



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.

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

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

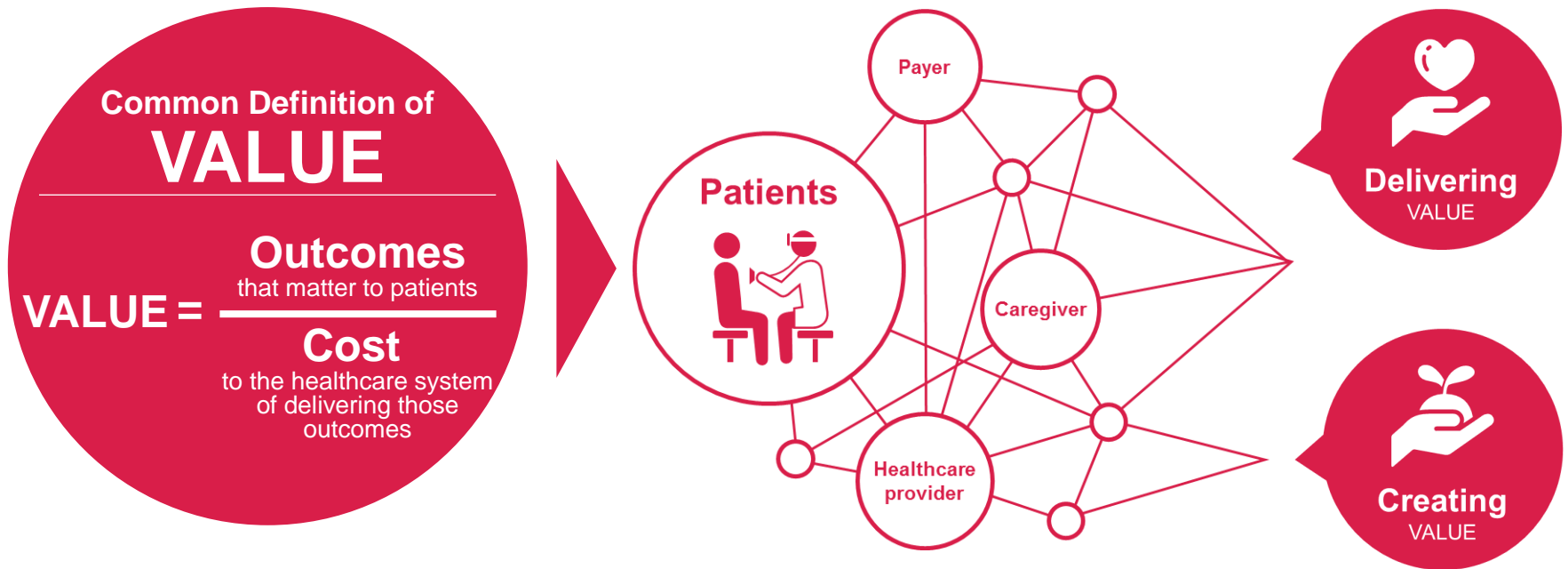
OUR VISION

Vision

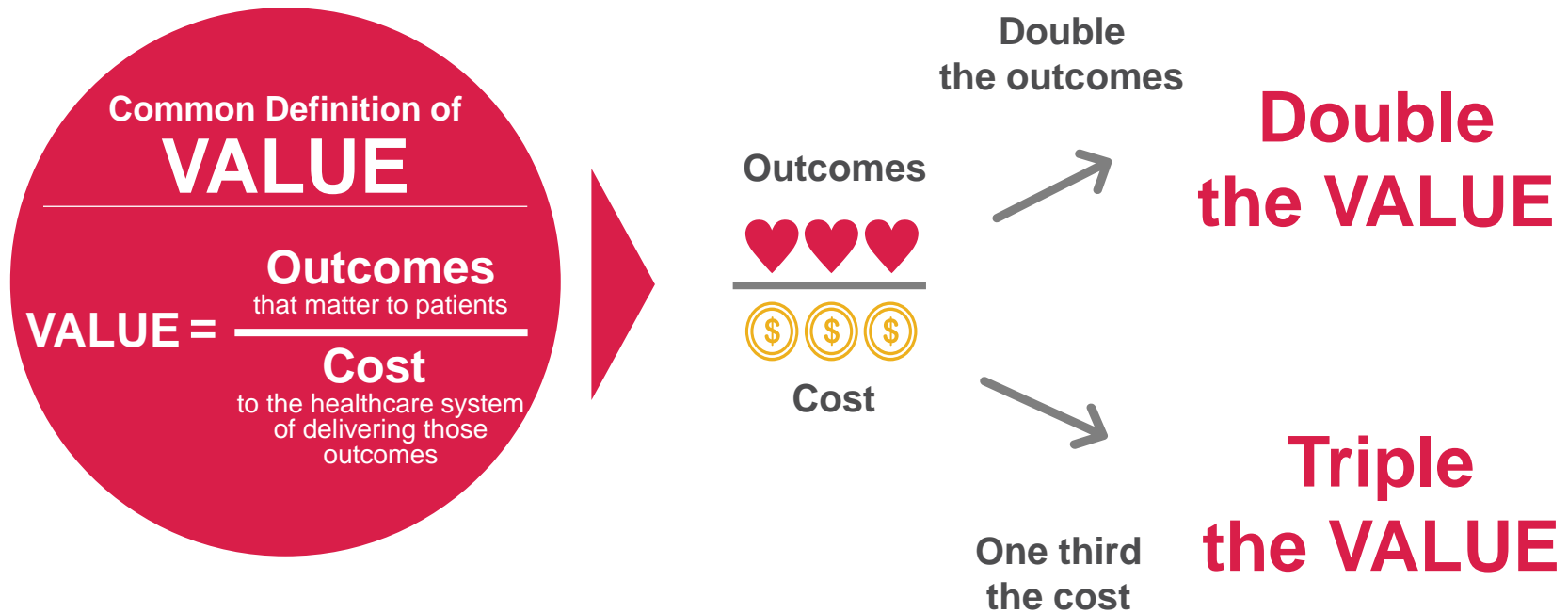
On the Forefront of
Healthcare Change to Turn
Innovative Science into
**VALUE for
Patients**

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

2005

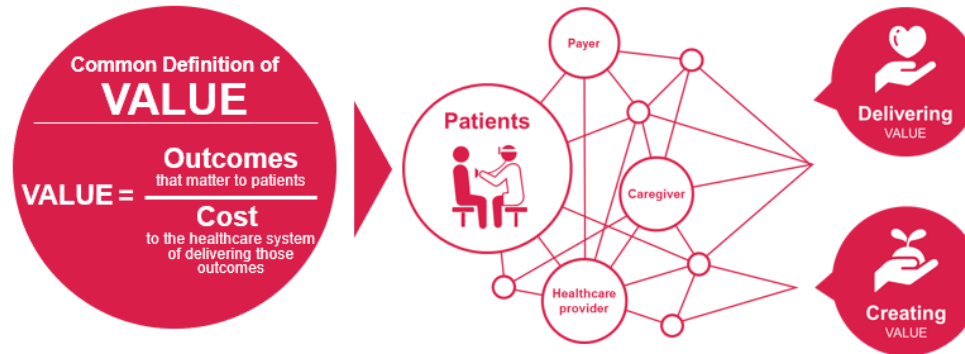


2013



WHY ASTELLAS DEVELOP Rx+[®] PROGRAMS

【Common definition of VALUE】



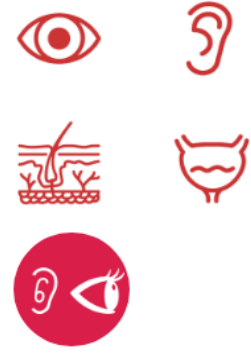
【Technological innovation and rapid changes in industrial structure】

2005



2013





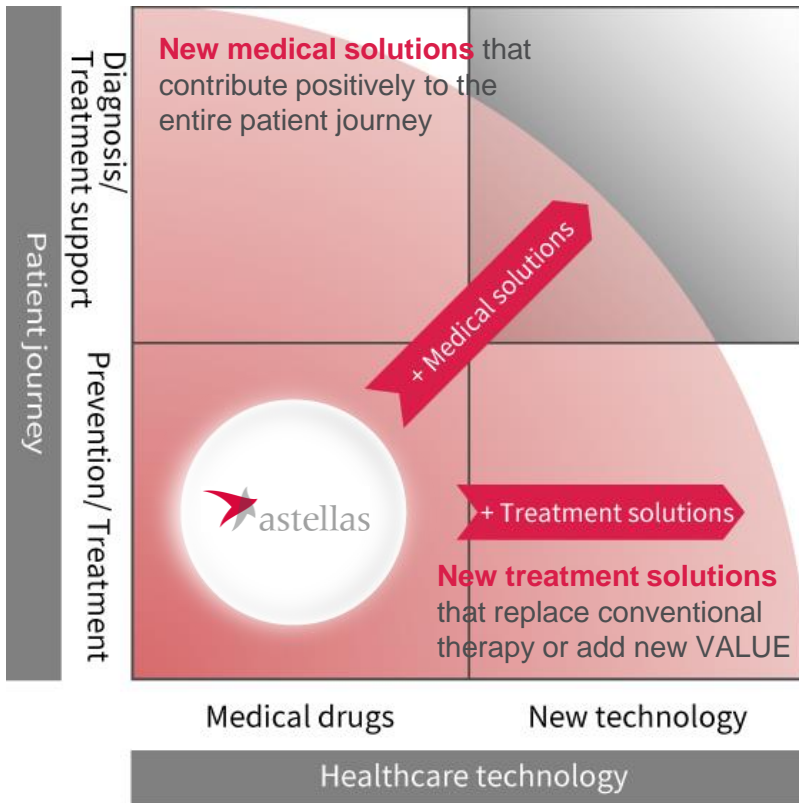
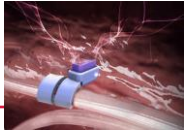
PART 2

