CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING INFORMATION

In this material, statements made with respect to current plans, estimates, strategies and beliefs and other statements that are not historical facts are forward-looking statements about the future performance of Astellas Pharma. These statements are based on management’s current assumptions and beliefs in light of the information currently available to it and involve known and unknown risks and uncertainties. A number of factors could cause actual results to differ materially from those discussed in the forward-looking statements. Such factors include, but are not limited to: (i) changes in general economic conditions and in laws and regulations, relating to pharmaceutical markets, (ii) currency exchange rate fluctuations, (iii) delays in new product launches, (iv) the inability of Astellas to market existing and new products effectively, (v) the inability of Astellas to continue to effectively research and develop products accepted by customers in highly competitive markets, and (vi) infringements of Astellas’ intellectual property rights by third parties.

Information about pharmaceutical products (including products currently in development) which is included in this material is not intended to constitute an advertisement or medical advice.
AGENDA

1. **Introduction**
   Naoki Okamura
   Representative Director, Executive Vice President, CStO and CFO, CBO

2. **New Research Organization**
   Yoshitsugu Shitaka, Ph.D.
   Corporate Executive, CScO
INTRODUCTION

Naoki Okamura
Representative Director, Executive Vice President
Chief Strategy Officer (CStO) and Chief Financial Officer (CFO)
Chief Business Officer (CBO)
Continuously create unique programs by driving Focus Area approach toward sustainable growth over the long term

Research based on Focus Area approach

Common Definition of VALUE

\[
VALUE = \frac{Outcomes}{Cost}
\]

Outcomes: that matter to patients

Cost: to the healthcare system of delivering those outcomes

FOCUS AREA APPROACH AND RESEARCH ORGANIZATION STRUCTURE

Acquired external technologies and assets under Focus Area approach strategy, leading to a variety of internal organizations and programs

Portfolio management in research phase
- Comprehensive management while maintaining autonomous program creation activities in each organization
- Establishment of Chief Scientific Officer (CScO) and new research organization structure

Portfolio management in Primary Focus
- Oversight of overall strategy by CStO
- Strategy development, program prioritization and life cycle management in each Primary Focus
- Decision-making process “Kachi”: Aiming for real-time project evaluation and portfolio management fitting with the characteristics of new modalities (to start in 2022)
NEW RESEARCH ORGANIZATION

Yoshitsugu Shitaka, Ph.D.
Corporate Executive
Chief Scientific Officer (CScO)
MY JOURNEY TO CHIEF SCIENTIFIC OFFICER

Yoshitsugu SHITAKA, Ph.D.
Corporate Executive, Chief Scientific Officer (CScO)

**Brief history:**

- 1996: Joined the Company
- 2012: Head of Frontier Disease Research, Pharmacology Research Labs
- 2016: President, Astellas Institute for Regenerative Medicine (AIRM)
- 2021: Present post
TODAY'S AGENDA

1 OUTLINE, CONCEPT, AND AIM OF RESEARCH REORGANIZATION

2 DEVELOPING AND OPERATING PRODUCT CREATION UNITS
**CONCEPT OF REORGANIZATION**

### Before
1. DDR*1 was a hierarchical and function-led organization
2. Strategy was not efficacious for DDR and the acquired bio-ventures to create synergy
3. Two organizations handle early- and late-stage partnering opportunities respectively

### After
1. DDR is dissolved and its product creation functions are transformed into agile in-house bio-ventures
2. Research divisions are integrated into CScO accountability, with a comprehensive strategy and a synergy-driven management system implemented
3. Partnering functions are consolidated

*1 Drug Discovery Research  *2 To be a new Business Development division under Chief Business Officer
THE NEW RESEARCH ORGANIZATION

CScO

Research Architect Lead

Affiliate Engagement

Research Strategy & Communications

Early-Stage Partnering

AIRM

Universal Cells

Xyphos

Immuno-Oncology

AGT

Mitobridge

Discovery Accelerator

Applied Research & Operations

Product Creation Units

★ : In-house bio-ventures established in the present reorganization

- ‘One Partnering Team’ for all potential partners and all stages
- Bio-venture-like agile research model
- Full use of proprietary technology/capability to boost VALUE
- Synergy-driven management system
RESEARCH ORGANIZATION OVERVIEW

Astellas

‘One Partnering Team’ for all potential partners and all stages

- Strengthening capabilities as a new Business Development division
- Established networks in key bio-clusters in the US, EU and Japan which cover diverse stakeholders

