Dr. Hatsuo Aoki, Ph. D.
Senior Advisor, Astellas Pharma Inc.
Drug’s Therapeutic Effect vs. Therapeutic Satisfaction

Diagnosis with low therapeutic satisfaction

Diagnosis with lower Drug’s therapeutic effect than therapeutic satisfaction

Note: Japan Health Science Foundation “Perspects on Medical Needs in Y2015”
Advancement of Life Science and Pharmaceutical R&D

-1950

1950-Per 1990s

High hurdle for further innovation

Control of chronic diseases

Efficient control of acute diseases

1973 Recombinant DNA Technology

1983 PCR System

1990 Gene Therapy

Late 1990s Biomarker Molecules and Disease-related-genes

1990 Genomics, Transcriptomics, Proteomics

2000 Sequencing human genes

Total Analysis of Diseases

System Biology

Pharmacogenomics/Toxicogenomics

Future

Biology/Chemistry

Biochemistry, Molecular Biology, Biomedical Science, Medicinal Chemistry

Now

Regenerative Medicine

Antibody Medicine

Nucleic acid Medicine

20th Century

Aspirin, Penicillin

NSAID

Insulin, Interferon

H2-receptor antagonist

HMG-CoA-R

ACE inhibitors

20th Century - Biology/Chemistry

Advance of Life Science and Pharmaceutical R&D

Medicinal Chemistry
“Innovation Policy” pursued

“Closed Type”

Seeds-oriented Policy
= R&D (Science & Technology) Policy

Advanced Science & Technology

The nation (region) with infrastructure of breaking out innovation can realize the prominent growth.
⇒ Considering policy in “Government-Industry Dialog”
  o Strengthening industries and/or companies with international competitiveness
    → Concrete target of policy
    = The 5-year strategy for creating of innovative drugs and medical equipment
  ⇒ Expectation and role of Industries
    = “New Vision of the Pharmaceutical Industry”
  o Rationalization & Efficiency of policy decision and management (Reform of government system)
    → Unification of management on budget and policy decision etc. (for example, DIUS in UK)

“Open Innovation Type”

Need-oriented Policy
= Integrated Innovation Policy
(R&D (Science & Technology), educational talented people, market formation, etc.)

Needs from Society & people
Advanced Science & Technology
Improvement of Infrastructure for Innovation

Improvement of Infrastructure for Basic and Clinical Research
- Promotion of advanced basic research in universities/public research institutions
- Strengthening translational research
- Reform of clinical research and clinical trial infrastructure
- Educational training of talented people

R&D Infrastructure

Environment to Accelerate Drug Development

Pricing System of New Drugs

Evaluation of Innovation

Policy on Intellectual Property Rights

Regulatory Reform

New drug review/approval system

Collaboration with academia & government
- Establishment of council for cooperation (budget allotment, focusing issues, etc.)

Improvement of access to innovative NMEs

Improveement of access to innovative NMEs

Policy on Intellectual Property Rights

Regulatory Reform

New drug review/approval system

Collaboration with academia & government
- Establishment of council for cooperation (budget allotment, focusing issues, etc.)

Improvement of access to innovative NMEs

Pricing System of New Drugs

Evaluation of Innovation

Policy on Intellectual Property Rights

Regulatory Reform

New drug review/approval system

Collaboration with academia & government
- Establishment of council for cooperation (budget allotment, focusing issues, etc.)

