Astellas Rx+® DAY
~ Beyond the Rx business ~
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) that is included in this material is not intended to constitute an advertisement or medical advice.
A society where people can become healthy while having fun
Digitalization can change behavior, change healthcare
Start with early detection of arrhythmias/Contribute to extending healthy life expectancy

AGENDA

1. Introduction
   Naoki Okamura  Executive Vice President, Chief Strategy Officer and Chief Financial Officer

2. Outcomes and Future Perspectives of Developing the Rx+® Programs
   Yuta Watanabe  Senior Vice President, Rx+ Business Accelerator

3. Topics of each program
   **Sphere: Patient outcome maximization** (via precise surgery/diagnosis)
   - Surgery cannot be performed with drugs, but surgery can be supported with drugs
   **Sphere: Chronic disease progression prevention**
   - A society where people can become healthy while having fun
   - Digitalization can change behavior, change healthcare
   - Start with early detection of arrhythmias/Contribute to extending healthy life expectancy
   **Sphere: Across all spheres**
   - Ultra-small medical devices beyond the pill
   Akira Suwa
   Motohiro Kanayama
   Naoyuki Kanda
   Makoto Ogino
   Kunitake Abe

4. Wrap up
   Naoki Okamura  Executive Vice President, Chief Strategy Officer and Chief Financial Officer
PART 1

Introduction

Naoki Okamura
Executive Vice President, Chief Strategy Officer
and Chief Financial Officer
OUR VISION

Vision
On the Forefront of Healthcare Change to Turn Innovative Science into VALUE for Patients

We will achieve sustainable growth by pursuing innovative science to produce medical solutions that provide VALUE to patients
DEFINITION OF VALUE

Common Definition of VALUE:

VALUE = \frac{Outcomes that matter to patients}{Cost to the healthcare system of delivering those outcomes}
DEFINITION OF VALUE

Common Definition of VALUE

\[
\text{VALUE} = \frac{\text{Outcomes that matter to patients}}{\text{Cost to the healthcare system of delivering those outcomes}}
\]

Double the outcomes → Double the VALUE

One third the cost → Triple the VALUE
TECHNOLOGICAL INNOVATION AND RAPID CHANGES IN INDUSTRIAL STRUCTURE

2005

2013

Photo: AP/Aflo
WHY ASTELLAS DEVELOP Rx+® PROGRAMS

【Common definition of VALUE】

Common Definition of VALUE
VALUE = \frac{Outcomes \text{ that matter to patients}}{Cost \text{ to the healthcare system of delivering those outcomes}}

【Technological innovation and rapid changes in industrial structure】
2005 2013

Photo: AP/Aflo
PART 2

Outcomes and Future Perspectives of Developing the Rx+® Programs

Yuta Watanabe
Senior Vice President, Rx+ Business Accelerator
**Rx+®**: HEALTHCARE SOLUTIONS BEYOND THE Rx BUSINESS

Combine our expertise and experiences with technology and knowledge from different fields to create new revenue streams separate from our core Rx products.

**New medical solutions** that contribute positively to the entire patient journey

**New treatment solutions** that replace conventional therapy or add new VALUE

**Bioelectronics** Ultra-small implant medical device

**Digital Health & Digital Therapeutics**
- Smartphone exercise app with gamification and 3D motion technologies
- Disease management digital platform

**Medical drug and device technologies combinations**
- Medical drug and device technologies combinations
- Image guided surgery
Given the broad business scope and market uncertainty in Rx+®, a unique approach is taken. 

1. Start from our ASPIRATIONS (a world realized by Rx+®: “Rx+ World”) 

2. FUTURE-DRIVEN and OUT-OF-THE-BOX thinking, breaking away from the traditional pharmaceutical business 

3. AGILE and ITERATIVE on the basis of hypothesis thinking
**Rx+® World**

A world where people can live mentally and physically healthy lives and be true to themselves through healthcare solutions based on scientific evidence.