Outcomes and Future Perspectives of Developing the Rx+[®] 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



Bioelectronics Ultra-small implant medical device

Digital Health & Digital Therapeutics



Disease management digital platform



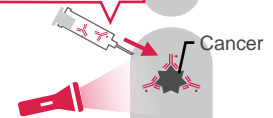
Smartphone exercise app with gamification and 3D motion technologies



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[®]: STRATEGIC DIRECTION OF RX+[®]

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

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



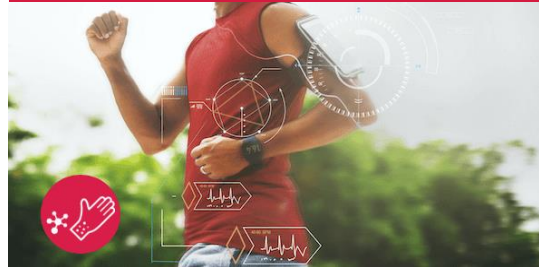
SUMMARY OF CURRENT SPHERES

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



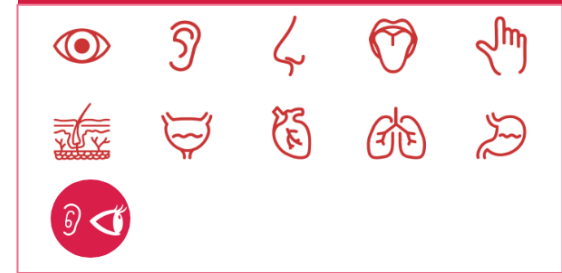
Solve health problems in perinatal and menopausal women and children with non-invasive solutions

Patient outcome maximization (via precise surgery/ diagnosis)



Improve accuracy of surgery and diagnosis to optimize treatment measures and maximize therapeutic outcome

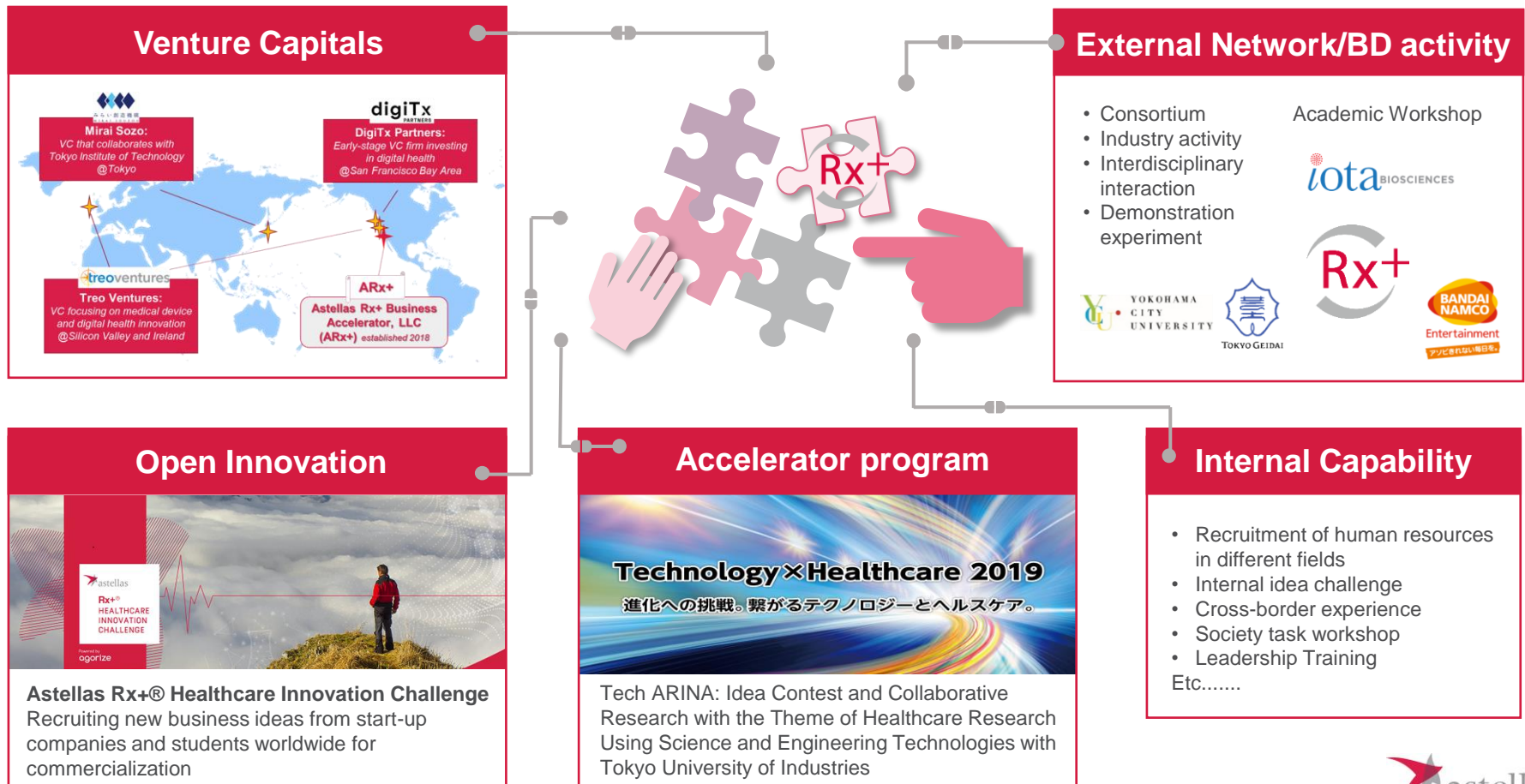
Sensory function support/ replacement



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

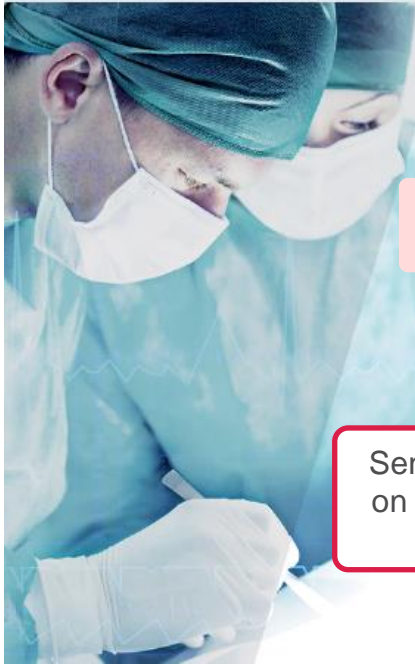
Akira Suwa
Business Producer,
Rx+ Business Accelerator

