JPMA’s Endeavors to Expedited Access of Innovative Medicines to Patients

Yoshihiko Hatanaka
President
Japan Pharmaceutical Manufacturers Association
Disclaimer

This presentation is made on behalf of the Japan Pharmaceutical Manufacturers Association (JPMA). Unless expressly stated otherwise by the speaker, information presented in the slides as well as positions taken and opinions expressed during this presentation are those of JPMA, not of the speaker in an individual capacity or any specific member company, including the one with which the speaker is affiliated.
Contents

1. JPMA
2. Drug-development in Japan
3. Changing Regulatory Landscape
4. Regulatory Convergence
5. MHLW/PMDA-JPMA Partnership Initiatives
6. Conclusion
1. **JPMA** (Japan Pharmaceutical Manufactures Association)

2. Drug-development in Japan

3. Changing Regulatory Landscape

4. Regulatory Convergence

5. MHLW/PMDA-JPMA Partnership Initiatives

6. Conclusion
Established in 1968
72 R&D Oriented Companies
As of January 1, 2017

President

Vice Presidents

General Assembly

Auditors

Board of Directors (Standing B/D)

Council on Planning & Policy

Code Compliance Committee (167)
Review Board of Ethical Drug Product Information Brochure
Japan Pharmaceutical Industry Legal Affairs Association
Pharmaceutical Industrial Policy Committee (81)
Distribution Improvement Committee (130)
Drug Evaluation Committee (919)
ICH Project (65)
Quality & Technology Committee (117)
Biopharmaceutical Committee (73)
Regulatory Affairs Committee (132)
Intellectual Property Committee (35)
R&D Committee (71)
International Affairs Committee (152)
Environmental & Safety Committee (116)
Public Affairs Committee (72)
Patient Cooperation Committee (23)
Consumer Consultation Review Committee (70)
Office of Pharmaceutical Industry Research (OPIR) (34)

Figures: number of committee member
JPMA’s Industry Vision 2025
Bringing Innovation in Drug Discovery to the World

Driving next-generation Medicine with advanced drug discovery
~Contribution to P4+1 medicine~

Supporting to create An advanced healthcare country
~Creating a society where people can live long, healthy lives with peace of mind~

Providing innovative drugs to 8 billion people worldwide

Leading the Japanese economy forward as a high value-added industry

Becoming a trustworthy industry with noble aspiration
Patient Centric Drug Development

Pharmaceutical Companies

Optimized medical care of each patient by utilizing patients’ medical information (Precision Medicine)

Resolution of “unapproved drugs and off-label drugs” issues

Patients

Access opportunity to investigational medicines for patients who were unable to join clinical trials (Compassionate Use)
Contents

1. JPMA
2. Drug-development in Japan
3. Changing Regulatory Landscape
4. Regulatory Convergence
5. MHLW/PMDA-JPMA Partnership Initiatives
6. Conclusion
Japan Stands Second in the World for New Drug Discovery

Countries of origin of top 100 sales of pharmaceutical products for medical use (2015)

- America: 48
- Japan: 13
- Switzerland: 11
- France: 3
- Denmark: 4
- Germany: 6
- Britain: 7
- Belgium: 2
- Sweden: 2
- Italy: 2
- Israel: 1
- Luxembourg: 1

Note: Classified based on the national origin of firms which hold patents. Tallied by countries of origin of top 100 sales of pharmaceutical products in 2016. Copyright©2017 QuintilesIMS. World Review, LifeCycle, ARK, Citeline, Evaluate Pharma, Orange Book (Reprinted with permission).

## Innovative Drugs Developed in Japan

<table>
<thead>
<tr>
<th>Related Technologies</th>
<th>Product</th>
<th>Usage</th>
<th>Inventor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medicinal Chemistry</td>
<td>ARICEPT® (donepezil)</td>
<td>Dementia (Alzheimer-type)</td>
<td>Eisai Pharmaceuticals</td>
</tr>
<tr>
<td>Immunology</td>
<td>ACTEMRA® (Tocilizumab)</td>
<td>Immuno-modulator (RA etc)</td>
<td>Osaka Univ. Chugai Pharmaceutical</td>
</tr>
<tr>
<td>Cancer immunology</td>
<td>OPDIVO® (nivolumab)</td>
<td>Cancer immunotherapy</td>
<td>Kyoto Univ. Ono Pharmaceuticals</td>
</tr>
</tbody>
</table>

