Science-based Initiatives of PMDA

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Today's Presentation

1. Introduction: Products from Japan
2. Current Status of Pharmaceutical Affairs Consultation on R&D Strategy
3. Updates of Science Board
4. Advanced Review/Consultation System

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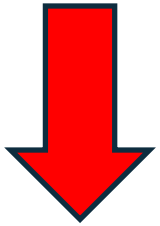
EML4-ALK fusion oncogene

Professor Hiroyuki Mano (Jichi Medical University, Japan) discovered EML4-ALK fusion oncogene in non-small-cell-lung cancer in 2007.

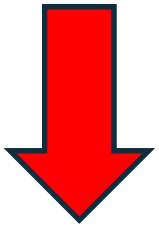
(Nature 2007; 448:561-6)



Crizotinib
Alectinib

PD-1 (programmed cell death 1)

Professor Tasuku Honjo (Kyoto University, Japan) identified PD-1 in 1992(EMBO J. 1992 Nov;11(11):3887-95.).



Anti PD-1 Antibodies

CCR4: Molecular target of Adult T-cell leukemia (ATL)

Professor Ryuzo Ueda (Nagoya City University, Japan) discovered CCR4 as the pathogenic factor of ATL (Clinical Cancer Res 2003; Sep 1; 9(10 Pt 1):3625-34)

Mogamulizumab : Anti CCR4 mAb

(POTELIGEO® Injection, Kyowa-Kirin Co., Ltd .)

Approved in JAPAN; March 2012 for ATL
(First marketing authorization)

POTELIGEO® (Mogamulizumab) is a humanized monoclonal antibody targeting CCR4 developed by Kyowa-kirin Co., Ltd . It is considered to bind with CCR4, suppressing tumor growth by antibody-dependent cellular cytotoxicity (ADCC).

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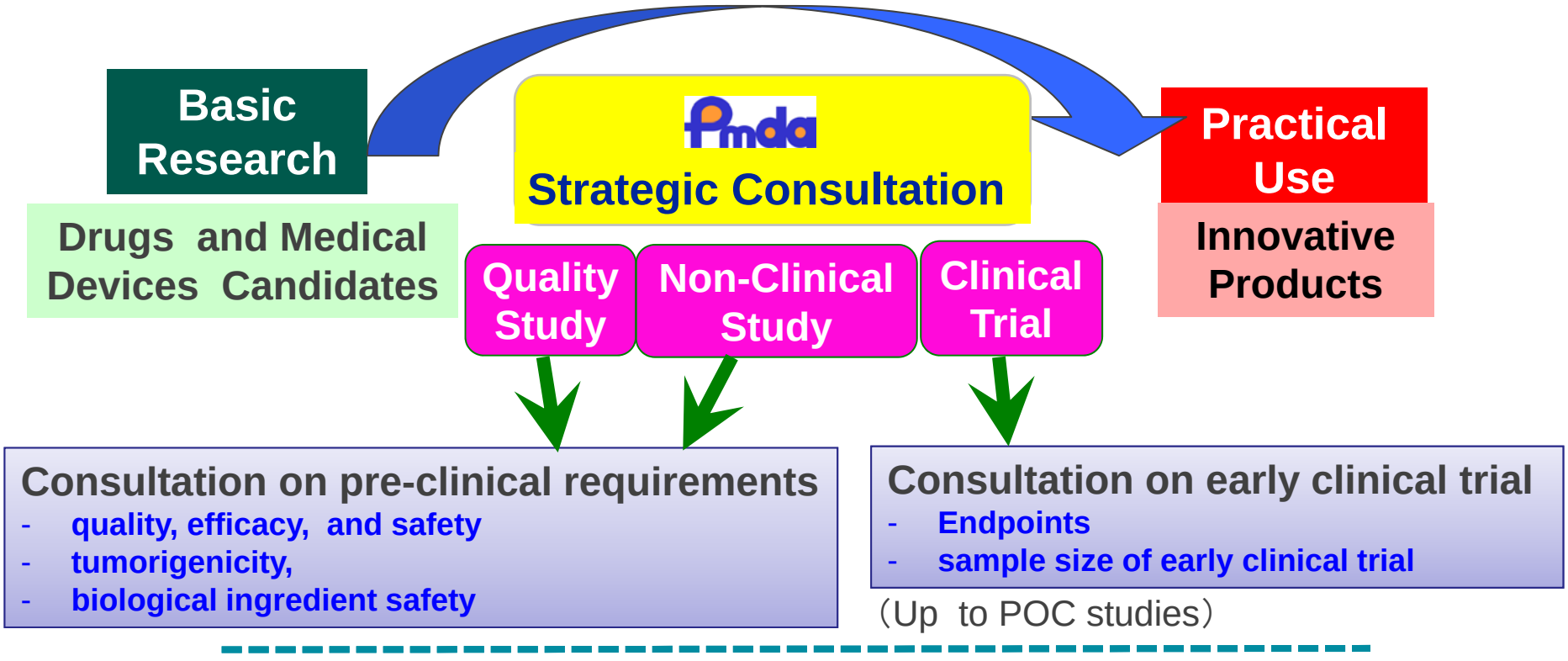
Pharmaceutical Affairs Consultation on R&D Strategy