**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**



Sensory surgery based on surgeon's skills and experiences

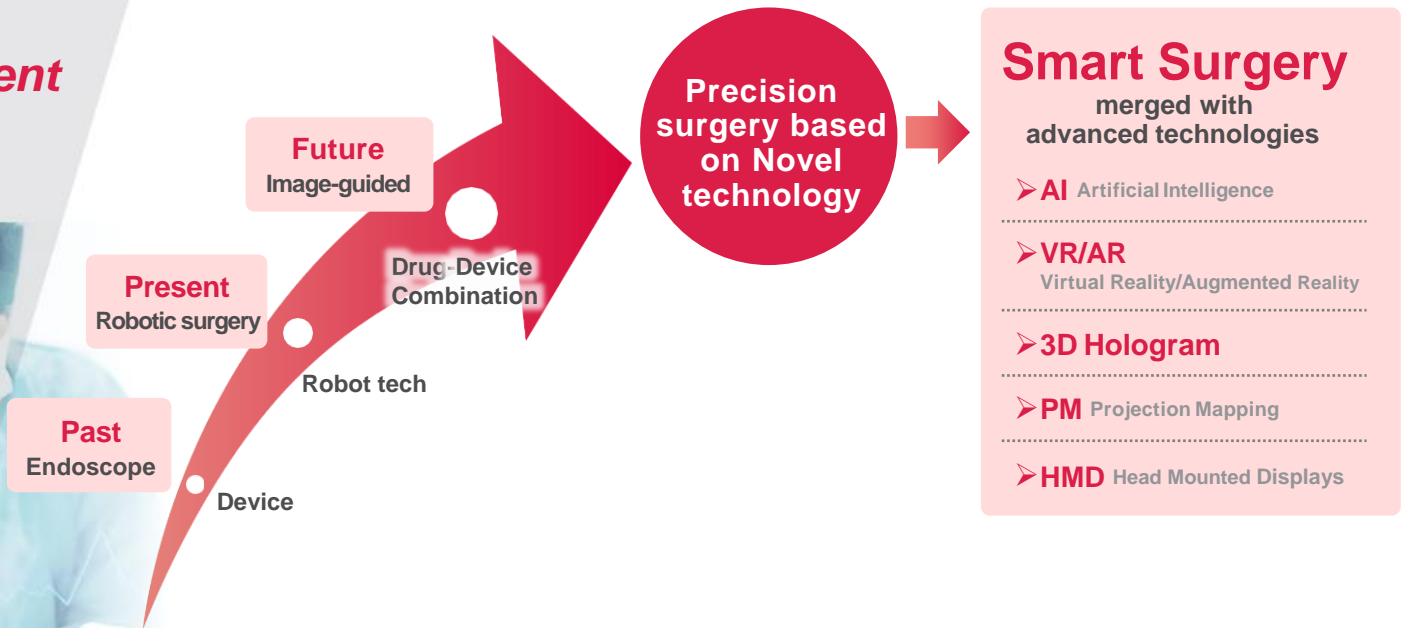
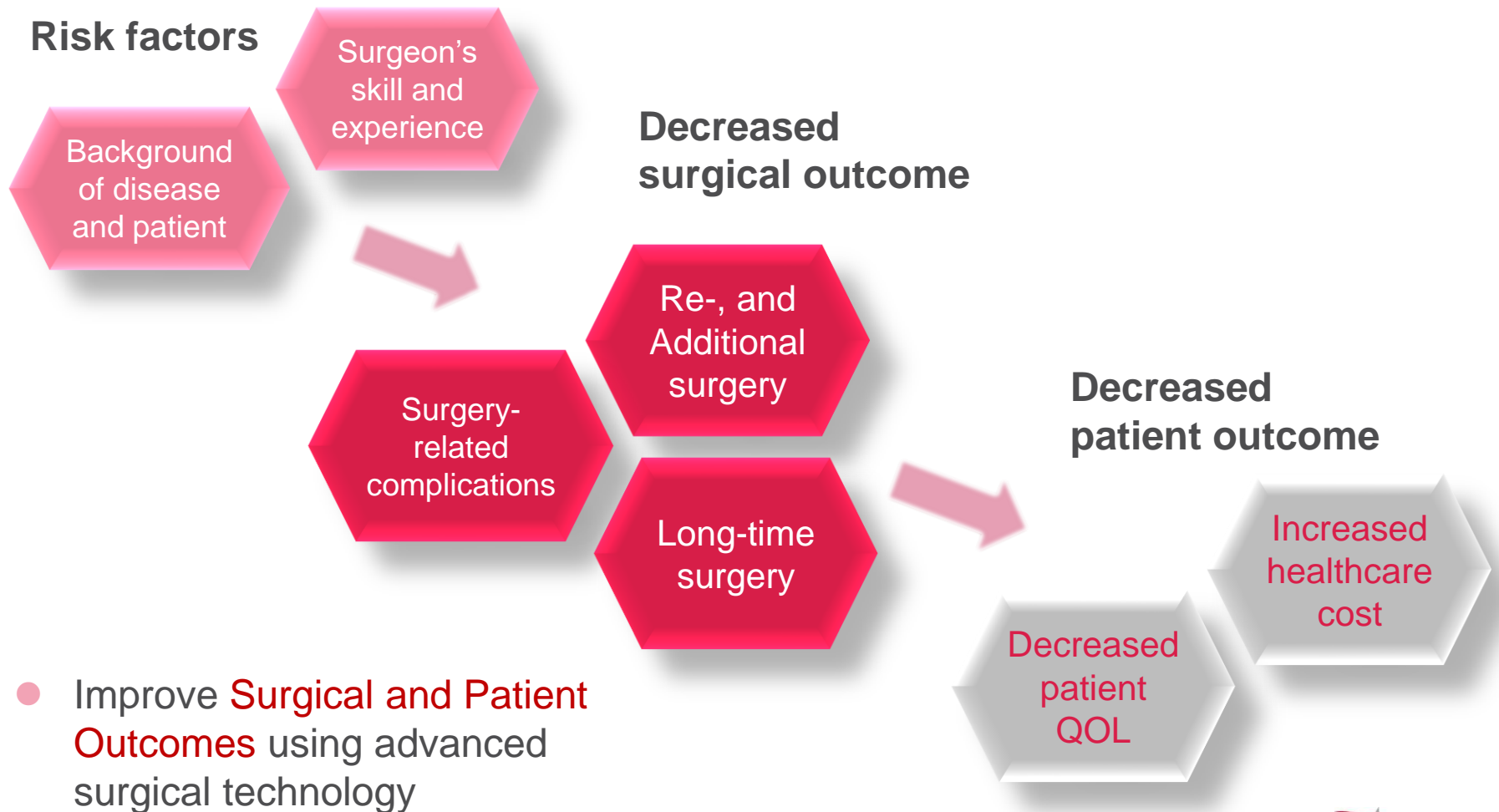


Image-guided surgery can be achieved by capitalizing on **device (Mechanical-based) and **pharma** (Biology-based) technology**

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 cost¹
- The best method for preventing IUI is intraoperative identification of both ureters²

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).

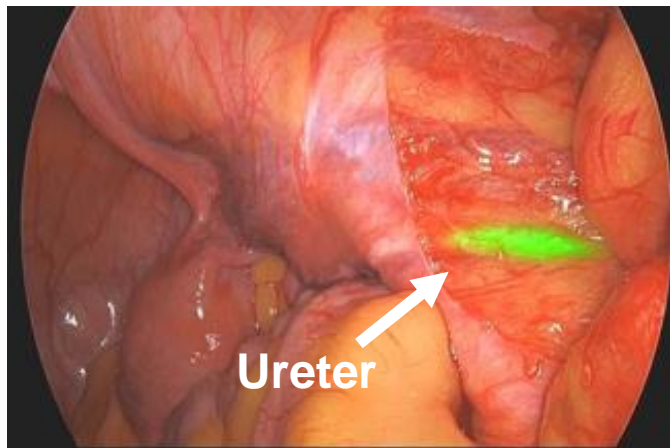


Challenges with the stenting method

- 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.)¹

Image-Guided Precision Surgery

Use Image: Image-Guided Precision Surgery



Graphical illustration of ureter imaging with ASP5354 in the clinical setting

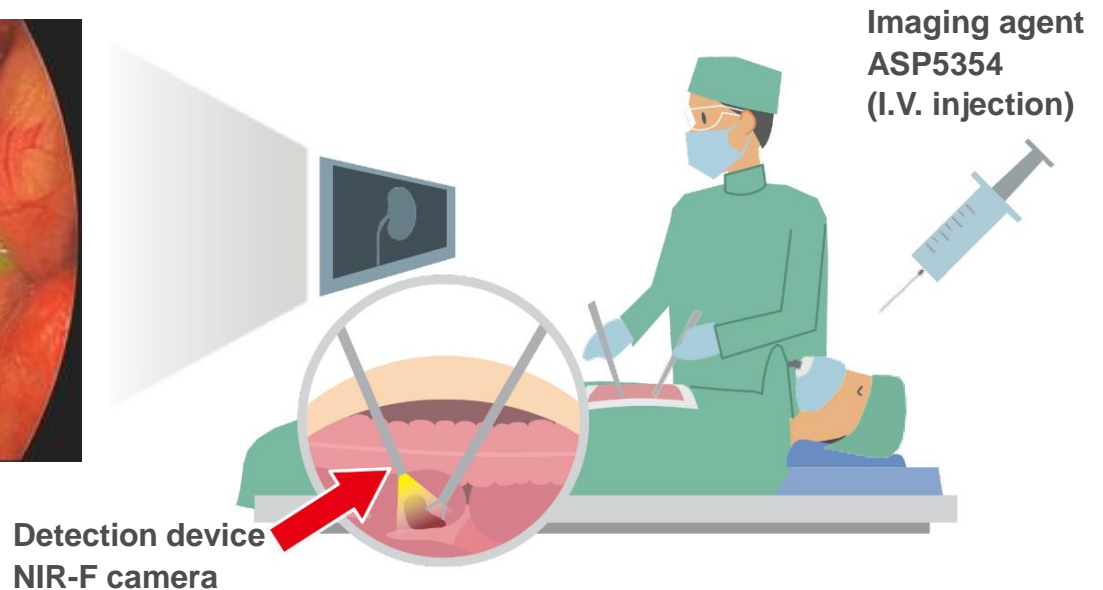


Image-guided precision surgery enables **easy, safe and precise** visualization of organs or tissues that are particularly difficult-to-identify, with improved **global post-operative outcomes**