**Rx+® Values**

- Prevent disease onset and slow progression by using personal data
- Expand options for people with limited access to current therapeutics
- Support active living by enhancing physical and sensory function

**Spheres (business areas)**

- Chronic disease progression prevention
- Motor Function support/replacement
- Digital x neuroscience
- Patient w/o effective medicines
- Patient outcome maximization (via precise surgery/diagnosis)
- Sensory function support/replacement
SUMMARY OF CURRENT SPHERES

**Chronic disease progression prevention**
Enable prevention of disease progression in accordance with individual constitution and lifestyle.

**Motor function support/replacement**
Free patients and caregivers from problems in daily life related to physical functions.

**Digital × Neuroscience**
Free patients and caregivers from problems in daily life caused by central nerve system-related diseases.

**Patient w/o effective medicines**
Solve health problems in perinatal and menopausal women and children with non-invasive solutions.

**Patient outcome maximization (via precise surgery/diagnosis)**
Improve accuracy of surgery and diagnosis to optimize treatment measures and maximize therapeutic outcome.

**Sensory function support/replacement**
Free patients and caregivers from problems in daily life related to sensory functions.

APPROACHES TO TECHNOLOGY AND EXPERTISE IN DIFFERENT FIELDS

Co-Creation: Accessing and working with state-of-the-art issues, findings, technologies, and capabilities

Venture Capitals

- Miraiz Soze: VC that collaborates with Tokyo Institute of Technology @ Tokyo
- digiTx: Early-stage VC firm investing in digital health @ San Francisco Bay Area
- Treo Ventures: VC focusing on medical device and digital health innovation @ Silicon Valley and Ireland
- Arx+ Astellas Rx+ Business Accelerator, LLC (Arx+) established 2018

External Network/BD activity

- Consortium
- Industry activity
- Interdisciplinary interaction
- Demonstration experiment

Open Innovation

Astellas Rx+ Healthcare Innovation Challenge
Recruiting new business ideas from start-up companies and students worldwide for commercialization

Accelerator program

Technology x Healthcare 2019

Tech ARINA: Idea Contest and Collaborative Research with the Theme of Healthcare Research Using Science and Engineering Technologies with Tokyo University of Industries

Internal Capability

- Recruitment of human resources in different fields
- Internal idea challenge
- Cross-border experience
- Society task workshop
- Leadership Training
Etc........
MAJOR EVENTS (FY18 ~ FY20)

**FY18**
- Newly established Rx+ Business Accelerator

**FY19**
- Astellas and Welldoc enter into Strategic Alliance for Digital Therapeutics
- Astellas and iota Biosciences enter into Collaborative Research and Development Agreement
- Yokohama City University, Tokyo University of the Arts and Astellas Launched Health Mock Lab. to Create New Digital Healthcare Solutions Using Gamification

**FY20**
- "Project ABC PAC-MAN Squat Challenge" by Astellas and BANDAI NAMCO Entertainment
- Research Collaboration with Actinium for Molecular Targeted Radiotherapy
- Completed acquisition of iota Biosciences
- U.S. FDA Fast Track Designation for ASP5354
- Service start of Fit-eNce®
- Astellas, City of Yokohama, and Yokohama City University Developed Science-Based Exercise Programs
- Astellas and BANDAI NAMCO Entertainment Enter into Agreement to Co-Develop and Co-Commercialize Smartphone Exercise Support Application
- Announcement of Rx+ Story® Story
- Astellas and BANDAI NAMCO Entertainment to Jointly Develop Smartphone Exercise Support App
PART 3

Surgery cannot be performed with drugs, but surgery can be supported with drugs

Akira Suwa
Business Producer,
Rx+ Business Accelerator
Establish More Precise, Safer and Efficient procedures

Key point
➢ Maximize patient outcome using Image-guided technology
➢ Realize precise procedures with drugs and devices

Image-guided surgery can be achieved by capitalizing on **device** (Mechanical-based) and **pharma** (Biology-based) technology
Challenges with current surgical treatments

Risk factors
- Surgeon’s skill and experience
- Background of disease and patient
- Surgery-related complications

Decreased surgical outcome
- Re-, and Additional surgery
- Long-time surgery

Decreased patient outcome
- Increased healthcare cost
- Decreased patient QOL

- Improve Surgical and Patient Outcomes using advanced surgical technology
Challenges with current surgical treatments - focus points