Valley of Death between Basic research & Practical Use

- Shortage of funds, Knowledge on Regulation and developmental strategy



Flow of Strategy Consultation

Introductory Consultation (775) → Pre-Consultation (937) → Face-to-Face Consultation (236)

(7/1/2011 – 10/31/2014)

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Case of Face to Face consultation

Consulter	Product under development	Intended performance, Intended use, Indications
National Institute of Neuroscience, NCNP Department of Molecular Therapy **Shin'ich Takeda**	Morpholino oligos (Antisense)	Remedy for Duchenne muscular dystrophy (DMD)
Molecular Medicine and Therapy, Medicine (ART), Tohoku University School of Medicine, **Toshio Miyata**	PAI-1 Inhibitor (TM5509)	Hematogenic recovery of cord blood transplantation
Center for iPS Cell Research and Application (CiRA), Kyoto University, **Shinya Yamanaka**	iPS Cell (Allo)	Starting Materials for cellular & tissue based products derived from iPS Cells
Sapporo Medical University, **Osamu Honmou**	Mesenchymal Stem Cell (Auto)	Improvement of neurological sign, activities of daily living disorders in daily activities, and dysfunction associated with Stroke
CYBERDYNE INC.	ROBOT SUIT HAL (Hybrid Assistive Limb®) and partial Equipment for the subset of function of HAL used for movement training	Devices for assistive movement with in patients. Planed to introduce models which differ in intended use or indications.

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PMDA To Be More Science-Based

Basic Research

Seeds of new drug / medical devices

Quality Tests → Non-clinical tests → Clinical Trial → Review → Approve → Post Marketing

Practical use

Innovative medical products

Pharmaceutical consultation on R&D Strategy | Clinical Trial Consultation | Review | Post Marketing Safety Measure

Offices of Review (Drugs & Medical Devices), Office of Safety

Office of Review Innovation

Establishment of the Science Board

The Science Board was established in May 2012 to discuss how PMDA can better cope with products with advanced science & technology, in each developmental stage such as basic research, development support, product review, and post market safety measures.

Board members

Academia

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Working policy of discussion in Subcommittees (1st Stage: Jul. 2012-Mar. 2014)

Pharmaceuticals　Bio-based Products

Recommendation for the review policy of the pharmaceuticals regarding personalized medicine and discussion of needed items in order of priority.

Cellular & Tissue-based Products

How to ensure the safety of cellular and tissue-based products and aiming at revealing the predictable risks in the products as possible.

Medical Devices

Starting from discussion about the common issues as many kind of medical devices as possible because of big differences among product attributes of the medical devices.

