

R&D to Support Our Business

Our R&D Organization

Fiscal 2022 Results
Pharmaceutical Business R&D Expenses
260.6 billion yen

Fiscal 2022 Results
In-house drug discovery ratio¹
79%

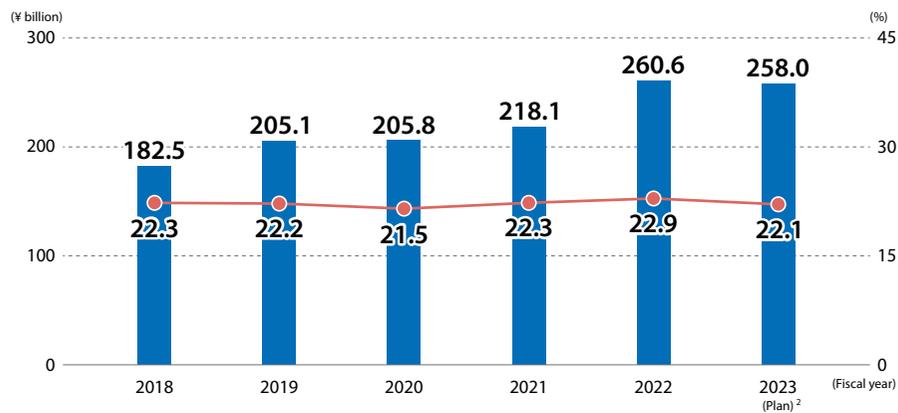
1. Among late-stage development projects (Phase 3 and beyond) percentage of Otsuka drugs discovered in-house

Fiscal 2022 Results
Percentage of Pharmaceutical Business R&D Expenses
22.9%

In order to research and develop innovative products that contribute to curing diseases and support good health, the Otsuka group has established a network of domestic and overseas group research institutes and is engaged in diverse drug discovery research under a global structure.

The Otsuka group's strength lies in its unique and diverse research base, and it will organically integrate its drug discovery research base, mainly small molecules accumulated through years of new drug research, with cutting-edge technologies to create innovation through a value creation process based on "Ryukan-godo," "Jissho," and "Sozosei."

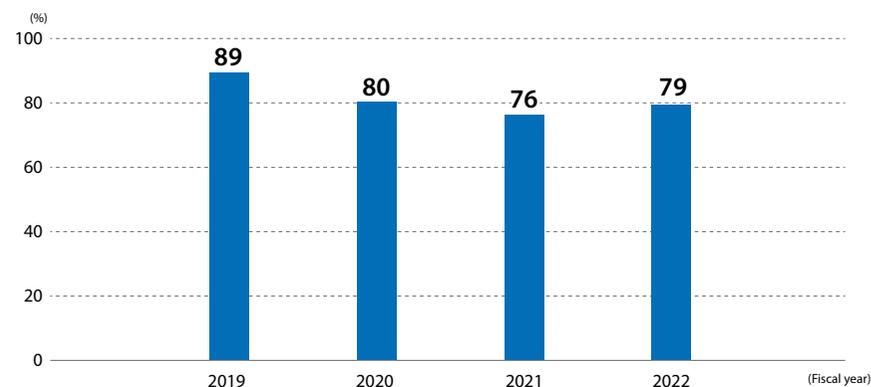
Pharmaceutical Business R&D Expenses and Ratio of R&D Expenses to Revenue



■ R&D expenses ● Ratio of R&D expenses to revenue

2. Announced February 2023

Percentage of In-house drug discovery¹



R&D to Support Our Business Representative Research Institutes for the Pharmaceutical Business

Astex

Astex, which conducts fragment-based drug discovery of small molecule compounds for oncology and psychiatric and neurological disorders, has created anti-cancer drugs such as *Kisqali*¹, *Balversa*² and *INQOVI*. Furthermore, in addition to drug design based on protein structure analysis using cryo-electron microscopy, Astex is working to create innovative drugs through target and mechanism analysis using quantum computers.

