

# Business Strategy Section

## Positioning of the Third Medium-Term Management Plan

# Advance in the Global Market as a Unique Total Healthcare Company —Five-Year Growth Phase (2019–2023)—

Existing Business Value Maximization and New Value Creation

### Performance Target: Business Profit CAGR of 10% or More

- Organic growth of mainstay products and brands in Pharmaceutical and Nutraceutical Businesses
- Actively invest in R&D to continue creating new drugs that will drive revenue during and beyond the next medium-term management plan

### Business Strategy: Existing Business Value Maximization and New Value Creation

Strategic initiatives for mainstay products and brands to accelerate growth

- Strengthen strategic initiatives for growth drivers—4 Global Products in the Pharmaceutical Business; 3 Major Brands and 3 Nurture Brands in the Nutraceutical Business

Initiatives for next-generation businesses and products

- Launch and nurture new drivers for sustainable growth in Pharmaceutical and Nutraceutical Businesses

Third Medium-Term Management Plan Targets	Business profit CAGR: 10% or more
	Revenue and business profit before R&D expenses: All-time highs
	ROE: 8.0% or higher
	R&D ratio in the Pharmaceutical Business: 20% or higher (versus revenue)

### Social Issues Relating to Strategies, and KPIs

	Social Issue	Strategic Theme	KPIs in the Third Medium-Term Management Plan
Pharmaceutical Business	Unmet medical and health needs	Existing Business Value Maximization	Revenue from 4 Global Products: Increase by ¥200 billion
		Challenge New Frontiers: Do what only Otsuka can do	Revenue from New Products: Increase by ¥90 billion
			Address unmet needs in the psychiatry and neurology area Projects to be filed for regulatory approval
			• REXULTI and AVP-786: Agitation associated with dementia of the Alzheimer's type • REXULTI: PTSD • centanafadine: ADHD • fremanezumab: Migraine
Generate Innovation From Creative and Diverse Research Platforms	Create first-in-class products in the oncology area Projects to be filed for regulatory approval		
	• TAS-116: Gastrointestinal stromal tumor • TBI-1301: Synovial sarcoma • TAS-120: Intrahepatic cholangiocarcinoma		
	Create first-in-class products in the cardiovascular and renal area Projects to be filed for regulatory approval		
Nutraceutical Business	Nutritional needs	Challenge New Categories and New Areas	Revenue from 3 Major Brands: Increase by ¥40 billion
			Revenue from 3 Nurture Brands: Increase by ¥40 billion
			POCARI SWEAT overseas revenue CAGR: 9.4%
			Daiya Foods revenue CAGR: 25%
	Continuous High Profit Structure		Fiscal 2023 business profit margin of Nutraceutical Business: 14.4%

## Linking Investments and Results

Across our entire value chain, we are investing in anticipation of changes and issues five to ten years in the future, and working to steadily generate results from those investments.

### A. 4 Global Products driving the group's growth

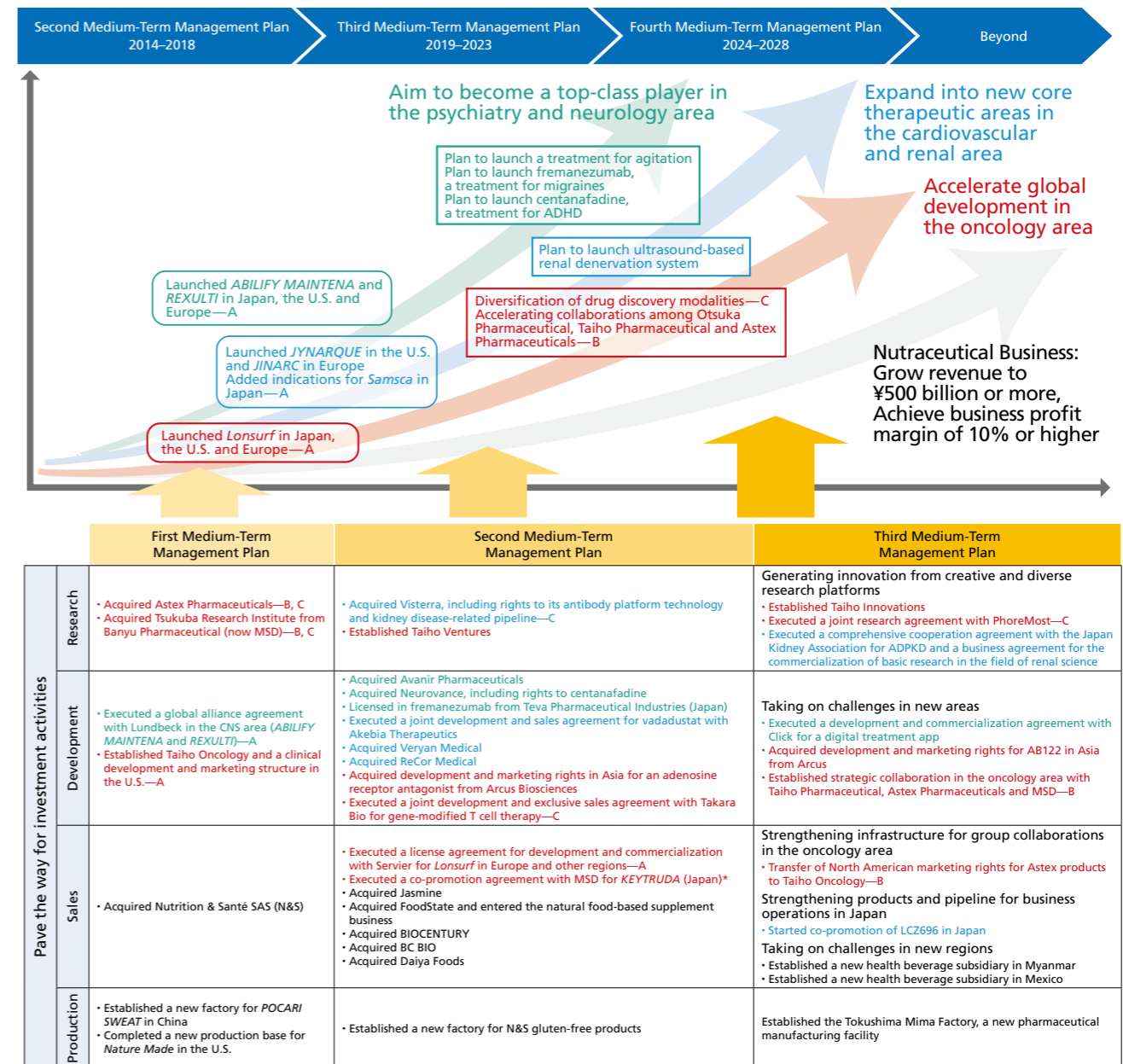
To maximize the value of our 4 Global Products—*ABILIFY MAINTENA*, *REXULTI*, *Samsca/JINARC/JYNARQUE*, and *Lonsurf*—we continued to invest for growth, including signing a joint development and sales agreement with Lundbeck for *ABILIFY MAINTENA* and *REXULTI*, establishing an in-house development and sales system in the U.S. oncology business, and signing a European licensing contract with Servier for *Lonsurf*. As a result, these products are now driving the group's growth.

