

Challenges Facing Japan’s Pharmaceutical Industry and Orientation of the Solution

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

December 14, 2016

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.



Today's Agenda

- 1. Overview of the Japanese Market**
- 2. Transition of Drug Discovery**
- 3. Challenges Facing Japan's Pharmaceutical Industry and Orientation of the Solution**
- 4. Chugai's Strategy**

Today's Agenda



1. Overview of the Japanese Market

2. Transition of Drug Discovery

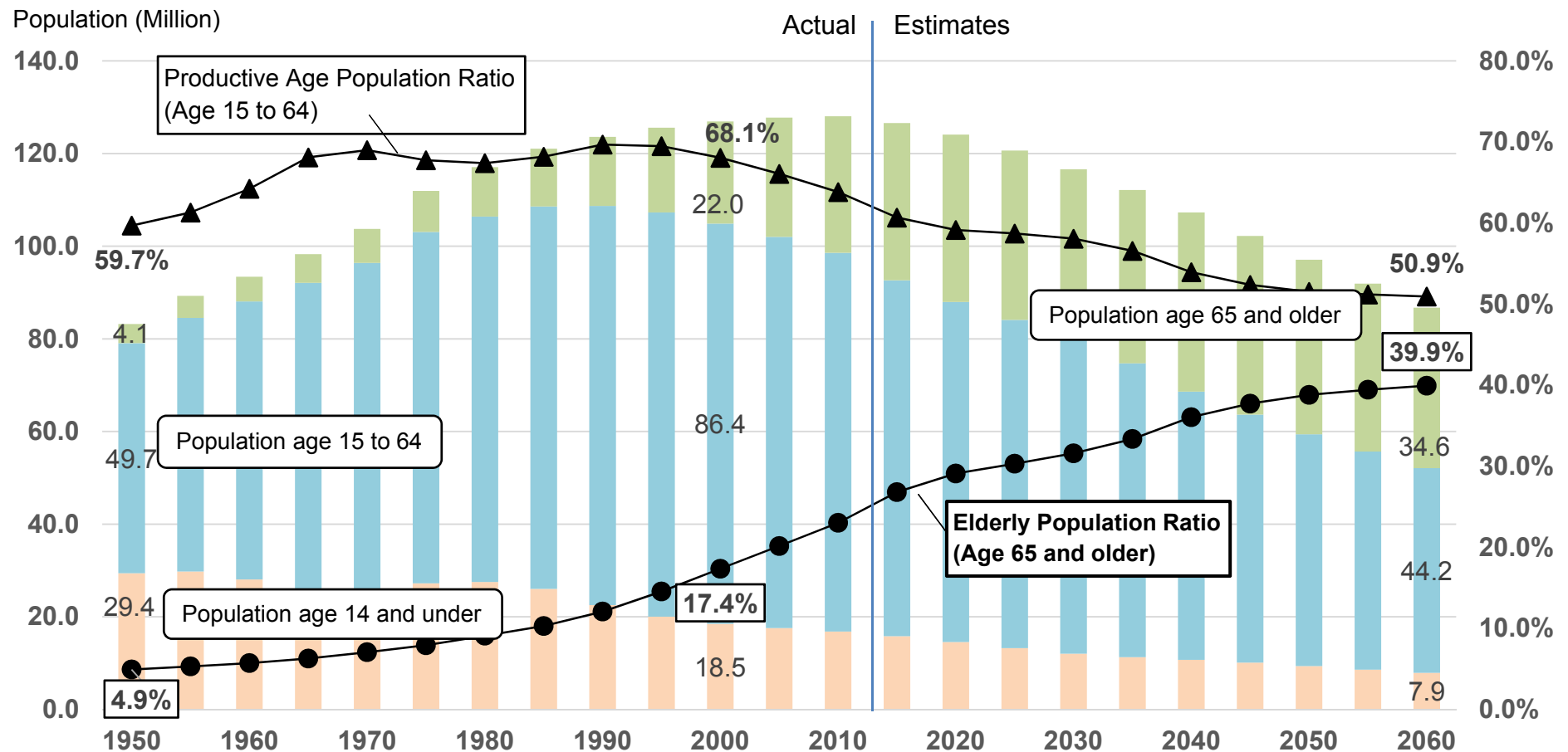
3. Challenges Facing Japan's Pharmaceutical Industry and Orientation of the Solution

