Research and Development at Shionogi

March 15, 2018

Shionogi & Co., Ltd.

SHIONOGI

Agenda

1. **Introduction**
   - **Isao Teshirogi**, Ph.D., President and CEO
2. **Research**
   - **Takeshi Shiota**, Ph.D., Senior Vice President
     Pharmaceutical Research Division
3. **CMC**
   - **Miyuki Hiura**, Senior Vice President, CMC R&D Division
4. **Development**
   - **Kazuhiro Hatanaka**, Senior Vice President
     Development Division
5. **Summary**
   - **Isao Teshirogi**, Ph.D., President and CEO
6. **Q&A**

Research

Takeshi Shiota, Ph. D.
Senior Vice President
Pharmaceutical Research Division

R&D Vision

R&D Vision

Research：Innovation in drug discovery for our society

CMC：Product development Bringing “Benefit for All”

Development: Efficient and Consistent Development

Actions：

- Continuous generation of new development products and drug candidates
- Enhancement of drug discovery platforms based on our strengths
- Expansion & refocusing of disease area strategy to optimize future prospects
- Creation of new value through collaboration with external organizations
- Expansion of drug pipeline through LCM* strategy
- Progression of biomarker research to increase probability of clinical success

* LCM: Life cycle management

Agenda：Pharmaceutical Research Division

- **Goals of drug discovery research and Shionogi's vision**
  - Innovation in drug discovery to meet societal needs
- **Targets and outcomes in 2017 (Summary)**
  - Development products / drugs
  - External collaborations / biomarker research
- **Outcomes in FY2017 and priorities for FY2018**
  - Disease strategies (infectious diseases, pain / nerves)
  - Enhancement of drug discovery modality
- **Targets for FY2018**

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Synergistic Research Innovation for Our Society

Issues for Drug Industry: Appropriate balancing between producing of novel medicine and social economy for medical & social needs

Concept for Drug Discovery

Powerful research points of infectious diseases and CNS**

+

Getting profound social issues in the future

Flexible research scope shift to "more valuable area"

Drug Discovery Modalities

SAR* Engine for small molecule drug discovery

+

Acquiring new modalities

Expanding the productive power of our original "SAR engine"

We produce novel medicines meeting medical & societal needs faster than other companies

* SAR: Structure activity relationship

** CNS: Central nervous system

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From Presentation of FY2016

FY2017 plans for Research

SONG for you!

Innovation in drug discovery

Ten or more development products to be created by FY2020

- **Continuous generation of new development candidates and development products**
  - Generation of development candidates for HIV
  - Designation(?) of two or more development candidates
- **Maximizing productivity of drug discovery through external collaborations**
  - Launch of innovative drug discovery programs
  - Initiation of new collaborations to drive progress in drug discovery programs
  - Achievement of study milestones in ongoing collaborations
  - Generate research results that improve predictability of clinical trial success
- **Verification of clinical applicability of newly created PET imaging compounds**

Accomplishments in FY2017 ~Drug Candidates/Development Products~

SONG for you!

Create 10 or more development products

derived from internal or collaborative research by FY2020

- **Goals for FY2017 - Continuous generation of development candidates and products -**
  - > Generating new development candidates in HIV area
  - > Producing two or more development products
- **Accomplishments in FY2017**

Created a novel HIV drug candidate (P.16)

Created a novel adjuvant as a development candidate for vaccines (P.32)

Selected S-004992 - anti-TB* drug from C&O in China (P.19)

Created S-005151 - a novel peptide drug for stroke (P.87)

Created S-637880 - a powerful CNS pain drug (P.23)

Created S-770108 – inhaled pirfenidone for IPF (P.50,83)

*TB: Tuberculosis

Achievements in FY2017 ~External Collaboration/Biomarker Research~

- **Goals for FY2017**
  - Maximizing drug discovery productivity external collaboration
    - > Launch of creative drug discovery programs
    - > Initiation of new product collaborations to promote drug discovery program
    - > Achieve milestones in collaborative drug discovery programs
    - > Generate research results that improve predictability of clinical success
  - Newly created PET* Verification of clinical applicability of imaging compounds
- **Achievements in FY2017**

Introduced PDPS technology and initiated some drug discovery programs based thereon (P.30)**

Initiated collaborative research with PharmaIN to apply their peptide modification and drug delivery technology (P.49)

Established business partnership with UMN Pharma (infectious disease prevention vaccine expertise)

Expanded collaboration with Nissan Chemical Industries

Preparing a microdosing test in humans for S-637880 (P.23)

Launched a new drug discovery program from SK project * (P.25)**

*PET: Positron emission tomography **PDPS: Peptide Discovery Platform System
*** SK: Drug discovery and medical research for the regeneration of synapses and neuronal function

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Most important compound in 2018

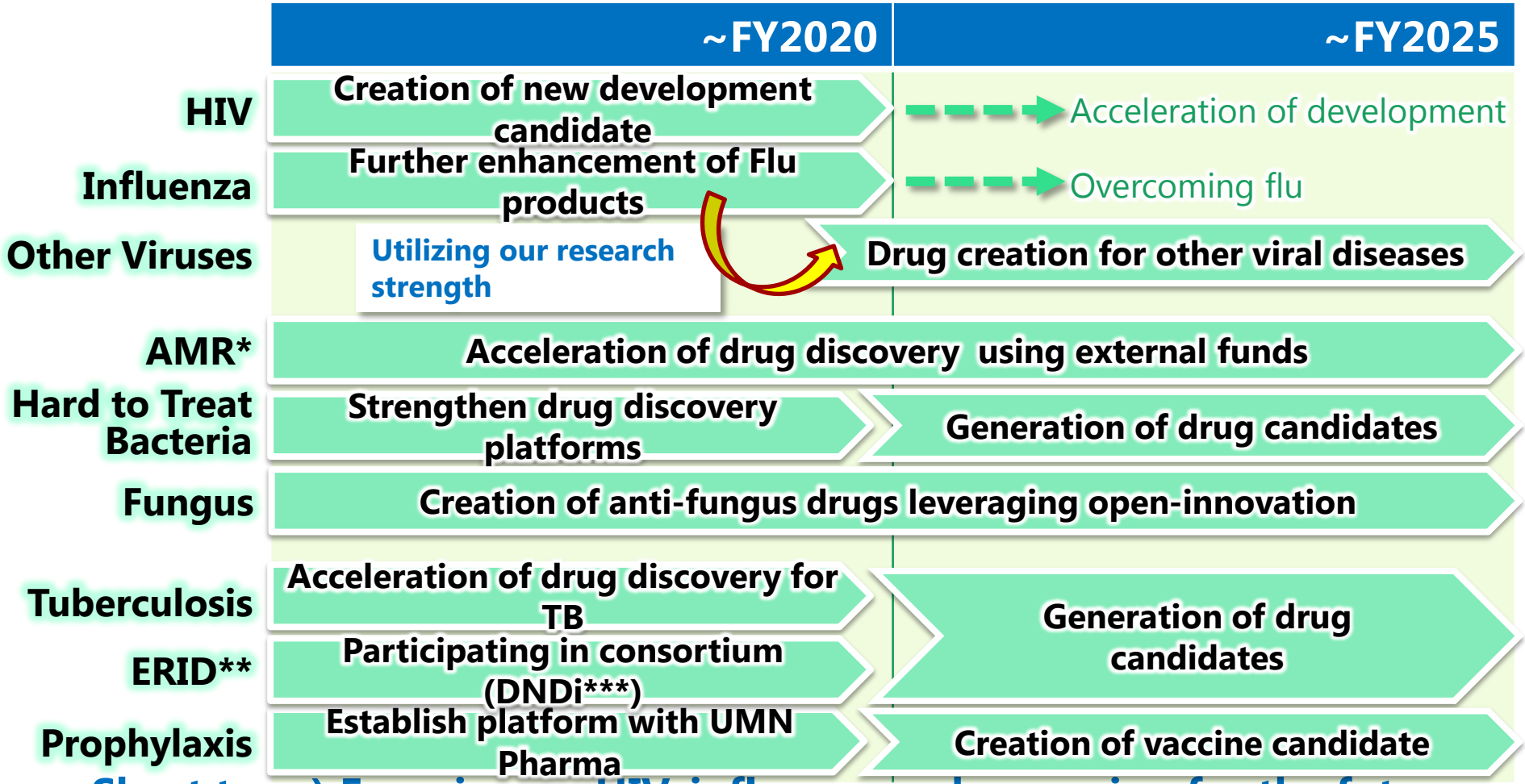
Novel HIV Drug ref. p109map

S-004992 (anti-Tuberculosis) ref. p111map

S-637880 (Neuropathic pain) ref. p111map

Please take a look at the map at from p109 to p111 as well.

Drug Discovery Strategies for Infectious Diseases



Short term) Focusing on HIV, influenza and preparing for the future
Medium to long term) Expand/shift scope to include other viruses, tuberculosis

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* AMR: Antimicrobial resistance
** ERID: Emerging and Re-emerging Infectious Diseases
*** DNDi: Drugs for Negrected Diseases initiative

Most important compound in 2018

SONG for you!

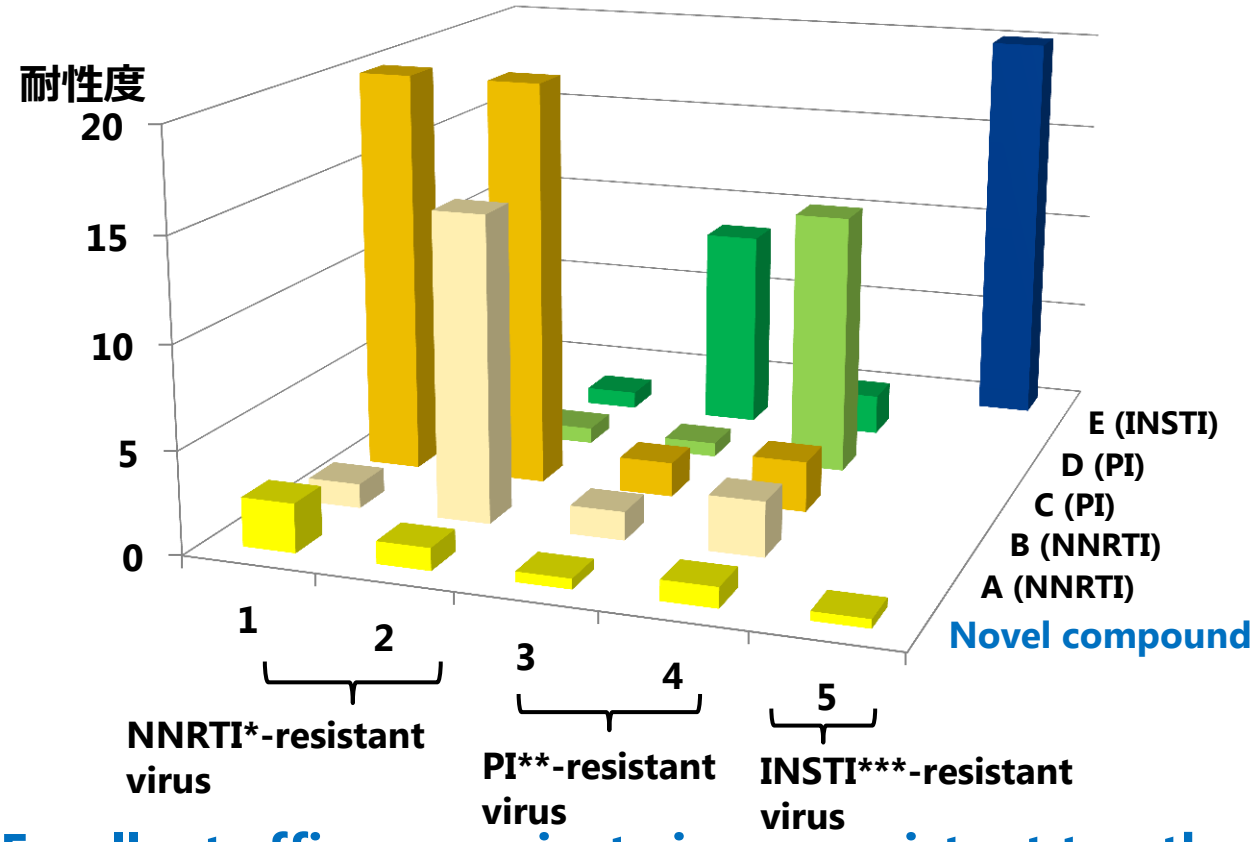
Novel HIV Drug

ref. p109map

SHIONOGI

HIV Drug Discovery Program

Succeeded in creating a novel drug candidate for HIV with a new mechanism



Phase I in FY2019

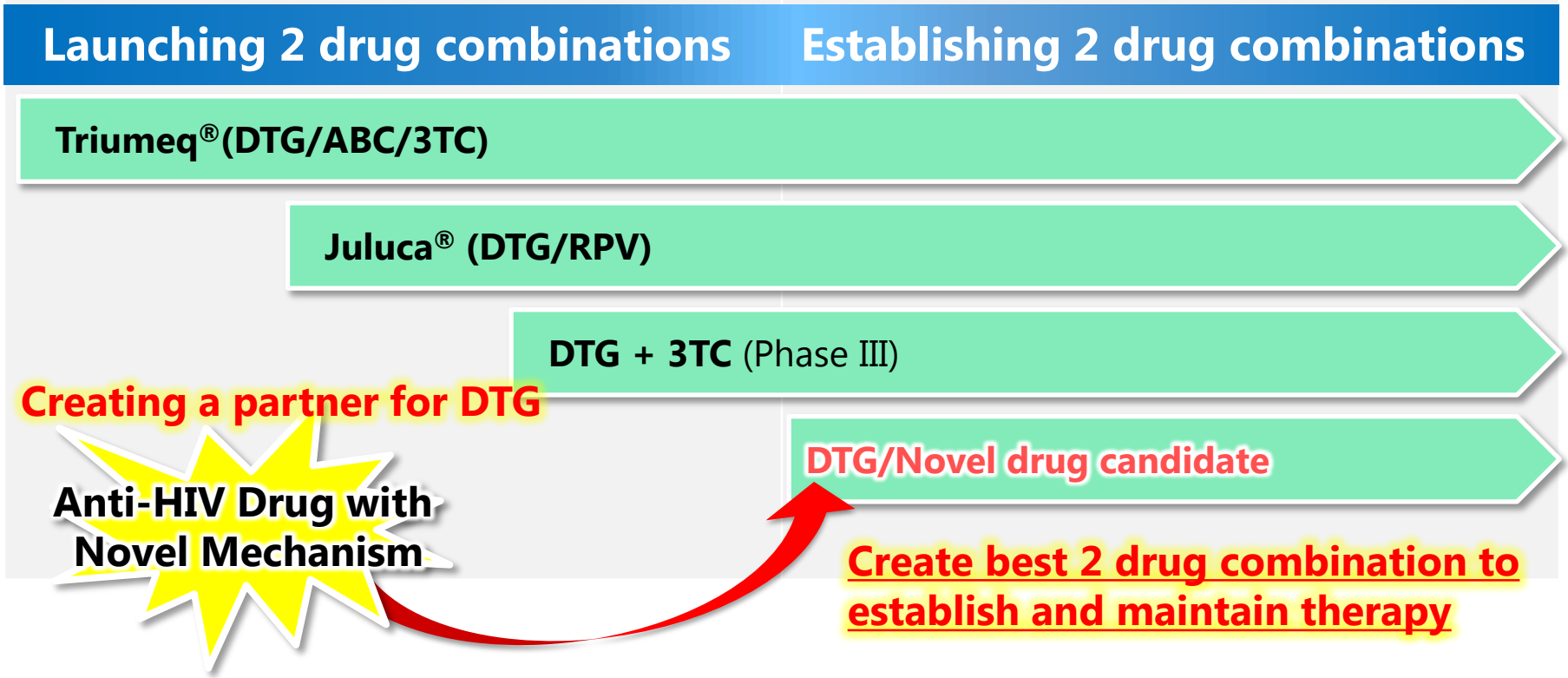
Excellent efficacy against viruses resistant to other anti-HIV drugs

Excellent candidate for combination with dolutegravir

* NNRTI: non-nucleoside reverse transcriptase inhibitor
** PI: Protease inhibitor　*** INSTI: integrase strand transfer inhibitor

Drug Discovery Strategies for HIV

From 3 drug combination therapy era to 2 drug combination therapy era



Offering the best partner for DTG to firmly establish 2 drug combination therapy

DTG: Dolutegravir ABC: Abacavir 3TC: Lamivudine RPV: Rilpivirine

Most important compound in 2018

SONG for you!

