In addition to advancing drug discovery in our three focus areas (Psychiatry & Neurology, Oncology, and Regenerative Medicine/Cell Therapy), we aim to contribute to global health through the Infectious Diseases area and the provision of new health solutions through the launch of Frontier Business.

We will enhance our innovation base with new approaches to drug discovery and strive to strengthen our development capabilities to produce concrete achievements.

We are promoting competitive drug discovery research based on unique platforms for drug discovery, developed through the incorporation of cutting-edge technology. Moreover, we are aiming to improve the success rate of research and development by selecting suitable drug discovery targets and biomarkers from big data. This includes genome information and imaging, and leveraging the knowledge obtained from clinical trials for our own products in translational research. We aim to optimize treatments for psychiatric disorders through drug discovery research based on neural circuit pathology. For neurological disorders, we aim to develop innovative disease-modifying treatments through drug discovery based on molecular pathophysiology.

We design a strategic development plan based on a globally integrated development organization, across Japan and U.S. businesses, with the aim of implementing efficient clinical development and obtaining approval as early as possible.

**Psychiatric disorders** (Schizophrenia, depression, psychiatric symptoms related to neurological disorders)
We aim to increase the probability of success and optimize treatments through drug discovery based on neural circuit pathology. We also strive to increase the probability of success in clinical development through patient stratification using new evaluation indicators.

**Neurological disorders** (Dementia, Parkinson’s disease, rare diseases)
We seek to develop innovative disease-modifying drugs through drug discovery based on molecular pathophysiology. We aim to increase the probability of success in research and development by investigating the causes of disease using analysis of big data to select drug discovery targets. We also are conducting drug discovery programs to support the research and development of preventive medicines.
Priorities in Psychiatry & Neurology area

We will promote the late-stage clinical development of SEP-363856, leveraging expertise accumulated through the research and development of our own pharmaceuticals.

SEP-363856
New generation of antipsychotics (Non-D2)
Aiming to contribute to society by creating a new treatment option
Growth potential beyond LATUDA®

SEP-363856 has the potential to have a broad effect on the negative symptoms of schizophrenia, and we will begin to expand its indications with the intent to develop it into a blockbuster drug that goes beyond LATUDA®.

Dasotraline (SEP-225289)
SEP-225289 is a dopamine and norepinephrine reuptake inhibitor (DNRI). SEP-225289 has an extended half-life (47-77 hours) that supports the potential for plasma concentrations yielding a continuous therapeutic effect over the 24-hour dosing interval.

We have submitted a New Drug Application to the FDA for binge eating disorder (BED) and are aiming for a U.S. launch during fiscal 2020.

The essential feature of BED is recurrent episodes of binge eating that occur at least once per week for three months (binge eating is defined as eating an abnormally large amount of food in a discrete period of time accompanied by a sense of lack of control). It is estimated that 4.1 million people are affected by BED in the U.S.

We received a Complete Response Letter (CRL) from the FDA for dasotraline in attention deficit hyperactivity disorder (ADHD), and we are currently considering our development plan for this indication.

Main late stage assets
New generation of antipsychotics aimed at creating new treatment paradigm: SEP-363856
SEP-363856, which has potential as a post-LATUDA® revenue replacement, is a non-D2 drug, which unlike the existing medications, does not show affinity to dopamine D2 receptors. Although the molecular targets involved in its efficacy profile are unclear, it is thought to work as an agonist for the serotonin 5-HT1A receptor and TAAR1 (trace amine-associated receptor 1).

It demonstrated positive results in a registration study for schizophrenia. In May 2019, it received Breakthrough Therapy designation* from the U.S. Food and Drug Administration (FDA), and the Phase 3 study is scheduled to commence in the U.S. in fiscal 2019 with the aim of market launch during fiscal 2023. We also aim for the fastest possible launch in Japan and China, and plan to start the Phase 2 study during fiscal 2019 in these regions. Our goal is to develop SEP-363856 into a new generation of antipsychotic to create a new treatment option.

SEP-363856 has the potential to treat positive and negative symptoms of schizophrenia, and it is thought to work as an agonist for the serotonin 5-HT1A receptor and TAAR1. It is also thought to work as an agonist for the serotonin 5-HT1B receptor.