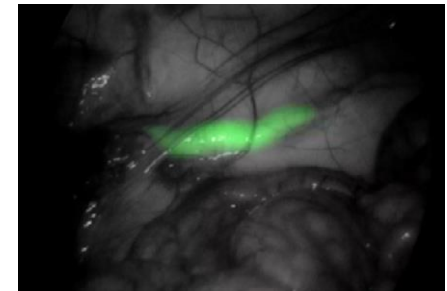
Create new value in collaboration with an external partner

Ureter imaging using ASP5354

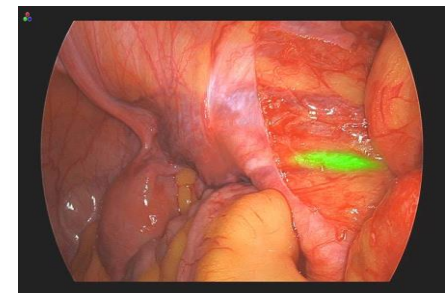
ASP5354 features

- 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

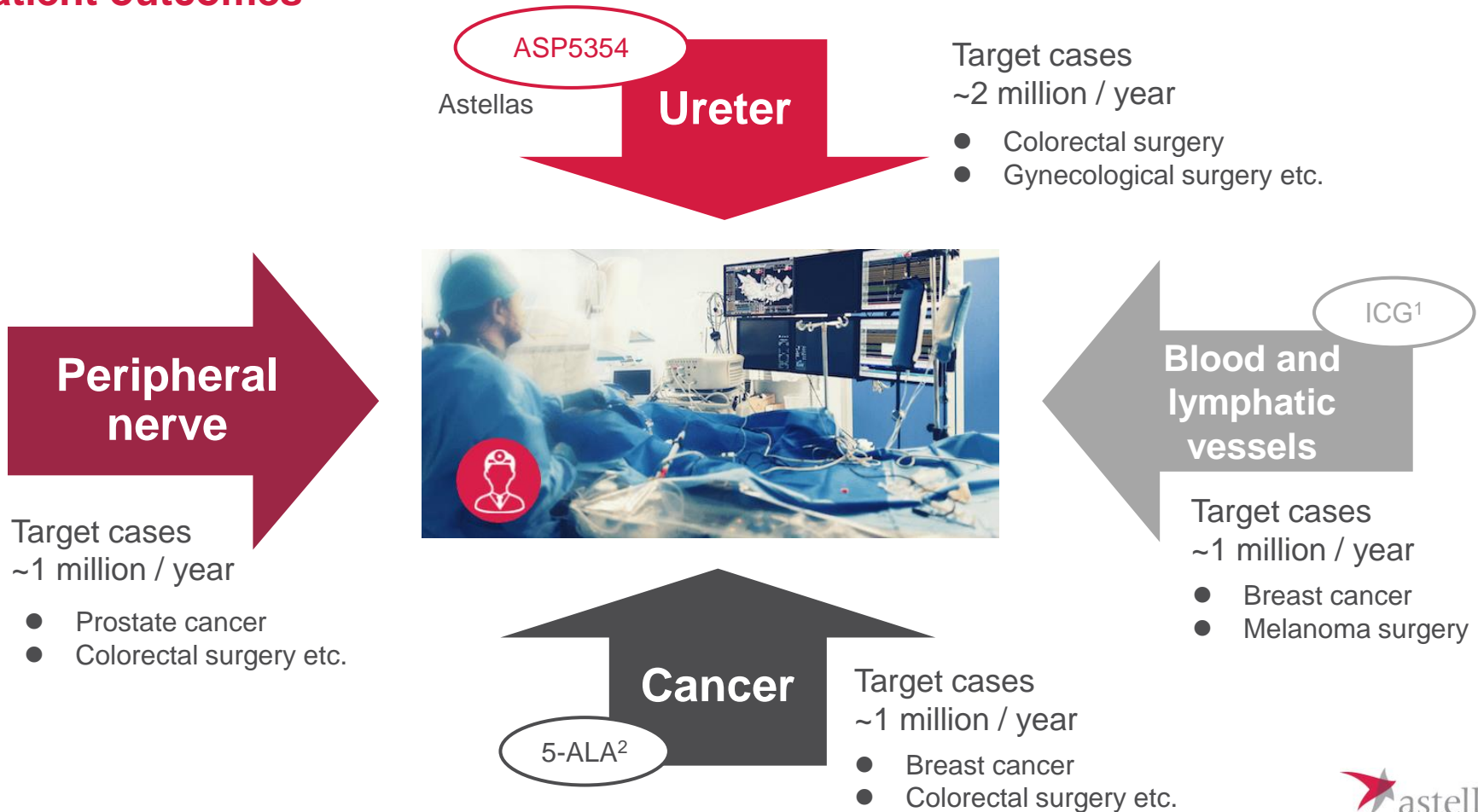
Ureter visualization using ASP5354 is an easy-to-use and effective method for minimizing the risk of IUI without the need for additional procedures or time.

- 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





Sphere:
Chronic disease
progression prevention

PART 4

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

Motohiro Kanayama
Business Producer,
Rx+ Business Accelerator

Connecting Medical to Exercise

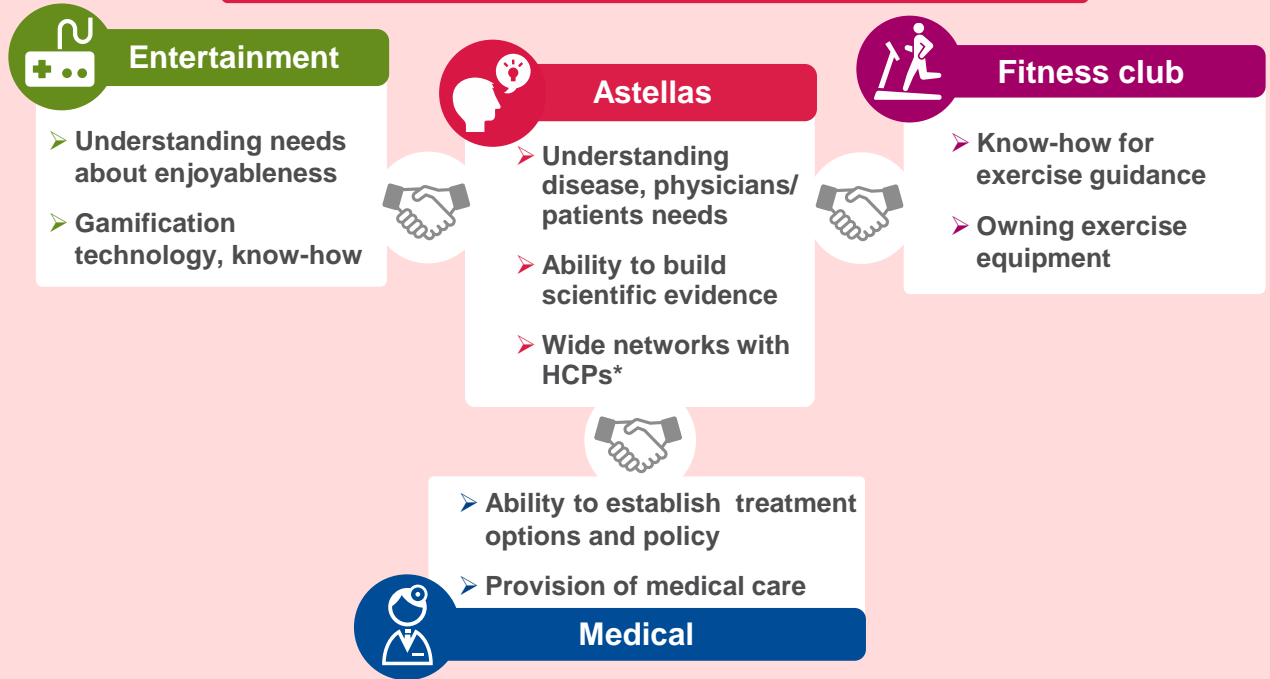
- Key point** Value creation and provision through
- "Astellas x Entertainment x Medical"
 - "Astellas x Fitness x Medical"

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

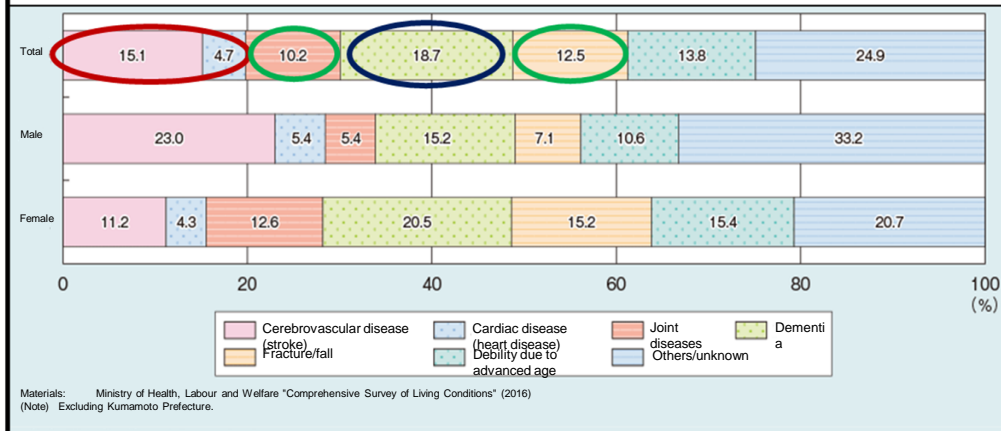
CHALLENGES

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%



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.