S-004992
Anti-Tuberculosis

ref. p111map

SHIONOGI

Status and Issues of Tuberculosis

It's our mission to treat tuberculosis, one of the top 3 major infectious diseases worldwide, to meet this global need

10.4 million new patients/year, about 400MM$ market worldwide (FY2016)
Recently, multidrug-resistant, and extensively drug-resistant tuberculosis are becoming an increasingly critical issue
Tuberculosis is a serious threat to HIV patients (No.1 cause of death)

S-004992 was discovered in C&O, our subsidiary in China
Shionogi is leading the global development

Initiate FTIH in FY2018 in China

Leveraging external funding and open-innovation, accelerate global development and build new discovery programs for tuberculosis

Non-Clinical Profiles of S-004992

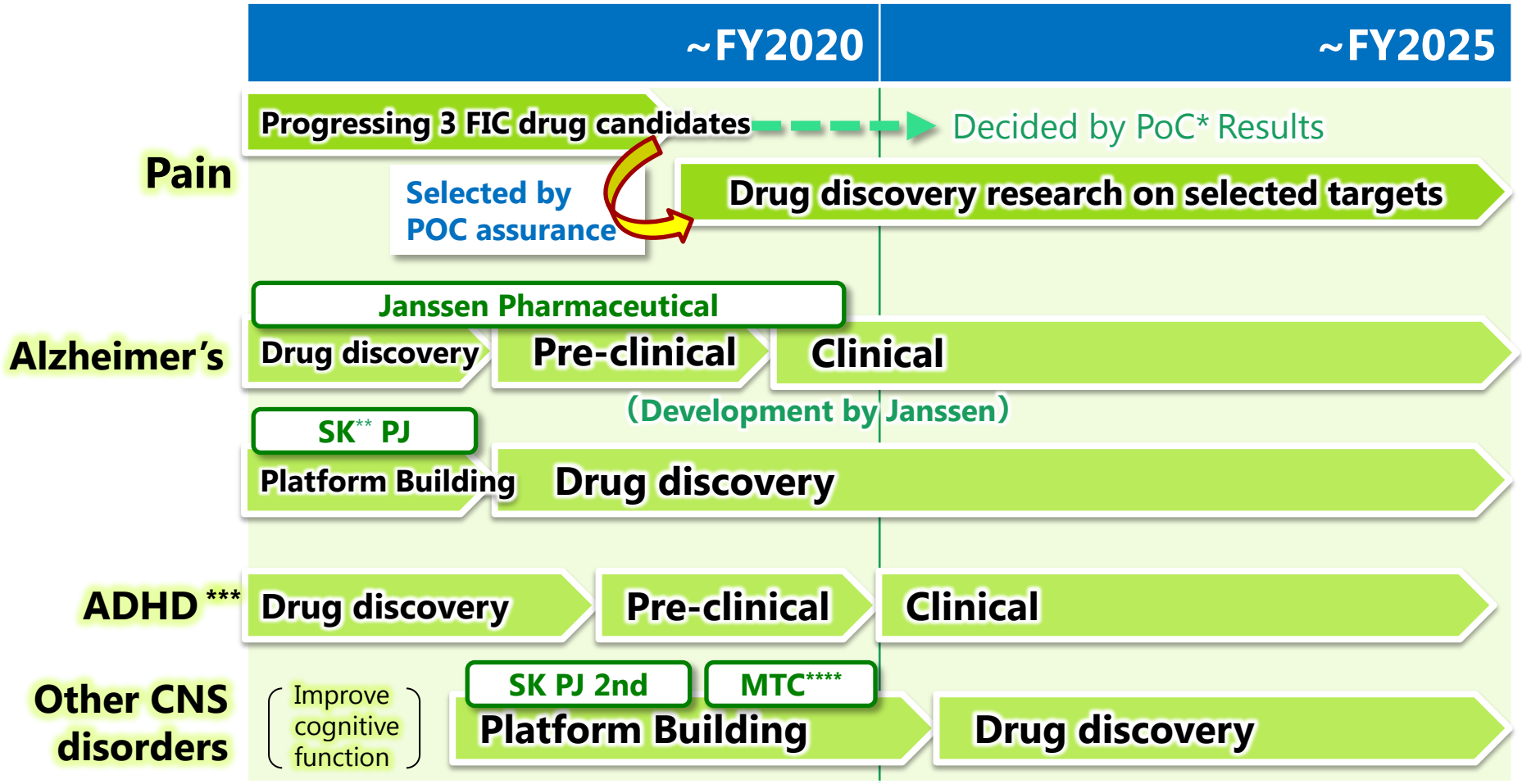
- Standard clinical regimen: Treatment with 3 or 4 drugs including Rifampicin and Isoniazid for 2 months, followed by treatment with Rifampicin and Isoniazid for another 4 months
- Recently launched drugs have not succeeded due to safety and price limitations

	S-004992	Launched comparison Drug
Dosage and Administration	**Once daily, low dosage**	Twice daily, 200mg/day
Solubility, Absorbance	**High**	Low
Lung Penetration	**Extremely High**	Medium
QT Prolongation	**Low risk**	High risk
CoGs*	**Low enough to allow access in LMICs****	Extremely High

S-004992 could fulfill the unmet medical needs of tuberculosis patients

* CoGs: Cost of goods sold
** LMICs：Lower Middle Income Countries

Drug Discovery Strategies for Pain and CNS



Pain: Focus on selected drug targets
CNS: Utilizing open-innovation to accelerate novel drug discovery

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* PoC: Proof of concept
** SK: Collaboration project of Shionogi and Kyoto Univ.
*** ADHD: attention deficit/hyperactivity disorder
**** MTC: Milner Therapeutics Consortium

Most important compound in 2018

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S-637880
Development compound for neuropathic pain

ref. p111map

SHIONOGI

Development Compound for Neuropathic Pain (S-637880)

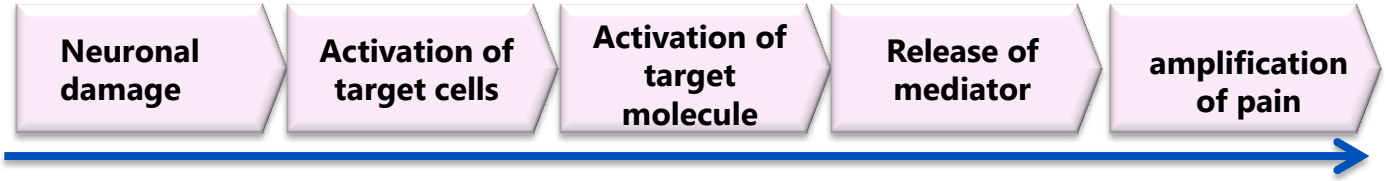
Creating a more vigorous society

SGS2020 updated on 31st October, 2016

Pain/CNS + **Addressing societal needs**

S-637880 acts through a new key mechanism related to the maintenance and exacerbation of neuropathic pain

Mechanism of Chronic pain



- Establish importance of mechanism with clinical evidence
- Identify reliable biomarker candidates

- To provide new treatment option, overcoming R&D challenges of the pain area

Development Compound for Neuropathic Pain (S-637880)

A new development process to support successful development of new pain therapies

➢ Identify patients with neuropathic pain in which the relevant mechanism is involved to improve development efficiency and accuracy	➢ Utilization of Clinical PET * imaging technology to optimize clinical dosage and usage

Increase probability of establishing PoC by utilizing biomarker effectively

Goals of SK Project

Discover drugs targeting improvement of cognitive dysfunction, distinct from early treatment intervention with Aβ-focused mechanism

Maximize Shionogi drug discovery assets

Invited cutting-edge researchers from academia

- Drug discovery know-how in our core disease area of Pain/CNS

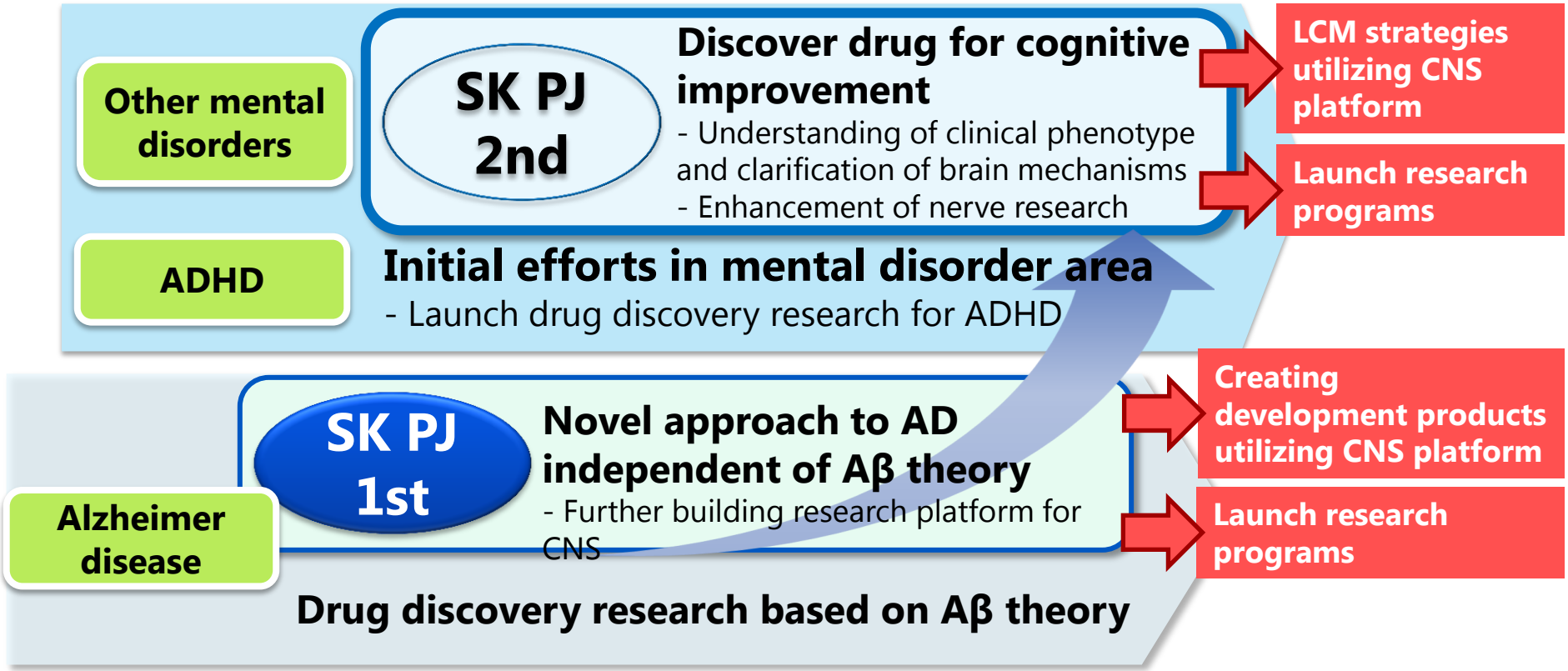
+

- World-class research capability in epigenetics / synapse / neural function research

Successfully building a nonclinical evaluation platform for memory and cognitive functions, and identification of novel drug discovery targets

SK Project in CNS

Aggressive targeting of mental disorders to meet patient's medical needs relieve financial and other burdens on society



Building drug discovery platform based on deep mechanistic understanding of the disorders

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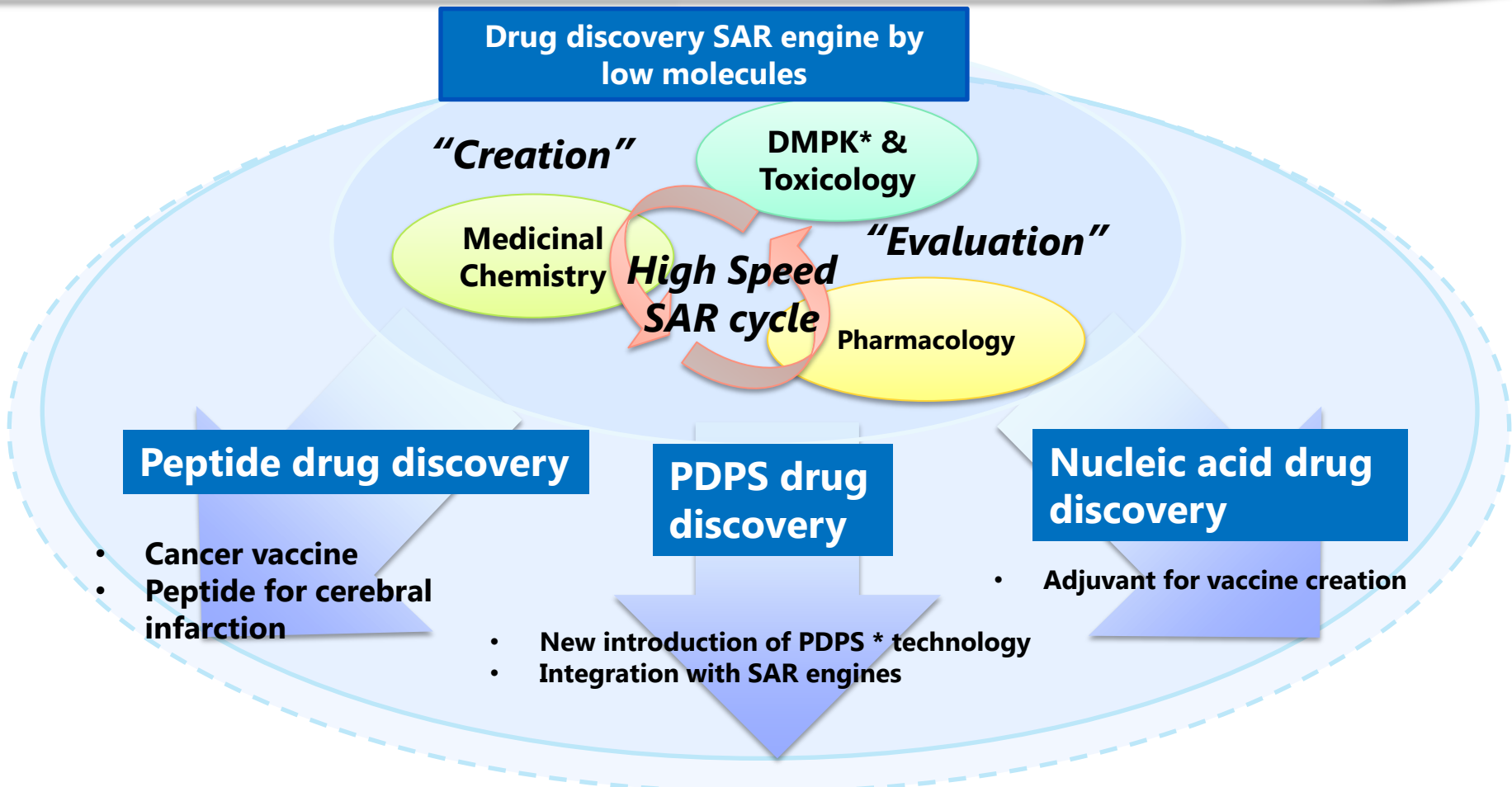
Expanded Range of Drug Discovery Modalities



Based on our strengths in small molecule drug discovery, we expanded into medium-sized molecule drug discovery modality (peptide / nucleic acid) to respond to a wider scope of medical needs

* DMPK: Drug Metabolism and Pharmacokinetics

Important compound in 2018

- **Peptide therapeutics**
- **Nucleic acid adjuvant for Vaccine**

ref. p110map

PDPS Drug Discovery Platform

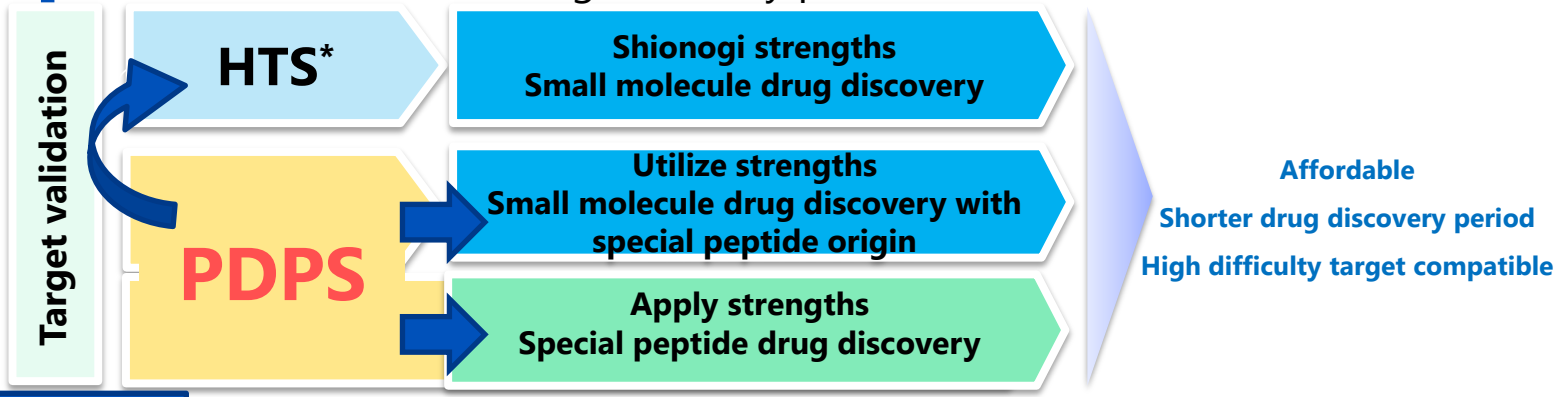
[PDPS]

Special cyclic peptide

- Quick screening with low costs and small tasks
- Generate highly selective and highly active peptides
- Hits can be acquired even for challenge in targets

[Platform]