Improvement of access to innovative NMEs
New York Pharma Forum
20th Annual General Assembly
December 4, 2009

Biopharma in 2029: A 20th Anniversary Perspective

James J. Dolan
SVP, Licensing and Business Development
Purdue Pharma L.P.
Specialty Pharma: Plays a Critical Role in the Global Biopharma Market

- Perspective on “Specialty Pharma” vs. global big pharma / big biotech

- Spec pharma sector thriving

- Will need continuous innovation to survive until 2029
Specialty Pharma....has come a long way in 20 years...much to do in the next 20 years

- Built high-performance, efficient, marketing / sales organizations which offer impressive avenues to market for specialty and GP products

- Strong commercial expertise based on market exclusivity, labeling, positioning, deep understanding of physician/patient/payor needs, i.e. all aspects of commercial value proposition
Specialty Pharma….has come a long way in 20 years…much to do in the next 20 years

• “Backward integrated” into R&D – looking for proprietary products to extend market positions…moved into NCEs…saw the benefit of development risk/reward and liked it; not just drug-delivery any more

• Always dependent on licensing/partnering and all forms of sophisticated commercial/development arrangements; willing/able to imagine creative partnerships in a few focused TAs
Specialty Pharma...where will the next 20 years take us?

• Our product life cycles are getting shorter; high % of our markets are generic already

• Our investment in marketing/sales demands longer periods of exclusivity for ROI – what to do?
Specialty Pharma...where will the next 20 years take us?

• Development will be guided by clear medical/patient benefits in well-defined populations, outcomes data / managed care will dictate the new proprietary products of the future

• Use our commercial expertise to convince private and gov’t insurance to pay for/recognize individual patient characteristics
Specialty Pharma….in 2029

- Innovation is the only answer; technical risk will increase; only the strong survive

- Shoulder-to-shoulder with our biotech partners

- Let biotech do what they do best…invent new medicines; leave them alone, i.e. Roche / Genentech models for our collaborations
Specialty Pharma….in 2029

- Spec pharma’s understanding of patient/physician needs and outcomes gets immediately translated back to the drug hunters in biotech

- Development will be guided by well-defined patient populations; gene mutations can be addressed by new drugs with diagnostics; spec pharma will execute multiple drug combo clinical trial strategies for best outcomes in the commercial world

- New proprietary medicines emerge because spec pharma and biotech are committed to novel, first-in-class drugs w/economic rationale
Biopharma in 2029: a 20th Anniversary Perspective

Introduction to the 20th Annual General Assembly of the NYPF
December 4, 2009

Dr. Sapan Shah
President & CEO
Shionogi USA Inc.
Today’s Program

• Introduction and quick look at the past 20 years
• Panelists thoughts on the next 20 years
  – **Mr. Richard Van Duyne**, Head of Global Business Development, Daiichi Sankyo Inc.
  – **Dr. Hatsuo Aoki**, former Chairman of both Astellas Pharma Inc. and Japan Pharmaceutical Manufacturers Association
  – **Mr. Soichi Matsuno**, Deputy President of Eisai Co., Ltd.
  – **Mr. James Dolan**, Senior Vice President, Licensing & Business Development of Purdue Pharma LLP
Why look back before looking ahead?

• “The distinction between past, present, and future is only a stubbornly persistent illusion”
  – Albert Einstein

• “To look backward for a while is to refresh the eye, restore it, and render it more fit for its prime function of looking forward”
  – Margaret Fairless Barber

• “Learn from the past, live in the present, plan for the future"
  – Audrey Farrell
So let’s go back to......
1989

- The first GWB took office
- Launch of Sega Genesis
- Tiananmen Square protests
- Exxon Valdez oil spill
- Nolan Ryan – 1st pitcher to record 5000 strikeouts
- Collapse of Berlin Wall
How has the Pharmaceutical Industry changed since 1989?

