PMDA’s Efforts in Medicinal Area

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Today’s Presentation

1. Introduction: Products from Japan

2. Current Status of Pharmaceutical Affairs Consultation on R&D Strategy

3. Establishment of the Science Board
Innovative Medicinal seeds from Academia in Japan
ACTEMRA® Injection (Tocilizumab (r-INN))

- Target Identification / Target Validation
Professor Tadamitsu Kishimoto (Osaka University, Japan) discovered IL-6 as the pathogenic factor of Castleman’s disease (Blood 1989; 74:1360-1367)

- Extensive research & Development
ACTEMRA® (Tocilizumab) is a humanized monoclonal antibody targeting the IL-6 receptor, developed by Osaka University and Chugai Pharmaceutical Co., Ltd. Approved in JAPAN; April 2005 (First marketing authorization)

Innovative Medicinal seeds from Academia in Japan
XALKORI® capsules (Crizotinib(INN))

- Target Identification / Target Validation
Professor Hiroyuki Mano (Jichi Medical University, Japan) discovered EML4-ALK fusion oncogene in non-small-cell-lung cancer (Nature 2007; 448:561-6 etc.,)

- Extensive research & Development
XALKORI ® (Crizotinib) is the ATP competitive inhibitor of tyrosine kinase of the Hepatocyte growth factor receptor developed by Pfizer Inc. Approved in JAPAN; May 2012 (International Birth Date: Aug. 2011)
Innovative Medicinal seeds from Academia in Japan

1950
University of Tokyo

OLYMPUS GASTROCAMERA GT-I
Copyright: The Japan Society of Mechanical Engineers.

201X
University of Tsukuba
"HAL" (Hybrid Assistive Limb®)

Copyright: CYBERDYNE INC

TOKYO SKY TREE
Completion: February 2012
Height: 634m
Today’s Presentation

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Pharmaceutical Affairs Consultation on R&D Strategy

Valley of Death
- Shortage of funds, Knowledge on Regulation and developmental strategy

- Basic Research
  - Pharmaceutical and Medical Devices candidates

- Strategic Consultation
  - Quality Study
  - Non-Clinical Study
  - Clinical Trial (Up to the level of POC studies)
  - Consultation on quality or toxicity study of biologics, cellular and tissue-based products
  - Consultation on endpoints or sample size of early clinical trial

- Practical Use
  - Innovative Products

* Further studies are handled by the Regular Consultation
Flow of R&D Strategy Consultation

**Introductory Consultation**
- Explain procedure
- No Charge

**Pre-Consultation**
- Sort out issues
- No Charge
- Not binding

**Face-to-Face Consultation**
- Scientific discussion
- 2 hours
- Charged
- Binding
- Minutes

- **420 Consultations**

Case of Face to Face consultation

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

- Achieved our targets
- What are the strategies and approaches PMDA could use to integrate the ever advancing technologies?

Issues of PMDA

① Conducting review and consultation understanding of the research activities in state-of-the-art technologies,

② Conducting review and consultation in the state of the art technologies from early stage of development,

③ Training reviewers to catch up on the accelerating innovative technologies and contributing in the establishment of practical use of state of the art technologies.

Science Board
For PMDA To Be More Science-Based

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.

Office of Review Innovation

Science Board and Office of Review Innovation
- Committee members: External experts from Academia
- Declare Conflicts of Interest
- Not involved in the Review Process of individual products

Mission
Reform PMDA review system and related services based on science with consideration of actual medical practices
Main Roles of Science Board

• Pick out Issue

• Coach for Issue

On the subject of advanced scientific technology, profound researchers and the PMDA reviewers deliberate assessment tools in order to provide review and consultation services appropriately.

- Pick out Issue -

Picking out Science & Technology which could be potentially applied to innovative products (Drug/Medical Device) in the near future among the Cutting-edge of Exploratory Research,

On the advanced scientific & technology, Requesting the subcommittee to discuss further for providing review and consultation services appropriately in PMDA.
Main Roles of Science Board
- Coach for Issue -

Committee
- Discussion on the proposed subjects
- Requesting adequate subcommittee to discuss further for the issues.

Subcommittee
- Profound researchers and the PMDA reviewers deliberate the referred issues from the Science Committee.

Review Offices
- Problem consciousesses in PMDA
- Anxious to exchange views on subjects with the Science Committee.

Exchange
Opinions

Propose

Request

Past Activities

Committee

Subcommittees

Pharmaceuticals

Bio-based Products

Cellular & tissue-Based products

Medical Devices

DIA 2013
49th Annual Meeting

DIA 2013
49th Annual Meeting
Outcome of Science Board

• A report on a summary of discussion by the subcommittee for each subject

• An annual report

Schedule of Science Board (Committee)

Aug 20, 2013 • Report from Subcommittee

The end of 2013 • Report from Subcommittee

Around Mar 2014 • Report from Subcommittee
• Annual report
Possible issue on each Subcommittee

**Pharmaceuticals & Bio-products**
- Non-clinical pharmacology studies of anticancer drugs
- Personalized medicine
  - Biomarkers

**Cellular & Tissue-based products**
- The subject on securing quality and safety of cellular and tissue-based products.
  - Tumorigenicity
  - Requirements of Cell Processing Center (CPC)

**Medical Devices**
- Challenges to develop registry
- Scope of the follow-on medical devices
- View on developing combination products

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.
Thank you for your attention!

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