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

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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.

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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

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History of Pharmaceutical Innovations that Changed the World

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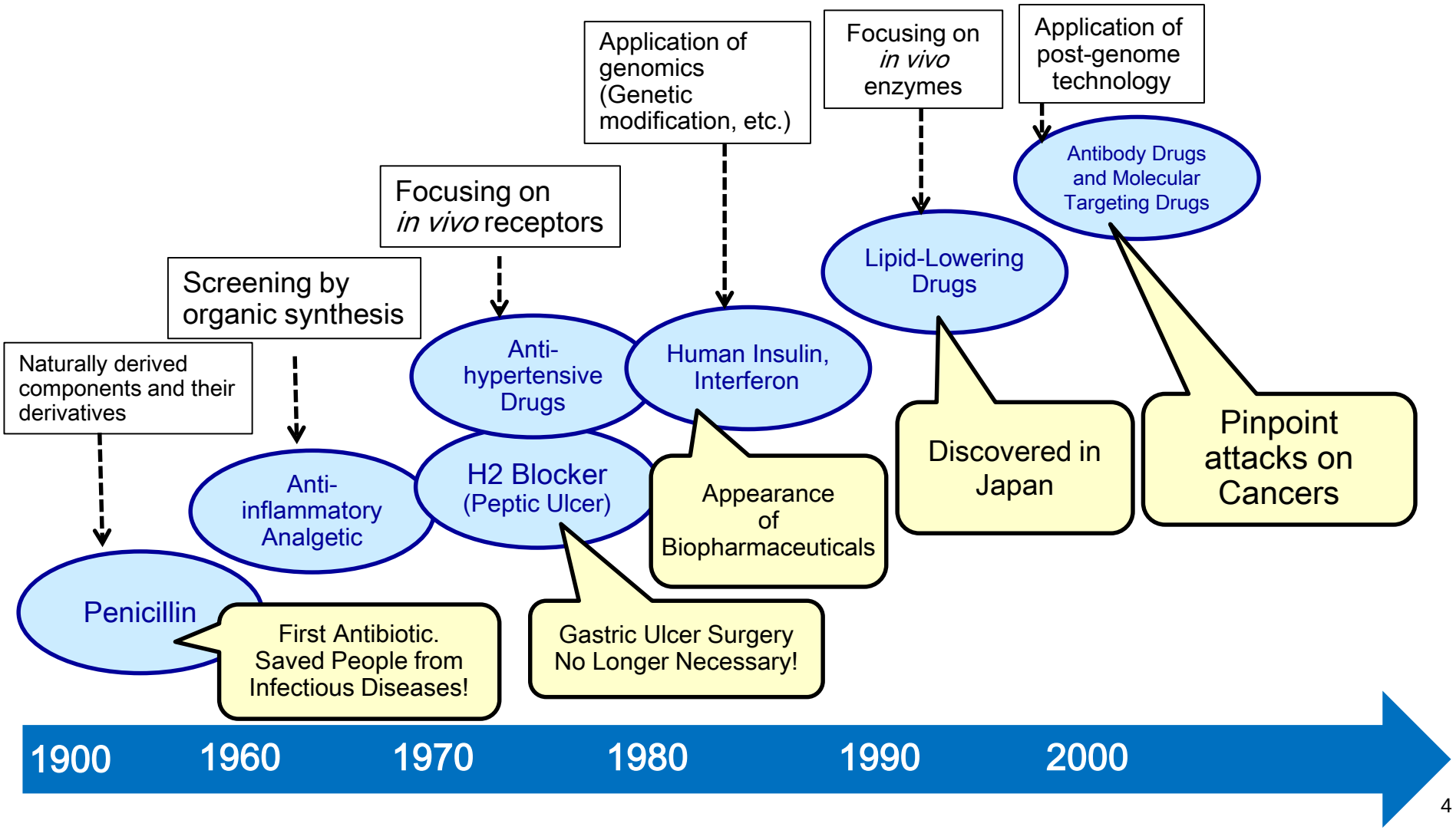
- Scientific developments have resulted in innovative medicines



The World has been Transformed Since the Decoding of the Human Genome Sequence

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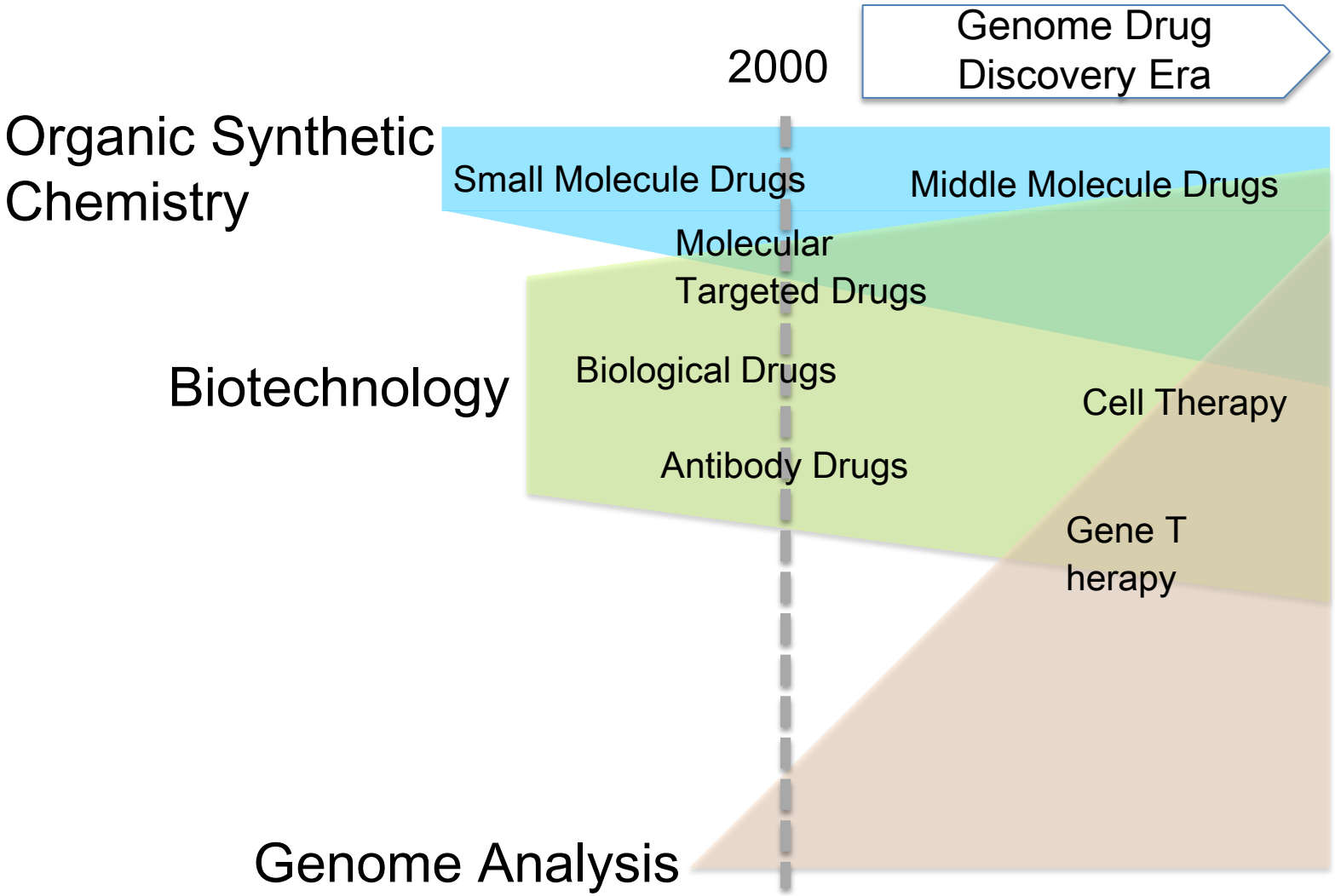
Human genome sequence was decoded and published in Nature (15 Feb, 2001) and Science (16 Feb, 2001)