Drug discovery process



3 spreading effects

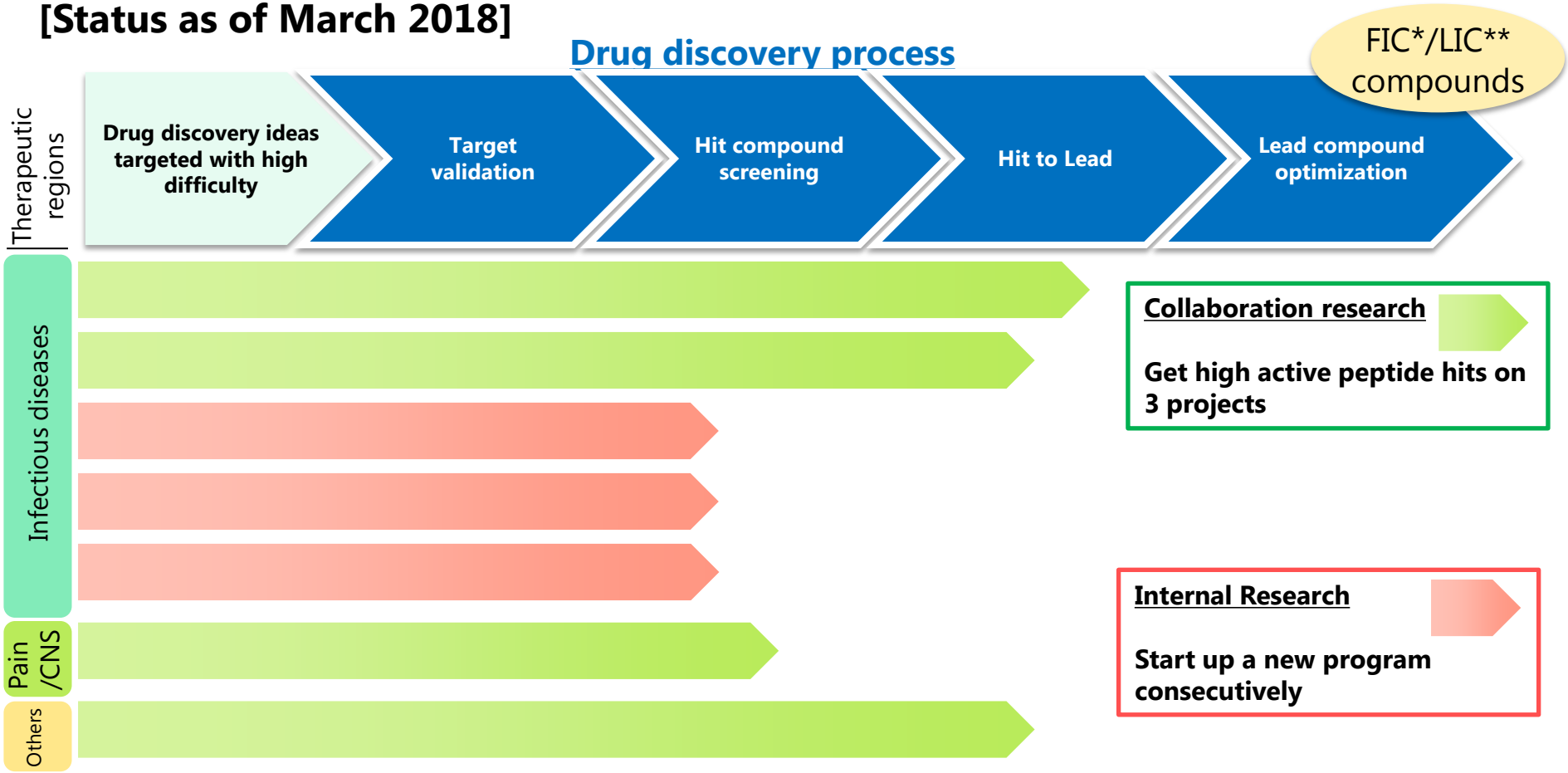
Utilizing new pharmacophore information by making full use of advanced SBDD ** technology	PDPS SAR further optimized by through Shionogi's knowledge base	Utilizing highly active peptides as a validation tool

Continually generate affordable drugs and dramatically improve productivity by synergistically using our strengths and PDPS

* HTS: High Throughput Screening ** SBDD: Structure Based Drug Discovery

Outcomes of PDPS drug discovery

[Status as of March 2018]



Continually create development /candidates for development products after 2020

* FIC: First-in-Class (Especially novelty/effectiveness is high, original medicinal products which greatly change traditional treatment)
** LIC: Last-in-Class (Drugs that have clear advantages over similar mechanisms and do not allow other new drugs to follow)

Nucleic acid drug discovery platform

Based on synthetic chemistry cultivated with low molecule drug discovery, building platform as a new drug discovery modality

Shionogi's original capability of nucleic acid chemistry modification and design

DDS * (Drug Delivery Technology)

A variety of physiological function control approaches based on nucleic acid

Adjuvant, siRNA, etc.

Nucleic acid platform

・Creation of nucleic acid adjuvant development candidate for vaccine
・Genetic controlled approaches to targets which are difficult for low molecule drugs to approach

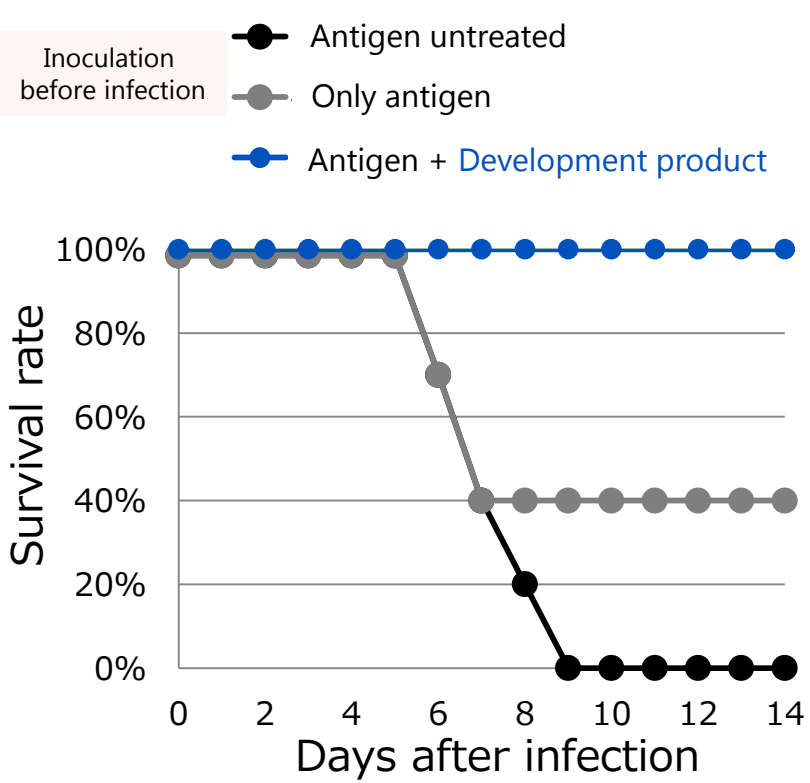
Build continuous output system with Adjuvant and siRNA technology

* DDS: Drug Delivery System

Success in nucleic acid drug discovery

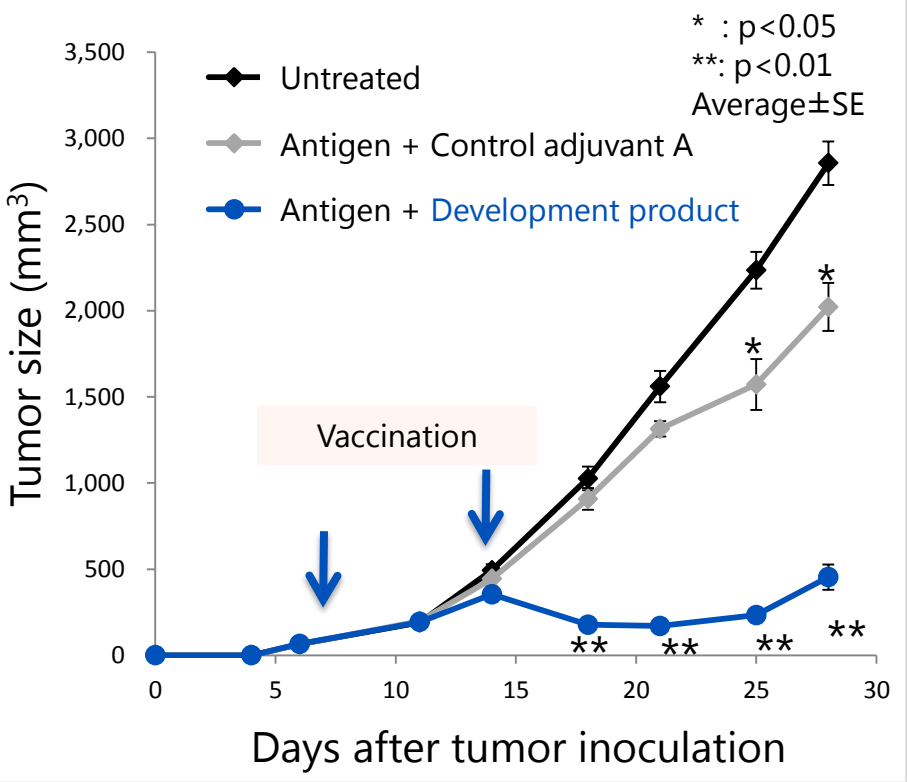
Infectious disease vaccine adjuvant effect (nonclinical)

To initiate clinical trials in 2020



Cancer vaccine Adjuvant effect (nonclinical)

To initiate clinical trials in 2019



Maximizing the value of a novel nucleic acid adjuvant arising from Shionogi internal research via collaborative efforts with the National Institutes of Biomedical Innovation, Health and Nutrition

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FY2018 Plans for Research

Innovation in Drug discovery for Our Society

10 or more development products to be created by FY2020

- **Continuous creation of development candidates and development products**
  - Creation of **3 development candidates** (Two candidates in FY2017)
  - Creation of **2 development products** (Four products in FY2017)

- **Beginning some actions for improvement of productivity**
  - Launch **5 programs** using PDPS, and obtainment Hit peptide
  - Launch **new business corporation** to promote drug discovery
  - Launch **new open recruitment project**, **FINDS Targets**, to acquire novel drug targets
  - Launch clinical trial using **novel PET imaging marker** to improve development productivity

FINDS Targets

New FINDS program * "FINDS Targets" scheduled to start in Fall 2018

Quickly providing tools for validation of potential disease targets identified in academia, based on Shionogi's world-class platform technologies

Academia

Provide potential targets and assays/models

⇒accelerate verification!

Shionogi

Quickly generate specific tools by using our technological strengths

⇒Rapidly generate drug leads!

【Shionogi specific tools】
- Nucleic acid: synthetic skills and DDS technology to create development candidates
- Peptide: PDPS technology – SHIONOGI is the only company to have this in-house in Japan
- Antibody: rapid antibody preparation technology utilizing unique antibody library

Highly productive partnerships leveraging complementary strengths

* FINDS（PHarma-Innovation Discovery competition）: Shionogi Drug Discovery Innovation Competition started in 2007

CMC

Miyuki Hiura
Senior Vice President
CMC R&D Division

Vision for R&D

R&D Vision

Research: Innovation in Drug Discovery to Serve Society

CMC：Product development Bringing “Benefit for All”

Development: Efficient and Consistent Development

Actions：
Create New Product Value Meeting Society’s Needs with Innovative CMC Technologies

- **Providing reliable & effective medicines**
- **Improving medical economics**
- **Increasing the success rate of drug development**

Agenda: CMC R&D Division

- **To Achieve SGS2020**
  - Responding to the Changing Needs of Society with New Drugs
- **Achievements in FY2017**
  - Breakthroughs by CMC Technologies
  - NDA Submissions and Market Launches of Pipeline Products
- **Targets for FY2018**
  - Towards Further Advances in CMC Technologies: Cooperation with Outside Organizations

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Society's Needs for New Drugs

- **Endless Effort to Create New Drugs Helping Patients' Live More Fulfilling Lives**
- **To Grow for the Future By Meeting Society's Needs**
  - **Maximizing the Value of Our Products**

Providing **reliable & good medicines**	Improving **medical economics**	Increasing **success rate** of our drug development
Creation of **High-Value Products** of good quality and meeting medical needs Delivering relief reliably to all people	Achievement of **Cost Reduction** and **Insightful Development** demonstrating cost-effectiveness	Application of CMC technology at **Early R&D Stage** Providing new solutions for drug discovery research

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From Presentation of FY2016

Targets for FY2017 (1)

Rapid/high quality NDAs and launches

Cefiderocol	Completion of NDA Submission in the US
Xofluza™	Establishment of Commercial Manufacturing Completion of NDA in Japan Trial for new LCM* Formulation
Pediatric ADHD (Guanfacine, Lisdexamfetamine)	Completion of Market Launch Preparations

Development approach that reliably meets the requirements of global regulatory authorities

- Drug development with predictive risk assessment and proactive resolution
- No delays in approval of NDA submissions due to quality of filing package and excellent communication with authorities

Consistent reduction of COGs in all stages through improvement of CMC technology**

* LCM: Life cycle management
** CoGs: Cost of goods sold

From Presentation of FY2016

Targets for FY2017 (2)

Maximize the value of the compound

Conventional NTE*: Targeting a wide range of therapeutic areas

⬇ As technologies are refined and developed

Strategic LCM: Focusing on our original drugs or candidates using advanced CMC technologies in NME trial**

NME Moving projects forward to RSC/S stage by innovative and advanced CMC technologies

➡ **Advance ≧ 4 projects to RSC/S by 2020**

Developing revolutionary CMC technologies for the next generation NME

➡ **Develop ≧ 3 technologies by 2020**

LCM Developing new LCMs utilizing improved technology created for NTEs

➡ **Advance ≧ 2 projects to RSC/S by 2020**

Collaborate to apply CMC core competencies across the value chain, beyond the traditional role of CMC

* NTE: New therapeutic entity ** NME: New molecular entity

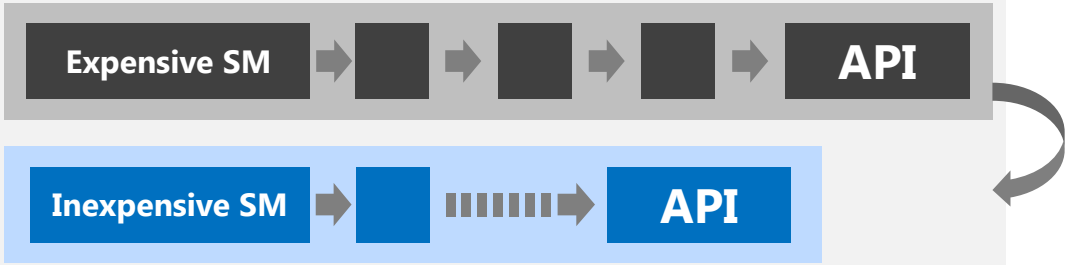
Achievements in FY2017 (1)

- Breakthroughs by CMC Technologies
  - **API Cost Reduction:**
    Manufacturing Technology for Small Molecule API
  - **API Productivity Improvement:**
    Manufacturing Technology for Medium-sized Molecule API
  - **Drug Absorption Control:**
    In Silico Prediction System (Internally-developed Technology)
  - **PharmaIN PGC™ Technology Introduction:**
    Drug Stability and Sustained Release
  - **Pulmonary Drug Delivery Technology of Pirespa Inhaled Product** (Self-developed Technology)

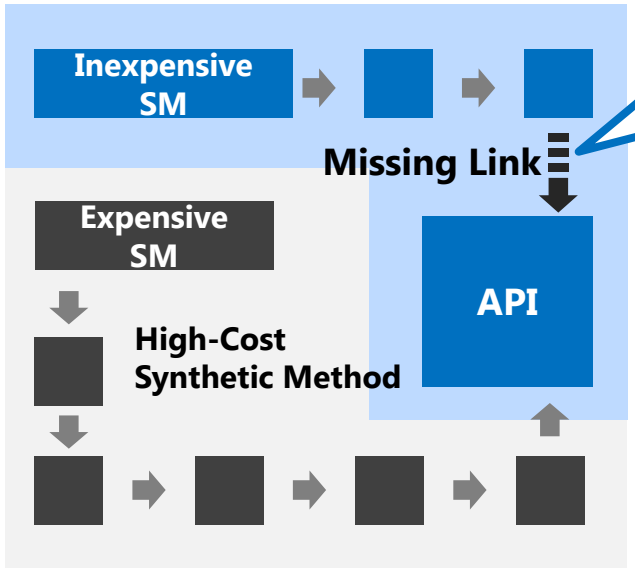
API Cost Reduction:
Manufacturing Technology for Small Molecule API

Resolving Synthetic Route Challenges

Inexpensive starting material (SM) and shorter synthetic steps are desirable, but difficult to achieve

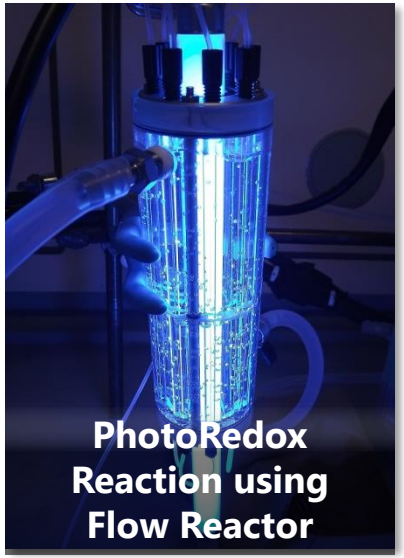


Adopting New Synthetic Technology



PhotoRedox Reaction[*1]
Enabling New Synthetic Route
Scale-up Study in Progress

50% Reduction of Starting Material Cost
Reduction of Steps



Proactive Adoption of New Synthetic Technology Leading **to Substantial Cost Reduction**

*1 PhotoRedox Reaction: Oxidation and Reduction Reaction using Visible Light

API Productivity Improvement:
Manufacturing Technology for Medium-sized Molecule API

SONG for you!