4. Chugai's Strategy



Japan is Facing Super-Aging & Depopulation

- Population is predicted to be under 90 Million by 2060.
The elderly population ratio will be close to 40%.



Reference: Actual Figures (until 2010) are based on "Population Estimates" (Statistic Bureau), and Estimated Figures (after 2015) are based on "Population projections for Japan (estimated in January, 2012): Projection based on medium fertility and medium mortality" (IPSS)



Healthcare Cost Containment Makes it Difficult to Value Innovation in Japan

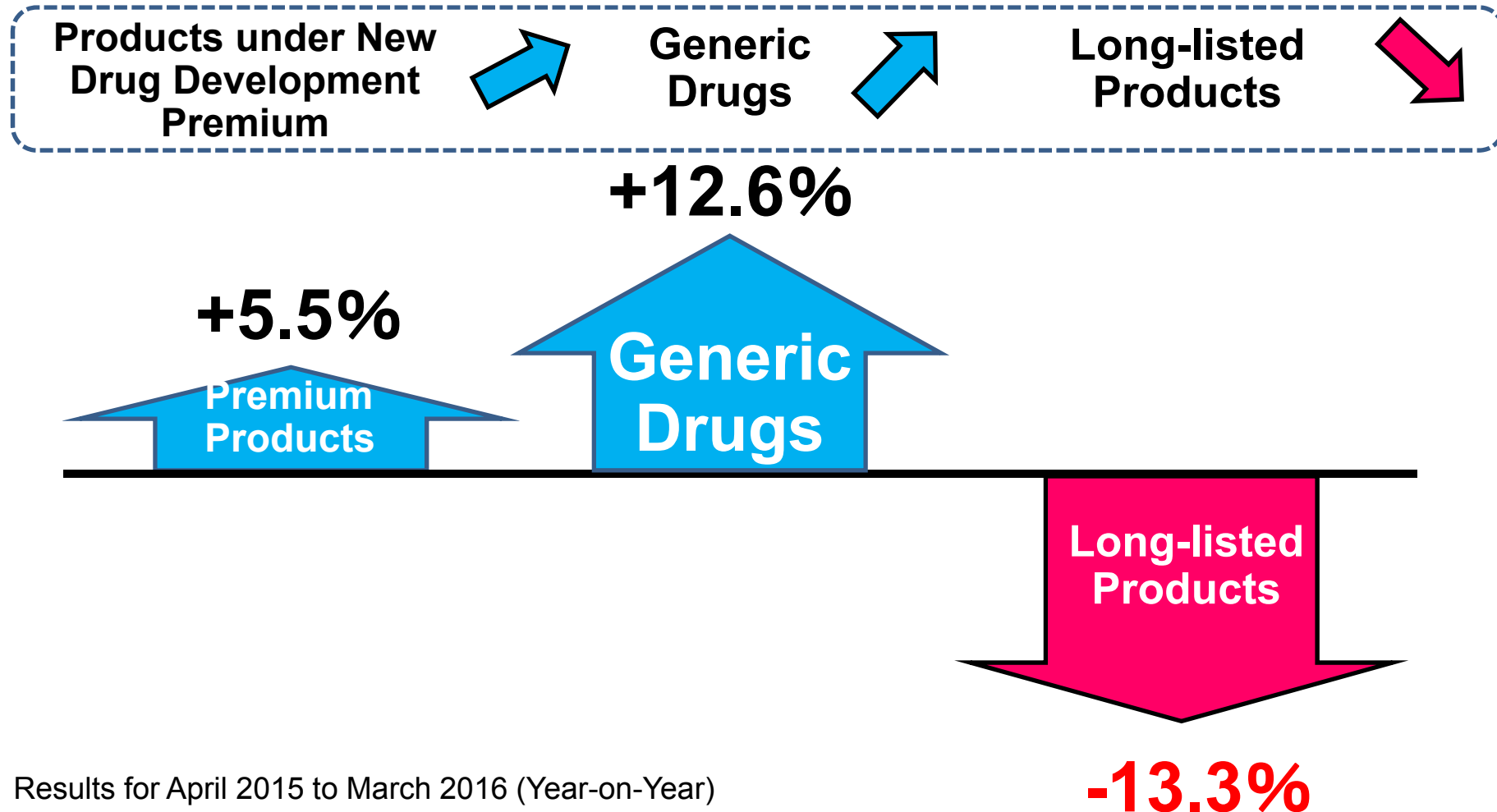
Rapid and Simultaneous Progression of
Aging & Birthrate Decline
(In 2025, baby-boomers will be late elderly)



