R&D meeting

March 3, 2020
Sumitomo Dainippon Pharma Co., Ltd.
Disclaimer Regarding Forward-looking Statements

This material contains forecasts, projections, targets, plans, and other forward-looking statements regarding the Group’s financial results and other data. Such forward-looking statements are based on the Company’s assumptions, estimates, outlook, and other judgments made in light of information available at the time of preparation of such statements and involve both known and unknown risks and uncertainties. Accordingly, plans, goals, and other statements may not be realized as described, and actual financial results, success/failure or progress of development, and other projections may differ materially from those presented herein.

Information concerning pharmaceuticals (including compounds under development) contained herein is not intended as advertising or as medical advice.
## Today’s Agenda

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<th>Representative Director President and CEO</th>
<th>Hiroshi Nomura</th>
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<td>Toru Kimura, Ph.D.</td>
<td>P.15-29</td>
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<td>3</td>
<td>Regenerative Medicine/Cell Therapy</td>
<td>Member, Board of Directors Senior Executive Officer</td>
<td>Toru Kimura, Ph.D.</td>
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<tr>
<td>4</td>
<td>Oncology</td>
<td>Senior Executive Officer Global Head of Oncology</td>
<td>Kazuo Koshiya, Ph.D.</td>
<td>P.48-61</td>
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<td>Development pipeline : SEP-363856</td>
<td>Sunovion Pharmaceuticals Inc. Chief Scientific Officer</td>
<td>Kenneth S. Koblan, Ph.D.</td>
<td>P.62-75</td>
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<td>Q&amp;As</td>
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</tr>
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</table>
To deliver innovation to patients with CHANTO

Hiroshi Nomura
Representative Director, President and CEO

CHANTO
Capability to continuously foster and deliver innovation to patients and other customers, while transforming our organization in flexible ways to adapt to changes in the world
To broadly contribute to society through value creation based on innovative research and development activities for the betterment of healthcare and fuller lives of people worldwide.
**Introduction**

**Value Creation Process (Research & Development)**

### Sources of value creation —— six types of capital

#### Our Strengths

- **R&D: Research & Development**
- **Global Platform**
- **Human Resources**

#### Value Chain

**Innovative Drug Discovery**
- Psychiatry & Neurology Area
  - New compounds under development: 11
- Oncology Area
  - New compounds under development: 11
- Regenerative Medicine/Cell Therapy Field
  - Projects under development: 6
- Infectious Diseases Area
  - Joint research with academia, etc.

**Drug Development, Production, Sale, and Information Provision**

- CSR-based Management /Corporate Governance

### Business Activities

- **Creating innovative pharmaceutical products and healthcare solutions in areas with high unmet medical needs**
- **Contributing to the development of science**
- **Contributing to improving quality of life (QOL) for patients and their families**
- **Improving sustained corporate value**
  - Returns to shareholders (stable dividends, increases in dividends linked to improvements in performance)
  - Strategic investment aimed at sustained growth (includes research and development investment)
  - Also contributing to achieving the Sustainable Development Goals (SDGs)

### Value provided to society

- **Returns to shareholders (stable dividends, increases in dividends linked to improvements in performance)**
- **Strategic investment aimed at sustained growth (includes research and development investment)**
- **Also contributing to achieving the Sustainable Development Goals (SDGs)**

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**R&D: Research & Development**

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**Six types of capital**
Introduction

Mid-to-Long Term Corporate Vision

We aspire to establish ourselves as a “Global Specialized Player” by 2033 with the ability to meet increasingly diversified healthcare needs.

Goal and Vision 2033

Vision

Position we aspire to establish in 2033

For Longer and Healthier Lives:
We unlock the future with cutting-edge technology and ideas

Global Specialized Player

Pharmaceuticals+Solutions

Global leader in 3 areas

Focus Research Areas

Best in class focused on value

Medicine / Cell Therapy

Healthcare Solution (Frontier business)

Psychiatry & Neurology

Oncology

Regenerative / Cell
Reshape business foundation through the “establishment of growth engine” and the “building of flexible and efficient organization”, preparing for the “Time for Change” and post-LATUDA® revenue replacement

I. Establishment of growth engine

1. Enhance innovation base with new approaches to drug discovery
2. Deliver highest performance of clinical development
3. Pipeline expansion through strategic investment
4. Regional strategy centering in Japan, North America and China
5. Launch frontier business

II. Building of flexible and efficient organization

Today’s presentation shows the progress in each area starting on page 15

“CHANTO”

Flexible and efficient operations  Digital innovation  Corporate culture and talent to drive innovation
## Main Progress of Development Pipeline in FY2019

### Introduction

One approval obtained (LONASEN® Tape)
Three NDAs submitted (dasotraline < BED in U.S. >, apomorphine <in U.S.>, lurasidone <in Japan>)
New Phase 1 study: DSP-1181 (proposed indication: obsessive compulsive disorder)

<table>
<thead>
<tr>
<th>Products</th>
<th>Status</th>
<th>Countries</th>
<th>Launch target</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lurasidone</td>
<td>NDA submitted for schizophrenia and bipolar depression in July 2019</td>
<td>Japan</td>
<td>FY2020</td>
</tr>
<tr>
<td>Dasotraline</td>
<td>NDA submitted for binge eating disorder (BED) (PDUFA date: May 14, 2020)</td>
<td>U.S.</td>
<td>FY2020</td>
</tr>
<tr>
<td>Apomorphine</td>
<td>NDA submitted for OFF episodes associated with Parkinson’s disease (PDUFA date: May 21, 2020)</td>
<td>U.S.</td>
<td>FY2020</td>
</tr>
<tr>
<td>SEP-363856</td>
<td>Started Phase 3 studies for schizophrenia</td>
<td>U.S.</td>
<td>FY2023</td>
</tr>
<tr>
<td>Imeglimin</td>
<td>Completed Phase 3 studies for Type 2 diabetes, preparing to submit NDA</td>
<td>Japan</td>
<td>FY2021</td>
</tr>
</tbody>
</table>

Obtained 10 products due to the strategic alliance with Roivant Sciences
(Pipeline includes the following: RVT-801, RVT-802, rodaristat ethyl, MVT-602, URO-902, SPIRO-2101, SPIRO-2102, ALTA-2530)

<table>
<thead>
<tr>
<th>Products</th>
<th>Status</th>
<th>Countries</th>
<th>Submit target</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vibegron</td>
<td>NDA submitted for overactive bladder Ongoing Phase 3 study for overactive bladder in men with BPH Ongoing Phase 2a study for IBS-associated pain</td>
<td>U.S.</td>
<td>Overactive bladder: NDA submitted in December 2019</td>
</tr>
<tr>
<td>Relugolix</td>
<td>Completed Phase 3 studies for uterine fibroids, preparing to submit NDA Completed Phase 3 studies for prostate cancer, preparing to submit NDA Ongoing Phase 3 study for endometriosis</td>
<td>U.S.</td>
<td>Uterine fibroids: April 2020 Prostate cancer: Q1 FY2020</td>
</tr>
</tbody>
</table>
## Development Pipeline (as of March 3, 2020)

