

# 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 ratio<sup>1</sup>**  
**79%**

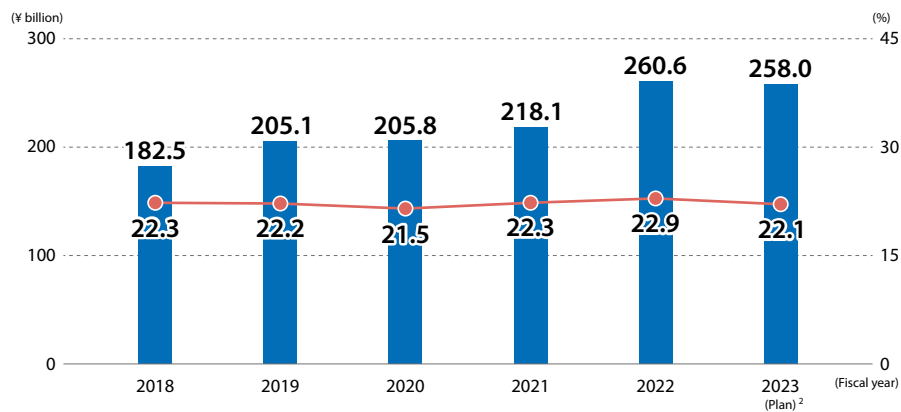
1. Among late-stage development projects (Phase 3 and beyond) percentage of Otsuka drugs discovered in-house

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."

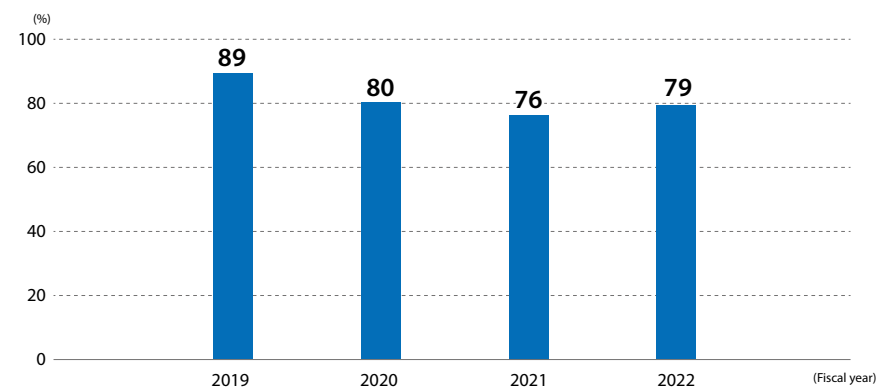
Pharmaceutical Business R&D Expenses and Ratio of R&D Expenses to Revenue



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

2. Announced February 2023

Percentage of In-house drug discovery<sup>1</sup>



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