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

https://www.ncbi.nlm.nih.gov/projects/genome/guide/human/

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



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

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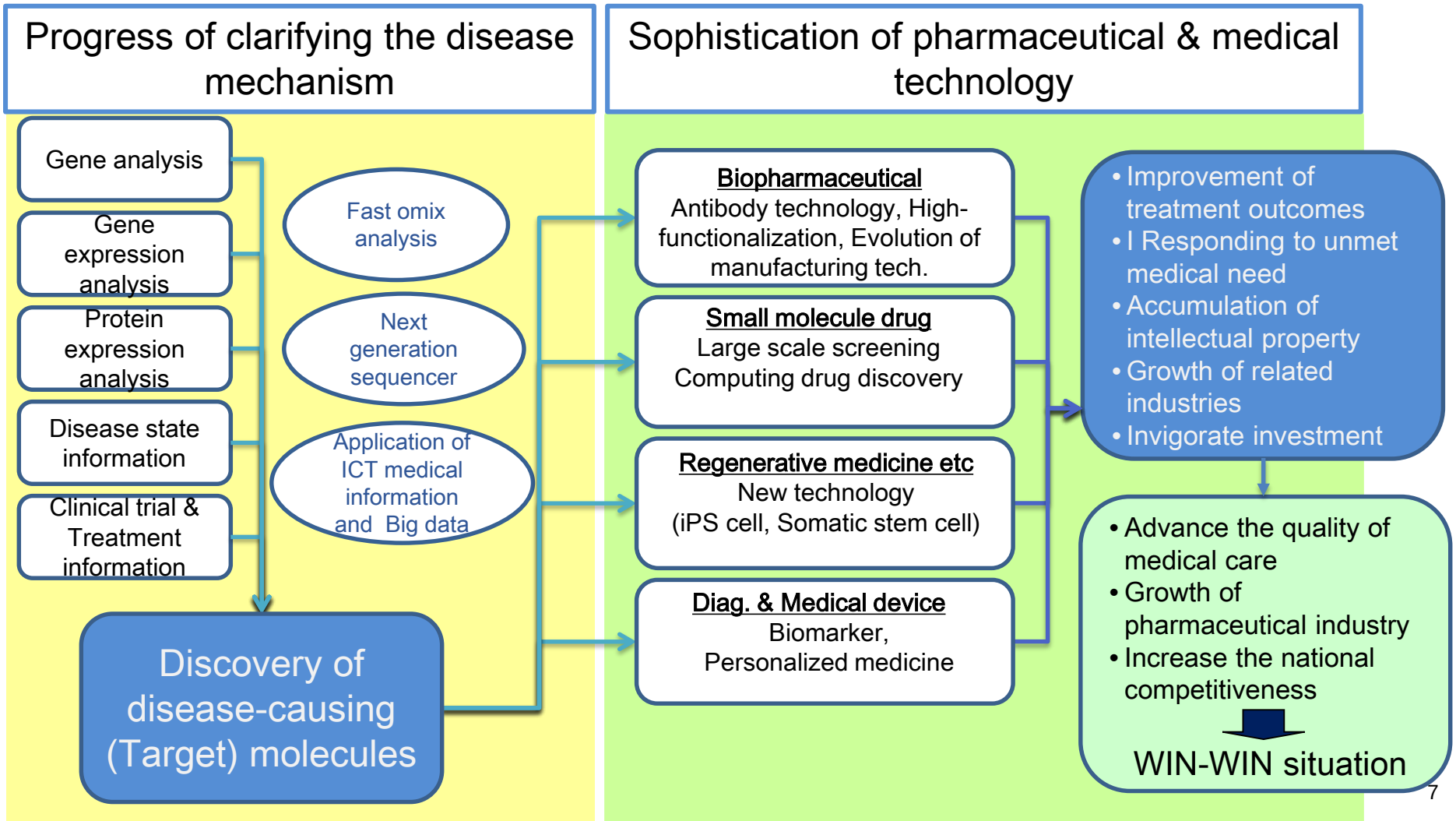
➢ Various technologies and multiple discovery approaches require high costs



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

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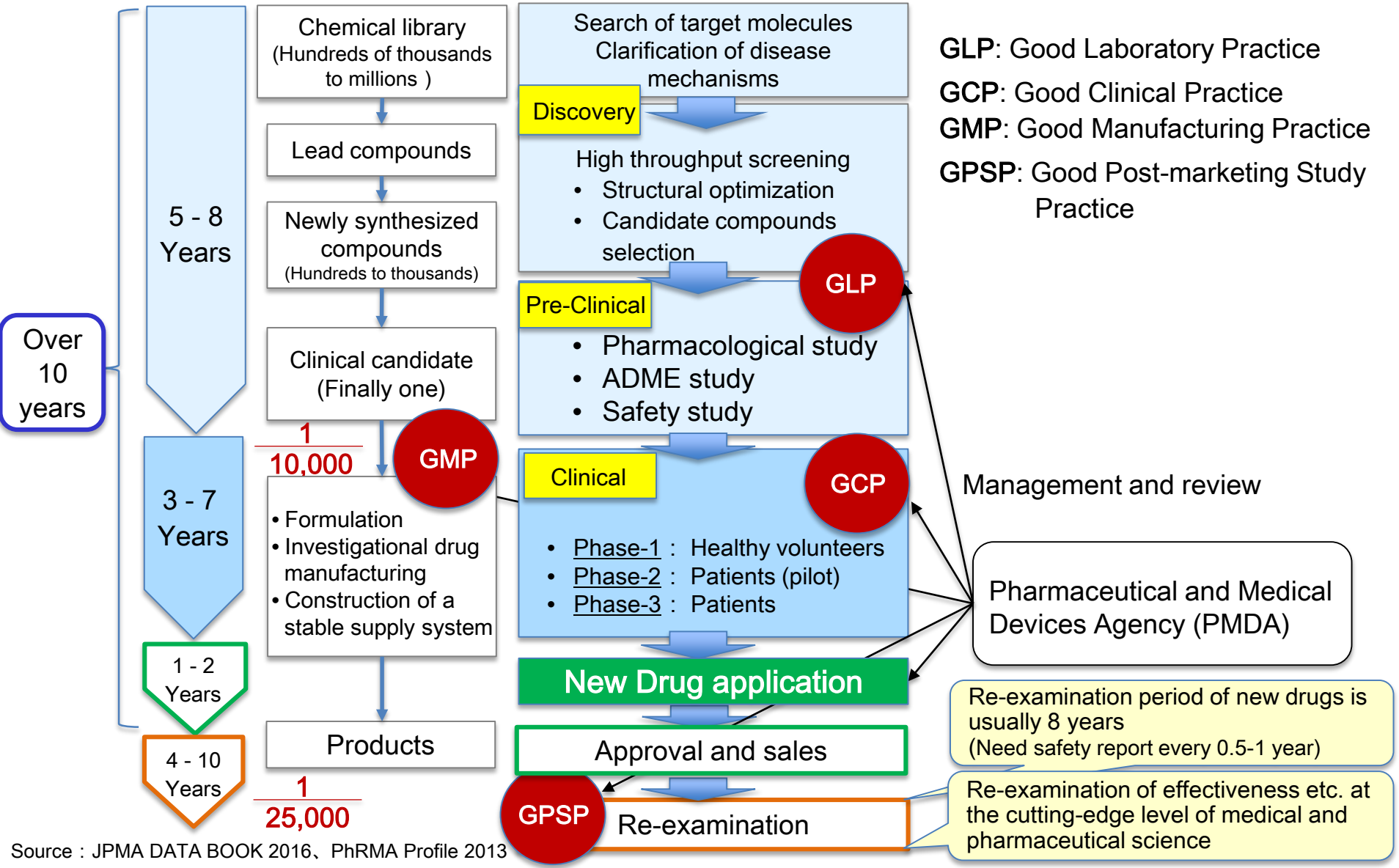

Source : JPMA DATA BOOK 2016、PhRMA Profile 2013

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Seven Out of the World's Top 10 Products are Biopharmaceuticals Now