**Introduction**

<table>
<thead>
<tr>
<th>Area</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>NDA/BLA submitted</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Japan</strong></td>
<td>dasotraline (ADHD)</td>
<td>alvodcidib (Hematologic malignancies)</td>
<td>SEP-4199 (Bipolar I depression)</td>
<td>lurasidone (Schizophrenia/Bipolar depression)</td>
</tr>
<tr>
<td></td>
<td>SEP-363856 (Schizophrenia)</td>
<td>duberminib (TP-0903) (Solid tumors)</td>
<td>DSP-7888 (Solid tumors/Hematologic malignancies)</td>
<td>RETHIO® (Conditioning treatment prior to autologous HSCT for malignant lymphoma)</td>
</tr>
<tr>
<td></td>
<td>EPI-589 (ALS)</td>
<td></td>
<td>imeglimin (Type 2 diabetes)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>DSP-1181 (Obsessive compulsive disorder)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>U.S.</strong></td>
<td>DSP-6745 (Parkinson’s disease psychosis)</td>
<td>alvodcidib (MDS)</td>
<td>EPI-589 (Parkinson’s disease/ALS)</td>
<td>dasotraline (BED)</td>
</tr>
<tr>
<td></td>
<td>SEP-378608 (Bipolar disorder)</td>
<td>duberminib (TP-0903) (Solid tumors/Hematologic malignancies)</td>
<td>SEP-363856 (Parkinson’s disease psychosis)</td>
<td>dasotraline (ADHD)</td>
</tr>
<tr>
<td></td>
<td>DSP-3905 (Neuropathic pain)</td>
<td>DSP-0509 (Solid tumors)</td>
<td>SEP-4199 (Bipolar I depression)</td>
<td>Development strategy under consideration</td>
</tr>
<tr>
<td></td>
<td>SEP-378614 (Treatment resistant depression)</td>
<td>TP-0184 (Solid tumors / Hematologic malignancies)</td>
<td>relugolix (Prostate cancer)</td>
<td>apomorphine (OFF episodes associated with Parkinson’s disease) NDA resubmitted in November 2019</td>
</tr>
<tr>
<td></td>
<td>SEP-380135 (Agitation in Alzheimer’s disease)</td>
<td>DSP-0337 (Solid tumors)</td>
<td>SEP-4199 (Parkinson’s disease psychosis)</td>
<td>RVT-802 (Pediatric congenital athymia) Received Complete Response Letter</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TP-1287 (Solid tumors)</td>
<td>relugolix (Uterine fibroids/Endometriosis)</td>
<td>vibegron (OAB)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TP-3654 (Solid tumors/Hematologic malignancies)</td>
<td>vibegron (OAB in men with BPH)</td>
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</tbody>
</table>
## Introduction

### Product Launch Target (as of March 3, 2020)

*Revisions since the announcement of January 2020 are shown in red*

<table>
<thead>
<tr>
<th>FY2019</th>
<th>FY2020</th>
<th>FY2021</th>
<th>FY2022</th>
<th>FY2023</th>
</tr>
</thead>
<tbody>
<tr>
<td>LONASEN®</td>
<td>LONASEN® (Schizophrenia/Transdermal patch) Launch in September 2019</td>
<td>dasotraline (ADHD) Launch target under consideration</td>
<td>apomorphine (OFF episodes associated with Parkinson’s disease)</td>
<td>dasotraline (BED)</td>
</tr>
<tr>
<td>REETHIO® (Conditioning treatment prior to autologous HSCT for malignant lymphoma)</td>
<td>napabucasin (Colorectal cancer) Launch target under consideration</td>
<td>imeglimin (Type 2 diabetes)</td>
<td>napabucasin (Colorectal cancer)</td>
<td>SEP-363856 (Schizophrenia)</td>
</tr>
<tr>
<td>alvocidib (MDS)</td>
<td>dubertaminib (TP-0903) (Solid tumors/Hematologic malignancies)</td>
<td>Allo iPS cell-derived products (Parkinson’s disease)</td>
<td>Allo iPS cell-derived products (AMD) Launch target under consideration</td>
<td></td>
</tr>
<tr>
<td>alvocidib (MDS)</td>
<td>dubertaminib (TP-0903) (Solid tumors/Hematologic malignancies)</td>
<td>Allo iPS cell-derived products (Parkinson’s disease)</td>
<td>Allo iPS cell-derived products (AMD) Launch target under consideration</td>
<td></td>
</tr>
</tbody>
</table>

* Plan to launch RVT-802, vibegron and relugolix from FY2019 to FY2023 (launch targets are not disclosed)
  - RVT-802 (Pediatric congenital athymia) Submitted in April 2019, Received Complete Response Letter in December 2019
  - Vibebron (OAB) Submitted in December 2019
  - Relugolix (Uterine fibroids) (Prostate cancer) Plan to submit NDA in April 2020

*1 Premise to utilize an application of accelerated approval program (Plan to consult with the FDA)
*2 Launch schedule is based on our goal pending agreement with partners
Basic policy: Concentrated investment in three focus research areas, bringing in open innovation, and allocation of R&D investment by priority

<table>
<thead>
<tr>
<th>Focus Research Areas</th>
<th>Psychiatry &amp; Neurology</th>
<th>Oncology</th>
<th>Regenerative Medicine/Cell Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Approach</strong></td>
<td>Target psychiatric disorders with poor treatment satisfaction; also aim at discovery of disease-modifying drugs in addition to drugs for treating peripheral symptoms of neurodegenerative diseases</td>
<td>Build diversified and innovative development pipeline through discovery research focused on tumor microenvironment (intercellular interaction) and other key cancer pathways</td>
<td>Pursue advanced manufacturing expertise and cutting-edge science to become a global leader</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Infectious Diseases</th>
<th>Frontier Business</th>
<th>Best in class focused on value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Approach</strong></td>
<td>Promote R&amp;D in collaboration with academia aiming at contributing to global health</td>
<td>Build a unique technology platform centering around our pharmaceutical business</td>
</tr>
</tbody>
</table>
**Introduction**

**Research & Development Base**

- **Sunovion Pharmaceuticals Inc. (U.S.)** R&D (Psychiatry & Neurology)
- **Sumitomo Pharmaceuticals (Suzhou) Co., Ltd. (China)** Development in China
- **Boston Biomedical, Inc. (U.S.)** R&D (Oncology)
- **Tolero Pharmaceuticals, Inc. (U.S.)** R&D (Oncology)
- **Myovant Sciences Ltd. (U.S.)** R&D (Women’s health, prostate cancer)
- **Urovant Sciences Ltd. (U.S.)** R&D (Urology)
- **Enzyvant Therapeutics Ltd. (U.S.)** R&D (Pediatric rare diseases)
- **Altavant Sciences Ltd. (U.S.)** R&D (Respiratory rare diseases)
- **Spirovant Sciences Ltd. (U.S.)** R&D (Cystic fibrosis gene therapy)
- **Sumitomo Dainippon Pharma Co., Ltd. (Japan)** R&D
- **Sumitomo Pharmaceuticals (Suzhou) Co., Ltd. (China)** Development in China
- **Sunovion Pharmaceuticals Inc. (U.S.)** R&D (Psychiatry & Neurology)
- **San Diego Office (U.S.)** R&D (Regenerative Medicine/Cell Therapy)
- **Boston Biomedical, Inc. (U.S.)** R&D (Oncology)
Introduction

Research & Development System (scheduled for April 1, 2020)

Appointment of Chief Scientific Officer

- Supervision of R&D activities in all areas
- Central management of R&D expense allocation and achievement of optimal R&D portfolio management

President and Chief Executive Officer

Chief Scientific Officer
Toru Kimura

Psychiatry & Neurology / Others
- Drug Research (Division)
- Drug Development (Division)
- Sunovion Pharmaceuticals Inc.
- etc.