### B. Accelerating collaborations among Otsuka Pharmaceutical, Taiho Pharmaceutical and Astex Pharmaceuticals

We are sharing proprietary cutting-edge technologies cultivated by each operating company.

### C. Diversification of drug discovery modalities

With a focus on generating innovation from creative and diverse research platforms, we plan to diversify drug discovery modalities and strengthen our in-house drug discovery platforms mainly by collaborating with and acquiring organizations with innovative and highly original drug discovery technologies.



\* Agreement terminated in 2019

## Progress of the Third Medium-Term Management Plan

### Overview of Fiscal 2019

In fiscal 2019, the first year of the Third Medium-Term Management Plan, we steadily executed priority measures aimed at maximizing existing business value. As a result, revenue was 1,396.2 billion yen, an increase of 8.1% from the previous year, indicating solid growth. Furthermore, business profit was 187.2 billion yen, a substantial increase of 54.8% from the previous year, outperforming the Third Medium-Term Management Plan forecast for the year.

	Progress to date			Third Medium-Term Management Plan Announced May 2019		
	2018A	2019A	2020E	2021E	2023E	CAGR 2018-2023
Revenue	1,292.0	1,396.2	1,445.0	1,500.0	1,700.0	5.6%
Business profit before R&D expenses	313.8	403.0	415.0	390.0	460.0	7.9%
R&D expenses	192.9	215.8	220.0	230.0	260.0	6.1%
Business profit	120.9	187.2	195.0	160.0	200.0	10.6%
ROE	4.7%	7.3%	8.0%	6.0% or higher	8.0% or higher	—

## Pharmaceutical Business

The Third Medium-Term Management Plan calls on us to maximize existing business value and create new value, to challenge new frontiers by doing what only Otsuka can do, and to generate innovation from creative and diverse research platforms. We will take advantage of this strategic framework to position our 4 Global Products—*ABILIFY MAINTENA*, *REXULTI*, *Samsca/JINARC/JYNARQUE* and *Lonsurf*—as growth drivers. We will further accelerate growth, targeting 200 billion yen in revenue, an increase of 90 billion yen, on the back of New Products scheduled to be launched during the current Medium-Term Management Plan.

### Progress of 4 Global Products

The 4 Global Products made smooth progress overseas, expanding regions and adding indications. Revenue in fiscal 2019 rose 34.9% from the previous year, outperforming plan targets and making a considerable contribution to growth in consolidated performance.

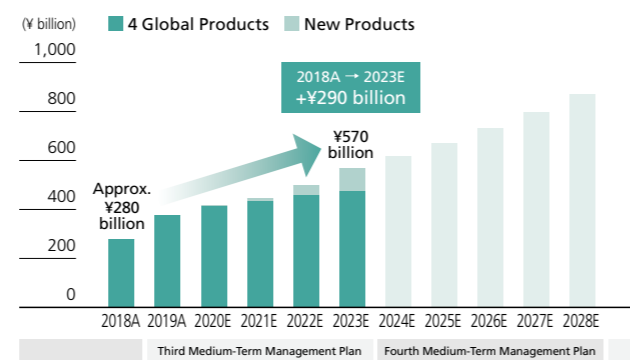
#### *ABILIFY MAINTENA*

##### aripiprazole | Atypical antipsychotic long-acting injectable

As a global treatment for schizophrenia, there is increased awareness of this drug's efficacy claims and convenient dosage formulation. Following U.S. approval in 2017 for an additional indication for the treatment of bipolar I disorder, prescriptions are increasing. In September 2019, we also filed for an additional indication for bipolar disorder in Japan.

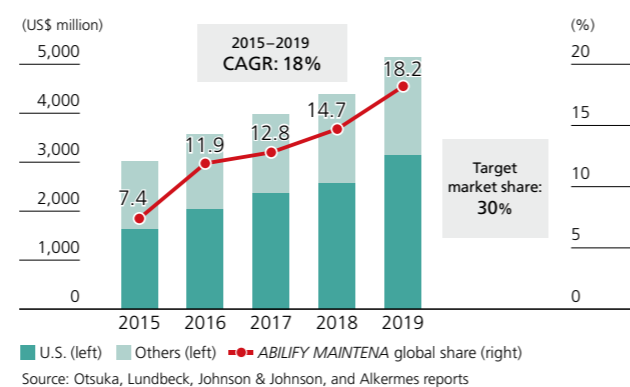
The global market for atypical antipsychotic long-acting injectables continues to grow as they can address the issue of medication adherence in schizophrenia and bipolar disorder. We will continue to contribute to patients around the world and aim to achieve a 30% global market share for *ABILIFY MAINTENA*.