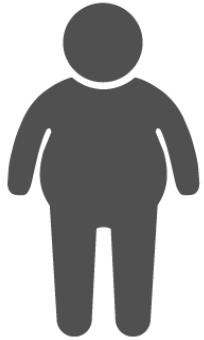
Player	Common challenges	Individual challenges
Exercise service provider 	Medical rationale It is not easy to build a medical rationale.	–
Physician 	Opportunities There are few opportunities to obtain information on exercise services.	Time It is difficult to secure time for exercise guidance.
Patient 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.

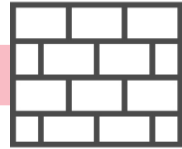
CHALLENGES

End user's perspective

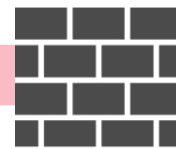
People who want to be healthy through exercise



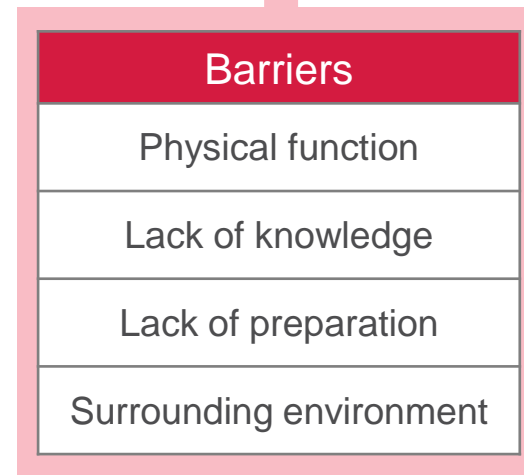
Psychological barrier



Implementation barriers

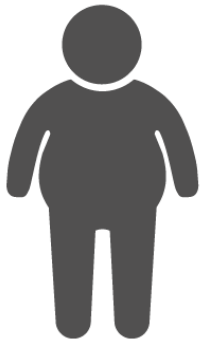


People who continue proper exercises



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

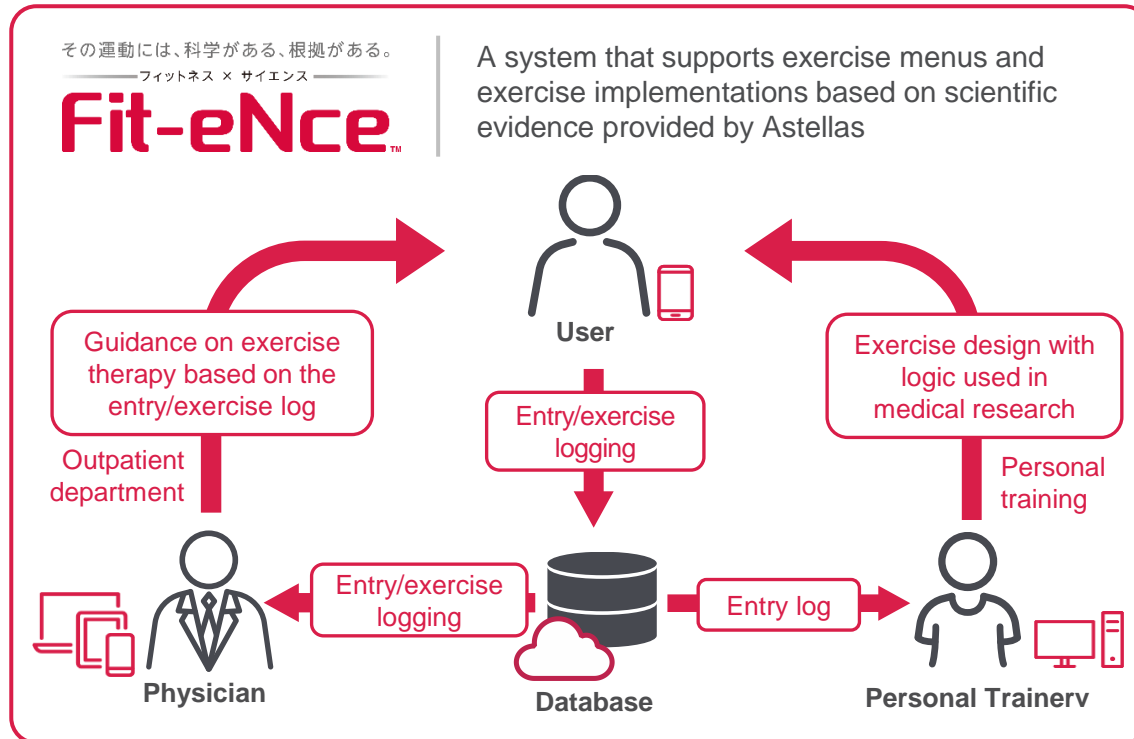


Collaboration with a fitness club

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)

