Astellas’ Corporate-wide Digital Transformation Driven by Analytics
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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. Information about investigational compounds in development does not imply established safety or efficacy of the compounds; there is no guarantee investigational compounds will receive regulatory approval or become commercially available for the uses being investigated.
Agenda

I. What Astellas is Aiming for with Corporate-wide Digital Transformation
   Naoki Okamura, Chief Strategy Officer

II. Corporate-wide Digital Transformation Driven by Analytics
    Masanori Ito, Ph.D., MBA, Senior Director, Advanced Informatics & Analytics
What Astellas is Aiming for with Corporate-wide Digital Transformation

Naoki Okamura, Chief Strategy Officer
VALUE Creation

Vision

On the forefront of healthcare change to turn innovative science into VALUE for patients

Business Activity

Strategy: Corporate Strategic Plan 2021

Portfolio

Primary Focus

Project

Talent and Organization

Output

XTANDI and Priority Strategic Products

Products derived from Focus Area Approach

VALUE = \frac{Outcomes}{Cost} to the healthcare system of delivering those outcomes

Astellas R&D Strategy
Analytics to turn innovative science into VALUE

**Focus Area Approach**

is designed to identify drug discovery opportunities flexibly and efficiently by combining innovative biologies and modalities/technologies to address diseases with high unmet medical needs

**Primary Focus**

<table>
<thead>
<tr>
<th>Biology/Modality/Technology 1</th>
<th>Genetic Regulation</th>
<th>Immuno-Oncology</th>
<th>Blindness &amp; Regeneration</th>
<th>Mitochondria</th>
<th>Targeted Protein Degradation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gene replacement (AAV)</td>
<td>Checkpoint</td>
<td>Artificial adjuvant vector cell (aAVC)</td>
<td>Cell replacement</td>
<td>Gene regulation (AAV)</td>
<td>Protein degradation</td>
</tr>
<tr>
<td>Checkpoint</td>
<td>Artificial adjuvant vector cell (aAVC)</td>
<td>Oncolytic virus (intratumoral)</td>
<td>Cell replacement (UDC)</td>
<td>Mitochondrial stress</td>
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<td>Oncolytic virus (systemic)</td>
<td>Bispecific immune cell engager</td>
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</tbody>
</table>

1. Not exhaustively listed.

AAV: Adeno-associated virus, UDC: Universal donor cell

Coordinate a portfolio of various possibilities
→ Analytics and modeling support this decision making
Corporate-wide DX: Data-Driven Management Decisions

Database of companies and products in the industry

Insights on business models from portfolio profiling

Revealing strengths and opportunities to identify partners that lead to increased corporate value

CF: Cash flow, D: Debt, EBITDA: Earnings Before Interest payments, Tax Depreciation, and Amortization
What Astellas is Aiming for with Corporate-wide Digital Transformation

A state in which all data, from management decisions to individual projects, is organically connected to maximize VALUE

**Input**
- Financial Capital
- Manufacturing Capital
- Intellectual Capital
- Social and Relational Capital
- Human Capital
- Natural Capital

**Output**
- XTANDI and Priority Strategic Products
- Products derived from Focus Area Approach

**Business Activity**
- Strategy: Corporate Strategic Plan 2021
- Portfolio
- Primary Focus
- Project
- Talent and Organization

**VISION**
On the forefront of healthcare change to turn innovative science into VALUE for patients

Corporate-wide Digital Transformation Driven by Analytics

Masanori Ito, Ph.D., MBA
Senior Director, Advanced Informatics & Analytics
AIA Responsible for Data Analytics across Entire Company

**Major divisions responsible for DX**

- **Transformation of Existing businesses**
  - AIA*
    - Advanced data analysis
      - Transformation of existing operations
        - Renewal of digital infrastructure
          (data analysis, AI utilization, workspace)
    - Information Systems
    - Integration in FY2023

- **New businesses**
  - Rx + Business Accelerator
    - Establishment of new businesses

**Groups in AIA**

- **Enterprise Insights and Digital Solutions**
  - Supporting the division’s strategic decision-making through advanced analytics and modeling solutions

- **Real World Data Innovations and Solutions**
  - Enable data-driven decision-making through innovative solutions leveraging real-world data to generate robust insights at scale and at speed

- **Digital Research Solutions**
  - Promotes and accelerates drug discovery R&D projects using the latest knowledge and technologies related to advanced medical big data, digital technologies, and advanced data analysis technologies

- **Technology, Governance and Informatics**
  - Expands and supports advanced analytical capabilities with technology, governance, and data engineering

*AIA: Advanced Informatics & Analytics*
Characteristics of the Pharmaceutical Industry:

High levels of uncertainty while needing a lot of investment

Success rate*¹
7.9%

Phase I to approval

Assumptions change over long development period
• Hypotheses about biology
• Number of patients, competitive products, social conditions, etc.