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World Drug Sales Ranking

2005

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

2016

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

★ Biologics

Global Growth of Biopharmaceuticals

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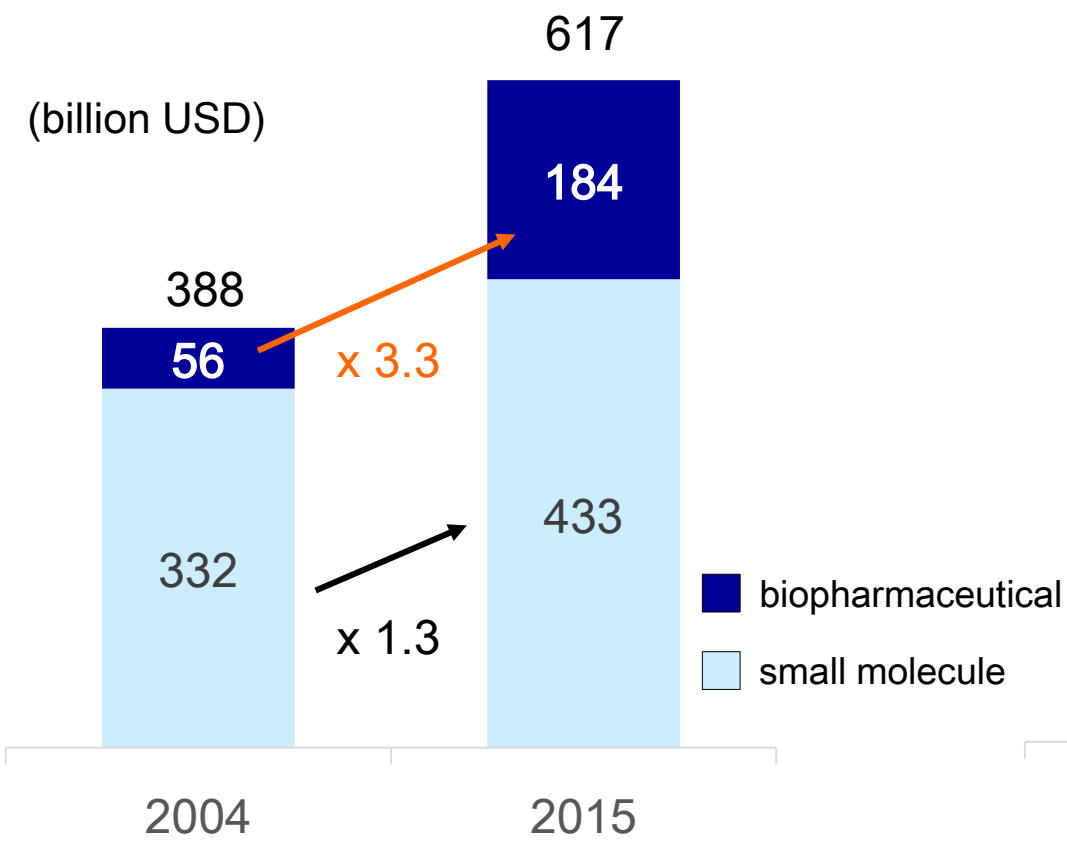
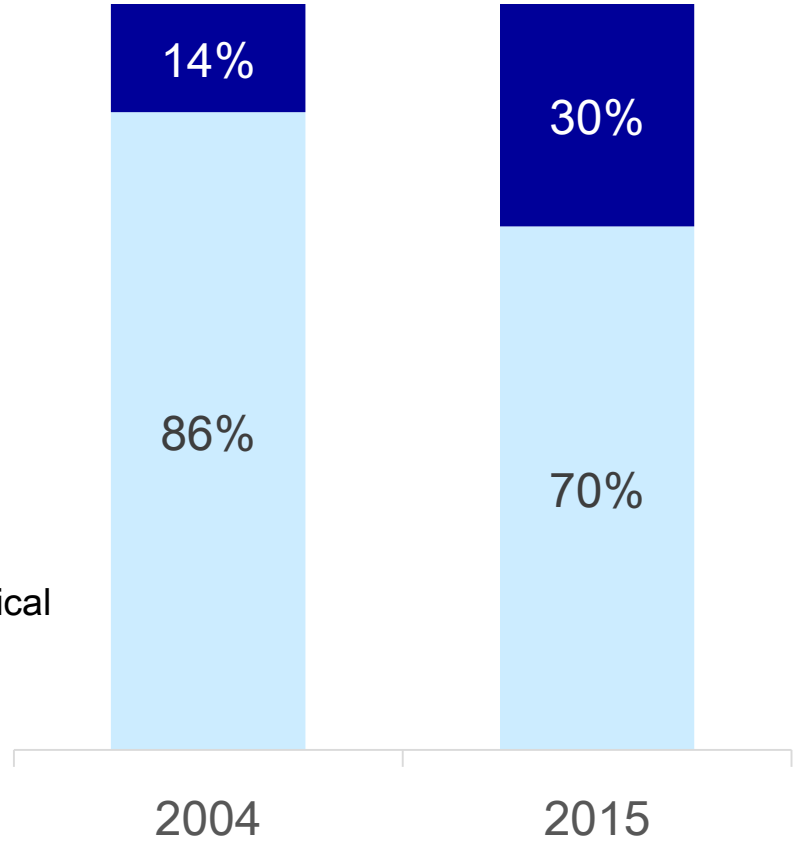
Sales of biopharmaceuticals



Sales increased by 3.3 times in 10 years

Sales ratio of biopharmaceuticals



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

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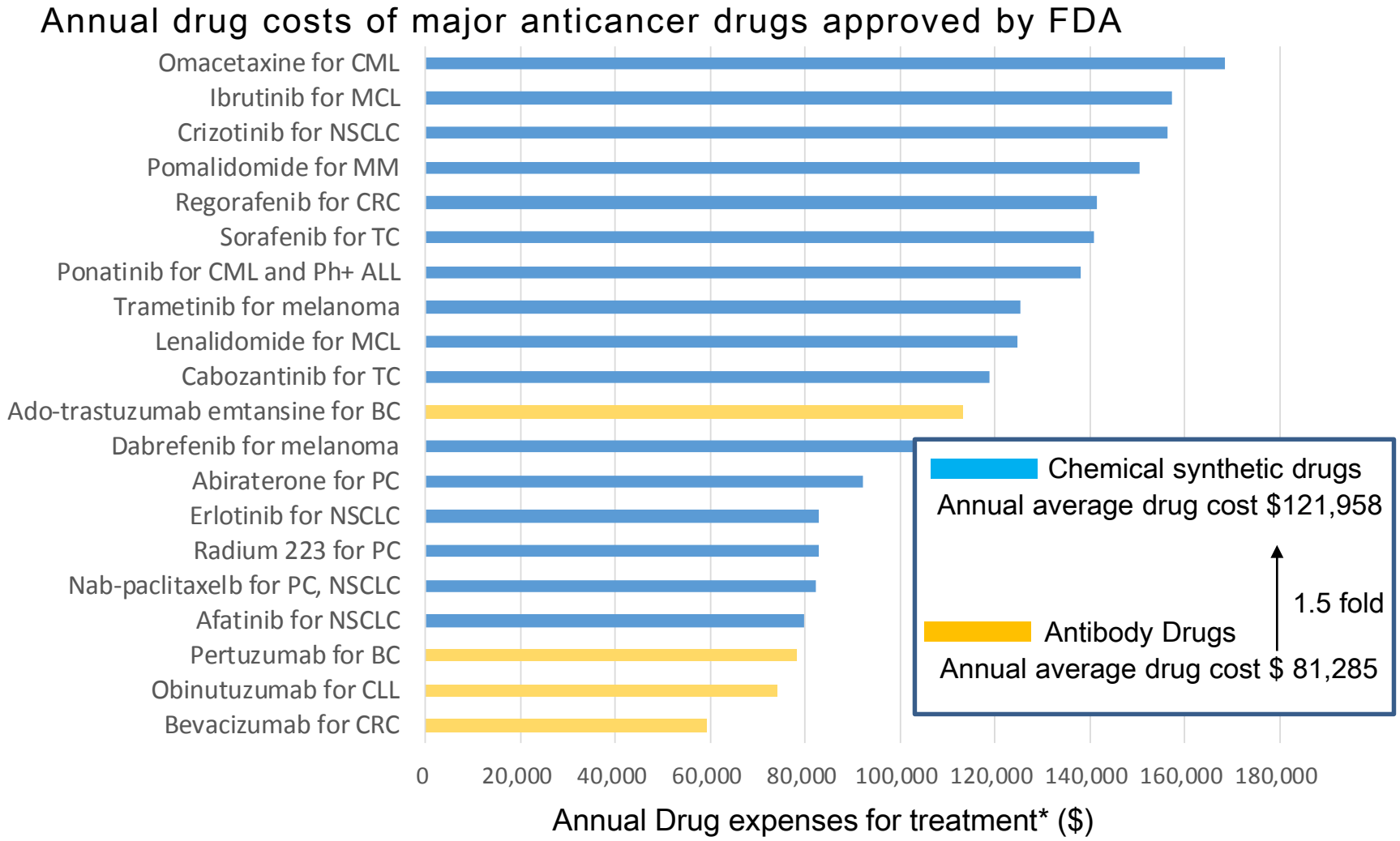

JAMA Oncology, 1: 539-540 (2015)

*average wholesale prices from Redbook

Clinical Development Success Rates (NDA vs BLA)