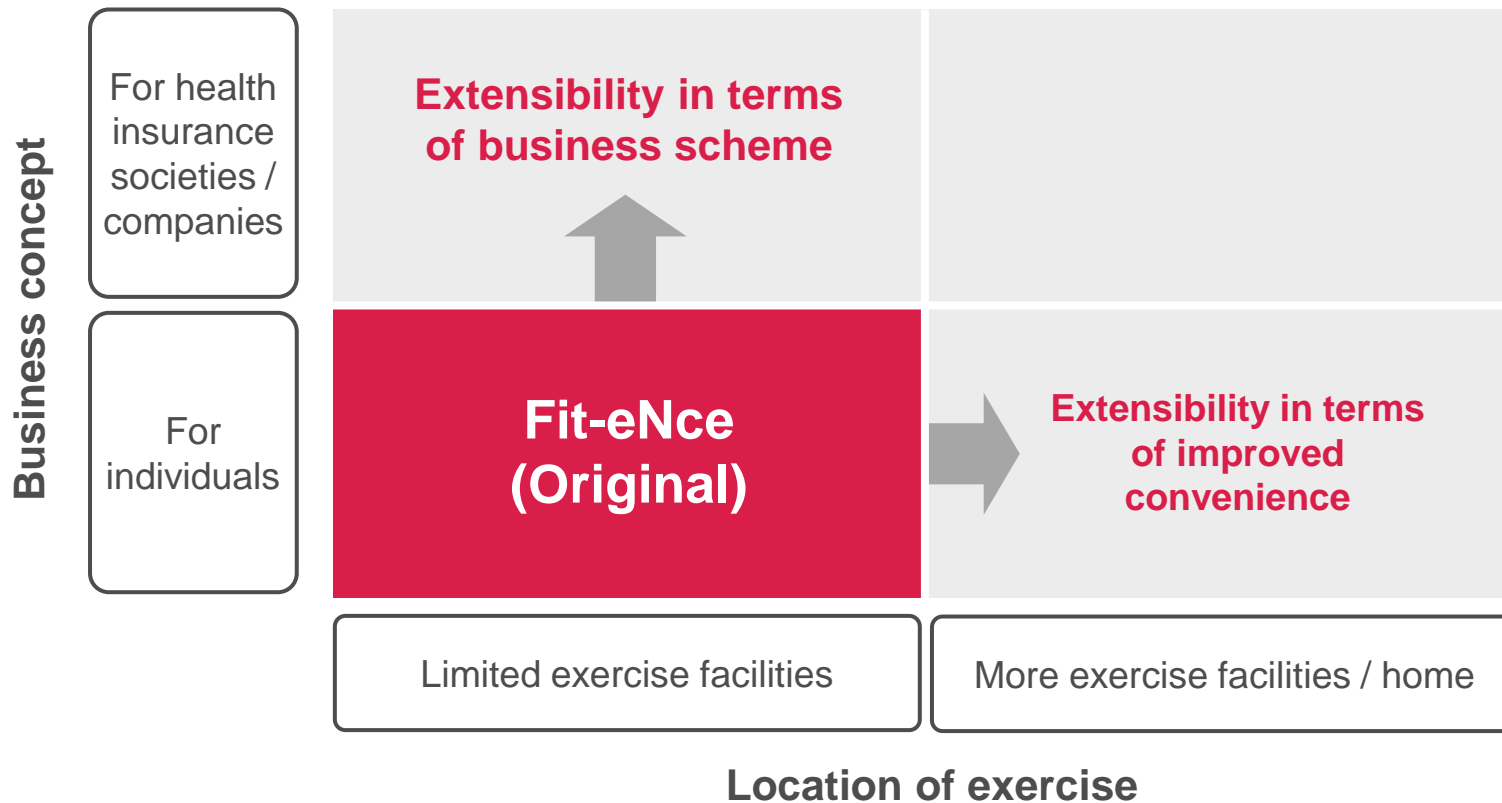


Fit-eNce

Future perspective

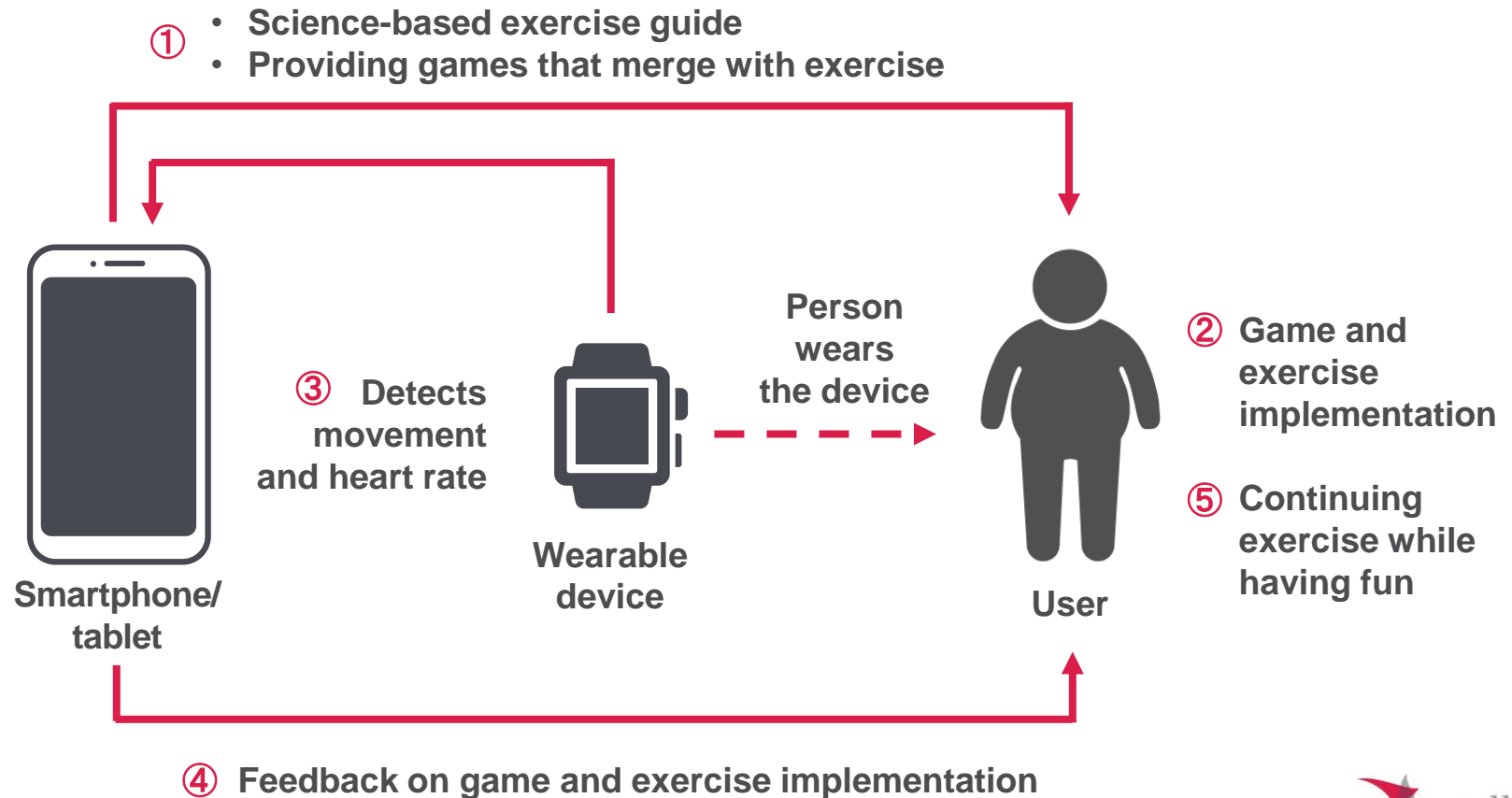


We will be exploring the optimal form of the service through small repeated trials.
We will work on service development with science-based exercise as a common value.



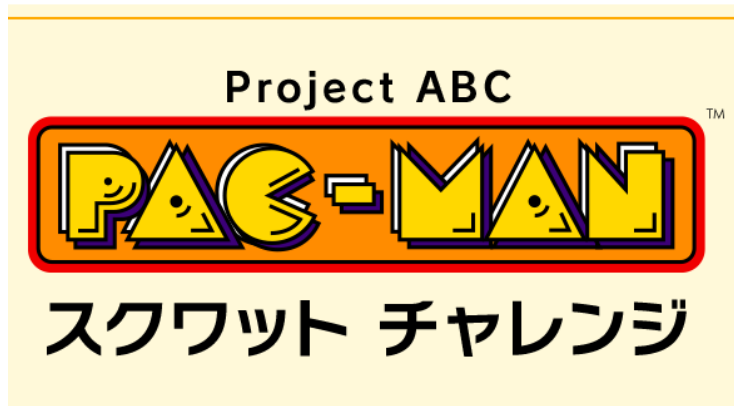
Example 1: Cooperation with BANDAI NAMCO Entertainment Exercise support application using game know-how

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!

遊び方

チーム選択
どちらかのチームを選んで
みんなでスクワットバトル！
あなたはどっち派？
【2021/1/26 17:29まで】
お家で一緒に過すなら？

イヌ VS ネコ
132pt 130pt
に参加! に参加!

遊び方
スクワットカウンター
12回

今日のキロク
13 スクワット
ダメージ
イヌ VS ネコ
145pt 130pt
チーム変更 シェアする
TAP
おたからを1個ゲット!
今日のおたから残り：1個
もう一度チャレンジ

チームを選択
参加するチームを決めよう！
好みができる『お題』が出
題されます。
あなたはどちら派？

チャレンジスクワット！
スマホを持ってスクワット！
スクワットの回数で、好みを
主張します！！

チームを勝利に導こう！
スクワットの回数は、参加す
るチームに集計され、勝敗が
決まります。
みんなで勝利を掴もう！！

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

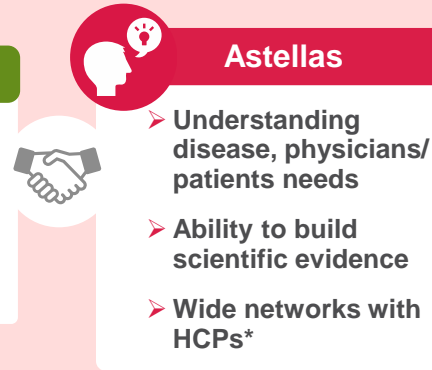
A society where people can become healthy while having fun



Developing new solutions/Market penetration

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

- Ability to establish treatment options and policy

- Provision of medical care

Medical

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

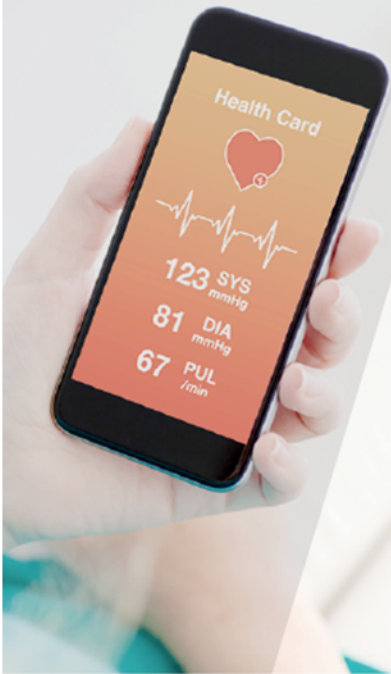
Principal, Project Lead, Digital Health,
Rx+ Business Accelerator