Development period*¹
10.5 years

R&D expenses*²
$1B

Huge investments

Success rate*¹ is very low

Difficult decision on what to invest in and when

*²: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7054832/
Adopt analytical techniques appropriate to “Focus Area Approach”

Since the innovative drug development we are working on is highly uncertain, it is necessary to support optimal management decisions based on simulation, in addition to "prediction from past data", which has been remarkably developed by AI in recent years.

<table>
<thead>
<tr>
<th>Available data</th>
<th>Current Focus Area Approach</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Much data accumulated in-house</td>
<td></td>
</tr>
<tr>
<td>• Many public databases</td>
<td>• Limited in-house data</td>
</tr>
<tr>
<td>• Many bibliographic references</td>
<td>• Limited public databases</td>
</tr>
<tr>
<td></td>
<td>• Limited bibliographic references</td>
</tr>
<tr>
<td></td>
<td>• Rare diseases</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Analysis method</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Prediction from historical data (Data-driven)</td>
<td>Prediction from historical data (Data-driven) + Inference based on simulation</td>
</tr>
</tbody>
</table>
Simulation-based Forecasting to Confront Uncertain Situations

Important Points for Simulation
• Forecasting by “range” rather than “single points”
• Identification of scenarios and countermeasures
• Accumulation of data to update assumptions and countermeasures
• Modeling to control uncertain situations

Benefits of Simulation
• Decision-making based on trade-offs
• Transparency and consistency in decision making
• Updating of actions in response to changes in the internal and external environment
Simulation of Project Valuation in Drug Development

VoLatility for sales is included at each phase

*Numbers are examples

DS: Discovery stage, P0~3: Phases of Clinical Trials, NDA: New Drug Application, NPV: Net Present Value
Portfolio-level Simulation
Advantage of Focus Area Approach

Non-Focus Area Approach
POC success is independent on each other with limited linkage between projects.

Focus Area Approach
POC success is dependent on each other. Success of lead program is likely to be followed by success of other programs based on the same platform.

Linkages between programs having Biology/Modality/Disease connection

Probability of occurrence in 1 million simulations

Focus Area Approach dramatically increases the probability of a highly profitable event.

POC: Proof of Concept, NPV: Net Present Value
Simulation-based forecasting and decision-making

Utilizing a model based on Monte Carlo simulations*, factors such as development success/failure and sales ups and downs are taken into account.

→Obtain possible scenarios and their probabilities of realization for pipeline outcomes

1 Generate 10,000 random observations 2 Calculated cashflows for each project 3 Output NPV Distribution

**Observation 1 | Baseline**
- Platform A
- Platform B
- Platform C

**Strategy A | Two failures allowed**
- Platform A
- Platform B
- Platform C

**Strategy B | Three failures allowed**
- Platform A
- Platform B
- Platform C

Monte Carlo simulation: A stochastic model that allows an element of uncertainty to be incorporated into future forecasts. The model can be used to produce different results each time based on the occurrence or non-occurrence of the uncertainty factor and the amplitude of its impact.

NPV: Net Present Value
Analytics is Utilized in All Areas of Enterprise to Maximize VALUE

On the forefront of healthcare change to turn innovative science into VALUE for patients

- Financial Capital
- Manufacturing Capital
- Intellectual Capital
- Social and Relational Capital
- Human Capital
- Natural Capital

Output

XTANDI and Priority Strategic Products
Products derived from Focus Area Approach

Outcome

VALUE = $\frac{\text{Outcomes that matter to patients}}{\text{Cost}}$

to the healthcare system of delivering those outcomes

Strategy: Corporate Strategic Plan 2021

Portfolio
Focus Area
Project

Analytics is Utilized in All Areas of Enterprise to Maximize VALUE

* Initiatives not introduced during the presentation are also listed in the Appendix.