### Revenue Plan for the 4 Global Products and New Products



	Fiscal 2019 revenue	Year-on-year	Achievement rate	Fiscal 2020 revenue plan
<i>ABILIFY MAINTENA</i>	101.8	+15.7%	102%	110.5
<i>REXULTI</i>	89.8	+29.3%	101%	106.0
<i>Samsca/JINARC/JYNARQUE</i>	149.1	+65.1%	102%	160.5
<i>Lonsurf</i>	34.5	+13.6%	101%	38.0
Total	375.1	+34.9%	102%	415.0

### Atypical Antipsychotic Long-Acting Injectables Market



#### *REXULTI*

##### brexpiprazole | Atypical antipsychotic

Marketed as an adjuvant treatment for major depressive disorder and as a treatment for schizophrenia in the U.S., this drug is highly evaluated for its efficacy and safety as a new treatment option for both diseases. In Japan, where the drug is marketed as a treatment for schizophrenia, prescriptions have grown significantly following the lifting of restrictions on maximum prescription period in May 2019. In Europe, sales began from April 2019.

At present, several clinical trials are under way with the aim of further contributing to treating unmet needs in the psychiatry and neurology area.

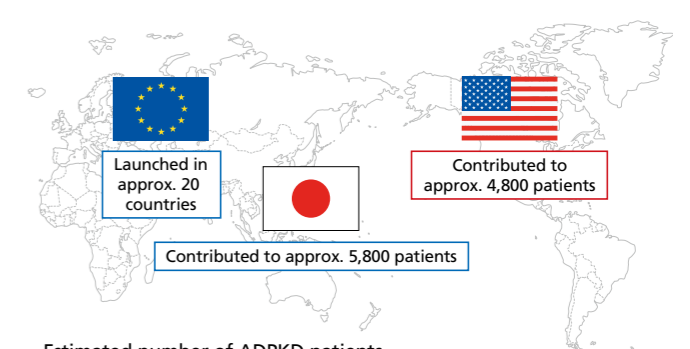
#### *Samsca/JINARC/JYNARQUE*

##### tolvaptan | V<sub>2</sub>-receptor antagonist

*Samsca* is highly evaluated in various guidelines in Japan, and prescriptions are increasing for the treatment of cardiac edema and hepatic edema. Prescriptions for the treatment of the intractable disease ADPKD are increasing due to the promotion of proper use guidelines and disease awareness activities.

In May 2018, *JYNARQUE* was launched in the U.S. as a treatment for ADPKD. Efforts to raise disease awareness and make clinical trial data available have helped spread recognition of both the disease and the drug, resulting in a steady increase in prescriptions. In Europe also, *JINARC* is sold in approx. 20 countries and the number of patients receiving treatment through the drug is on the increase.

### Global Use as an ADPKD Treatment



Estimated number of ADPKD patients  
 U.S.: 140,000, Europe: 205,000, Japan: 31,000  
 (As of March 31, 2020, in-house survey)

#### *Lonsurf*

##### trifluridine/tipiracil | Anti-cancer agent

*Lonsurf* is growing as a treatment option for advanced colorectal cancer with the help of enhanced promotion activities. *Lonsurf* has also received marketing authorization for the additional indication of previously treated metastatic gastric cancer in the U.S. (February 2019), Japan (August 2019), and Europe (September 2019). Further clinical studies are currently ongoing or being planned with business partners and academia to maximize the value of *Lonsurf*.

	Treatment line	Regimen	Country/Region	Development status
Colorectal cancer	First-line	Study in combination with bevacizumab for patients who are not candidates for intensive therapy (SOLSTICE study)*	Europe	Phase III
	Second-line	Study in combination with bevacizumab (Specified Clinical Study)	Japan	Phase II/III
Gastric cancer	Second-line/ Third-line	Study in combination with ramucirumab	Japan	Phase II

\* Trial sponsored by Servier

(As of March 31, 2020)



**Kabir Nath**  
 President and  
 CEO, Otsuka  
 North America  
 Pharmaceutical  
 Business

### Initiatives to Maximize the Value of Global Products

In 2019, our North American prescription Pharmaceutical Business contributed to an impressive start of the Third Medium-Term Management Plan.

We continued to see strong revenue growth across our CNS and nephrology franchises. Established products like *REXULTI*, *ABILIFY MAINTENA*, and our newest, *JYNARQUE*, continued to perform well and exceeded sales forecasts.

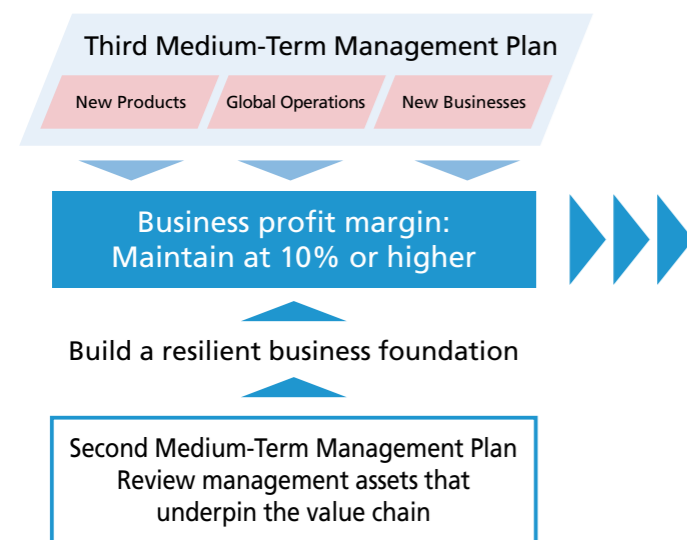
This not only speaks to the efficacy and clinical value that these products are bringing to patients and healthcare professionals, but it is also a direct result of the hard work and dedication of Otsuka people across the organization.

The whole leadership team of the North American Pharmaceutical Business is committed to maximizing the value of our entire portfolio of global products. Concurrently, we seek out new business opportunities to drive future growth and ensure that we continue to operate from a position of strength and innovation.

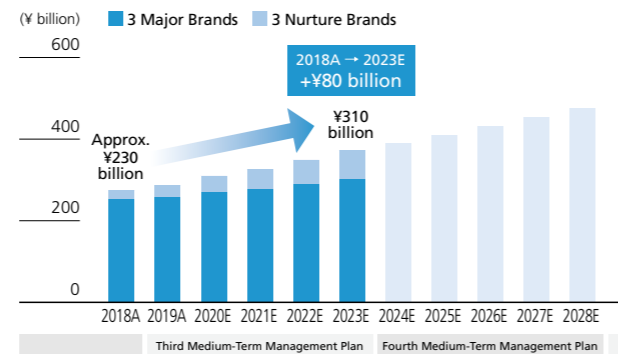
## Nutraceutical Business

The Third Medium-Term Management Plan calls for revenue growth of 40 billion yen in the 3 Major Brands—*POCARI SWEAT*, *Nature Made*, and *N&S*—and 40 billion yen in the 3 Nurture Brands—*BODYMAINTÉ*, *EQUELLE* and *Daiya*.

