



# Astellas Rx+<sup>®</sup> 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.

# AGENDA

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## Introduction

**Naoki Okamura**

Executive Vice President, Chief Strategy Officer and Chief Financial Officer

2

## Outcomes and Future Perspectives of Developing the Rx+<sup>®</sup> 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 .....

**Akira Suwa**

### 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 .....

**Motohiro Kanayama**

**Naoyuki Kanda**

**Makoto Ogino**

### Sphere: Across all spheres

- Ultra-small medical devices beyond the pill .....

**Kunitake Abe**

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## 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

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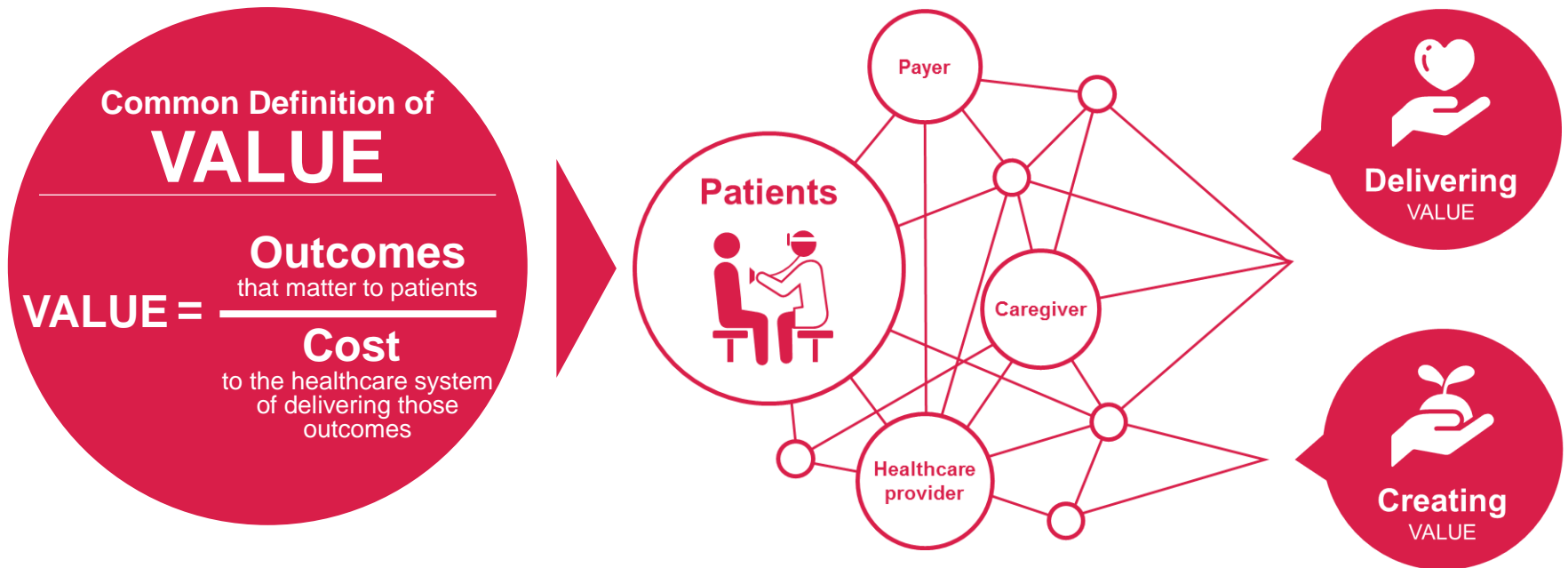
# OUR VISION

## Vision

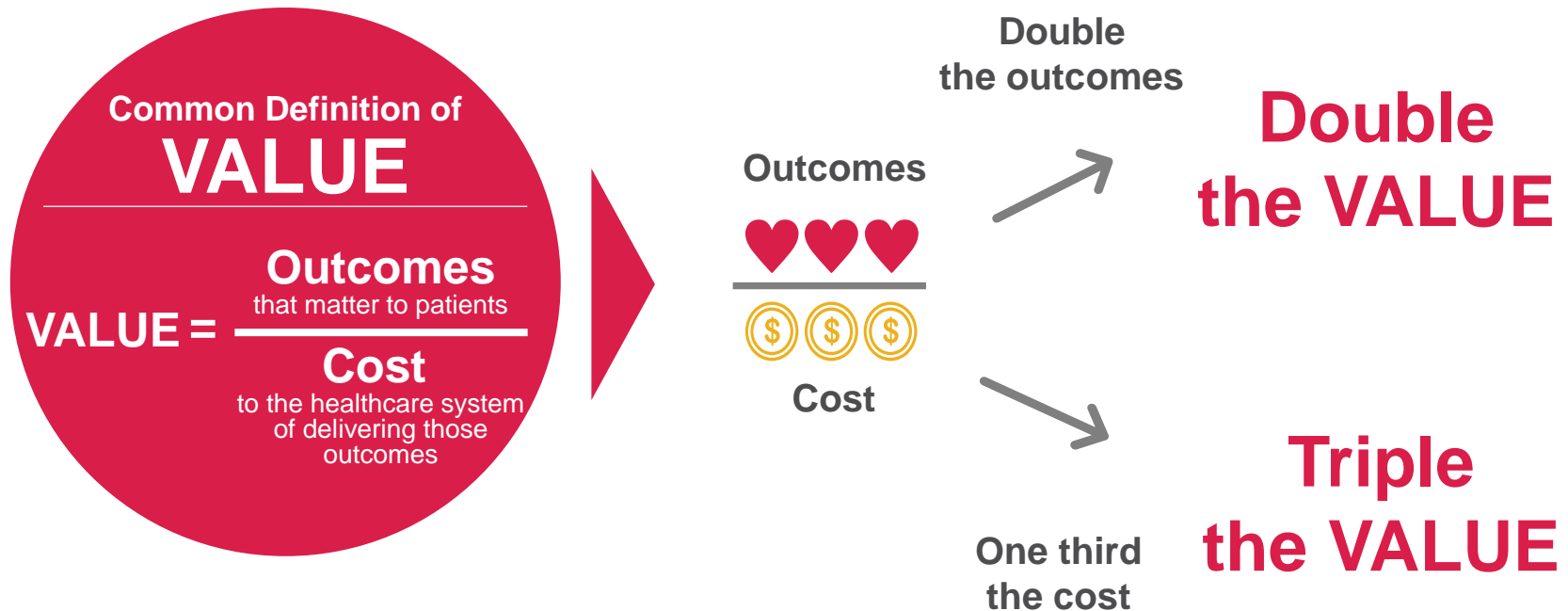
On the Forefront of  
Healthcare Change to Turn  
Innovative Science into  
**VALUE for  
Patients**

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

# DEFINITION OF VALUE



# DEFINITION OF VALUE



# TECHNOLOGICAL INNOVATION AND RAPID CHANGES IN INDUSTRIAL STRUCTURE

8

2005



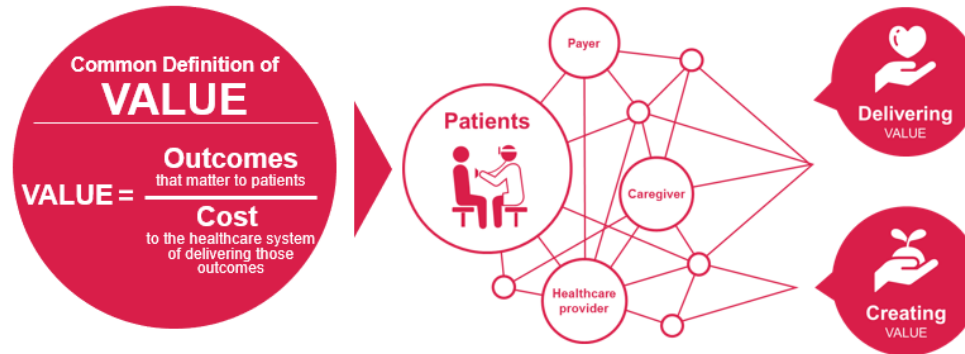
2013





# WHY ASTELLAS DEVELOP Rx+<sup>®</sup> PROGRAMS

## 【Common definition of VALUE】



## 【Technological innovation and rapid changes in industrial structure】

2005



2013





## PART 2

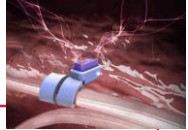
# Outcomes and Future Perspectives of Developing the Rx+<sup>®</sup> Programs

**Yuta Watanabe**  
Senior Vice President,  
Rx+ Business Accelerator

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# 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



