Dramatic Changes in the Environment for New Drug Creation and Challenges Facing Japan’s Pharmaceutical Industry

Chugai Pharmaceutical Co., Ltd.
Chairman & CEO
Osamu Nagayama

October 30, 2017
Forward-Looking Statements

This presentation may include forward-looking statements pertaining to the business and prospects of Chugai Pharmaceutical Co., Ltd. (the “Company”). These statements reflect the Company’s current analysis of existing information and trends. Actual results may differ from expectations based on risks and uncertainties that may affect the Company’s businesses.
Agenda

1. Dramatic changes in the environment for drug discovery research for creating innovation

2. Changing pharmaceutical market

3. Challenges facing Japan’s Pharmaceutical Industry and the direction of solutions toward the continuous creation of innovation
Agenda

1. Dramatic changes in the environment for drug discovery research for creating innovation

2. Changing pharmaceutical market

3. Challenges facing Japan’s Pharmaceutical Industry and the direction of solutions toward the continuous creation of innovation
History of Pharmaceutical Innovations that Changed the World

- Scientific developments have resulted in innovative medicines

- **1900**
  - Penicillin
  - Naturally derived components and their derivatives
  - Focusing on **in vivo** receptors
  - Screening by organic synthesis
  - Application of genomics (Genetic modification, etc.)

- **1960**
  - First Antibiotic. Saved People from Infectious Diseases!
  - Pinpoint attacks on Cancers

- **1970**
  - H2 Blocker (Peptic Ulcer)
  - Antihypertensive Drugs
  - Focusing on **in vivo** receptors

- **1980**
  - Human Insulin, Interferon
  - Appearance of Biopharmaceuticals
  - Lipid-Lowering Drugs
  - Antihypertensive Drugs

- **1990**
  - Discovered in Japan
  - Antibody Drugs and Molecular Targeting Drugs
  - Focusing on **in vivo** enzymes

- **2000**
  - Antihypertensive Drugs
  - Application of post-genome technology
The World has been Transformed Since the Decoding of the Human Genome Sequence

Human genome sequence was decoded and published in Nature (15 Feb, 2001) and Science (16 Feb, 2001)

Human Genome Information Database (Link to various genome related information)
NIH/NCBI (National Center for Biotechnology Information)

Drug Discovery Approach has Changed Dramatically with Genome Drug Discovery Era since 2000

- **Genome Drug Discovery Era**
  - Small Molecule Drugs
  - Middle Molecule Drugs
  - Molecular Targeted Drugs
  - Biological Drugs
  - Antibody Drugs
  - Cell Therapy
  - Gene Therapy

- **Biotechnology**
  - Organic Synthetic Chemistry
  - Antibody Drugs

- **Genome Analysis**
Clarification of Disease Mechanisms and the Advancement of Emerging Drug Discovery Technologies are Creating Innovative New Drugs

- Various technologies and multiple discovery approaches require high costs

**Progress of clarifying the disease mechanism**
- Gene analysis
- Gene expression analysis
- Protein expression analysis
- Disease state information
- Clinical trial & Treatment information
- Discovery of disease-causing (Target) molecules
- Fast omix analysis
- Next generation sequencer
- Application of ICT medical information and Big data

**Sophistication of pharmaceutical & medical technology**
- **Biopharmaceutical**
  - Antibody technology, High-functionalization, Evolution of manufacturing tech.
- **Small molecule drug**
  - Large scale screening
  - Computing drug discovery
- **Regenerative medicine etc**
  - New technology
  - (iPS cell, Somatic stem cell)
- **diag. & Medical device**
  - Biomarker, Personalized medicine

**Advantages**
- Improvement of treatment outcomes
- Responding to unmet medical need
- Accumulation of intellectual property
- Growth of related industries
- Invigorate investment
- Advance the quality of medical care
- Growth of pharmaceutical industry
- Increase the national competitiveness

WIN-WIN situation
Drug Development Takes a Long Time and the Process is Based on Advanced Regulatory Science

- **Phase-1**: Healthy volunteers
- **Phase-2**: Patients (pilot)
- **Phase-3**: Patients

### Chemical library
(Hundreds of thousands to millions)

- Lead compounds
- Newly synthesized compounds
(Hundreds to thousands)

- Clinical candidate
(Finally one)