Clinically Relevant Holistic Mobile Healthcare Solutions

Key Points

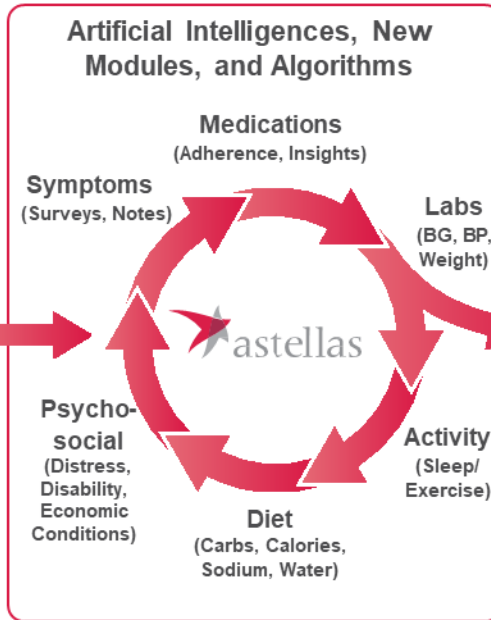
- Provides a personalized treatment and continuous interaction with the healthcare providers (HCPs)
- Optimal timing of medical intervention leading to improved outcomes and cost saving

Fosters patients and HCPs **behavioral** changes and coaching using **novel technology**



Welldoc

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



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



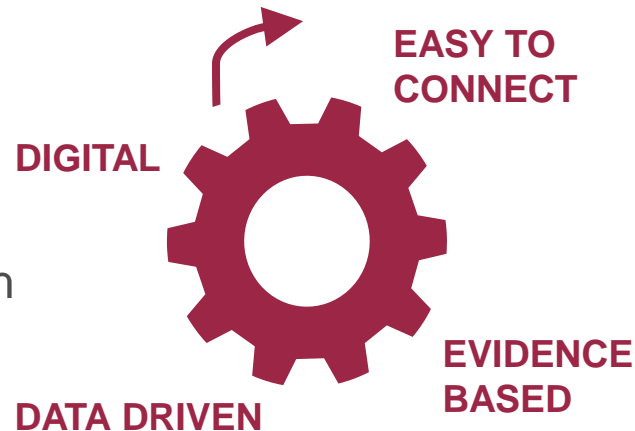
Escalating of
Healthcare Cost



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



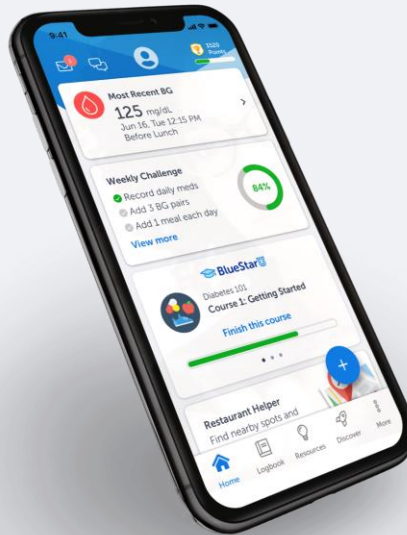
Device Agnostic

Syncs with 300+ devices



Comprehensive Platform

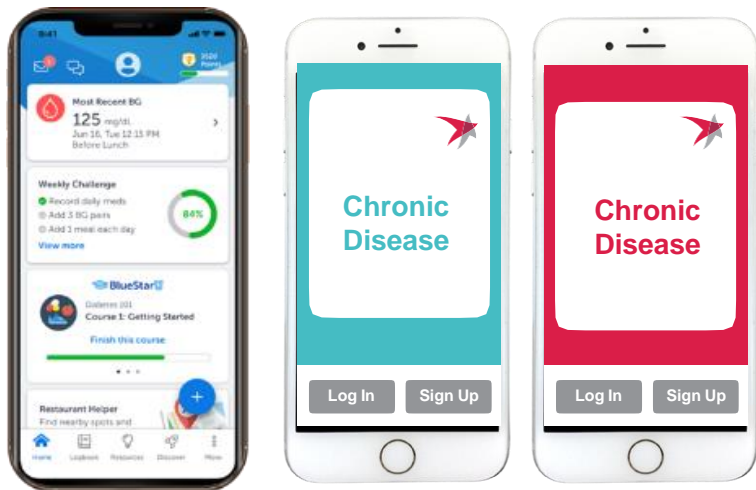
Supports seven chronic conditions



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

Key point

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

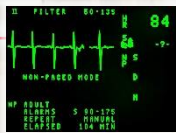
Support ecosystems for patients with heart disease

At home

Medical institutions

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

Seeking medical attention before illness worsens



Patients



Timely Follow-up



Doctor

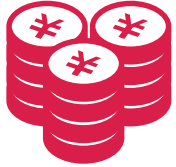
Convenient measuring devices

Communication Tools

Data linkage

Tools to support patients with heart disease

Impact of heart disease on society



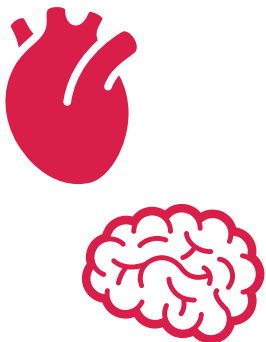
Medical costs for cardiovascular diseases was **highest at 6 trillion yen (19.7%)**

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.



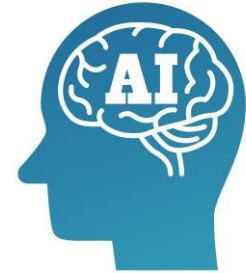
If the efficiency and accuracy of the automatic analysis are improved, more Holter ECG tests will be possible more easily.

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.

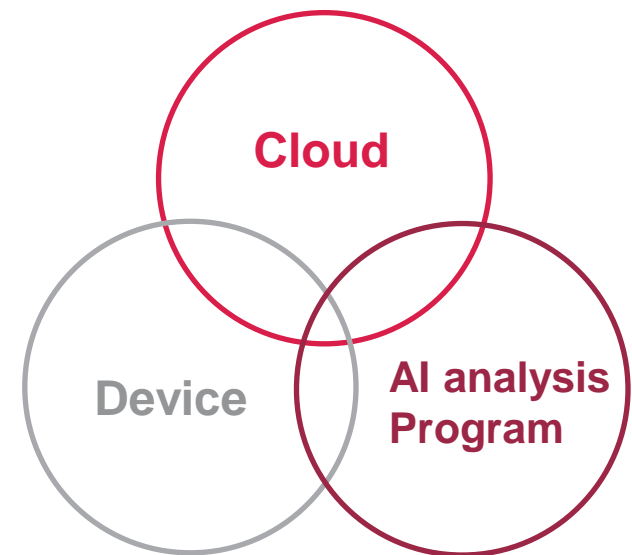
If this Holter ECG analysis system is described in the international standard rules, **MFER**, an analysis of the data obtained from any type of Holter ECG device is possible **on the cloud**.



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 *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-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

iota platform technology

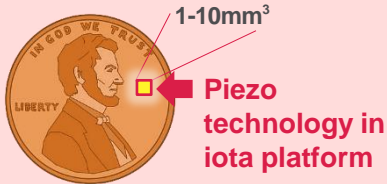
Key point

- 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

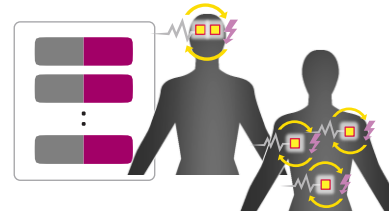
Lead bioelectronics to our future core business

? What is the iota platform?



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

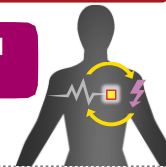
Closed-loop control for Organ Brain-Machine-Interface



Future step
Feedback control from multiple linked implants

Closed-loop modulation

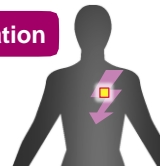
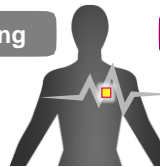
sensing and stimulation