- Healthcare Cost Containment due to Increased Social Welfare Costs
 - Generic Drugs: Target 80% (By early 2020)
 - Additional Repricing Rule
 - Optimal Usage Promotion Guideline
 - Trial Implementation of Cost Efficiency Analysis



Progress of Domestic Market Category Change



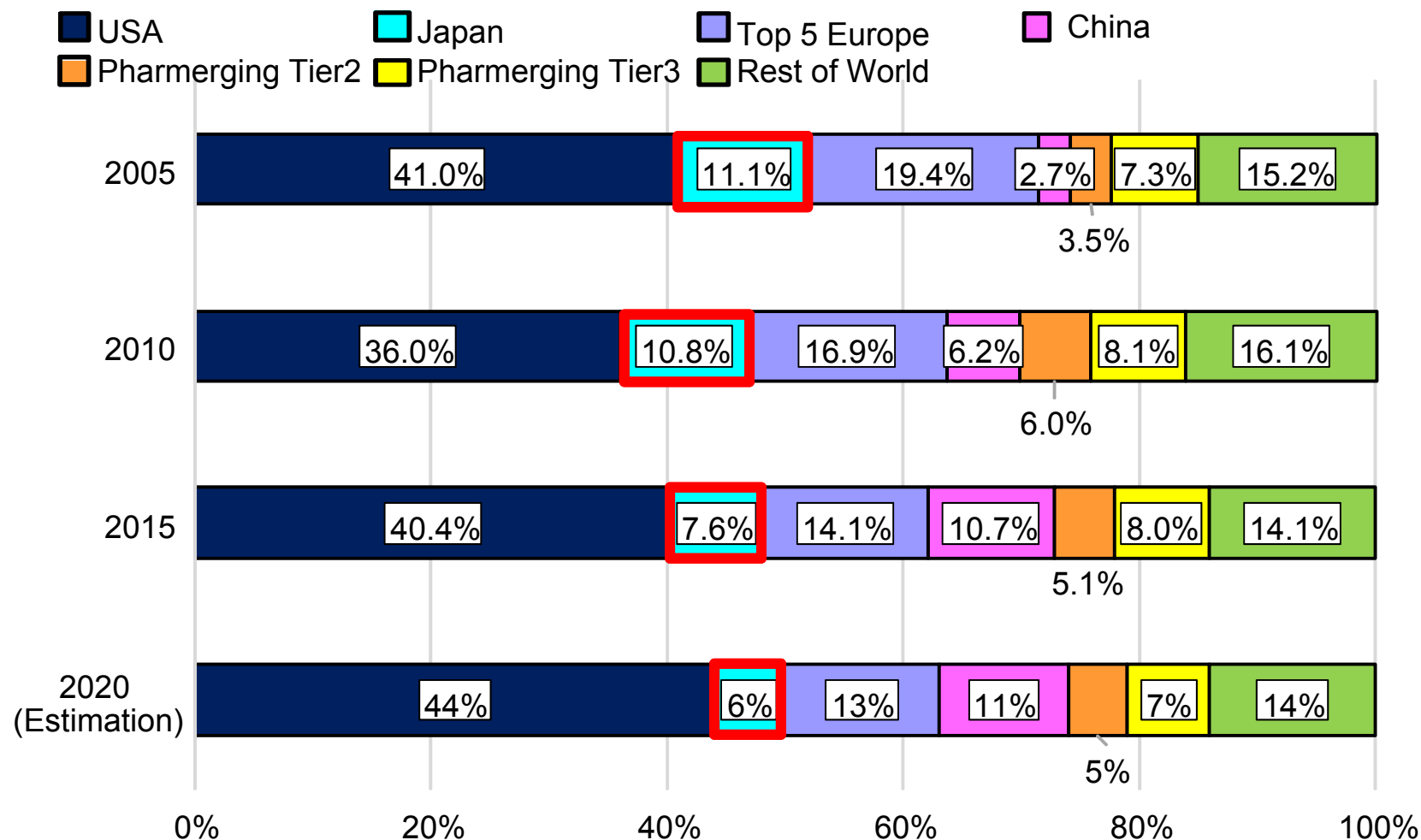
Results for April 2015 to March 2016 (Year-on-Year)
Based on data by Crecon Research