### Search of target molecules
Clarification of disease mechanisms

#### Discovery
- High throughput screening
  - Structural optimization
  - Candidate compounds selection

#### Pre-Clinical
- Pharmacological study
- ADME study
- Safety study

#### Clinical
- Phase-1: Healthy volunteers
- Phase-2: Patients (pilot)
- Phase-3: Patients

### New Drug application

- Approval and sales

### Products

- Newly synthesized compounds
(Hundreds to thousands)

- Lead compounds

- Clinical candidate
(Finally one)

**Over 10 years**

**5 - 8 Years**

**3 - 7 Years**

**1 - 2 Years**

**4 - 10 Years**

**1,000**

**10,000**

**25,000**

**GLP**: Good Laboratory Practice

**GCP**: Good Clinical Practice

**GMP**: Good Manufacturing Practice

**GPSP**: Good Post-marketing Study Practice

Management and review

Pharmaceutical and Medical Devices Agency (PMDA)

Re-examination period of new drugs is usually 8 years
(Need safety report every 0.5-1 year)

Re-examination of effectiveness etc. at the cutting-edge level of medical and pharmaceutical science

Source: JPMA DATA BOOK 2016, PhRMA Profile 2013

Drug Development Takes a Long Time and the Process is Based on Advanced Regulatory Science

GLP: Good Laboratory Practice

GCP: Good Clinical Practice

GMP: Good Manufacturing Practice

GPSP: Good Post-marketing Study Practice
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Seven Out of the World’s Top 10 Products are Biopharmaceuticals Now

**World Drug Sales Ranking**

### 2005

<table>
<thead>
<tr>
<th>Rank 2005</th>
<th>Product Name</th>
<th>Company</th>
<th>Disease for treatment</th>
<th>Sales ($M)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Lipitor</td>
<td>Pfizer/Yamanouchi</td>
<td>hyperlipidemia</td>
<td>12,963</td>
</tr>
<tr>
<td>2</td>
<td>Plavix</td>
<td>Sanofi/BMS</td>
<td>Anti-platelet</td>
<td>6,223</td>
</tr>
<tr>
<td>3</td>
<td>Epogen/Procrit/Espo</td>
<td>Amgen/J&amp;J/Kirin/Sankyo</td>
<td>renal anemia</td>
<td>6,145</td>
</tr>
<tr>
<td>4</td>
<td>Norvasc</td>
<td>Pfizer/Sumitomo</td>
<td>hypertension</td>
<td>5,245</td>
</tr>
<tr>
<td>5</td>
<td>Seretide/Advair</td>
<td>GSK</td>
<td>asthma</td>
<td>5,168</td>
</tr>
<tr>
<td>6</td>
<td>Nexium</td>
<td>AstraZeneca</td>
<td>ulcer</td>
<td>4,633</td>
</tr>
<tr>
<td>7</td>
<td>Takepron/Prevacid</td>
<td>Takeda/TAP/Abbott/Wyeth</td>
<td>ulcer</td>
<td>4,394</td>
</tr>
<tr>
<td>8</td>
<td>Zocor</td>
<td>Merck</td>
<td>hyperlipidemia</td>
<td>4,328</td>
</tr>
<tr>
<td>9</td>
<td>Zyprexa</td>
<td>Eli Lilly</td>
<td>schizophrenia</td>
<td>4,202</td>
</tr>
<tr>
<td>10</td>
<td>Mabthera/Rituxan</td>
<td>Roche/Chugai</td>
<td>cancer</td>
<td>3,867</td>
</tr>
</tbody>
</table>