**Bioelectronics** Ultra-small implant medical device

## Digital Health & Digital Therapeutics



Disease management digital platform



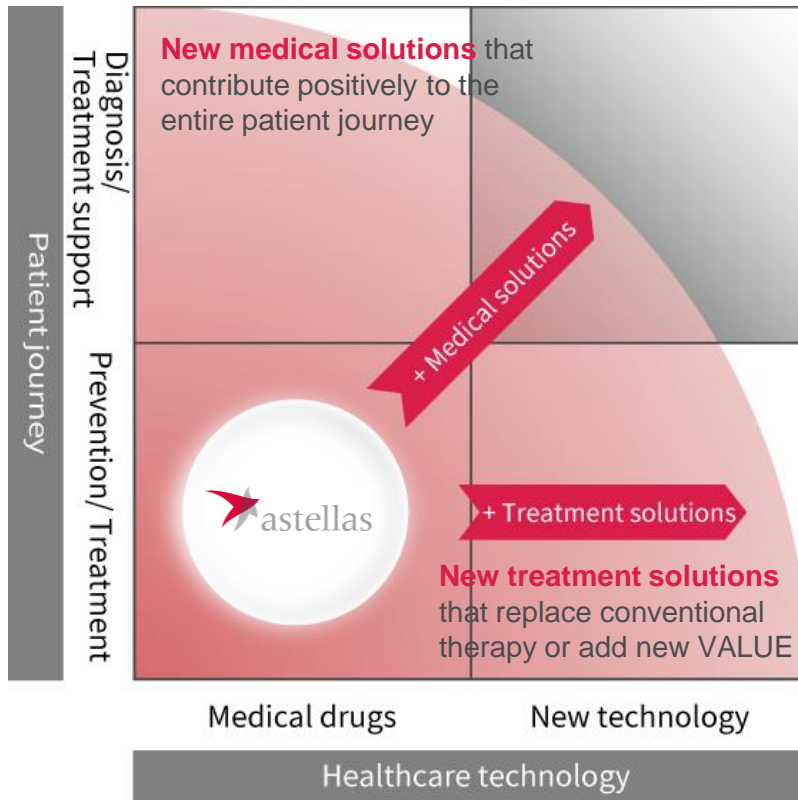
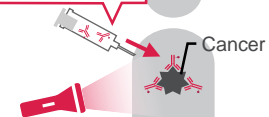
Smartphone exercise app with gamification and 3D motion technologies



## Medical drug and device technologies combinations



Image guided surgery



# APPROACH TO CREATING THE Rx+ STORY®

Given the broad business scope and market uncertainty in Rx+®, a unique approach is taken



# Rx+ STORY<sup>®</sup>: STRATEGIC DIRECTION OF Rx+<sup>®</sup>

**Rx+<sup>®</sup> 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+<sup>®</sup> 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

Updated whenever necessary



## 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





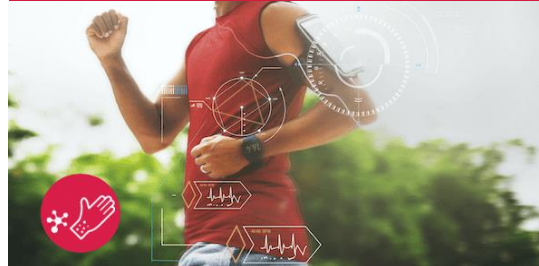
# SUMMARY OF CURRENT SPHERES

## 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



# MAJOR EVENTS (FY18 ~ FY20)





# SPEAKER



Business Producer,  
Rx+ Business Accelerator  
**Akira Suwa**



Business Producer,  
Rx+ Business Accelerator  
**Motohiro Kanayama**



Principal, Project Lead,  
Rx+ Business Accelerator  
**Naoyuki Kanda**



Business Producer,  
Rx+ Business Accelerator  
**Makoto Ogino**



Business Producer,  
Rx+ Business Accelerator  
**Kunitake Abe**





**Sphere :**  
**Patient outcome maximization**  
(via precise surgery/diagnosis)

## PART 3

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

**Akira Suwa**  
Business Producer,  
Rx+ Business Accelerator

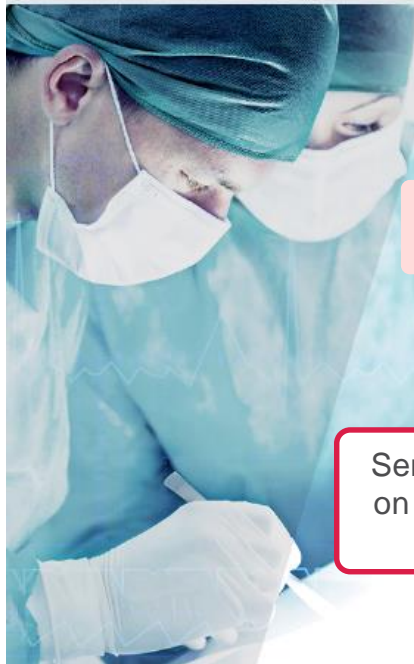
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## Image-guided Precision Surgery / Image-guided Precision Surgery

### Key point

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

Establish  
*More Precise,*  
*Safer* and *Efficient*  
procedures



**Past**  
Endoscope

**Present**  
Robotic surgery

**Future**  
Image-guided

Device

Robot tech

Drug-Device  
Combination

Precision  
surgery based  
on Novel  
technology

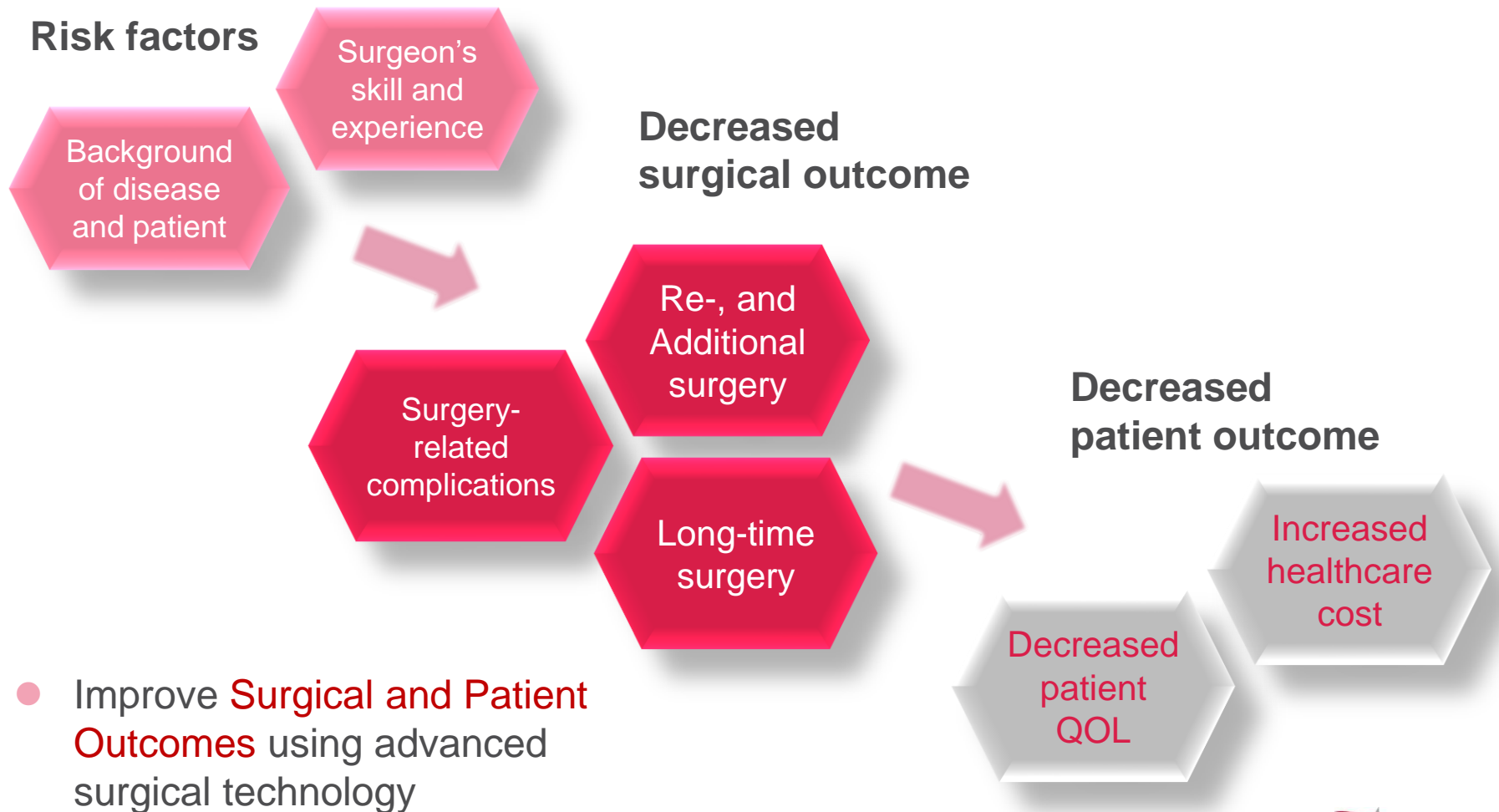
**Smart Surgery**  
merged with  
advanced technologies

- **AI** Artificial Intelligence
- **VR/AR** Virtual Reality/Augmented Reality
- **3D Hologram**
- **PM** Projection Mapping
- **HMD** Head Mounted Displays

Sensory surgery based  
on surgeon's skills and  
experiences

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

# Challenges with current surgical treatments



# 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<sup>1</sup>
- The best method for preventing IUI is intraoperative identification of both ureters<sup>2</sup>

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).