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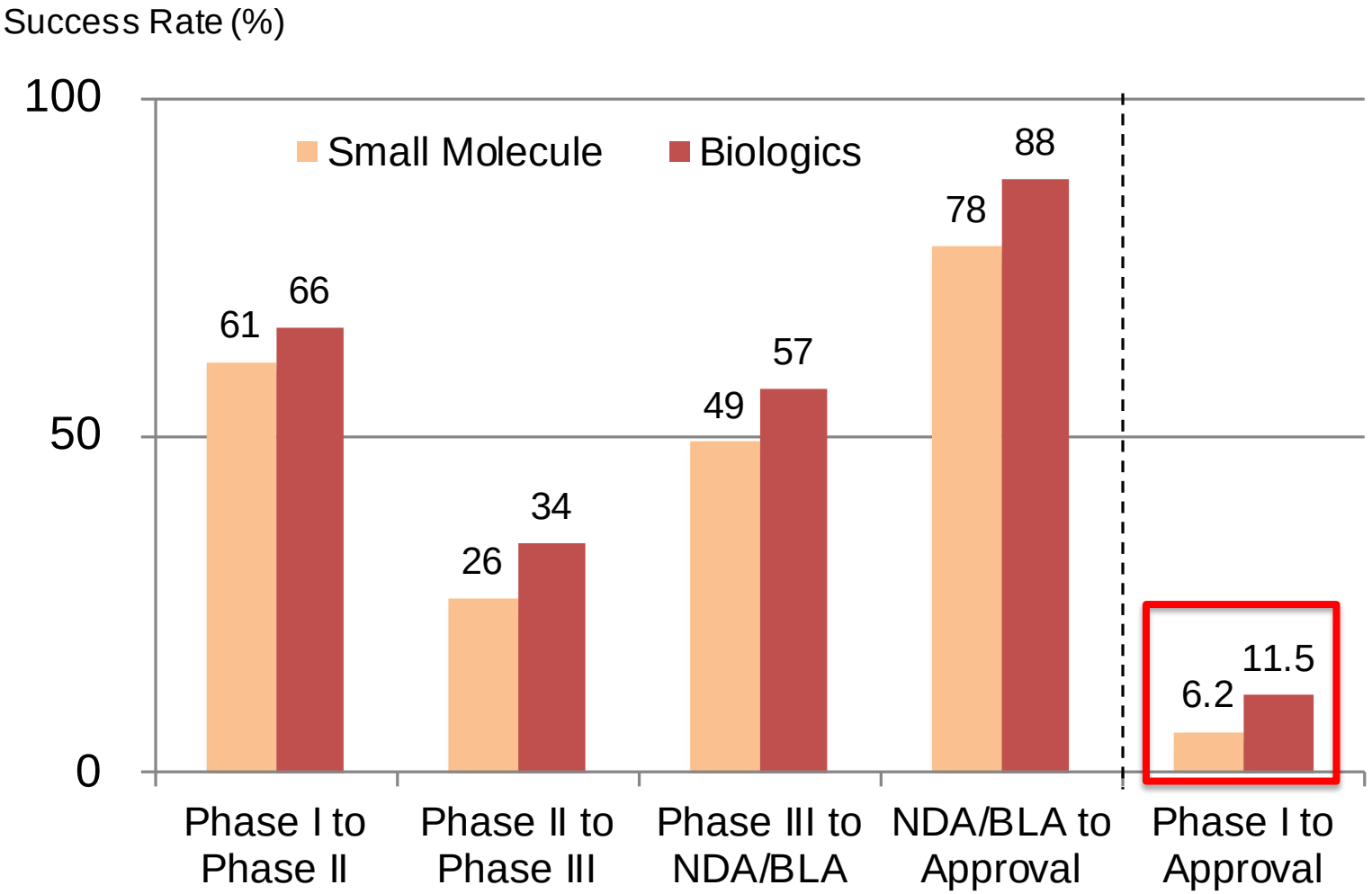

Source: Clinical Development Success Rate 2006-2015, BIO (2016)

As Targets of Antibody Drugs are Finite, Competition is Intensifying due to Concentration of Development on the Same Antigens

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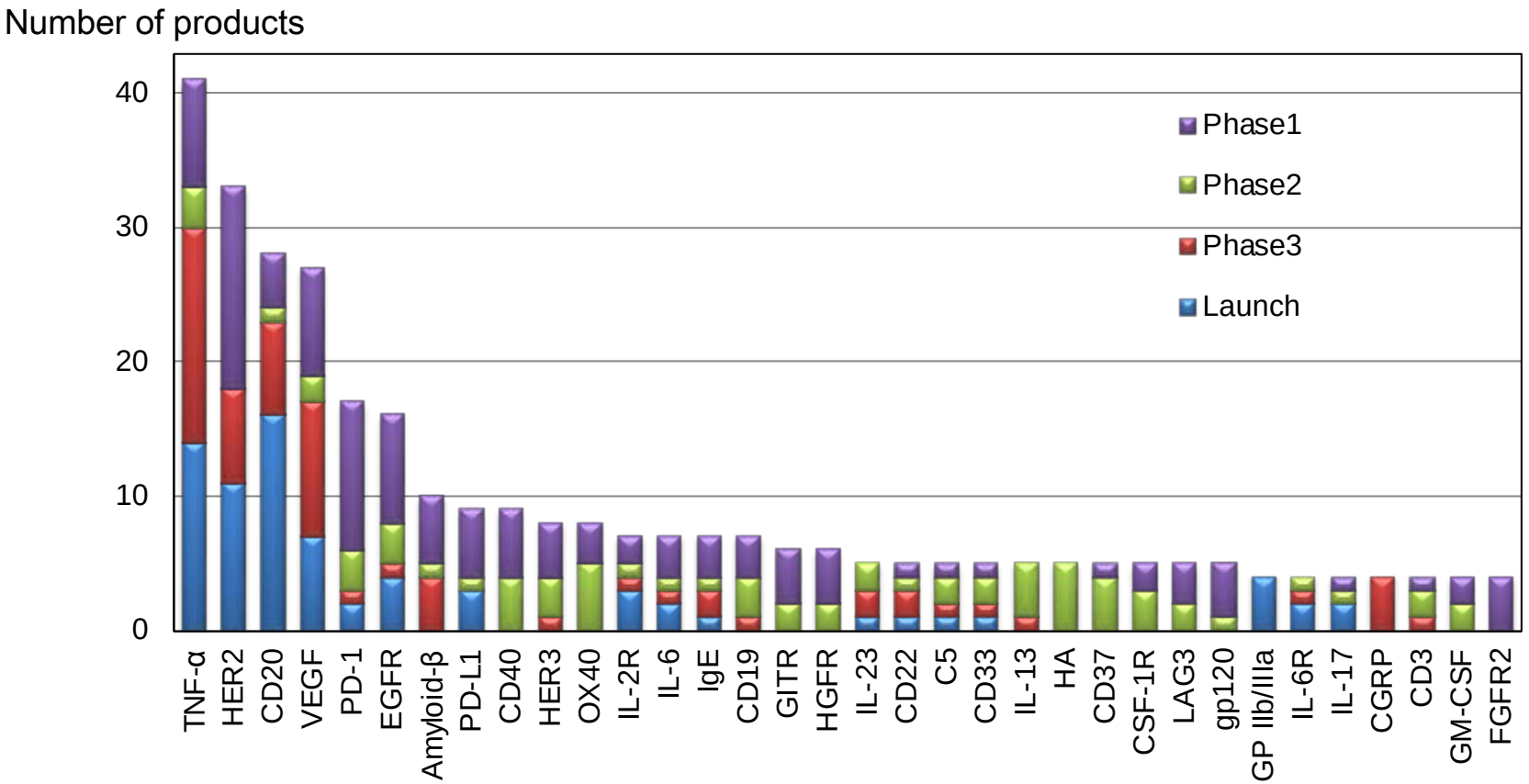
- All mega pharma are focusing on antibody drugs due to the success and market expansion of these products
- More than 730 antibody drugs are currently in clinical development
- 324 antibodies for 34 promising target antigens are in development