It is also thought to work as an agonist for the serotonin 5-HT1A receptor and TAAR1. It is also thought to work as an agonist for the serotonin 5-HT1A receptor and TAAR1.

* Breakthrough Therapy designation: The drugs targeted by the system need to show that significant improvements on existing treatments can be expected at key clinical endpoints through the results of preliminary clinical trials.
Apomorphine hydrochloride (APL-130277)
APL-130277 is a sublingual film formulation of apomorphine, a dopamine agonist approved for acute intermittent treatment of OFF episodes associated with Parkinson’s disease.

We received a CRL from the FDA for the New Drug Application to treat OFF episodes in Parkinson’s disease. However, we plan to reapply for APL-130277 during 2019 with the aim of a U.S. launch during fiscal 2020.

One million people in the U.S. and an estimated four to six million people worldwide live with Parkinson’s disease. Parkinson’s disease is a chronic, progressive neurodegenerative disease characterized by motor symptoms such as tremors at rest and rigidity (muscle stiffness) and significant non-motor symptoms, including cognitive impairment and mood disorders.

OFF episodes are the re-emergence or worsening of symptoms (motor and non-motor) despite appropriate treatment, and can occur multiple times a day. OFF episodes are experienced by 40 to 60% of Parkinson’s disease patients and may worsen in frequency and severity over the course of the illness.

Latuda (lurasidone hydrochloride)
We submitted a New Drug Application in Japan in July 2019 for schizophrenia and bipolar depression. We are aiming for a Japan launch during fiscal 2020.

Fiscal 2019 Events/Objectives
- LONASEN® tape: obtained approval for schizophrenia in Japan
- Dasotroline: applied for binge-eating disorder in the U.S.
- Lurasidone hydrochloride: applied for schizophrenia and bipolar depression in Japan
- SEP-363856: commenced next-phase studies for schizophrenia
  - Phase 3 study in the U.S.
  - Phase 2 study in Japan

Vision 2033
We aim to be an innovator that makes a high quality contribution in specific diseases and categories.

Oncology Area
We will work on unique seeds and themes through research focused on cell-cell interaction in the tumor microenvironment* with the aim of discovering innovative new drugs. Moreover, we will strive for innovative technologies utilizing external collaboration and promote drug discovery and development leveraging big data and digital technologies. We will also promote network-based drug discovery between Sumitomo Dainippon Pharma, its U.S. subsidiaries, and external institutions with the aim of integrating research and development to move to clinical trials as early as possible.

At the development stage, we steadily promote the development of late stage assets in addition to actively striving for early-stage clinical development.

*Tumor microenvironment: the microenvironment formed around a tumor and surrounding host-derived cells is related to tumor pathology, and significantly influences prognosis, sensitivity and resistance to treatment.
Priorities in Oncology area

We will ensure development of napabucasin, a late stage asset, with the aim of application, approval, and launch as soon as possible. For early stage assets, we will accelerate POC approval through cutting-edge technologies, and establish an oncology franchise.

Main late stage assets
Napabucasin (BBI608)
Napabucasin is a small molecule oral medication with a novel mechanism. It is activated in vivo by the enzyme NQO1, which is expressed in cancer cells, and inhibits the pathways involved in cancer cell stemness, including STAT3, and cancer progression by producing reactive oxygen species. It is expected to ultimately lead to cancer cell death.

We are promoting a joint international Phase 3 study in a combination for colorectal cancer with the aim of launch in Japan and the U.S. during fiscal 2021.

Main early stage assets
Alvocidib (DSP-2033)
Alvocidib is a small molecule inhibitor of cyclin-dependent kinase 9 (CDK9), a member of cyclin-dependent kinase family, which activates transcription of cancer-related genes. The subsequent down-regulation of MCL-1, an anti-apoptotic gene, may be responsible for the potential clinical anticancer activity observed with alvocidib.

We are conducting a joint international Phase 2 study (combination / Zella 201 study) for patients with relapsed/refractory acute myeloid leukemia (AML). We have commenced a Phase 1 study for first-time AML patients and are conducting a clinical study for myelodysplastic syndrome (MDS) as well. We are also in the process of conducting a clinical study for AML in Japan.