Input
- Financial Capital
- Manufacturing Capital
- Intellectual Capital
- Social and Relational Capital
- Human Capital
- Natural Capital

Output
- Corporate
  - Monitoring achievement of each goal to achieve Corporate Strategic Plan 2021
- Dev
  - Capturing Real Needs that Lead to VALUE through Social Listening
- Commercial
  - Leveraging RWD to Model Patient Journeys and Forecast Marketability
- Dev
  - Utilizing RWE to Expand Indications without Clinical Trials
- Tech
  - Demand Analysis for Stable Supply of Products

Business Activity
- Corporate
  - Portfolio Management
- Corporate
  - Portfolio Management (introduced)
- HR
  - Providing Information that Contributes to Investment Decisions with Limited Data
- Marketing
  - Marketing Strategies Based on Long-term Sales Forecasts

VISION
On the forefront of healthcare change to turn innovative science into VALUE for patients

Outcomes = VALUE* to the healthcare system of delivering those outcomes

Outcome

HR: Human Resource, Dev: Development, RWD: Real World Data, RWE: Real World Evidence
Monitoring Achievement of Each Goal to Achieve Corporate Strategic Plan 2021

Data Visualization

**Problem**
- To transform into an innovative organization, cross-divisional and ambitious goals (Shared Objectives) are set. Data on initiatives related to goals and their progress are centrally managed, but the volume of information is increasing.
- As the amount of information to be aggregated and checked increases, the time available for sense-making is reduced.

**Solution**
- Developed a dashboard to support management decision-making by automating the analysis and processing of large amounts of data
- Visualization of initiatives and progress, enabling prioritization of critical information and extraction of trends

**Value**
- Time from data entry to visualization reduced from 3 days to 15 minutes.
- Report creation is focused on meaning-making over production.

Verified in FY2021, currently being utilized
Demand Analysis for Stable Supply of Products
Supply Chain Management

Problem
• Demand forecasting is critical to avoid inventory shortages and surpluses
• Accurate forecasting requires customization to account for seasonality, calendar, and market-specific patterns

Solution
• New supply chain forecasting platform with eight freely selectable time-series algorithms
• Improved forecasting accuracy by allowing selection of the best algorithm for each product

Value
• Improved forecasting accuracy for stable product supply and cost optimization
• Reduction of external vendor dependence/costs

Verified in FY2022, currently being utilized in several projects
Providing Information that Contributes to Investment Decisions with Limited Data
Real-Option Valuation

Problem
• Speed is important in asset evaluation, but human evaluation is time-consuming and expensive
• Especially in the early stage, there are many cases where data is insufficient, and the results will differ if different people perform the estimation.

Solution
• Developed a Python-based methodology based on an external dataset of tens of thousands of compounds that can be evaluated even in the presence of missing data (e.g., how long and how much does it cost to target a certain indication with a certain compound, how much sales, etc.)

Value
• Quick valuation of early-stage assets
• Increased information for early-stage investment decisions

Currently under verification

POC: Proof of Concept, NPV: Net Present Value, P3: Phase 3 clinical trial
What Astellas is Aiming for with Corporate-wide Digital Transformation
From point solutions to end-to-end

A state in which all data, from management decisions to individual projects, are organically connected to maximize VALUE

VISION
On the forefront of healthcare change to turn innovative science into VALUE for patients

Business Activity

Input

• Financial Capital
• Manufacturing Capital
• Intellectual Capital
• Social and Relational Capital
• Human Capital
• Natural Capital

Output

Calculating VALUE based on RWD and Selecting Optimal Indications

Portfolio Management
Providing Information that Contributes to Investment Decisions with Limited Data

Insights into Innovative Organizational Structures through the Use and Analysis of Human Resources Data

Marketing Strategies Based on Long-term Sales Forecasts

Demand Analysis for Stable Supply of Products

Capturing Real Needs that Lead to VALUE through Social Listening

Leveraging RWD to Model Patient Journeys and Forecast Marketability

Utilizing RWE to Expand Indications without Clinical Trials

Outcome

VALUE = Outcomes that matter to patients

Cost
to the healthcare system of delivering those outcomes

VALUE*


HR: Human Resource, Dev: Development, RWD: Real World Data, RWE: Real World Evidence
Appendix
Calculating VALUE based on RWD and Selecting Optimal Indications

**RWD Data Hub**

**Problem**
- VALUE of a drug is not only its therapeutic effect, but also its cost of care, quality of life, burden on caregivers, etc.
- Optimizing VALUE through clinical trials alone is time-consuming and expensive.

**Solution**
Build a uniquely processed data hub based on RWD
- Capable of quantifying VALUE (within 1 day)
- Can perform clinical analysis and evaluation at various stages of the drug development cycle

**Value**
- Faster time-to-market
- Reduction of study costs

Verified in FY2021 and currently being utilized in multiple projects

**Key components of VALUE e.g.**
- Direct medical costs
- Morbidity/quality of life
- Indirect costs: family burden, etc.

**Examples of data processing:**
- Population/Weights
- ML-Based Data Enhancements
- Identification of Meaningful Sub-groups, etc.

