Targeting further advances in our four businesses

Business strategy

Business strategy driven by social issues

Through total healthcare, we contribute to the Well-being of society as a whole.

To the heart of health issues through a human-centered approach

Social issues in focus under the 4th MTMP

Global environment

Heat is a common global problem

Women's health

Great health needs in various age groups

Aging societies with declining birthrates

Population aging is progressing rapidly, especially in developed regions

Business strategy

Pharmaceutical Business

Our business activities focus on clearly emerging medical needs that remain unmet. We will utilize expertise in our established strengths of oncology and psychiatry and neurology, as well as knowledge accumulated through development and marketing in the renal area, to further expand initiatives in the autoimmune and rare disease area, which has a high level of unmet needs. To deliver novel therapies and new patient support options amid the increasingly diverse medical needs of today, we are also actively devoting resources to development in areas such as medical devices and digital tools in order to offer more comprehensive solutions and generate medical value.

1. Psychiatry and neurology area
2. Oncology area
3. Autoimmune and rare disease area
4. New approaches to treatment and support

Nutraceutical Business

We are centered on such products as functional foods and beverages and nutritional supplements, which support the maintenance and improvement of day-to-day health. Leveraging our know-how acquired through the Pharmaceutical Business, we are working to develop unique products based on scientific evidence and conduct business globally, including in Asia, the U.S., Europe, the Middle East, and Africa. While actively making upfront investments to further expand the scale of our business, we will maintain a high level of profitability as we aggressively promote our business through global expansion of the many Otsuka products with unique characteristics.

1. For climate & environmental risk
2. For women's health
3. For healthier life

Consumer Products Business

We operate food and beverage businesses around the themes of flavor, safety, peace of mind, and better health, aiming to develop products that are ahead of the times. As an example, we created *Bon Curry*, the world's first food product to be sold in a sealed hygienic plastic pouch (retort bag). We use our unique ideas and development capabilities to continue to create products that are needed by the world, and contribute to the diversifying needs of our customers and solve various issues through the dinner table.

1. Beverages
2. Foods

Other Businesses

Our Other Businesses contribute in a wide range of fields across the Otsuka group. The chemicals business, for instance, provides functional materials and also components that utilize these materials; the warehousing and transport business handles the distribution of total healthcare products such as pharmaceuticals, foods, and beverages, achieving efficient and environmentally friendly transportation and delivery through standardization; and the electronic equipment business supports leading-edge science and technology.

1. Chemicals
2. Warehousing and transportation

Contribute to the health and Well-being of people around the world

At a glance

Pharmaceutical Business

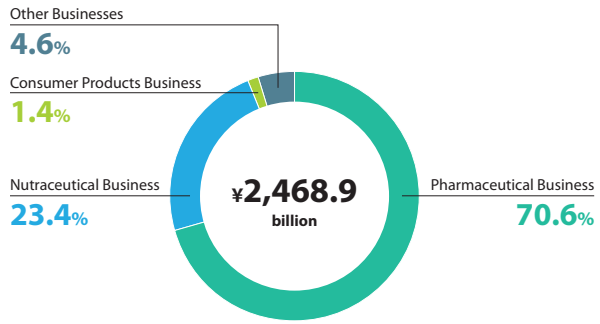
Nutraceutical Business

Consumer Products Business

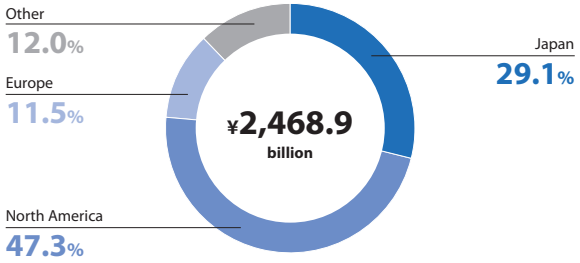
Other Businesses

Revenue*

By business segment (FY2025)



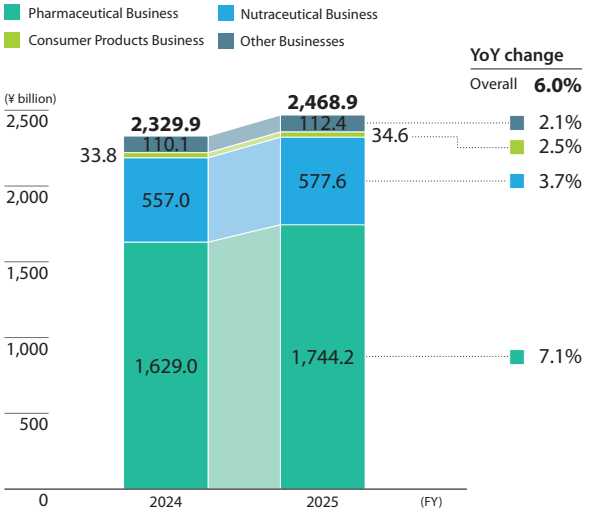
By region (FY2025)



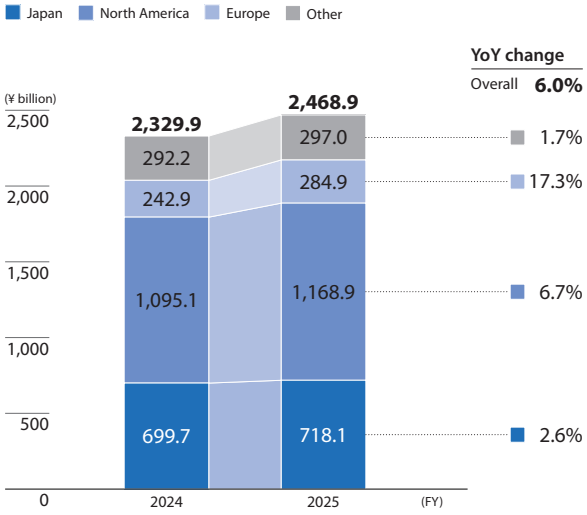
* Revenue from sales to external customers

Revenue YoY change

By business segment



By region



Pharmaceutical Business

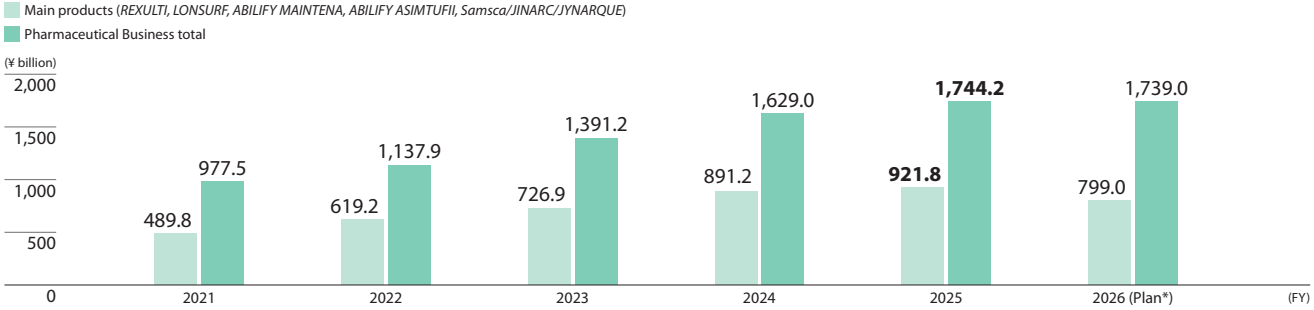
Committed to enhancing not only individual health but also the Well-being of society as a whole

Materiality

Contribute to the health and Well-being of people around the world

Summary of results

Progress in revenue



* Announced February 2026

2025 results

Item	Main results	
Development product results	**Approvals obtained**	• *REXULTI* (Europe: Additional indication for schizophrenia in adolescents) • *NEXLETOL* (Japan: Hypercholesterolemia) • *VOYXACT* (U.S.: Accelerated approval for the reduction of proteinuria in adults with primary IgA nephropathy at risk for disease progression) • Paradise Ultrasound Renal Denervation System (Japan: Resistant hypertension) • Povidone Iodine Solution/Olanedine Antiseptic Solution Cartridges (Japan: Antiseptics for external use)
	Regulatory submissions	• centanafadine (U.S.: ADHD*) • zipalertinib (U.S.: Non-small cell lung cancer) • *INQOVI* in combination with venetoclax (U.S.: Acute myeloid leukemia) * Attention-deficit hyperactivity disorder
Value delivery through digital tools		• eMind for Medical Research: Joint research started toward implementation of epilepsy treatment support system • FACEDUO: Frailty Prevention Support VR and content for family support of people with severe social withdrawal (*hikikomori*) • Vivoo: Joint research agreement with the National Cerebral and Cardiovascular Center to examine behavioral changes toward salt reduction • Rejoyn: Launch in the U.K.
Strengthened pipeline		• In-licensing of 4D-150, CAN10, HBM7020, casdatifan, and risovalisib
Strengthening of platforms		• Araris Biotech made a subsidiary • Technology validation started to expand the Cysteinomix drug discovery platform using generative AI • Joint basic research agreement with Keio University for infrastructure development toward the social implementation of psychedelics in Japan • Collaborative research using real-world data to develop treatment methods for recurrent early-stage cancer • Three-party joint research agreement between Taiho Pharmaceutical, the Japanese Foundation for Cancer Research (JFCR), and NEC Corporation to develop new cancer vaccines

Overview of Pharmaceutical Businesses

In the Pharmaceutical Business, amid changes in the social environment, we are incorporating new technologies and responding to evolving needs to create innovative pharmaceuticals and services that help solve social issues and to provide comprehensive healthcare solutions.

Business strengths

- Expertise and distinctive approaches in the respective fields of each group company, including in psychiatry and neurology at Otsuka Pharmaceutical, oncology at Taiho Pharmaceutical, clinical nutrition at Otsuka Pharmaceutical Factory, and medical devices at Otsuka Medical Devices.
- A strong drug discovery platform that features research sites in Japan and overseas, distinctive drug discovery platforms, and an extensive development pipeline and track record in psychiatry, neurology, oncology and other areas.
- A culture of pursuing originality from research and development to sales, continuously applying Otsuka's unique innovation to address unmet needs and emerging challenges, and striving to create innovative products and services.

Opportunities

- Prospects for sustained growth driven by high unmet needs in the group's areas of strength and the accelerated creation of new treatment options through proprietary technologies and digital applications.
- Expectations for further market growth as we leverage the group's global business development capabilities and diverse product portfolio to respond to growing global needs arising from population aging, increased prevalence of chronic diseases, and improved access to healthcare.
- Advancement of drug discovery capabilities through collaboration with academia and industry, AI-driven drug discovery, and digital health applications, alongside expansion of value delivery through personalized medicine and integration with diagnostic technologies.

Risks

- Significant uncertainty in R&D outcomes and intensifying competition, creating a need for rapid and clear differentiation.
- Changes in healthcare systems, including drug price cuts and reimbursement system reforms, which may affect earnings and require stronger value communication and product strategies.
- Disruptions in raw material procurement and supply chains, or quality-related issues, which could have significant impacts on business continuity and supply systems.

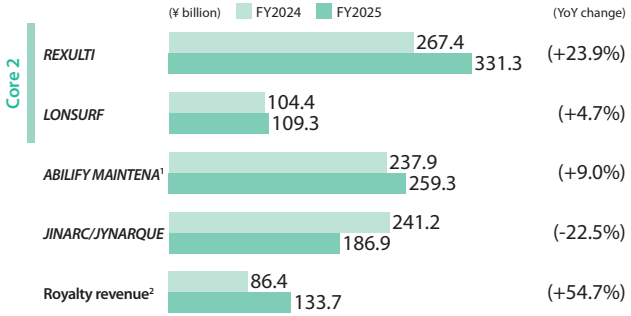
Progress of the 4th Medium-Term Management Plan

- **Growth in the Pharmaceutical Business and stronger platforms for the future**

Under the 4th MTMP, we have established the strategic focus of "Achieve sustainable growth by taking on challenges in new areas." As a unique total healthcare company, we are enhancing our global presence while steadily growing our Pharmaceutical Business.

In FY2025, revenue reached ¥1,744.2 billion, an increase of 7.1% year on year, while business profit rose by 2.9% to ¥402.0 billion. Although the second half was impacted by LOE for *JINARC/JYNARQUE*, earnings were driven by increased revenue from *REXULTI* and *ABILIFY MAINTENA* and higher royalty revenue.

FY2025
¥1,744.2 billion (up 7.1% YoY, achievement rate: 102.3%)



1. Includes *ABILIFY ASIMTUFII*
2. Excludes some product royalties

For research and development, we continue to actively invest in new clinical trials and other activities with a view to growth beyond the 5th MTMP beginning in FY2029. In FY2025, we obtained approval for five products (including additional indications), including *VOYXACT* that is expected to become a new growth driver.

We are also strengthening our drug discovery platform and pipeline through in-house drug discovery and access to external assets from acquisitions and strategic alliances. In FY2025, we acquired Araris Biotech, a company with next-generation ADC drug discovery technology. We also built distinctive drug discovery platforms and established systems to generate innovation through horizontal collaboration. Looking ahead, we aim to deepen collaboration within the group and achieve sustained growth by acquiring external assets that maximize synergies with existing businesses and management assets.

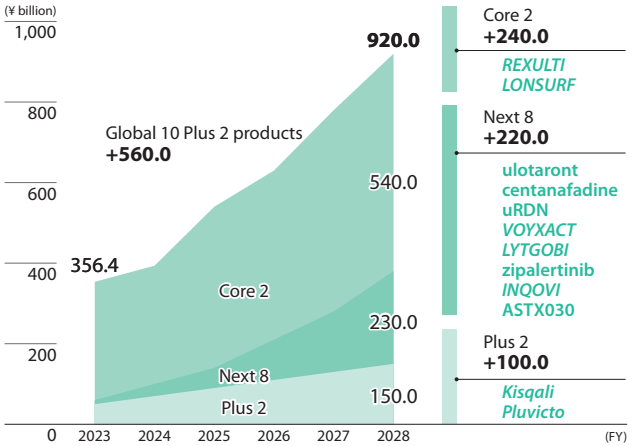
Business strategy for FY2026

- **Nurturing Global 10 Plus 2 to support future growth**

Revenue for FY2026 will be impacted by generic competition versus *JINARC/JYNARQUE* and other core products, but we expect to achieve revenue at the same level as the previous fiscal year due to growth by *REXULTI*, *ABILIFY ASIMTUFII*, *VOYXACT*, and other products, as well as increased royalty revenue.