### 2016

<table>
<thead>
<tr>
<th>Rank 2016</th>
<th>Product Name</th>
<th>Company</th>
<th>Disease for treatment</th>
<th>Sales ($M)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Humira ⭐</td>
<td>Abbvie/Eisai</td>
<td>rheumatoid arthritis</td>
<td>16,513</td>
</tr>
<tr>
<td>2</td>
<td>Enbrel ⭐</td>
<td>Amgen/Pfizer/Takeda</td>
<td>rheumatoid arthritis</td>
<td>9,245</td>
</tr>
<tr>
<td>3</td>
<td>Harvoni</td>
<td>Gilead Sciences</td>
<td>HCV</td>
<td>9,081</td>
</tr>
<tr>
<td>4</td>
<td>Remicade ⭐</td>
<td>J&amp;J/Merck/Tanabe M</td>
<td>rheumatoid arthritis</td>
<td>8,848</td>
</tr>
<tr>
<td>5</td>
<td>Mabthera/Rituxan</td>
<td>Roche/Chugai</td>
<td>cancer</td>
<td>8,719</td>
</tr>
<tr>
<td>6</td>
<td>Revlimid ⭐</td>
<td>Celgene</td>
<td>multiple myeloma</td>
<td>6,974</td>
</tr>
<tr>
<td>7</td>
<td>Avastin ⭐</td>
<td>Roche/Chugai</td>
<td>cancer</td>
<td>6,879</td>
</tr>
<tr>
<td>8</td>
<td>Herceptin ⭐</td>
<td>Roche/Chugai</td>
<td>cancer</td>
<td>6,878</td>
</tr>
<tr>
<td>9</td>
<td>Januvia/Glactiv</td>
<td>Merck/Ono/Almira II</td>
<td>diabetes/DPP4</td>
<td>6,431</td>
</tr>
<tr>
<td>10</td>
<td>Lantus ⭐</td>
<td>Sanofi</td>
<td>diabetes/insulin</td>
<td>6,317</td>
</tr>
</tbody>
</table>

⭐ Biologics
Global Growth of Biopharmaceuticals

Sales of biopharmaceuticals

<table>
<thead>
<tr>
<th>Year</th>
<th>Sales (billion USD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2004</td>
<td>332</td>
</tr>
<tr>
<td>2015</td>
<td>617</td>
</tr>
</tbody>
</table>

Sales increased by 3.3 times in 10 years

Sales ratio of biopharmaceuticals

<table>
<thead>
<tr>
<th>Year</th>
<th>Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>2004</td>
<td>14%</td>
</tr>
<tr>
<td>2015</td>
<td>30%</td>
</tr>
</tbody>
</table>

Biopharmaceutical sales ratio now reached 30%

Source: Evaluate Pharma as of July, 2016
Annual Drug Costs of Biological Drugs are not Always Expensive Compared with Chemical Synthetic Drugs

Annual Drug costs of major anticancer drugs approved by FDA

- Omacetaxine for CML
- Ibrutinib for MCL
- Crizotinib for NSCLC
- Pomalidomide for MM
- Regorafenib for CRC
- Sorafenib for TC
- Ponatinib for CML and Ph+ ALL
- Trametinib for melanoma
- Lenalidomide for MCL
- Cabozantinib for TC
- Ado-trastuzumab emtansine for BC
- Dabrafenib for melanoma
- Abiraterone for PC
- Erlotinib for NSCLC
- Radium 223 for PC
- Nab-paclitaxel for PC, NSCLC
- Afatinib for NSCLC
- Pertuzumab for BC
- Obinutuzumab for CLL
- Bevacizumab for CRC

JAMA Oncology, 1: 539-540 (2015)

Annual average drug cost $121,958
Annual average drug cost $81,285

*average wholesale prices from Redbook
Clinical Development Success Rates (NDA vs BLA)

Source: Clinical Development Success Rate 2006-2015, BIO (2016)
As Targets of Antibody Drugs are Finite, Competition is Intensifying due to Concentration of Development on the Same Antigens

- All mega pharma are focusing on antibody drugs due to the success and market expansion of these products
- More than 730 antibody drugs are currently in clinical development
- 324 antibodies for 34 promising target antigens are in development

Number of products

Source: Clarivate Analytics, Citeline, Springer (As of Jan., 2017)
Volume Share of Generic Drugs Increasing at a High Pace Towards the 80% Target in September 2020

Percentage of generic drugs in dispensed medical expenses (volume basis)

Source: Japan Generic Medicines Association HP
Domestic Market Share of Long-listed Products Shrinking due to Market Changes

<table>
<thead>
<tr>
<th></th>
<th>2012</th>
<th>2016</th>
</tr>
</thead>
<tbody>
<tr>
<td>Long-listed products</td>
<td>29.3%</td>
<td>21.9%</td>
</tr>
<tr>
<td>Standard brands products</td>
<td>26.7%</td>
<td>26.7%</td>
</tr>
<tr>
<td>Premium brands products</td>
<td>25.0%</td>
<td>30.0%</td>
</tr>
<tr>
<td>Generic products</td>
<td>7.2%</td>
<td>10.8%</td>
</tr>
<tr>
<td>Others (Kanpo, non-NHI listed products)</td>
<td>11.8%</td>
<td>10.7%</td>
</tr>
</tbody>
</table>