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

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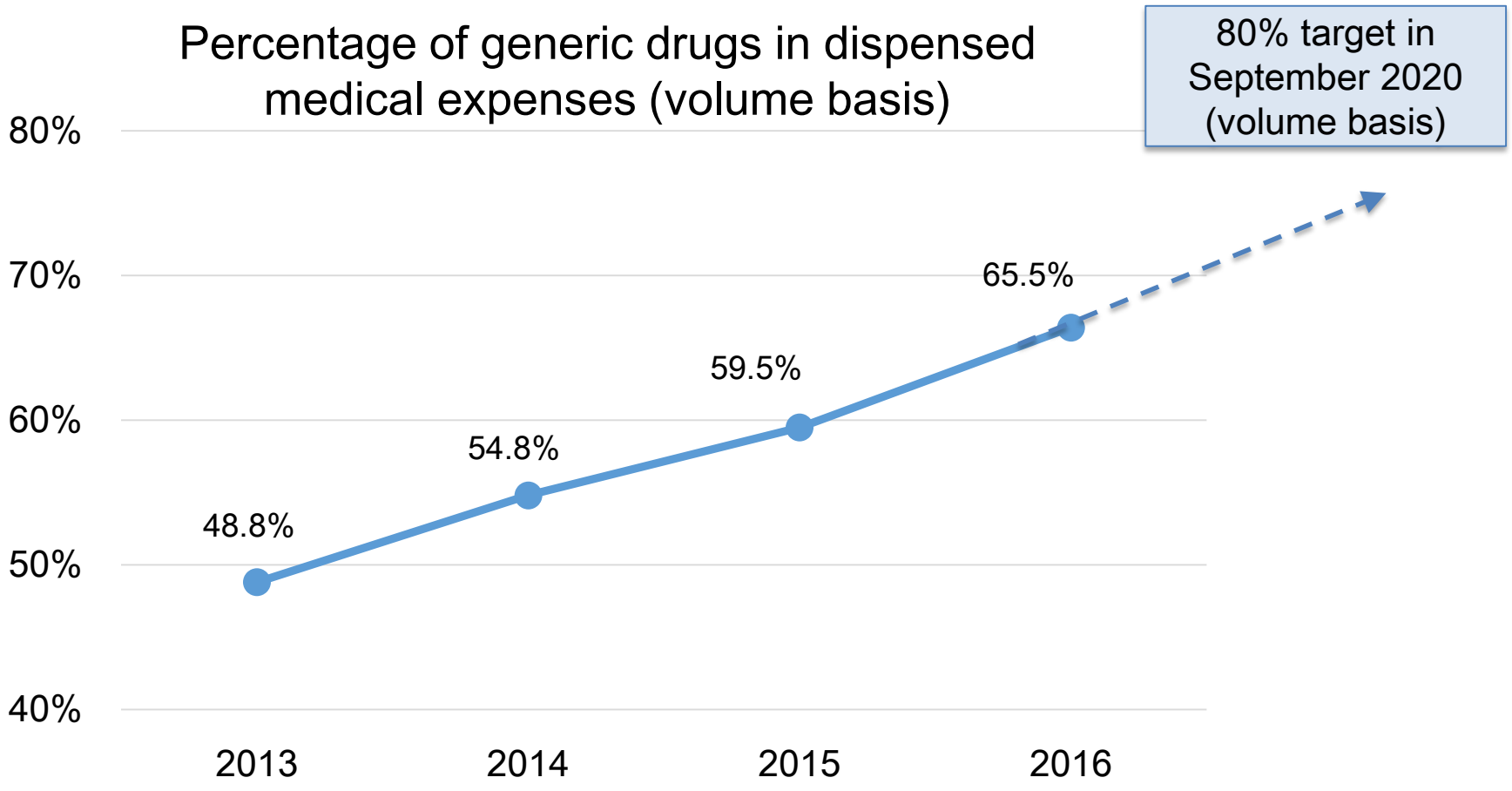

Source：Japan Generic Medicines Association HP

Domestic Market Share of Long-listed Products Shrinking due to Market Changes

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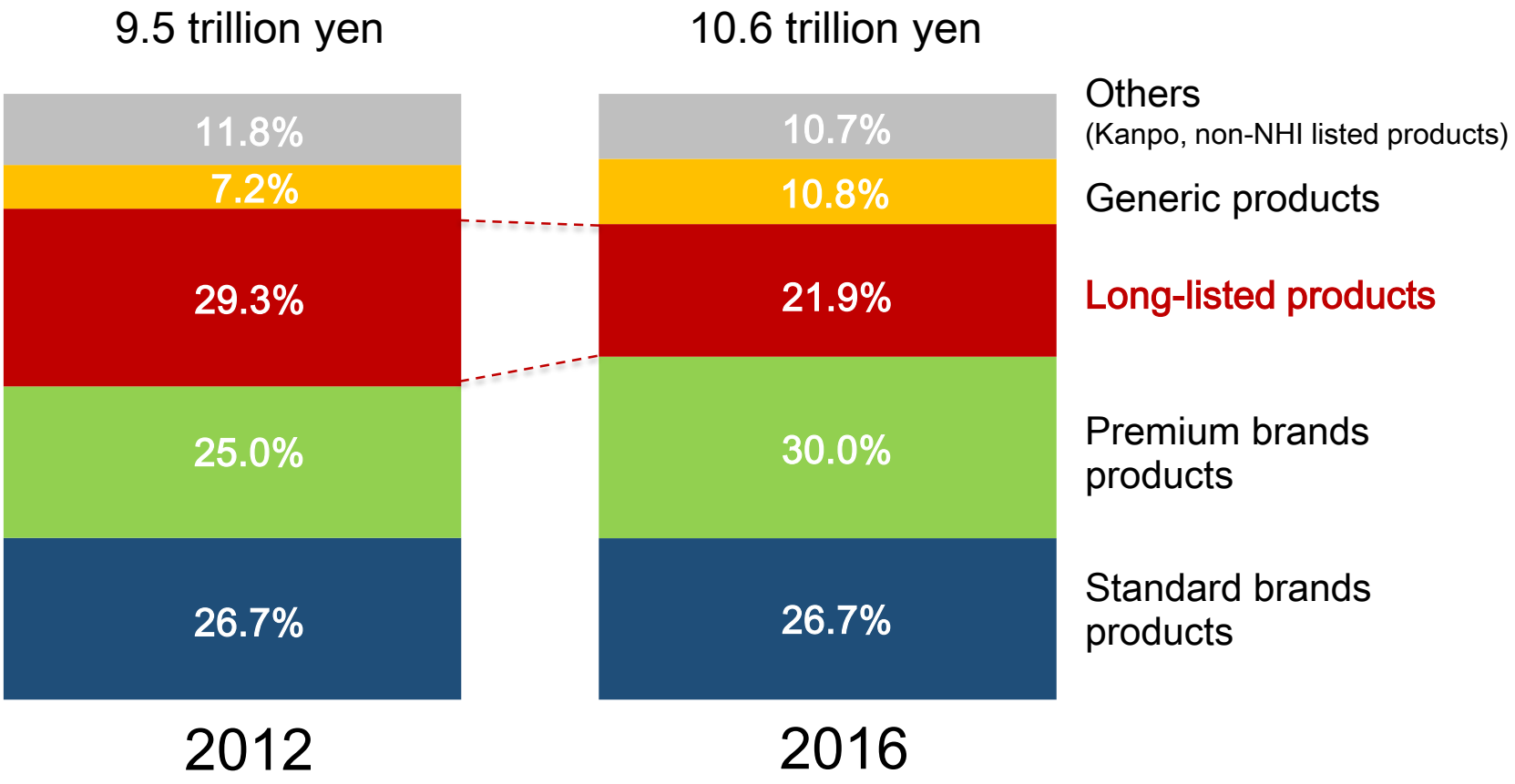

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Challenges Facing Japan’s Pharmaceutical Industry and the Direction of Solutions toward the Continuous Creation of Innovation

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- 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

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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

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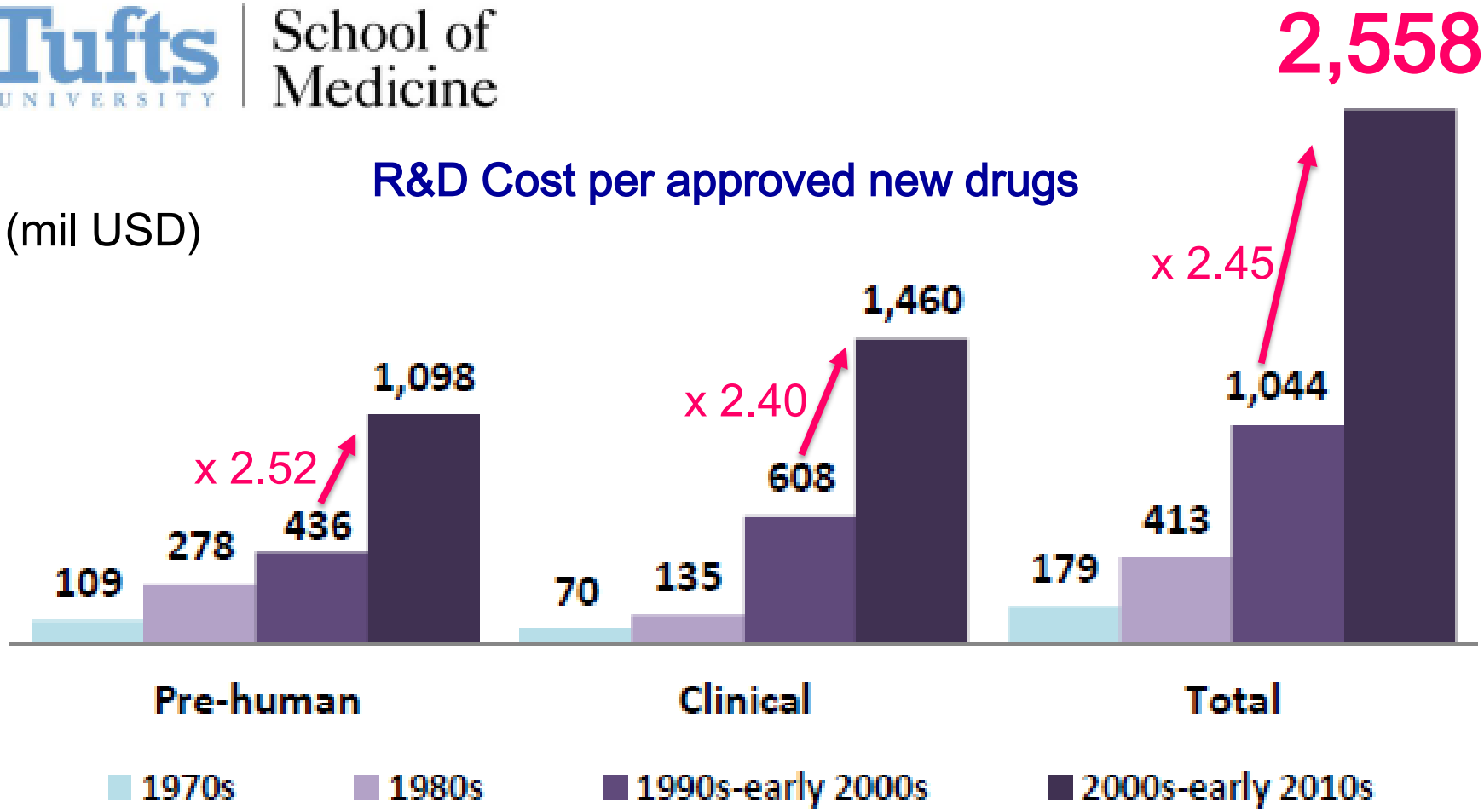
Tufts UNIVERSITY | School of Medicine