The Global 10 Plus 2 refers to 10 global products and two out-licensed products that will drive earnings growth under the 4th MTMP. During the 4th MTMP, we plan to launch multiple new products in addition to the Global 10 Plus 2, minimize the impact of LOE on core products as much as possible, and strive to firmly establish sustainable growth beyond the 4th MTMP. We aim to keep the adjustment period caused by LOE to a minimum and achieve overall revenue of ¥1,680 billion (with an average annual growth rate of 3.8%) by FY2028 through growth driven by Global 10 Plus 2 and other initiatives.

Revenue plan for Global 10 Plus 2 products



The products among the Global 10 Plus 2 expected to serve as growth drivers for the 5th MTMP have been designated as the Next 8. We have continued to actively invest in the development of next-generation growth drivers, including the Next 8. While some trials have not progressed as planned and certain projects have required revisions to launch timelines, the growth potential of several development products has steadily increased compared with when the 4th MTMP was announced.

We are also continuing to invest in our new core areas of autoimmune and rare diseases, and look to create new value in fields beyond our existing areas of expertise.

Going forward, we will solidify our foundations for future growth even further by deepening our presence in existing areas and expanding into new fields. In this way, we aim to strengthen the foundations for continuous, proprietary innovation and achieve sustained growth over the long term.

Development progress for next-generation growth drivers

Products	Plans for 2026	Country
ulotaront	• Completion of Phase 3 trial for schizophrenia • Initiation of Phase 3 trial for generalized anxiety disorder	Japan, U.S.
centanafadine	• Regulatory approval for ADHD indication	U.S.
uRDN	• Advancement of activities toward broad insurance reimbursement coverage • Initiation of sales	U.S. Japan
VOYXACT	• Approval of IgA nephropathy indication • Regulatory submission for IgA nephropathy indication • Regulatory submission for IgA nephropathy indication (full approval)	China Japan, Europe U.S.
LYTGOBI	• Initiation of Phase 3 trial for biliary tract cancer	Japan
zipalertinib	• Development underway for non-small cell lung cancer with EGFR[1] exon 20 insertion mutations: 2L therapy: Regulatory submission completed 1L therapy: Phase 3 enrollment completed	U.S. Japan, U.S., Europe
INQOVI	• Regulatory approval for AML[2] indication	U.S., Europe
ASTX030	• Ongoing Phase 3 trial for AML and MDS[3]	U.S.
repinatrabit	• Ongoing Phase 3 trial for phenylketonuria	U.S.

1. EGFR: Epidermal growth factor receptor
2. AML: Acute myeloid leukemia
3. MDS: Myelodysplastic syndromes

Psychiatry and neurology area

- **Enhancing not only individual health but also solving issues impacting society as a whole**

Otsuka Pharmaceutical has a portfolio of development assets and products with high potential for the treatment of schizophrenia, major depressive disorder, and other psychiatric disorders. During the development and commercialization of *ABILIFY*, we achieved success in clinical trials previously considered difficult and obtained approvals for new indications. In the psychiatry and neurology area, there are still many disorders where therapeutic methods have yet to be established due to the difficulties of treating the condition and the low chances of success in product development. Leveraging our expertise accumulated thus far as a platform for growth, we are accelerating development, including through the acquisition of various external science assets. We have made steady progress in the development of ulotaront and centanafadine, including conducting clinical trials and regulatory submissions for approval. Both of these new drugs have novel mechanisms of action and are expected to become first-in-class[1] therapeutic drugs.

Clinical trials have now started for MSP-2020, originated by Mindset Pharma that Otsuka acquired as a subsidiary in 2023, for mental health disorders that remain inadequately controlled with existing therapies. New treatment options for treatment-resistant mental health disorders are eagerly awaited, and psychedelics have come under the spotlight as treatments with novel mechanisms of action. We are working to address challenges related to the social implementation of psychedelics, including through an industry-academia collaboration with Keio University, to ensure that these therapies can be delivered to patients safely and appropriately.

We are also developing the nucleic acid drug ulefnersen, in-licensed from Ionis Pharmaceuticals, Inc., as a treatment for amyotrophic lateral sclerosis (ALS), a serious neurodegenerative disease characterized by the rapid progression of muscle weakness and respiratory impairment. Ulefnersen has the potential to become the world's first treatment for FUS-ALS, a form of ALS caused by mutations in the FUS gene and that typically develops around the age of 40 and progresses very rapidly.

Alongside efforts to address the social challenges associated with each disease, we are advancing research and development to satisfy unmet medical needs in the psychiatry and neurology area, with the aim of providing treatment options that benefit patients, their families, and caregivers. Through these efforts, we seek to help create a society in which patients and their families can live with greater peace of mind.

1. A breakthrough drug with a new mechanism and target that differs from conventional treatments for specific diseases

R&D activities in FY2025	
centanafadine	• Regulatory submission in the U.S. as a first-in-class therapeutic drug for ADHD
ulotaront	• Phase 3 trial started for schizophrenia • Concept validity confirmed for generalized anxiety disorder; Phase 3 trial planning ongoing
MSP-2020	• Phase 1 trial started as a psychedelic therapy
ulefnersen	• Phase 1/2/3 trial ongoing in ALS

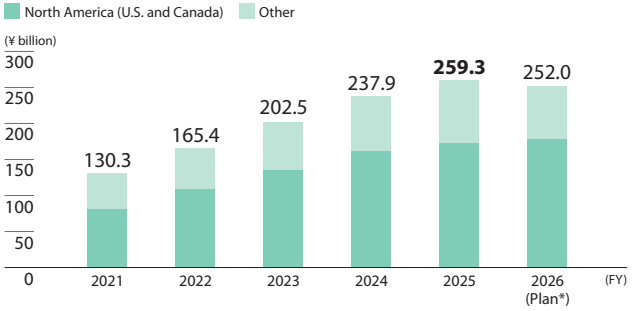
ABILIFY MAINTENA / ABILIFY ASIMTUFII

aripiprazole | Antipsychotic long-acting injectable

For bipolar I disorder and schizophrenia patients, who often find medication adherence difficult, Otsuka Pharmaceutical has developed and sells *ABILIFY MAINTENA* and is promoting this once-monthly long-acting injectable formulation of aripiprazole. As a result, sales are steadily growing for this product in the U.S., Europe, and Japan.

Furthermore, the long-acting injectable formulation (2-month formulation) *ABILIFY ASIMTUFII* received marketing approval in the U.S. in 2023, followed by approval in Europe in March 2024 as the first 2-month formulation for the maintenance treatment of schizophrenia in that region. Sales are continuing to grow steadily as more patients transition from the 1-month to the 2-month formulation.

Revenue of *ABILIFY MAINTENA / ABILIFY ASIMTUFII*



* Announced February 2026

REXULTI

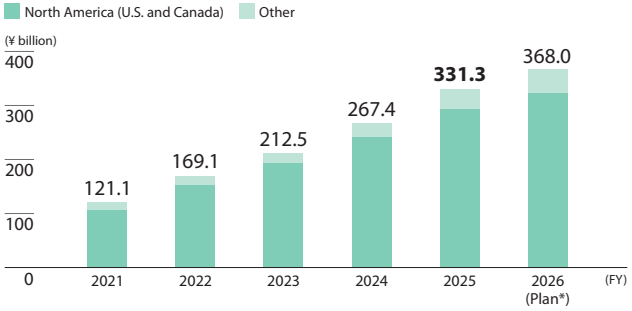
brexpiprazole | Atypical antipsychotic

REXULTI has been approved for schizophrenia and major depressive disorder, and has also received approval as the first treatment for agitation associated with dementia due to Alzheimer's disease (AAD). AAD presents with both aggressive and non-aggressive symptoms and impedes a patient's daily life or human relations. It reduces the quality of life of people with dementia and places an enormous emotional and physical burden on families and caregivers. Otsuka Pharmaceutical is conducting information-sharing and awareness-raising activities to promote a better understanding of dementia and broaden the circle of support, helping to create an environment in which people living with dementia and their families can live with greater peace of mind.

In the U.S., *REXULTI* was approved for AAD in 2023 and awareness-raising activities have helped to drive growth in prescription numbers. In Japan, in addition to an increase in the number of new prescriptions due to product detailing activities related to its use for schizophrenia, depression, and depressive states, sales have significantly increased following the approval of the AAD indication[2] in September 2024.

2. The treatment indication in the package insert in Japan is described as the treatment of "excessive motor activity or physically/verbally aggressive behavior due to rapid changes in mood, irritability, and/or outbursts associated with dementia due to Alzheimer's disease."

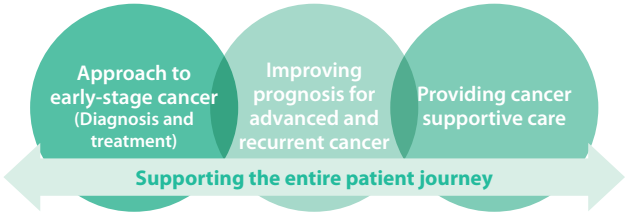
Revenue of *REXULTI*



* Announced February 2026

Oncology area

- **Discovery of new drugs through world-class drug discovery platforms and robust collaboration**



For fulfilling lives "Today and Every Day"

The Otsuka group views the cancer patient journey as consisting of three stages, and aims to provide comprehensive support throughout the journey by addressing the specific needs at each stage. In Japan, the 10-year survival rate for cancer is reported to be 54.0%,[1] and although treatment outcomes are improving every day, there remains considerable room for improvement.

The Otsuka group is committed to enhancing the lives of all people—patients, their families, and those living in good health—and to taking a holistic approach to health by focusing not only on treatment, but also on early intervention and disease prevention. We will continue to pursue the development of innovative new products that make a meaningful impact on society.

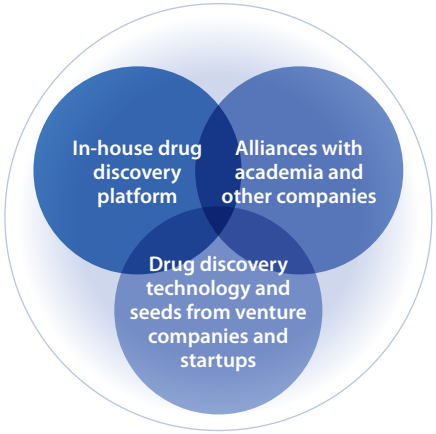
Our diverse and distinctive drug discovery platform technologies support the creation of a broad and competitive product portfolio. These technologies include biochemical modulation drug discovery,[2] which Taiho Pharmaceutical was quick to start work on; cysteinomix drug discovery,[3] which is distinguished by specific covalent modification of therapeutic targets; and Astex Pharmaceuticals' fragment drug discovery.4

Araris Biotech, which became a subsidiary in March 2025, is pioneering the development of best-in-class antibody-drug conjugates (ADCs) to overcome the challenges with conventional ADCs. The Otsuka group now has strengths in both small-molecule drugs and ADCs through its existing drug discovery platforms and the newly acquired innovative ADC drug discovery technology from Araris. This will allow us to accelerate the continued expansion of our oncology development portfolio.

In terms of developing key growth drivers, we have systematically advanced plans for clinical trials and regulatory submissions for zipalertinib, *INQOVI*, ASTX030, and other projects, and have made progress that contributes to both pipeline expansion and future business growth. Our goal is to obtain approvals during the 4th MTMP and maximize commercial potential in the next MTMP.

Furthermore, through investments in corporate venture capital and open innovation funds, we are strengthening collaborations with promising biotech startups and academic institutions both inside and outside Japan, thereby gaining access to more unique and innovative technologies and early-stage drug discovery assets that we do not have in-house. We will pursue innovation through in-house drug discovery and collaboration with diverse partners, and continue to take on the challenge of research and development into innovative new drugs.

R&D activities in FY2025	
zipalertinib	• Development underway for non-small cell lung cancer with specific gene mutations - 2L therapy: Regulatory submissions completed in the U.S. - 1L therapy: Phase 3 trial ongoing - Postoperative adjuvant chemotherapy: Phase 3 trial started
INQOVI	• Regulatory submissions completed in the U.S. and Europe as an oral therapeutic drug used in combination with venetoclax for hematological cancer
ASTX030	• Oral formulation of azacitidine for injection that is widely used worldwide • Phase 3 trial ongoing as an oral therapeutic drug for hematological cancer



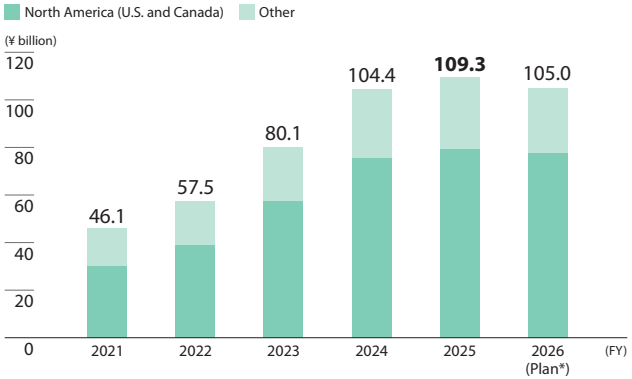
LONSURF

trifluridine/tipiracil | Anticancer agent

LONSURF, developed by Taiho Pharmaceutical, has been widely approved around the world for the treatment of unresectable advanced or recurrent colorectal cancer, and prescription volumes are steadily increasing.

In Japan, the U.S., and Europe, awareness of *LONSURF* has increased following its recommendation in various guidelines[5] as combination therapy with bevacizumab to treat colorectal cancer. Increased prescribing led to revenue growth in FY2025.

Revenue of *LONSURF*



* Announced February 2026

1. Cases diagnosed in 2012; National Cancer Center Japan, 2025
2. Drug discovery approach aimed at enhancing anti-tumor effects and reducing toxicity to normal cells by adding other drugs (modulators) to alter the pharmacokinetics of anti-cancer drugs
3. A unique drug discovery platform technology, which allows for the formation of strong bonds and high target selectivity by covalently binding drugs to the specific cysteine residues of therapeutic target proteins
4. Technology to create new compounds through molecular design. It clarifies interactions between small-molecular fragments showing pharmacological activity that cannot be measured in high-throughput screening, and large molecule proteins with complicated 3D structures that have been implicated in diseases and are potential drug targets.
5. Includes the NCCN Guidelines (cancer treatment guidelines used broadly throughout the world).

Autoimmune and rare disease area

- **Creating first-in-class products for diseases that lead to renal failure**

Otsuka Pharmaceutical is leveraging its drug discovery and development capabilities accumulated in the renal area to deliver innovative treatments to respond to unmet medical needs for diseases that lead to renal failure and improve treatment satisfaction.