Oncology
- DSP Cancer Institute
- Boston Biomedical, Inc.
- Tolero Pharmaceuticals, Inc.
- etc.

Regenerative Medicine/Cell Therapy
- Regenerative & Cellular Medicine Office
- Regenerative & Cellular Medicine Kobe Center
- Regenerative & Cellular Medicine Manufacturing Plant
- etc.

Sumitovant Biopharma Group
- Myovant Sciences Ltd.
- Urovant Sciences Ltd.
- Enzyvant Therapeutics Ltd.
- Altavant Sciences Ltd.
- Spirovant Sciences Ltd.

R&D resource allocation policy will be discussed in the Management Committee.
Continuously foster and deliver innovation to patients and other customers

Transform our organization to adapt to changes in the world and to continue a sustained growth
Psychiatry & Neurology

Toru Kimura, Ph.D.
Member, Board of Directors
Senior Executive Officer
Psychiatry & Neurology

R&D Strategy

- Achieve precision medicine through pathophysiology-based drug discovery
- Provide total health care solutions through combining pharmaceuticals with digital technologies
- Overcome neurodegenerative diseases and move toward preventive medicine

**Direction**
- Psychiatry: Drive “genetics and neural circuit anomalies”-based drug discovery for the treatment of schizophrenia, depression, psychiatric symptoms in neurological disorders, and developmental disorders
- Neurology: Identify disease modifying drugs for dementia, Parkinson’s disease, and rare diseases, maximizing the opportunities of advance in science

**Measures**
- Maximize our strengths in monoamine drug discovery
- Take advantage of our original technologies; in silico-, iPS-, and ion channel-based drug discoveries
- Deepen genetics- and neural circuit-based research to achieve precision medicine
- Utilize big data and explore surrogate biomarkers in collaboration with industries, governments, and academia.
- Advance use of digital devices for patient support, diagnosis, and treatment
- Strengthen open innovation
Established a top-class position in global market and building unique R&D pipeline

- **Market share of pharma companies (2018)**
  
  Global market size: 55.6 B$

- **Numbers of new active ingredients in neuroscience clinical pipeline (as of Jan. 2020)**

<table>
<thead>
<tr>
<th>Company</th>
<th>Phase1</th>
<th>Phase2/Phase3/Submitted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biogen</td>
<td>3</td>
<td>12</td>
</tr>
<tr>
<td>J&amp;J</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>Roche</td>
<td>4</td>
<td>8</td>
</tr>
<tr>
<td>Eli Lilly</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Lundbeck</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>Novartis</td>
<td>6</td>
<td></td>
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<tr>
<td>Takeda</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Eisai</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>Otsuka</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Astellas</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>
Psychiatric and neurological disorders cause enormous loss for society

- Highest disease burden in disability-adjusted life year (DALY)
- Increasing economic loss worldwide
  USD 2,493 B (2010) to USD 6,046 B (2030)
  (Source: The Global Economic Burden of Non-communicable Diseases 2011.9)

- Patients with schizophrenia or depression are often resistant to current therapy and facing difficulty in social reintegration
  - Approx. 30% of patients are treatment resistant
  - No approved drugs for negative symptoms/cognitive impairment of schizophrenia
  - >150K schizophrenia patients hospitalized in Japan
    (Source: Ministry of Health, Labor and Welfare 2017 patient survey)

- Burden of care for patients with behavioral and psychiatric symptoms in dementia (BPSD) is increasing
  - Number of patients increasing rapidly in Japan, likely to exceed 7 million by 2025
    (Source: 78th Social Security Council Nursing Care Insurance Subcommittee Reference Material 2-1)
  - Importance of prevention and handling of BPSD is emphasized in the Framework for Promoting Dementia Care
    (psychiatric symptoms include anxiety, depression, apathy, agitation, delusion, hallucination, sleep disorders, etc)
Heterogeneity in Psychiatric and Neurological Disorders

Psychiatric Disorder
- Drug-responsive patients
- Drug-resistant patient/patient with residual symptoms

Neurological Disorder
- Core symptoms: Cognitive and Memory dysfunction, etc.
- Psychiatric symptoms: Anxiety, depression, apathy, agitation, delusions, hallucinations, sleep disorders, etc.

High Unmet Medical Needs
Initiatives Leveraging Strengths in Science & Technology

**Psychiatry & Neurology**

Biology
- Novel disease models
  - Genetic modification
  - Abnormal neural circuit model
- Patient-derived iPSCs
  - Human disease model
- Other advanced technologies
  - AI-driven behavior analysis
  - Neuroimaging
  - EEG
  - GWAS

Chemistry
- Med-Chem in CNS
  - Know-how
  - Accumulated data
- In silico prediction
  - Chemical structure
  - Physicochemical property
  - ADMET

Clinical Science
- Abundant clinical experiences and rich clinical data

Psychiatry
- Behavioral and psychiatric symptoms in neurological disorders
Organizational Activation: Research Project (PJ) System (from October 2017)

- Hit to Lead
- Lead Generation & Lead Optimization
- Pre Clinical
- Early Clinical
- Late Clinical

Approval as a Research PJ

- Team grows as the PJ proceeds
- Passionate initiator to be the PJ leader
- Core research PJ members remain to accelerate clinical PJ
  (° = PJ member(s) from research division)
  Leaders have budget authority and performance evaluation authority

Collaborate with CRO

CRO

Nomination
TR: Translational Research

All other functions in the company support PJs
Organizational Activation: Virtual One Team (V1T) Initiatives

Researchers from different PJ’s/departments with common interest gather, discuss and share ideas/knowledge/technologies ~ key for open, creative culture

V1T “Protein aggregation”
- Common Interest: protein aggregation in cells
- Exchange idea, share technologies/topics

V1T “Neuro-inflammation”
- Common Interest: Glial neuro-inflammation etc
- Exchange idea, share technologies/topics

V1T “What’s new as a psychiatry discovery program”
- Common interest: Find good seeds/targets, etc.
- New research program proposal(s)

This initiative leads to organizational activation, resulting in new program proposals
In-house advanced technologies platform

- Patients-derived iPSC
- In silico drug discovery
- New modalities
- Neural circuits
- Higher brain function
- Ion channels
- Optogenetics
- Monoamines
- Genetic modifications

Clinical candidates Nominations per FY

- 2013: 2
- 2014: 1
- 2015: 2
- 2016: 1
- 2017: 4
- 2018: 2
- 2019: 2
- 2020 (estimated): 11

Advanced technologies platform built through internal effort and external alliances aggressively utilized in drug discovery research process