Source: Journal of Health Economics, 47:20-33 (2016)

There is a Big Difference between the Domestic Companies and the Global Leading Pharmaceutical Companies Investing Huge Costs in R&D

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(million USD)

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

Source : NEW Pharma Future No.7 2017/June-July by Ken Pharma Brain

Difference in Resources between Japan and the World's Pharmaceutical Companies

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

	Global Mega Pharma	Major Japanese Pharmaceutical Companies
R&D Costs	2 to 10 times higher	When this is 1
Number of R&D Personnel	3 to10 times higher	When this is 1
Development Pipelines	90 to 170	20 to 50
Compound Library	2 to 3.5 million compounds	0.5 to 1 million compounds
Strategy Scope	Covers wide spectrum	Specific disease area
Technology Scope	Wide spectrum, Long-term perspective (Small molecules, Bio, Vaccines)	Limited area, Short-term perspective Focus on small molecules (Except CHUGAI)
Blockbusters*	125 Products	13 Products (9% of world total)
No. of biopharmaceuticals*	48 products (38%)	2 products (15%)

*source: *NEW* Pharma Future 2016/06/30

Major Pharma Companies Rely Heavily on Top Sellers

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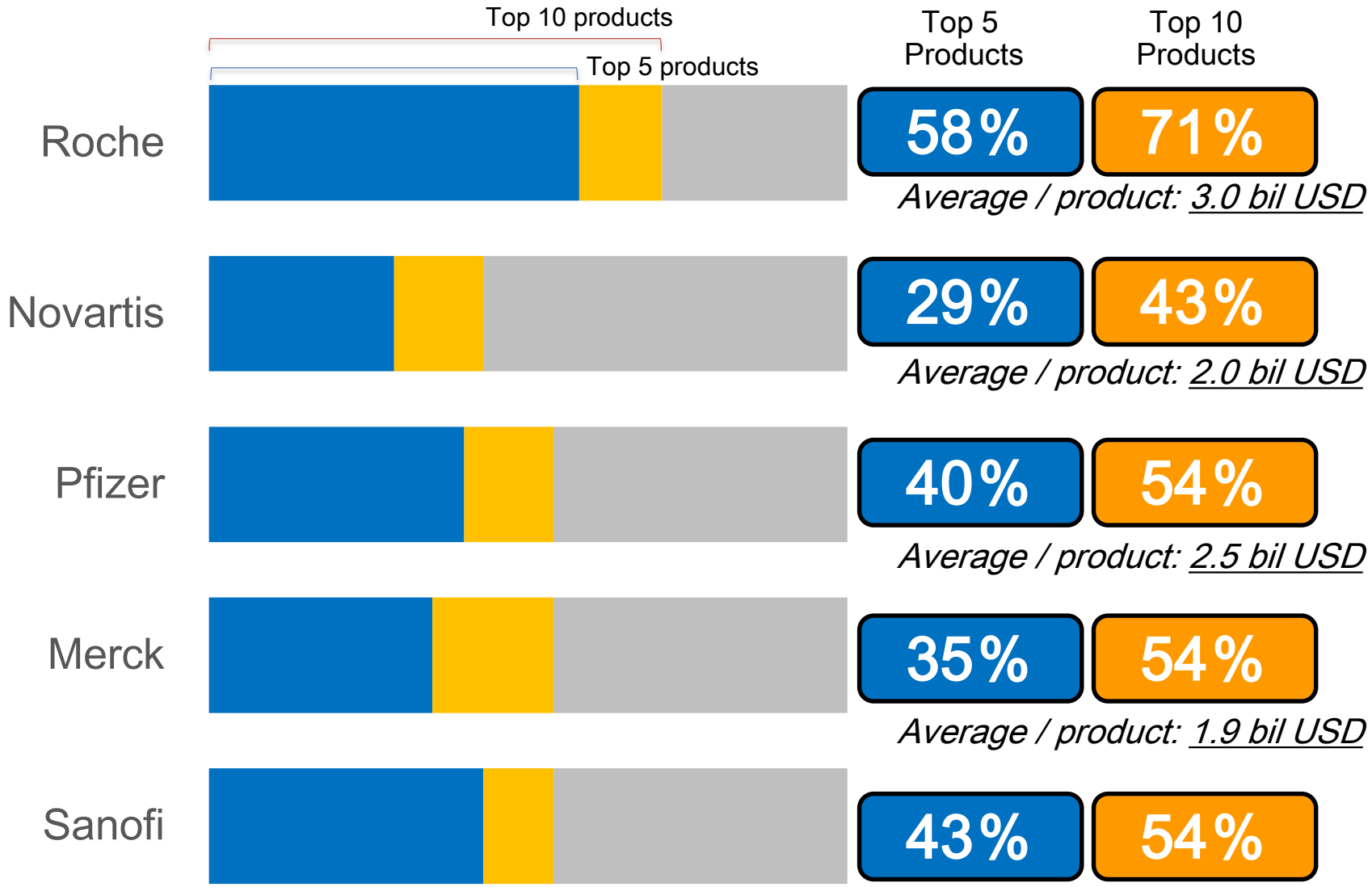

Based on the companies' financial reports

Sales Breakdown of Major Japanese Pharmaceutical Companies

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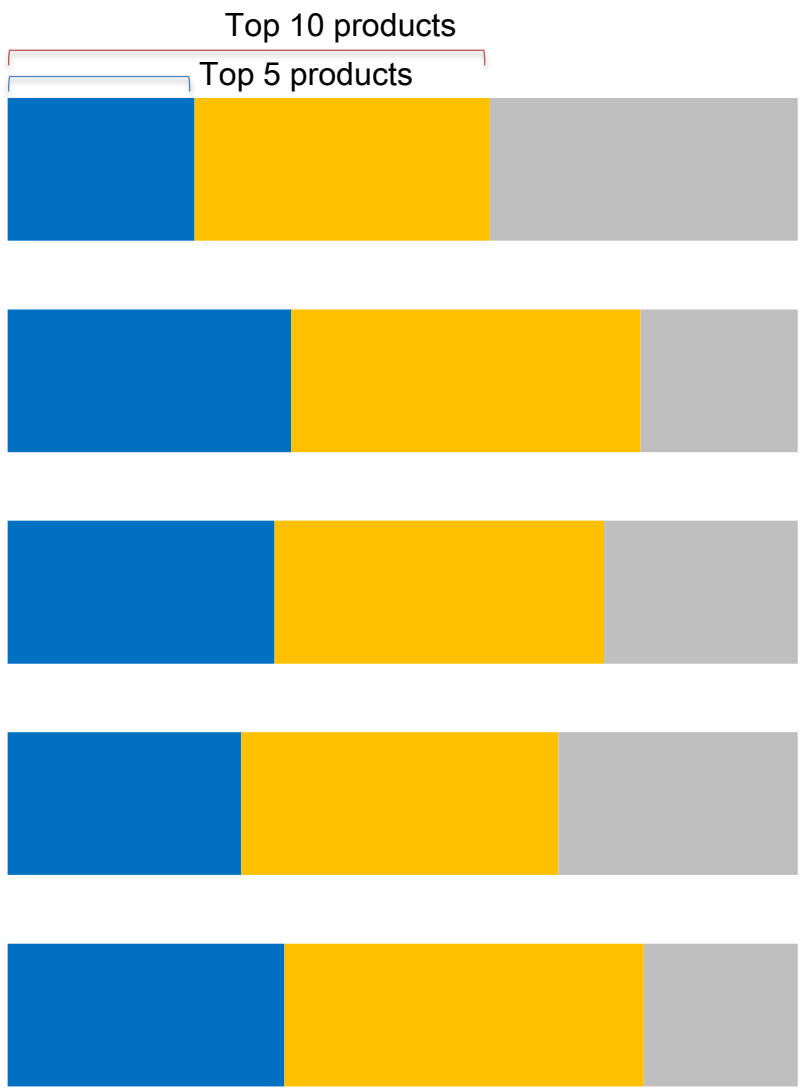