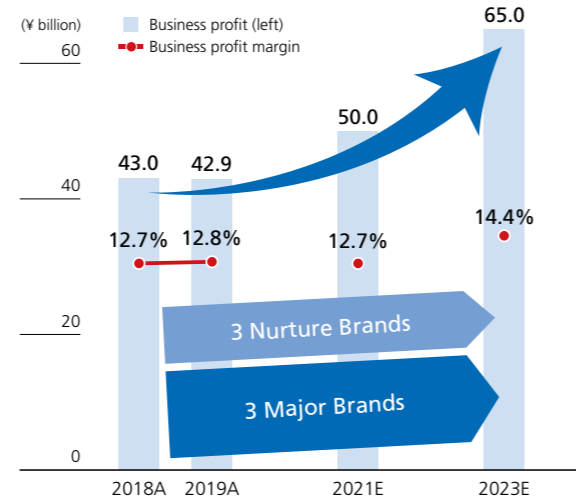
Furthermore, we are working to maintain a high-profit structure capable of a sustained business profit margin of 10% or higher by creating new product concepts in anticipation of changes in business and other landscapes and by expanding into new categories and new regions.



### Revenue Plan for 3 Major Brands and 3 Nurture Brands



### Business Profit Plan

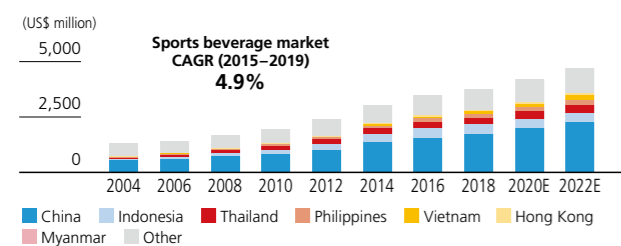


## Progress of 3 Major Brands

### POCARI SWEAT

Overseas, mainly in Asia, sales volume for *POCARI SWEAT*, a beverage for replenishing fluids and electrolytes, is increasing due to awareness activities tailored to the characteristics and needs of each region. The CAGR of the Asia-Pacific sports beverage market was 4.9% for the period 2015 to 2019. We intend to outpace recent market growth, forecasting a CAGR of 9.4% in overseas revenue for *POCARI SWEAT* during the period of the Third Medium-Term Management Plan.

### Sports Beverage Market (Asia-Pacific\*)



Euromonitor International of the U.K. \* Excluding Japan

Furthermore, given higher levels of health consciousness, we are strengthening our global sales structure to expand into new regions where we expect growth in demand for health beverages.

In the future, we aim to grow *POCARI SWEAT* into a 100-billion-yen brand by further enhancing brand strength through original marketing that thoroughly communicates the product concept.

## Nature Made

Pharmavite is a leading company in the U.S. supplement industry. Under the *Nature Made* supplement brand, Pharmavite develops and markets products free from flavorings, colorings and preservatives. With a lineup of high-quality supplements, key items of which have been verified as meeting the strict quality criteria set by the United States Pharmacopeia (USP), *Nature Made* is the leading choice of U.S. pharmacists in nine product categories.



1. Based on total U.S. retail sales aggregate data reported through the Scantrack® service in the supplement vitamin category for the 52-week period ended December 29, 2019. ©2020 Information Resources Inc.
2. INTAGE SRI Health Food Multivitamin Market, cumulative market share by brand for January–December 2019
3. US News & World Report and *Pharmacy Times* 2019 survey: Product categories: Letter Vitamins (A–E), Coenzyme Q10, Omega-3/Fish Oil, Flax Seed Oil, Herbal Supplements, Mood Health Supplements, Diabetic Multivitamins, Cholesterol Management—Natural, Garlic Supplements



Self-medication is increasingly prevalent in the U.S., and in recent years, related demand has continued to increase, driven by factors that include medical cost inflation. The U.S. supplement market continues to grow at a CAGR of 3.7%. We aim to turn *Nature Made* into a 100-billion-yen brand by developing products that incorporate cutting-edge science and by taking on challenges in new categories.

## Nutrition & Santé (N&S)

The organic food market in Europe has grown in recent years as more health-conscious consumers demand safer and more trustworthy foods. Trends such as “free-from” foods and alternative products are attracting the attention of the millennial generation. In fiscal 2019, the European meat-free food market was worth approximately 1.8 billion U.S. dollars, having grown rapidly over the past five years at a CAGR of 11.9%, while the gluten-free food market was worth around 2.5 billion U.S. dollars after expanding at a CAGR of 12.3%.<sup>4</sup>

N&S, a health and nutritional food company, provides health foods and other products in more than 40 countries around the world, centered on Europe. At each of its factories, N&S has obtained ISO 14000 and ISO 12000, as well as IFS Food Standard certification, the international

4. Euromonitor International of the U.K. (Retail Value RSP)

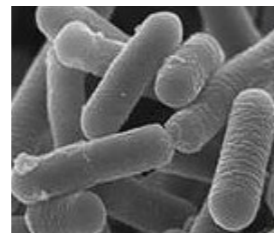
standard for auditing food manufactures, and conducts production with concern for the environment and a high level of quality management. In 2017, N&S built a new factory for gluten-free products in France and strengthened the development of free-from products to meet evolving consumer needs.



## Progress of 3 Nurture Brands

### BODYMAINTÉ

*BODYMAINTÉ* was commercialized based on research conducted by Otsuka Pharmaceutical on the themes of “intestines and nutrition” and “exercise and nutrition.” Focusing on health management for athletes exposed to risks related to intense training, we developed *BODYMAINTÉ Jelly*, a conditioning food that has won the support of many athletes and sports trainers. Its main ingredients include lactic acid bacteria B240, a proprietary ingredient, as well as BCAA, arginine and whey protein. In addition, we developed *BODYMAINTÉ Drink*, a conditioning beverage containing lactic acid bacteria B240, to help replenish fluids and electrolytes that support proper hydration. *BODYMAINTÉ Drink* expands the value of this product line by supporting the health management of more consumers.