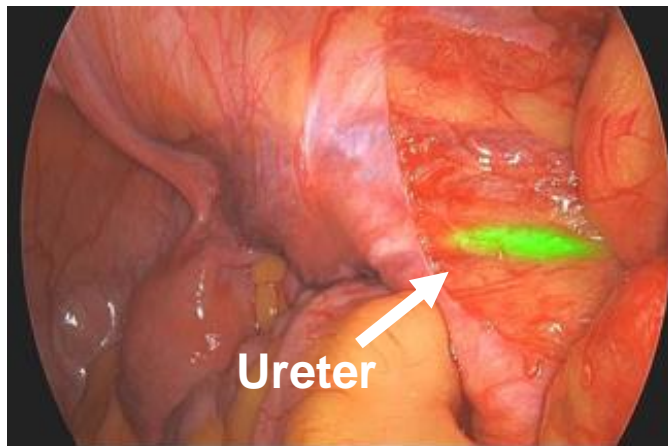
### Challenges with the stenting method

- 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.)<sup>1</sup>



# Image-Guided Precision Surgery

## Use Image: Image-Guided Precision Surgery



Graphical illustration of ureter imaging with ASP5354 in the clinical setting

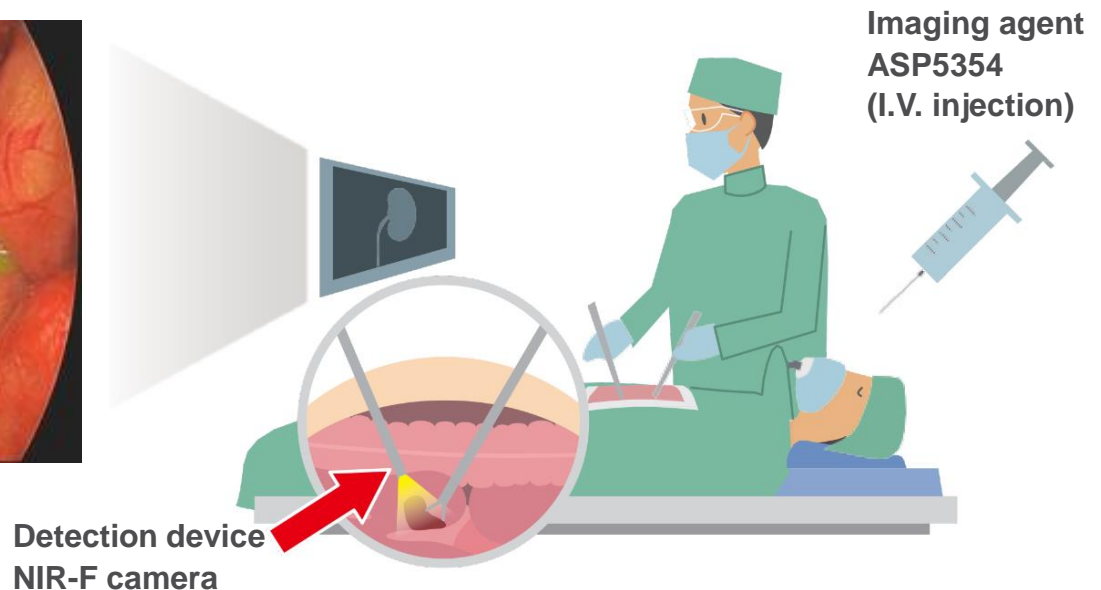


Image-guided precision surgery enables **easy, safe and precise** visualization of organs or tissues that are particularly difficult-to-identify, with improved **global post-operative outcomes**

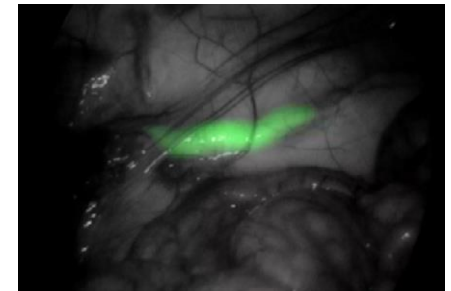
# Create new value in collaboration with an external partner

## Ureter imaging using ASP5354

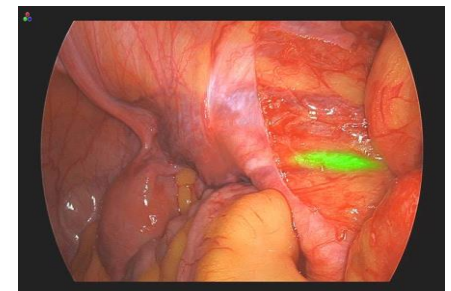
### ASP5354 features

- 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

### Ureter visualization data using ASP5354



Non-clinical (Porcine)



Clinical Setting



# Current situation and future plan

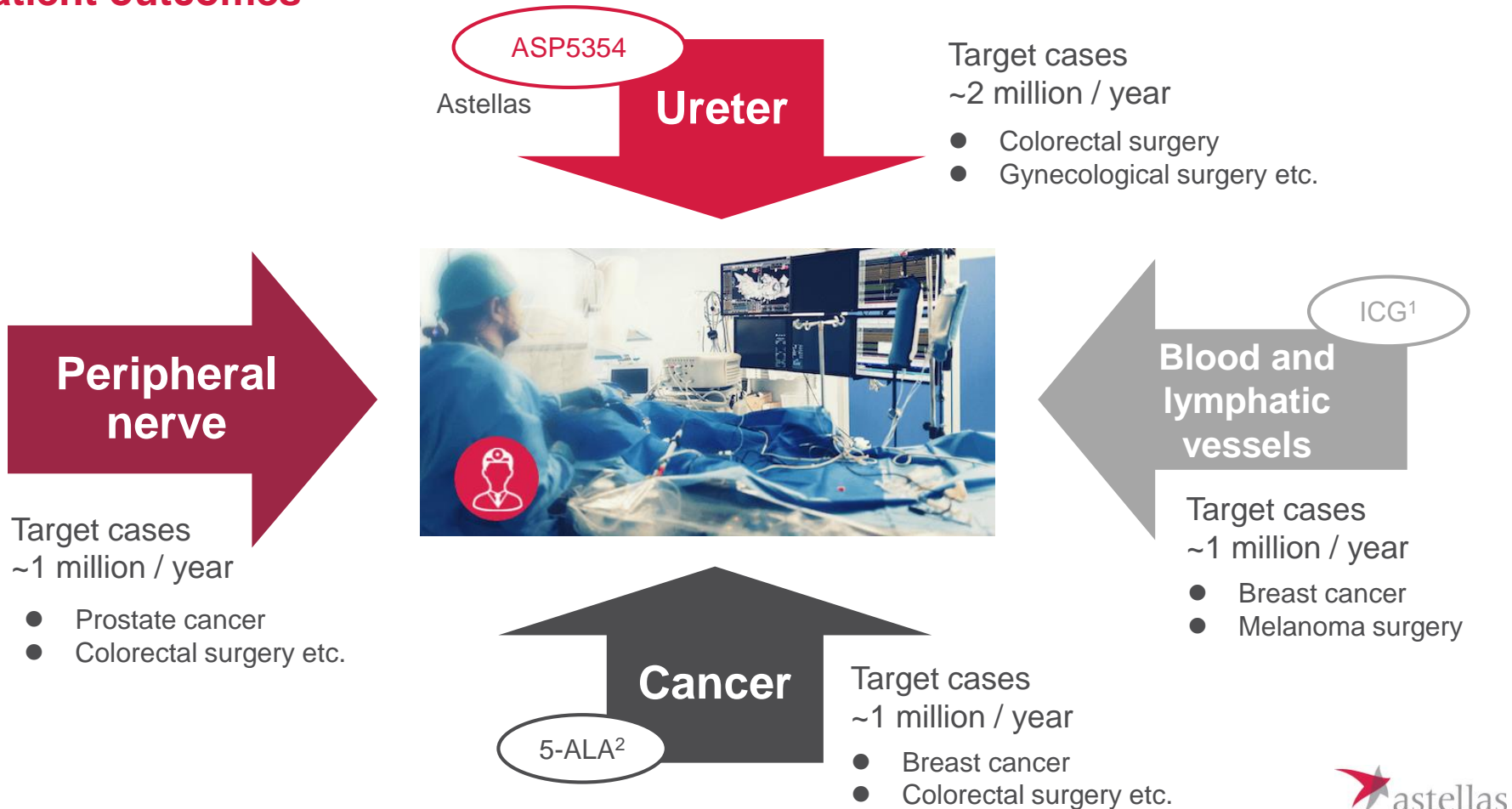
**Ureter visualization using ASP5354 is an easy-to-use and effective method for minimizing the risk of IUI without the need for additional procedures or time.**

- Completed First-subject-first-treatment in P2 (U.S.): Oct 2020
- Received U.S. FDA Fast Track Designation: Oct 2020
- Target approval: FY2023
- Investigating global development in addition to U.S. (Japan, China, EU)



# Future perspective

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



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.