Challenge in Production

Medium-sized Molecule API

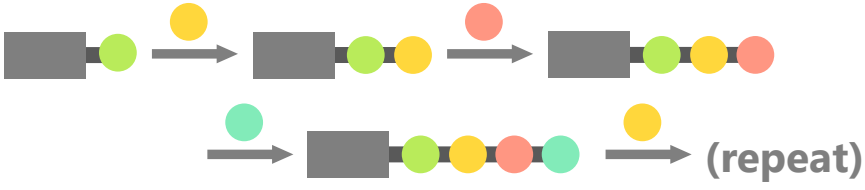
Peptides, Nucleic Acids:
API with Molecular Weight between Small Molecule and Antibody

Issues for Manufacturing

Yield, Cost, Environment, Productivity, and Quality

Low Productivity in Synthesis of Peptides

Coupling Amino Acid **One by One**
Long Reaction Time for Each of Many Reactions ➡ **Low Productivity**



Reaction Acceleration with MicroWave (MW) Irradiation

Reaction Time for Cancer Peptide Vaccine (S-288301) (Laboratory Scale)

Without MW — Reaction Time **40 hrs**

With MW — **1hr with Equal Quality**

MW Acceleration of Each Reaction

40 hrs to **1 h** for Reaction Time

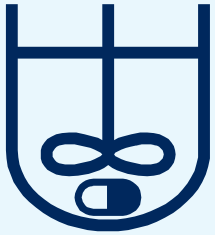
Adopting New Technology Leading to **Productivity Improvement**

Drug Absorption Control:
In Silico Prediction System (Self-developed Technology)

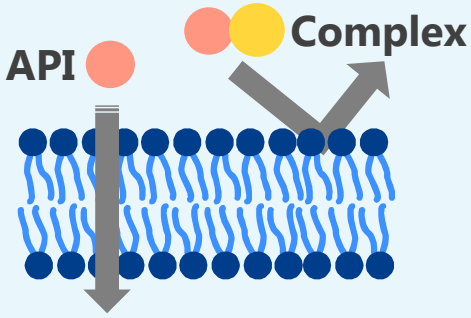
SONG for you!

in vitro testing

Dissolution test arranged to **simulate behavior in human gastrointestinal tract**

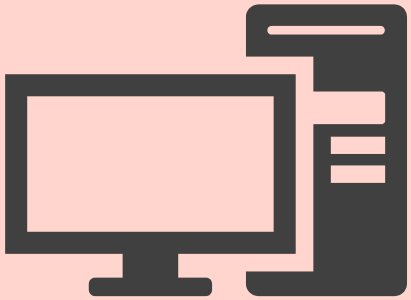


Permeability/ interaction analysis
(PAMPA* system)



in silico prediction

Predict drug absorption behavior using *in silico* absorption model



in vivo testing

in **animal**

in vivo testing

in **human**

Other information

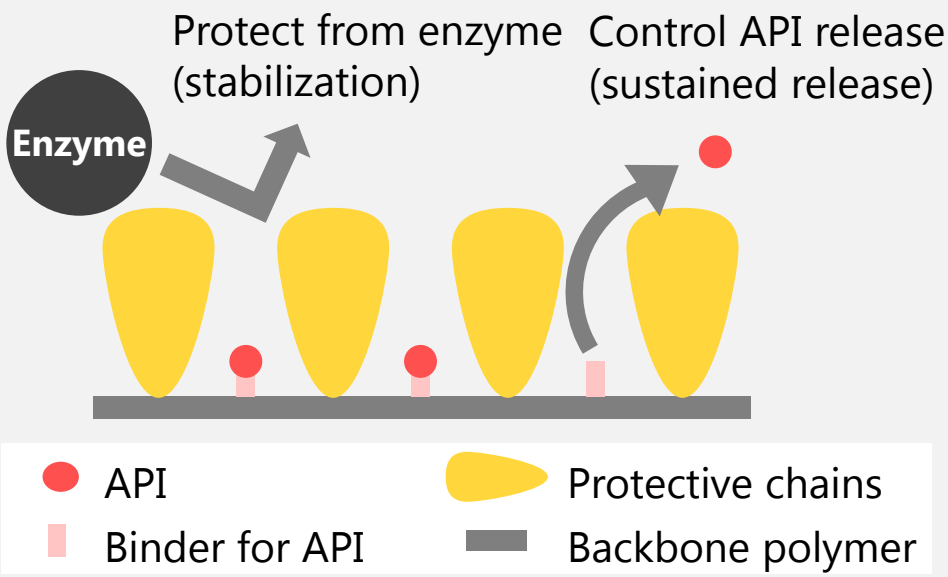
Absorption site
API Physical properties
Standard dissolution test result
Disease associated information

Develop drug product with highly predictable absorption

* PAMPA: Parallel Artificial Membrane Permeation Assay

PharmaIN PGC™ Technology Introduction:
Drug Stability and Sustained Release

Mechanism to optimize pharmacokinetics using PGC™*

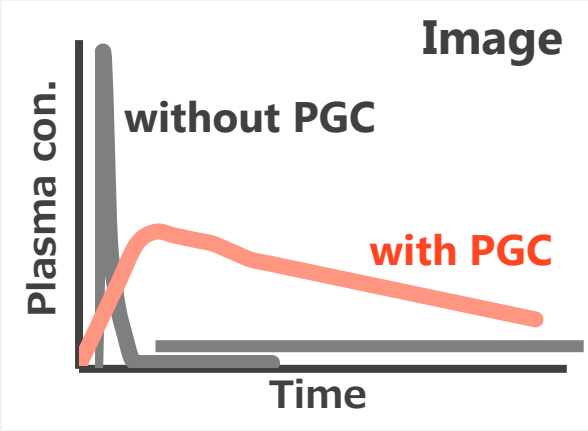


Pharmacokinetics can be optimized by optimization of

- the binder for API ➡ **Rate of Release**
- the protective chains ➡ **Stability**

Image of plasma concentration profile w/o PGC™

Example where API is degraded by plasma enzymes



Without PGC: Eliminated from body quickly

With PGC: Long acting is achieved by controlling API release speed and protecting enzymatic degradation

Pharmacokinetics can be optimized using PGC™ introduced from PharmaIN

* PGC™: Protected Graft Copolymer (Novel drug carrier developed by PharmaIN)

Pulmonary Drug Delivery Technology of Pirespa Inhaled Product (Internally-developed Technology)

Purpose & challenge of inhaled product development

Pirespa Tablet

Side effects due to whole body exposure

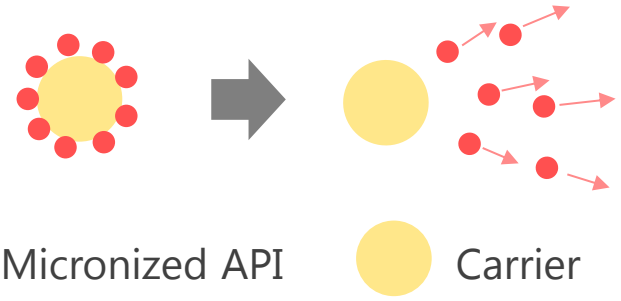
Inhaled product

Minimize side effects by pulmonary targeting

Challenges for inhaled product development

1. **Difficulty in micronization**
2. **High drug load** will be needed

Dry powder inhalation technology



1 Pulmonary drug delivery

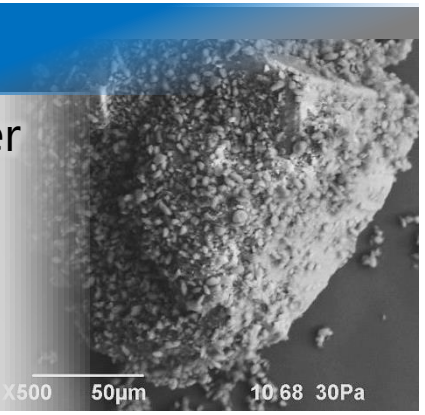
Patent pending

- Micronize API with lipid
  ➡ Micronized down to a size permitting pulmonary drug delivery
- An new inhaler device is under development with a device maker

2 Dose maximization

- Select appropriate carrier
- Optimize complex formation process

Achieve **high drug load**



Developed Pirespa inhaled product
to minimize side effects (LCM*) using dry powder inhalation technology

* LCM: Life cycle management, formulation improvement

Achievements in FY2017 (2)

- **Rapid/high quality NDAs and launches**
  - **Xofluza™**
    - > **NDA (Oct. 25), Approval (Feb. 23) in Japan under Sakigake Designation Scheme**
    - > Completion of NDA Preparation in the US, Completion of Trial for Pediatric Granular Formulation
  - Cefiderocol
    - > Support for Phase III, NDA Preparation in the US
  - Pediatric ADHD
    - > Guanfacine Approval in Japan, Launch
    - > Lisdexamfetamine Completion of NDA in Japan
  - Naldemedine
    - > Launch in Japan and the US
    - > Completion of submission in EU, Preparation for Launch
  - Oxycontin™ TR Tablet
    - > Approval in Japan, Launch

Agenda: CMC R&D Division

- **To Achieve SGS2020**
  - Responding to the Changing Needs of Society with New Drugs
- **Achievements in FY2017**
  - Breakthroughs by CMC Technologies
  - NDA Submissions and Market Launches for Pipeline Products
- **Targets for FY2018**
  - Toward Further Advances in CMC Technologies: Cooperation with Outside Organizations

Targets for FY2018 (1)

Maximize the Value of the Compound

NME and LCM* by CMC Technologies

NME

Moving Projects forward to Drug Candidate status using Innovative and Advanced CMC Technologies

➡ **Advance ≧ 4 Projects by 2020**

FY2017: 0 Project **FY2018: 2 Projects**

Developing Revolutionary CMC Technologies through In-House Development and Collaborations

➡ **Develop≧ 3 Technologies by 2020**

FY2017: 2 Tech. **FY2018: 1 Tech.**

LCM

Develop New LCMs Utilizing Improved CMC Technology

➡ **Advance ≧ 2 Projects by 2020**

FY2017: 1 Project **FY2018: 1 Project**

Collaborate to apply CMC core competencies across the value chain, beyond the traditional role of CMC

Targets for FY2018 (2)

Rapid/High Quality NDAs and Launches

Xofluza™	Completion of NDA and Preparation for Launch in the US, Completion of NDA for Pediatric Granular Formulation in Japan
Lisdexamfetamine	Approval in Japan, Launch
Rizmoic® (Naldemedine)	Completion of Preparation for Launch in EU
Mulpleta®	Completion of Preparation for Launch in the US
Cefiderocol	Completion of NDA preparation in the US

Rapid/high quality NDAs that reliably meet the requirements of global regulatory authorities

- Drug development with predictive risk assessment and proactive resolution
- No delays in approval of NDA submissions due to quality of filing package and excellent communication with authorities

Toward Further Advances in CMC Technologies:
Cooperation with Outside Organizations

ACADEMIA	Collaboration with academia, university, laboratory etc.
PHARMAIN Enabling and improving human therapeutics	Collaborative research utilizing PGC™ platform technology
PeptiStar	Creation of CMO* for revolutionizing production of API for constrained peptides
UMN	Capital and business alliance, technology for prophylactic vaccine against infection disease
BIKEN 一般財団法人 阪大微生物病研究会	Process technology development for "A2NTX" Botulinum toxin bio-pharmaceutical

* CMO: Contract Manufacturing Organization

Development

Kazuhiro Hatanaka
Senior Vice President
Development Division

Vision for R&D

Vision for R&D

Research: Innovation in Drug Discovery to Serve Society

CMC: Product Development Bringing "Benefit for All"

Development: Efficient and Consistent Development

Actions:

・Establish development framework that can respond flexibly to environmental changes

・Cost saving by streamlined development packages and focused clinical trials

Agenda: Global Development Division

- **To Achieve SGS2020**
  - Development Targets for FY2020
  - Targeted Milestones for FY2017
- **Achievements in FY2017**
  - Current Status and Actions
  - Pipeline
  - Core Development Products
    - > Infectious disease
      - = Xofluza™
      - = Cefiderocol
- **Top priority Development Products in FY2018**
  - **S-600918**
    Neuropathic pain・Refractory Chronic Cough
  - **S-770108**
    Pirfenidone inhalant（Idiopathic pulmonary fibrosis ）
- **Other developed products**
  - S-005151
    Epidermolysis bullosa, stroke
- **Targeted Milestones for FY2018**

Agenda: Global Development Division

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From Presentation of FY2016

Development Targets for FY2020

Goals

10 or more compounds, including out-licensed products and products currently approved in a limited number of countries, to be launched globally

Currently 3 compounds

Further improvement of productivity is essential to achieve our goals

- Further improvement in the efficiency of strategic decision making
- Establish a solid framework for high quality, rapid, and efficient global development

From Presentation of FY2016

Targeted Milestones for FY2017

Efficient and Consistent Development

To consistently bring our new products to the global market

- **Global operations framework**
  - Review of implementation and management system for global studies at the portfolio level and at various clinical trial phases
  - Efficient study management through use of new IT systems
- **Cost management**
  - Endure realistic and predictable cost projections by thoroughly checking the feasibility of each clinical trial
- **Utilization of investigator-initiated clinical research**

NDA submissions: 5 (6 indications)

Approvals: 2

Agenda: Global Development Division

- **To Achieve SGS2020**
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Actions in FY2017

To consistently bring our products into the global market

Global Operations Framework

One Global SHIONOGI

- ✓ Sharing fundamental policy, mission and decision
- ✓ Standardization of Roles & Responsibilities and business processes

Concentration of resources on global studies

- ✓ Increase team members devoted to global studies

Cost Management

Selection and Concentration of Development Products

- ✓ Xofluza ™, Cefiderocol, ADHD*

Business Process Re-engineering

- ✓ Shift monitoring methodology to risk based approach and utilize electronic TMF**
- ✓ Reduce clinical research associate
- ✓ Utilize AI and big data

Utilization of investigator-initiated clinical research

NDA Submitted: 4 (6 indications)

[Targeted: 5 (6 indications)]

- Lisdexamfetamine（pediatric）
- Xofluza™ （Adult：Japan）
- Xofluza™ （pediatric：Japan）
- Mulpleta® （US）
- Mulpleta® （EU）
- Osphena® （Vaginal dryness ：US (2018.03)）

Approved: 4

[Targeted: 2]

- OxyContin®TR(Cancer pain(Abuse-deterrent tablets))
- Actair®(Pediatric allergic rhinitis caused by house-dust mite allergen)
- Xofluza™ （Adult）
- Xofluza™ （pediatric）

*ADHD: Attention-deficit/hyperactivity disorder
** TMF: Trial Master File

Achievements in FY2017: Approvals and NDA Submissions

Product (indication)	Phase I	Phase II	Phase III	NDA submission	Approval
OxyContin®TR* (Cancer pain（Abuse-deterrent tablets))				Japan (2016.11)	Japan (2017.8)
Actair® (Pediatric allergic rhinitis caused by house-dust mite allergen)				Japan (2017.3)	Japan (2018.2)
Xofluza™ (Influenza virus infection)			Global	Japan (2017.10)	Japan (2018.2)
Xofluza™ (Influenza virus infection (pediatric))			Japan	Japan (2017.10)	Japan (2018.2)
Mulpleta® (Thrombocytopenia)			Global	US(2017.12) EU(2018.1)	
Cefiderocol (Multidrug-resistant Gram-negative bacteria infection)			Global : ongoing	US:NDA submission in FY2018	
Lisdexamfetamine (ADHD(pediatric))			Japan	Japan (2017.4)	
Osphena® (Vaginal dryness associated with postmenopausal VVA)**			US	US (2018.3)	

* Development for expansion of indications

** Grant Duchesnay Inc. the right to develop, manufacture and sell in North America

Achievements in FY2017: Phase I - III

Product (indication)	Phase I	Phase II	Phase III	NDA submission	Approval
Xofluza™ (Influenza virus infection・granule)			Japan : initiated		
Cymbalta® (Depression (pediatric))			Japan : initiated		
Intuniv® (ADHD(adult))			Japan : confirmatory trial completed		
S-588410 (Esophageal cancer)			Japan : registration completed		
S-600918 (Neuropathic pain)	Japan : completed	Initiation (regions to be determined)			
S-770108 (Idiopathic pulmonary fibrosis)	Japan : initiated				
S-637880 (Neuropathic pain)	Japan : initiated				

Xofluza™
Influenza Virus Infection

Profile

Indication	Influenza virus infection
Mechanism of action	Cap-dependent endonuclease inhibition (novel mechanism of action)
Special characteristics	✓ Single oral dose ✓ Potent antiviral activity against seasonal influenza (type A and B viruses) and virus with potential pandemic risk including highly pathogenic avian viruses ✓ Confirmed safety/tolerability
Stage	✓ Japan: Approved in Feb 2018 (adults and pediatrics) ✓ US: NDA submission(in preparation)
Future plans	✓ Japan: Launch (Mar 2018), NDA submission for granule formulation, clinical development for prophylaxis indication ✓ US: NDA submission in FY2018

First approval under Sakigake designation on Feb 23, 2018

Launch of Xofluza™

Shionogi
Accelerating global development

- **Shionogi led global Phase III trial and succeeded.**
- **Intensive resource investment enabled us to rapidly achieve his goal**
- **About 3 years from Phase I to launch**