1. A product sold by Novartis
2. A products sold by Janssen Biotech



Visterra

Visterra, with its strength in antibody drug discovery, has made steady progress in its clinical development since joining the Otsuka group in 2018, including the start of Phase 3 studies for VIS649 and Phase 1 studies for VIS171 in immune-mediated and renal diseases where treatment satisfaction has been low. The proprietary Hierotope® platform enables the design of antibody drugs for many biological substances by calculating and predicting protein-antibody binding. As part of Otsuka Pharmaceutical's Open Innovation Strategy, the company is collaborating with universities and hospitals in the Boston area.



Otsuka Pharmaceutical Tokushima Research Center for Drug Discovery

The Tokushima Drug Discovery Research Center has provided new therapeutic agents such as *REXULTI* and *SAMSCA/JINARC/JYNARQUE* for the areas of psychiatric and neurological diseases, and cardiovascular and renal diseases that were not being met by existing therapeutic agents. 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. We also conduct safety and pharmacokinetic studies to advance our products to clinical trials (investigational new drugs).

Taiho Pharmaceutical Discovery and Preclinical Research Division (Tsukuba Area)

At the Tsukuba Area research facility, we are taking on the challenge of creating bold new drug candidate compounds, in the same vein as futibatinib and pimitespib, with superior efficacy and safety, mainly in the fields of oncology and immunology. In addition to our proprietary drug discovery platforms, such as the Cysteinomix Drug Discovery Platform and the RAS Drug



Discovery Platform, we are actively working to improve and expand our drug discovery platform technologies, including the introduction of robotics technology to increase and accelerate research productivity and the use of artificial intelligence (AI) in the search for drug targets and compound design.

Otsuka Pharmaceutical Osaka Research Center for Drug Discovery

The Osaka Research Center for Drug Discovery is engaged in research centered on biologics drug discovery, with *OPC-415* (MMG49 CAR-T cells), a gene-cell therapy development product, at the forefront, through collaboration with external organizations in Japan and overseas. In addition, the Center has a facility for



biologics process development research and a dedicated facility equipped with a cryo-electron microscope with the world's highest resolution and high throughput. While continuing with small molecule drug discovery, which has been our strength, we are conducting drug discovery research that incorporates immunology, organoids, and digital technology.

Product Development Pipelines

Major Development Progress in 2022

Product	Indication	Country/Region	Progress
Psychiatry and neurology			
brexpiprazole weekly formulation	Schizophrenia	Japan	Started Phase 3
brexpiprazole	Schizophrenia	China	Filed
aripiprazole 2-month long-acting injection injectable	Schizophrenia	U.S. and Europe	Filed
	Bipolar I disorder	U.S.	Filed
centanafadine	major depressive disorder	U.S.	Started Phase 2
ulotaront	Adjuvant treatment for major depressive disorder	U.S.	Started Phase 2 and 3
	Generalized anxiety disorder	Japan and U.S.	Started Phase 2 and 3
Oncology			
futibatinib	Intrahepatic bile duct cancer	U.S.	Approved
	Cholangiocarcinoma	Europe	Filed
	Bile duct cancer	Japan	Filed
pimipitespib	Gastrointestinal stromal tumor exacerbated after cancer chemotherapy	Japan	Approved
zimberelimab + pimipitespib	Solid tumors	Japan	Started Phase 1
zimberelimab + pamufetinib	Solid tumors	Japan	Started Phase 1
zipalartinib	Non-small cell lung cancer with epidermal growth factor receptor exon 20 insertion mutation	U.S. and Europe	Started Phase 1 and 2
ASTX727	Acute myeloid leukemia	Europe	Filed
fosnetupitant	Nausea and vomiting associated with administration of antineoplastic agents	Japan	Approved
Cardiovascular and renal system			
OPC-61815	Fluid retention in heart failure	Japan	Approved
sibeprenlimab	Immunoglobulin A (IgA) nephropathy	Japan, U.S., and Europe	Started Phase 3
voclosporin	Lupus nephritis	Europe	Approved
Ultrasonic renal denervation system	Uncontrolled hypertension	U.S.	Filed
Other categories			
TAS5315	Chronic idiopathic urticaria	Japan	Started Phase 2
quabodepistat	Tuberculosis	U.S.	Started Phase 2