- Commercial
- R&D/Innovation
- Government/Regulatory
Global pharmaceutical sales have experienced steady growth

Global Pharmaceutical Sales
$ Billion

CAGR 8%

Source: McKinsey & Company; IMS
North American market has captured a larger share over this period

Global Pharmaceutical Sales

1991
Total = $201B

- AAA: 26%
- NA: 34%
- EU: 34%

2008
Total = $774B

- AAA: 23%
- NA: 40%
- EU: 30%

Source: McKinsey & Company; IMS
US Market Has Grown in Importance

Percent of new compounds that are first marketed in the US

Then
20% of new compounds

Now
75% of new compounds


Source: Tufts Center for the Study of Drug Development
More recent period shows growth is coming from “new” markets

Pharmaceutical Sales by Country

$ Billion

- US
- Japan
- Germany
- France
- Italy
- Other

Source: McKinsey & Company; IMS

“Other” CAGR 14%
Japanese domestic market has held flat, growing reliance on global sales

*Data from 14 TSE-listed JPMA member companies

Source: Company financial reports
Scale of top global pharma companies has increased dramatically

**Percent of global pharma sales accounted for by Top 10 Companies**

<table>
<thead>
<tr>
<th>Then</th>
<th>Now</th>
</tr>
</thead>
<tbody>
<tr>
<td>20%</td>
<td>48%</td>
</tr>
</tbody>
</table>

* 1985 vs. 2002

Source: Congressional Budget Office October 2006 Pharmaceutical Industry Report
The same trend of increasing size has occurred in Japan

**Combined pharma sales of Top 5 Japanese pharmacos**

<table>
<thead>
<tr>
<th>Then</th>
<th>Now</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.2 trillion JPY</td>
<td>4.4 trillion JPY</td>
</tr>
</tbody>
</table>

* 1998 vs. 2007

Source: Company financial reports
Japanese Market Leaders Have Changed Due to Consolidation and Growth of MNCs

Top 10 pharmacos by pharma sales in Japan

<table>
<thead>
<tr>
<th>Then</th>
<th>Now</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Takeda</td>
<td>1. Takeda</td>
</tr>
<tr>
<td>2. Sankyo</td>
<td>2. Astellas</td>
</tr>
<tr>
<td>3. Shionogi</td>
<td>3. Daiichi Sankyo</td>
</tr>
<tr>
<td>4. Fujisawa</td>
<td>4. Eisai</td>
</tr>
<tr>
<td>5. Tanabe</td>
<td>5. Otsuka</td>
</tr>
<tr>
<td>6. Yamanouchi</td>
<td>6. Pfizer</td>
</tr>
<tr>
<td>7. Eisai</td>
<td>7. Mitsubishi Tanabe</td>
</tr>
<tr>
<td>8. Daiichi</td>
<td>8. Novartis</td>
</tr>
<tr>
<td>9. Chugai</td>
<td>9. GSK</td>
</tr>
<tr>
<td>10. Kyowa Hakko</td>
<td>10. Shionogi</td>
</tr>
</tbody>
</table>

* 1989 vs. 2007

Source: Company financial reports
Competition Has Increased Dramatically

Average period of US market class exclusivity for a first-in-class compound

Then

10.2 years

Now

2.5 years

* 1970s vs. 2003
Source: Tufts Center for the Study of Drug Development
Biologics have become a large and growing segment of the pharma market

 Evolution of Biologics

**Then**

Procrit/Epogen launched in 1989

**Now**

4 of top 12 pharmaceutical products by sales are biologics

Source: IMS Health
How has the Pharmaceutical Industry changed since 1989?

![Diagram showing the changes in the Pharmaceutical Industry with categories: Commercial, R&D/Innovation, Government/Regulatory.](image)
Drug Development Costs Have Increased Dramatically

* Fully capitalized cost to develop a new drug

**Then**

$318m

**Now**

$897m

* 1991 vs. 2003; adjusted for inflation; includes total average pre-clinical, clinical and post-marketing clinical study costs; based on analysis of data covering 68 drugs from 10 pharmacos

Source: Tufts Center for the Study of Drug Development
As an industry, total R&D spending has increased significantly

**Figure 4-1.**

Annual Spending on Research and Development by Drug Companies and the National Institutes of Health

(Billions of 2005 dollars)


Note: Spending was adjusted for inflation using the biomedical research and development price index from the Bureau of Economic Analysis.
In Japan R&D Expenses Have Doubled in Ten Years

*Data from 14 TSE-listed JPMA member companies
Source: Company financial reports
How has increased R&D spending impacted approvals?