Based on this understanding of the challenges, Otsuka Pharmaceutical is engaged in research and development with the aim of providing new treatment options to people living with disease and supporting patients throughout their journey.

- **Tackling highly specialized autoimmune and rare diseases using new drug discovery technologies**

Otsuka Pharmaceutical is stepping up efforts in highly specialized disease areas, including autoimmune diseases related to kidney disorders and rare diseases with significant unmet needs. Building on the expertise gained with *JINARC/JYNARQUE* for autosomal dominant polycystic kidney disease (ADPKD), we are expanding our capabilities through the in-licensing of advanced drug discovery technologies, external partnerships, and the strengthening of our development organization, including the addition of autoimmune disease expertise.

In areas like autoimmune diseases, effective treatment options remain limited and major social challenges persist due to safety concerns associated with long-term treatment, significant declines in patient quality of life, and the burden on family caregivers.

The U.S. subsidiary Visterra, Inc. has a proprietary drug discovery platform to optimize antibody drugs against biological substances, and this is helping us build a pipeline of antibody drugs for autoimmune diseases. *VOYXACT*, originated by Visterra, was granted accelerated approval in the U.S. at end-2025 for the indication of proteinuria in adults with primary IgA nephropathy at risk for disease progression. The drug got off to a positive start after launch.

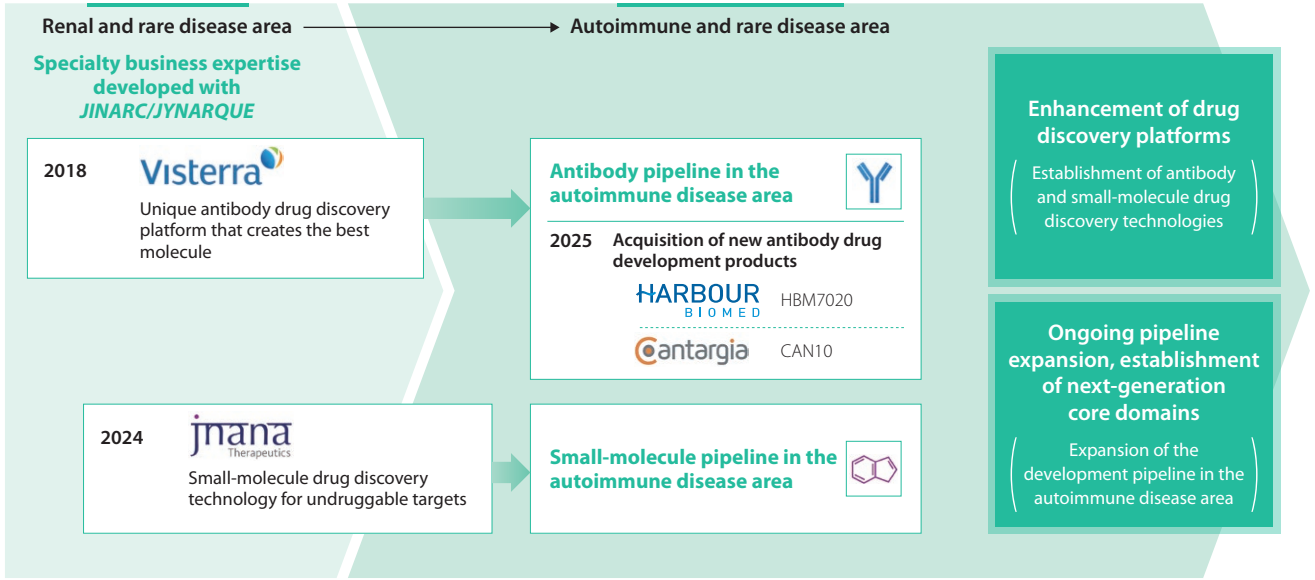
Additionally, the U.S. subsidiary Jnana Therapeutics Inc. possesses a drug discovery platform designed to discover medicines for targets considered undruggable. Repinatrabit (JNT-517) was originated using this drug discovery technology and has the potential to become a first-in-class treatment for phenylketonuria, a rare disease that requires strict dietary restrictions and where many patients cannot be adequately treated with existing therapies. The goal is to develop these drugs into future blockbusters. Clinical trials are currently underway aimed at securing early approval. Furthermore, we are exploring new possibilities in small-molecule drug discovery for autoimmune diseases, including by acquiring active compounds for challenging drug targets such as interferon regulatory factor 3 (IRF3), a master transcription factor for the production of interferon.

We have also added to our pipeline the bispecific T-cell engager HBM7020 and the multi-cytokine inhibitory antibody CAN10, expanding our R&D portfolio and accelerating development for regulating various pathways in autoimmune diseases. Currently our pipeline covers a wide range of target areas, including B cells, complement, and cytokines that are involved in the immune response, and we have various development programs focused on drug discovery targets that play a role in underlying disease pathologies. We believe these programs have the potential to become a top player in this disease area.

Building on these efforts, we continue to bring in innovative science approaches from outside the Company while also deepening our connections within the group to leverage our technological capabilities in autoimmune and rare diseases, such as the antibody drug discovery platform from Visterra and the small-molecule drug technologies from Jnana Therapeutics. In addition to further expanding our R&D pipeline, we will work to establish the next generation of core domains by pursuing innovation through our proprietary drug discovery technologies. Through the creation of new value based on cutting-edge science, we aim to contribute to patients by providing innovative treatment options.

R&D activities in FY2025	
VOYXACT	• Approved and launched in the U.S. for IgA nephropathy • POC trial started for Sjögren's disease
VIS171, VIS954	• Development underway for specific autoimmune diseases
HBM7020	• In-licensed from Harbour BioMed • Preparations underway for Phase 1 trials as an antibody drug for autoimmune diseases
CAN10	• Phase 1 trial ongoing as an antibody drug for autoimmune diseases

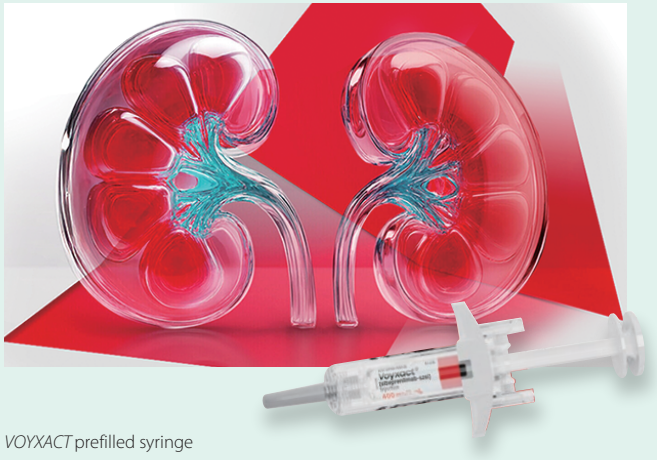
Leveraging strengths in renal diseases for autoimmune and rare disease area



Focus

VOYXACT: World first therapy that blocks APRIL to address the root cause of IgA nephropathy
Accelerating global growth through distinctive new drugs

VOYXACT is a monoclonal antibody that selectively binds to A-PRoliferation-Inducing Ligand (APRIL) to block its activity.
VOYXACT was launched in the U.S. at the end of 2025 as the world's first therapy targeting APRIL.



VOYXACT prefilled syringe

Novel approach targeting upstream pathogenetic mechanisms to address root cause of disease

IgA nephropathy (IgAN) is a disease that typically manifests in adults aged 20–40 years and causes progressive loss of kidney function as immune complexes accumulate in the kidneys. With current standard treatments, IgAN can lead to end-stage kidney disease (ESKD) over the lifetime of many patients and is associated with reduced life expectancy, imposing a significant burden on patients. Treatments to date have focused on slowing the progressive loss of kidney function and have not adequately addressed the root cause of the disease.

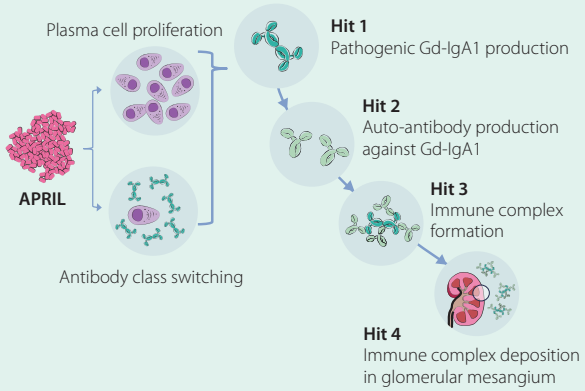
IgAN onset and progression to kidney damage are thought to involve a 4-hit process of four sequential immune abnormalities. APRIL, a cytokine in the tumor necrosis factor (TNF) family, is integral to the pathogenesis and progression of IgAN. It promotes the class switching of B cells, a type of white blood cell, to produce IgA, particularly the pathogenic galactose-deficient IgA1 (Gd-IgA1) that forms immune complexes in the kidneys in IgAN patients.

VOYXACT, developed by Visterra, blocks the action of APRIL. The drug suppresses production of pathogenic Gd-IgA1 at the upstream stage of IgAN onset and slows progressive loss of kidney function. This is a different mechanism of action to current treatment methods. The targeting of upstream pathogenesis represents a novel approach aimed at addressing the root cause of the disease.

Founding of Visterra and development of *VOYXACT*

2007		Visterra founded as a spinout from Massachusetts Institute of Technology (MIT)
2018		Visterra acquired by Otsuka Pharmaceutical
		First-in-human study started
2020		Phase 2 (ENVISION) study started
2022		Phase 3 (VISIONARY) study started
2025	March	Biologics license application (BLA) submitted to the FDA
	November	Accelerated approval granted by the FDA
	End-2025	Launched under the brand name *VOYXACT*

Four-hit process involved in IgAN onset



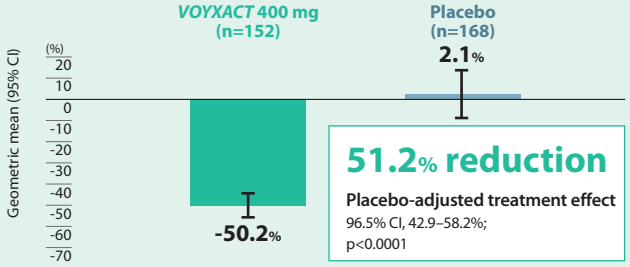
Validating clinical benefit and maximizing value

VOYXACT was granted accelerated approval in the U.S. based on an interim analysis of the VISIONARY Phase 3 study currently underway. Proteinuria reduction is a recognized surrogate marker correlating with delaying progression to kidney failure. In the VISIONARY study, the primary endpoint is the 24-hour urine protein-to-creatinine ratio (uPCR) at month nine compared with baseline. The interim analysis demonstrated a statistically significant and clinically meaningful improvement in the *VOYXACT* group, including a 51.2% reduction in proteinuria when compared to placebo. The VISIONARY study is still underway and the company plans to continue validating the clinical benefit of *VOYXACT* by evaluating long-term change in kidney function as measured by estimated glomerular filtration rate (eGFR).

Otsuka Pharmaceutical submitted an approval application in China in August 2025 and is advancing a global development program, with regulatory submissions and approvals to be pursued sequentially in other countries. The Company is also investigating additional indications beyond IgAN, including the initiation of a Phase 2 study in the U.S. for Sjögren's disease where there are limited effective treatment options.

Otsuka Pharmaceutical seeks to maximize the value of *VOYXACT* at an early stage by establishing it as a first-in-class and best-in-class therapy, while also pursuing future expansion through a life-cycle management (LCM) strategy, with the goal of benefiting as many patients as possible.

Primary endpoint: uPCR-24h (g/g) at month nine



uPCR-24h: 24-hour urine protein-to-creatinine ratio; CI: confidence interval

New approaches to treatment and support

- **Looking beyond pharmaceuticals to address new social issues**

The Otsuka group provides products and services that support all stages of people's healthcare, while also helping address social issues through its unique product and service offerings. We are actively working to address diverse unmet needs, not only through pharmaceuticals, but also through digital tools for health, such as medical devices and therapeutic apps, and employment support for cancer patients.

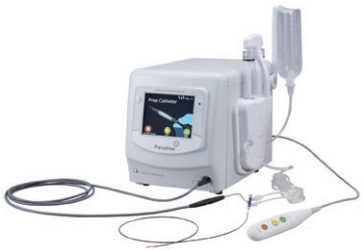
Paradise uRDN system

- **Medical device provides a new treatment option for hypertension**

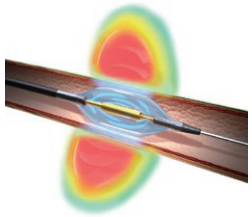
While multiple antihypertensive drugs have been developed and used in clinical practice over the years, many hypertension patients still have poorly controlled blood pressure and are at risk of serious cardiovascular events such as stroke and myocardial infarction.

Otsuka Medical Devices' Ultrasound Renal Denervation (uRDN) system was first approved by the U.S. FDA in November 2023 as an adjunctive treatment option for hypertension in patients with inadequately controlled blood pressure. This system is designed to lower blood pressure by delivering ultrasound energy to the sympathetic nerves surrounding the renal arteries and reducing their overactivity. The system has also been introduced into key European markets, and was first approved in Japan in August 2025 for the indication of resistant hypertension, followed by insurance coverage and commercial launch in March 2026.

Three independently powered, sham-controlled randomized clinical trials conducted in the U.S. and Europe demonstrated significant blood pressure-lowering effects with the uRDN system. This system is expected to provide a novel treatment option for hypertension.



Paradise Ultrasound Renal Denervation (uRDN) system



Conceptual illustration of treatment mechanism

FACEDUO

- **Learning and support through simulated VR training programs**

Launched in September 2024, Dementia Care Support VR is a module of the *FACEDUO* VR training program that was developed by Otsuka Pharmaceutical in collaboration with Jolly Good Inc. The module is an experiential VR program to help families and caregivers understand the background to the feelings and behaviors of people with dementia and to learn practical approaches to care. By improving dementia care, we aim to realize a society living in harmony with dementia, where both people with dementia and caregivers can lead more fulfilling lives in a way that respects their individuality.

In December 2025, Otsuka Pharmaceutical started offering the Frailty Prevention Support VR program. This module promotes early recognition of the signs of frailty through realistic simulated VR experiences, supporting health maintenance and preventing the need for long-term care. Frailty is a condition of age-related physical and cognitive decline, but is potentially reversible. Early recognition and preventive action may help slow progression and improve outcomes. Otsuka is looking beyond pharmaceuticals and working to address unmet needs through comprehensive programs using digital technologies.