	Top 5 Products	Top 10 Products	
Takeda	31%	49%	Average / product: 88.7 bil JPY
Astellas	56%	69%	Average / product: 94.5 bil JPY
Daiichi Sankyo	51%	63%	Average / product: 61.9 bil JPY
Eisai	42%	57%	Average / product: 31.1 bil JPY
Chugai	54%	70%	Average / product: 34.8 bil JPY

Based on the companies' financial reports

Challenges Facing Japan’s Pharmaceutical Industry and the Direction of Solutions toward the Continuous Creation of Innovation

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Japan's Issues with the Valuation of Innovation

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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

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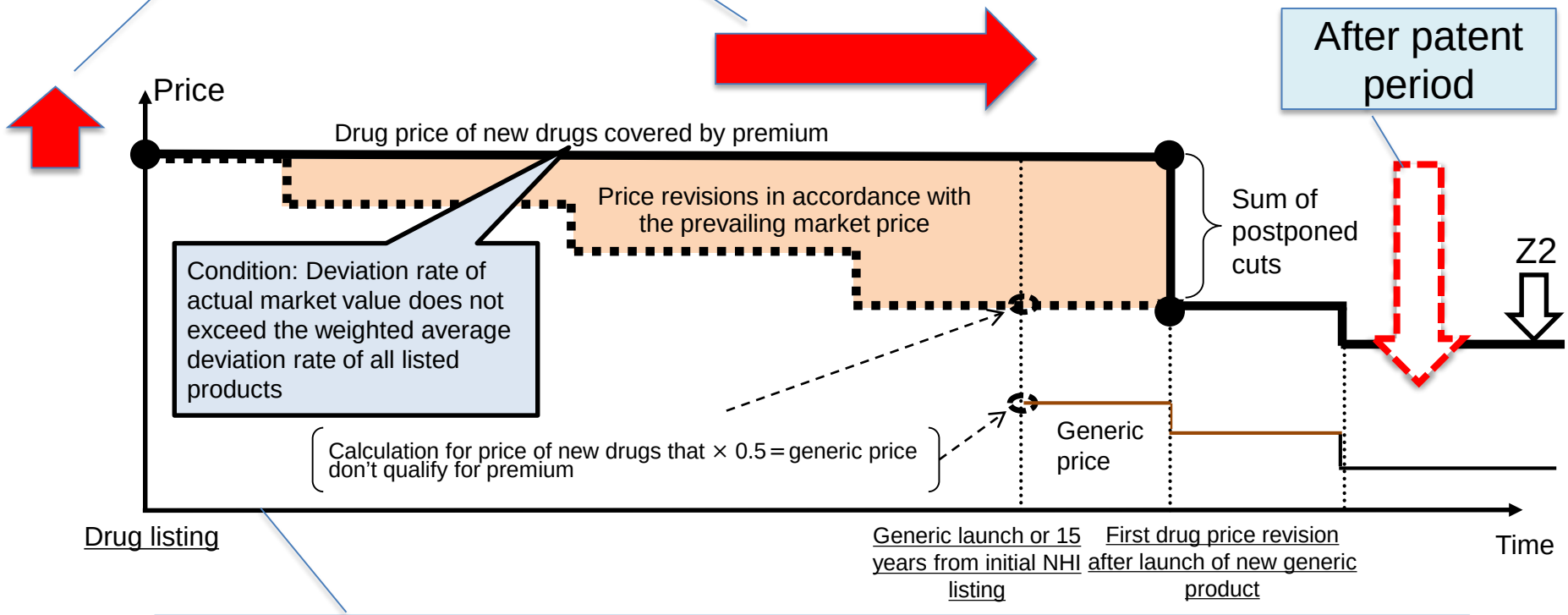
Reform of the Drug Pricing System

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



- 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

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Necessity of Open Innovation

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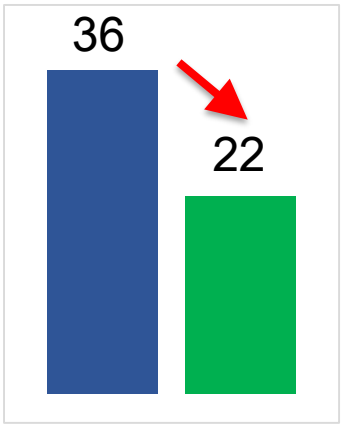
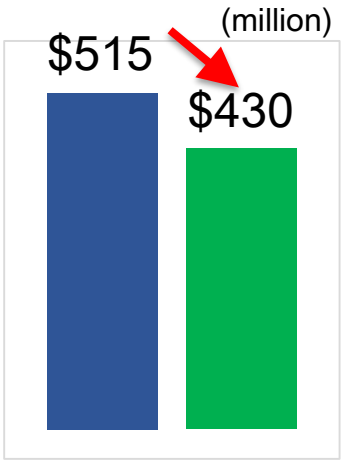
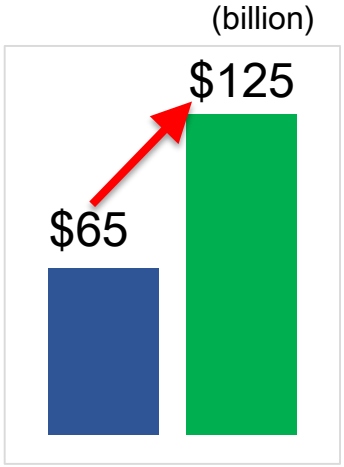
1. Decline of R&D productivity in the pharmaceutical industry



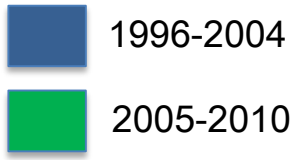
No. of new drugs / year



Average annual sales of products



R&D cost / year



Source：Hewitt, J., et al., Beyond the Shadow of a Drought: The Need for a New Mindset in Pharma R&D, 2011, Health & Life Sciences

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

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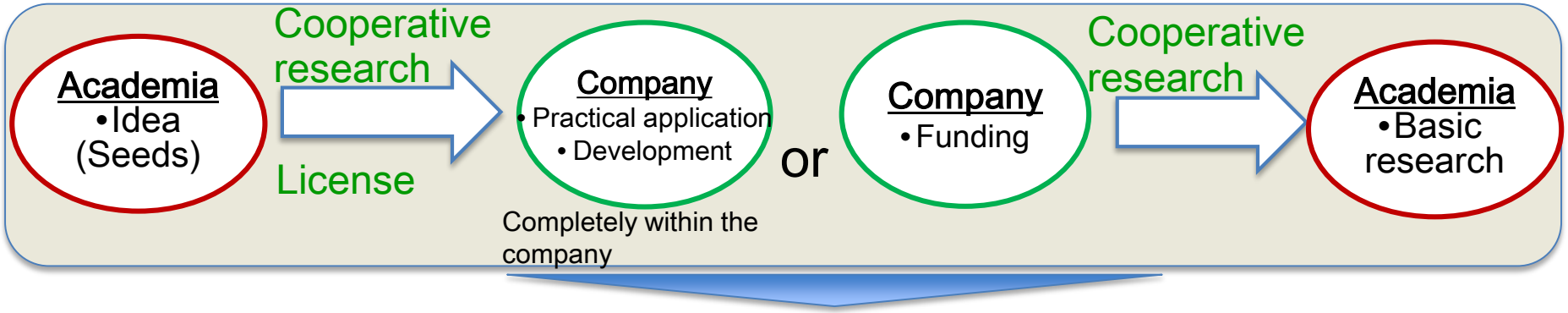
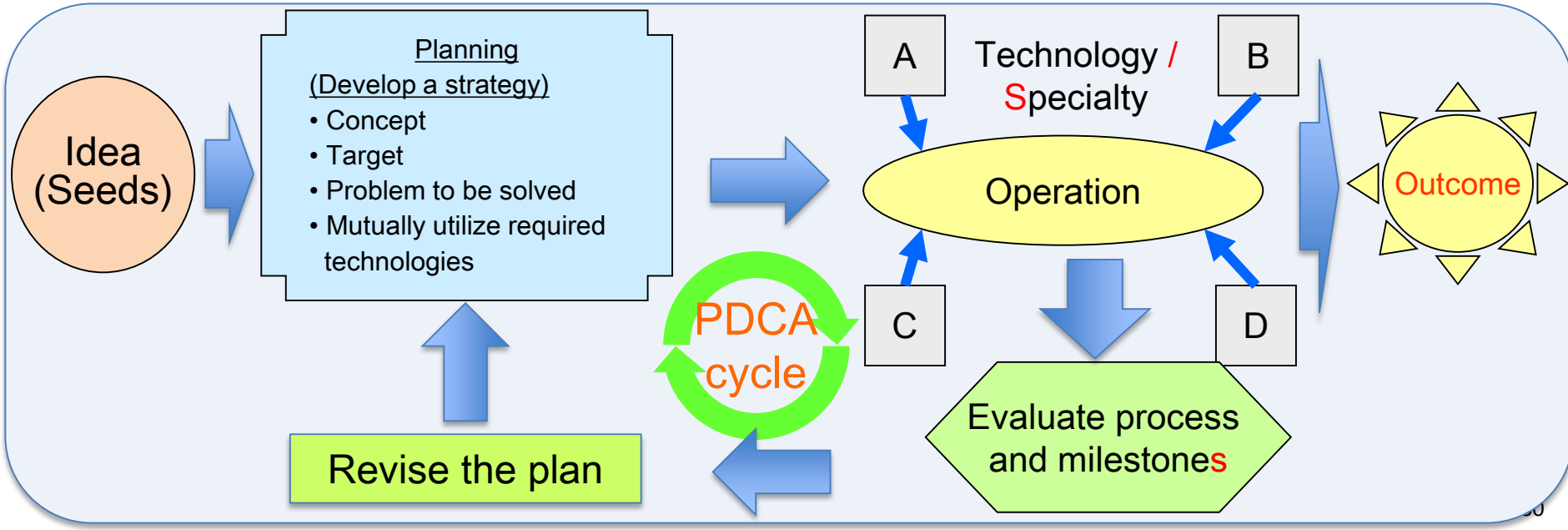
Before