Key success factor to proceed research PJs
DSP-1181, a 5-HT$_{1A}$ Receptor Full Agonist, As an OCD Drug Candidate

Reported in BBC news and Science Translational Medicine
OCD; Neural Circuits and Pathophysiology

Positive cortico-striatal connectivity in OCD patients

- Increased cortico-striatal connectivity
- Pathophysiology of OCD

Challenges in Drug discovery:
Lack of reliable disease models in Psychiatry area

Optogenetics technology to produce pathophysiology-related models

Optogenetics, a technology to control specific neuronal activities using opto-stimulation in specific brain region

The efficacy of DSP-1181 was evaluated in the animal model with human OCD pathophysiology
Efficacy of DSP-1181 in OCD Model

Grooming (OCD-like behavior) suppressed in DSP-1181-treated mice

Optical stimulation + DSP-1181

<table>
<thead>
<tr>
<th>Condition</th>
<th>Grooming time (Mean±SEM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-stimulation</td>
<td>10±2</td>
</tr>
<tr>
<td>Stimulation</td>
<td>80±3</td>
</tr>
<tr>
<td>Stimulation+DSP-1181 Low</td>
<td>20±1</td>
</tr>
<tr>
<td>Stimulation+DSP-1181 High</td>
<td>10±2</td>
</tr>
</tbody>
</table>

n=7-9, *p<0.01 (Parametric Dunnett's test)
Aiming for Global Leading Company in Psychiatry & Neurology Area

Value creation

- Experiences/know-how achieved from long term history of CNS research
- Aggressive incorporation/utilization of advanced technologies
- Flexible and challenging Organizational management

Strength in Research and Development

Innovative drug discovery to fulfill unmet medical needs
Tackling Infectious Diseases; Also Considering the Contribution to Society

**Sumitomo Dainippon Pharma**
- Accumulated R&D experience (MEROPEN®, TLR7 agonist, etc.)

**Academia, etc.**
- Scientific expertise and insights in respective specialty fields
- Global network

**Drug discovery to treat Antimicrobial resistance (AMR*1)**
- Joint project with the Kitasato Institute, supported by AMED*2’ CiCLE*3

**Adjuvanted vaccines R&D**
- Combination of our TLR7 agonist (adjuvant) and promising external antigen
  - Universal influenza vaccine supported by AMED CiCLE)
  - Blood-stage malaria vaccine supported by GHIT fund*4

- (Collaboration supported by AMED*2)

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*1 AMR : Antimicrobial resistance
*2 AMED : Japan Agency for Medical Research and Development
*3 CiCLE : Cyclic Innovation for Clinical Empowerment
*4 GHIT Fund: Global Health Innovative Technology Fund
Regenerative Medicine/Cell Therapy

Toru Kimura, Ph.D.
Member, Board of Directors
Senior Executive Officer
Area
From the central nervous system (including ophthalmology) to peripheral tissues

Modality
From single cell to tissues and organs
iPS cell, mesenchymal stem cell (MSC)

Region
From Japan to the U.S.

Open innovation
Academia, biotech companies, companies of other industries, governmental institutions
### Regenerative Medicine/Cell Therapy

#### Business Plan (as of March 3, 2020)

<table>
<thead>
<tr>
<th>Proposed indication, etc.</th>
<th>Partnering</th>
<th>Region (planned)</th>
<th>Cell type</th>
<th>status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pediatric congenital athymia (RVT-802)</td>
<td>Duke University</td>
<td>Global</td>
<td>Cultured thymus tissue</td>
<td>BLA submitted in the U.S. in April 2019 Under consideration to resubmit BLA</td>
</tr>
<tr>
<td>AMD (age-related macular degeneration)</td>
<td>Healios RIKEN</td>
<td>Global</td>
<td>Allo iPS cell-derived retinal pigment epithelium</td>
<td>In progress: clinical research Preparing to start clinical study (Japan)</td>
</tr>
<tr>
<td>Parkinson’s disease (Designated as a &quot;SAKIGAKE&quot;)</td>
<td>Kyoto University CiRA</td>
<td>Global</td>
<td>Allo iPS cell-derived dopamine neural progenitor</td>
<td>In progress: investigator-initiated clinical study (Phase 1 / 2 study) (Japan)</td>
</tr>
<tr>
<td>Retinitis pigmentosa</td>
<td>RIKEN</td>
<td>Global</td>
<td>Allo iPS cell-derived photoreceptor (3D)</td>
<td>Preparing to start clinical research</td>
</tr>
<tr>
<td>Spinal cord injury</td>
<td>Keio University Osaka National Hospital</td>
<td>Global</td>
<td>Allo iPS cell-derived neural progenitor</td>
<td>In progress: clinical research</td>
</tr>
<tr>
<td>Kidney failure</td>
<td>Jikei University Bios PorMedTec</td>
<td>Japan, North America</td>
<td>Auto/ Allo iPS cell-based induced nephron progenitor cells (organ)</td>
<td>In progress: pre-clinical study</td>
</tr>
</tbody>
</table>

*Launch schedule is based on our goal pending agreement with partners*
Expand the Business through Strategic Alliance with Roivant

Regenerative Therapy
Enzyme Replacement Therapy

**Enzyvant Therapeutics**
- US Headquarters: Cambridge, Massachusetts
- Number of employees: 26 (as of December 31, 2019)
- Representative: Rachelle Jacques, CEO
- Focus Area: Pediatric Rare Diseases
- Pipeline: RVT-802, RVT-801
- Wholly owned

**Spirovant Sciences**
- Number of employees: 11 (as of December 31, 2019)
- Representative: Joan Lau, CEO
- Focus Area: Cystic Fibrosis Gene Therapy
- Pipeline: SPIRO-2101, SPIRO-2102, SPIRO-2110
- Wholly owned

Early entry in the U.S. market
Expand into gene therapy business
Profile of RVT-802

- **Originator:** Duke University
- **Phase:** BLA submitted in the U.S. in April 2019, Complete Response Letter received in December 2019
- **Characteristics:**
  - One-time regenerative tissue-based therapy indicated for immune reconstitution when implanted in pediatric patients with congenital athymia, a condition that is fatal when untreated, usually by the age of 2
  - Produced from human thymus tissue that has been removed during unrelated pediatric cardiac surgeries
  - Granted Breakthrough Therapy, Regenerative Medicine Advanced Therapy, Orphan Drug and Rare Pediatric Disease designations by the FDA

In 85 RVT-802 treated patients with congenital athymia, Kaplan-Meier estimated survival rates at Year 1 and Year 2 were 76% and 75%, respectively.