Japan's Share is Shrinking in the Global Pharmaceutical Market

Innovation all for the patients



Roche A member of the Roche group



Top 5 Europe = France, Germany, Italy, Spain, UK

Pharmerging Tier2 = Brazil, India, Russia

Pharmerging Tier3 = Algeria, Argentina, Columbia, Egypt, Indonesia, Mexico, Nigeria, Pakistan, Poland, Romania, Saudi Arabia, South Africa, Thailand, Turkey, Ukraine, Venezuela, Vietnam

Source: Copyright ©2016 QuintilesIMS. IMS Japan Conference2016 "Global Forecast and Opportunities for Japanese Pharma." Reprinted with permission (IMS Market Prognosis, Ex-manufacture price excluding discounts/rebates. Audited and unaudited)



Today's Agenda

1. Overview of the Japanese Market
- 2. Transition of Drug Discovery**
3. Challenges Facing Japan's Pharmaceutical Industry and Orientation of the Solution
4. Chugai's Strategy



Japan's Advanced Science Level

- Number of Nobel Laureates since 2000 is Second to the U.S. (17 people)

Nobel Laureates with a Deep Relationship to Drug Development

1987	2001	2008	2010	2012	2015	2016
Prof. Susumu Tonegawa Genetic mechanism producing antibody diversity	Prof. Ryoji Noyori Asymmetric synthesis by chiral catalyst	Prof. Osamu Shimomura Green fluorescent protein	Prof. Akira Suzuki / Prof. Ei-ichi Negishi Cross coupling	Prof. Shinya Yamanaka iPS cell formation	Prof. Satoshi Omura Method for treating infectious disease	Prof. Yoshinori Ohsumi Mechanisms for autophagy
Physiology or Medicine	Chemistry			Physiology or Medicine		