TP-0903
TP-0903 is an AXL receptor tyrosine kinase inhibitor, which is known to be involved in acquiring resistance to conventional agents and developing metastatic capacity in cancer cells. TP-0903 may have anti-cancer activities on various cancer types through blocking transition from epithelial to mesenchymal phenotype by inhibiting AXL.

We are conducting a Phase 1/2 study for chronic lymphocytic leukemia in the U.S. and a Phase 1 study for solid tumors in the U.S. and Japan.

TP-0184
TP-0184 inhibits activin A receptor type 1 (ACVR1, also known as ALK2) kinase, part of the transforming growth factor beta (TGFβ) receptor superfamily. Mutations in the ACVR1 gene have been identified in various tumors, including diffuse intrinsic pontine glioma (DIPG; one of common pediatric brain tumors).

We are conducting a Phase 1 study in the U.S. for solid tumors

Fiscal 2019 Events/Objectives

Events/objectives completed as of July 2019

Napabucasin: promote joint international Phase 3 study for colorectal cancer and pancreatic cancer

Completed interim analysis in H1 FY2019

Colorectal cancer: received recommendation to continue study from independent Data and Safety Monitoring Board (DSMB) as a result of interim analysis in June 2019

Pancreatic cancer: received recommendation to terminate study from DSMB as a result of interim analysis in July 2019

Vision 2033

We will possess several global products and aim to establish a worldwide “DSP oncology” brand.
Value Chain

Research & Development

We are working to achieve early commercialization through our open innovation-based unique growth model, which pursues advanced industrialization and manufacturing expertise, and cutting-edge science, and are implementing six research and development projects. We are steadily promoting research projects mainly in Neurology and Ophthalmology seeking early commercialization. We are also setting our sights on next-generation regenerative medicine (gene therapy, organ regeneration, genome editing, autologous cell therapy, and peripheral services including diagnosis and rehabilitation), including the regeneration of organs, and aim for global expansion (Japan, the U.S., and Asia). First, we will aim to realize financial contributions mainly in Japan and the U.S. during the next MTBP period (fiscal 2023—2027).

Regenerative Medicine / Cell Therapy field

Main Projects

Chronic stroke (SB623)
SB623 is an allogeneic cell product, derived from bone marrow stromal cells. SB623 has been studied for chronic stroke, which currently has no effective treatments available, by promoting regeneration of central nerve cells. Unlike autologous cell therapies that require individualized cell preparation at the clinical site, SB623 production can be scaled up from a single donor’s cells, enabling delivery of uniform-quality products to a large number of stroke patients.

In 2014, Sumitomo Dainippon Pharma concluded a joint development and license agreement for exclusive marketing rights in North America. A Phase 2b study was conducted in the U.S. with SanBio, Inc. to evaluate the effects of SB623 on chronic stroke, and detailed analysis is currently ongoing. We plan to determine the future development policy based on the results of the detailed analysis.

AMD (Age-related macular degeneration)
Sumitomo Dainippon Pharma concluded a joint development agreement with Healios K.K. in December 2013, and established a joint venture company SighRegen K.K. through investment with Healios K.K. in February 2014. In June 2019, we modified the joint development system, with Sumitomo Dainippon Pharma becoming the development entity and both companies now able to apply for manufacturing and marketing approval based on the results of clinical trials. In collaboration with Healios K.K., Sumitomo Dainippon Pharma is preparing to commence sponsor-initiated clinical trials of retinal pigment epithelial cells using iPS cells for age-related macular degeneration in Japan.

Parkinson’s disease
In February 2017, allogeneic iPS cell-derived dopaminergic neural progenitor cells, which we are working to use in practice in collaboration with the Center for iPS Cell Research and Application (CiRA) at Kyoto University, were designated as a “SAKIGAKE Designation System” product for regenerative medicine & cell therapy by the Ministry of Health, Labour and Welfare.

Kyoto University Hospital started, in fiscal 2018, an investigator-initiated clinical study in regenerative medicine for Parkinson’s disease using dopaminergic neural progenitor cells derived from iPS cells of healthy (allogeneic) donors. Based on the results of the investigator-initiated clinical study, we are aiming to acquire approval for the cells as a regenerative medicine product.