**Selecting the best indications for maximizing VALUE**

RWD: Real World Data
Capturing Real Needs that Lead to VALUE through Social Listening
Patient Insights from Social Media

Problem
• Learning about the patient experience is critical to understanding the outcomes that truly matter to patients
• On the other hand, it is difficult to filter out the noise and gain insight from social media posts

Solution
• Using natural language processing technology to filter data on relevant content and identify, for example, key themes in posts by patients and caregivers

Value
• Understanding the needs of patients (more efficient market research)
• Insight into the patient environment, not only the patient, but also potential patients before diagnosis, untreated patients after diagnosis, and caregivers

Being utilized in multiple projects in FY2022

Social Media Listening
Gain insight into which symptoms patients are struggling and/or coping with, how they relate to other diseases, etc.

Perception/Sentiment Trends
Needs/Opportunities Competitor Analysis
Reader Analysis Share of Voice
Conversation Analysis
Marketing Strategies Based on Long-term Sales Forecasts
Long-Range Forecasting

Problem

- Long-term sales forecasting is uncertain and difficult because of the impact of multiple uncontrollable factors, such as government price controls and increasing market share of competing products. On the other hand, using only a single point estimate based on a variety of assumptions.

Solution

1. Assumptions are made about the impact and probability of occurrence of each of the factors affecting sales. Monte Carlo simulations generate a "range" of numerous possibilities and outcomes.

Value

- Marketing strategies with appropriate estimates of risk
- Improved understanding of possible scenarios
- Ability to pre-test the impact mitigation strategies

1. Monte-Carlo Simulation

<table>
<thead>
<tr>
<th>Input Data Sets (e.g.)</th>
<th>A (number of patients)</th>
<th>B (competing product)</th>
<th>C (insurance reimbursement)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assumed distribution</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| Take random sample and model outputs
| Repeat 1000s of time to generate a distribution of model outputs |

\[ NPV = f_{NPV}(X_A, X_B, X_C) \]

2. Time Series Forecasting

Verified in FY2021, currently being used in multiple projects

NPV: Net Present Value
Leveraging RWD to Model Patient Journeys and Forecast Marketability
Dynamic Patient Flow Model

**Problem**
- To predict marketability, it is necessary to predict how a candidate compound will be incorporated into actual therapy.
- This is especially challenging for diseases with complex or evolving therapeutic pathways.

**Solution**
Modeling the Patient Journey with RWD
- What paths patients follow
- How the patient journey itself changes
- Reflects individual patient characteristics and treatment history

**Value**
- Improving the robustness of pipeline product forecasting
- Insights into marketing strategies

Verification has been conducted for 1 project in FY2022

**Patient Journey on Treatment (image)**

**Elements of the model** (e.g.)
- Patient type/segment
- Treatment type
- Outcome of treatment
- Decisions made by the patient (and/or physician) based on symptom progression and market events
Utilizing RWE to Expand Indications without Clinical Trials
Expansion of Prograf (tacrolimus) Indications

**Problem**
- No immunosuppressant drug approved for lung transplantation in US, and access issues were reported
- Tacrolimus is a drug that prevents organ rejection and was only indicated for liver, kidney, and heart transplant patients in 2018

**Solution**
Application to expand the indication to adult and pediatric lung transplant patients utilizing the FDA’s new RWE framework
- Leveraged data from more than 25,000 patients over 20 years
- Approved less than 3 years after the framework was presented

**Value**
- Expanding indications without clinical trials to help address unmet medical needs

<table>
<thead>
<tr>
<th>Date</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>December 2018</td>
<td>FDA “Framework for RWE”</td>
</tr>
<tr>
<td>April 2019</td>
<td>Project approved</td>
</tr>
<tr>
<td>December 2020</td>
<td>Submission to FDA</td>
</tr>
<tr>
<td>July 2021</td>
<td>FDA approval</td>
</tr>
</tbody>
</table>

FDA approves expansion of indication to include lung transplantation in July 2021

FDA: Food and Drug Administration, RWE: Real World Evidence
Insights into Innovative Organizational Structures through the Use and Analysis of Human Resources Data

**Problem**

- The large number of hierarchical positions (up to 10) has been an impediment to innovation, causing delays in decision-making and making it difficult for ideas from the field to be raised.

**Solution**

- Multidimensional quantitative analysis of the percentage of managers with subordinates, divisional and country differences, hierarchical structure, etc., using the HR database.

**Value**

- Insights into optimal organizational structure → Transformation underway to innovative organizational structure

**Verification conducted for 1 project in FY2022**

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SPOC: Span of Control (Number of members that one people manager manages)