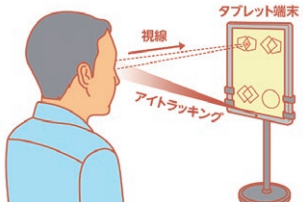
MIREVO

- **Neuropsychological testing program to support dementia treatment**

Otsuka Pharmaceutical has worked with Ai-BrainScience Inc. to develop the *MIREVO* neuropsychological testing program to support dementia treatment. *MIREVO* is a neuropsychological testing program that uses eye tracking technology. The test can be easily conducted and results obtained in approximately three minutes using the *MIREVO* app on a tablet. It allows for a quantitative and objective evaluation that is not dependent on the examiner's knowledge or experience.

In January 2025, this product became the first Software as a Medical Device (SaMD) in the field of dementia to obtain NHI coverage in Japan.

As early detection and early intervention become increasingly important in the treatment of dementia, *MIREVO* offers a new option for testing and contributes to early detection of dementia.



ARIRGE

- **Addressing social issues related to cancer that cannot be solved with pharmaceutical products alone**

ARIRGE Co., Ltd. aims to resolve social issues related to cancer and realize a society where people can continue to work with vigor even if they have cancer, and where everyone can receive cancer screenings as a matter of course. Drawing on the expertise and experience of the Otsuka group, ARIRGE provides education, support, and other solutions to resolve key social issues, such as employment support for cancer patients, as well as services to promote cancer screening and smoking cessation.

Cancer patients and their families face concerns and challenges that cannot be solved with pharmaceutical products alone, and many social issues surrounding cancer remain unresolved. We are working to address the social issues related to cancer by looking beyond pharmaceutical products and providing solutions to support all those affected, so that cancer patients and their families can continue to enjoy the precious moments of daily life, today and every day.

Focus

Our commitment to saving lives: Otsuka's global initiatives to eradicate tuberculosis

Tuberculosis (TB) is a serious infectious disease that still claims the lives of around 1.2 million people each year.

"We must continue our research if nobody else does it." Guided by this deep commitment, the Otsuka group has continued its drug discovery research efforts for over 50 years.

From delivering proprietary therapeutics to running workplace programs on TB eradication, we continue to address social issues and deliver Well-being to people around the world through our unique approach of connecting healthcare with local communities.

To address unmet medical needs, the group continues its ongoing collaboration with the WHO to promote clinical trial strategies and strengthen evidence-building.

The commitment that has sustained Otsuka's R&D efforts: "We are committed to advancing our initiatives"

The Otsuka group's history in anti-tuberculosis drug development goes back as far as 1971. At that time, it had only 14 scientists working on drug discovery and TB was selected as one of the first projects. TB remains a serious public health threat even today. Globally, more than 10 million people continue to become infected with TB every year. The emergence of bacteria resistant to mainstay anti-tuberculosis drugs has made treatment even more challenging. While many pharmaceutical companies closed their TB R&D programs after encountering various difficulties, we have been continuing our research with a mission that TB remains a critical global challenge and we must carry on the fight if no one else is willing to. These efforts embody the Otsuka group DNA expressed in the principles of *Sozosei* (creativity) and *Jissho* (actualization), as we strive to do "what can only be done by Otsuka."

Developing delamanid and expanding global access

This commitment ultimately bore fruit with the development of delamanid (brand name *DELTYBA*) in 2014, the first new treatment for multidrug-resistant TB in some 40 years. Delamanid has been included in the WHO Model Lists of Essential Medicines, which identify medicines necessary to meet minimum healthcare needs in developing countries. As of June 2025, delamanid has been supplied to over 130,000 cases in 135 countries and regions around the world.

Our approach to TB has also grown to encompass international partnerships. Through our collaboration with the Global Drug Facility, we are enabling sustainable access to TB drugs in developing countries. We are also partnering with numerous other stakeholders, such as participating in the Global Health Innovative Technology Fund, cooperating with Médecins Sans Frontières, and developing a new anti-TB compound with grants from the Bill & Melinda Gates Foundation.

Launching "Free Tuberculosis at Workplaces" with the Ministry of Manpower in January 2023

From Indonesia and the Philippines to the world: Social implementation rooted in local communities

Today, the Otsuka group's efforts against TB go beyond just therapeutic drug supply, and have evolved into activities rooted in local communities.

Indonesia has the second-highest number of TB cases globally. Two of the Otsuka group companies in Indonesia have initiated the program, "Free Tuberculosis at Workplaces" (FTBAW), in collaboration with Indonesia's Ministry of Manpower and Ministry of Health. We conducted awareness-raising and engagement (socialization) initiatives with more than 840 partner companies across 12 provinces, reaching a total of over 240,000 employees who underwent TB screening. In addition, we have implemented a comprehensive workplace approach that spans prevention through treatment management, including medication adherence support via the Sembuh TB app, nutritional assistance through high-protein diets, and access to medical support services. In recognition of the impact of this unified effort by the government and private sector, the FTBAW program received the Ending Workplace Tuberculosis (EWTB)* 2024 Exemplar Award. This program has been implemented in the Philippines as well, where TB is also a serious issue. In recognition of these initiatives, we received the 2025 Exemplar Award. Alongside these initiatives, we are accelerating the development of a new anti-tuberculosis drug, quabodepistat, and have started joint global clinical studies (Phase 3).

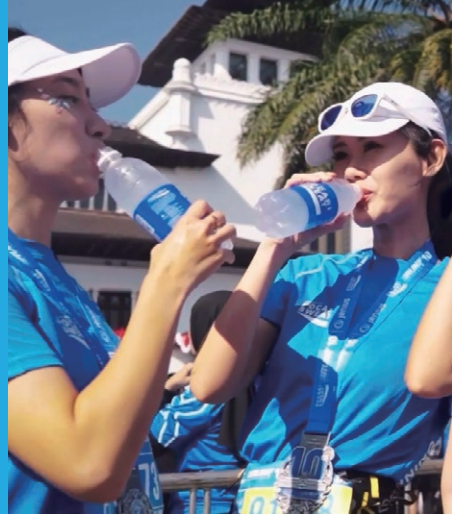
* Established at the World Economic Forum Annual Meeting (Davos) to promote the participation of leading companies in the fight against TB

Nutraceutical Business

Creating unique health value through products based on medical expertise and scientific evidence

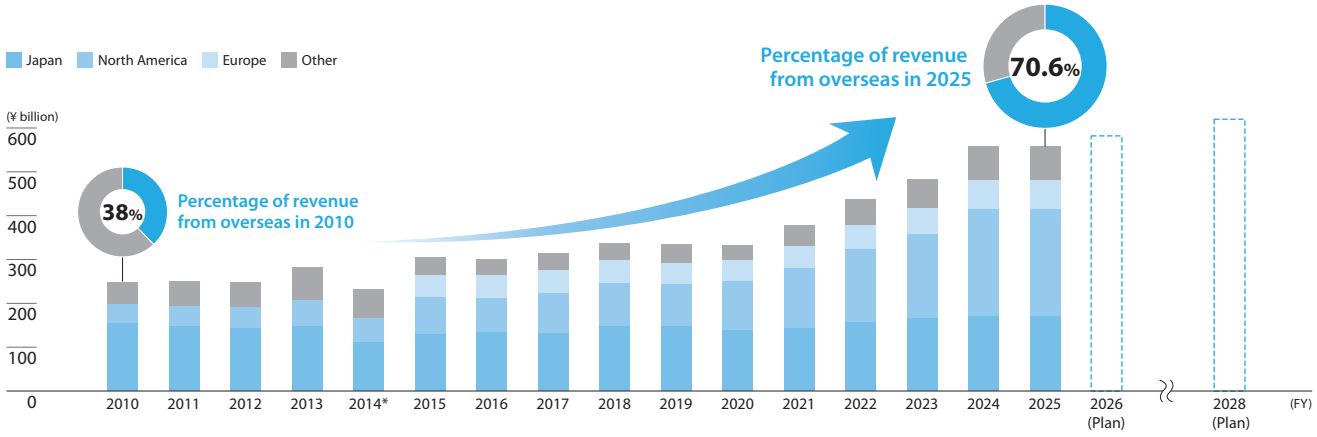
Materiality

Contribute to the health and Well-being of people around the world



Summary of results

Accelerating global expansion of the Nutraceutical Business: Revenue



Notes: 1. For 2014, figures used are for the nine-month period from April 1, 2014 to December 31, 2014 due to a change in the fiscal year-end.
2. European revenue prior to 2014 is included in Other.

Main results in FY2025 (initiatives to address social issues)

Otsuka Pharmaceutical's initiatives to address social issues are mostly focused on various types of events in Japan and overseas to raise awareness of heat illness due to climate change. At World Athletics Championships Tokyo 25, the Company conducted joint research on athletes' heat acclimatization and fluid/nutrition strategies in order to provide practical insights for future generations of athletes and people involved in sports around the world.

Nutraceutical Business outline

The Otsuka group's Nutraceutical Business conducts business centered on such products as functional beverages, functional foods, and supplements, which support the maintenance and improvement of day-to-day health. Leveraging our know-how acquired through the Pharmaceutical Business, we are working to develop unique products based on scientific evidence and conduct business globally, including in Asia, the U.S., Europe, the Middle East, and Africa. We will continue to pursue and elevate a high-margin strategy based on brand value, and further enhance the value and reputation of our business. While actively making upfront investments, we will maintain a high level of profitability and aggressively promote our business through the global expansion of many products with unique characteristics.

Business strengths

- **Product development capabilities based on scientific evidence**: Developing functional beverages and foods by leveraging our expertise from the Pharmaceutical Business
- **Strong presence on global markets**: Operating businesses in a wide range of regions, including Asia, U.S., Europe, Middle East, and Africa; high percentage of revenue from overseas markets (70.6% in FY2025); and growing as a global business
- **Brand value supporting high margins**: Profit margins improving as Otsuka pursues a high-margin strategy based on brand value; forecast is for sustained expansion, with EBITDA rising from around ¥89 billion in FY2025 to over ¥100 billion in FY2028

Opportunities

- **Further growth in global markets**: Amid rising health awareness, demand in preventive areas is rising worldwide
- **Creation and fostering of the next generation of growth drivers**: Innovation in nutrition and health areas could be the source of future market expansion and profit growth
- **Business growth driven by social issues**: Growing global demand for products that support and promote good health amid the shift to a super-aging society and climate change

Risks

- **Risks from changing external environment due to dependence on sales overseas**: 70.6% of revenue comes from overseas markets, raising concerns over the impact from forex fluctuations, political risk, or import regulations
- **Intensifying global competition**: Across functional beverage and food markets, competition continues to intensify, with ongoing battles for market share against local companies and international brands
- **Changing costs for raw materials and logistics**: Increasing uncertainties in supply chains due to sharp increases in materials prices, logistics constraints, and geopolitical risk
- **Burden of regulatory or scientific evidence requirements**: Ongoing compliance with country- and region-specific regulations governing labeling, advertising claims, and ingredients

Progress of the 4th Medium-Term Management Plan

Through the 4th MTMP, we are committed to tackling social issues in each country and region and to continue contributing to the health and Well-being of people around the world—as a total healthcare company—through Otsuka's unique product lineup. To that end, we have defined three categories of growth drivers from the viewpoint of social issues.

In FY2025, all three categories grew and revenue reached ¥577.7 billion (up 3.7% year on year).

- **Three categories that are addressing social issues**
- For climate & environmental risk | Develop overseas *POCARI SWEAT* business to be a ¥100 billion brand
- For women's health | Build growth foundation to become a leader by developing the category, mainly in North America
- For healthier life | Further maximize value with unique product line-up geared toward life stages of consumers

Business strategy for FY2026

FY2026 revenue for the Nutraceutical Business as a whole is forecast to increase 6.5% from the previous fiscal year to ¥615 billion.

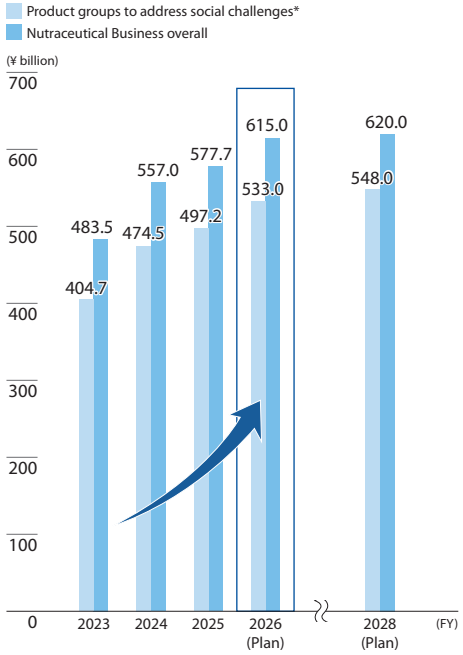
In each of the three categories tied to social issues, which we have set as growth drivers, we expect growth in each category and higher revenue, led by *POCARI SWEAT*, *Bonafide*, and *Nature Made*. We will continue our proactive efforts to address the growing global challenge of heat illness while strengthening the business infrastructure needed to support the expansion of *POCARI SWEAT* into new markets and further growth.

In March 2026, we launched */zeroz*, a self-conditioning food containing the plant-derived ingredient kaempferol, with a focus on oxygen that is an essential element for sustaining life.

Nutraceutical business: Revenue overview and progress by category for product groups to address social challenges

FY2025 results ¥577.7 billion	+3.7% (YoY change)	Reasons for change	FY2026 plan ¥615.0 billion		MTMP targets
For climate & environmental risk					
¥201.7 billion	+1.6% (YoY change)	***POCARI SWEAT*** Japan | Although consumer activity levels declined during the summer, we continued to create opportunities for drink consumption through marketing and other activities Overseas | Increased brand recognition drove revenue growth ***N&S*** Europe | Strong sales of *Gerblé* and other health foods drove revenue growth	FY2026 plan ¥221.0 billion	CAGR ('23–'26) 6.4%	CAGR ('23–'28) 6%
For women's health					
¥60.8 billion	+7.4% (YoY change)	***Bonafide*** U.S. | e-commerce and August 2025 start of retail store sales drove revenue growth ***EQUELLE*** Japan | Greater awareness through broad-based product detailing activities (e.g., women's health seminars) drove revenue growth	FY2026 plan ¥66.0 billion	CAGR ('23–'26) 21.1%	CAGR ('23–'28) 17%
For healthier life					
¥234.7 billion	+7.0% (YoY change)	***Nature Made*** U.S. | Strong sales through e-commerce channels and large retail outlets drove revenue growth	FY2026 plan ¥246.0 billion	CAGR ('23–'26) 10.2%	CAGR ('23–'28) 4%

Sales trends of product groups to address social challenges



* Product groups to address social challenges: For climate & environmental risk | For women's health | For healthier life

For climate & environmental risk category

POCARI SWEAT

- **Strengthening business infrastructure to support expansion into new markets and further growth**

The Asia-Pacific (ex-Japan) sports drink market has continued to grow due to strong health awareness. As a result of continuing educational activities on hydration and electrolyte replenishment tailored to the culture and circumstances of each region, sales volume grew in response to demand and revenue increased. More recently, we have opened new factories in Vietnam and Tianjin, China and also begun marketing in the new markets of India and Nigeria.