Renal failure
Sumitomo Dainippon Pharma has commenced efforts for joint research and development with The Jikei University School of Medicine and others on renal regeneration with the fetal organ niche method using iPS cells as a new business in the Regenerative Medicine/Cell Therapy business.

Sumitomo Dainippon Pharma aims to realize renal regeneration by fiscal 2027. We expect to provide renal regeneration for patients who are waiting for kidney transplants for a long time due to problems such as organ shortages and medical expenses, contributing to medical treatment.
Renal Regeneration Project Using iPS Cells

Proposed indication, etc. | Partnering | Region (planned) | Cell type | status |
--- | --- | --- | --- | --- |
Chronic stroke (SB623) | SanBio | North America | Allo mesenchymal stem cell | Completed Phase 2b study Development strategy and launch target under consideration |
AMD (age-related macular degeneration) | Healios RIKEN | Global | Allo iPS cell-derived retinal pigment epithelium | In progress: clinical research Preparing to start clinical study (Japan) |
Parkinson's disease (Designated as a "SAKIGAKE") | Kyoto University CiRA | Global | Allo iPS cell-derived dopamine neural progenitor | In progress: investigator-initiated clinical study (Phase 1 / 2 study) (Japan) |
Retinitis pigmentosa | RIKEN | Global | Allo iPS cell-derived photoreceptor (3D) | Preparing to start clinical research |
Spinal cord injury | Keio University Osaka National Hospital | Global | Allo iPS cell-derived neural progenitor | In progress: clinical research |
Kidney failure | Jikei University Bios PorMedTec | Japan, North America | Auto/ Allo iPS cell-based induced nephron progenitor cells (organ) | In progress: pre-clinical study |

* Launch target is based on our goal pending agreement with partners.

Fiscal 2019 Events/Objectives
- SB623: Determine development plan for chronic stroke in the U.S.
- Allogeneic iPS cell-derived pharmaceuticals (age-related macular degeneration): start sponsor-initiated clinical trials

Vision 2033
We will aim for sales revenue in the Regenerative Medicine/Cell Therapy business of around ¥200 billion on a global scale in 2033.
Imeglimin (PXL008)
Imeglimin was in-licensed from Poxel SA in October 2017 and is the first clinical candidate in a new chemical class of oral agents called the Glimins by the World Health Organization. Imeglimin has a unique mechanism of action that targets mitochondrial bioenergetics. Imeglimin acts on all three key organs which play an important role in the treatment of type 2 diabetes: the pancreas, muscles, and the liver, and it has demonstrated glucose lowering benefits by increasing insulin secretion in response to glucose, improving insulin sensitivity and suppressing gluconeogenesis.

We have conducted three Phase 3 studies for Type 2 Diabetes in Japan and obtained positive test results for the Phase 3 studies of monotherapy and combination therapy with an insulin formulation. We plan to confirm the results of the remaining Phase 3 study during 2019 and aim to apply for approval in Japan in fiscal 2020 based on these results.

Fiscal 2019 Events/Objectives
Events/objectives completed as of July 2019
- Obtain two Phase 3 study results in Japan
- TIMES 2: long term monotherapy or combination therapy with existing hypoglycemic agents
- TIMES 3: insulin combination therapy

Product Launch Target (as of July 29, 2019)

<table>
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<tr>
<th>Area</th>
<th>FY2019</th>
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<th>FY2021</th>
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<td>LONASEN®</td>
<td>dasotraline (ADHD) Launch target under consideration</td>
<td>lurasidone (Schizophrenia/ Bipolar depression)</td>
<td>napabucasin (Colorectal cancer)</td>
<td>Allo IPS cell-derived1 products (AMD)</td>
<td>Allo IPS cell-derived products2 (Parkinson’s disease)</td>
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<td>RETHIO®</td>
<td>dasotraline (BED) Launch target under consideration</td>
<td>Apomorphine (OFF episodes associated with Parkinson’s disease)</td>
<td>napabucasin (Colorectal cancer)</td>
<td>Allo IPS cell-derived products2 (Parkinson’s disease)</td>
<td>Allo IPS cell-derived products2 (Parkinson’s disease)</td>
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<td>dasotraline (BED) Launch target under consideration</td>
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<td>napabucasin (Colorectal cancer)</td>
<td>SB62335 (Chronic stroke) Launch target under consideration</td>
<td>SEP-363856 (Schizophrenia)</td>
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*1 Premise to utilize an application of accelerated approval program (Plan to consult with the FDA)
*2 Launch target is based on our goal pending agreement with partners.