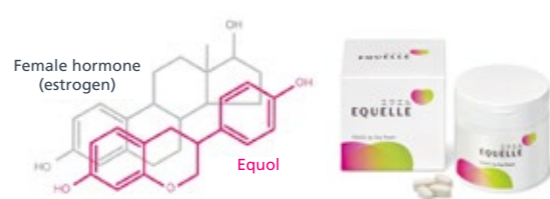
#### Plant-Derived Lactic Acid Bacteria B240

Lactic acid bacteria B240 is a plant-derived lactic acid bacteria isolated through the fermentation of a type of tea leaf, traditionally consumed in northern Thailand. It was isolated by Sanae Okada, Professor Emeritus of Tokyo University of Agriculture\* and its efficacy was confirmed by Otsuka Pharmaceutical.

\* J Gen Appl Microbiol. 1986; 32:57-65

### EQUELLE

*EQUELLE* originated from research conducted at Otsuka Pharmaceuticals' Saga Nutraceuticals Research Institute, where women's health is a research theme. *EQUELLE*, which contains equol, is sold in Japan and the U.S. as a food product that supports women's health and beauty at a time when aging brings physical and mental changes. In Japan, we have deployed dedicated staff with expert knowledge of women's health nationwide. With the cooperation of physicians, pharmacists and other healthcare professionals we convey the importance of personal care to women who are experiencing physical and mental changes, among other activities aimed at maintaining and improving the health of women and enhancing quality of life.



#### Equol

Equol is an ingredient produced when daidzein, a soybean isoflavone, is metabolized by intestinal bacteria. One aspect of Otsuka Pharmaceutical's many years of soybean research was a focus on the properties of equol. The Saga Nutraceuticals Research Institute succeeded in isolating the lactococcus 20-92 strain, a lactic acid bacteria that produces equol. We publicize the progress results of a variety of research and continue to be a leader in global research in this field.

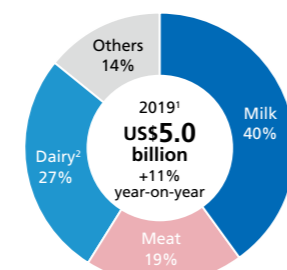
The U.S. plant-based alternatives market continues to grow. Daiya Foods is expanding its sales channels and product lineup, mainly in the area of cheese alternatives, which are a core product. Under the Third Medium-Term Management Plan, we plan to achieve a revenue CAGR of 25%.

### Daiya

Daiya Foods develops, manufactures, and sells high-quality, creative plant-based food products such as cheese alternatives, yogurt alternatives, dressings, and desserts. Its brand, *Daiya*, is enjoyed not only by vegetarians and people with food allergies, but also by the health-conscious millennial generation.



#### U.S. Plant-Based Alternative Food Market



1. PBFA-commissioned data from Nielsen (52 weeks U.S. dollar sales ending December 2019)  
2. Ice cream, yogurt, cheese, creamer, butter and dressing

Daiya Foods Revenue Plan  
**CAGR**  
(2018–2023)  
**25%**

## Social Issues Targeted by the Nutraceutical Business

Today, pressing social issues include extended healthy life expectancy, declining birthrates, aging populations, and soaring medical costs. The Otsuka group engages in product development and awareness activities aimed at solving a variety of social and health issues.

### Social Issues Targeted by Otsuka

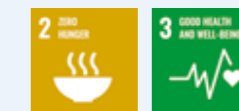
#### 1. Irregular and Unbalanced Diets

While there is seemingly an abundance of food in the developed world, diversification in daily routines and an increase in single-person households contribute to eating alone, skipped meals, and unbalanced diets. This can lead to poor physical and mental well-being. The Otsuka group is tackling various social issues related to nutrition by developing nutritional products and implementing dietary education activities.

Leveraging expertise in concentrated liquid diets from our clinical nutrition business, we created *Calorie Mate*, which provides nutrition for general consumers. It supports healthy dietary life in busy modern lifestyles, and is a pioneer in nutritionally balanced foods in Japan. As the top-selling brand,\* it continues to lead the field. Compact and with a long shelf life, *Calorie Mate* is convenient as

a nutritional food for use during sports, when there is no time for breakfast or other meals, and during work or study, and can also be kept as a disaster provision.

\* Intage SRI, Nutritionally Balanced Food Product Market (category: cookies, biscuits, cereals and cakes), January–December 2019



#### 2. Women's Health

Women experience mental and physical changes throughout their lives. The effects of rapid hormonal changes are felt by women in their 40s and 50s in particular, which can impact their social life.

The Otsuka group has identified women's health as one of the priority areas of its Nutraceutical Business. We are disseminating information to promote better understanding of physical changes in women and developing related products.

Otsuka Pharmaceutical's Saga Nutraceuticals Research Institute conducts research on total health maintenance for women in their 40s and older, including research into symptoms of menopause, bone and skin issues, and blood vessel health, and continues to generate evidence on active ingredients. In addition, our experts in women's health carry out activities across Japan to spread accurate understanding of the mental and physical changes experienced by women and related health issues, as well as solutions to those issues.



#### 3. Environmental Issues

Given that global warming is a major social issue, public attention is focused on CO<sub>2</sub> emissions from food production as part of realizing a carbon-free society. The plant-based foods that Daiya Foods develops, manufactures and sells have a low carbon footprint, reduce environmental load, and are more sustainable. Daiya Foods was founded on the belief that plant-based living is better for people's health and better for the planet. Its range of plant-based foods resonates with many people and as a category leader it is evolving into a high-growth company.