Due to the expectation of continued strong growth, we aim to further spread the brand in existing markets and expand into new markets by educating consumers on the importance of hydration and electrolyte replenishment. Through the spread of the *POCARI SWEAT* product concept via unique marketing activities cultivated over the years, *POCARI SWEAT* has grown mainly in Asia, including China and Indonesia, and we are taking on the challenge of nurturing *POCARI SWEAT* into a ¥100 billion brand overseas.

- **Activities in Asia**

We have launched the Dream Project to support the aspirations and efforts of young people. The project encompasses promotional activities in the medical field, collaboration with government authorities, and engagement through popular sports such as soccer in Japan, Cambodia and Vietnam and basketball in the Philippines and Taiwan. The initiative has contributed to expanding demand for *POCARI SWEAT*. The Dream Project was selected as one of 11 case studies in the Ministry of Economy, Trade and Industry collection of "problem-solving partnerships" between companies and sports.

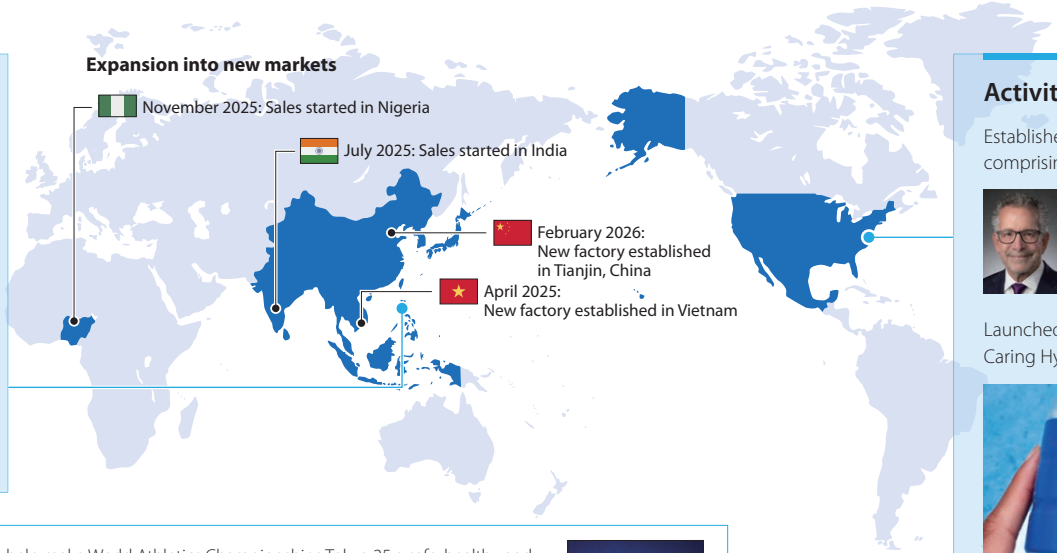
- **Establishing the concept of Caring Hydration in the U.S.**

As climate change makes extreme heat a regular part of life, heat-related health impacts and dehydration have become public health issues rather than just individual concerns. Now that adapting to climate change is becoming increasingly important, our aim is to establish the concept of *POCARI SWEAT* as a way of looking out for others and not just something consumed for one's own benefit. This is part of our unique approach to value creation. In the U.S., we have developed the new concept of Caring Hydration and have started to communicate this idea to consumers through *POCARI SWEAT*. Drawing on scientific evidence, we will collaborate with key opinion leaders, government agencies, and other stakeholders to pursue value-creation initiatives that contribute to addressing various environmental and social issues.

Overseas expansion of *POCARI SWEAT*

Activities in Asia

Started *POCARI SWEAT* Basketball Dream Project in the Philippines to support aspirations and efforts of children around the world through basketball



Activities in the U.S.

Established the POCARI SWEAT SCIENCE ADVISORY BOARD comprising experts in this field

Launched a brand website to promote the concept of Caring Hydration

Source: U.S. *POCARI SWEAT* brand website

Spotlight

Believing in human potential—Learning from athletes: Supporting World Athletics Championships Tokyo 25

To help make World Athletics Championships Tokyo 25 a safe, healthy and sustainable event, we supported athletes, event personnel, and spectators not only by providing *POCARI SWEAT*, which was developed by translating medical knowledge into everyday practice, but also by sharing scientifically grounded information on hydration.

For healthier life category

Nature Made

- **Striving to generate additional growth, particularly in the U.S., based on brand strength and high trust in quality**

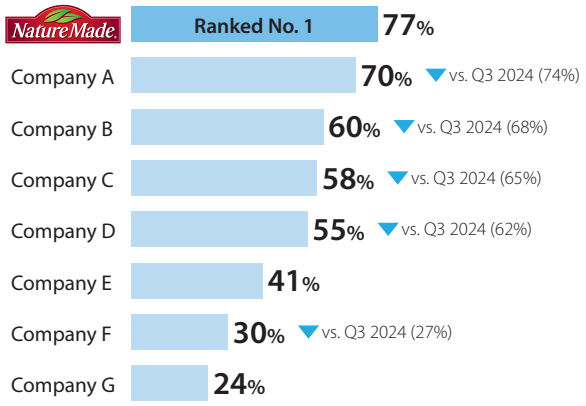
While it continues to conduct R&D on supplements, Pharmavite LLC manufactures and sells *Nature Made* brand products, which were first launched in California, U.S., in 1971. The brand has captured the top retail market share[1] for vitamins in the U.S.

Highly regarded as the most recommended supplement brand[2] by U.S. pharmacists for 28 consecutive years in the U.S. market, the brand has grown to exceed ¥100 billion in revenue, backed by its brand strength and high trust in quality. In order to meet the rapidly growing demand for gummy products in recent years in the U.S., Pharmavite has invested $250 million in New Albany, Ohio, to establish a new factory dedicated to gummy production. The factory site will be used for manufacturing of *Nature Made* gummy products and also for research and development into new products at the forthcoming Gummies Innovation Center of Excellence planned for the site. In 2024, gummy-type products became the fastest-growing category in the U.S. supplement market, and *Nature Made* recorded the highest dollar-based growth rate[3] in the vitamin category for gummy formulations.

In the Japan market, we have been offering a high-quality lineup and product designs tailored to the needs of Japanese consumers since sales launched in 1993. Going forward, we will continue to further grow our business through global expansion and the creation of next-generation products.

1. Based on data collected using the Complete Market Service from Circana, LLC, covering the general vitamin category (©2025, Circana, LLC) for the 52-week data through December 28, 2025, in the retail store category (U.S. MULO) adopted by Pharmavite
2. U.S. News & World Report / Pharmacy Times 2024 survey
3. Circana Market Advantage and Panel

Nature Made market penetration (FY2025 Q3, U.S.)



Source:
Continuous tracking survey by Pharmavite (sample size: 100 per week, approximately 400 per month, and approximately 1,200 per quarter)
Circana MULO POS data (food, drug, mass merchandise and club channels [excluding Costco])
Survey period: From year start (to December 28, 2025)
Circana panel data
All-channel household penetration (latest 52 weeks ending September 7, 2025)
Reach: Nielsen Media Impact (NMI)

Pharmavite New Albany

Selected *Nature Made* gummy products in the U.S.

/zeroz: Our new product

- **Launch of self-conditioning food product */zeroz* with a focus on oxygen that is essential for life**

It is well known that water, nutrients, and oxygen are essential elements for sustaining life. Thus far, we have created and proposed various forms of value, including *POCARI SWEAT*, which supports hydration, and *Calorie Mate*, which provides balanced nutrients.

As the final piece in this portfolio of products, */zeroz* focuses on oxygen and offers a new form of value as a self-conditioning food designed to support everyday Well-being. */zeroz* was developed under the concept of "Active Inner Resource" and contains kaempferol, a plant-derived ingredient that activates the innate strengths within the body.

/zeroz

- **Discovery of kaempferol**

Otsuka focused on the diets of people living in highland areas where the environment is low in oxygen, which is difficult for plants as well as animals. Our research scientists investigated 341 foods consumed in highland areas and ultimately identified the plant-derived compound kaempferol. They discovered that horseradish leaves contain particularly high levels of high-quality kaempferol.

The body's capacity to utilize oxygen is influenced by age and lifestyle habits. We therefore undertook some 13 years of clinical research on kaempferol and have published numerous scientific papers on its benefits.

Focus | Launch of a new concept: A product focused on the body's ability to utilize oxygen

In March 2026, Otsuka Pharmaceutical launched */zeroz*, a new "self-conditioning" food product based on the novel concept of "Active Inner Resource" that means reawakening the power innate in the human body. Developed with the insight that the ability to make effective use of oxygen is key to maintaining health, this product will enable us to deliver new value to everyone who aspires to good health.

Why we named it */zeroz*

Theme **The ultimate answer that unlocks infinite possibilities through the power of oxygen**

***/zero*:** In mathematics, as the value of a divisor moves infinitely closer to zero, the value of the division becomes infinitely greater. By the same principle, we give /zero (division by zero) the meaning **"unlocking the infinite possibilities of humankind."**

Final "Z": Signifies **Z as the "ultimate"** endpoint of the serial lines of inquiry we followed starting with A.

Final "OZ": Alludes to the **chemical symbol for oxygen, O_2**.

Key features of */zeroz*

It is widely recognized that water, nutrients, and oxygen are all essential for energy production in the body. Otsuka Pharmaceutical has created and proposed various forms of value, including *POCARI SWEAT*, which supports hydration, and *Calorie Mate*, which provides balanced nutrients. Our new product, */zeroz*, focuses on oxygen and offers a new form of value as a self-conditioning food designed to support everyday Well-being.

/zeroz was developed under the concept of Active Inner Resource. Unlike the conventional approach of replenishing deficient nutrients and other substances, it helps the body make more effective use of oxygen, activating the body's innate capabilities and enhancing performance in all daily activities.

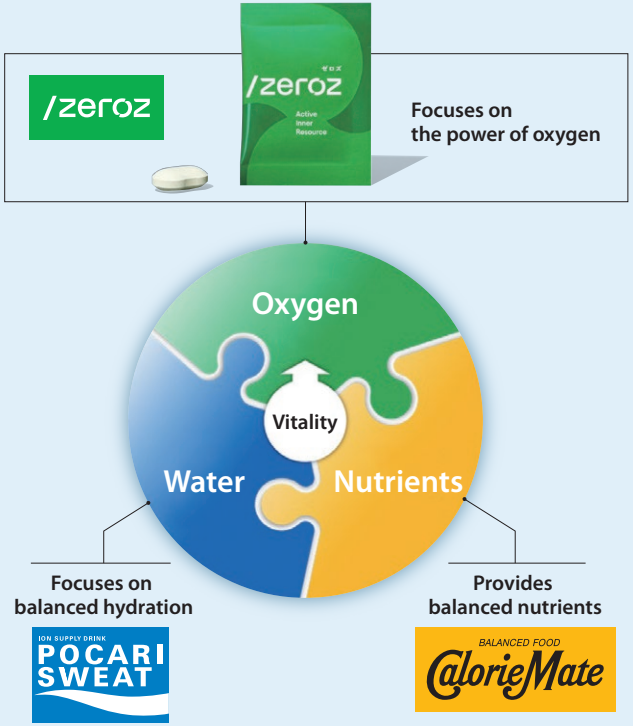
The */zeroz* development concept

The utilization of oxygen is intimately connected with energy production and everyday performance. However, the ability to use oxygen is known to change with age and lifestyle.

In a research project to investigate the body's utilization of oxygen that extended over some 13 years, Otsuka Pharmaceutical conducted numerous studies on the benefits of kaempferol, a substance derived from horseradish leaves. We then confirmed its safety and established proprietary technologies to improve its absorption efficiency within the body. The launch of the new product is the culmination of these efforts.

/zeroz features a citrus & tea flavor, combining refreshing citrus notes with a hint of matcha in a chewable tablet. As it can be sucked or chewed without water, it is simple to take in any situation.

One tablet a day provides our recommended daily intake of 10 mg of kaempferol. */zeroz* supports people to stay healthy and true to themselves in every moment—whether they are switched on for action or switched off for rest.



Giveaway samples at the Tokyo Marathon
Otsuka Pharmaceutical has sponsored the Tokyo Marathon in each of its 19 years, starting with the inaugural event. At Tokyo Marathon 2026, held on March 1, */zeroz* was distributed in the finish area to all runners who completed the course. In this way, we provided the */zeroz* experience to athletes who had run the whole 42.195 km.
(Otsuka Pharmaceutical was an official sponsor of Tokyo Marathon 2026.)

The road to developing */zeroz* —By the scientist who developed it

Yasutaka Ikeda
Director, Advanced Science Research Institute
Otsuka Pharmaceutical Co., Ltd.

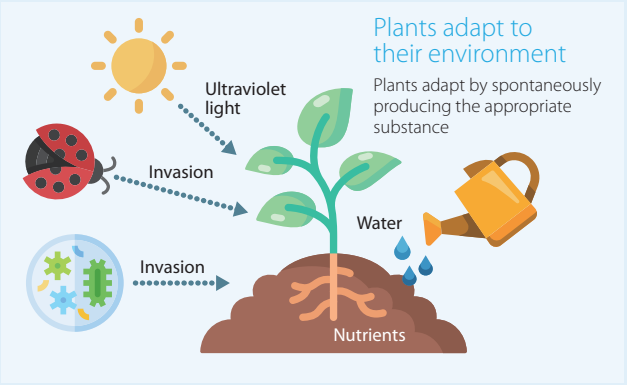
Profile • March 2007: Completed doctorate in Food Science and Biotechnology at the Faculty/Graduate School of Agriculture, Kyoto University
April 2007: Began postdoctoral research at Tokyo Metropolitan Institute of Gerontology (TMIG; now Tokyo Metropolitan Institute for Geriatrics and Gerontology)
December 2008: Joined Otsuka Pharmaceutical Co., Ltd. at its Nutraceuticals Research Institute (Saga research site)
March 2025: Became director of Otsuka's Advanced Science Research Institute with overall responsibility for the research organization
April 2026: Took up concurrent appointment as adjunct professor at the University of Pittsburgh School of Medicine

Q What was the original starting point of the research?