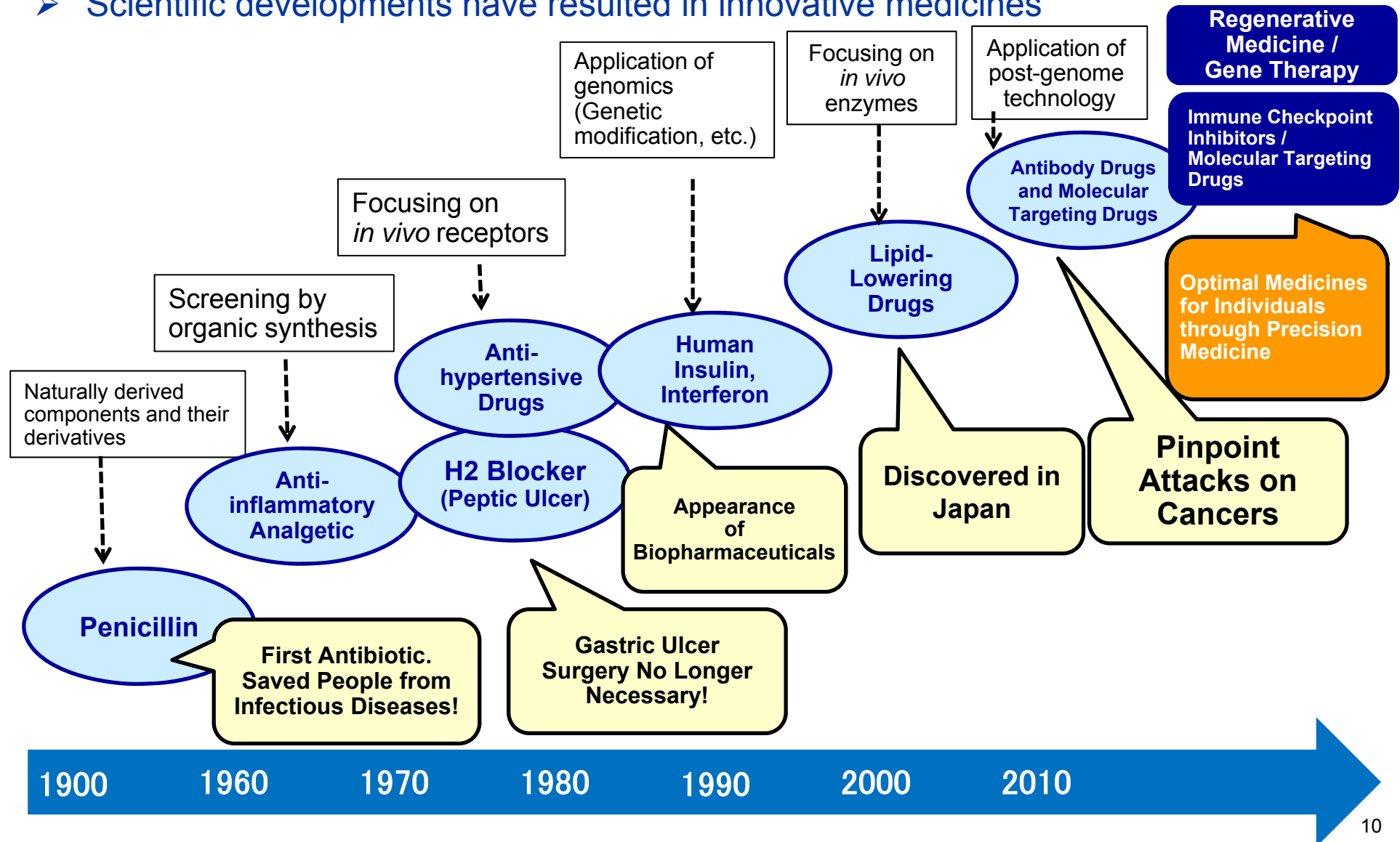
History of Pharmaceutical Innovations that Changed the World

- Scientific developments have resulted in innovative medicines

Innovation all for the patients



Roche A member of the Roche group



Small Molecule Drug Discovery Underpinned Japan's Pharmaceutical Industry until Early 2000s



Blockbuster Product Originated in Japan

1997: 3 Products

Million USD

Rank	Product	Developer	Sales
3	Mevalotin	Sankyo	2,748
8	Gaster	Yamanouchi	1,708
15	Leuplin	Takeda	1,181