9.5 trillion yen (2012)
10.6 trillion yen (2016)

Copyright: (C)2017 QuintilesIMS, this figure was created based on Quintiles IMS JPM 2012, 2016 (Copy / Reprint prohibited)
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Challenges Facing Japan’s Pharmaceutical Industry and the Direction of Solutions toward the Continuous Creation of Innovation

- Investment in R&D Comparable to Global Companies
- Appropriate evaluation of Innovation
- Promotion of open Innovation
- Japan as International Arena for Drug Discovery and Development
Challenges Facing Japan’s Pharmaceutical Industry and the Direction of Solutions toward the Continuous Creation of Innovation

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R&D Expenditure of Global Pharmaceutical Companies Has Expanded 2.5 Times and More than 2.5 Billion Dollars Compared with Previous 10 Years

R&D Cost per approved new drugs
(mil USD)

Pre-human
1970s 1980s
109 278
x 2.52

Clinical
1990s-early 2000s 2000s-early 2010s
70 135
1,098
x 2.40

Total
1,460
1,044
x 2.45

Source: Journal of Health Economics, 47:20-33 (2016)
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There is a Big Difference between the Domestic Companies and the Global Leading Pharmaceutical Companies Investing Huge Costs in R&D

<table>
<thead>
<tr>
<th>Pharma Rx Sales Ranking</th>
<th>Company</th>
<th>Pharma Rx Sales</th>
<th>Pharma Rx Sales Growth rate</th>
<th>Total Sales</th>
<th>R&amp;D Expenditure</th>
<th>R&amp;D Expenditure % to Total Sales</th>
</tr>
</thead>
<tbody>
<tr>
<td>2016</td>
<td>2015</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>1  Pfizer</td>
<td>48,259</td>
<td>8.3%</td>
<td>52,824</td>
<td>7,872</td>
<td>14.9%</td>
</tr>
<tr>
<td>2</td>
<td>2  Novartis</td>
<td>42,706</td>
<td>-1.6%</td>
<td>48,518</td>
<td>8,523</td>
<td>17.6%</td>
</tr>
<tr>
<td>3</td>
<td>3  Roche</td>
<td>41,626</td>
<td>4.0%</td>
<td>51,289</td>
<td>10,299</td>
<td>20.1%</td>
</tr>
<tr>
<td>4</td>
<td>5  Merck</td>
<td>35,151</td>
<td>1.1%</td>
<td>39,807</td>
<td>7,194</td>
<td>18.1%</td>
</tr>
<tr>
<td>5</td>
<td>4  Sanofi</td>
<td>34,692</td>
<td>0.0%</td>
<td>37,392</td>
<td>5,718</td>
<td>15.3%</td>
</tr>
<tr>
<td>6</td>
<td>7  J&amp;J</td>
<td>33,464</td>
<td>6.5%</td>
<td>71,890</td>
<td>6,967</td>
<td>9.7%</td>
</tr>
<tr>
<td>7</td>
<td>6  Gilead</td>
<td>30,390</td>
<td>-6.9%</td>
<td>30,390</td>
<td>5,098</td>
<td>16.8%</td>
</tr>
<tr>
<td>8</td>
<td>8  GSK</td>
<td>28,629</td>
<td>16.2%</td>
<td>32,468</td>
<td>3,852</td>
<td>11.9%</td>
</tr>
<tr>
<td>9</td>
<td>10 AbbVie</td>
<td>25,638</td>
<td>12.2%</td>
<td>25,638</td>
<td>4,366</td>
<td>17.0%</td>
</tr>
<tr>
<td>10</td>
<td>9  AstraZeneca</td>
<td>23,002</td>
<td>-6.9%</td>
<td>23,002</td>
<td>5,890</td>
<td>25.6%</td>
</tr>
<tr>
<td>17</td>
<td>17 Takeda</td>
<td>14,415</td>
<td>-4.8%</td>
<td>15,915</td>
<td>2,869</td>
<td>18.0%</td>
</tr>
<tr>
<td>20</td>
<td>19 Astellas</td>
<td>12,052</td>
<td>-4.4%</td>
<td>12,052</td>
<td>1,912</td>
<td>15.9%</td>
</tr>
<tr>
<td>25</td>
<td>25 Daichi Sankyo</td>
<td>8,163</td>
<td>-4.8%</td>
<td>8,775</td>
<td>1,969</td>
<td>22.4%</td>
</tr>
<tr>
<td>26</td>
<td>24 Otsuka HD</td>
<td>6,919</td>
<td>-27.4%</td>
<td>10,984</td>
<td>1,551</td>
<td>14.1%</td>
</tr>
<tr>
<td>31</td>
<td>35 Eisai</td>
<td>4,696</td>
<td>-0.5%</td>
<td>4,953</td>
<td>1,310</td>
<td>26.4%</td>
</tr>
<tr>
<td>35</td>
<td>36 Chugai</td>
<td>4,519</td>
<td>-1.4%</td>
<td>4,519</td>
<td>781</td>
<td>17.3%</td>
</tr>
<tr>
<td>39</td>
<td>40 Mitsubishi Tanabe</td>
<td>3,864</td>
<td>-1.7%</td>
<td>3,895</td>
<td>594</td>
<td>15.3%</td>
</tr>
<tr>
<td>42</td>
<td>44 Sumitomo Dainippon</td>
<td>3,381</td>
<td>1.9%</td>
<td>3,782</td>
<td>742</td>
<td>19.6%</td>
</tr>
<tr>
<td>45</td>
<td>46 Shionogi</td>
<td>2,894</td>
<td>4.3%</td>
<td>3,114</td>
<td>458</td>
<td>14.7%</td>
</tr>
<tr>
<td>48</td>
<td>50 Kyowa Kirin</td>
<td>2,412</td>
<td>-6.0%</td>
<td>3,151</td>
<td>464</td>
<td>14.7%</td>
</tr>
</tbody>
</table>