⇒ Stronger partnership with Roche

Japanese authority
Fast track approval & emergent price listing

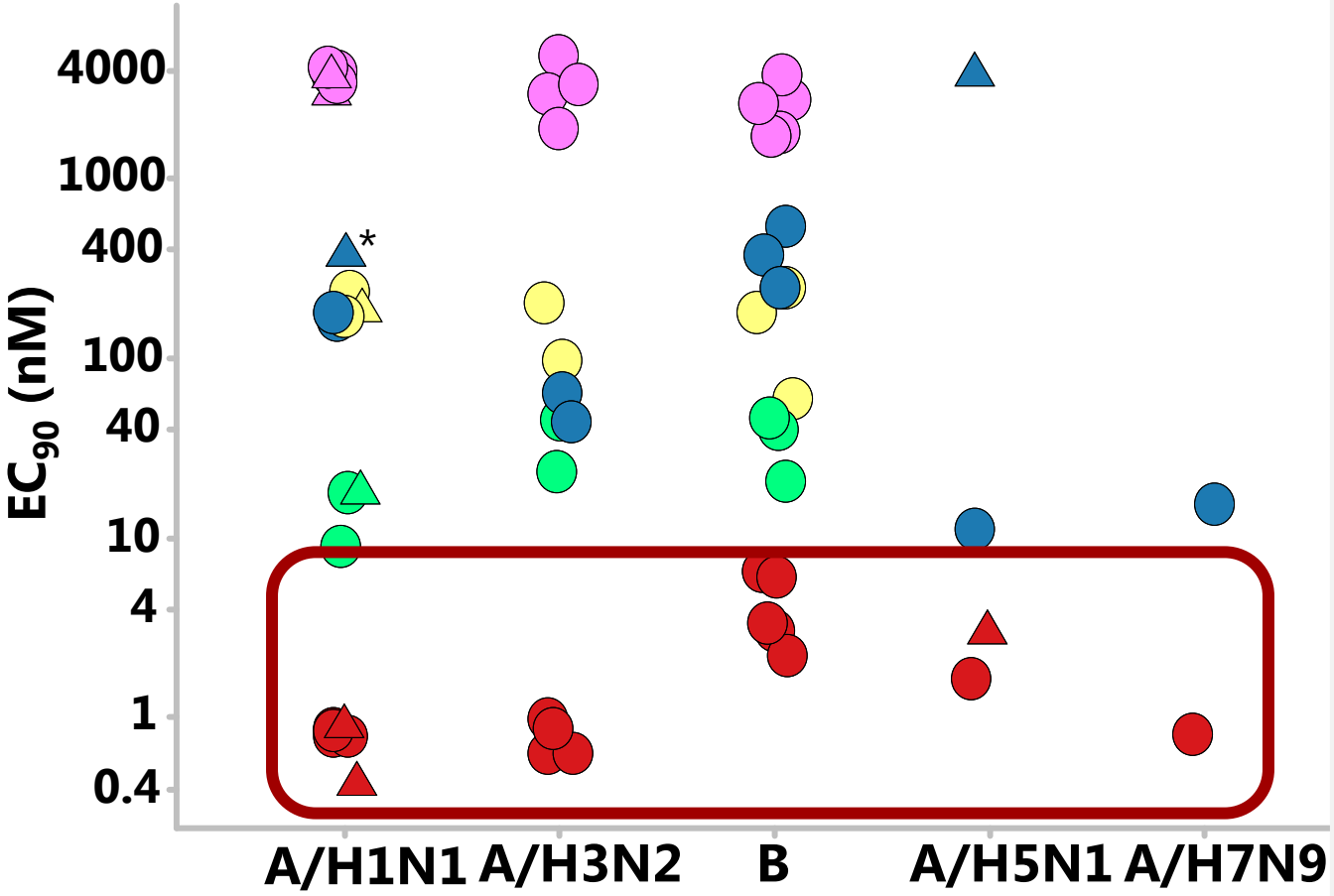
- **"Sakigake" designation**
  - Neuraminidase inhibitor resistant viruses, more virulent viruses
  - Oct.25th (2017)：NDA
    Feb.23rd (2018)：Approval
    Mar.14th (2018)：Price listing

⇒ about 4 months from NDA to approval

Promptly providing the medicine to those in need

Superior Inhibitory Effect on Virus Replication Compared to Existing Antivirals

Inhibitory effect on virus replication in MDCK cells (yield reduction assay)



Color by compound

- S-033447
- Oseltamivir acid
- Zanamivir hydrate
- Laninamivir
- Favipiravir

Shape by NA/274

H Y

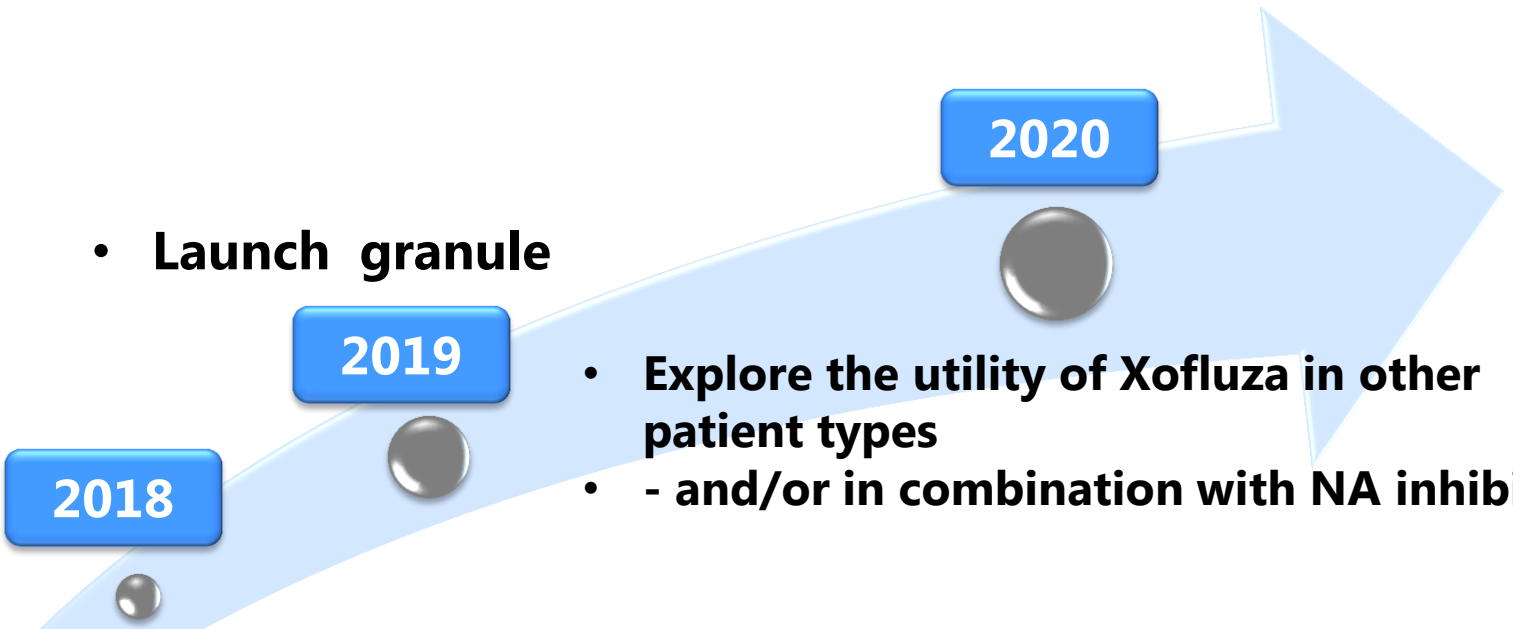
Viral strains tested

A/H1N1	A/WSN/33 A/WSN/33-NA/H274Y A/PR/8/34 A/Kadoma/3/2006 A/Osaka/129/2009 A/Osaka/180/2009-NA/H274Y
A/H3N2	A/Victoria/3/75 A/Hong Kong/8/68 A/Niigata/12F392/2013 A/Hokkaido/12H048/2013
B	B/Lee/40 B/Hong Kong/5/72 B/Maryland/1/59 B/Gunma/12G045/2013 B/Hokkaido/11H011/2012
A/H5N1	A/Hong Kong/483/97 A/Hong Kong/483/97-NA/H274Y
A/H7N9	A/Anhui/1/2013

*>400nM

Superior antiviral activity against influenza viruses, oseltamivir resistant (H274Y) and avian flu (A/H5N1, H7N9) strains, compared to existing antivirals

Future Clinical Development/Research Plans



- US NDA submission(2018)
- Confirm efficacy evidence in patients at high-risk for complication (HR study)
- Start clinical trial for prophylaxis indication (2018/19 flu season)

Life cycle management plan to maximize Xofluza™ with taking key advantages, ie potent antiviral efficacy, convenience in single oral dose, improved adherence.

Cefiderocol
Multidrug-resistant Gram-negative bacteria infection

Profile: Cefiderocol

Indication	Multidrug-resistant Gram-negative bacteria infection
Mechanism of action	Cell-wall synthesis inhibition
Special characteristics	Injectable siderophore cephalosporin Wide range of Gram-negative pathogens
Stage	APEKS*-cUTI：Phase II complicated urinary tract infection study (Global)(Complete) CREDIBLE-CR：Phase III Gram-negative carbapenem – resistant study (Global) APEKS*-NP：Phase III hospital-acquired pneumonia/ ventilated-associated pneumonia study (Global)
Future plan	US: NDA submission in 2H FY2018 (QIDP** designated compound)

* APEKS = Acinetobacter, Pseudomonas, E. coli, Klebsiella, Stenotrophomonas
** QIDP: Qualified infectious disease product

WHO/CDC Priority Pathogens List

Bacteria (WHO category)	WHO (2017)	CDC (2013)
Acinetobacter baumannii, carbapenem-R	Critical	Serious (MDR)
Pseudomonas aeruginosa, carbapenem-R	Critical	Serious (MDR)
Enterobacteriaceae, carbapenem-R, 3rd-gen ceph-R (ESBL+)	Critical	Urgent (carbapenem-R) Serious (ESBL+)
Enterococcus faecium, vancomycin-R	High	Serious (VRE)
Staphylococcus aureus, methicillin-R, vancomycin-I/R	High	Serious (MRSA) Concerning (VRSA)
Helicobacter pylori, clarithromycin-R	High	
Campylobacter spp., fluoroquinolone-R	High	Serious (drug-R)
Salmonellae spp., fluoroquinolone-R	High	Serious (drug-R)
Neisseria gonorrhoeae, 3rd-gen ceph-R, fluoroquinolone-R	High	Urgent (drug-R)
Streptococcus pneumoniae, penicillin-NS	Medium	Serious (drug-R)
Haemophilus influenzae, ampicillin-R	Medium	
Shigella spp., fluoroquinolone-R	Medium	Serious
Clostridium difficile		Urgent

SHIONOGI

WHO: GLOBAL PRIORITY LIST OF ANTIBIOTIC-RESISTANT BACTERIA TO GUIDE RESEARCH, DISCOVERY, AND DEVELOPMENT OF NEW ANTIBIOTICS, 2017
CDC : Antibiotic Resistance Threats in the United States, 2013

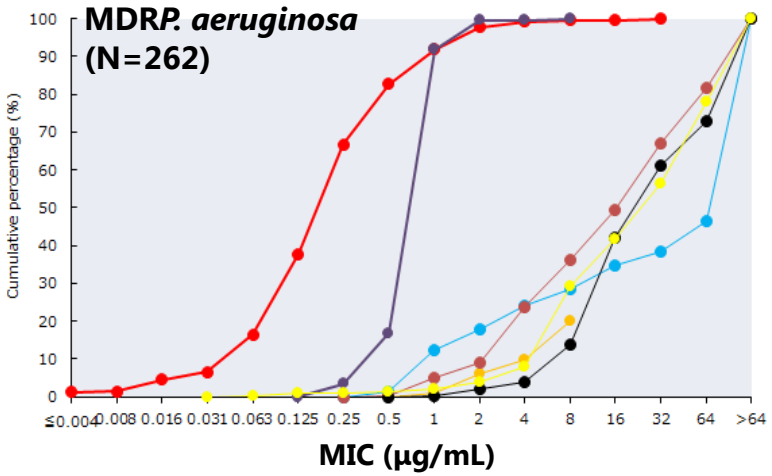
Antibacterial Activities against Three WHO Priority Pathogens

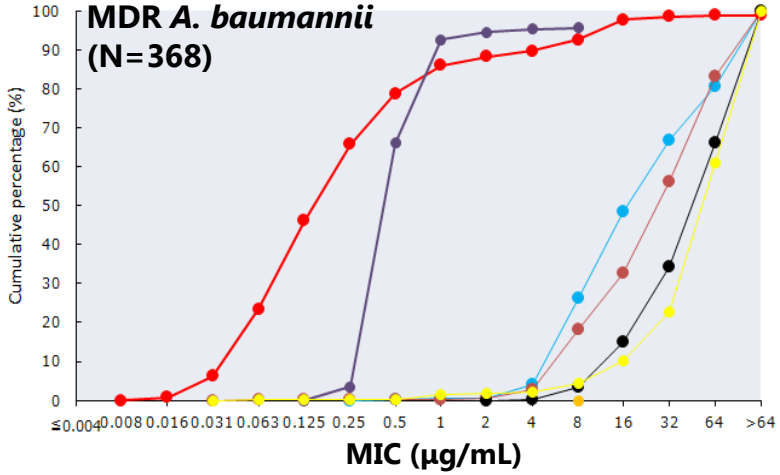
Name (synonym)	Antibiotic class	Route of Administration (Developer)	Expected activity against priority pathogens: CRAB	CRPA	CRE	OPP
Vaborbactam + meropenem (Carbavance)	Boronate BLI + carbapenem	IV (The Medicines Co)	■	■	■	[b]
Cefiderocol	Siderophore-cephalosporin	IV (Shionogi)	■	■	■	
Relebactam + imipenem/ cilastatin	DBO-BLI + carbapenem/ degradation inhibitor	IV (Merck & Co)	■	■	■	[b]
Sulopenem	Carbapenem	IV & oral (Iterum)	■	■	■	[c]
Plazomicin	Aminoglycoside	IV (Achaogen)	■	■	■	
Lascufloxacin	Fluoroquinolone	IV & oral (Kyorin)	■	■	■	■
Eravacycline	Tetracycline	IV & oral (Tetraphase)	■	■	■	

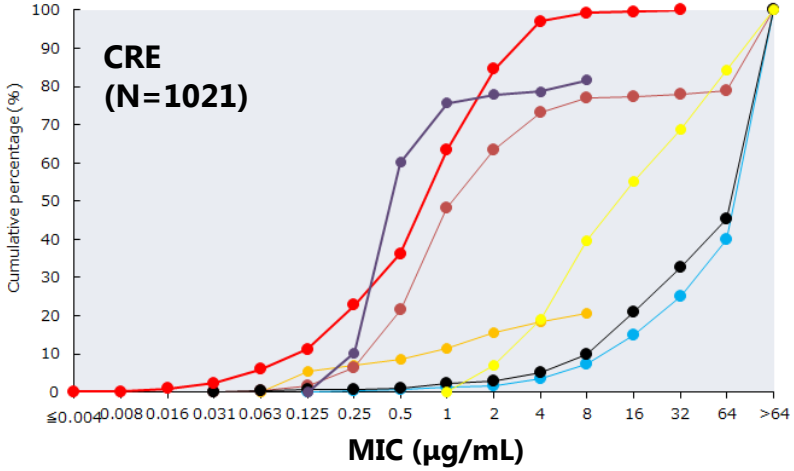
Pathogen activity: ■ active, ■ possibly active, ■ not or insufficiently active.

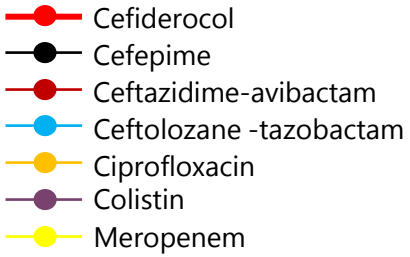
CRAB: Carbapenem-Resistant *Acinetobacter baumannii,* CRPA: Carbapenem-Resistant *Psudomonas aeruginosa,* CRE: Carbapenem-Resistant Enterobacteriaceae, OPP: Other Prioritized pathogen

MDR Non-fermenters and CRE Collected Globally in 2014-2016 (SIDERO-CR-2014/2016)









Enhanced activity against Gram-negative bacteria especially, MDR* non-fermenters and CRE**

* MDR = Multidrug-resistant
** CRE = Carbepenem-resistant Enterobacteriaceae

Antimicrobial Resistance (AMR): Current Situation

Wide spread of AMR infections

- **The estimated impact of antimicrobial resistance (AMR) by 2050***
  - Failing to tackle AMR could cause 10 million extra deaths a year by 2050 and cost up to US$100 trillion
- **Significant unmet medical needs for new antibacterial agents that have activity against priority pathogens, especially CR pathogens**

  ⇒ Cefiderocol would be a valuable drug to tackle AMR
- **Over 80% of carbapenem-resistant (CR) pathogens are non-fermenters, such as *A. baumannii* and *P. aeruginosa,* in the US****

  ⇒ Cefiderocol is an important drug that can tackle CR non-fermenters, such as *A. baumannii* and *P. aeruginosa*, in addition to CRE

Recent competitors' situation in the US

- **Among antibacterials targeting MDR*** Gram-negative infections (GNIs), some products released clinical data in CR-GNI at the time of submission or acceptance of their NDA filing. However, the target pathogens for these products are CRE**** and they do not have activity against CR non-fermenters (*A. baumannii* and *P. aeruginosa*).**

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* The Review on Antimicrobial Resistance Chaired by Jim O'Neill, December 2014
** Open Forum Infectious Diseases, Volume 4, Issue 3, 1 July 2017, ofx176
*** MDR = Multidrug-resistant, **** CRE = Carbepenem resistant Enterobacteriaceae

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  - S-005151
    Epidermolysis bullosa, stroke
- **Targeted Milestones for FY2018**

Most important compound in 2018

ref. p111map

S-600918

Neuropathic pain, refractory chronic cough and others

ref. p111map

S-770108

Idiopathic Pulmonary Fibrosis (IPF)

Please take a look at the map at from p109 to p111 as well.