2nd step
Feedback control for stimulation by sensors on implant

sensing

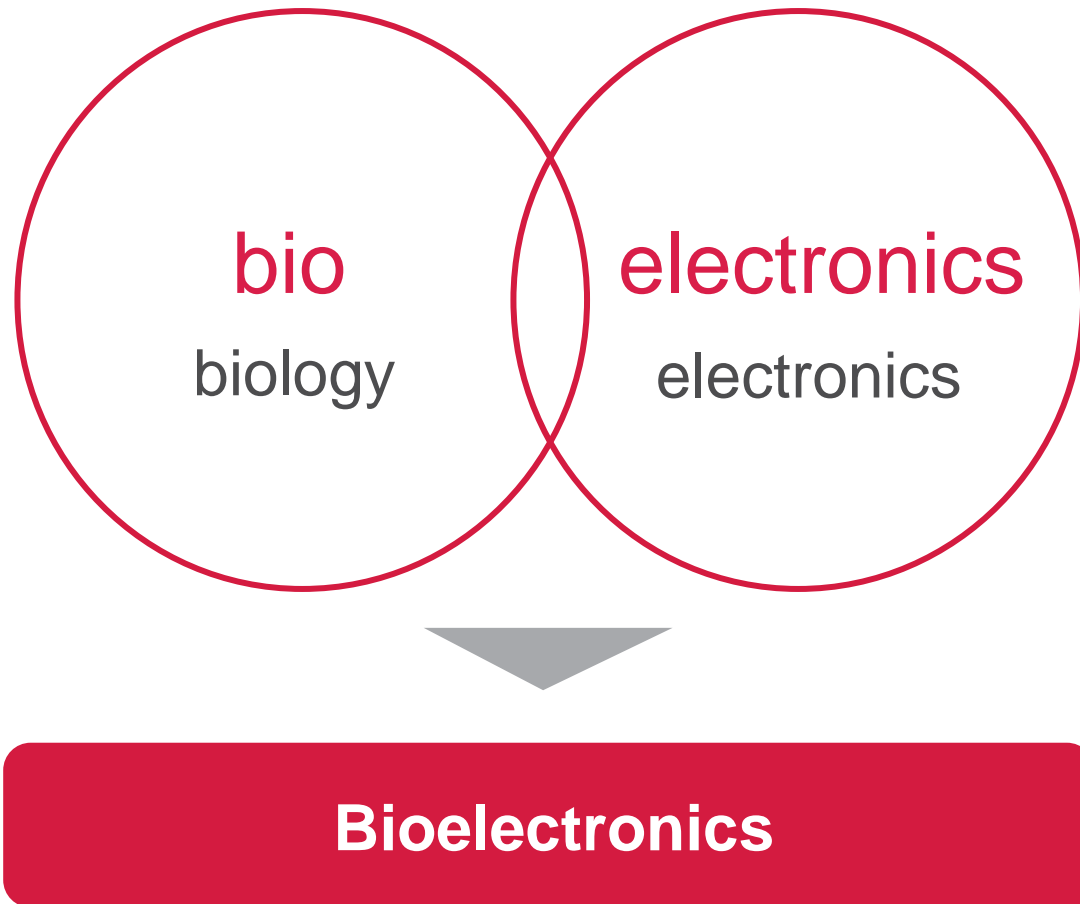
stimulation



1st step
feasibility evaluation of the technology individually

We are here!

What is bioelectronics?

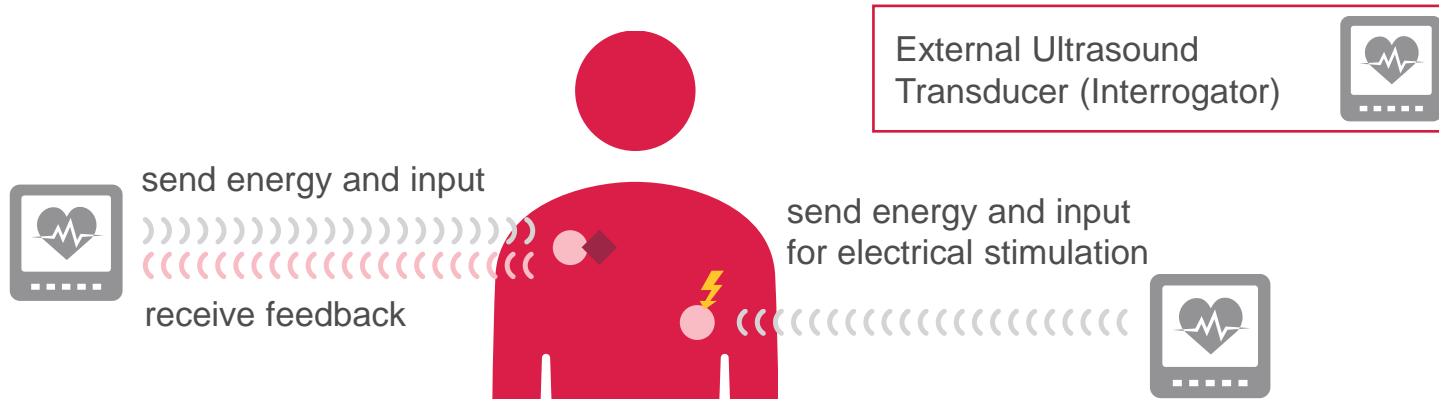


- Interdisciplinary field of biology and electronics
- Aims to improve lives of people with disabilities or diseases through obtaining biological data through methods using electronics or transmitting signals into organisms
- Examples include cardiac pacemakers, deep brain stimulation devices, vagus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

O₂ 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...

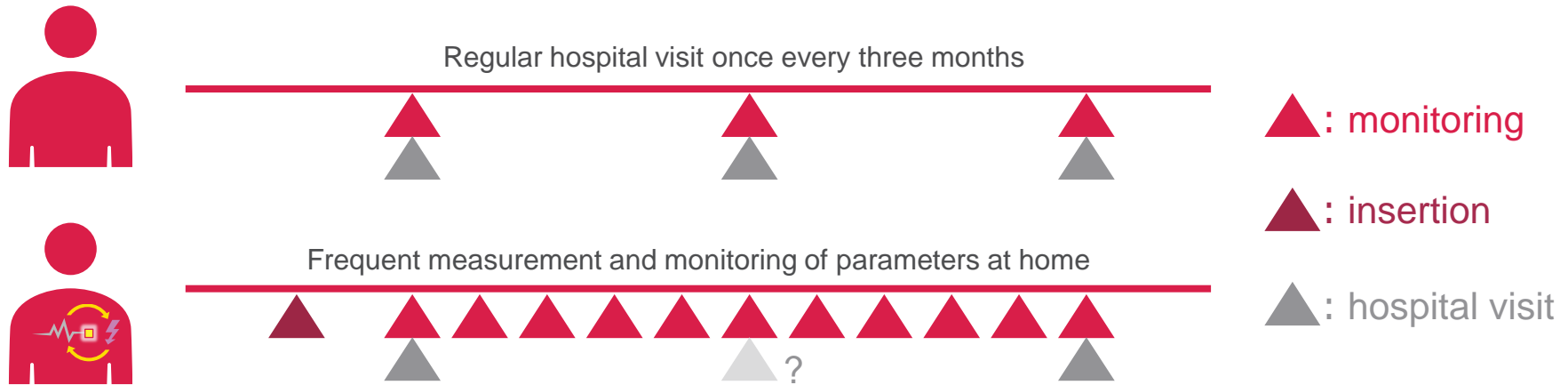
- Measure organ temperature to monitor a disease?
- Would pressure measurement provide useful insights?



- Would consistency/discrepancy of the O₂ level within the blood and organs locally provide useful insights?
- Can pH be monitored as an indicator of inflammation?

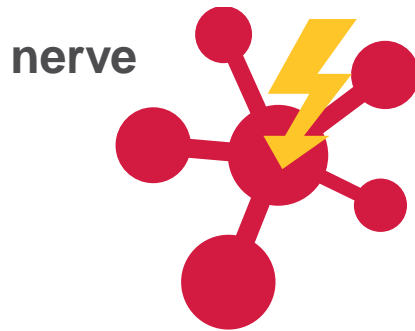
- **Potential to discover new parameters and data, leading to novel treatments and disease monitoring methods**
- **A major point of consideration is how to lower the invasiveness of device implanting**

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 effectsxx
- 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)

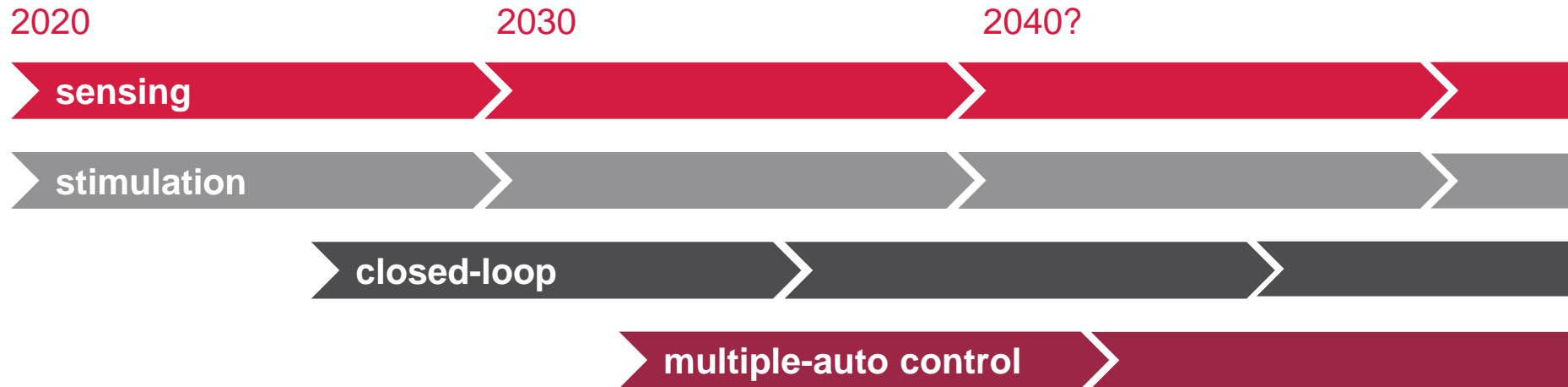
Digestive/ metabolic

- 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

DEFINITION OF VALUE