For patients surviving 12 months post-treatment, there was a 93% probability of surviving 10 years post-treatment.
Regenerative Medicine/Cell Therapy: Introduction of New Project

Started Renal Regeneration Project Using iPS Cells

Started collaborative efforts including joint research and development with the goal of developing renal regenerative medicine

Aim to launch before FY2027 in Japan
Regenerative Medicine/Cell Therapy: Progress of Existing Project

Cell Transplantation Therapy for Parkinson's disease Using iPS Cells

Collaboration partner: CiRA, Kyoto University (Prof. Jun Takahashi)

- Most common neurodegenerative disease, which causes motor symptoms
- Number of patients: 1.5 million in the USA, 163,000 in Japan; 7.3% of patients at level 5 of nursing care needed (ranks 5th)
- Cardinal symptoms are motor symptoms associated with degeneration of substantia nigro/striatal dopaminergic neurons
- Efficacy of implanted embryonic dopaminergic neurons has been confirmed

Establishment of protocol for creating dopamine precursor cells from iPS cells has opened up the possibility of practical application of cell therapy

Safety and ethical issues

Investigator-initiated clinical trial in Kyoto University is ongoing.
* Transplantation of iPS cells completed in 3 of 7 patients in 2019. The remaining 4 patients to receive transplantations in FY2020.

We plan to proceed with commercialization based on the results of the investigator-initiated clinical study.
* Product designated for Sakigake
Retinal Structure and Disease

Retinal pigment epithelium (RPE) → Age-related macular degeneration
Photoreceptor cells → Retinitis pigmentosa
Intermediate neurons
Ganglion cells

Cross section of the retina
Direction of excitement

Causes of visual impairment in Japanese

- Glaucoma: 28.6%
- Retinitis pigmentosa: 14.0%
- Macular degeneration: 8.0%
- Retinopathy of diabetes: 12.8%
- Choroidal retinal atrophy: 4.9%
- Others: 31.7%

Cell Transplantation Therapy for AMD Using iPS Cells

Collaboration partner: RIKEN/Healios K.K.

- Clinical research conducted by RIKEN (Prof. Masayo Takahashi)
  - Auto RPE sheet (1 patient) → world's first
  - Allogeneic cell suspension (5 patients)
Regressive Medicine/Cell Therapy: Progress of Existing Project

Cell Transplantation Therapy for Retinitis Pigmentosa Using iPS Cells

Sumitomo Dainippon Pharma

Self-organizing culture

Allo human iPS cell

3D retina
(including neural photoreceptors)

Transplanted cells

Partnering: RIKEN (Dr. Mandai)

Retinitis pigmentosa

Kobe Eye Center Hospital applied for clinical research

Sumitomo Dainippon Pharma is in charge of cell production

Photoreceptor cells

Normal retina
Outline of cell transplantation therapy for spinal cord injury (SCI)

- iPS cells
- Neural precursor cells
  - Neuron
  - Astrocyte
  - Oligodendrocyte

- Relay damaged neural circuit
- Release of neurotrophic factor
- Smooth transmission of neural information

Clinical research ongoing at Keio University
Regenerative Medicine/Cell Therapy
Pursuit of Open Innovation

- Biotech companies: Initial development
- Companies of other industries: devices, production equipment

- Basic research for new seeds
- Clinical research/ Clinical study

- PMDA: Clarify development path
- MHLW: Drug designated for SAKIGAKE
- AMED: Research Grant

Promotion of business using open innovation

Sumitomo Dainippon Pharma
- Overall coordination
- Research & Development, Manufacture, Sales
  Swift decision making
  Cutting-edge science/ Cell manufacturing technology

Academia

Industry

Government

- PMDA: Pharmaceuticals and Medical Devices Agency
- MHLW: Ministry of Health, Labor and Welfare
- AMED: Japan Agency for Medical Research and Development
Regenerative Medicine/Cell Therapy

In Order for Cells to Become “Medicines"

Pharmaceutical product means:
stable supply of cells of the same specifications

* Long-term, sterile, mass culture
* Established quality specifications
* Guaranteed safety
* Low cost
Regenerative Medicine/Cell Therapy

For the Manufacture of Regenerative Medicine Products

Kyoto University
CiRA

Master cell bank

Working cell bank

Freeze-preservation

Differentiation induction

Target cell

Large-scale cell culture

Regenerative medicine products

iPS cells
For the Manufacture of Regenerative Medicine Products

Regenerative Medicine/Cell Therapy

Kyoto University
CiRA

iPS cells

Quality Control

Master cell bank

Working cell bank

Large-scale
cell culture

Freeze-preservation

Differentiation induction

Regenerative
medicine products

Quality Control

Quality Control

Quality Control

Quality Control

Quality Control

Quality Control

Quality Control
Regenerative Medicine/Cell Therapy

Building a Stable and High-Quality Production System

**Improvement of work environment**

“Aseptic room” + Safety cabinet

Isolator

**Securing stability and reducing costs by automating production processes**

High speed cell sorter

Closed automatic cell culture

Remove non-target cell and collect the target cells only

Expansion culture of iPS cells
Induction of differentiation of mass culture cells
Profile of SMaRT

SMaRT: Sumitomo Dainippon Manufacturing Plant for Regenerative Medicine & Cell Therapy

Regenerative and cell medicine business based on solid production technology

- Building area: 1,997㎡, Total floor area: 2,915㎡, Structure: 12-m-tall steel construction with 2 above ground levels
- Construction cost: approximately 3.6 billion yen
- Function: Manufacturing of investigational agents and early-stage commercial production using retinal pigment epithelium (age-related macular degeneration), dopamine neural progenitor (Parkinson's disease), 3D retina (retinitis pigmentosa), neural progenitor (spinal cord injury), and other ailments
- Construction start in FY2016, construction end and operation in March 2018
Regenerative Medicine/Cell Therapy
Mid-Term Strategy

Actively pursue open innovation-based unique growth model, integrating internal advanced manufacturing expertise and external cutting-edge science, to achieve early commercialization

- Introduce next-generation seeds/technology
  - iPS cell-derived organ (kidney, etc.)
  - Autologous iPS cell-derived cell/tissue
  - Gene transfer/modification
  - Next-generation stem cell

- Contribute to early commercialization and expand pipeline
  - MSC/somatic stem cell

Realize next-generation regenerative medicine (including application to peripheral organs)

- Accelerate on-going projects
  (mainly in Neurology and Ophthalmology)

- Related business
  (diagnosis, rehabilitation, etc.)

- Organ regeneration
- Gene therapy
- Genome editing
- Autologous cell therapy

- Allogenic iPS cell-derived differentiated cell
  - Dopaminergic neuron progenitor
  - Retinal pigment epithelium
  - Neural progenitor

- Mesenchymal stem cell (MSC)
  Collaboration with DS Pharma Animal Health

Aim to realize financial contributions during the next MTBP period (FY2023 to FY2027)
Oncology

Kazuo Koshiya, Ph.D.
Senior Executive Officer
Global Head of Oncology
Build diversified and innovative development pipeline through discovery research focused on tumor microenvironment (intercellular interaction) and other key cancer pathways.
Oncology Development Pipeline