Most important compound in 2018

SONG for you!

S-600918
Neuropathic pain, refractory chronic cough and others

ref. p111map

Profile: S-600918

Indication	Neuropathic pain, refractory chronic cough and others
Mechanism of action	Undisclosed (new mechanism)
Product profile	✓ Once-daily, oral ✓ Good and well-tolerated safety profile
Stage	✓ Phase I completed (JP)
Future plan	✓ PoC study will be initiated in FY2018 (JP)

In development for diseases caused by afferent nerve sensitization such as neuropathic pain, refractory chronic cough and so on.

S-600918 development: Meeting Societal Needs

Creating a more vigorous society

SGS2020update

Pain/CNS + **Addressing society's needs**

Refractory chronic cough

- **Cough lasting ≥ 8 weeks**
- **Underlying causes: asthma, sinobronchial syndrome, GERD etc.**
- **Persisting cough despite appropriate treatment(s)**

- There are no approved drugs
- Long-term use of centrally-acting antitussive is not recommended

Contribute to the creation of a more vigorous society that is relieved from long-lasting cough/pain by providing new therapeutic options

GERD: Gastroesophageal Reflux Disease

Most important compound in 2018

SONG for you!

S-770108

ref. p111map

Idiopathic Pulmonary Fibrosis (IPF)

SHIONOGI

Profile：S-770108 (Pirfenidone Inhalant)

Indication	Idiopathic pulmonary fibrosis
Mechanism	Anti-fibrosis
Profile	✓ Dry powder inhaler (convenient use) ✓ Specific inhalation device designed for pirfenidone inhalant ✓ Favorable safety and tolerability profile
Stage	✓ Japan: Phase I study
Plan	✓ Planning a study to investigate the distribution in the lung after inhalation of radio-labelled pirfenidone

S-770108 Development Concept

Oral pirfenidone (Pirespa®, Esbriet®)

- Global guideline[1] ; conditional recommendation for use to IPF
- Intolerable in some patients
  - GI events (decreased appetite, nausea), photosensitivity ; cannot reach recommended dose (60%), drop-out due to adverse reactions (20%/year)[2]

Inhalant pirfenidone (S-770108)

- Markedly decrease in systemic exposure, and favorable safety profile
  - Improved treatment compliance, enable to continue treatment
  - Direct exposure to lung lesions, possibly enhancing efficacy

Provide treatment with markedly improved safety to IPF patients, who cannot be adequately treated with existing drugs due to adverse reactions.

1) ATS/ERS/JRS/ALAT clinical practice guidelines on the treatment of IPF (2015)
2) Post-marketing surveillance report of pirfenidone for IPF patients in Japan

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S-005151
Epidermolysis bullosa, stroke

Profile：S-005151

Indication	Epidermolysis bullosa (EB), acute ischemic stroke (AIS)
Mechanism of action	Mobilization of mesenchymal stem cells (MSCs) to peripheral blood
Product property	Drip intravenous infusion Anti-inflammatory effect and induction of regeneration by mobilized MSCs
Stage	EB: Phase II（Investigator-initiated study） AIS：Preparation for Phase I
Future plan	AIS：Phase I in 2018 1H

Clinical Development of S-005151: Meeting Society's Needs

Creating a more vigorous society

SGS2020update

Pain/CNS + **Addressing society's needs**

Through regeneration-inducing effects, medium-sized peptide molecule S-005151 is anticipated to show effects similar to regenerative medicine, balancing innovation and accessibility

- In Japan, more than 1 million patients suffer from cerebrovascular disorders including acute ischemic stroke (the leading cause of long-term care*). The annual medical cost expands to 1.7 trillion Yen.
- t-PA or endovascular therapy are used only in the limited number of stroke patients (0.9-6%) ** with treatment satisfaction being 60%***.

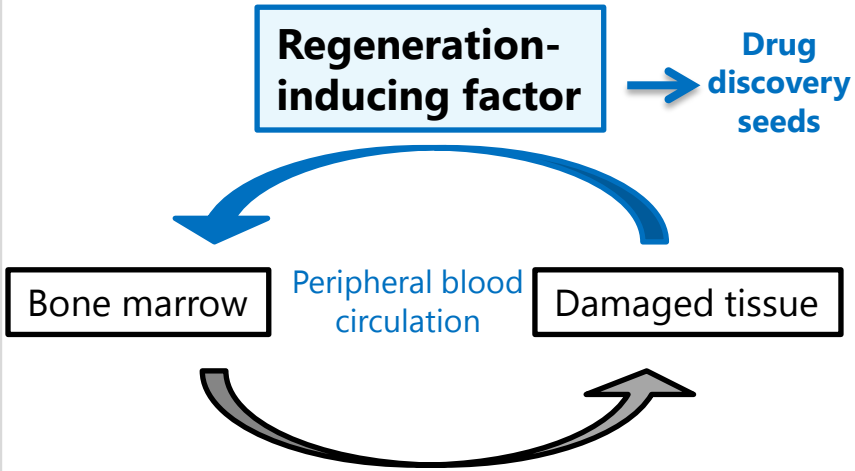
Clinical development of S-005151 will contribute to making society more vibrant by helping stroke patients by reducing their disability

*: MHLW Comprehensive Survey of Living Conditions 2010
**: Stroke databank2015
*** : Report from the Japan Health Sciences Foundation (2014)

Mechanism of Action of Novel Development Product for Ischemic Stroke (S-005151)

Mechanism to promote tissue regeneration

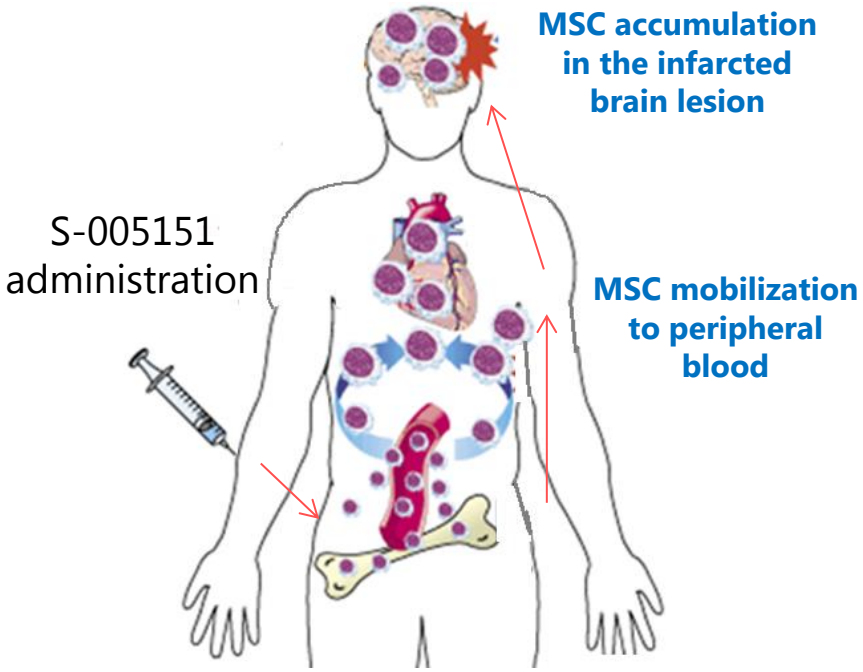
In vivo self-regeneration mechanism discovered by collaborative research with academia and venture



Mesenchymal stromal cells (MSC)

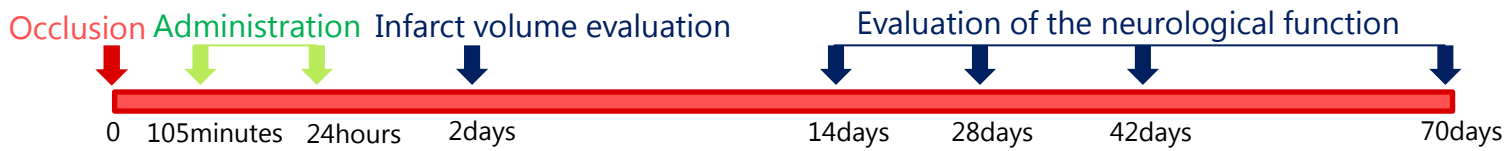
Genomix Co Ltd
世界初「再生誘導医薬」の実現を目指して

Supposed action of S-005151



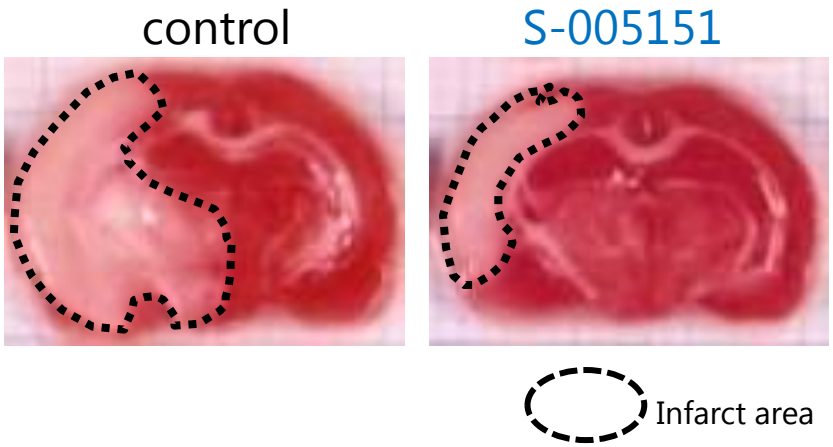
The peptide with regeneration-inducing effects for treating ischemic stroke arose from drug seeds derived from a collaboration with an Osaka University-originated venture

Pharmacological Effects of S-005151 in Nonclinical Studies



Neuroprotection

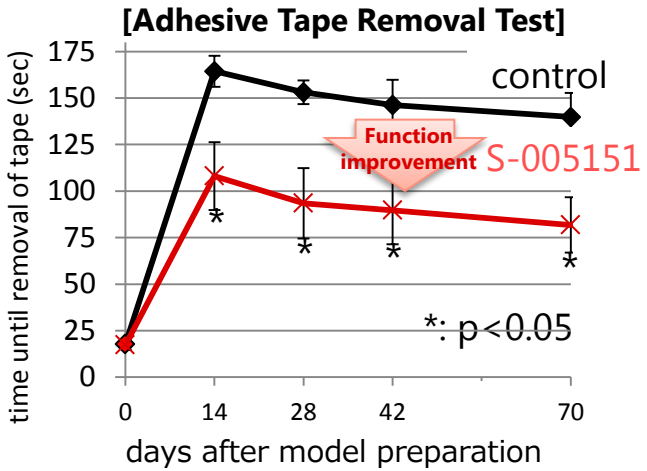
Reduction of cerebral infarction area



Neuro-function improvement

Recovery of sensory motor function

The time until removal of tape from impaired side forelimb was timed up to 180 seconds.



S-005151 demonstrated neuroprotection and neuro-function improvement by administration after cerebral infarction

⇒ Phase I clinical trial will start in first half of FY2018

Agenda: Global Development Division

- **To Achieve SGS2020**
  - Development Targets for FY2020
  - Targeted Milestones for FY2017
- **Achievements in FY2017**
  - Current Status and Actions
  - Pipeline
  - Core Development Products
    - > Infectious disease
      - = Xofluza™
      - = Cefiderocol
- **Top priority Development Products in FY2018**
  - **S-600918**
    Neuropathic pain・Refractory Chronic Cough
  - **S-770108**
    Pirfenidone inhalant（Idiopathic pulmonary fibrosis ）
- **Other developed products**
  - S-005151
    Epidermolysis bullosa, stroke
- **Targeted Milestones for FY2018**

Development Targets for FY2018

Issues for FY2017

Accuracy of clinical trial planning

Progress of global studies

Increasing outsourcing fees

- **Establish development framework that can respond flexibly to environmental changes**
  - Centralized management and oversight for global clinical trials
  - Rapid decision making by data driven approach
- **Cost saving by streamlining development packages and focusing clinical trials**
  - Increasing skillis in forecasting and planning
  - Increase the predictability from feasibility studies

NDA Submissions: 3 (4 indications)

Approvals: 3

Target Milestones for FY2018: Approvals and NDA Submissions

Product (indication)	Phase I	Phase II	Phase III	NDA submission	Approval
Mulpleta® (Thrombocytopenia)				US (2017.12) EU (2018.1)	US
Rizmoic® (Opioid-induced constipation)				EU (2017.3)	EU
Lisdexamfetamine (ADHD(pediatric))				Japan (2017.4)	Japan
Xofluza™ (Influenza virus infection)			Global : ongoing		US
Xofluza™ (Influenza virus infection(granule))			Japan : ongoing		Japan
Cefiderocol (Multidrug-resistant Gram-negative bacteria infection)			Global : ongoing		US
Intuniv® (ADHD(adult))			Japan : extension study ongoing		Japan

Target Milestones for FY2018: Phase I - III Study

Product (indication)	Phase I	Phase II	Phase III	NDA submission	Approval
Xofluza™ (Influenza virus infection (prophylaxis))			Asia(Japan・Taiwan) : initiated		
OxyContin®TR (Treatment of moderate to severe chronic pain*)			Japan : initiated		
S-120083 (Inflammatory pain)		US : completed			
S-588410 (Bladder cancer)		Japan・EU : completed			
S-600918 (Neuropathic pain or Refractory Chronic Cough)		Japan : initiated			
S-770108 (Idiopathic pulmonary fibrosis)	Japan : completed				
S-637880 (Neuropathic pain)	Japan : completed				
S-005151 (Acute ischemic stroke)	Japan : initiated				
S-004992 (Tuberculosis)	Asia (China) : initiated				

Development Targets for FY2020 from FY2017

Direction for FY2020

Goals **10 or more compounds, including out-licensed products and products currently approved in a limited number of countries, to be launched globally**

Establish global development framework

- **One Global SHIONOGI**
  - ✓ Sharing fundamental policies, mission and decisions
  - ✓ Standardization of Roles & Responsibilities and business processes

Fast and accurate making decision

- **Strategy-based prioritization**
- **ROI* based efficient investment**
- **Science-based go/no-go decision**

Efficient development

- **Streamline development packages**
- **Control development costs**
- **Reduce development time**

*Return on investment

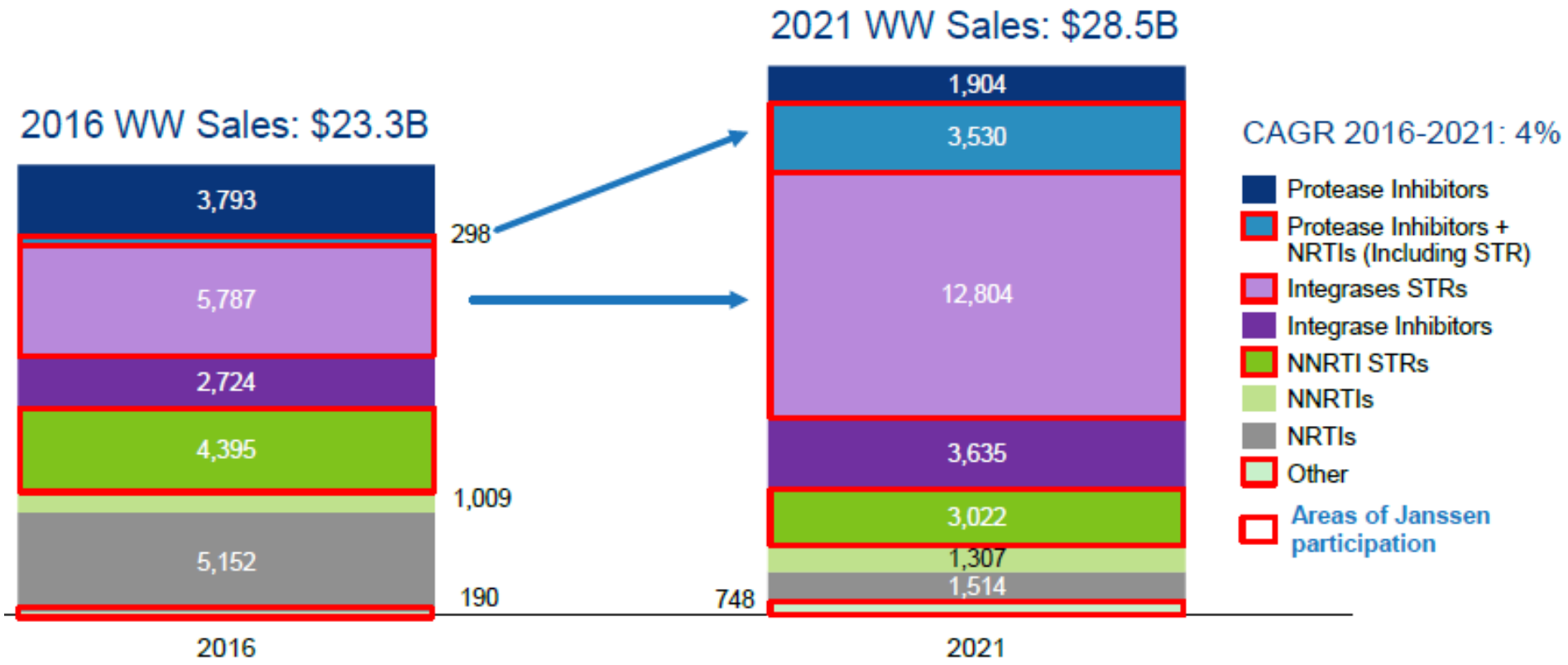
Summary

Isao Teshirogi, Ph.D.
President and CEO

Future Action Plan for HIV Integrase Inhibitor Franchise

Isao Teshirogi, Ph.D.
President and CEO

Trends in the HIV Market



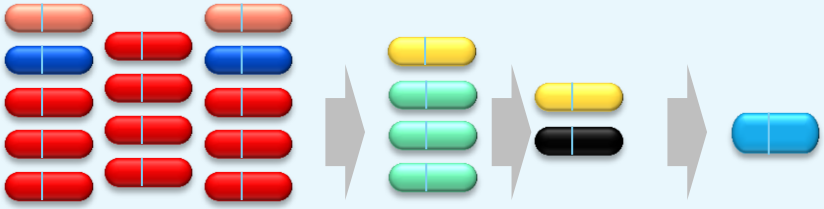
EvaluatePharma, April, 2017

Source: Johnson & Johnson Pharmaceutical Business Review Day in May, 2017

Therapeutic Strategy for HIV

1996	2000	2010	2020
Deadly illness	Treatable disease	Restore and maintain their health	