Iatrogenic Ureteral Injury (IUI)

- Caused by accidental injury to the ureter during abdominal and pelvic surgeries
- IUIs are associated with higher mortality, morbidity, longer length of hospital stays, and increased healthcare cost\(^1\)
- The best method for preventing IUI is intraoperative identification of both ureters\(^2\)
  
  There is no approved method for non-invasively visualizing ureters in clinical practice

Iatrogenic Ureteral Injury - Challenges with current method

Current method to identify ureters

The ureter position is approximated or possibly identified by the surgeon’s experience.

There is a method of inserting a ureteral stent before surgery. The stenting allows the ureter to be located haptically (and partly visually if lighted).

Challenges with the stenting method

- Low efficacy: May not effectively identify the ureter
- Needs the support from experts: The stenting procedure is difficult and requires the consultation of a urologist
- Extended surgery time: Additional time for stenting required
- Risk of adverse events: Hematuria, ureteral damage, renal dysfunction, etc.
- High medical costs: Around $1,500 including the stenting method fee (U.S.)

Image-guided precision surgery enables easy, safe and precise visualization of organs or tissues that are particularly difficult-to-identify, with improved global post-operative outcomes.

NIR-F: Near InfraRed fluorescence

The safety and efficacy of this investigational agent has not been established. ASP5354 is not approved for use in any jurisdiction.
Create new value in collaboration with an external partner

Ureter imaging using ASP5354

ASP5354 features

- A derivative of indocyanine green that fluoresces upon excitation with a near-infrared light, a hydrophilic and iodine-free compound
- ASP5354 was discovered by Mie University and Nagoya University. Astellas acquired exclusive development and marketing rights worldwide
- Combined with the detection device (partnering with a medical device company), intraoperative identification of the ureters is expected to minimize the risk of IUI
- Nonclinical and clinical data to date indicate ASP5354 has been well tolerated with no related adverse events
- The nonclinical (porcine model) and preliminary human findings are consistent showing that ASP5354 illuminated the full extent of ureters under near-infrared light in both laparoscopic and open surgeries

The safety and efficacy of this investigational agent has not been established. ASP5354 is not approved for use in any jurisdiction.
Ureter visualization using ASP5354 is an easy-to-use and effective method for minimizing the risk of IUI without the need for additional procedures or time.

- Received U.S. FDA Fast Track Designation: Oct 2020
- Target approval: FY2023
- Investigating global development in addition to U.S. (Japan, China, EU)

The safety and efficacy of this investigational agent has not been established. ASP5354 is not approved for use in any jurisdiction.
Future perspective

Multiple needs exist for which image-guided precision surgery can improve patient outcomes

**Ureter**
- Target cases
  - ~2 million / year
  - Colorectal surgery
  - Gynecological surgery etc.

**Peripheral nerve**
- Target cases
  - ~1 million / year
  - Prostate cancer
  - Colorectal surgery etc.

**Blood and lymphatic vessels**
- Target cases
  - ~1 million / year
  - Breast cancer
  - Melanoma surgery

**Cancer**
- Target cases
  - ~1 million / year
  - Breast cancer
  - Colorectal surgery etc.

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1: indocyanine green, 2: 5-aminolevulinic acid

The safety and efficacy of this investigational agent has not been established. ASP5354 is not approved for use in any jurisdiction.
PART 4

A society where people can become healthy while having fun

Sphere:
Chronic disease progression prevention

Motohiro Kanayama
Business Producer,
Rx+ Business Accelerator
Toward a society in which people become healthy with enjoying.

Key point

Value creation and provision through
- "Astellas x Entertainment x Medical"
- "Astellas x Fitness x Medical"

Developing new solutions/Market penetration

Entertainment
- Understanding needs about enjoyableness
- Gamification technology, know-how

Astellas
- Understanding disease, physicians/patients' needs
- Ability to build scientific evidence
- Wide networks with HCPs*

Fitness club
- Know-how for exercise guidance
- Owning exercise equipment

Medical
- Ability to establish treatment options and policy
- Provision of medical care

Society implementing health actions

World where people can live mentally and physically healthy lives and be true to themselves

*HCPs: Health Care Professionals
The prevention of (the exacerbation of) "metabolic syndrome," "locomotive syndrome," and "dementia" are important issues for extending healthy life expectancy.