Outcomes of the Science Board
(1st Stage: Jul. 2012-Mar. 2014)

Cellular & Tissue-based Products

- Current Perspective on Evaluation of Tumorigenicity of Cellular and Tissue-based Products Derived from iPSCs and iPSCs as Their Starting Materials (Aug. 21, 2013)

Pharmaceuticals, Bio-based Products

- Summary of Discussion on Non-clinical Pharmacology Studies of Anticancer Drugs (Dec. 10, 2013)

- Summary of the discussion on assessment of the current status of personalized medicine related to development and review (Mar. 11, 2014)

Outcomes of the Science Board (1st Stage)

平成25年8月20日

iPS 細胞等を

1. はじめに

独立行政法人医

（以下、本専門部

懸念事項である「

細胞組織加工

し、現時点で認識

れるべきである。

中であり、現時点

分析と対応を提

必要があることを

「造腫瘍性(tum

Japane

Provisional Translation (as of September 30, 2013)†

August 20, 2013

Current Perspective on Evaluation of Tumorigenicity of Cellular and Tissue-based Products Derived from induced Pluripotent Stem Cells (iPSCs)* and iPSCs as Their Starting Materials

Tatsutoshi Nakahata, Chair, Cellular and Tissue-based Products Subcommittee
Hideyuki Okano, Vice-chair, Cellular and Tissue-based Products Subcommittee

1. Introduction

The Cellular and Tissue-based Products Subcommittee (hereinafter, the subcommittee) of the Science Board to Pharmaceuticals and Medical Devices Agency (PMDA) has held multiple discussions from the scientific point of view on "tumorigenicity" that is the major safety concern of induced pluripotent stem cells (iPSCs)* for cellular and tissue-based products, and come to conclusion at present of

English（Provisional Translation）

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Subcommittees on 2nd Stage (Apr 2014- Mar 2016) and Their Activities (till Feb 2014)

Drug Area

1. Subcommittee on Placebo-controlled Trials (held twice)
2. Subcommittee on Non-clinical Studies (held 3 times)

Medical Device Area

3. Subcommittee on Application of Numerical Analysis to Non-clinical Evaluation (held 3 times)
4. Subcommittee on Evaluation of Medical Devices for Pediatric Use (held twice)

Cellular & Tissue-based Products Area

5. Subcommittee on Cell Processing Center (held 4 times)

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Advanced Review/Consultation System

Analysis by PMDA

Giving additional scientific value to submitted data

Cooperation with Academia

Regulatory Science

Practical use of Innovative Medical Products

A rational & effective evaluation process for regulatory decision

NDA etc.

e-Submission of study data

Data Accumulation

Database

Sophisticated NDA review

- Each reviewer utilizes innovative assessment techniques

Cross-Products Analysis

- Innovative evaluation methods
- Active utilization of Modeling & Simulation
  - Disease model
  - Objective B/R assessment
  - Identifying AE-related factors etc.

Sophisticated Consultation

- More evidence-based consultation

Effective and High Quality Review

- More predictable efficacy/safety after approval
- Reduction of applicant's work load
- More scientific regulatory decision