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



Chugai's Technology Driven Approach

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- 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

Next generation (high functionalized) antibody

Small molecule drugs

Middle molecule drugs

Academia

Research network

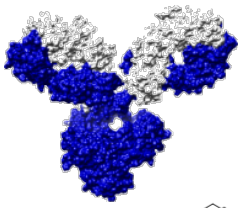
Joint research

Satellite Lab.

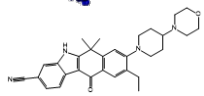
Matching of technology & target

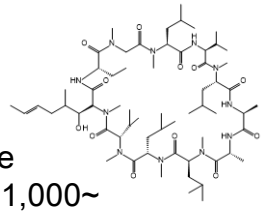
Solution for unmet medical needs

Antibody
mw: 150,000



Small molecule
Alectinib, mw: 482





Middle molecule
Cyclic peptide, mw: ~1,000~

Med-term Comprehensive Collaboration with Osaka University Immunology Frontier Research Center (IFReC)

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- 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	Chugai
Great source of drug seeds with the world's most advanced science in Immunology, Bioimaging & Bioinfomatics	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

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- **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

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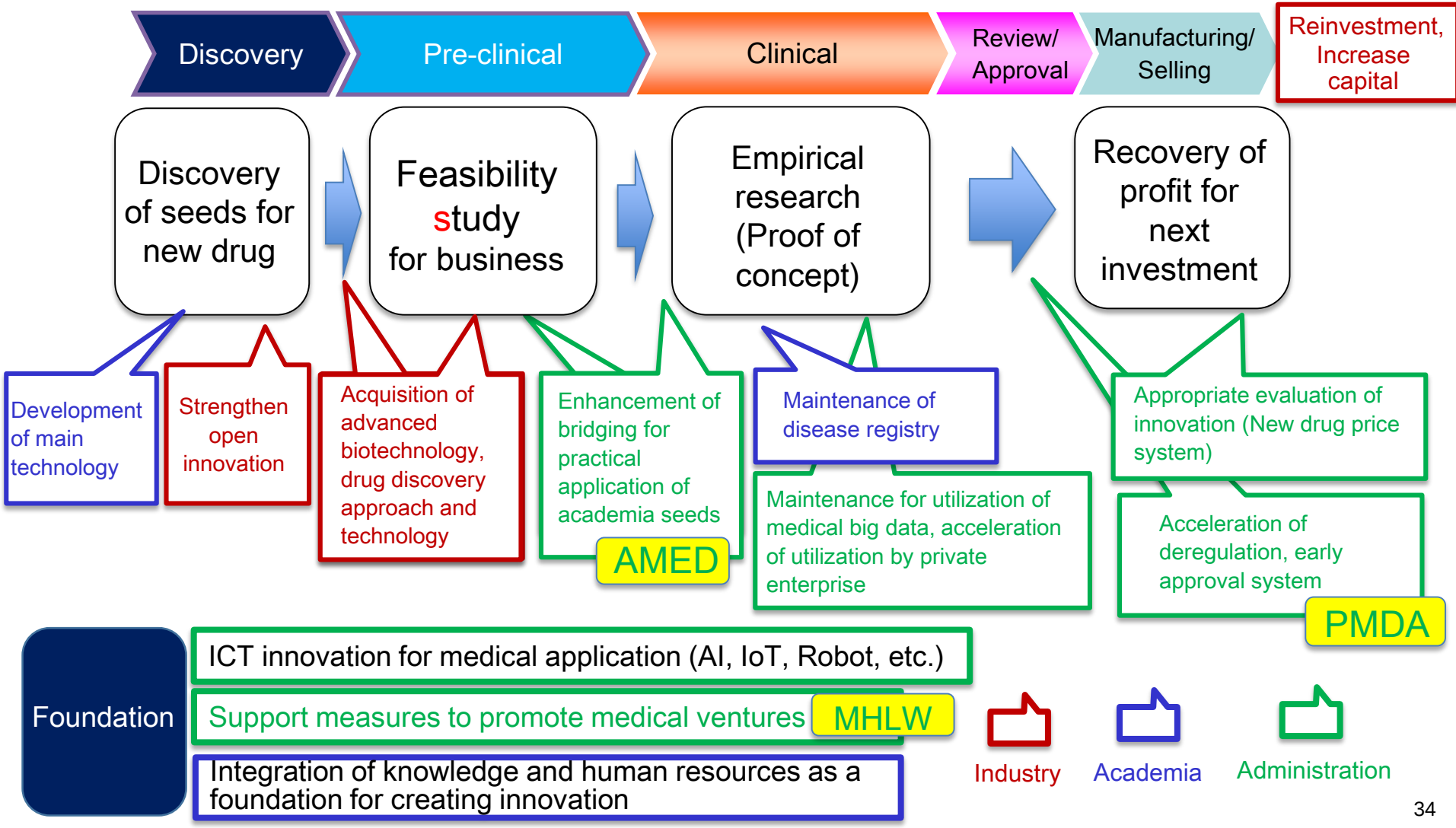

Special Features of U.S. Industry Clusters Leading to the Creation of Innovation

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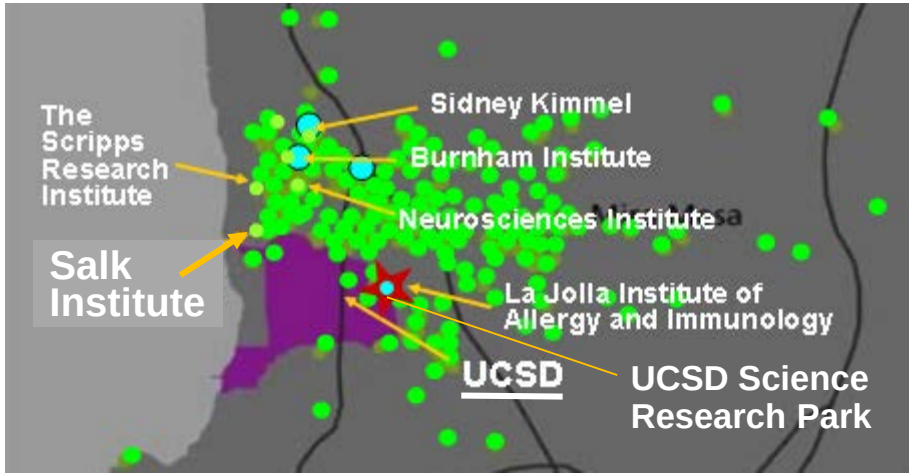
San Diego Research Cluster
(No.1 Bio-cluster in the US)



Life science companies

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.

- **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

Japan as International Arena for Creating Innovation and World Healthcare Center through Innovative Drugs Creation

Innovation all for the patients

CHUGAI

Roche A member of the Roche group

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

Contacts: Corporate Communications Dept.

Media Relations Group

Tel: +81 (0)3-3273-0881 Fax: +81 (0)3-3281-6607
e-mail: pr@chugai-pharm.co.jp

Koki Harada, Hiroshi Araki, Sachiyo Yoshimura,
Chisato Miyoshi, Yayoi Yamada

Innovation all for the patients

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