### Major causes of conditions requiring long-term-care*

- Cerebrovascular disease + cardiac disease: 19.8%
- Joint disease + fracture/fall: 22.7%
- Dementia: 18.7%

![Bar chart showing major causes of conditions requiring long-term-care](https://www8.cao.go.jp/kourei/whitepaper/w-2018/html/zenbun/s1_2_2.html)

**Challenges concerning extending healthy life expectancy**

- Metabolic syndrome
- Locomotive syndrome
- Dementia

Prevention of (exacerbation of) the above conditions is important for extending healthy life expectancy.

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* Major causes of conditions requiring long-term-care for persons aged 65 or older and receiving care. Persons requiring long-term-care refer to persons at home among those who are certified as requiring support or care.
CHALLENGES
Continuing exercise

A system to support health promotion through exercise is expected to be enhanced even further.

< Preventive viewpoint >
● It is clear that a decrease in physical activity due to household and work automation, as well as the development of transportation along with changes in eating habits, has contributed to the recent increase in lifestyle diseases.
● Although the effects of physical activity and exercise on health have become well known to the public, the percentage of people who actually exercise is small.

Source: Ministry of Health, Labour and Welfare website

< Viewpoint of clinical practice for diabetes mellitus >

<table>
<thead>
<tr>
<th>Frequency of guidance during medical visit</th>
<th>Dietary guidance (%)</th>
<th>Exercise guidance (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Almost every time</td>
<td>11.4</td>
<td>11.1</td>
</tr>
<tr>
<td>Often (about 1 in 2-5 times)</td>
<td>16.8</td>
<td>14.5</td>
</tr>
<tr>
<td>Sometimes (about 1 in 6-10 times)</td>
<td>25.1</td>
<td>19.0</td>
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<tr>
<td>Rarely (about once a year)</td>
<td>36.7</td>
<td>25.4</td>
</tr>
<tr>
<td>Never</td>
<td>9.9</td>
<td>30.0</td>
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</tbody>
</table>

Prepared with reference to Current Situation of Diet and Exercise Therapy in Terms of Medical Consultations in Patients with Diabetes Mellitus in Japan: A Nationwide Survey - [Diabetes mellitus 58 (4): 265-278, 2015]
CHALLENGES
Each player’s perspective

In order to become a society where "health promotion through science-based exercise" is practiced, several unmet needs must be met.

<table>
<thead>
<tr>
<th>Player</th>
<th>Common challenges</th>
<th>Individual challenges</th>
</tr>
</thead>
</table>
| Exercise service provider             | Medical rationale
It is not easy to build a medical rationale. | –                                         |
| Physician                             | Opportunities
There are few opportunities to obtain information on exercise services. | Time
It is difficult to secure time for exercise guidance. |
| Patient or person who wants to be healthy | –                                                      | Emotion/implementation
There are psychological and practical issues. |

Source: Prepared by Astellas based on the results of interviews with exercise service providers, physicians, and web surveys.
CHALLENGES
End user’s perspective

People who want to be healthy through exercise

Psychological barrier

- Motivation
- Resistance to change
- Cumbersome
- Giving up

Implementation barriers

- Physical function
- Lack of knowledge
- Lack of preparation
- Surrounding environment

People who continue proper exercises

Source: Created by Astellas based on the results of web-based surveys
Direction to solutions

People who want to be healthy through exercise

Envisioned services
- Science-based
  - Exercise-support services with physician approval to exercise regularly at a fitness club
  - Exercise support app that uses gamification and IoT technology which allows one to enjoy and continue proper exercises

Provide science-based services

With an appropriate provision channel

Provided as a new healthcare tool

People who continue proper exercises
Collaboration with a fitness club
Service overview

- We provide exercises tailored to the physical strength of individuals through exercise design with logic used in medical research.
- You can share your exercise log with your primary care physician.
- The app allows you to start the service and record your exercising, helping you to start and continue exercising.