**Imuno-oncology**  
**Cancer metabolism**  
**Oncogenic signaling (including kinase inhibitor)**

<table>
<thead>
<tr>
<th>Compound</th>
<th>Mechanism of Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>napabucasin</td>
<td>(ROS generator)</td>
</tr>
<tr>
<td>alvocidib</td>
<td>(CDK9 inhibitor)</td>
</tr>
<tr>
<td>DSP-7888</td>
<td>(WT1 cancer peptide vaccine)</td>
</tr>
<tr>
<td>duberminib</td>
<td>(AXL kinase inhibitor)</td>
</tr>
<tr>
<td>DSP-0509</td>
<td>(TLR7 agonist)</td>
</tr>
<tr>
<td>DSP-0337</td>
<td>(napabucasin prodrug)</td>
</tr>
<tr>
<td>TP-1287</td>
<td>(CDK9 inhibitor)</td>
</tr>
<tr>
<td>TP-0184</td>
<td>(ALK2 inhibitor)</td>
</tr>
<tr>
<td>TP-3654</td>
<td>(PIM kinase inhibitor)</td>
</tr>
<tr>
<td>TP-1454</td>
<td>(PKM2 activator)</td>
</tr>
<tr>
<td>TP-5809</td>
<td>*</td>
</tr>
<tr>
<td>DSP-5336</td>
<td>*</td>
</tr>
<tr>
<td>DSP-0390</td>
<td>*</td>
</tr>
</tbody>
</table>

* The mechanism of action is not disclosed
Cocktail vaccine containing “peptide inducing WT1-specific CTL” and “peptide inducing helper T cells”

- One of the front-runner WT1 peptide vaccines
- Treatment with DSP-7888 resulted in longer, overall survival (OS) in WT1-positive patients compared with WT1-negative patients (Figure 2)

**Figure 1: The mechanism of DSP-7888**

- Injection
- Peptides
- Antigen presenting cell
- Peptides are presented on antigen presenting cell
- CTLs and helper T cells are induced. Helper T cell enhance the activity of CTL
- Clonally expanded WT1-specific CTLs attack WT1-expressing cancer cells

**Figure 2: Overall survival and WT1 immune response**

**Phase 1/2 study for Myelodysplastic syndrome (NCT02436252)**

<table>
<thead>
<tr>
<th></th>
<th>Median overall survival, months (90% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All (N=37)</td>
<td>9.4 (7.3-13.6)</td>
</tr>
<tr>
<td>Positive (n=29)</td>
<td>10.3 (7.6-16.3)</td>
</tr>
<tr>
<td>Negative (n=8)</td>
<td>4.9 (2.6-8.8)</td>
</tr>
</tbody>
</table>

Log-Rank P=0.0045 (Positive vs Negative)

**EHA 2019 (#1344)**
In a Phase 1 study of WT1 peptide vaccine WT2725, complete response (CR) was observed in 2 patients with glioblastoma (GBM).

A global Phase 2 study of DSP-7888, a next-generation drug after WT2725, is ongoing in patients with glioblastoma (GBM) (WIZARD-201G study, NCT03149003)

- Patient recruitment has been completed, and follow-up of overall survival is ongoing.
A phase 1/2 study of DSP-7888 in combination with an immune checkpoint inhibitor is ongoing

- Synergic effect of DSP-7888 in combination with immune checkpoint inhibitor was confirmed in mice (Figure)
- Tolerability in human subjects has been confirmed and the recommended dose is determined
- Progressed to Phase 2 study in patients with platinum-resistant ovarian cancer who do not respond well to immune checkpoint inhibitor monotherapy

**Figure: Preclinical result in mice resistant to immune checkpoint inhibitors**

- Anti-tumor activity was enhanced by a combination with immune checkpoint inhibitor

- **DSP-7888**
  - Increase tumor-infiltrated CTL

- **Anti-PD-1 antibody**
  - Eliminate exhaustion of tumor-infiltrated CTL

**Mechanism of combination effect**

ASH 2016 (#4715)
Dubermatinib (TP-0903) (Immuno-oncology, Oncogenic signaling)

- An inhibitor of multikinase including AXL\(^1\) kinase, being explored in various indications
  - Discovered by phenotypic screening targeting epithelial-to-mesenchymal transition (EMT) which is involved in tumor proliferation, infiltration, and metastasis and therapeutic resistance
  - Potent inhibitory activity against multiple kinases including AXL, potential targets of tumor therapy
  - A Phase 1b basket study to explore indications is ongoing

1) AXL receptor tyrosine kinase inhibitor
Systemically deliverable TLR7 agonist with anti-tumor efficacy by activating dendritic cell for cytokine induction and CTL activation

- Rapid elimination from the body ensures safety with maintaining efficacy and makes intravenous administration possible (Figure 1)
- Long-lasting anti-tumor immunity is expected through induction of immune memory T-cells (Figure 2)
- Anti-tumor activity mediated by CTL activation (Figure 3)
- Synergistic effect was confirmed in mice treated with DSP-0509 in combination with immune checkpoint inhibitor (Figure 4)
- Phase 1 study (dose escalation therapy) is ongoing for monotherapy and combination therapy

**Figure 1: PK profile (rat)**

**Figure 2: Induction of memory T-cells in combination therapy with immune checkpoint inhibitor**

**Figure 3: CTL activation mediated by immunomodulation**

**Figure 4: Synergic effect with immune checkpoint inhibitor (mice)**

AACR 2018 (#4726)
**Expected efficacy in the treatment of myelofibrosis patients with high unmet medical needs**

- PIM kinases are main effector molecules in JAK/STAT signaling pathway and play an important role in cell proliferation and oncogenesis (Figure 1).
- Expression of PIM kinases is increased in myelofibrosis patients and hematopoietic cells of animal models (Figure 2).
- In animal model, TP-3654 in monotherapy and in combination with ruxolitinib\(^1\) showed reduction in fibrosis in the spleen and bone marrow (Figure 3).
- A Phase 1 study with myelofibrosis patients is ongoing.

---

1) JAK inhibitor
Expected to treat various cancer types through inhibition of ALK2, ALK5, and other members of the TGF-β superfamily

- TGF-β regulates cell differentiation, proliferation, and apoptosis and is involved in a variety of physiological and pathological processes including cancer (Figure 1)
- Genetic mutation of ALK2 is found in various types of cancer including endometrial cancer, melanoma, colorectal cancer, bladder cancer, breast cancer
- In myelodysplastic syndrome (MDS), ALK5-pathway is activated, increasing the downstream SMAD2/3 complex phosphorylation and resulting in altered erythroid differentiation (Figure 2)
- A Phase 1 study in solid cancer is ongoing, and a Phase 1 study in hematologic cancer will be started

1) ALK: Activin-like receptor kinase

Figure 1: Physiological/pathological processes in which TGFβ is involved

Figure 2: ALK2 signaling pathway
With a new mechanism influencing on glucose metabolism in tumor cells to improve immune environment, anti-tumor efficacy in combination with immune checkpoint inhibitor is expected

- Promotes formation of PKM2 tetramer (highly active form) from its dimeric form which is predominant in tumor cells
- Activation of PKM2 converts anaerobic environment of tumor cells into aerobic conditions (Figure 1)
- Synergistic effect was confirmed in mice treated with DSP-1454 in combination with immune checkpoint inhibitor (Figure 2)

A phase 1 study is scheduled to start in Q1 FY2020

Figure 1: Major mechanism of action of TP-1454

Figure 2: Synergic effect with immune checkpoint inhibitor (mice)

1) PKM2 : Pyruvate kinase M2
Reinforcement of Development

Oncology

Characteristic features of Oncology Area

- Pursuing R&D with higher success rate, more agility and more compact than before, by utilizing cutting-edge technologies, regulatory systems, and development methodology unique to Oncology Area.