Figure 5-1.
NME Approvals and Drug Companies’ Spending on Research and Development

(Billions of 2005 dollars)


Note: Spending was adjusted for inflation using the biomedical research and development price index from the Bureau of Economic Analysis.
Clinical Development Times Have Actually Decreased

Average amount of time to move through clinical and approval phases for approved compounds (US)


Source: Tufts Center for the Study of Drug Development

<table>
<thead>
<tr>
<th>Then</th>
<th>Now</th>
</tr>
</thead>
<tbody>
<tr>
<td>9.4 years</td>
<td>8 years</td>
</tr>
</tbody>
</table>

Source: Tufts Center for the Study of Drug Development
Emphasis on external licensing for innovation has increased

* 1993-1997 vs. 2003-2005

Source: Tufts Center for the Study of Drug Development

Share of licensed compounds in the pipeline of leading pharmacos

Then
1 in 7 compounds

Now
1 in 4 compounds
How has the Pharmaceutical Industry changed since 1989?

- Commercial
- R&D/Innovation
- Government/Regulatory
NME approvals have remained flat, with periods of high activity

Source: Drugs@FDA Database, approvals with NDA Chem Type 1 (NME); As of 10/2009
Generic approvals have increased significantly.

Source: Drugs@FDA Database, approvals with ANDA designation; As of 10/2009
Overall Healthcare Budget Has Increased Dramatically

**US Government Health Care Budget**

**Then**

Total $155.8b
- Medicare $98.1b
- Medicaid** $47.6b
- Other $10.1b

**Now**

Total $846.8b
- Medicare $457.8b
- Medicaid** $348.2b
- Other $40.8b

*1990 compared to 2010E, **Includes welfare and other related services

Source: www.usgovernmentspending.com
How has the Pharmaceutical Industry changed since 1989?

- Commercial
- R&D/Innovation
- Government/Regulatory
Summary of key trends over the past 20 years

- Rise in importance of the US market, recent flattening of traditional markets with growth from new areas
- Significant consolidation and increase in size/scale of top companies
- Increased competition commercially, rise of biologics as a major driver of sales
- R&D costs/spend increasing dramatically, more reliance on external licensing for innovations
- Regulatory approvals of NME’s have largely remained flat overall, current period below average
- Generic approvals have increased significantly
- Healthcare costs rising dramatically for governments and individuals
What do the next 20 years hold for the industry......
Today’s Program

• Panelists thoughts on the next 20 years
  – **Mr. Richard Van Duyne**, Head of Global Business Development, Daiichi Sankyo Inc.
  – **Dr. Hatsuo Aoki**, former Chairman of both Astellas Pharma Inc. and Japan Pharmaceutical Manufacturers Association
  – **Mr. Soichi Matsuno**, Deputy President of Eisai Co., Ltd.
  – **Mr. James Dolan**, Senior Vice President, Licensing & Business Development of Purdue Pharma LLP
Biopharma in 2029:
A 20th Anniversary Perspective

New York Pharma Forum
General Assembly
December 4, 2009

Richard Van Duyne
Head of Global Business Development
Daiichi Sankyo Group
The pharmaceutical industry continues to evolve...