A system that supports exercise menus and exercise implementations based on scientific evidence provided by Astellas

Change in HbA1c at Week 13
(Results of medical research)

<table>
<thead>
<tr>
<th>Changes from baseline</th>
<th>Least squares mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exercise group (n = 97)</td>
<td>-0.31</td>
</tr>
<tr>
<td>Non-exercise group (n = 108)</td>
<td>0.13</td>
</tr>
</tbody>
</table>

*: Cases analyzed: Full Analysis Set
Mixed-effect model for repeated measures (explanatory variables include study group, assessment time point, value at Week 0, interaction between assessment time point and study group, interaction between assessment time point and value at Week 0)
We will be exploring the optimal form of the service through small repeated trials. We will work on service development with science-based exercise as a common value.
Example 1: Cooperation with BANDAI NAMCO Entertainment
Exercise support application using game know-how

We are aiming to provide the value of "preventing metabolic syndrome or improving obesity by continuing proper exercise while having fun."

1. Science-based exercise guide
   • Providing games that merge with exercise

2. Game and exercise implementation

3. Detects movement and heart rate

4. Feedback on game and exercise implementation

5. Continuing exercise while having fun

Smartphone/tablet

Wearable device

User

Person wears the device
Project ABC was launched with the aim of providing opportunities for health promotion through exercise and creating a feeling of unity and cheerfulness to overcome the current situation.

We provided this WEB application between 26 January to 23 February 2021.
We did squats 149,429 times together!

Example 2: Cooperation With Bandai Namco Entertainment
Project ABC Pac-Man Squat Challenge

https://abc.asobistore.jp/
You can try the Pac-Man Squat Challenge today only!

- The special website for the Project ABC Pac-Man Squat Challenge
  https://abc.asobistore.jp/
- Recommended environment
  [Recommended OS] iOS: iOS 10 or later, Android: Android 6.0 or later
  [Recommended browser] iOS: the latest version of Safari, Android: the latest version of Chrome

Previous topics

Which *Aoharu* (adolescence)-like Squat Situation would you choose?

Squats during an after-school club activity

Voluntary training squats by idols

*Okonomiyaki* could be a side dish?

Yes!

No!
A society where people can become healthy while having fun

Desired image

Society implementing health actions

World where people can live mentally and physically healthy lives and be true to themselves

Developing new solutions/Market penetration

Entertainment
- Understanding needs about enjoyableness
- Gamification technology, know-how

Astellas
- Understanding disease, physicians/patients needs
- Ability to build scientific evidence
- Wide networks with HCPs*
- Ability to establish treatment options and policy
- Provision of medical care

Fitness club
- Know-how for exercise guidance
- Owning exercise equipment

Medical

*HCPs: Healthcare Professionals
PART 5

Digitalization can change behavior, change healthcare

Naoyuki Kanda
Principal, Project Lead, Digital Health, Rx+ Business Accelerator
Clinically Relevant Holistic Mobile Healthcare Solutions

Fosters patients and HCPs behavioral changes and coaching using novel technology

Key Points
- Provides a personalized treatment and continuous interaction with the healthcare providers (HCPs)
- Optimal timing of medical intervention leading to improved outcomes and cost saving

Artificial Intelligences, New Modules, and Algorithms

Symptoms (Adherence, Insights)

Labs (BG, BP, Weight)

Medications

Psychosocial (Distress, Disability, Economic Conditions)

Activity (Sleep/Exercise)

Diet (Carbs, Calories, Sodium, Water)

Software and/or hardware as a novel Digital Therapeutics (DTx)

Ease Access Using Digital Technology

Chronic disease Mobile Non-Prescription Therapy

- Regulatory Clearance (or, as appropriate, approval)
- Clinical and health-economic value
- Enhance user engagement
- Evidence-based business models
Medical needs

Healthcare Challenges

- Escalating of Healthcare Cost
- Increasing health care disparities
- Difficult to continue or intensify treatment

Changed World

- Significant cost saving with digital
- Universal Access
- Personalized goals and outcomes
Our collaboration