- Highly Efficient R&D
  - Cutting-edge analytic technology
  - Network-oriented R&D
  - Cutting-edge regulatory affairs systems
  - Cutting-edge diagnostic tools and biomarkers
  - Cutting-edge clinical trial designs

- Segmented diseases
- More flexible and rapid regulatory path
- Frequent collaborative development (e.g. consortium)
- Opportunities for expanding indications
- High expectations for fulfilling unmet medical needs
- Importance of biomarkers
- Standard therapies continue to change rapidly
- Ready to adopt advanced technology (such as AI)
Toward the Future: Bring in External Innovations

With the objective to bring in external innovations, such as cutting-edge technologies and candidate drugs, venture capital investment specialized in oncology and collaboration with academia have been initiated through Boston Biomedical, Inc. as the Hub, in addition to the ongoing DSK project with Kyoto University.

- Investment has been made into MPM Oncology Innovations Fund, a venture fund that makes investments mainly in drug discovery seeds from Dana-Farber Cancer Institute
- Alliance in research with Columbia University, Harvard University, and Wistar Institute has been initiated
Oncology Mid-Term Strategy

To advance development in a steady and speedy manner to establish oncology franchise.

Late stage assets
- napabucasin

Mid/Early stage assets
- Highly efficient R&D supported by cutting-edge technology and methodology
- Internal discovery
- External innovation
  - Alvocidib
  - Dubematinib
  - DSP-7888
  - TP-1454
  - DSP-0509
  - TP-0184
  - TP-3654
  - TP-1287
  - DSP-0337
  - DSP-5336
  - TP-5809

Early establishment of Oncology franchise
- Network-oriented R&D
- Cutting-edge regulatory affairs systems
- Cutting-edge clinical trial designs
- Cutting-edge diagnostic tools and biomarkers
- Diversified and innovative pipeline
Development Pipeline: SEP-363856
Advancing Life-Transforming Therapies in Neuropsychiatry

Kenneth S. Koblan, Ph.D.
Chief Scientific Officer
Sunovion Pharmaceuticals Inc.
Global Neuropsychiatric Challenges with Significant Need

SEP-363856 has the potential to treat the positive and negative symptoms of schizophrenia, including cognitive impairment, as well as the hallucinations and delusions commonly experienced by patients with Parkinson’s disease (PD).

**SCHIZOPHRENIA**
- Affects **23 million** people worldwide\(^1\)
- Approximately **2.4 million** people diagnosed in the U.S.\(^2\)
- Limited treatment options exist, and currently available products:
  - Have significant side effects that may affect adherence
  - No new MOAs approved in >60 years – target either dopamine 1 and/or dopamine 2 receptors and Serotonin 5-HT\(_{2A}\)
- Significant cognitive impairment is common, affecting up to 75% of patients,\(^5\) with no currently approved therapies

**PARKINSON’S DISEASE PSYCHOSIS (PDP)**
- PD is the second most common neurodegenerative disease and is expected to affect ~1.2 million people in the U.S. and an ~10 million people worldwide within the next 10 years\(^3\)
- Affects up to **60 percent** of patients with PD\(^3\)
- Includes hallucinations and delusions
- Is a strong predictor of nursing home placement and mortality\(^4\)
- Current treatment options are limited

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\(^4\) Aarsland 2000 Journal of American Geriatric Society, v48, pg 938, conclusion

\(^5\) Talreja 2013 Industrial Psychiatry Journal v22(1), pg 47-53, conclusion
Sunovion’s phenotypic discovery approach is target agnostic and begins with in vitro anti-target screening and in vivo screening followed by additional medicinal chemistry efforts based on our deep expertise in neuropsychiatry.

Sunovion discovered SEP-363856 in collaboration with PsychoGenics based in part on a mechanism-independent approach using the in vivo phenotypic SmartCube® platform and associated artificial intelligence algorithms.


Sunovion discovered SEP-363856 in collaboration with PsychoGenics based in part on a mechanism-independent approach using the in vivo phenotypic SmartCube® platform and associated artificial intelligence algorithms.
SEP-363856 does not bind to D₂ or to serotonergic receptors (except for 5-HT₁A), which are thought to mediate the effects of currently available antipsychotic medicines.

SEP-363856 is a TAAR1 (trace amine-associated receptor 1) agonist in development for the treatment of schizophrenia.
Development Pipeline: SEP-363856 PET Imaging

Lack of Blockade of Dopamine D₂ Receptors in All Animal Species Tested

In vivo PET imaging of [¹⁸F]-fallypride binding to D₂ receptors in rhesus at 20x effective clinical concentrations of SEP-363856
Mechanism of Action on Dopamine Neurocircuitry

fMRI probes core dopaminergic reward circuitry including ventral striatum, insula and medial orbitofrontal cortex (mOFC) brain regions.

Placebo

Dopamine D₂ Antagonist

SEP-363856
Unique “Proof-of-Concept” Development Approach

Designed global, registration studies to evaluate SEP-363856

**STUDY 201**
- Double-blind Treatment
  - (4 Weeks - Inpatient)
  - 245 patients

**STUDY 202**
- Open-Label Extension
  - (6 Months - Outpatient)
  - 157 patients

201 PRIMARY ENDPOINT:
- Change from baseline in Positive and Negative Syndrome Scale (PANSS) total score versus placebo at Week 4

201 SECONDARY ENDPOINTS:
- CGI-S score
- PANSS subscale scores
- Brief Negative Symptom Scale (BNSS) total score
- Montgomery Asberg Depression Rating Scale (MADRS) total score
- Proportion of PANSS responders (>20% decrease in PANSS total score)

SAFETY/TOLERABILITY:
- Incidences of adverse events, serious adverse events, and adverse events leading to discontinuation from study
SEP-363856 showed statistically significant and clinically meaningful improvement in the Positive and Negative Syndrome Scale (PANSS) total score compared to placebo after four weeks of treatment (-17.2 vs. -9.7, respectively; p=0.001).
Development Pipeline: SEP-363856 201 study
Statistically Significant Improvement in Brief Negative Symptom Scale (BNSS) Score Over Four Weeks

Improvement was found in the Brief Negative Symptom Scale (BNSS) total score (p<0.001) and all major PANSS (positive, negative and general psychopathology) subscales (p<0.02)

Improvement was found in the the Brief Negative Symptom Scale (BNSS) total score (p<0.001) and all major PANSS (positive, negative and general psychopathology) subscales (p<0.02)
Effectiveness Sustained Over Six Months

Clinically meaningful improvement seen in the Positive and Negative Syndrome Scale (PANSS) total score.
SEP-363856 was associated with functional improvement as measured by the UPSA-B over six months.
## Development Pipeline: SEP-363856