**Era of Therapeutic Improvement**

1980—2000

- Therapeutic area focus
- Blockbuster model flourishes
- Hatch-Waxman Act
- DTC advertising empowers patients
- Sales force arms race

2000—2009

- Managed markets influence
- Biotech dominance
- Patent expirations
- Regulatory pressures

**Era of Payer Influence**

2010+

- US healthcare reform
- Personalized medicine
- Disease management
- Emerging markets
- Emerging technologies (e.g., nanotechnology)
- Biosimilars
- ????
...some developments will impact the direction of companies

**Portfolio Transformation**
Transition from traditional follow-on primary care products to specialty products to realize higher margins

**Value Proposition**
All stakeholder groups (government, employers, payers, providers, and patients) are demanding more value (health economics)

**Payer Influence**
Payers will exert more influence on selection, development, utilization, and marketing of products

**Selling Model**
Sales force sizes are returning to moderate size—specialty product focus will transform sales force structure

*Pharma companies must be flexible enough to quickly and effectively react to both the internal and external developments*
Increasing Globalization of Big Pharma

- Japanese companies in the U.S.
- Foreign-based companies in Japan
- Expansion of Big Pharma in the Emerging Markets
Increasing Globalization of Big Pharma

• Japanese companies in the U.S.

From

- small, “representative” offices or clinical oversight groups
- an out-licensing model
Increasing Globalization of Big Pharma

• Japanese companies in the U.S.

From

• small, “representative” offices or clinical oversight groups
• an out-licensing model

To

• large, “full capabilities” organizations
• launching internally developed products … and seeking to in-license

<table>
<thead>
<tr>
<th></th>
<th>Estimated 2009 Sales ($ Millions)</th>
<th>Number of US Sales Representatives</th>
</tr>
</thead>
<tbody>
<tr>
<td>Takeda</td>
<td>5,566</td>
<td>3,500</td>
</tr>
<tr>
<td>Astellas</td>
<td>2,024</td>
<td>855</td>
</tr>
<tr>
<td>Eisai</td>
<td>----</td>
<td>920</td>
</tr>
<tr>
<td>Daiichi Sankyo</td>
<td>1,474</td>
<td>1,850</td>
</tr>
</tbody>
</table>

Increasing Globalization of Big Pharma

• Japanese companies in the U.S.

• Foreign-based companies in Japan
  – from small organizations; out-licensing
  – to large organizations, self-launching internal global compounds,
    e.g., Pfizer, Sanofi
Increasing Globalization of Big Pharma

• Japanese companies in the U.S.
• Foreign-based companies in Japan
• Expansion of Big Pharma in the Emerging Markets
  – slowing rate of growth (pharmaceutical sales and population) in Developed Markets
    o growth of generics
    o patent expirations for major products
  – increasing growth – and increasing Big Pharma investment - in Emerging Markets
  – example: the Daiichi Sankyo “hybrid business model”
Increasing Globalization of Big Pharma

- Japanese companies in the U.S.
- Foreign-based companies in Japan
- Expansion of Big Pharma in the Emerging Markets

Question: In addition to globalization, what will be the pace of industry consolidation?
“Doing Deals”

• Increasingly necessary…but increasingly more difficult
• More competitive
• More complex
• More expensive
• The impact of globalization and R&D productivity challenges:
  – fewer Big Pharma/Japan licensing deals
  – biotech is now the common target
Increasing Importance of True Innovation

• In the past, a “fast follower” approach was commercially successful, with multiple drugs within a therapeutic class.

• Today and in the future, the regulatory authorities and reimbursement agencies/payers are raising the bar.
  - Regulators
    o Increasingly making assessments of drugs relative to standard of care.
    o Increase in risk aversion driven by public and government pressure.
  - Reimbursement agencies/payers
    o Government paying for an increasing percentage of drug costs.
    o Increasing concentration and professionalism; high quality care at lowest possible cost.
    o Increase in co-pays.
    o Increase in tiers; and increase in drugs in tiers 3 and 4.
  - Health technology agencies – e.g., NICE in the UK.
• Consequences

  - all stakeholders demand – “Show me the value (from my perspective)!"

  - Health Economics & Outcomes Research (HEOR) becoming increasingly important
    - generate evidence to demonstrate value to health policy makers, reimbursement agencies/payor groups and consumers

  - increased pressure on R&D organizations
    - order of entry increasingly important
    - higher demand for novel approaches means more technical risk and higher attrition rates