Soybeans are a part of Japan's traditional food culture and contain quality dietary proteins, and have been referred to as “the meat of the fields.” Focusing on the high nutritional value and potential of soybeans, Otsuka Pharmaceutical has developed and commercialized soy-derived nutritional foods under three brands at its in-house research center—

*SOYJOY*, *SOYSH* and *SoyCarat*. Soybeans directly consumed by people around the world account for a mere 6% of total soybean production. Beef is one source of protein, but to produce 1 kilogram of beef, it is said to take 10 kilograms of grain, such as soybeans. There is data suggesting that the production of soybeans requires one-fiftieth the water and one-twentieth the amount of energy needed to produce the same volume of beef. Based on the concept of “Soylution” (soy + solution), Otsuka Pharmaceutical provides solutions for both human health and environmental issues through a range of soy products.



## Looking ahead to the Fourth Medium-Term Management Plan

### Opportunities and Risks

As a total healthcare company, the Otsuka group conducts activities not only related to diagnosis and medication, but also to contribute to maintaining and improving the health of healthy people. Medical cost inflation due to aging populations and the increasing sophistication of medical treatment are a serious issue for Japan and the rest of the world, and in particular pose a risk to the Pharmaceutical Business. However, from the perspective of the Nutraceutical Business, we regard increased awareness of self-medication, prevention and daily health as an opportunity.

## Pharmaceutical Business

<ul style="list-style-type: none"> <li>Providing total healthcare solutions, from diagnosis to treatment.</li> <li>Global R&amp;D and marketing assets in the psychiatry and neurology area, and the cardiovascular and renal area</li> <li>Presence in the oncology area in Japan</li> <li>Stable profit in the intravenous solutions business</li> </ul> <p style="text-align: center; font-size: 2em; color: #4CAF50;">Strength</p>	<ul style="list-style-type: none"> <li>Global operations in the oncology business</li> <li>Management personnel for diversifying businesses</li> <li>Patent expiration of mainstay products</li> </ul> <p style="text-align: center; font-size: 2em; color: #4CAF50;">Weakness</p>
<ul style="list-style-type: none"> <li>Advances in science and technology, progress of basic research related to diseases</li> <li>Promotion of personalized medicine</li> </ul> <p style="text-align: center; font-size: 2em; color: #4CAF50;">Opportunity</p>	<ul style="list-style-type: none"> <li>Global drug price control policies and promotion of generic drug use due to medical cost inflation</li> <li>Intensifying competition in core areas</li> <li>Restrictions on sales promotion activities due to stricter regulations</li> </ul> <p style="text-align: center; font-size: 2em; color: #4CAF50;">Threat</p>

## Nutraceutical Business

<ul style="list-style-type: none"> <li>Creative products and marketing backed by scientific evidence</li> <li>Ability to nurture brands</li> <li>Overseas businesses that incorporate solutions to social issues with their core business processes</li> <li>Steady earnings power</li> </ul> <p style="text-align: center; font-size: 2em; color: #4CAF50;">Strength</p>	<ul style="list-style-type: none"> <li>Management personnel for diversifying businesses</li> <li>Cultural differences regarding raw materials and taste preferences</li> </ul> <p style="text-align: center; font-size: 2em; color: #4CAF50;">Weakness</p>
<ul style="list-style-type: none"> <li>Rising consumer awareness of self-medication, prevention and daily health in tandem with medical cost inflation</li> <li>Diversification of diet</li> </ul> <p style="text-align: center; font-size: 2em; color: #4CAF50;">Opportunity</p>	<ul style="list-style-type: none"> <li>Sluggish overall beverage market due to unseasonal weather</li> <li>Intensification of competition in core areas due to entry of new competitors</li> </ul> <p style="text-align: center; font-size: 2em; color: #4CAF50;">Threat</p>

### Our Approach to Issues

Global operations in the oncology business	In recent years, Taiho Pharmaceutical, a pioneer in oral oncology products in Japan, has been actively promoting further globalization, mainly by establishing its own marketing structure in the U.S. and expanding its sales networks in other regions. In addition, group companies, including Otsuka Pharmaceutical, Astex Pharmaceuticals and Taiho Pharmaceutical, are combining their assets to strengthen group-wide global operations, as well as promoting strategic alliances with external partners.	➔ Page 34 Maximizing business value by combining group strengths
Management personnel for diversifying businesses	Otsuka Holdings plans and implements executive human resource development programs, and collaborates with external organizations to train managers capable of leading the next generation. In addition, individual group companies are vigorously promoting human resource development.	➔ Page 43 People
Intensifying competition in core areas	Based on our unique and diverse businesses, we will continue to create new value by taking on challenges, applying an original approach that addresses the health needs of people, always looking to the future.	➔ Page 6 What we can achieve because we are Otsuka ➔ Page 7 Taking on the challenge of doing what only Otsuka can do

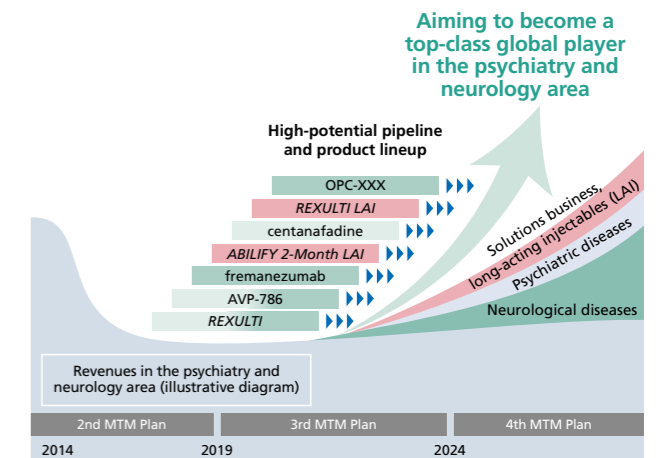
## Initiatives in the Pharmaceutical Business

### Psychiatry and Neurology

Aiming to become a top-class global player in the psychiatry and neurology area, with a high-potential pipeline and product portfolio

Psychiatric diseases such as schizophrenia, bipolar disorder, and major depressive disorder can develop at any age and affect a person's social life, career, and studies. Moreover, concerns are growing about the increasing frequency of Alzheimer's-related dementia as populations worldwide continue to age. These diseases affect not just the patient's quality of life; they also place a strain on family members and caregivers, as well as on the healthcare economy. There are still many psychiatric and neurological diseases for which satisfactory treatments have yet to be established. This is because their causes and mechanisms are not fully understood, which makes the discovery of new drugs extremely difficult. The Otsuka group entered the psychiatry and neurology area in the 1970s and has continued to take on the challenge of new drug discovery with the goal of contributing to medical needs.