Source: NEW Pharma Future No.7 2017/June-July by Ken Pharma Brain
Difference in Resources between Japan and the World’s Pharmaceutical Companies

- Huge gaps lay in various factors in addition to R&D costs

<table>
<thead>
<tr>
<th></th>
<th>Global Mega Pharma</th>
<th>Major Japanese Pharmaceutical Companies</th>
</tr>
</thead>
<tbody>
<tr>
<td>R&amp;D Costs</td>
<td>2 to 10 times higher</td>
<td>When this is 1</td>
</tr>
<tr>
<td>Number of R&amp;D Personnel</td>
<td>3 to 10 times higher</td>
<td>When this is 1</td>
</tr>
<tr>
<td>Development Pipelines</td>
<td>90 to 170</td>
<td>20 to 50</td>
</tr>
<tr>
<td>Compound Library</td>
<td>2 to 3.5 million compounds</td>
<td>0.5 to 1 million compounds</td>
</tr>
<tr>
<td>Strategy Scope</td>
<td>Covers wide spectrum</td>
<td>Specific disease area</td>
</tr>
<tr>
<td>Technology Scope</td>
<td>Wide spectrum, Long-term perspective (Small molecules, Bio, Vaccines)</td>
<td>Limited area, Short-term perspective Focus on small molecules (Except CHUGAI)</td>
</tr>
<tr>
<td>Blockbusters*</td>
<td>125 Products</td>
<td>13 Products (9% of world total)</td>
</tr>
<tr>
<td>No. of biopharmaceuticals*</td>
<td>48 products (38%)</td>
<td>2 products (15%)</td>
</tr>
</tbody>
</table>

*source: NEW Pharma Future 2016/06/30
Major Pharma Companies Rely Heavily on Top Sellers

Based on the companies’ financial reports

Roche

Top 10 products

Top 5 products

58% 71%

Average / product: 3.0 bil USD

Novartis

Top 5 products

Top 10 products

29% 43%

Average / product: 2.0 bil USD

Pfizer

Top 5 products

Top 10 products

40% 54%

Average / product: 2.5 bil USD

Merck

Top 5 products

Top 10 products

35% 54%

Average / product: 1.9 bil USD

Sanofi

Top 5 products

Top 10 products

43% 54%

Average / product: 2.0 bil USD
Sales Breakdown of Major Japanese Pharmaceutical Companies