Sphere:  
Chronic disease  
progression prevention

## PART 4

**A society where people can  
become healthy while having fun**

**Motohiro Kanayama**  
Business Producer,  
Rx+ Business Accelerator

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## Connecting Medical to Exercise

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

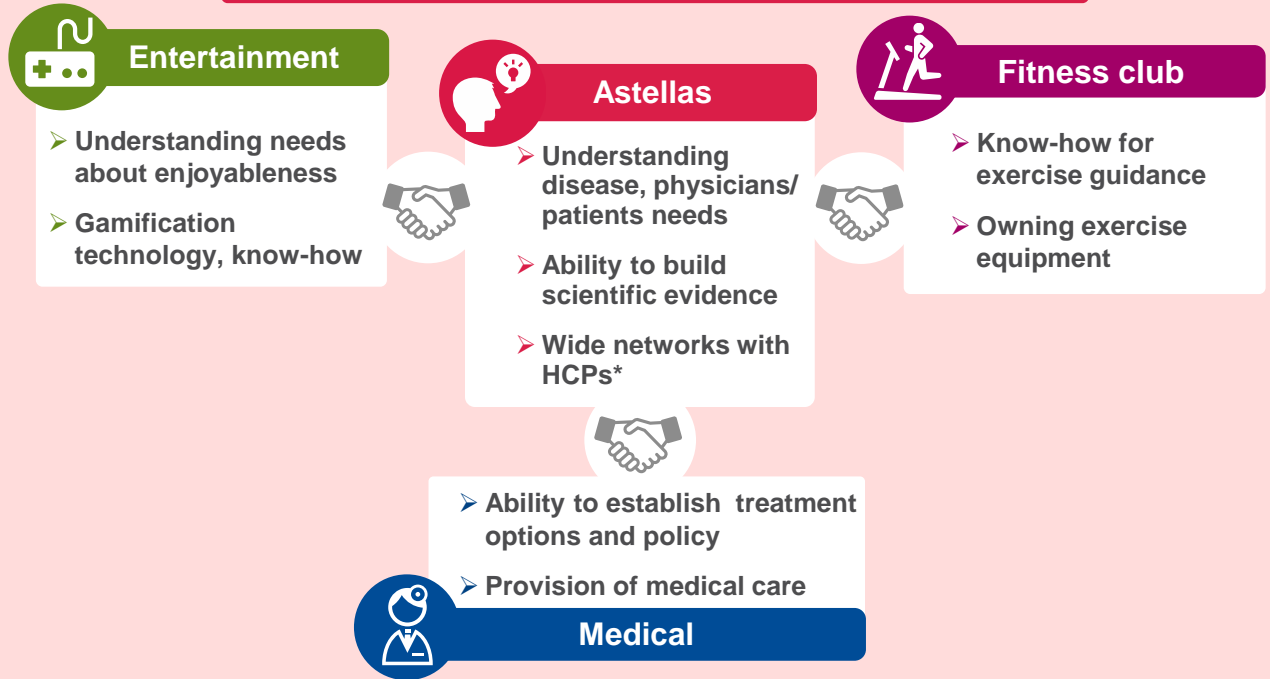
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Toward a society in which *people become healthy* with enjoying.



\*HCPs: Health Care Professionals

### Developing new solutions/Market penetration



### Society implementing health actions

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

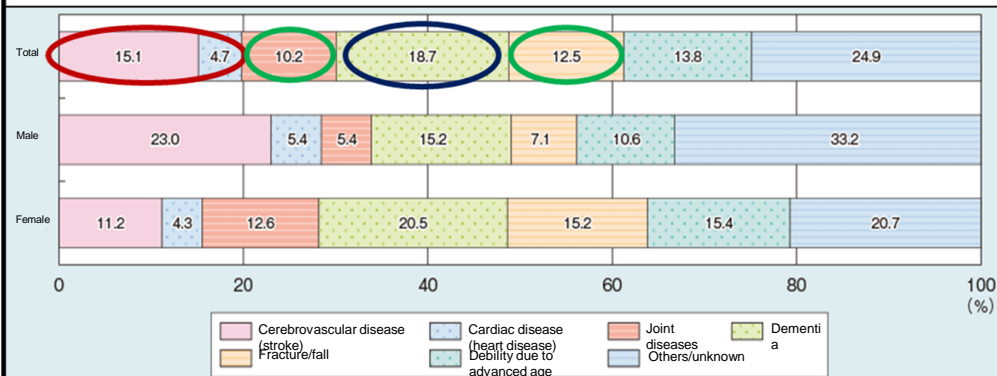
# CHALLENGES

## Macro perspective

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%



Materials: Ministry of Health, Labour and Welfare "Comprehensive Survey of Living Conditions" (2016)  
(Note) Excluding Kumamoto Prefecture.

[https://www8.cao.go.jp/kourei/whitepaper/w-2018/html/zenbun/s1\\_2\\_2.html](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.



\* 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 >




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



# 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.

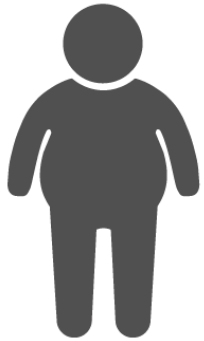
Player	Common challenges	Individual challenges
<b>Exercise service provider</b> 	<b>Medical rationale</b> It is not easy to build a medical rationale.	—
<b>Physician</b> 	<b>Opportunities</b> There are few opportunities to obtain information on exercise services.	<b>Time</b> It is difficult to secure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

Source: Prepared by Astellas based on the results of interviews with exercise service providers, physicians, and web surveys.

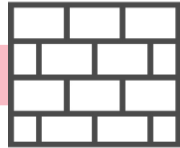
# CHALLENGES

## End user's perspective

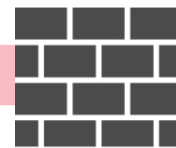
People who want  
to be healthy  
through exercise