We have a high-potential pipeline and product lineup, and aim to become a top-class global player in this area.



#### Agitation Associated with Dementia of the Alzheimer's Type

It is estimated that approximately 3.4 million people\* in the U.S. have Alzheimer's disease, and it is thought that a large number of those patients exhibit some form of behavioral disorder (agitation), such as excessive motor activity, and verbal or physical aggression. This kind of disorder places a burden on patients and caregivers, impacting quality of life. The Otsuka group aims to market the world's first treatment for agitation associated with dementia of the Alzheimer's type. Clinical trials are under way on two drugs with different mechanisms of action, brexpiprazole (REXULTI) and AVP-786.

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(As of March 31, 2020)

Pipeline	Features	Indication	Country/Region	Development status
aripiprazole (long-acting injectable)	Dopamine partial agonist	Bipolar disorder	Japan	Filed ●
		Major depressive disorder	Japan/Europe/China	Phase III
brexpiprazole	Dopamine partial agonist	Agitation associated with dementia of the Alzheimer's type	Japan/U.S./Europe	Phase III
		Post-traumatic stress disorder	U.S.	Phase III ●
		Borderline personality disorder	U.S.	Phase II ●
		Schizophrenia; long-acting injectable	U.S.	Phase I
OPC-64005	Serotonin, norepinephrine and dopamine reuptake inhibitor	Attention deficit hyperactivity disorder	U.S.	Phase II
AVP-786	NMDA receptor antagonist; serotonin and norepinephrine reuptake inhibitor; sigma-1 receptor agonist	Agitation associated with dementia of the Alzheimer's type	U.S./Europe	Phase III
		Negative symptoms of schizophrenia	U.S.	Phase II/III ●
		Traumatic brain injury	U.S.	Phase II
centanafadine	Norepinephrine, dopamine and serotonin reuptake inhibitor	Intermittent explosive disorder	U.S.	Phase II
		Attention deficit hyperactivity disorder	U.S.	Phase III ●
TAS-205	PGD synthase inhibitor	Duchenne muscular dystrophy	Japan	Phase II
fremanezumab	Anti-CGRP antibody	Migraine	Japan	Phase II/III ●
OPC-214870	—	Epilepsy	U.S.	Phase I ●

■ Development project in an unmet needs area (defined by Otsuka based on data from PatientsMap) ● Project that has advanced in or after fiscal 2019

## Oncology

Maximizing business value by combining group strengths

Taiho Pharmaceutical engages in drug discovery, leveraging its long-standing proprietary platform focused on biochemical modulation, as well as drug discovery based on its research platform, such as the newly established Cysteinomix and kinase target drug discovery. Furthermore, through its collaboration with relation to Astex Pharmaceuticals' fragment-based drug discovery technology, Taiho Pharmaceutical continues to discover new molecular targeting drugs.

Meanwhile, centering on external collaborations, Otsuka Pharmaceutical is taking on the challenge of establishing therapies with a focus on the future. This includes creating synergies with new modalities, in areas such as gene-modified T cell therapies and oncolytic virus therapies.

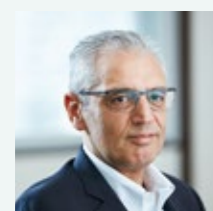
Individual group companies are combining their drug discovery technologies and assets to bolster global operations and enhance business value.



**Teruhiro Utsugi**  
Managing Director,  
Taiho Pharmaceutical

### Strengths in Drug Discovery at Taiho Pharmaceutical

As a specialty pharmaceutical company in the oncology area, Taiho Pharmaceutical is utilizing its proprietary drug discovery platforms and developing highly-effective, novel anti-cancer agents that contribute to the diversification of cancer treatment. In addition to further developing and enhancing our platform technologies for drug discovery, we are accelerating our R&D by complementing our proprietary technologies through collaborations with research organizations both in and outside Japan. Furthermore, through our corporate venture capital, we have built a proprietary network that gives us access to creative and innovative technologies and drug discovery seeds outside the company. Through research and development of promising new drugs, Taiho Pharmaceutical will contribute to a society enriched by smiles, and pursue the realization of a sustainable society.



**Harren Jhoti**  
CEO,  
Astex Pharmaceuticals

### Strengths in Drug Discovery at Astex Pharmaceuticals

As an established world leader in fragment-based drug discovery, Astex celebrated its 20th anniversary in 2019. In that time we have created a broad portfolio of programs in oncology and CNS and a successful track record of strategic alliances with pharmaceutical collaborators resulting in two approved anti-cancer agents within the last three years. Our innovative culture and collaborative spirit have continued to flourish as part of the Otsuka group as we have established new collaborations and further developed our technology that we hope will result in many new product approvals in the future.

(As of March 31, 2020)

Pipeline	Features	Indication	Country/Region	Development status
TAS-118	Anti-metabolite	Gastric cancer	Japan	Phase III
		Ovarian cancer	U.S./Europe	Phase II
guadecitabine	DNA methyltransferase inhibitor	Acute myeloid leukemia	Japan/U.S./Europe	Phase III
		Myelodysplastic syndromes	Japan/U.S./Europe	Phase III
ASTX727	DNA methyltransferase inhibitor	Myelodysplastic syndromes	U.S.	Filed ●
		Acute myeloid leukemia	Japan	Phase I ●
			Europe	Phase III ●
ASTX660	IAP inhibitor	Solid tumors, lymphomas	U.S.	Phase II
ASTX029	ERK1/2 inhibitor	Solid tumors	U.S.	Phase I/II
ASTX295	MDM2 inhibitor	Solid tumors	U.S.	Phase I/II ●
OPB-111077	—	Diffuse large B-cell lymphoma	Japan	Phase I ●
		Hematological cancer	U.S.	Phase I
TAS-114	dUTPase inhibitor	Non-small cell lung cancer	Japan/U.S./Europe	Phase II
TAS-115	Multi-kinase inhibitor	Prostate cancer	Japan	Phase II
TAS-116	HSP90 inhibitor	Gastrointestinal stromal tumor	Japan	Phase III
		Solid tumors	U.S./Europe	Phase I
TAS-117	—	Solid tumors	Japan	Phase I
TAS-119	—	Solid tumors	U.S./Europe	Phase I
futibatinib	FGFR inhibitor	Intrahepatic cholangiocarcinoma	Japan/U.S./Europe	Phase II
TAS0313	Peptide vaccine	Urothelial cancer	Japan	Phase II ●
TAS3681	—	Prostate cancer	U.S./Europe	Phase I
TAS0728	—	Solid tumors	U.S./Europe	Phase I/II
trabectedin	—	Ovarian cancer	Japan	Phase I
canerpaturev	Oncolytic virus	Pancreatic cancer	Japan	Phase I
TBI-1301	NY-ESO-1 siTCR™ gene therapies	Synovial sarcoma	Japan	Phase I/II
TBI-1501	CD19 CAR gene therapies	Acute lymphoblastic leukemia	Japan	Phase I/II
fosnetupitant	NK1 receptor antagonist	Chemotherapy-induced nausea and vomiting	Japan	Phase III ●