- **PLATFORM**
  - Innovative Technology
  - Artificial Intelligence
  - Machine Learning Algorithms
  - Continuous monitoring and tracking

- **PRODUCT QUALITY**
  - QA Compliance
  - PV Compliance
  - Privacy
  - Cybersecurity
  - User Friendly Design

- **REGULATORY**
  - Pharmaceuticals
  - Medical Device
  - Digital Therapeutics
  - Regulatory approval / clearance
  - Reimbursement

- **EVIDENCE**
  - Evidence-based clinically relevant solutions
  - Clinical Trial
  - HEOR
  - Real World Evidence and/or Data

- **COMMERCIAL**
  - Awareness to patients
  - Delivering Value
  - Demonstrating Value
  - Driving Use

Strength of Welldoc in DTx field

Strength of Astellas in Rx field
Welldoc platform value

**FDA-Cleared**
Class II Medical Device with eight 510(k) clearances

**Personalized Digital Coaching**
Real-time feedback, anytime, anywhere

**Proven Clinical & Economic Rigor**
Over 50+ peer-reviewed publications

**Patented Technology**
18 patents on artificial intelligence and algorithms

**Device Agnostic**
Syncs with 300+ devices

**Comprehensive Platform**
Supports seven chronic conditions
# Product pipeline

<table>
<thead>
<tr>
<th>PRODUCT</th>
<th>INDICATION</th>
<th>REGION</th>
<th>PLANNING</th>
<th>DEVELOPMENT</th>
<th>CLINICAL TRIAL</th>
<th>COMMERCIAL</th>
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<tbody>
<tr>
<td>BlueStar</td>
<td>Diabetes</td>
<td>Japan</td>
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<td>ASIA*</td>
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<tr>
<td>New DTx</td>
<td>Chronic Disease</td>
<td>Global</td>
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</table>

*Countries outside of Japan*
Further expansion of the platform

Diabetes: JAPAN
- 10 million people are strongly suspected of having diabetes
- 10 million people who cannot rule out the possibility of diabetes

Cardiovascular: US
- Number of Americans projected to have CVD by 2035 will have increased to nearly half of the U.S. population
- By age 45, cardiovascular disease risk is 50%, at 65 it jumps to 80%

Sources: 1) Cardiovascular Disease: A Costly Burden for America Study, AHA; 2) Heart Disease and Stroke Statistics—2019 Update: A Report From the American Heart Association; 3) 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation; 4) 厚生労働省健康局「平成28年国民健康・栄養調査」
Start with early detection of arrhythmias
Contribute to extending healthy life expectancy
Support ecosystems for patients with heart disease

Key point
➢ Ecosystems to support patients with heart disease
➢ A Simple, Cost-Effective Solution Incorporating Novel Technologies

Current problems:
Home management is patient-dependent and lacked sufficient tools

At home

Seeking medical attention before illness worsens

Patients

Timely Follow-up

Data linkage

Doctor

Convenient measuring devices

Communication Tools

Tools to support patients with heart disease

Medical institutions

Innovation of Heart Disease
Patient Management
Medical costs for cardiovascular diseases was highest at 6 trillion yen (19.7%)

The major cause of the need for long-term care:
Cerebrovascular disease accounted for 16.1% and heart disease for 4.5%, and 20.6%, the highest, when both were combined

Heart disease is the second leading cause of death, and cerebrovascular disease is the fourth leading cause of death. Together, it is the second leading cause of death after cancer, with more than 310,000 people dying annually.

2017, "National Health Expenses" (MHLW)
2019, National Basic Survey of Life (MHLW)
Our focus
- Early detection of atrial fibrillation (AF) -

- About sixty percent of strokes are cerebral infarctions (blocked blood vessels)
- Cerebral infarction (cardiogenic cerebral embolism) caused by a clot (thrombus) in the heart that blocks an artery in the brain or neck accounts for 2-30% of cerebral infarctions.
  Cardiogenic cerebral embolism is associated with a high mortality rate (20%) due to the large size of the infarct, and severe sequelae, such as bedridden, often remain (40%).
- Three-fourths of the causes of cardiogenic cerebral embolism are AF, and prevention of the development of cardiogenic cerebral embolism from AF is crucial.