I started out from the idea that health is not inborn, in other words not determined by genetics. Identical twins are born with exactly the same set of genes, but we know that their state of health can diverge greatly with the cumulative influence of the environment they grow up in, their daily diet, and other factors. So we are aware that health is something that is gradually shaped by the choices we make from day to day.

In the course of my research, I took particular inspiration from the survival strategies of plant life. As plants are unable to move independently, they have to survive under constant exposure to stresses from the external environment such as ultraviolet light, microorganisms, and insects. Plants have adapted by evolving systems to protect against different environmental factors. For instance, they secrete protective substances when ultraviolet light becomes too harsh, emit bitter flavors and odors when attacked by insects, and produce antibacterial substances when invaded by microorganisms.

I realized that this vital ability to change in response to the environment was also an important element in our approach to human health. Animals and plants have different ways of adapting to the environment, but they also share the fundamental similarity of needing water, nutrients, and oxygen. I felt that this indicated some essential property that deserved to be investigated.



Q How did your research into oxygen utilization take shape?

It was studying people who live in highland areas that sparked my interest. People who live at high altitudes where the environment is low in oxygen can run faster and for longer distances than any other group. It was this observation that made me start my investigations 13 years ago.

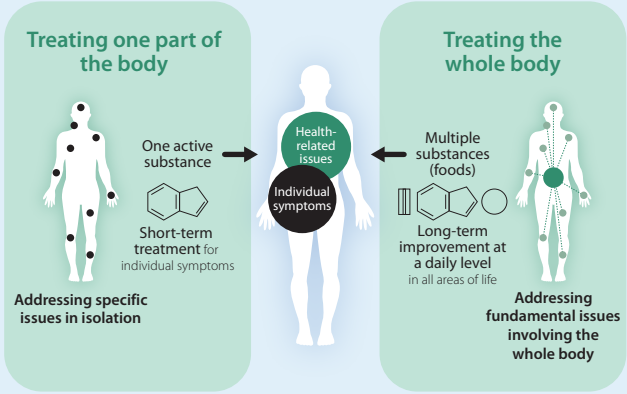
Beginning with the premise that health is not determined by genetics, we carried out an exhaustive investigation into what these people eat and how they have adapted to their environment. One by one, we tested 341 different foodstuffs found in highland regions around the world and eventually identified a common ingredient. That ingredient was a flavonoid called kaempferol. Areas with low oxygen levels represent a harsh environment for plants as well as humans. We decided that this kaempferol might be the substance that plants produce spontaneously to survive in these low-oxygen environments.

However, even after this insight, there was still the major issue of securing enough of this substance to supply a large number of people. We spent eight years working on this task and followed successive lines of inquiry that finally led us to the horseradish leaf. We discovered that kaempferol can be harvested in large quantities from horseradish leaves. By extracting it as a natural substance according to a careful procedure, we were able to develop a way of making it safely available to large numbers of people.

Q What is the core concept of this research and development project?

In the course of our development, we came to fundamentally rethink our whole approach to the question of health. Before, I would say that the main focus was on a localized approach that treats in isolation the part of the body where symptoms appear. However, what we aimed for is a systemic approach that improves day-to-day living over the long term by thinking of the body as a whole.

With the complex nature of modern health issues, an approach restricted to individual symptoms or parts of the body cannot address the root causes. That's why I see potential new value in taking a fresh look at the body's existing inner abilities and working to activate them. It was this idea that led us to develop the Active Inner Resource concept. That means reawakening the power innate in the human body. Underlying that statement is the strong conviction that we still have a long way to go in uncovering the hidden potential of humankind.



For women's health category

Women's health is one of the categories of social issues identified as a growth driver in the 4th MTMP. The Otsuka group is developing products based on scientific evidence, and, through the scientific know-how we have cultivated and our ongoing educational activities, we will work to quickly address the increasingly complex health issues faced by women and propose new solutions.

In Japan, product recognition for *EQUELLE*, which contains equol and supports women's health and beauty, increased significantly due to our extensive provision of information through women's health seminars. Women are also known to face different health challenges at different stages of life due to the significant influence of hormonal changes. In addition, these challenges are known to vary considerably among individuals and across populations, and women need individually tailored solutions. As women continue to advance in society and are expected to play more active roles, many suffer from various symptoms affecting both their mind and body. The Otsuka group will work to provide solutions to women around the world that address the needs of individuals according to their circumstances and stage of life.

EQUELLE, Uqora, and *Bonafide*

• Activities in North America

In North America, we are addressing various women's health issues with three brands, the first of which is *EQUELLE*, followed by *Uqora*, which supports women's urinary tract health, and *Bonafide*, which supports women's needs as they become more complex.

Uqora, in particular, has seen steady growth in North America in OTC sales at pharmacies, expanding its distribution channels to drugstores such as CVS and Walgreens, in addition to expanding e-commerce. For *Bonafide*, which we added to our portfolio in FY2023 through the acquisition of women's health company Bonafide Health, LLC, in September 2024 we launched *Thermella*, a product that has been confirmed to be effective through research. It was developed as a plant-based supplement based on scientific evidence to support women experiencing hot flashes and night sweats. *Thermella* contains curcumin extract, decaffeinated green tea extract, and spirulina extract, naturally derived ingredients with a functional claim* to relieve hot flashes and night sweats. This product offers a new treatment option to support women with menopausal symptoms.

* This statement has not been evaluated by the U.S. FDA. The product is not intended to diagnose, treat, cure, or prevent any disease.

Strengths in the for women's health category

Bonafide

1.1 million	Consumers using these products
40+	Clinical studies on the product/active ingredients
13,000	Physicians recommending product

uqora

700,000	Consumers using these products
No. 1	UTI brand sales in the U.S.

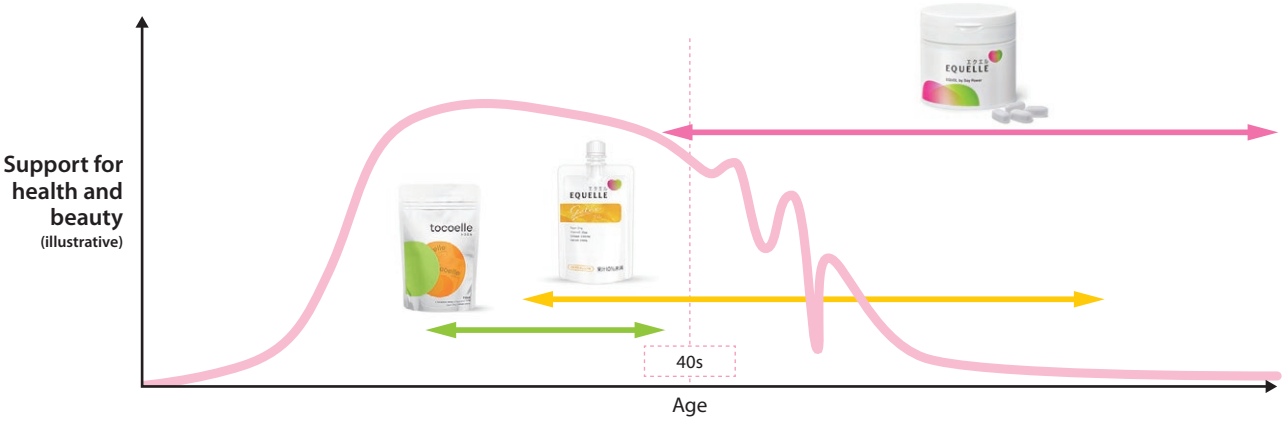
• Accelerating expansion in Asia

To expand our business in Asian markets, we need to comply with different regulations in each country or region, so we are making preparations by drafting country/region-specific plans.

The regulatory requirements are particularly strict in South Korea, where we need to obtain both temporary food ingredient registration and functional ingredient registration (to support health claims). We started working to obtain the necessary approvals in FY2018. In FY2023, Lactococcus 20-92, one of the ingredients in *EQUELLE*, became the first ingredient to receive certification from the South Korean authorities under the temporary food ingredient registration system. Because products marketed in tablet form, a dosage form generally associated with pharmaceuticals, require approval as a Health Functional Food (health claim) in South Korea, we applied for Health Functional Food approval for SE5-OH (*EQUELLE*) in FY2023. In May 2025, the product became the first in South Korea to receive certification for the health claim "supports the health of menopausal women." After seven years of effort, the groundwork for launch is now in place.

EQUELLE was launched in Hong Kong in April 2026 and there are plans to launch in Singapore. We are steadily advancing preparations to expand our sales footprint beyond Japan and into Asia.

Product development to support women at different life stages



Bonafide

EQUELLE (Japan)

Consumer Products Business

Contributing to society by creating new foods in response to consumer issues

Materiality

Contribute to the health and Well-being of people around the world

Progress of the 4th Medium-Term Management Plan

Otsuka Foods, the core of the Consumer Products Business in the group, is expanding its business in the beverage and food categories with a mission to contribute to consumer Well-being through food. As an indispensable presence in society through the creation of new foods, Otsuka Foods aims to achieve sustained growth and is pursuing business growth that balances revitalization of existing brand value and creation of new value under the 4th MTMP.

In the Beverages Business, the core brand *MATCH* has expanded its following among younger consumers through engagement- and experience-based initiatives and continues to outpace overall market growth despite challenging conditions in the carbonated beverages market. The Foods Business has outperformed the growth rate* of the retort pouch food market by leveraging the *Bon Curry* brand's offerings tailored to increasingly diverse dietary needs and by strengthening communication of the *MY SIZE* brand's low-calorie and reduced-sodium benefits.

Otsuka Foods is focusing its new product development on the three core themes of creating deliciousness, helping to address social issues, and evidence-based proprietary technology.

Based on our original concepts and technologies, we aim to develop new products with value to meet potential consumer needs as only Otsuka Foods can.

* Intage SRI

Beverages Business

- **Building brands that earn long-standing customer loyalty**

The Beverages Business offers a wide range of brands, including *MATCH*, *CRYSTAL GEYSER*, *Sinvino JAVA TEA Straight*, and *Sugoi Daizu*, and proposes solutions that contribute to richer daily lives for consumers.

MATCH will celebrate its 30th anniversary and is a brand cherished by all generations as a vitamin-enhanced carbonated beverage with a refreshing taste. We will step up communication programs to foster greater appreciation of this brand, and work to expand the *MATCH* fan base and increase brand value.

For *CRYSTAL GEYSER*, we are working to highlight the absence of detectable perfluoroalkyl and polyfluoroalkyl substances (PFAS) including perfluorooctanoic acid (PFOA) and perfluorooctane sulfonate (PFOS) in this product, position its soft-water profile as a quality attribute suited to Japanese tastes, and expand the customer base on a foundation of trust in its safety and reliability. For *Sugoi Daizu*, we are maximizing brand value through a full product refresh and by strengthening communication of the dietary fiber benefits derived from the use of whole soybeans, in addition to the established positioning on protein intake.

MATCH (left), *MATCH Vitamin Mikan* (right)

CRYSTAL GEYSER

Sugoi Daizu series

Foods Business

- **Responding to increasingly diverse dietary needs and health issues**

We are staying attuned to changes in the social environment and lifestyles and working to respond to increasingly diverse dietary needs and health issues. With the sharp increase in rice prices, more consumers are turning to noodles with their meals. We have launched *Umami-Rich Japanese-Style Bon Curry* as a new offering that goes well with both noodles or rice. We have also brought to market *Health-Conscious Bon Curry with Full Serving of Japan-Grown Vegetables* that retains the distinctive flavor of *Bon Curry* but is also made with a full serving of Japan-grown vegetables and is free from 28 allergens, gluten, and animal-based ingredients. In the *My Size Plus Support* series, we have expanded our lineup with two new products that only contain 1g salt to help address the national public health challenge of reducing salt intake. We have also developed *Main Dip*, an innovative series of freezer marinades that enhance flavor by marinating meat before freezing. These products help reduce the burden of daily meal planning and cooking stress amid the rise in dual-income households and increasingly diverse lifestyles. By enabling consumers to stock their freezers with ready-to-cook dishes, *Main Dip* helps reduce the effort involved in planning daily meals and satisfies demand for meals that deliver time savings, homemade quality, and great taste.

Bon Curry GOLD

Umami-Rich Japanese-Style Bon Curry

Health-Conscious Bon Curry with Full Serving of Japan-Grown Vegetables

My Size Plus Support

Mannanhikari

Main Dip freezer marinades

Other Businesses

Expanding into new markets in Japan and overseas, leveraging strengths in our specialist technologies and shared platforms

Materiality

Contribute to the health and Well-being of people around the world

Progress of the 4th Medium-Term Management Plan

In Other Businesses, FY2025 revenue reached ¥115.9 billion, an increase of 2.0% year on year, while business profit rose by 7.4% to ¥7.5 billion. In the chemicals field, revenue increased slightly following the acquisition of hakkai inc. as a wholly owned subsidiary in order to strengthen our KATACHI* Business. In the warehousing and transport field, revenue increased after we won business with new customers.

* KATACHI = Parts

Chemicals business (Otsuka Chemical)

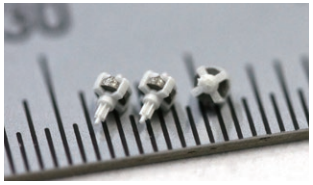
- **Transform the potential of materials to KATACHI**

Otsuka Chemical supports comfortable lifestyles and industrial development in the information electronics, mobility, housing, and pharmaceutical fields by supplying functional materials and proprietary intermediates— and leveraging the power of these materials to supply components and active pharmaceutical ingredients. Starting with the refinement of nigari (bittern) from seawater, we have developed a wide range of chemical products based on our proprietary technologies, including the first successful industrialization of hydrazine in Japan. In the information electronics field, we offer plastics and polymer materials that meet miniaturization and high-resolution needs; in the mobility field, we provide brake pad materials, foaming agents, and tire rubber additives that enhance safety, comfort, and energy efficiency; and in the pharmaceutical field, we supply raw materials for antibiotics and proprietary intermediates, among other products, to address the advanced needs of various industries. In the 4th MTMP, we are promoting KATACHI Business, which offers components that embody the material capabilities we have cultivated over the years. In the semiconductor and robotics industries, where further growth is anticipated, our precision gear and molding business is meeting demand for precise, lightweight, and quiet components; our high-performance, multifunctional Films Business is meeting wide-ranging demand from automotive parts to information devices; and our CDMO Business is focused on medium-molecule pharmaceuticals and their raw materials. We will leverage our material and technological capabilities to realize new value for society under our vision: A company that collaborates with customers to find creative new usage by utilizing advanced materials.