Bio-venture-like agile research model

- Full use of proprietary technology/capability to boost VALUE

Ideation & Creation

Venture Unit

Research Engine

- Autonomous VALUE creation by each Product Creation Unit
- Lifecycle and growth mechanism mimicking venture ecosystems
- Provision of leading platform technology, regulatory science, translational science, etc.
- Co-innovation/Co-creation with Manufacturing from early drug development stages

Synergy-driven management system

- New decision-making system to create synergy
- Fit-for-purpose administration function

External

Academia Start up Bio-venture

12
‘One Partnering Team’ for all potential partners and all stages

**Bio-venture-like agile research model**
- Autonomous VALUE creation by each Product Creation Unit
- Lifecycle and growth mechanism mimicking venture ecosystems

- Full use of proprietary technology/capability to boost VALUE
- Synergy-driven management system

**AIRM**: Astellas Institute for Regenerative Medicine,
**AGT**: Astellas Gene Therapies, in which Gene Therapy Research & Technical Operations is referred to here
CHALLENGES IN PREVIOUS ORGANIZATION

Hierarchical, Function-led Organization

Hierarchy-dependent Decision Making

- **Slow Decision Making**
  Researchers participate in research programs on behalf of each department. Decision making takes time as each member requires internal discussion and manager's approval for it.

- **Difficulty in following latest technology trends**
  As technology becomes more sophisticated and diverse, it is difficult for the managers to provide professional and appropriate instruction to all issues.

Sequential Operation (Waterfall Model)

- **Risk of bottlenecks and turning back**
  Each function conducts tasks as ordered and hands over to the subsequent process, once the outcome meets the pre-defined criteria. It efficiently works in well-experienced areas, while it may become stuck or sometimes be forced to turn back when faced with unprecedented problems in new areas.
Members with various expertise get together to iterate by trial and error to continuously improve solutions. Highly delegated mission-specific units make quick decisions and act autonomously.

Transfer of authority and allocation of resources in line with the growth of each Product Creation Unit (PCU)

**Strategic Stage**

<table>
<thead>
<tr>
<th>Exploratory Research</th>
<th>PF Candidate</th>
<th>Primary Focus</th>
</tr>
</thead>
</table>

**Research Organization**

- **Goal**: Establishing a Research Platform
  - To conduct research following the approved research plan

- **Participants**
  - 1 – 5

- **Programs**
  - 1 – 2

- **Authority**
  - 10 – 30
  - 3 – 5

**Focus Area**

- Ideation & Creation
- Incubation / Start-up
- Venture Unit
- Research Engine

**PF Candidate**

- Lead Program Creation
- Resource allocation to create VALUE continuously

**Primary Focus**

- Drug Candidate Creation and Program Expansion
- Selection of product candidates

PF: Primary Focus
Each Research Engine led by outstanding CSO and SAB members attracts competitive talent to grow

**Universal Cells**
President: Noboru Yamaji  
Immuno-Oncology, Immune Homeostasis

**Mitobridge**
President: Mike Patane  
SAB: H. Robert Horvitz, Ron Evans etc.  
Mitochondria Biology

**AIRM**
President: Hide Goto  
CSO: Robert Lanza  
Blindness & Regeneration, Mitochondria Biology, Immuno-Oncology, Immune Homeostasis

**Xyphos**
President: Noboru Yamaji  
CSO: Gary Starling  
Immuno-Oncology

**AGT**
Div. Head: Mathew Pletcher  
Genetic Regulation

**Immuno-Oncology**
Div. Head: Taku Yoshida  
Immuno-Oncology

**PCU Headcount Growth**
- Figures at each fiscal year end (forecasted for FY2021)
- IO: Immuno-Oncology, UCells: Universal Cells

PCU: Product Creation Unit, CSO: Chief Scientific Officer, SAB: Scientific Advisory Board, Div: Division, AIRM: Astellas Institute for Regenerative Medicine, AGT: Astellas Gene Therapies, in which Gene Therapy Research & Technical Operations is referred to here, IO: Immuno-Oncology, UCells: Universal Cells
Full use of proprietary technology/capability to boost value

- Provision of leading platform technology, regulatory science, translational science, etc.
- Co-innovation/Co-creation with Manufacturing from early drug development stages

Synergy-driven management system

‘One Partnering Team’ for all potential partners and all stages

Bio-venture-like agile research model

AIRM: Astellas Institute for Regenerative Medicine,
AGT: Astellas Gene Therapies, in which Gene Therapy Research & Technical Operations is referred to here
NEEDS FOR EARLY COLLABORATION BETWEEN RESEARCH AND MANUFACTURING: EXAMPLE OF CELL THERAPY

Uniqueness in cell therapy: “Process is Product”