Psychological  
barrier



Implementation  
barriers



People who  
continue proper  
exercises



### Barriers

Motivation

Resistance to change

Cumbersome

Giving up

### Barriers

Physical function

Lack of knowledge

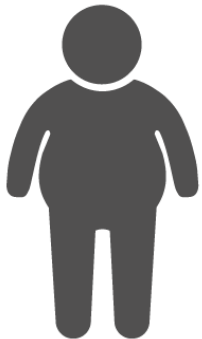
Lack of preparation

Surrounding environment



# 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**

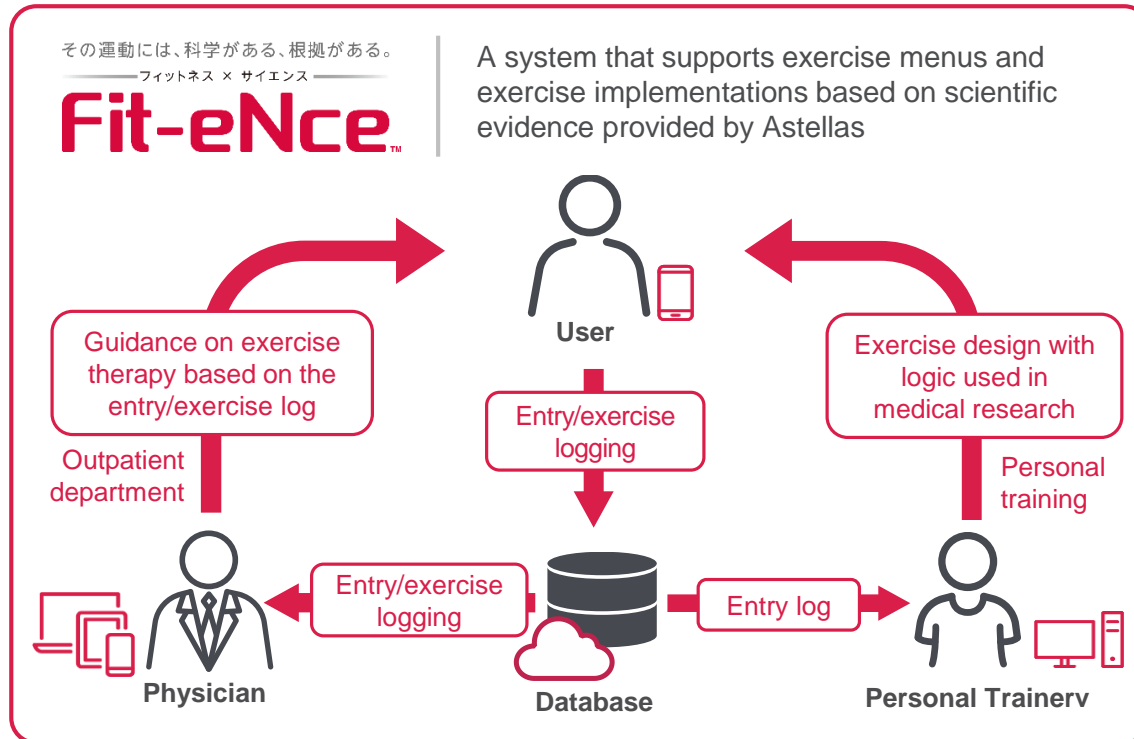


# Collaboration with a fitness club

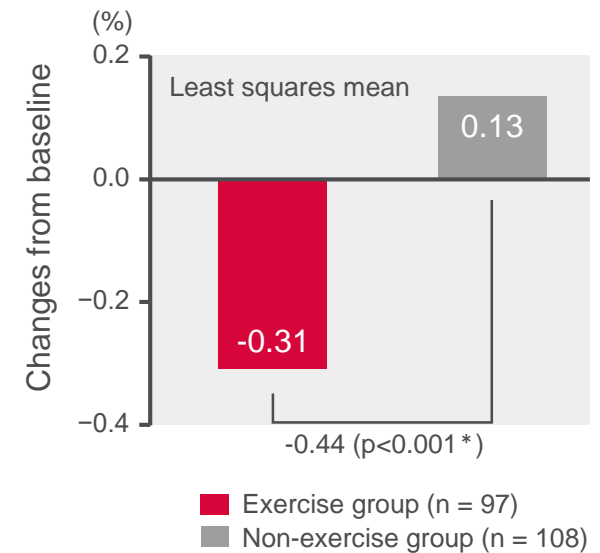
## Service overview



- 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.



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



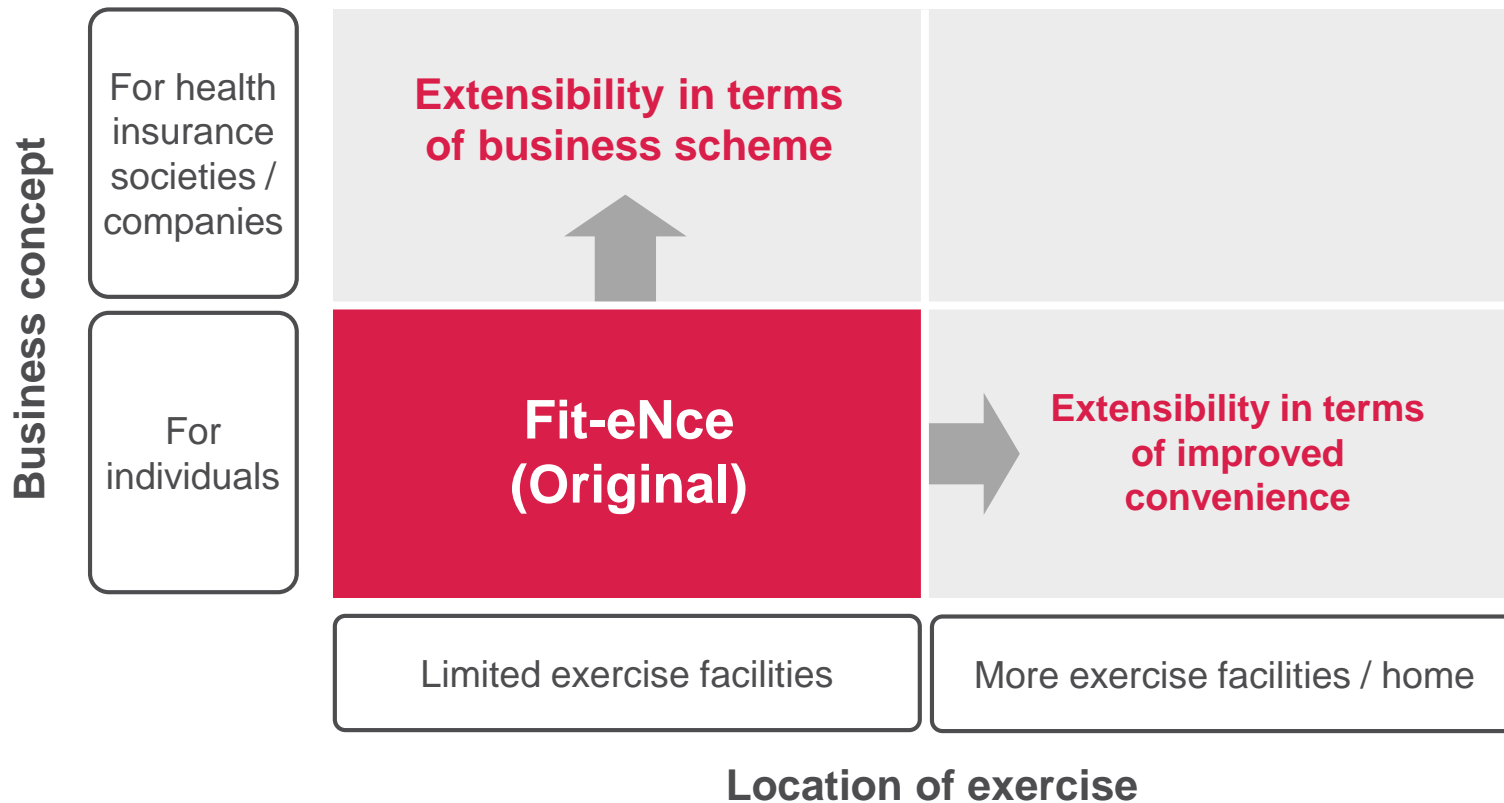
# Fit-eNce

## Future perspective



35

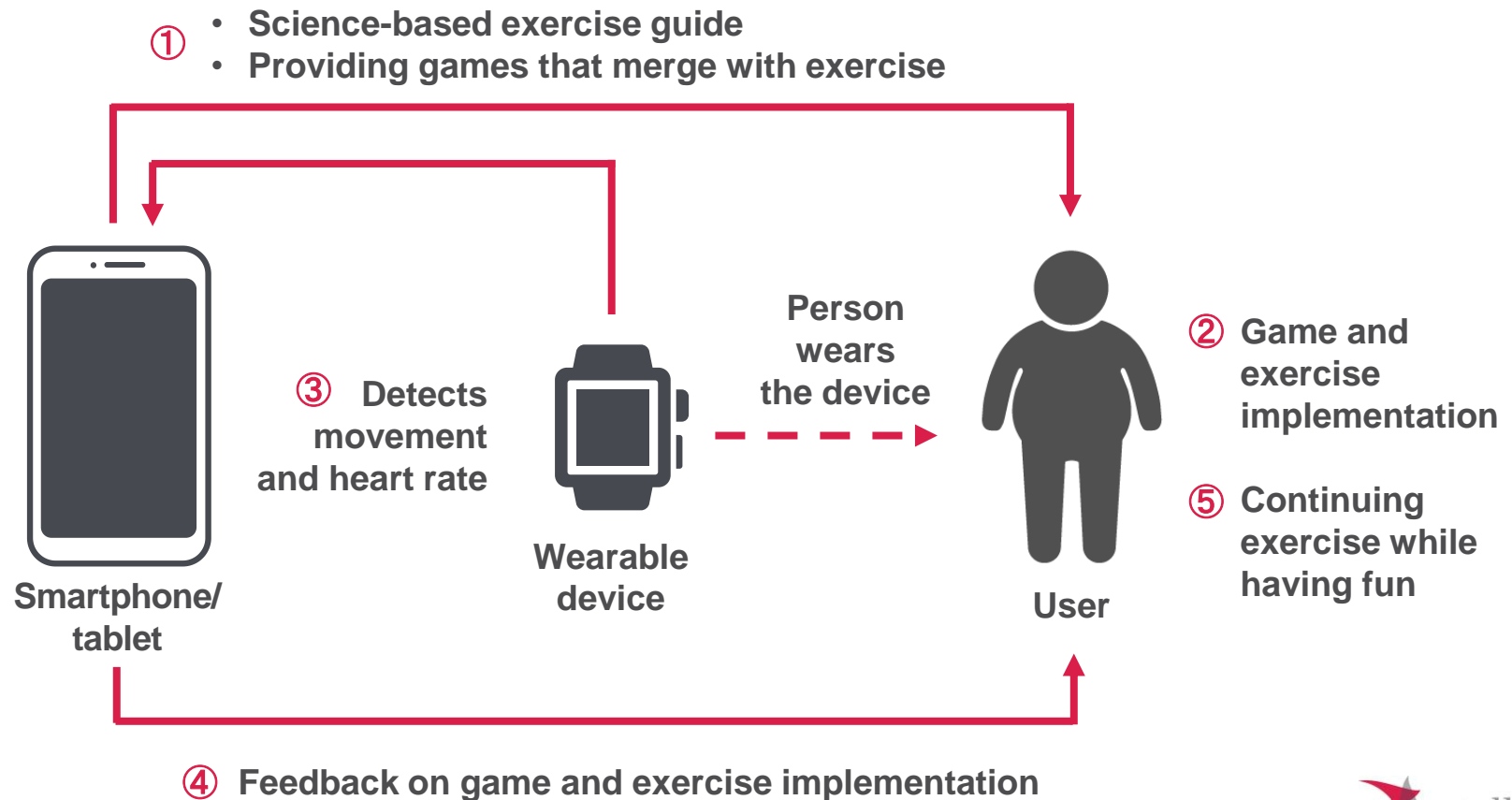
We will be exploring the optimal form of the service through small repeated trials.  
We will work on service development with science-based exercise as a common value.