- **Acquired hakkai as a wholly owned subsidiary to further our KATACHI Business**

In October 2025, Otsuka Chemical acquired hakkai inc. as a wholly owned subsidiary. By combining hakkai's advanced technological capabilities in precision plastic molding and mold design and manufacturing with Otsuka Chemical's materials development capabilities and customer base, we can create value through an integrated value chain spanning research and development through manufacturing. Through this acquisition, we will further enhance the competitiveness of our value-added products in growth markets, including automotive, electrical/electronics, and pharmaceutical fields.

Wholly owned subsidiary hakkai



Miniature gear that combines technologies from Otsuka Chemical and hakkai

Warehousing and transport business (Otsuka Warehouse)

- **Tackling optimization and efficiency across industry through a comprehensive digitalization strategy**

Otsuka Warehouse is a logistics company specializing in the distribution of total healthcare products such as pharmaceuticals, foods, and beverages, and plays an important role in supporting people's richer and healthier lifestyles.

Currently, the logistics industry as a whole is facing labor shortages. To address this and other issues, we are moving forward with reforms to our warehousing and delivery operations by leveraging technology to create systems that anyone can use without relying on intuition or experience. By prioritizing standardization and systematization under the 4th MTMP, we are aiming to optimize the entire supply chain by establishing a versatile framework that enables coordination with other companies such as shippers (manufacturers), transportation companies, and wholesalers, without relying on specific equipment or proprietary systems. For example, we have built a system that visualizes the flow of goods from order receipt to delivery, offering real-time tracking of the current location and status of goods. Furthermore, by using an incoming goods reservation system and changing the first-come, first-served rule for vehicle arrivals to a reservation-based system, we have leveled arrival times. This has allowed us to visualize scheduled arrivals and waiting vehicles, which has helped to reduce the work hours of receiving staff and improve on-site operational efficiency. The system has also reduced vehicle wait times, leading to reduced CO_2 emissions and other environmental benefits.

In line with our mission to deliver total healthcare products safely and reliably, we will strive to realize sustainable logistics to support health for people and for society as a whole.

CROSS DOCK HARUMI: Headquarters building converted from a warehouse

Research and development

Using a creative approach to focus on areas with unmet needs

Materiality

Contribute to the health and Well-being of people around the world

R&D policy

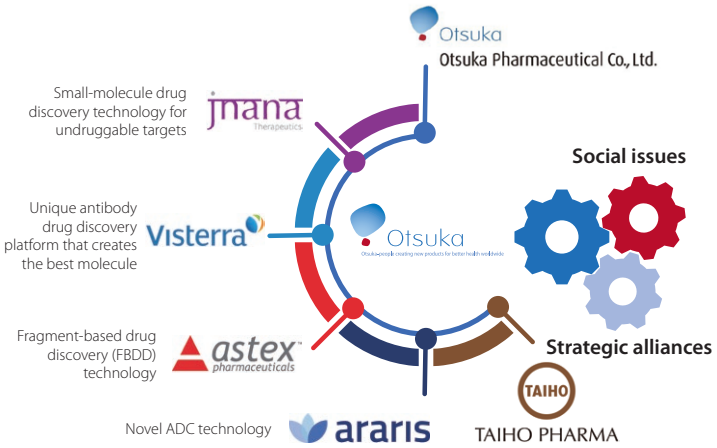
The Otsuka group is working to strengthen its business portfolio for medium- and long-term growth by combining internal and external science resources with a focus on healthcare-related social issues and proprietary science. We are aiming for consolidated revenue of ¥3,500 billion in FY2035. Over the long term, we will invest the management resources needed to continuously develop original pipeline assets and products at our research facilities.

One of the distinctive features of the Otsuka group is our management style of horizontal collaboration, whereby each operating company contributes its respective strengths independently and the group collaborates with the most suitable partners while providing them with maximum support. In the Pharmaceutical Business, we have drug discovery sites at Otsuka Pharmaceutical, Otsuka Pharmaceutical Factory, Taiho Pharmaceutical, Astex Pharmaceuticals, Visterra, Jnana Therapeutics, and Araris Biotech. Based on this concept of horizontal collaboration, we have fostered organic connections across the group and integrated the expertise and technologies of these companies to evolve our capabilities into a robust drug discovery platform. While many programs that leverage the strengths of our operating companies are progressing toward launches in FY2030 or later, we also plan to obtain approval for three additional drug candidates beyond the Next 8 by FY2030.

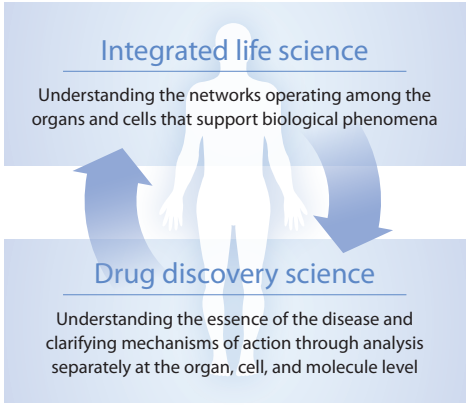
At Otsuka Pharmaceutical, we have launched a mechanism for managing development priorities and promoting collaboration among subsidiaries from an overall perspective, allowing us to accelerate strategic research and development by leveraging the strengths of each subsidiary. Furthermore, from a group-wide perspective, we have begun exploring ways to apply technologies developed by individual operating companies to drug discovery in other therapeutic areas. For example, we have started leveraging the next-generation antibody-drug conjugate (ADC) drug discovery platform acquired by Taiho Pharmaceutical for drug discovery research beyond oncology. Through efforts like these, we are advancing collaboration across operating company boundaries.

By deepening cooperation within the group while strengthening collaboration with external scientific resources and improving the speed and likelihood of success of clinical development, we expect more programs to make it to market.

Horizontal collaboration in research



Mutually connecting drug discovery science and integrated life science



An approach that only the Otsuka group can deliver

The Otsuka group aims to combine drug discovery science and integrated life science. Our approach to drug discovery research is to seek to understand the essence of the disease and clarify mechanisms of action through analysis separately at the organ, cell, and molecule level.

The Nutraceutical Business takes an integrated life science approach, which aims for a deeper understanding of the actual networks operating among the organs and among the cells that support biological phenomena. The development of *Zeroz*, launched in March 2026, leveraged our research platforms accumulated as a total healthcare company.

Looking ahead, we will continue efforts to mutually connect drug discovery science and integrated life science and to combine their respective strengths in order to create new value focused on individual lifestyles. This unique approach is a strength that only the Otsuka group can deliver as a total healthcare company.

Research and development

R&D sites

Europe

U.K.:
- Astex Pharmaceuticals

Germany:
- Otsuka Novel Products GmbH

Switzerland:
- Taiho Oncology Europe GmbH
- Araris Biotech AG

Ireland:
- ○ Veryan Medical Ltd.

Asia

China:
- Otsuka Shanghai Research Institute
- Shanghai Otsuka Foods Co., Ltd.
- Otsuka Beijing Research Institute
- Taiho Pharmaceutical of Beijing Co., Ltd.

Korea:
- Korea Otsuka Pharmaceutical Co., Ltd.

Singapore:
- Taiho Pharma Asia Pacific Pte. Ltd.

Japan

Tokushima:
Otsuka Pharmaceutical Co., Ltd.
- Tokushima Research Center for Drug Discovery
- Chemistry, Manufacturing and Control (CMC) Headquarters
- Diagnostic Division, Research Department

Taiho Pharmaceutical
- Pharmaceutical Technology Division

Otsuka Pharmaceutical Factory, Inc.
- Research and Development Center
- Technical Center
- Medical Foods Research Institute

Ibaraki:
Taiho Pharmaceutical
- Research Division
- Consumer Healthcare Research and Development Department

Tokyo:
Otsuka Pharmaceutical Co., Ltd.
- Diagnostic Division, Clinical Development Department
- Advanced Science Research Institute

Taiho Pharmaceutical
- Development Division

Otsuka Pharmaceutical Factory, Inc.
- Research and Development Center

Otsuka Medical Devices
- ○ HARUMI Technology Center

Gunma:
JIMRO
- ○ R&D Headquarters

Saitama:
Taiho Pharmaceutical
- Pharmaceutical Technology Division

Osaka:
Otsuka Pharmaceutical Co., Ltd.
- Osaka Research Center for Drug Discovery
- Headquarters of Clinical Development

Shiga:
Otsuka Pharmaceutical Co., Ltd.
- Nutraceuticals Research Institute (Otsu research site)
- Otsu Skin Care Research Institute

Otsuka Foods Co., Ltd.
- Biwako Research Institute

Saga:
Otsuka Pharmaceutical Co., Ltd.
- Nutraceuticals Research Institute (Saga research site)

U.S.

- Visterra, Inc.
- Jnana Therapeutics Inc.
- Otsuka Pharmaceutical Factory America, Inc.
- Otsuka Pharmaceutical Development & Commercialization, Inc.
- Taiho Oncology, Inc.
- ○ Recor Medical, Inc.
- Bonafide Health

- Research divisions
- Development divisions
- ○ Medical devices
- Nutraceutical and Consumer Products Businesses

Main R&D sites

Tokushima Research Center for Drug Discovery, Otsuka Pharmaceutical

The Tokushima Research Center for Drug Discovery has provided new therapeutic agents such as *REXULTI* and *Samsca/JINARC/JYNARQUE* in the psychiatric and neurological and the cardiovascular and renal area. We continue to conduct research activities focusing on drug discovery approaches with small molecules, both phenotypic drug discovery and targeted drug discovery, utilizing the experience we have accumulated over the years. In collaboration with the Osaka Research Center for Drug Discovery and other global research institutes, we are also conducting drug discovery research by leveraging new technologies. From the early stages of drug discovery to the submission of applications for approval, we are conducting research and evaluation studies of safety and pharmacokinetics, while also preparing application documents and responding to inquiries.

Osaka Research Center for Drug Discovery, Otsuka Pharmaceutical

In addition to carrying on Otsuka Pharmaceutical's drug discovery history and culture, the Osaka Research Center for Drug Discovery generates new innovation. Having built a network with research institutes and biotech companies both in Japan and overseas, we are engaged in drug discovery research for small-molecule compounds and biologics. Equipped with cutting-edge research equipment, including one of the world's most advanced cryo-electron microscopes and automated organoid culture equipment, we are undertaking new drug discovery, including that which incorporates cutting-edge immunology and digital transformation.

Research and development

Discovery and Preclinical Research Division (Tsukuba), Taiho Pharmaceutical

In the Tsukuba area, Taiho Pharmaceutical's Discovery and Preclinical Research Division is taking on the challenge of discovering new original drug candidate compounds that indicate outstanding efficacy and high safety, mainly in the fields of oncology and immunology. In addition to expanding our proprietary Cysteinomix drug discovery platform, which led to the discovery of *LYTGOBI* and zipalertinib, we are actively working to improve and expand our drug discovery platform technologies by introducing robotics technology to increase and accelerate research productivity and AI in the search for drug targets and compound design.

Astex Pharmaceuticals

Astex Pharmaceuticals has established a method (FBDD[1]) for efficiently designing and discovering new drugs based on small-molecule organic compounds. In the oncology area, the company has developed multiple new drugs and clinical development compounds, including *Kisqali*[2] and *Truqap*,[3] and is recognized worldwide as a leading company in FBDD. Furthermore, in addition to creating innovative drugs by using cryo-electron microscopy for drug design, Astex Pharmaceuticals is also exploring the potential of quantum computers for such drug design.

1. Fragment-based drug discovery
2. Product sold by Novartis
3. Product sold by AstraZeneca

Visterra

Leveraging its strength with antibodies and biologics, Visterra is undertaking R&D in the fields of immune-mediated and renal diseases where current treatment options are limited. *VOYXACT* was launched in December 2025 for the treatment of adults with primary IgAN at risk for disease progression, and clinical studies are underway to develop additional indications. Additionally, VIS171 is currently in Phase 1 trials, and clinical development is progressing steadily. Our proprietary technology Hierotope® platform makes it possible to design antibody drugs for many biological substances by calculating and predicting the protein-antibody binding. As part of Otsuka Pharmaceutical's Open Innovation Strategy, we are collaborating with universities and hospitals in and around Boston.

Jnana Therapeutics

Jnana Therapeutics Inc., which joined the Otsuka group in 2024, is conducting research based in Boston. Its proprietary drug discovery platform, RAPID* enables the identification of compounds that bind to targets previously considered difficult to address using conventional screening methods, particularly for small-molecule drugs. This technology has shown promising results in challenging therapeutic areas such as autoimmune and rare diseases. Repinatrabit, currently in clinical development, is a small-molecule compound discovered through this platform that inhibits amino acid reabsorption in the kidneys. It is expected to become an effective treatment option for phenylketonuria.

* Reactive Affinity Probe Interaction Discovery

Araris Biotech

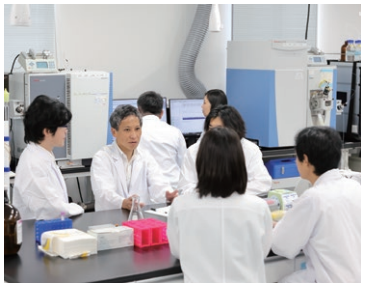
In March 2025, Taiho Pharmaceutical acquired Araris Biotech, a Switzerland-based biotechnology company developing next-generation antibody-drug conjugates (ADCs). Araris is now a member of the Otsuka group.

Araris owns the proprietary next-generation ADC drug discovery platform AraLinQ™, an innovative technology with the potential to address the toxicity and limited efficacy that remain key challenges for current-generation ADCs. Araris is currently progressing the development of three programs created using the AraLinQ™ technology for the treatment of hematological and solid tumors. Clinical studies are scheduled to start from FY2026.

Advanced Science Research Institute, Otsuka Pharmaceutical (Nutraceutical Business)

In 2025, Otsuka Pharmaceutical established the Advanced Science Research Institute as part of the Nutraceutical Business to pursue cutting-edge science and advance the development of innovative new products. Rather than focusing on dysfunction in individual parts of the body, the Institute operates under a policy of studying the body as an integrated whole. As a virtual research institute without dedicated laboratory or research facilities, it conducts collaborative research with leading research institutions and universities in Japan and abroad.*

* The Advanced Science Research Institute is conducting joint research with overseas institutions such as Cornell University, University of Pittsburgh, and University of North Carolina, and is collaborating with Kyoto University, Tohoku University, Keio University, Yamaguchi University, the National Cerebral and Cardiovascular Center, and other institutions in Japan.