Based on the companies’ financial reports

**Takeda**
- Top 5 Products: 31%
- Top 10 Products: 49%
- Average / product: 88.7 bil JPY

**Astellas**
- Top 5 Products: 56%
- Top 10 Products: 69%
- Average / product: 94.5 bil JPY

**Daiichi**
- Top 5 Products: 51%
- Top 10 Products: 63%
- Average / product: 61.9 bil JPY

**Sankyo**
- Top 5 Products: 42%
- Top 10 Products: 57%
- Average / product: 31.1 bil JPY

**Eisai**
- Top 5 Products: 54%
- Top 10 Products: 70%
- Average / product: 34.8 bil JPY

**Chugai**
- Top 5 Products: 56%
- Top 10 Products: 69%
- Average / product: 94.5 bil JPY
Challenges Facing Japan’s Pharmaceutical Industry and the Direction of Solutions toward the Continuous Creation of Innovation

- Investment in R&D Comparable to Global Companies
- Appropriate evaluation of Innovation
- Promotion of open Innovation
- Japan as International Arena for Drug Discovery and Development
Japan’s Issues with the Valuation of Innovation

Drug pricing rules change suddenly when the scale of sales is the only factor for evaluation

Introduction of Special Expansion Repricing Rule

✓ Sovaldi, Harvoni, Plavix, Avastin

Decision by Prime Minister’s Office on measure to halve drug prices

✓ Opdivo

Issues from the perspective of pharmaceutical industry

● Significantly impairs the management of predictability, lowers continuous investments in R&D and the desire to pursue innovation

● Drug price recalculations which are simply based on the scale of sales is not a model for creating innovation

● Drug price recalculation does not take into account the total reduction of costs provided by treatments with high therapeutic effect nor the positive economic impact of reintegrating a patient back into society
Reform of the Drug Pricing System

**NHI price calculation**
- Assess the diverse value of a new drug, realize a price that reflects the value

**Maintenance of drug price**
- Maintaining the price during the patent period promotes faster recovery of development costs and encourages the pursuit of new challenges

- Drug price of new drugs covered by premium
  - Condition: Deviation rate of actual market value does not exceed the weighted average deviation rate of all listed products
  - Calculation for price of new drugs that \( \times 0.5 = \) generic price
don’t qualify for premium

- Price revisions in accordance with the prevailing market price
  - Sum of postponed cuts

- After patent period
  - Z2

- Drug listing

- First drug price revision after launch of new generic product
  - Generic launch or 15 years from initial NHI listing

- Implement measures so that prices quickly reflect changes in the preconditions of market forecasts after market launch
- Move to abolish special expansion repricing rules that are based solely on scale of sales
Challenges Facing Japan’s Pharmaceutical Industry and the Direction of Solutions toward the Continuous Creation of Innovation

- Investment in R&D Comparable to Global Companies
- Appropriate evaluation of Innovation
- Promotion of open Innovation
- Japan as International Arena for Drug Discovery and Development
Necessity of Open Innovation

1. Decline of R&D productivity in the pharmaceutical industry

<table>
<thead>
<tr>
<th></th>
<th>1996-2004</th>
<th>2005-2010</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of new drugs / year</td>
<td>36</td>
<td>22</td>
</tr>
<tr>
<td>Average annual sales of products</td>
<td>$515 (million)</td>
<td>$430 (million)</td>
</tr>
<tr>
<td>R&amp;D cost / year</td>
<td>$65 (billion)</td>
<td>$125 (billion)</td>
</tr>
</tbody>
</table>


2. Meaning of Open Innovation

In order to improve R&D productivity...
- Increase and diversify new drug seeds
- Utilize each other’s high technology
- Human capital exchange
Future Direction of Academia-Industry Cooperation

Before

**Academia**
- Idea (Seeds)
- License

**Company**
- Practical application
- Development

**Company**
- Funding

**Academia**
- Basic research

Cooperative research

**PDCA cycle**
- Plan
- Do
- Check
- Act

Completely within the company

Going forward: Cooperation utilizing mutual strengths (Technology and human capital exchanges)

**Planning**
- Develop a strategy
- Concept
- Target
- Problem to be solved
- Mutually utilize required technologies

**Operation**

**Evaluate process and milestones**

A: Technology / Specialty
B: Outcome
C
D

Revise the plan
Chugai’s Technology Driven Approach

- Select best approach to target diseases with an arsenal of technologies including antibody engineering, small molecule and the next generation middle molecule
- Gain innovative drug seeds with enhanced research capabilities in oncology and immunology