The total number of patients with AF was estimated to be 33.5 million males and 12.6 million females worldwide (2010).

Circulation 2014; 129: 837-847

Early Detection of AF Is One of the Starting Points for Solving Large Social Problems

Regions focused on realizing Rx+ Story®
The Holter ECG is a test that takes an electrocardiogram for about 24 hours and is useful for detecting arrhythmias.

[Problems with the Holter ECG examination]

- Since a 24-hour heart rate is about 100,000 beats, many people such as clinical laboratory technicians are required to analyze the test results.
- Further accuracy improvement is desired for the current automatic analysis.

If the efficiency and accuracy of the automatic analysis are improved, more Holter ECG tests will be possible more easily.

Early detection of AF and appropriate medical intervention will contribute to extending healthy life expectancy
Providing value through collaboration with partners
Development of program for holter analyzer using AI

We have developed a program that analyzes data using an AI (artificial intelligence) algorithm so that Holter ECG data can be analyzed more efficiently in collaboration with M.Heart Co., Ltd.

Features in Development:
No just AI, but successful proprietary development of more efficient analysis algorithms (patent pending) with less computer load and less motion

Received pharmaceutical certification as a program medical device (class II)
- Product name: My Holter II
- Certification number: 303AGBZX00015000

Acquired Pharmaceutical Product Law Certification in March 2021 as a program for Holter analyzers using AI.
If this Holter ECG analysis system is described in the international standard rules, **MFER**, an analysis of the data obtained from any type of Holter ECG device is possible on the cloud.
The MYHOLTER II, certified as a program medical device, will be implemented into the Holter ECG analysis service of M. Heart and commercialized in fiscal 2021.

- Using the cloud to build environments where medical professionals can perform analysis tasks remotely from home or outside.

- In an effort to further improve the accuracy and efficiency of MYHOLTER II, the development of the next version was initiated.

- **Discussion on collaboration with Holter ECG device manufacturers were started.** We are considering providing a total solution using the device and data analysis as a set.
Future Perspectives: Possibilities of an AI-ECG

The AI-ECG holds the promise to transform clinical care *1

- **Supporting the long recording time of the Holter ECG device**
  Considered to be able to detect paroxysmal arrhythmia, ECG devices that can record even longer times will likely be in demand in the future. Since even larger amounts of data will need to be analyzed as well, the AI-ECG will play an active part.

- **Real-time ECG analysis**
  If wearable ECGs are improved, performance that can be analyzed to some extent in situ will be expected. At this time, it is believed that the implementation of an AI analysis software that can be operated even on a smartphone will be in demand.

- **Applied to 12-read ECG**
  The application of AI to the so-called ECG data analysis is being studied. It is anticipated that ECG will enable not only pulse disturbance, but also some of the heart's functional assessments. Research is underway.

We will contribute to the early detection of AF by maximizing the potential of AI-ECG

*1 Nat Rev Cardiol. 2021 Feb 1;1-14
Ultra-small medical devices beyond the pill

Kunitake Abe
Business Producer,
Rx+ Business Accelerator
Deliver *innovative value to medicine* with bioelectronics

**iota platform technology**

**Lead bioelectronics to our future core business**

**Key point**
- Iota’s Platform technology for tiny wireless medical implantables
- Building our core business of the future in three steps

**What is the iota platform?**
- No wire, no battery
- Bi-directional communication
- Can provide power to sensors
- Electrical stimulation

**Future step**
- Feedback control from multiple linked implants

**2nd step**
- Feedback control for stimulation by sensors on implant

**1st step**
- Feasibility evaluation of the technology individually

**We are here!**
Why iota? - background-

**Background 1**

Our intent is to keep providing new VALUE to society even in the next era, when everything will be measured, and the value of data mounts.

- In 2013, it was predicted that by year 2022, trillion sensors will be used per year.
- Many IT companies and other different industries are coming into the healthcare market to capture and utilize healthcare data.

→ The acquisition and utilization of biological information deep within the body is a competitive advantage for pharmaceutical companies.