Small molecule drugs
- Changes in manufacturing process do NOT drastically affect the product characteristics (e.g. efficacy)
- Not difficult to demonstrate comparability

Cell therapy
- Changes in manufacturing process (raw materials, culture method, etc.) drastically affect the product characteristics (e.g. efficacy)
- Difficult to demonstrate comparability

Challenges in waterfall model
- Return to the first step in case that change occurs after the process handed to manufacturing

Form: Formulation, Dev: Development, GMP: Good Manufacturing Practice, Mfg: Manufacturing
Advantages of an agile model

- Avoid trouble after handover by collaborating from research stage
- In-house manufacturing capabilities enable flexible collaboration and know-how accumulation
- Effective model also for DDS-integrated products (gene therapy, mRNA, local administration, etc.)

Research and manufacturing are co-located as agile organizations

- In addition to AIRM, Universal Cells and AGT, collaboration in Tsukuba is being strengthened

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**Research and manufacturing are co-located as agile organizations**

<table>
<thead>
<tr>
<th>Research</th>
<th>Manufacturing</th>
</tr>
</thead>
<tbody>
<tr>
<td>GMP mfg</td>
<td>5 Process dev for stable production under GMP</td>
</tr>
<tr>
<td>Process/form dev</td>
<td>4 Formulation dev for efficient supply chain</td>
</tr>
<tr>
<td>1 Establishment of cell differentiation process based on efficacy</td>
<td>3 Process dev for mfg cost reduction</td>
</tr>
<tr>
<td>2 Raw materials complying with regional standard</td>
<td>2 Raw materials complying with regional standard</td>
</tr>
</tbody>
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**Research and manufacturing are co-located as agile organizations**

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<table>
<thead>
<tr>
<th>AIRM</th>
<th>Universal Cells</th>
<th>AGT*1</th>
<th>Tsukuba*2</th>
</tr>
</thead>
<tbody>
<tr>
<td>(HC: 202)</td>
<td>(HC: 101)</td>
<td>(HC: 310)</td>
<td>(HC: 1,013)</td>
</tr>
<tr>
<td>71%</td>
<td>36%</td>
<td>79%</td>
<td>35%</td>
</tr>
<tr>
<td>29%</td>
<td>64%</td>
<td>21%</td>
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<td>21%</td>
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<td>79%</td>
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</tr>
</tbody>
</table>

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**Abbreviations**

- DDS: Drug delivery system
- mRNA: Messenger ribonucleic acid
- GMP: Good Manufacturing Practice
- Mfg: Manufacturing
- Form: Formulation
- Dev: Development
- AIRM: Astellas Institute for Regenerative Medicine
- AGT: Astellas Gene Therapies
- HC: Headcount

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*1 Gene Therapy Research & Technical Operations of AGT
*2 Tsukuba Research Center and Tsukuba Biological Research Center

HC as of Oct 2021
**EARLY-STAGE PARTNERING**

- ‘One Partnering Team’ for all potential partners and all stages
  - Strengthening capabilities as a new Business Development division
  - Established networks in key bio-clusters in the US, EU and Japan which cover diverse stakeholders

- Bio-venture-like agile research model
- Full use of proprietary technology/capability to boost VALUE
- Synergy-driven management system

**Product Creation Units**

- AIRM: Astellas Institute for Regenerative Medicine
- Universal Cells
- Xyphos
- Immuno-Oncology
- AGT
- Mitobridge
- Discovery Accelerator
- Applied Research & Operations

AIRM: Astellas Institute for Regenerative Medicine,
AGT: Astellas Gene Therapies, in which Gene Therapy Research & Technical Operations is referred to here
Challenges in External Partnership

- Two organizations operate side-by-side and lead early- and late-stage alliance/asset acquisition projects; respectively Early-Stage Partnering (ESP) and Business Development (BD), in order to better handle different types of deals.
- The increasing size and complexity of early-stage deals make them closer to late-stage deals.
- As a result, frequent project hand-over occurs, and more coordination is required between the two organizations.
- The drawbacks become more apparent than the advantages of operating the two organizations.