Expect peak annual sales to be 50 billion yen or more (described in the first launch)
Infectious diseases & vaccines (AMR and adjuvanted vaccines)

Collaborating with Academia to Contribute to Global Health
In addition to contributing to global health through joint research with academia and others, we will aim for commercialization during the next MTBP period (fiscal 2023—2027). We also expect that it will contribute to earning profit.

Main Projects
Drug discovery to treat antimicrobial resistance (AMR)
We are promoting joint drug discovery research with Kitasato Institute to treat antimicrobial resistance (AMR) covered by the Japan Agency for Medical Research and Development (AMED)’s CiCLE (Cyclic Innovation for Clinical Empowerment).

Drug discovery of adjuvanted vaccines
We are implementing drug discovery of adjuvanted vaccines by combining TLR7 agonist adjuvant, our foundation technology, with promising antigens from outside. We are working on a malaria vaccine with Ehime University, etc. and a universal influenza vaccination with the National Institute of Infectious Diseases, etc.

Fiscal 2019 Events/Objectives
Promote joint research with academia and others

Frontier business
Sumitomo Dainippon Pharma has launched frontier business with the objective of providing new solutions to solve issues in healthcare fields other than pharmaceuticals. We will work for commercialization during the current MTBP period and aspire to establish frontier business as a growth engine during the next MTBP period (fiscal 2023—2027).

Vision of frontier business:
Contribute to “wide-ranging well-being” together with pharmaceutical products
We will build a business platform consisting of key technologies (including ICT and engineering) and networks (including partnership with startups and venture capitals) in areas where we can create synergies with our pharmaceutical business to respond to future needs for healthcare. We will initiate multiple pilot trials for business seeds and explore commercialization mainly in Japan, the U.S. and China.

Main Projects
Investment in MELTIN MMI and conclusion of joint research and development agreement
In October 2018, Sumitomo Dainippon Pharma concluded an agreement for a joint research and development utilizing bio-signal processing and robotics.

As part of our pioneering of frontier business, we will engage in joint research and development that includes medical equipment utilizing the technologies of MELTIN MMI.
Commencement of joint research into medical equipment to alleviate behavioral and psychological symptoms of dementia

In February 2019, Sumitomo Dainippon Pharma concluded a joint research agreement with Aikomi Co., Ltd., to develop and examine the business potential of medical equipment to alleviate behavioral and psychological symptoms of dementia, an area in which there are significant unmet medical needs.

Consideration in clinical studies

Clinical studies put the human rights of subjects first

We conduct human clinical studies required for new drug applications in accordance with the utmost consideration of the subjects’ human rights.

Since clinical studies are conducted during the intermediate stages of confirming the efficacy (effectiveness) and safety of drug candidates, our clinical studies follow such regulations as Japan’s ministerial ordinance on GCP (Good Clinical Practice), which was established to protect the human rights, maintain the safety and improve the welfare of subjects participating in studies.

Ethical approach to human tissue research

Sumitomo Dainippon Pharma has established the Research Ethical Review Committee which reviews the appropriateness of implementing research from the perspectives of the significance and necessity of research, the scientific rationality of plans, the provision of adequate prior explanations to donors of human tissues, etc. and the acquisition of consent based on free will (informed consent), rigorous protection of personal information and other points of view. We also disclose the Rules for the Research Ethics Investigation Committee, the composition of the committee members, and the content of the committee proceedings.

Intellectual property

Sumitomo Dainippon Pharma recognizes that intellectual property is an essential part of the business of a pharmaceutical company. In filing patent applications, we are building up a patent portfolio including not only substance patent applications but also patent applications that encompass uses, manufacturing processes and formulations to comprehensively protect our commercial and development products. In addition, we are working to establish intellectual property in the regenerative medicine/cell therapy field in order to promote the business.

Fiscal 2019 Events/Objectives

Promote current projects and pioneer new themes