2004: 13 Products

Rank	Product	Developer	Sales
7	Takepron	Takeda	4,740
9	Mevalotin	Sankyo	4,252
21	Cravit	Daiichi	2,777
27	Blipress	Takeda	2,358
28	Harnal	Yamanouchi	2,323
33	Leuplin	Takeda	2,093
37	Pariet	Eisai	2,030
46	Aricept	Eisai	1,889
44	Actos	Takeda	1,873
48	Epogin	Chugai	1,840
85	Clarith	Taisho	1,634
75	Prograf	Fujisawa	1,194
78	Campto	Yakult	1,160

Biopharmaceutical

Biopharmaceutical Era Started in Western Countries in Late 1990's

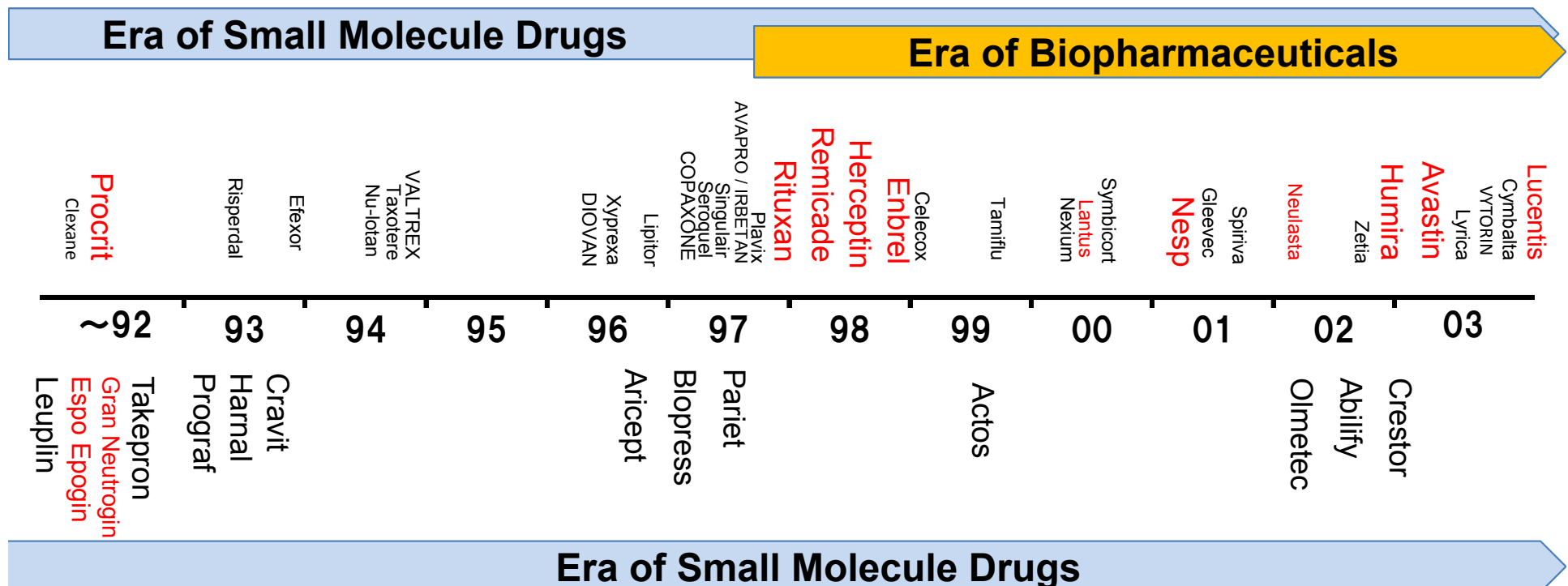
Innovation all for the patients



Roche A member of the Roche group

- European/US companies started to develop major biopharmaceutical products from the latter half of 1990's while the Japanese Pharma kept focused on small molecule drugs

Products Developed by European / American Companies



Products Developed by Japanese Companies

Red: biopharmaceutical

Eight out of the World's Top 10 Products are Biopharmaceuticals Now

Innovation all for the patients



Roche A member of the Roche group

- Japanese companies focusing on small molecule drugs have been left in the dust of western peers