April 2022

ESP and BD will integrate into a new Business Development division, which will report to Chief Business Officer (CBO)

New BD

- Unified and consistent partnering capability and talent development through early to late stage
- Speedy decision making
- Clearer point of contact to external partners
We have established network hubs in key Bio-Clusters on the West and East coast in North America, UK, and Japan

Achievements of networking

- Expansion of Global Network
  - Academia: Univ of California / Harvard Univ / Milner Institute / Kyoto Univ, The Univ of Tokyo, Tohoku Univ
  - Incubators: BioLabs (SF) / LabCentral (Boston) / WAPG (UK)
  - Venture capitals: US, EU, Japan

- Investment by Corporate Venture Capital
  - >$200M cumulative investment
  - Global top 7 ranking activity in first half of FY2020-2021 public report*

Achievements of Research Collaboration

- Academia
  - aAVC (RIKEN)
  - Oncolytic virus (Tottori Univ)
  - Engineered Phage (Gifu Univ)

Achievements of Biotech Acquisition
Synergy-driven management system

- New decision-making system to create synergy
- Fit-for-purpose administration function

‘One Partnering Team’ for all potential partners and all stages
Bio-venture-like agile research model
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## Challenges in Previous Research Management

- Lack of comprehensive research strategy that efficaciously guides each division to create synergy
- Rigid resource allocation incapable of flexible reallocation across divisions
- Lack of timely information transmission as Research
- Slowness of value enhancement of acquired assets

## New decision-making system to create synergy

**Research Leadership Summit**
- Consists of Division Leaders under CScO, chaired by CScO
- Members with diverse background discuss entire strategy, cross-divisional cooperation, portfolio management, resource allocation, etc. to make transparent and unbiased decisions

## Fit-for-purpose administration function

<table>
<thead>
<tr>
<th>Research Strategy &amp; Communications</th>
<th>Secretariat for Research Leadership Summit; integrating and optimizing research-wide total strategy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Conduct strategic and timely communications as Research</td>
</tr>
<tr>
<td>Affiliate Engagement</td>
<td>Support for newly joining research organizations</td>
</tr>
<tr>
<td>Research Architect Lead</td>
<td>Drive research transformation activities</td>
</tr>
<tr>
<td></td>
<td>Supporting individual activities such as operation design, cross-divisional collaboration mechanism, etc.</td>
</tr>
</tbody>
</table>
TODAY'S AGENDA

1. OUTLINE, CONCEPT, AND AIM OF RESEARCH REORGANIZATION

2. DEVELOPING AND OPERATING PRODUCT CREATION UNITS
   - CREATE VALUE FROM THE COMBINATION OF CUTTING-EDGE TECHNOLOGIES: CAR-NK FAMILY
   - GROWTH OF VENTURE UNIT: PROTACs
CREATE VALUE FROM COMBINATION OF CUTTING-EDGE TECHNOLOGIES: CAR-NK FAMILY

Creating VALUE that our competitors cannot follow from the combination of cutting-edge technologies

**CAR-NK (PF: Immuno-oncology)**
- Though the pharmaceutical efficacy of CAR-NK in B-cell tumor is being confirmed, there are many challenges for the current developed products.
- We aim to overcome these challenges with products differentiated from allogeneic pluripotent stem cells and aim to expand indications especially for solid tumor.
- As this requires multiple advanced technology elements, many divisions in Research and Manufacturing are collaborating.

CAR: Chimeric antigen receptor, NK: Natural killer, PF: Primary Focus, AIRM: Astellas Institute for Regenerative Medicine, PSC: Pluripotent stem cell, HLA: Human leukocyte antigen, UCells: Universal Cells, UDC: Universal donner cell, cCAR: convertibleCAR, GMP: Good Manufacturing Practice
GROWTH OF VENTURE UNIT: PROTACs

Venture Units steadily growing

I&C  |  Venture Unit  |  Research Engine
---|---|---
Research platform establishment  |  Lead program creation  |  Drug candidate creation and program expansion

- Microglia
- Innate Immunity
- Human Genetics
- Engineered Phage Therapy
- Tumor-directed Inhibition
- Specific Treg
- PF Candidate
- PF Candidate

PROTACs (Venture Unit: Tumor-directed Inhibition, PFC: Cancer Genomic Alteration)

**POI Binder:**
Component that binds to the target protein

**E3 Binder:**
Ligand that recruits E3 ubiquitin ligase

**Linker:**
Crosslinker between POI binder and E3 binder

PROTAC: PROteolysis TArgeting Chimera, I&C: Ideation & Creation, PF: Primary Focus, POI: Protein of interest
RESEARCH ORGANIZATION OVERVIEW

Astellas

- Strengthening capabilities as a new Business Development division
- Established networks in key bio-clusters in the US, EU and Japan which cover diverse stakeholders

Bio-venture-like agile research model

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Full use of proprietary technology/capability to boost VALUE

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- Fit-for-purpose administration function

Synergy-driven management system

- ‘One Partnering Team’ for all potential partners and all stages

External

Academia  Start up  Bio-venture
ON THE FOREFRONT OF HEALTHCARE CHANGE