- Disease-causing molecule
- Selection of proper drug discovery target
- Development of innovative drug discovery technology
- Matching of technology & target
- Solution for unmet medical needs

- Next generation (high functionalized) antibody
- Small molecule drugs
- Middle molecule drugs

- Antibody, mw: 150,000
- Small molecule Alectinib, mw: 482
- Middle molecule Cyclic peptide, mw: ~1,000~

 Select best approach to target diseases with an arsenal of technologies including antibody engineering, small molecule and the next generation middle molecule
 Gain innovative drug seeds with enhanced research capabilities in oncology and immunology
Med-term Comprehensive Collaboration with Osaka University Immunology Frontier Research Center (IFReC)

- Create innovation from the fusion of IFReC’s cutting-edge Immunology and Chugai’s Drug Discovery Technology
- Mid-long term support for basic research in academia

IFReC
- Great source of drug seeds with the world’s most advanced science in Immunology, Bioimaging & Bioinformatics

Chugai
- Drug discovery approach driven by innovative technology capable of tackling various drug discovery target

Understand the mechanism of Immune Diseases
Identify the Innovative new Target Molecule

Lead the global Immunology
Create Innovative New Drugs
Challenges Facing Japan’s Pharmaceutical Industry and the Direction of Solutions toward the Continuous Creation of Innovation

- Investment in R&D Comparable to Global Companies
- Appropriate evaluation of Innovation
- Promotion of open Innovation
- Japan as International Arena for Drug Discovery and Development
Specific Actions that Industry, Government and Academia should Promote towards Continuous Creation of Pharmaceutical Innovation in Japan

- **Discovery**
  - Discovery of seeds for new drug
  - Strengthen open innovation

- **Pre-clinical**
  - Feasibility study for business
  - Acquisition of advanced biotechnology, drug discovery approach and technology

- **Clinical**
  - Empirical research (Proof of concept)
  - Enhancement of bridging for practical application of academia seeds
  - AMED

- **Manufacturing/Selling**
  - Recovery of profit for next investment
  - Maintenance for utilization of medical big data, acceleration of utilization by private enterprise
  - Acceleration of deregulation, early approval system

- **Foundation**
  - ICT innovation for medical application (AI, IoT, Robot, etc.)
  - Support measures to promote medical ventures
  - Integration of knowledge and human resources as a foundation for creating innovation

**Support measures**
- MHLW
- PMDA
- Administration
- Industry
- Academia
Special Features of U.S. Industry Clusters Leading to the Creation of Innovation

San Diego Research Cluster (No.1 Bio-cluster in the US)

- **Top rank research centers** focused around universities
- Coexistence of large enterprises and small scale, high growth **venture** companies
- **Diverse business base** to support venture companies (legal, accounting, etc.)
- Continuous economic and industrial development activities by **regional entities** (local government, companies, universities, individual citizens)
- **Highly mobile** labor force
- **Diverse educational system** of specialists who become entrepreneurs

Characteristics of industrial clusters in Japan (differences with U.S.):

- Cluster formations stay in the administrative districts of prefectures and city governments
- Short- and mid-term policies (Suspension of Industrial Cluster Plan)
- Location and facilities prioritized, not accompanied by development of human resources, etc.
Japan as International Arena for Creating Innovation and World Healthcare Center through Innovative Drugs Creation

Diversity (Nationality/expertise) • Excellent Talent (W-major etc.)

Investment

Research base

Europe
Asia
U.S.A

Investment in technology development
• Further development and application of biotechnology to technology
• Establish and utilize emerging ICT technology such as AI and IoT
• Establishment and utilization by private enterprise of integrated database of health, medical care, nursing care including genome data

Infrastructure development
• Acceptance of diversity (Nationality/expertise)
• High level basic research at university
• Appropriate assessment mechanism of innovation and regulatory reform
• Collaboration based on human resources mobility between industry, government and academia
• Acceleration of medical venture promotion

Japan as international R&D arena for creating innovation

Further development of drug discovery technology
Further growth of talent in drug discovery

Continuous creation of innovative medicines

Contribution to the health of 8 billion people around the world
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Innovation all for the patients

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