ART



Three HIV medicines from at least two different drug classes

Improve dosage and administration by improving therapeutic agents

STR

2-drug treatment regimens
2-drug regimens

1-drug treatment

cure

Unmet patient needs

- Same quality of life as uninfected individuals
- Prevention
- Cure

HIV Discovery at Shionogi

Created Tivicay® (DTG)

STR Triumeq® (DTG/ABC/3TC)

Created long-acting injectable Cabotegravir (CAB) Phase III study

Drug discovery strategy to advance HIV Therapy

- Create compounds for STR with DTG
- Create compounds suited for injectable combination therapy
- Establish our agents in prevention

STR: Single tablet regimen, DTG: Dolutegravir, ABC: Abacavir, 3TC: Lamivudine

Dolutegravir: Trust Built on Extensive Experience

Dolutegravir (DTG)

- Dolutegravir is #1 core agent globally
- **500,000 patients** worldwide taking a dolutegravir based regimen
- **No dolutegravir-resistant viruses have observed** in clinical sites since the launch of Tivicay®, 2013.
- Unmatched trial results; **superiority** in 5 studies and data in broad populations

vs. efavirenz	vs. raltegravir	vs. darunavir	vs. atazanavir	vs. lopinavir
Superiority (naïve)	**Superiority** (experienced)	**Superiority** (naïve)	**Superiority** (women/naïve)	**Superiority** (experienced)

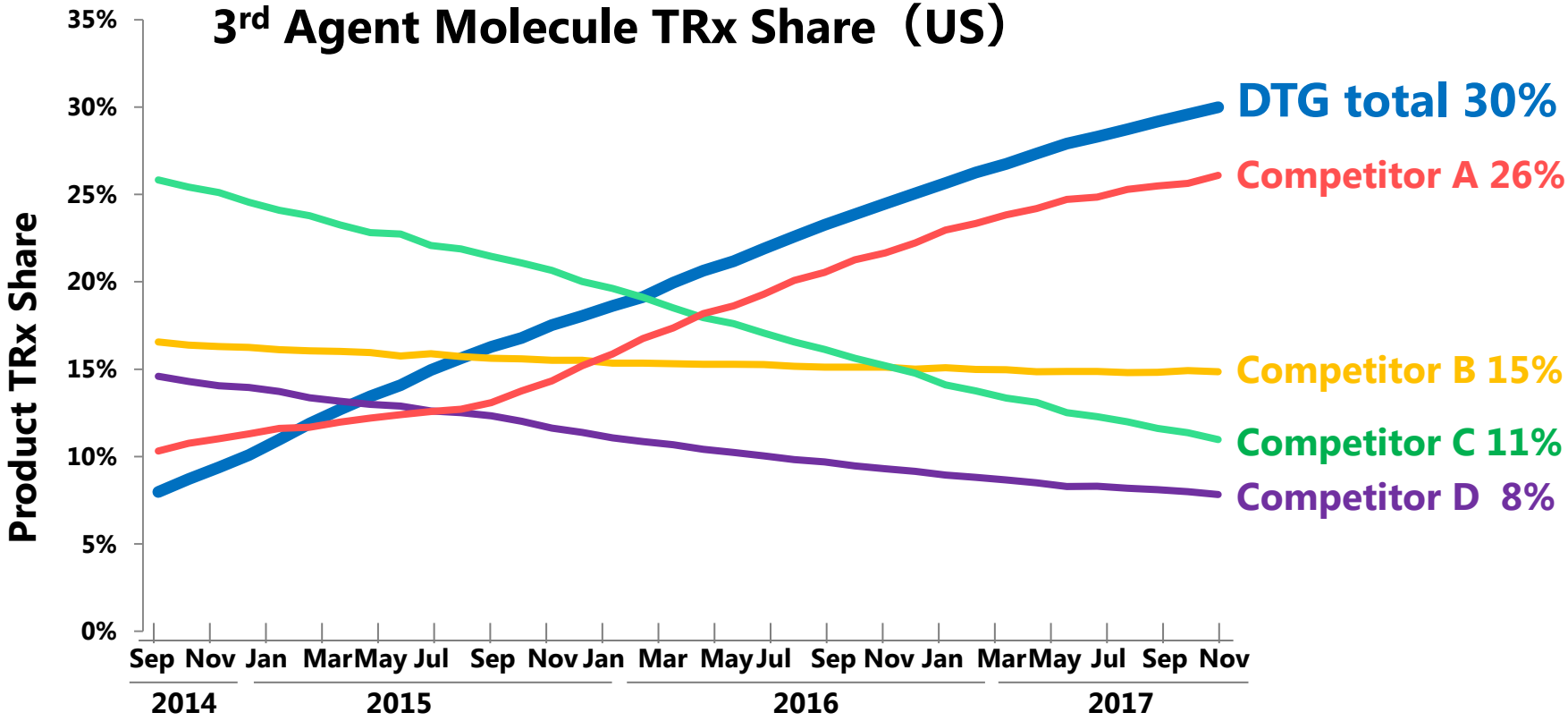
These were non-inferiority studies with a pre-specified analysis for superiority. Tables shows primary endpoint outcomes.

efavirenz : Sustiva® and Stocrin® , raltegravir : Isentress®, darunavir : Prezista® atazanavir : Reyataz® lopinavir : Kaletra®

Cited from presentation material of 3Q FY2017 Financial Results

Growth and Progress of HIV Franchise

Prescription trend in US（TRx Share）



Dolutegravir (DTG) Leads the Market as the #1 Core Agent in the US

New Regimens for HIV Treatment

Two-Drug Regimen

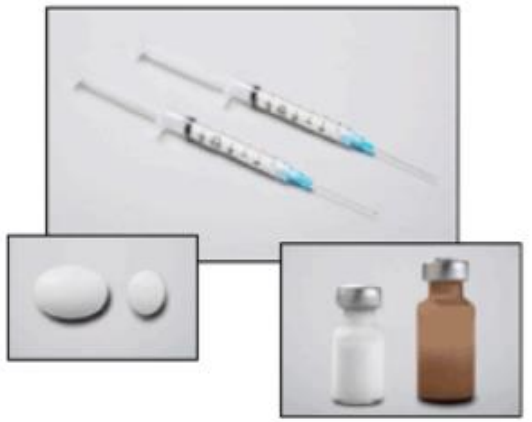
- Future growth driven by innovative oral and long-acting two-drug regimen pipeline
- **66% of patients** want to take less medicine*
- **Juluca®(DTG/RPV):** Approved by FDA November 2017 and already included in DHHS/EACS guidelines for suppressed switch
- Strong commercial execution building on success of Tivicay® and Triumeq®
- **DTG/3TC:** GEMINI data and regulatory submission expected **in 2018**
- **Long acting CAB+RPV:** Phase III data expected **by end of 2018**

* Patient Pathways survey presented at IAS 2017.
DHHS: Department of Health and Human Services; EACS: European AIDS Clinical Society

Further Improvement of Patient Satisfaction

- **Cabotegravir (CAB)**
  - Integrase inhibitor
  - Oral tablet and intramuscular long-acting injection
    - > Oral: 30mg tablet ($t_{1/2}$* ~40 hours)
    - > Long-acting injection: 200mg/mL ($t_{1/2}$ 20~40 days)

    →Only anti-HIV injectable drug



- **Rilpivirine (RPV)**
  - NNRTI
  - Oral tablet and intramuscular long-acting injection
    - > Oral: 25mg tablet ($t_{1/2}$* ~50 hours)
    - > Long-acting injection: 300mg/mL ($t_{1/2}$ 30~90 days)

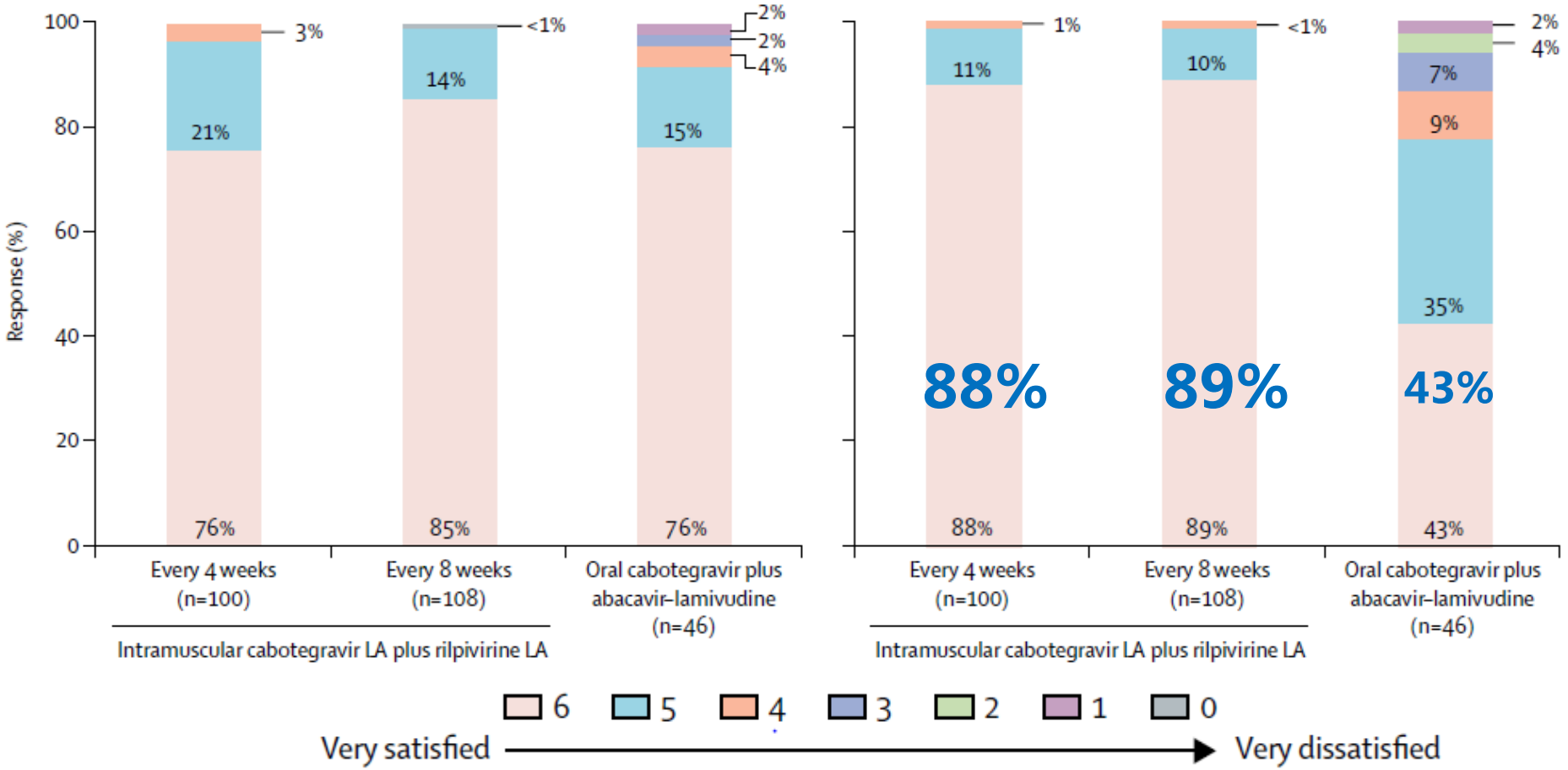
→ Cabotegravir + Rilpivirine (long-acting injection)

- **Expect to improve adherence**
  - > Intramuscular injection: every one month administration
  - > Initiated Phase III study of every two months administration (in Nov. 2017)
- **Planning to launch in FY2020**

CAB+RPV (LATTE-2 Study): Week 96 Patient Satisfaction with Maintenance Therapy vs Oral Induction

How satisfied are you with your current treatment?

How satisfied would you be to continue with your present form of treatment?



LA=long-acting.

Source: *Lancet* 2017; 390: 1499–510

Cabotegravir for HIV prevention

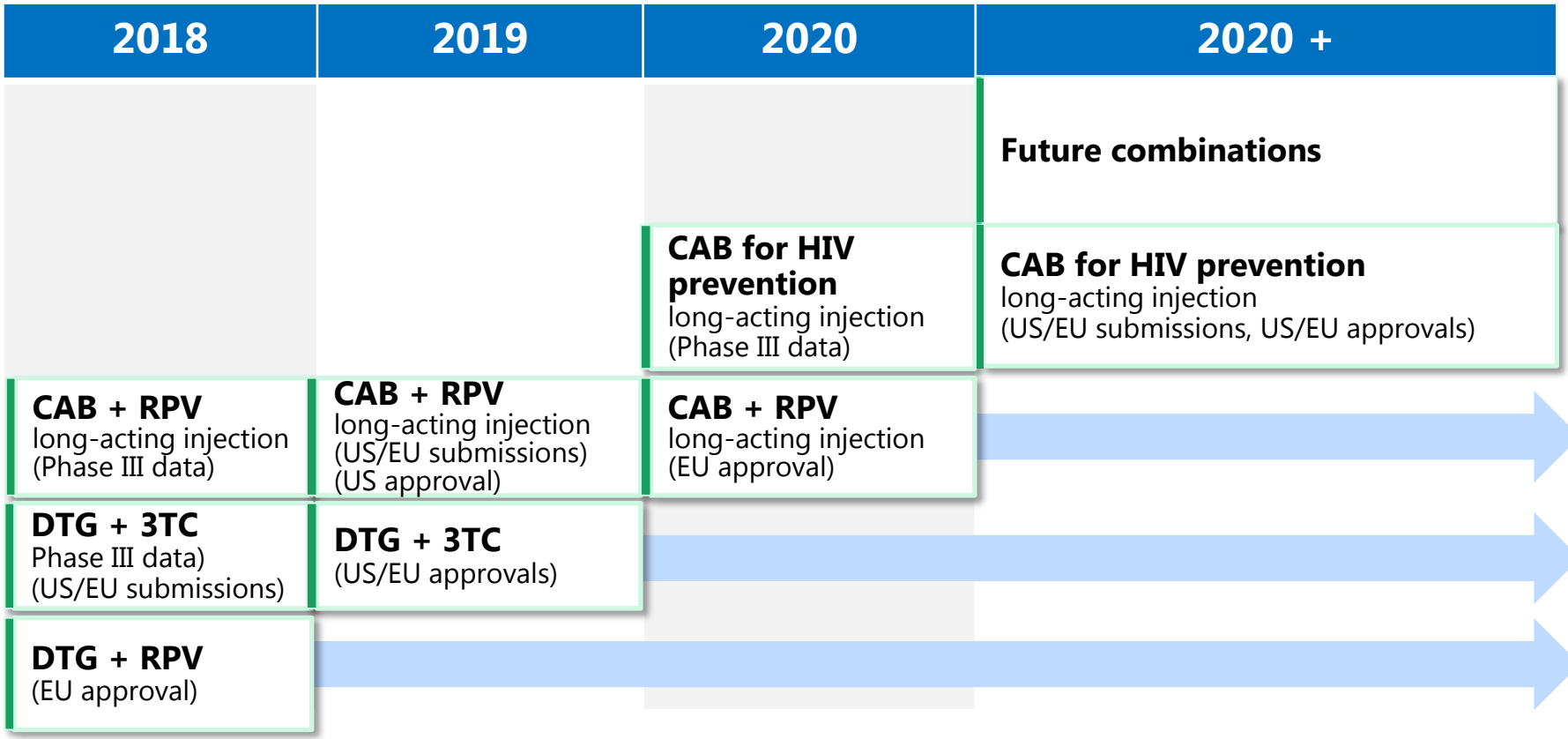
- **Development status of cabotegravir for HIV prevention**

CAB studies	Study Design*
ECLAIR ・Phase IIa (N=127)	• Long-acting CAB injections (every 12 weeks administration) vs placebo • Enrollment of HIV-uninfected men not at high risk for acquiring HIV infection
HPTN 083 ・Phase IIb/III (N=4500 in the plan)	• Long-acting CAB injections (every 8 weeks administration) vs oral Truvada tablets (once daily) • Enrollment of HIV-uninfected MSM and TGW at risk for acquiring HIV infection
HPTN 084 ・Phase III (N=3200 in the plan)	• Long-acting CAB injections (every 8 weeks administration) vs oral Truvada tablets (once daily) • Enrollment of HIV-uninfected women aged 18 to 45 years