## Example 1: Cooperation with BANDAI NAMCO Entertainment

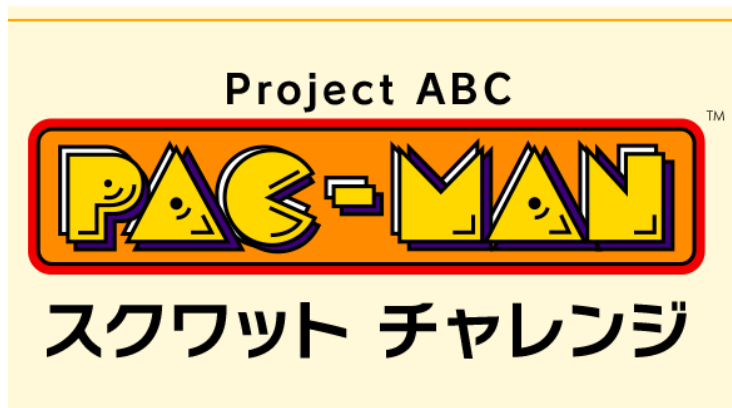
### Exercise support application using game know-how

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



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

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!

# Project ABC Pac-Man Squat Challenge

## Available today from noon to 10 p.m.

＼ 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?



VS



Squats during an after-school club activity

Voluntary training squats by idols

*Okonomiyaki* could be a side dish?



Yes!

VS



No!

The current “topic” can be viewed in the WEB application.

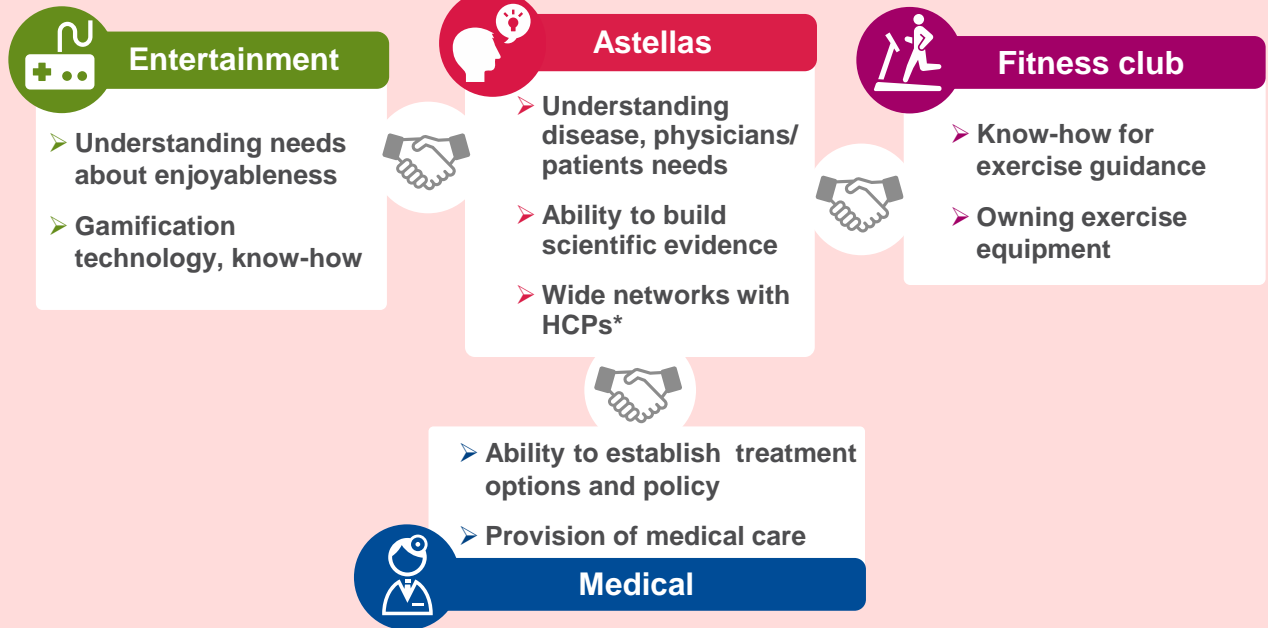
<https://abc.asobistore.jp/>

# Desired image

A society where people can become healthy while having fun



## Developing new solutions/Market penetration



## Society implementing health actions

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



Sphere:  
Chronic disease  
progression prevention

## 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

 **WellDoc**



- BlueStar regulatory clearance (Class II)
- HIPAA compliant
- SOC 2 certified
- ISO 13485 for International Business
- Cybersecurity functionality

### Artificial Intelligences, New Modules, and Algorithms



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

### Ease Access Using Digital Technology



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

# Medical needs

## Healthcare Challenges



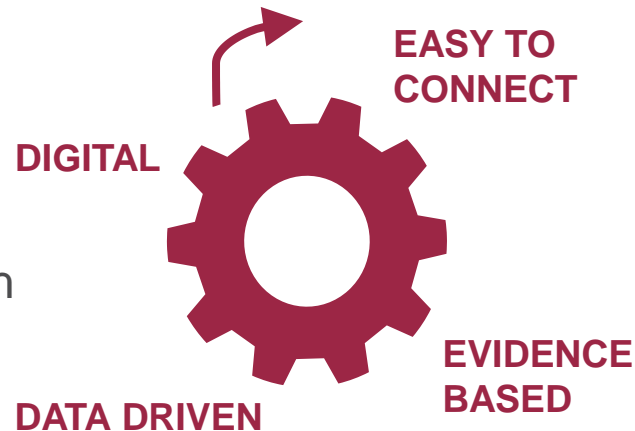
Escalating of  
Healthcare Cost



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



## Patented Technology

18 patents on artificial intelligence and algorithms



## Proven Clinical & Economic Rigor

Over 50+ peer-reviewed publications



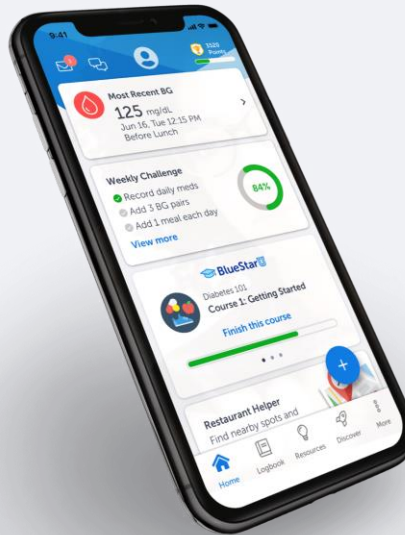
## Device Agnostic

Syncs with 300+ devices



## Comprehensive Platform

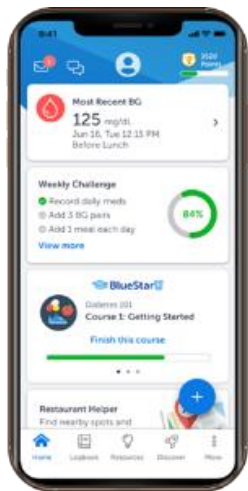
Supports seven chronic conditions



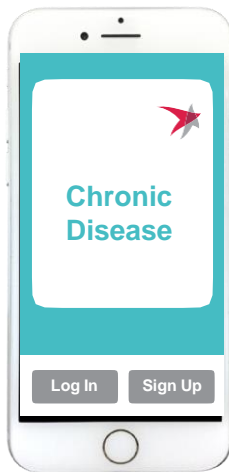
# Product pipeline

PRODUCT	INDICATION	REGION	PLANNING	DEVELOPMENT	CLINICAL TRIAL	COMMERCIAL
BlueStar	Diabetes	Japan				
		ASIA*				
New DTx	Chronic Disease	Global				
New DTx	Chronic Disease	Global				