### Drugs in Development which Received “Sakigake” Designation

<table>
<thead>
<tr>
<th>Category</th>
<th>Product Components</th>
<th>Potential Indications</th>
<th>Inventor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regenerative</td>
<td>Bone marrow mesenchymal stem cell</td>
<td>Spinal cord injury</td>
<td>Sapporo Medical Univ., Nipro</td>
</tr>
<tr>
<td>Regenerative</td>
<td>Gene-recombination herpes simplex virus</td>
<td>Malignant brain tumor</td>
<td>Tokyo Univ. Daiichi-Sankyo</td>
</tr>
<tr>
<td>Device</td>
<td>Titanium metal bridge</td>
<td>Thyroplasty (spastic dysphonia)</td>
<td>Kyoto Univ. Novel Pharma</td>
</tr>
</tbody>
</table>

* 22 products have designated as “Sakigake” or the Japanese expedited approval system
New Drugs have Significantly improved Satisfaction with treatment
Continued efforts to develop innovative drugs is required to meet unmet medical needs

Correlation chart between satisfaction with treatment and drug contributions

Source: Japan Health Sciences Foundation, 2014, Research report on basic domestic technologies (Research on medical needs for 60 disorders and new medical needs)
Development Period in Japan Has Hit a Plateau

Changes in domestic clinical development period (months)

Note: Dotted-line indicates median value, 45.6 months.
**Success Rate of Drug Development**

Key Factors to determine success probability of drug development

1. Appropriateness of drug discovery seeds
2. Clinical trial assessable clinical effects/safety

**Phase shift rate by starting year of clinical trial**

- NDA → Approval
- Phase III → NDA
- Phase I → II
- Phase II → III

※ Prepared based on database of pharma-projects
Values are moving averages over three years. However, the values for 1990 are the average of two years, 1990 and 1991, and the values for 2009 are the average of two years, 2008 and 2009.
New Challenges in Current Clinical Trials

Controlled clinical trials are not always suitable for diseases where:

- **Numbers of patients are too few**
  - Rare disorders
  - Precision medicine: Narrowed downed patient number by pathogenesis study

- **Proving reduction of “serious but less frequent” events is required**

- **Lifelong assessment of prognosis is required**

- **Significant physical burdens on subjects is required to assess treatment effect**
Contents

1. JPMA
2. Drug-development in Japan
3. Changing Regulatory Landscape
4. Regulatory Convergence
5. MHLW/PMDA-JPMA Partnership Initiatives
6. Conclusion
But based on the advances that have been made in **personalized medicine and health information technology**, including the use of real world data, **is the randomized, double-blinded, placebo-controlled model the best approach in all cases?**

PMDA “Rational Medicine” Initiative

February 2017
Tatsuya Kondo M.D., Ph.D.
Chief Executive, PMDA

(1) Suitable methodologies for clinical assessment of rare diseases

In order to support future clinical development activities in such rare disease areas, the Board will review the current status of clinical assessments and clarify possible methods of assessment.
Approved Number of New Drugs Shows Upward Trends

Changes in the number of approved NASs (New Active Substance)

<table>
<thead>
<tr>
<th>Year</th>
<th>EMA</th>
<th>FDA</th>
<th>PDMA</th>
</tr>
</thead>
<tbody>
<tr>
<td>2007</td>
<td>28</td>
<td>60</td>
<td>32</td>
</tr>
<tr>
<td>2008</td>
<td>22</td>
<td>48</td>
<td>28</td>
</tr>
<tr>
<td>2009</td>
<td>20</td>
<td>40</td>
<td>22</td>
</tr>
<tr>
<td>2010</td>
<td>18</td>
<td>30</td>
<td>20</td>
</tr>
<tr>
<td>2011</td>
<td>16</td>
<td>28</td>
<td>18</td>
</tr>
<tr>
<td>2012</td>
<td>14</td>
<td>22</td>
<td>16</td>
</tr>
<tr>
<td>2013</td>
<td>12</td>
<td>20</td>
<td>14</td>
</tr>
<tr>
<td>2014</td>
<td>10</td>
<td>18</td>
<td>12</td>
</tr>
<tr>
<td>2015</td>
<td>8</td>
<td>16</td>
<td>10</td>
</tr>
<tr>
<td>2016</td>
<td>6</td>
<td>14</td>
<td>8</td>
</tr>
</tbody>
</table>

Expedite Access to Innovative Medicine

- Breakthrough Therapy Designation (2012~)
- PRIME (PRIority MEdicines) scheme (2016~)
- The “sakigake” designation scheme (2015~)
- Others: Designated orphan

Source: The Centre for Innovation in Regulatory Science (CIRS), New drug approvals in ICH countries 2007-2016, R&D Briefing 62, April 2017
Contents