* Clinicaltrial.gov参照

** MSM：men who have sex with men 、TGW：transgender women

ViiV's Development Plan of HIV Integrase Inhibitor Franchise



ViiV's strategy to develop new treatment regimens to address the needs of people living with HIV places our HIV integrase inhibitors at the core of therapy

DTG: Dolutegravir , 3TC: Lamivudine, RPV: Rilpivirine, CAB: Cabotegravir

Closing Remarks

Isao Teshirogi, Ph.D.
President and CEO

To Achieve Sustainable Growth beyond 2020

First-priority R&D action in FY2017

- **Focusing our R&D resources on the next growth driver following the HIV franchise, Xofluza™**
- **Maximally accelerated the development of Xofluza™**
  - **Japan: Price listing and launched on Mar. 14, 2018**
  - **NDA submission in US and future global studies will be conducted by Roche**

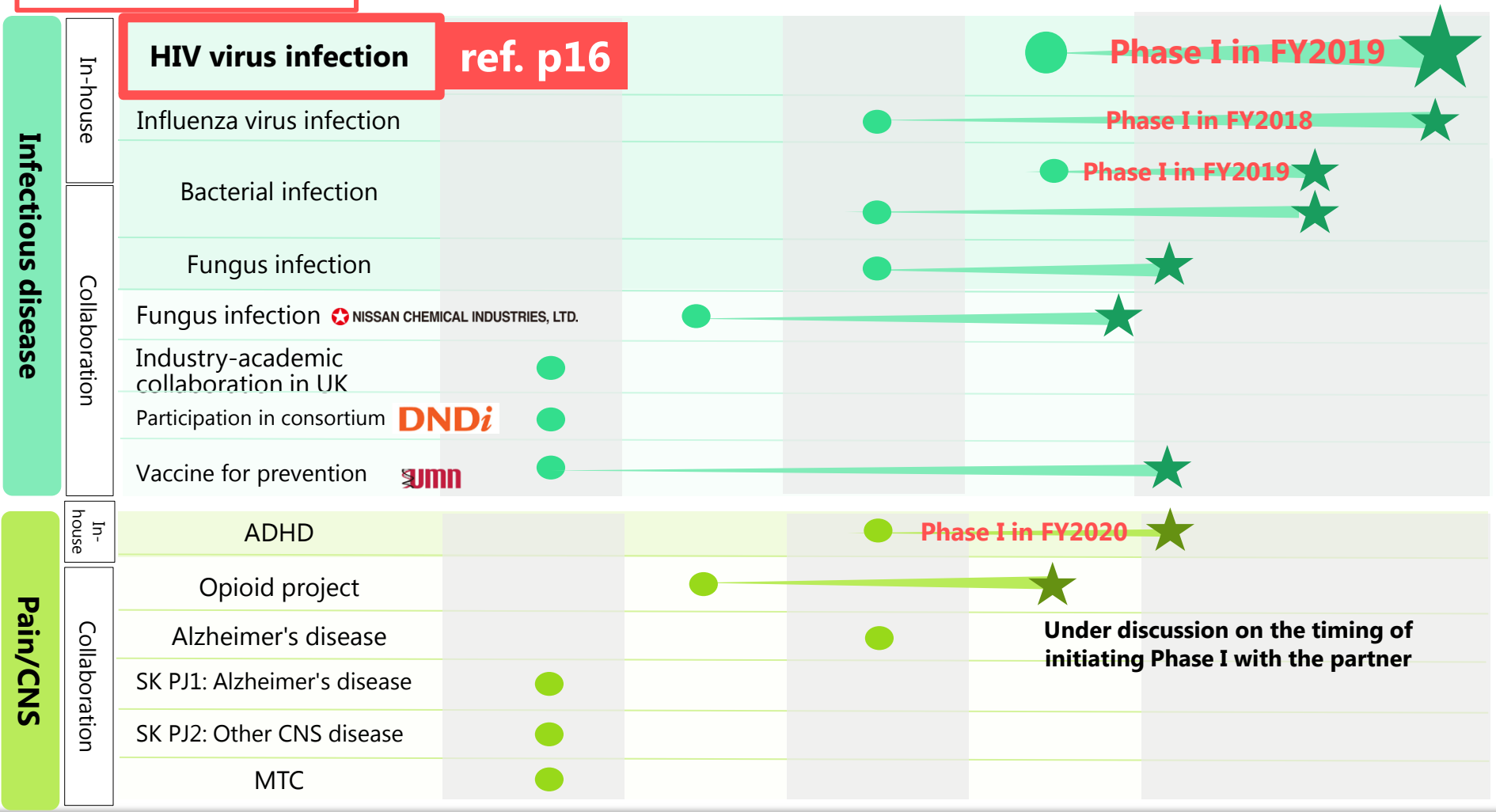
Entering a stage of continuous creation and progression of growth drivers

Actions to Create Further Growth Drivers

1: Generate a Large Variety of Compounds in Phase I (Infectious disease, Pain/CNS)

Focus on 7 projects marked by red frame in FY2018

Preclinical (Basic research) → Preclinical (Early phase) → Preclinical (Late phase) → Preclinical (Candidate) → Phase I



SHIONOGI

As of Mar. 2018

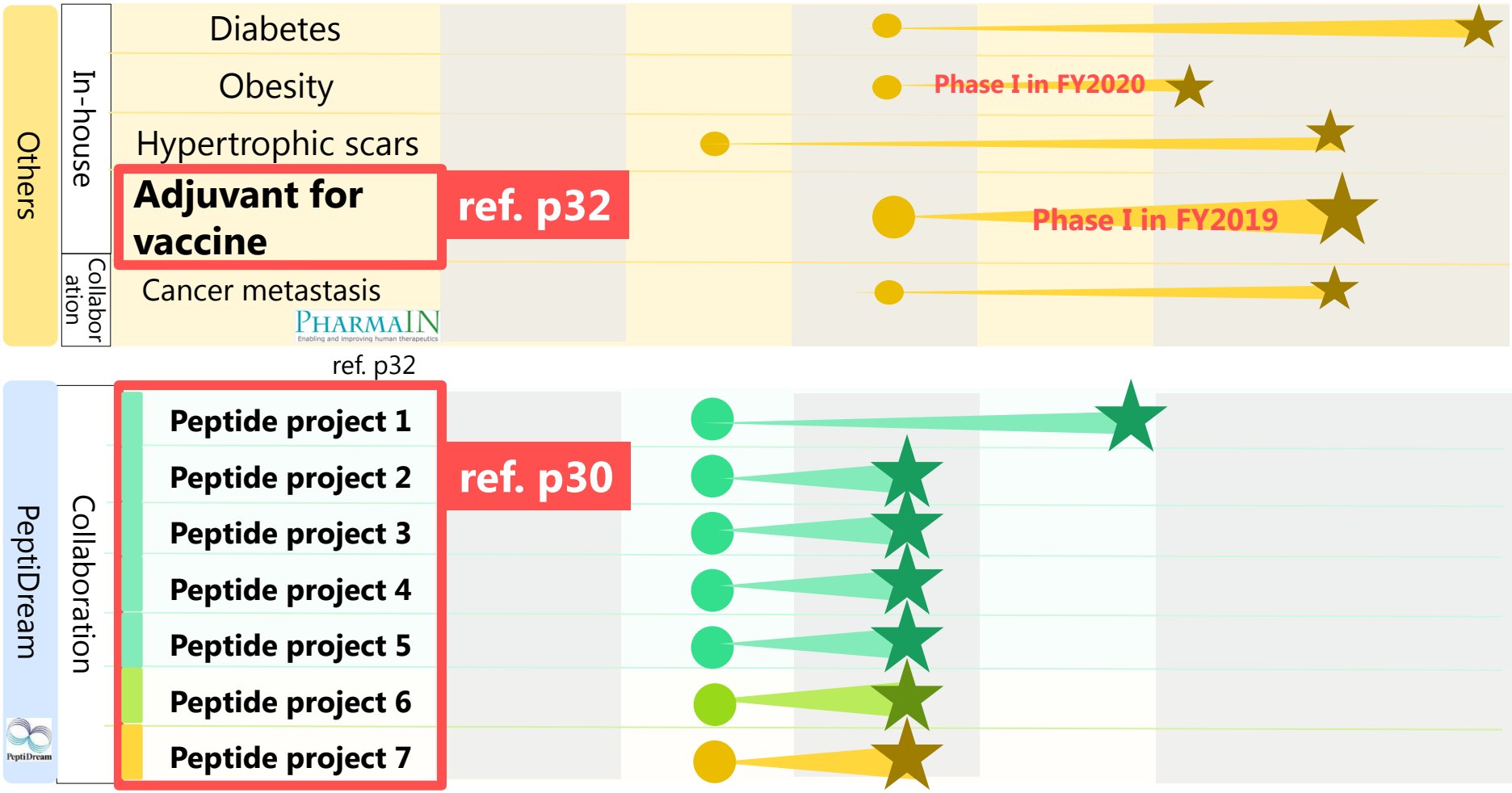
Target Milestones in Mar. 2021

Actions to Create Further Growth Drivers
1: Generate a Large Variety of Compounds in Phase I (Others)

SONG for you!

Focus on 7 projects marked by red frame in FY2018

Preclinical (Basic research) → Preclinical (Early phase) → Preclinical (Late phase) → Preclinical (Candidate) → Phase I



SHIONOGI

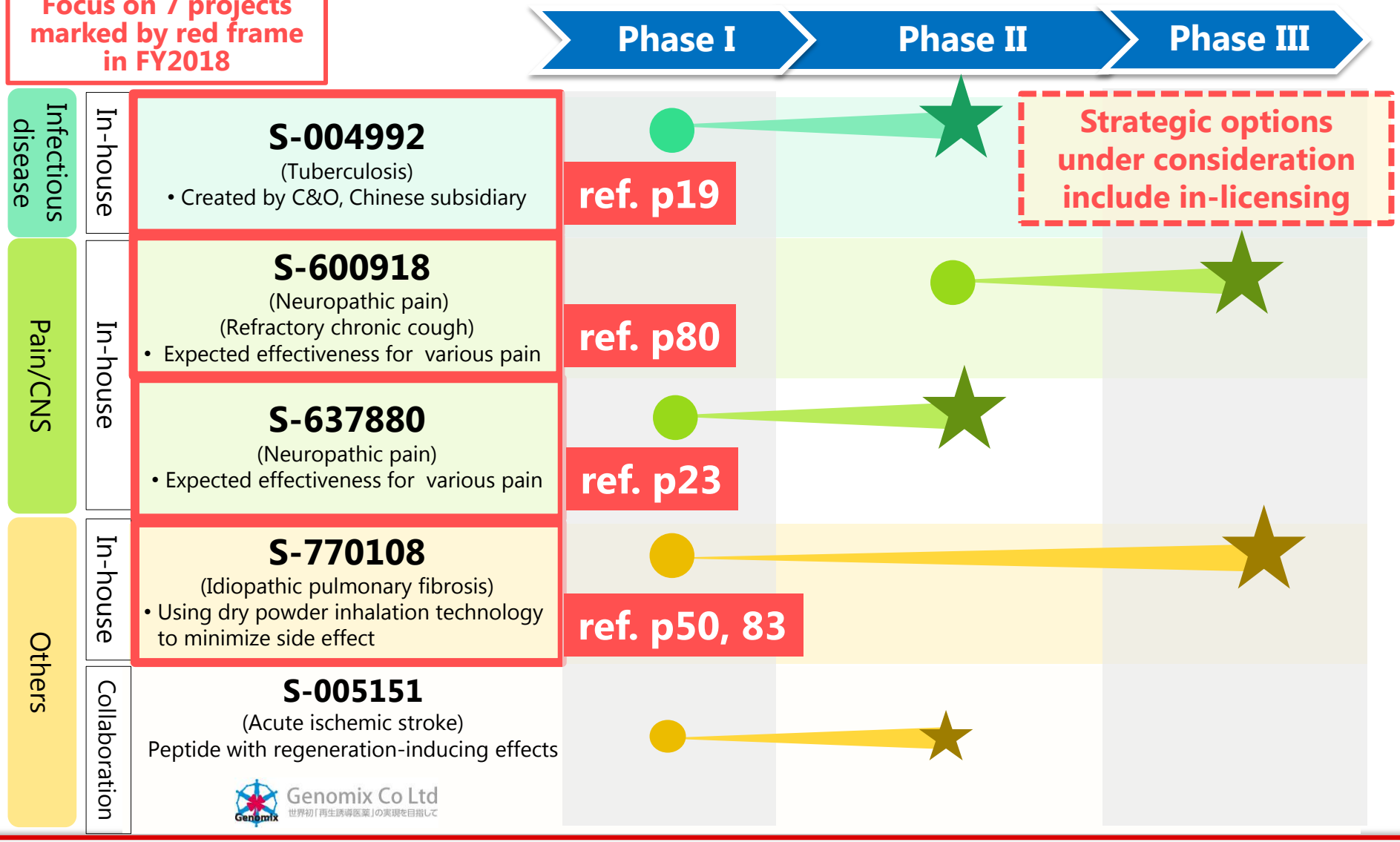
As of Mar. 2018

Target Milestones in Mar. 2021

Actions to Create Further Growth Drivers
2: To expand the Phase II and III pipeline

SONG for you!

Focus on 7 projects marked by red frame in FY2018



To Accomplish the Further Sustainable Growth beyond 2020

Actions for further continuous creation of the growth driver

Completed *shifting gears* in R&D activities

Strengthening, expanding and accelerating our internal research and collaborative research with partners

- **Advancing early research programs**
- **Establishing research base**

To generate a large number of development assets in Phase I and II by FY2020

Targets for FY2018 (Summary)

	Achievements in FY2017	Targets for FY2018	Targets from FY2017 to FY2020
Research	Drug candidate: 1 candidate	3 candidates	10 development products
	Development products: 4 products	2 products	
CMC	Moving projects forward to drug candidate: 0 project	2 projects	4 or more projects
	Obtaining revolutionary CMC technologies: 2 technologies	1 technology	3 or more technologies
	Developing new LCMs: 1 project	1 project	2 or more projects
Development	NDA submissions: 4 compounds (6 indications)	3 compounds (4 indications)	10 or more compounds to be launched globally*
	Approvals: 4 compounds	3 compounds	

Pipeline (as of Mar. 2018)

SONG for you!

Preclinical	Phase I	Phase II	Phase III	Filed
Influenza virus infection	**Global**	**Cefiderocol** Multidrug-resistant Gram-negative bacterial infections	**Baloxavir marboxil** Influenza virus infection	**Rizmoic® (EU)** Opioid-induced constipation
HIV virus infection	**S-004992** Tuberculosis	**S-120083** Inflammatory pain	**Cefiderocol** Multidrug-resistant Gram-negative bacterial infections	**Mulpleta® (US)** Thrombocytopenia
Bacterial infection	**S-117957** Insomnia	**S-707106** Type2 diabetes		**Mulpleta® (EU)** Thrombocytopenia
Antibody drug candidate against pseudomonas	**S-237648** Obesity	**S-488210** Head and neck squamous cell carcinoma		
Fungus infection		**epertinib** Malignant tumor		
Fungus infection		**S-588410** Bladder cancer		
Peptide	**In Japan**	**Cefiderocol** Multidrug-resistant Gram-negative bacterial infections	**Cefiderocol** Multidrug-resistant Gram-negative bacterial infections	**Oxycodone** Moderate to severe chronic pain
Vaccine for prevention	**S-637880** Neuropathic pain	**S-237648** Obesity	**Intuniv®** ADHD (adult)	**Lisdexamfetamine** ADHD (pediatric)
ADHD	**S-600918** Neuropathic pain Refractory chronic cough	**S-525606** Allergic rhinitis caused by Japanese cedar allergen	**Cymbalta®** Depression (pediatric)	
Opioid	**S-010887** Neuropathic pain	**S-588410** Bladder cancer	**S-588410** Esophageal cancer	
Peptide	**S-770108** Idiopathic pulmonary fibrosis		**Xofluza™** Influenza virus infection (oral, granule)	
Alzheimer's disease	**S-005151** Acute ischemic stroke			
Diabetes				
Obesity				
Hypertrophic scars				
Cancer metastasis				
Adjuvant				
Peptide				

Red frame:
High-priority projects in FY2018

- Infectious diseases
- Pain/CNS
- Metabolic disorder
- Frontier

Pipeline (as of Mar. 2018)

Preclinical	Phase I	Phase II	Phase III	Filed
Out-licensed	**GSK3342830** Multidrug-resistant Gram-negative bacterial infections		**DTG+3TC** Treatment for HIV infection **CAB LAP** Prevention for HIV infection **CAB+RPV LAP** Treatment for HIV infection **Janssen/Shionogi BACE inhibitor** Alzheimer's disease **Osphena®** Vaginal dryness associated with postmenopausal VVA	• **Infectious diseases** • **Pain/CNS** • **Metabolic disorder** • **Frontier**

Q&A

Forward-Looking Statements

- Forecast or target figures in this material are neither official forecasts of earnings and dividends nor guarantee of target, achievement and forecasts, but present the midterm strategies, goals and visions. Official earnings guidance should be referred to in the disclosure of the annual financial report (*kessan tanshin*) in accordance with the rules set by Tokyo Stock Exchange.
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