### Safety and Tolerability Comparable to Placebo

No new safety or tolerability effects during the 6-month open label period

### 4-WEEK DOUBLE-BLIND PERIOD

<table>
<thead>
<tr>
<th>Preferred Term</th>
<th>Placebo (N = 125)</th>
<th>SEP-363856 (N = 120)</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (%)</td>
<td>n (%)</td>
<td></td>
</tr>
<tr>
<td>Somnolence</td>
<td>6 (4.8%)</td>
<td>8 (6.7%)</td>
</tr>
<tr>
<td>Agitation</td>
<td>6 (4.8%)</td>
<td>6 (5.0%)</td>
</tr>
<tr>
<td>Nausea</td>
<td>4 (3.2%)</td>
<td>6 (5.0%)</td>
</tr>
<tr>
<td>Insomnia</td>
<td>13 (10.4%)</td>
<td>4 (3.3%)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>1 (0.8%)</td>
<td>3 (2.5%)</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>0</td>
<td>3 (2.5%)</td>
</tr>
<tr>
<td>Anxiety</td>
<td>9 (7.2%)</td>
<td>2 (1.7%)</td>
</tr>
<tr>
<td>Patients with any extrapyramidal symptom</td>
<td>4 (3.2%)</td>
<td>4 (3.3%)</td>
</tr>
</tbody>
</table>

**RETENTION RATE**

- **Placebo:** 79.2%
- **SEP-363856:** 78.3%

### CLINICAL SAFETY AND TOLERABILITY

- Favorable profile, without class-related side-effects of currently marketed antipsychotics
- Effects on extrapyramidal symptoms, weight, lipids, glucose, prolactin, and ECG parameters did not differ significantly from placebo
- Low discontinuation rates
Phase 3 DIAMOND Program Underway

- End of Phase 2 meeting with U.S. Food and Drug Administration (FDA) completed
- DIAMOND program determined to be suitable to support registration, if successful
  - Replication of pivotal SEP-856-201 study
- Global, multicenter program includes four studies that are designed to evaluate the safety, efficacy and tolerability of SEP-363856

### DIAMOND 1
A six-week, randomized, double-blind, parallel-group, placebo-controlled, fixed-dose, multicenter study to evaluate the efficacy and safety of SEP-363856 in acutely psychotic adults and adolescents (13 to 17 years of age) with schizophrenia [ClinicalTrials.gov: NCT04072354]

### DIAMOND 2
A six-week, randomized, double-blind, parallel-group, placebo-controlled, fixed-dose, multicenter study to evaluate the efficacy and safety of SEP-363856 in acutely psychotic adults with schizophrenia [ClinicalTrials.gov: NCT04092686]

### DIAMOND 3
A 52-week, outpatient, multicenter, flexible-dose, open-label long-term safety and tolerability extension study of SEP-363856 in adults and adolescents with schizophrenia who completed either the DIAMOND 1 or DIAMOND 2 study [ClinicalTrials.gov: NCT04109950]

### DIAMOND 4
A 52-week, randomized, double-blind, active comparator-controlled long-term safety and tolerability study of SEP-363856 in adults with schizophrenia [ClinicalTrials.gov: NCT04115319]
Summary and Next Steps in the SEP-363856 Program

**SEP-363856**
- Is a novel agent with a non-D\(_2\) mechanism of action, distinct from currently marketed antipsychotics
- Efficacy, safety and tolerability demonstrated in multi-center global 4-week study and 6-month extension study
- Absence of movement disorder symptoms; no weight, metabolic impairment observed to date

**Innovative drug profile**
- Non binding to dopamine D\(_2\) receptor
- Potential for high efficacy to treat positive and negative symptoms
- Potential for major improvement in differentiated drug safety and tolerability

**SCHIZOPHRENIA**
- Breakthrough Therapy Designation received (May 2019)
- Phase 3 studies (DIAMOND) underway
  - Data readouts expected to begin in FY2021
  - Includes both adolescents and adults

**ADDITIONAL INDICATIONS**
- Phase 2 Parkinson's disease psychosis (PDP) results expected in 1H2020
- A number of additional indications are under consideration, including mood disorders
Appendix
Strength in Productivity to Produce Psychiatry & Neurology Drugs

● Success rate in R&D
(Ratio of drugs approved/drugs entered in clinical phase 1)

Historically productive in this area, with higher success rate than industrial average

27 compounds in Clinical phase
4 products launched

- LONASEN (2008)
- TRERIEF (2009)
- LATUDA (2011)
- APTIOM (2014)

Success Rate in Psychiatric & Neurologic area has been very low industry-wide; our success rate above industry average
Appendix (Psychiatry & Neurology)

In-Silico Driven First-In Class Drug Discovery in Our Company

The series of sophisticated in-silico technologies to create real drug on computer

1. Seed exploration
   (Effective Concepts)
   Integrated analysis of scientific big data
   Validation with real word data
   - Compounds
   - Biological response (Clinical)

2. Lead discovery
   (Effective Drugs)
   Synergy of AI and simulation
   - Biomolecules
   - Biological function
   - iSIDE

3. Biomarker identification
   (Efficacy Evidences)
   Deep biomedical profiling of patients
   - Biological response (Non-clinical)
Patients treated with SEP-856 showed improvement in the overall severity of illness as assessed by the Clinical Global Impression Scale - Severity (CGI-S) \( (p<0.001) \)

**Statistically Significant Improvement in Clinical Global Impression Scale Over Four Weeks**

**Appendix (Development Pipeline: SEP-363856 SEP856-201 study)**

Patients treated with SEP-856 showed improvement in the overall severity of illness as assessed by the Clinical Global Impression Scale - Severity (CGI-S) \( (p<0.001) \)

- **Effect size:** 0.52
- **p-value:** <0.001

**WEEK 4 SECONDARY ENDPOINT**

Effect size: 0.52
p-value: <0.001

- **placebo**
- **SEP-363856**
  - (50 or 75 mg/d)

**N=245**

![Graph showing improvement in CGI-S over 4 weeks](image-url)
PANSS responders increased 30% from baseline over time
Appendix

Becoming a Data-Driven Pharmaceutical Company

For greater efficiency in R&D, Global Data Design Office in cooperation with Sumitovant is considering utilization of DrugOme and Digital Innovation within the Sumitomo Dainippon Pharma Group

DrugOme

- Computational Ecosystem centering around a Computational Research Team with a high degree of professional knowledge in data science
- Swiftly provides high quality solutions to various business problems by integrating a myriad of data

Digital Innovation

- Dedicated Digital Innovators will be assigned to each business department. Applying digital technologies, Digital Innovators will help solve business problems and improve business efficiency
- Application of successful measures to other groups with similar problems

Data source → Integrated database → Analysis → Output

**Collect data**
- Structured data sources
  - Pharmaceutical data
  - Target molecule data
  - Clinical trial registry
  - FDA data
  - Insurance claims data
- Unstructured data sources
  - FDA filings
  - SEC filings
  - Press releases
  - Academic research

**Synthesize data**
- Analysis tools
- Bespoke analyses
- Analysis tools
- Support for clinical development
- Search for promising assets

**Conduct analysis**

**Output**

- Improved decisions

- New asset idea generation
- Interactive map of asset landscape
- Detailed market assessment
- Formulation of development strategy
- Toxicology risk assessment
- Clinical trial enrollment

Example Digital Solutions

Rare disease patient identification
Operational risk monitoring
Salesforce optimization

Automation of trial oversight
Automated sub-group efficacy analyses
Innovation today, healthier tomorrows