■ Development project in an unmet needs area (defined by Otsuka based on data from *PatientsMap*) ● Project that has advanced in or after fiscal 2019

## Cardiovascular and Renal System

Creating first-in-class products through new drug discovery technologies, and medical devices

In the cardiovascular and renal area, in addition to strengthening our proprietary drug discovery platforms, we also plan to actively make growth investments, examples of which have included our business alliance with Akebia Therapeutics for vadadustat, and the acquisition of Visterra, a company with a renal disease-related pipeline. We also strive to find solutions to unmet needs in non-

pharmaceutical areas too. We are advancing development of unique medical devices, drawing on our innovative technology and our strengths in drugs and clinical research. Examples include a device for ultrasound renal denervation treatment and a peripheral artery stent system. We aim to create first-in-class products leveraging these new drug discovery technologies and medical devices.

(As of March 31, 2020)

Pipeline	Features	Indication	Country/Region	Development status
tolvaptan	V <sub>2</sub> -receptor antagonist	Syndrome of inappropriate antidiuretic hormone secretion	Japan	Filed ●
OPC-61815	V <sub>2</sub> -receptor antagonist	Cardiac edema	Japan	Phase III ●
vadadustat	HIF-prolyl hydroxylase inhibitor	Renal anemia	U.S./Europe	Phase III

● Project that has advanced in or after fiscal 2019

## Initiatives in the Nutraceutical Business

Our two research institutes of the Nutraceutical Business investigate themes such as nutrition and exercise from original viewpoints that utilize expertise honed in our

Pharmaceutical Business. Their goal is to develop and provide the world with creative products that maintain and improve people's health and are backed by scientific evidence.

### Saga Nutraceuticals Research Institute

Since its establishment in 1984 as Japan's first private research institute for clinical exercise and nutrition, the Saga Nutraceuticals Research Institute has conducted R&D in various fields related to exercise and nutrition, women's health, and other health issues. In 2014, one of the largest controlled-environment rooms in Japan was completed at the institute, enabling the recreation of hypoxic environments equivalent to those found at up to an altitude of 5,000 meters, which were previously difficult to recreate, as well as high-temperature/high-humidity and low-temperature/low-humidity conditions. This facility helps advance research into sports nutrition, such as by verifying the effects of fluid and nutritional intake in such environments.



### Otsu Nutraceuticals Research Institute

The Otsu Nutraceuticals Research Institute was established in 2000 to advance research on intestinal immunity, with a particular focus on the intestines, which play a key role in overall health. One example of the institute's research is related to enhancing the body's biological barrier by increasing the secretion of immunoglobulin A (IgA), an antibody that plays a crucial role in mucosal immunity. Exploratory R&D demonstrated that lactic acid bacteria B240 heightens the function of mucosal immunity and lowers the probability of catching the common cold.



# Beyond 2030

Envisaging a variety of changes, including an increase in aging populations, rapid climate change, and advances in precision medicine\* associated with the spread of preventive medicine and genetic testing, the Otsuka group aims to be an indispensable provider of products and services that meet the healthcare needs of the times.

\* Therapeutic approaches that achieve greater precision by applying detailed genetic and other information about each patient

## Pharmaceutical Business

Driven by the corporate philosophy “Otsuka-people creating new products for better health worldwide,” the Otsuka group aims to achieve highly innovative drug discovery to find solutions for unmet medical needs. With this goal in mind, we engage in drug discovery research through multiple approaches. We will strengthen our proprietary drug discovery platform to be capable of generating new strengths and innovation. This will include utilizing the

fragment-based drug discovery technology of Astex Pharmaceuticals, the unique antibody manufacturing platform technology from Visterra, and the cysteinomix drug discovery platform of Taiho Pharmaceutical, as well as building a network with and providing research support to academia and bio-ventures that possess advanced research technologies and drug discovery seeds.

### Initiatives for Innovation in Research and Development Areas



TAIHO PHARMA

- Generate innovation through collaboration and integration of proprietary R&D platforms and technologies in core areas
- Generate results from innovation seeds through various collaborations



Promote group-wide research collaborations



Collaborations with external institutions



\* Consortium members: Alzheimer's Research UK, AbbVie, Astex, CRL, Eli Lilly, Eisai, Evotec, MSD, JPNV, and Takeda

## Nutraceutical Business

Awareness of health issues is rising, including issues related to aging populations, medical costs, and the spread of infectious diseases. Our goal in the Nutraceutical Business is to support the maintenance and improvement of people's health worldwide, and thereby contribute to longer healthy life expectancy. To this end, we will utilize the expertise we have cultivated in the Pharmaceutical Business while proposing solutions based on new concepts that address yet-to-emerge needs and social issues. With an eye on changes in the global landscape, we will take on the

challenge of creating new value and expanding into new categories and regions by combining cutting-edge scientific and technological developments with our unique business model. Going forward, we will respond to various health-related social issues by continuing to implement health awareness activities that bring those issues to the forefront and offering solutions from each brand. Furthermore, we will promote these activities by strengthening collaborations with external institutions.