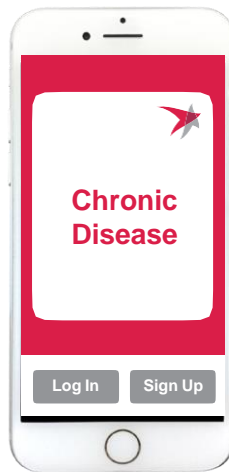
# Further expansion of the platform



BlueStar



New DTx



New DTx



## 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%



**Sphere:**  
**Chronic disease**  
progression prevention

## PART 6

# **Start with early detection of arrhythmias Contribute to extending healthy life expectancy**

**Makoto Ogino**  
Business Producer,  
Rx+ Business Accelerator

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

Support ecosystems  
for patients with  
heart disease

At home

Medical  
institutions

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

Seeking medical attention  
before illness worsens



Patients

Convenient  
measuring  
devices

Communication  
Tools

Timely  
Follow-up

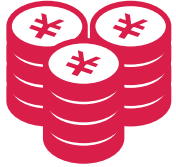
Data linkage

Doctor



Tools to support patients with heart disease

# Impact of heart disease on society



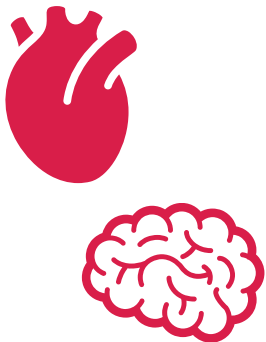
Medical costs for cardiovascular diseases was **highest at 6 trillion yen (19.7%)**

2017, "National Health Expenses" (MHLW)



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

2019, National Basic Survey of Life (MHLW)



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.

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.

<http://www.shinbousaidou-week.org/>

**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**



**Chronic disease  
progression prevention**

Regions focused on realizing Rx+ Story®

## Early detection of AF

### - Holter electrocardiography (ECG) -

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.



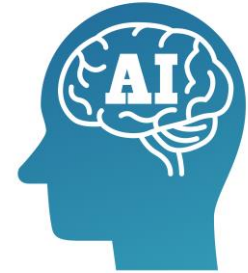
If the efficiency and accuracy of the automatic analysis are improved, more Holter ECG tests will be possible more easily.

**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.

## Providing value through collaboration with partners

### Introduction to M.Heart Co., Ltd.



M-Heart Co., Ltd. (Morioka-shi, Iwate, Japan)  
MedTech ventures established in 2016

While developing business with the cloud-type Holter ECG analysis system, “MYHOLTER”, the company is promoting DX (Digital Transformation) of medical services to create a society where electrocardiography can be performed more closely and more easily.

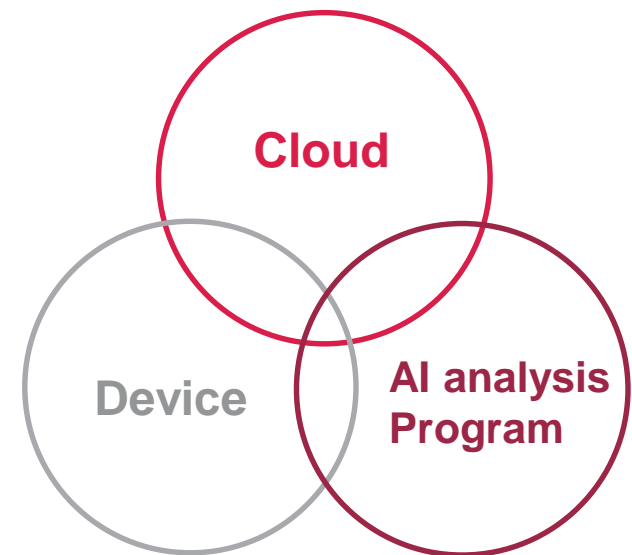
If this Holter ECG analysis system is described in the international standard rules, **MFER**, an analysis of the data obtained from any type of Holter ECG device is possible **on the cloud**.



## The development of a program for the holter analyzer using AI Future developments

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 <sup>\*1</sup>**

- **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-lead 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**





Sphere: Across all spheres

## PART 7

# Ultra-small medical devices beyond the pill

**Kunitake Abe**  
Business Producer,  
Rx+ Business Accelerator

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## iota platform technology

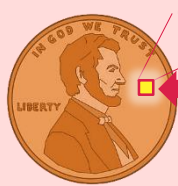
### Key point

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

Deliver *innovative value to medicine* with bioelectronics



What is the iota platform?



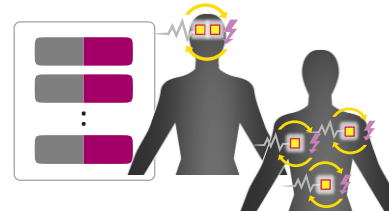
1-10mm<sup>3</sup>

Piezo technology in iota platform

- No wire, no battery
- Bi-directional communication
- Can provide power to sensors
- Electrical stimulation

## Lead bioelectronics to our future core business

Closed-loop control for Organ  
Brain-Machine-Interface

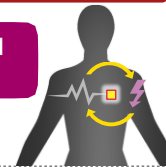


### Future step

Feedback control from multiple linked implants

Closed-loop modulation

sensing and stimulation

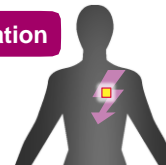
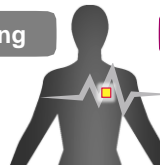