Focus | Business growth delivered by drug discovery research

The key to future growth lies in technology innovation through drug discovery. The Otsuka group has built drug discovery platforms around the world and is tackling cutting-edge research.
In this section, we focus on the proprietary technologies at Otsuka Pharmaceutical (Astex Pharmaceuticals, Jnana Therapeutics) and Taiho Pharmaceutical (Araris Biotech).

Drug discovery at Astex Pharmaceuticals | Next-gen discovery engine: FBDD, AI and cryo-EM

Pyramid: A proprietary drug discovery platform

Based in Cambridge (U.K.), Astex Pharmaceuticals has pioneered fragment-based drug discovery (FBDD) and has developed a world-class FBDD and structure-based drug discovery (SBDD) technology platform (Pyramid) which it is utilizing to develop small-molecule therapeutics for oncology and central nervous system (CNS) disorders. FBDD utilizes atomic resolution, protein–ligand, structures to identify novel chemotypes (fragment "hits") and ligand binding sites on a protein which can be exploited for drug discovery. Fragment "hits" are optimized via iterative cycles of SBDD to generate safe and efficacious drug molecules. To date, Pyramid has contributed to the identification of multiple small-molecule clinical candidates and three approved drugs (Kisqali, Balversa and Truqap).

Cutting-edge technologies in structural analysis: Cryo-EM

Since Astex's inception, protein-ligand structures have been determined using high-throughput protein X-ray crystallography. However, over the past decade, advances in electron cryo microscopy (cryo-EM), a complementary structure determination method, have meant that cryo-EM can now also be used to support FBDD and SBDD programs. Typically, X-ray crystallography can be utilized for small, soluble proteins that purify at scale. Conversely, cryo-EM has greater utility for large, flexible and/or low yielding proteins, or multi-protein complexes, that are refractory to X-ray crystallography.

In 2016 it was unclear if cryo-EM would have utility for drug discovery, so Astex founded the Cambridge Pharmaceutical Cryo-EM Consortium, as a means of evaluating this emergent technology. The consortium involved multiple pharmaceutical company partners, the cryo-EM microscope manufacturer Thermo Scientific, the University of Cambridge, and the Medical Research Council Laboratory of Molecular Biology (MRC LMB), home to the cryo-EM Nobel Laureate Professor Richard Hendeson (CH FRS FMedSci). The success of this partnership is reflected in the consortium celebrating its 10-year anniversary and by the fact that all pharma affiliates have now established in-house cryo-EM capabilities. Through the consortium, Astex was able to demonstrate proof of concept that cryo-EM could be used for FBDD and could be transformational for prosecuting drug discovery with challenging target classes (Saur et al., doi.org/10.1016/j.drudis.2019.12.006). Consequently, Astex has established a state-of-the-art, in-house, cryo-EM facility, housing a fleet of 4 cryo-EM microscopes (2 Glacios, 1 Krios G4 and a recently commissioned Krios 5 (Figure 1)).

This represents the most advanced industrial cryo-EM facility in Europe. Astex has also developed proprietary platform technologies to maximize cryo-EM throughput and to minimize the timelines required for atomic resolution cryo-EM structure determination. Astex is routinely using cryo-EM to enable and support multiple FBDD and SBDD CNS drug discovery programs.

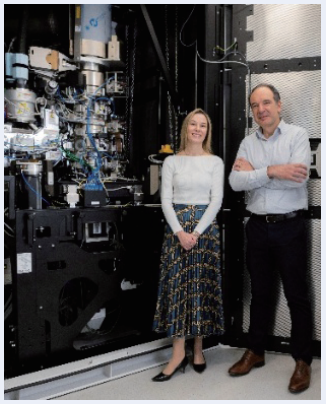


Figure 1
Dr Michelle Jones and Dr Gianni Chessari (Astex's President & CSO, respectively) by Astex's new Krios 5 microscope

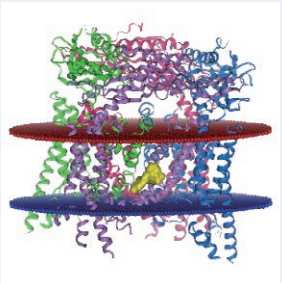


Figure 2
Astex cryo-EM structure of an agonist bound to an ion channel

Future outlook

Many CNS relevant drug targets, including within the challenging integral membrane protein family (e.g., neurotransmitter receptors, transporters, GPCRs, ion channels, and membrane associated enzymes), are inherently more amenable to cryo-EM than X-ray crystallography. Ion channels are of particular interest given their diverse cellular roles and as channel dysfunction is associated with various neurological disorders. Astex is leveraging the power of cryo-EM to elucidate the mechanism of action of small-molecule agonists and antagonists at high resolution, revealing how subtle structural changes associated with ion-channel opening and closing occur. This work demonstrates the value of cryo-EM in enabling structure-based drug discovery. (Figure 2)

Additionally, Astex is further exploring opportunities for streamlining cryo-EM data processing via enhanced automation of workflows and using deep learning approaches which leverage Astex's proprietary dataset of more than 19,000 protein-ligand complexes (Sanchez Garcia et al., doi.org/10.1101/2025.03.04.641536). This unique dataset is also being used to develop cutting-edge computational co-folding capabilities (AstexFold) and generative AI models which are being ubiquitously deployed to support FBDD and SBDD programs.

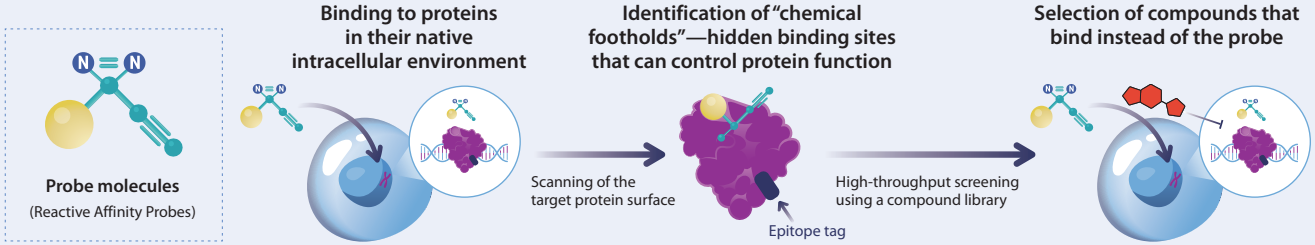
Over the past 25 years, Astex has continually evolved its Pyramid platform, integrating cryo-EM and advanced AI/ML methodologies with the original X-ray crystallographic technologies, to maintain a cutting-edge drug discovery engine capable of delivering safe and efficacious new medicines with clear patient benefit.

Drug discovery at Jnana Therapeutics | Unlocking the undruggable: The RAPID platform

Jnana's Reactive Affinity Probe Interaction Discovery (RAPID) platform is a proprietary drug discovery engine designed to unlock high-value therapeutic targets that traditional technologies cannot reach. While standard discovery methods often rely on purified proteins in isolation, RAPID analyzes protein targets in their native environment—inside living cells. This approach is critical for complex targets, ensuring we address the protein in its natural, biologically active structure.

The platform employs a streamlined two-step process to identify novel medicines. First, RAPID introduces a library of light-activated "probe" molecules (Reactive Affinity Probes) into the cell. These probes scan the target protein's surface to identify "chemical footholds"—hidden binding sites that are capable of controlling the protein's function. Unlike other methods, RAPID can immediately verify if binding to these sites produces the desired therapeutic effect, such as blocking a disease pathway.

Once a functional foothold is secured, the platform initiates a high-throughput screen of massive compound libraries to identify a lead-like molecule that can precisely engage that same site. By utilizing an automated readout that is over 100 times faster than comparable technologies, RAPID dramatically accelerates discovery timelines. This efficiency enabled the discovery of JNT-517, which targets a previously unknown allosteric site on SLC6A19, and currently powers Jnana's pipeline of first-in-class programs for autoimmune diseases.



Drug discovery at Araris Biotech | Accelerating cancer treatment innovation using the next-generation ADC technology AraLinQ™

Antibody-drug conjugates (ADCs) are therapeutic drugs comprising antibodies attached to anticancer agents (payloads) to selectively attack cancer cells.

Drug discovery research at Araris Biotech, which became part of the Otsuka group in 2025, is founded on its proprietary ADC linker platform AraLinQ™. This platform allows the discovery of highly uniform, stable and potent ADC therapeutic candidates that have demonstrated a wider range of safety and increased antitumor effects compared to conventional ADCs in preclinical studies. The use of this technology is expected to address the shortcomings of current-generation ADCs.

Through these features, the AraLinQ™ platform simultaneously enables high homogeneity, bloodstream stability, flexible payload design, and one-step manufacturing. Several drug candidates have been created using this proprietary platform and the company expects clinical studies to start in the near future.

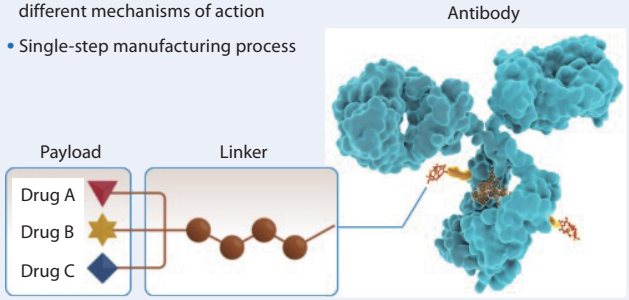
Araris' unique ADC technology represents a quantum leap for the ADC field, potentially offering precise payload delivery of multiple mechanisms of action simultaneously to the tumor, with less toxicity.

Special features of Araris' drug discovery technology

- Araris' linker technology enables site-specific payload attachment to a privileged attachment site on a specific amino acid (Q295) within the antibody IgG-Fc framework, which allows efficient payload delivery and maximum ADC potency.
- AraLinQ™ can insert the linker in a one-step process, enabling the efficient creation of ADCs with high homogeneity and reproducibility. The linker-payload is connected to the antibody through a very strong peptide bond resulting in exceptional stability in the bloodstream and reduced non-specific damage to healthy tissue.
- The platform allows the accurate attachment of multiple types of payload with different mechanisms of action to a single antibody, thereby maximizing the antitumor effects.

Special features of next-generation ADCs enabled by AraLinQ™

- Good safety profile and potency against a wide range of tumors
- Extremely high uniformity
- Improved physicochemical properties and stability in the bloodstream
- Carries multiple payloads with different mechanisms of action
- Single-step manufacturing process



Product development pipelines and research and development activities (at least in Phase 3 as of December 31, 2025)

Programs that made progress in FY2025

Category	Brand name (Generic name) Development code	Indication / Dosage form	Development status in major countries/regions								FY2025 progress (from phase 3)
			Japan		U.S.		Europe		China		
			Phase 3	Filed	Phase 3	Filed	Phase 3	Filed	Phase 3	Filed	
Psychiatry and neurology area	*REXULTI/RXULTI* (brexpiprazole) OPC-34712 / OPC-34712 FUM	Schizophrenia / Once-weekly oral	●								
	(centanafadine) EB-1020	Attention-deficit hyperactivity disorder / Oral	●[1]			●					May | Phase 2/3 initiate (Japan) Nov | Filing (U.S.)
	(ulotaront) SEP-363856	Schizophrenia / Oral	●		●						Mar | Phase 3 initiate (Japan and U.S.)
		Major depressive disorder / Oral			●[1]						
		Generalized anxiety disorder / Oral	●[1]		●[1]						
	(ulefnersen) ION363	Amyotrophic lateral sclerosis (ALS) / Injection	●[2]		●[2]		●[2]				
	(pizuglanstat) TAS-205	Duchenne muscular dystrophy / Oral	●								
	(Software as a Medical Device) ONB-01	Post-traumatic stress disorder / Medical device	●[3]								
Oncology area	*INQOVI/INAQOVI* (decitabine, cedazuridine) ASTX727	Acute myeloid leukemia / Oral				●		●			Jul | Filing (U.S.) Nov | Filing (Europe)
	(azacitidine, cedazuridine) ASTX030	Myelodysplastic syndromes, chronic myelomonocytic leukemia, acute myeloid leukemia / Oral			●						Feb | Phase 3 initiate (U.S.)
	(zipalertinib) TAS6417	Non-small cell lung cancer / Oral	●		●	●	●				Nov | Rolling Submission initiate (U.S.)
	(zimberelimab + domvanalimab) AB122 + AB154	Upper gastrointestinal tract cancer / Injection	●								
		Non-small cell lung cancer / Injection	●								
	Abraxane (quemliclustat + paclitaxel [albumin-bound particles for injectable suspension]) AB680 + ABI-007	Pancreatic ductal adenocarcinoma / Injection	●								Feb | Phase 3 initiate (Japan)
Autoimmune and rare disease area	*VOYXACT* (sibeprenlimab) VIS649	IgA nephropathy / Injection	●				●			●	Nov | Approval (U.S.) Aug | Filing (China)
	Dawnzera (donidalorsen) ISIS 721744	Hereditary angioedema / Injection						●			
	(repinatrabit) JNT-517	Phenylketonuria / Oral			●						Nov | Phase 3 initiate (U.S.)
Other categories	*NEXLETOL* (bempedoic acid) ETC-1002	Hypercholesterolemia, familial hypercholesterolemia / Oral									Sep | Approval (Japan)
	SAMTASU (tolvaptan sodium phosphate) OPC-61815	Cardiac edema / Injection									Sep | Approval (China)
	DELTYBA (delamanid) OPC-67683	Multidrug-resistant tuberculosis / Oral			●						
	(quabodepistat) OPC-167832	Multidrug-resistant tuberculosis / Oral			●						Nov | Phase 3 initiate (U.S.)
	Moizerto (difamilast) OPA-15406	Atopic dermatitis / Ointment								●	Aug | Filing (China)
	Mikeluna (carteolol, latanoprost) OPC-1085EL	Glaucoma, ocular hypertension / Eye drops								●	Dec | Filing (China)
	Paradise Ultrasound Renal Denervation (uRDN) system PRDS-001	Resistant hypertension / Medical device									Aug | Approval (Japan)
	(Enteral nutrition) EN-P11	Enteral nutrition / Liquid		●							Oct | Filing (Japan)

1. Phase 2/3
2. Phase 1/2/3
3. Pivotal clinical trial