1. JPMA
2. Drug-development in Japan
3. Changing Regulatory Landscape
4. Regulatory Convergence
5. MHLW/PMDA-JPMA Partnership Initiatives
6. Conclusion
Improve the Success Rate of Drug Development

Improve predictive rates for clinical effect/safety

- Biomarker Searching
- Companion Diagnostic
- Gene Panels

Develop New Clinical Trial Methods

- Adaptive Design
- Real-World Data
- Cohort-Type Clinical Trials

These New Clinical Trial Methods and Testing Means Need to be accepted globally to expedite launch of Innovative Drugs for Patients around the World
Regulatory Convergence for Early Access

Innovative Drugs are Common Properties of Humankind

Equal and Prompt Access Opportunity for Patients Worldwide

Assessment Based on the Same NDA Data Set

Review Processes  Required Data Items  Required Data Quality
Advance Regulatory Convergence

Structure of discussions on regulatory harmonization/convergence

- **Summit, ICMRA**
  - Exchanging opinions at top levels
  - Play a role in strategic coordination and leadership

- **ICH**
  - Develop guidelines concerning drug regulations from the view points of science and technology
  - Discuss rationalization and standardization of NDA review

- **Public-Private Partnership**
  - Conduct promoting activities of regulatory convergence
  - Aiming consistency among regulatory requisites in the implementing phase of guidelines
Contents

1. JPMA

2. Drug-development in Japan

3. Changing Regulatory Landscape

4. Regulatory Convergence

5. MHLW/PMEDA-JPMA Partnership Initiatives

6. Conclusion
Productive Dialogues between MHLW/PMDA and JPMA

1. Participating Discussions at ICH
   - Dispatching experts to the Expert Working Group

2. Supporting Biostatistician Training Programs
   - Installation of training classes in two universities
   - Utilizing matching fund among industries and government

3. Involving MHLW’s Assessment Method Development Projects for Pharmaceutical Products
   - Conducting shared research / Providing related data

MHLW: Ministry of Health, Labour and Welfare
JPMA and Asian Japanese Pharma Groups are Contributing to Regulatory Authorities for the Successful Bilateral Symposiums* in Asia and PMDA Asia Training Center’s Programs*

### Japanese Pharma Groups

- Chinese Taipei-Japan Symposium @Taipei
- India-Japan Symposium @Tokyo
- Indonesia-Japan Symposium @Jakarta
- Japan delegation visit China @Beijing
- Korea-Japan Symposium @Seoul
- Malaysia-Japan Symposium @KL
- Thailand-Japan Symposium @Bangkok

### Bilateral Meetings

- Instructor assignment to Workshops
- GMP training at JPMA member company’s plant

* Regulatory Authorities’ Initiatives
APAC is an Industry-Driven Initiative Led by R&D-Based Pharmaceutical Associations in Asia

- Established by 12 R&D based pharmaceutical associations in Asia in 2012
- PhIRDA (China) is accepted as 13th APAC member association in Sep. 2017
- 7th APAC 2018 is scheduled on April 10th in Tokyo
APAC’ Mission
To Expedite the Launch of Innovative Medicines for the Peoples in Asia

330 participants from 11 Asian economies gathered at 6th APAC held on April, 5th, 2017 in Tokyo

Source: http://apac-asia.com/
Asian Regulatory Authorities will Further Enhance Mutual Understanding and Partnership during APAC Week

Schedule of 7th APAC and related meetings in 2018

April 9th

MHLW/PMDA-Asian Regulatory Authority Bilateral Meeting

April 10th

7th APAC
Keidanren-Kaikan, Tokyo

- Opening Remarks
- Keynote Lecture
  Dr. Tatsuya Kondo,
  Chief Executive, PMDA
- Photo Taking
- ATIM Session
- DA-Session
- RA-Session
- Closing Remarks
- Reception Party

April 11th

APAC Convention Press Conference
MHLW/PMDA-Asian Regulatory Authority Bilateral Meeting
Contents

1. JPMA
2. Drug-development in Japan
3. Changing Regulatory Landscape
4. Regulatory Convergence
5. MHLW/PMDA-JPMA Partnership Initiatives
6. Conclusion
Conclusion

◆ We are committed to contributing to:
  
  • the improvement of global medical care through new drug discovery
  
  • public-private partnership initiatives to expedite the launch of innovative medicines to the patients around the world

◆ We are anticipating regulatory authorities’ leadership towards global regulatory convergence in the course of drug development.

◆ JPMA and the regulatory authorities share the ultimate goal. Let’s continue to work together for the patients.
Bringing Innovation in Drug Discovery to the World