### 2nd step

Feedback control for stimulation by sensors on implant

sensing

stimulation



### 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.

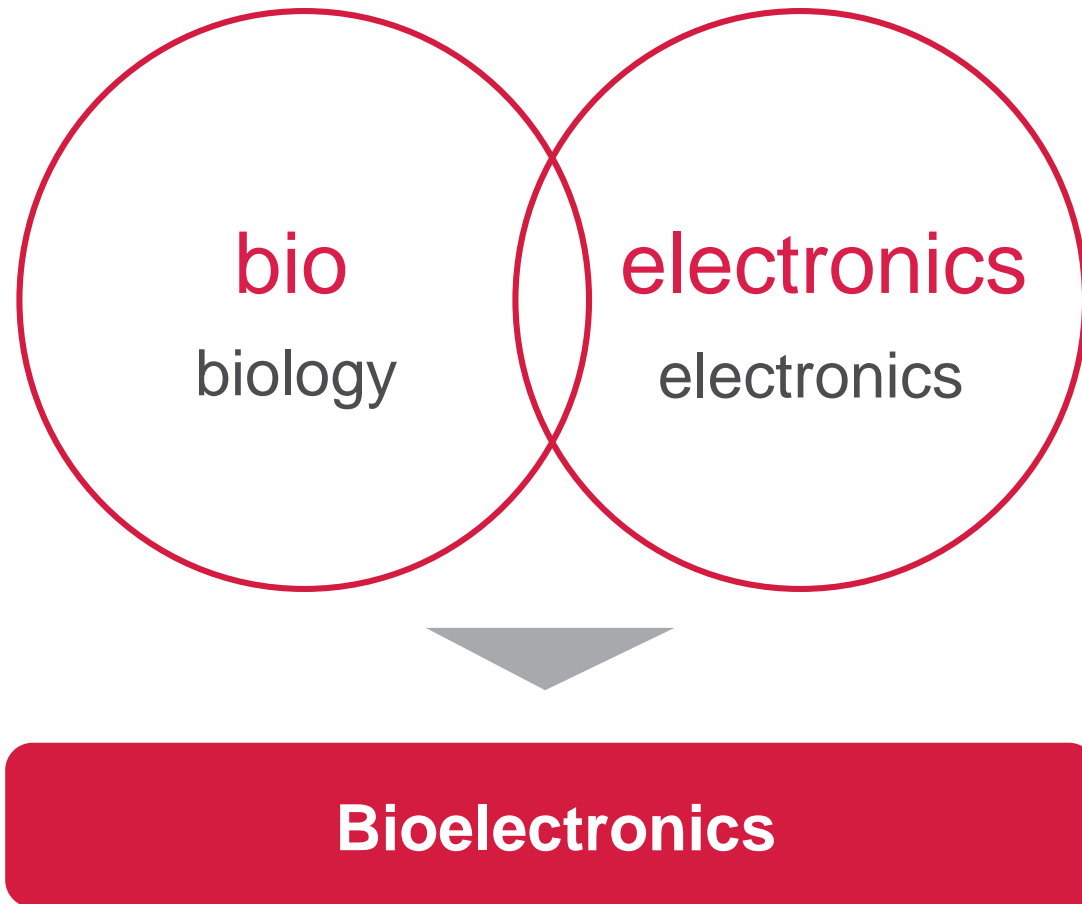
## Background 2

**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?

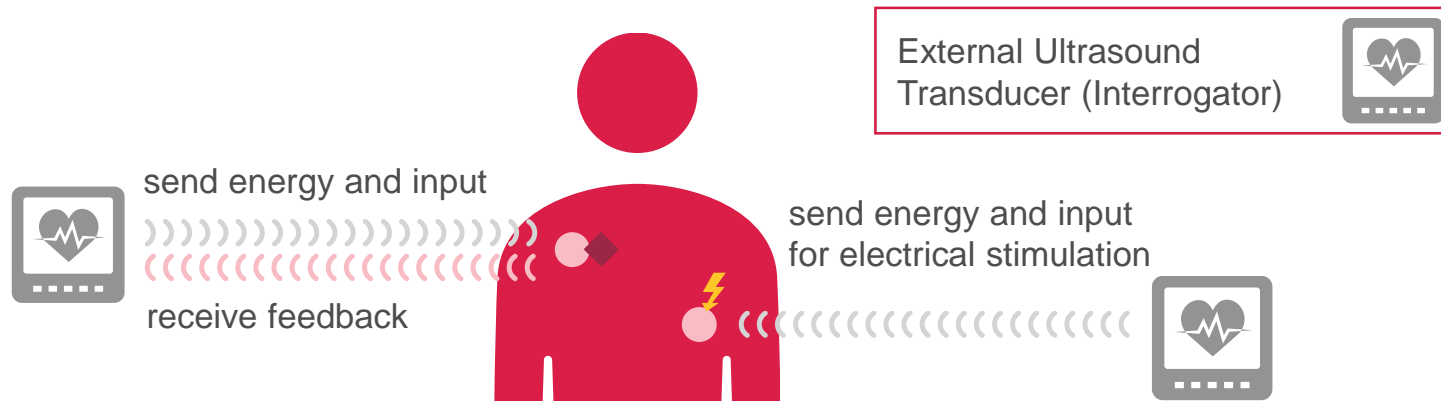


- Interdisciplinary field of biology and electronics
- Aims to improve lives of people with disabilities or diseases through obtaining biological data through methods using electronics or transmitting signals into organisms
- Examples include cardiac pacemakers, deep brain stimulation devices, vagus 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<sub>2</sub> 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

# What change would Iota's platform provide?

- 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?

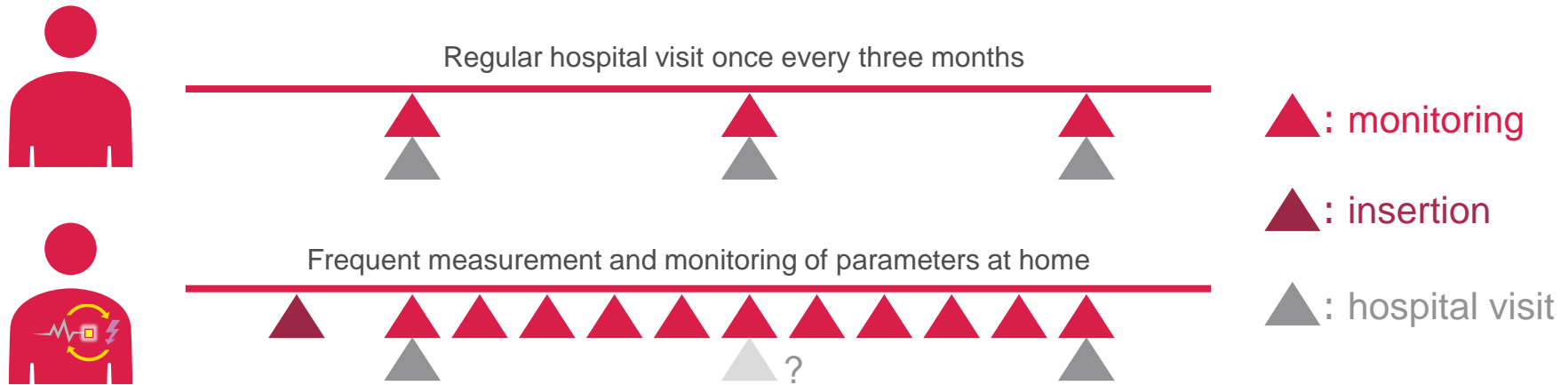


- Would consistency/discrepancy of the O<sub>2</sub> level within the blood and organs locally provide useful insights?
- Can pH be monitored as an indicator of inflammation?

- **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**

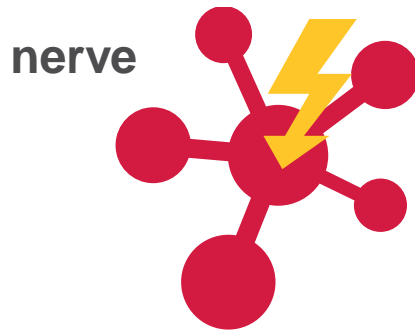


# What change would Iota's platform provide?



- 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?



**electrical stimulation to where the device is implanted**

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

○ Acts locally; less systemic adverse effects

- no wire
- no battery
- tiny

## Conventional implantables

- ✗ 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

## Neuro

- PD
- AD
- ET OCD
- ALS
- PTSD
- Depression
- Pain
- Anxiety
- BMI
- Sleep apnea
- Phantom pain
- Obesity
- Trauma
- Schizophrenia
- ED
- Brain pressure sensing
- MS
- Memory storage ("time machine")
- Spleen neuro paralysis
- Autonomic failure
- Epilepsy
- Motor Dysfunction

## Respiratory

- COPD
- Airway pressure sensor

## Urology

- Neurogenic bladder / Urination disorder (stimulation)
- Reflux esophagitis (monitoring)

## Locomotive / Muscular

- RA
- Muscular dystrophy

## Others

- Alcoholism
- Drug addiction

## Oncology

- Immuno-Oncology
- Tumor (monitoring)

## Ophthalmology

- Glaucoma (monitoring)
- AMD
- Intraocular (monitoring)
- Blindness
- Presbyopia

## Ear

- Tinnitus
- Cochlear implant
- Hearing loss, difficulty

## Cardiovascular

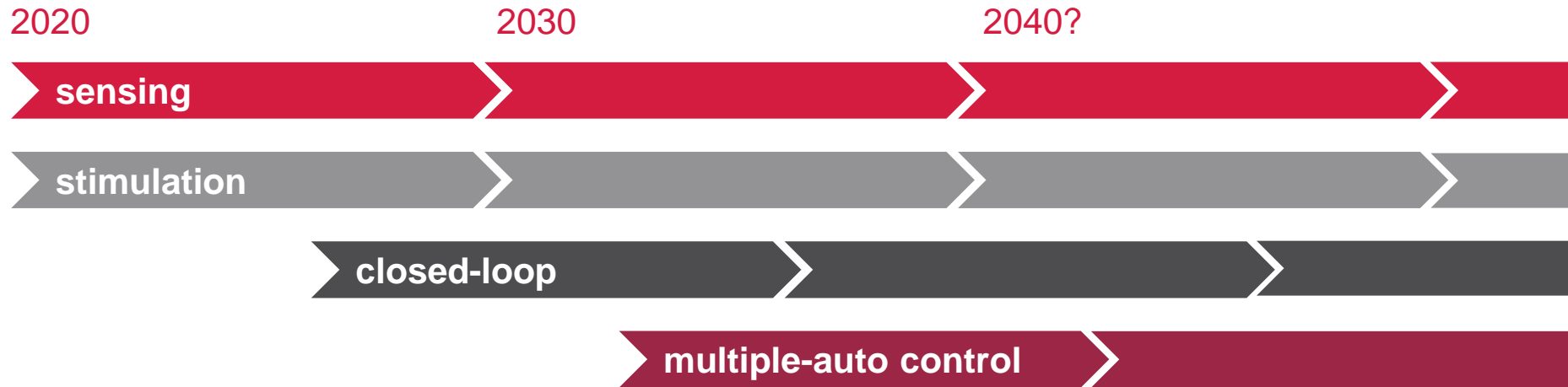
- Heart diseases (pacemaker)
- Chronic heart failure (monitoring)
- Abdominal aneurysm (monitoring)
- Intracardiac pressure (monitoring)

## Digestive/ metabolic

- CD
- FI/GERD
- NASH
- Diabetes (Glucose monitoring)

There is various potential upsides to the value of the platform

# 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

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# DEFINITION OF VALUE