Effective and Successful Development

- Epoch-making proposal leading the world
- Proactive publication of guideline

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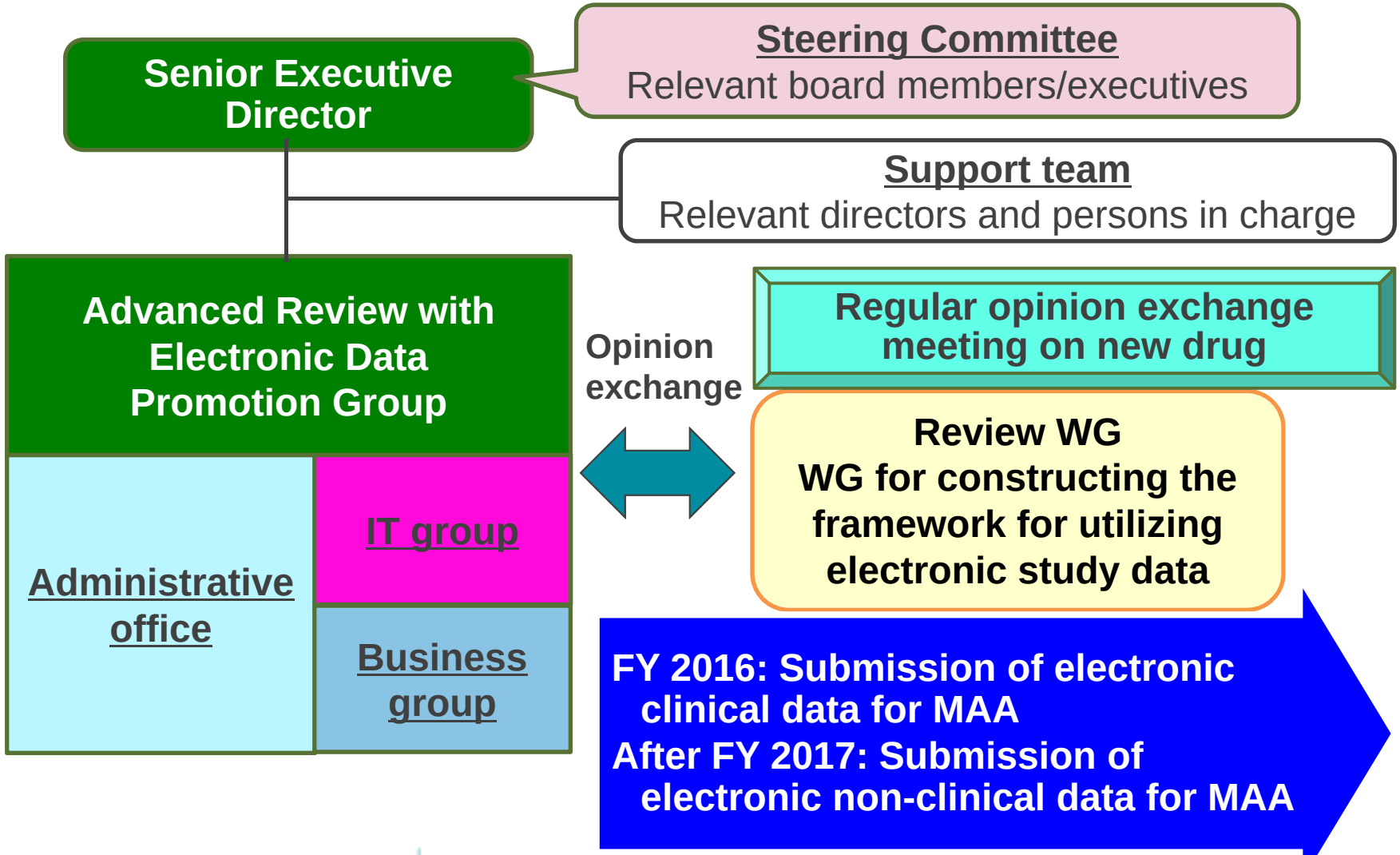
Utilization of study data and expected outcomes

Subject	Outcome
Prediction of drug interaction using a model	•Increase of study success rate •Avoidance of unnecessary studies •Confirmation of model •Appropriateness in the review process •Decrease of regulatory inquiries
Development of a dose-response model and prediction of optimal dose	
Development of a new evaluation indicator for disorders with no appropriate indicator	
Identification of factors affecting efficacy or safety	
Evaluation of class effect in rare adverse events	•Enhanced safety prediction, etc.
Prediction of QT prolongation based on simulated blood concentration-QT relationship	

Others: Evaluation of clinical data from Japanese subjects, comparison with those from non-Japanese subjects, etc.

Task Force for Advanced Review / Consultation

Established on Sep.1st, 2013



Summary

- *Pharmaceutical Affairs Consultation on R&D Strategy* is offering consultation for innovative products developed by academia/venture businesses.
- *Science board* was established for review/consultation in PMDA to become more science based.
- PMDA is going to develop a *next generation reviewing system* by accumulating electronic data.

Thank You for attention!

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Pharmaceuticals and Medical Devices Agency (PMDA)

http://www.pmda.go.jp/

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