**Background 2**

What is an ideal treatment solution that utilizes new technology?

- Rx: Compounds, Antibodies, Nucleic acid, cell, virus
- Rx+: Software modality Apps, visual, games, contents
  Physics modality radiations, heats, RF, magnetics, **electronics**

iota's technology could be the platform technology that underpins the Rx+ business across all spheres of the Rx+ Story.
What is bioelectronics?

- Interdisciplinary field of biology and electronics
- Aims to improve lives of people with disabilities or diseases through obtaining biological data through methods using electronics or transmitting signals into organisms
- Examples include cardiac pacemakers, deep brain stimulation devices, vagus nerve stimulation devices, or neuroprosthetics
- The market growth rate of implantable nerve stimulation devices is 12.5%
What is the iota platform?

Core Technology
An implantable device and an external interrogator communicates information using ultrasound. The implants can be tiny as energy is provided externally and does not require batteries. The implant can be placed deep within the body as ultrasound does not largely attenuate due to muscle, fat, blood etc.

Sensing: Output
Sense biological parameters around the device location by combining multiple sensors.
※ Application examples
  - $O_2$ level, pH, pressure, temperature...
  - Different sensors lead to wider possibilities

Stimulation: Input
Implement an electrical stimulation apparatus to locally stimulate the area where the device was implanted.
※ Application examples
  - local muscle stimulation, local nerve stimulation...
  - Different implant locations lead to wider possibilities
Provide easier measurement for biological parameters that currently cannot be obtained outside of hospitals

Discovery of novel, useful parameters that measure deep within the body that cannot be measured otherwise and that may indicate a disease status (measurements that cannot be done even in hospitals or with wearable devices)

For example...

- Measure organ temperature to monitor a disease?
- Would pressure measurement provide useful insights?
- Would consistency/discrepancy of the $O_2$ level within the blood and organs locally provide useful insights?
- Can pH be monitored as an indicator of inflammation?

Potential to discover new parameters and data, leading to novel treatments and disease monitoring methods

A major point of consideration is how to lower the invasiveness of device implanting

What change would iota’s platform provide?
What change would iota’s platform provide?

- If more frequent measuring of certain parameters with equal or higher accuracy than hospital measurements are possible at home, patients could respond to sudden changes in their disease status.
- Hospital visits may be reduced by feeding self-measured data into hospital databases.
- Patients can self-confirm the effect of treatments. Healthcare providers have more data to assess the suitability of treatments.
- In the future, a secondary-use data business can be considered. A major point of consideration would be data privacy.
What can electrical stimulation do?

- Control nerve excitation/inhibition
- Control organ activity
- Control muscle contraction/relaxation

Aim for disease treatment and control with different approaches to prescription medicines

Astellas no longer limits our business domain to prescription medicines because there are variety of ways to create and deliver VALUE to patients
What can electrical stimulation do?

**iota’s implantables**
- no wire
- no battery
- tiny

**Conventional implantables**
- Acts locally; less systemic adverse effects
- requires wires, limiting MRI use
- requires batteries, may need surgery for battery change
- large implantables cause burden on surgeons and patients

**iota’s implantables**
- patients utilize the implantables at home utilized about 1 – few times per day

**Conventional prescription medicine**
- regular intake leads to efficacy
- can be taken at home
- systemic delivery may cause adverse effects

iota’s implantables have a potential to become a new treatment option with strengths of both conventional medical devices and prescription medicines
Wide opportunities were identified through expert interviews

There is various potential upsides to the value of the platform

Source: Expert interviews
Aiming to make this one of Astellas’ core businesses

- Existing sensing/electrical stimulation projects planned for launch in later 2020s
- Once concepts are validated, aim for closed-loop systems
- Reach for more complex, multiple closed-loop, auto-controlled projects

Astellas will grow its expertise in the bioelectronics field as one of its core business capabilities and aim to deliver value to patients
PART 8

Wrap up

Naoki Okamura
Executive Vice President, Chief Strategy Officer and Chief Financial Officer
DEFINITION OF VALUE

Common Definition of VALUE

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