World Drug Sales Ranking

2004

	Product Name	Disease for treatment	Company	Sales (\$M)
1	Lipitor	hyperlipidemia	Pfizer/Yamanouchi	11,692
2	Epogen/Procrit/Espo	renal anemia	Amgen/J&J/Kirin/Sankyo	6,701
3	Plavix	Anti-platelet	SanofiA/BMS	5,638
4	Zocor(Ripobasu)	hyperlipidemia	Merck	5,197
5	Norvasc/Amlodin	hypertension	Pfizer/Sumitomo	5,019
6	Seretide/Advair	asthma	GSK	4,741
7	Takepron/Prevacid	ulcer	Takeda/TAP/Abbott/Wyeth	4,740
8	Zyprexa	schizophrenia	Eli Lilly	4,420
9	Mevalotin/Pravachol	hyperlipidemia	Sankyo/BMS	4,252
10	Nexium	ulcer	AstraZeneca	3,883
21	Cravit/Levaquin	antibiotics	Daiichi/J&J/SanofiA	2,777
27	Biopress/Atacand	hypertension	Takeda/AstraZeneca	2,358
28	Harnal/Flomax	prostatomegaly	Yamanouchi/BI	2,323
33	Luprin/Lupron	prostatic cancer	Takeda/TAP/Abbott	2,093
37	Pariet/Aciphex	ulcer	Eisai/J&J	2,030
43	Aricept	alzheimer	Eisai/Pfizer	1,889
44	Actos	diabetes	Takeda/Eli Lilly	1,873
45	Epogin/Neorecormon	renal anemia	Chugai/Roche	1,840
52	Clarith/Biaxin	infection	Taisho/Abbott/Dainippon	1,634
75	Prograf	immunosuppression	Fujisawa	1,193
78	Campto/Camptosar	cancer	Yakult/Pfizer/Daiichi	1,160

2015

	Product Name	Disease for treatment	Company	Sales (\$M)
1	Harvoni + Sovaldi	HCV	Gilead Sciences	19,140
2	Humira	rheumatoid arthritis	Abbvie/Eisai	14,357
3	Enbrel	rheumatoid arthritis	Amgen/Pfizer/Takeda	9,036
4	Remicade	rheumatoid arthritis	J&J/Merck/TanabeM	8,931
5	Mabether/Rituxan	cancer	Roche/Chugai	8,675
6	Lantus	diabetes/insulin	Sanofi	7,090
7	Avastin	cancer	Roche/Chugai	6,959
8	Herceptin	cancer	Roche/Chugai	6,807
9	Januvia/Glactiv	diabetes/DPP4	Merck/Ono/Almirall	6,324
10	Prevenar	vaccine	Pfizer	6,245
12	Crestor	hyperlipidemia	Shionogi/AstraZeneca	5,775
26	Gilenya	multiple sclerosis	TanabeM/Novartis	3,205
31	Abilify	schizophrenia	Otsuka/BMS	2,884
43	Benicar/Olmetec	hypertension	Daiichi Sankyo	2,357
44	Tivicay/Triumeq	HIV	Shionogi/ViiV Healthcare	2,351
56	Actemra/RoActemra	rheumatoid arthritis	Chugai/Roche	2,019
65	Leuplon/Lupron	cancer	Takeda/Abbvie	1,858
72	Prograf	organ rejection	Astellas	1,689
88	Invokana/Canaglu	diabetes/SGLT2	TanabeM/J&J	1,479
115	Vesicare	overactive bladder	Astellas	1,125
118	Opdivo	cancer	Ono/BMS	1,118
126	Biopress/Atacand	hypertension	Takeda/AstraZeneca	1,062
137	Latuda	schizophrenia	Sumitomo Dainippon	1,002

Copyright © 2016 QuintilesIMS. Pharma Future June 2005



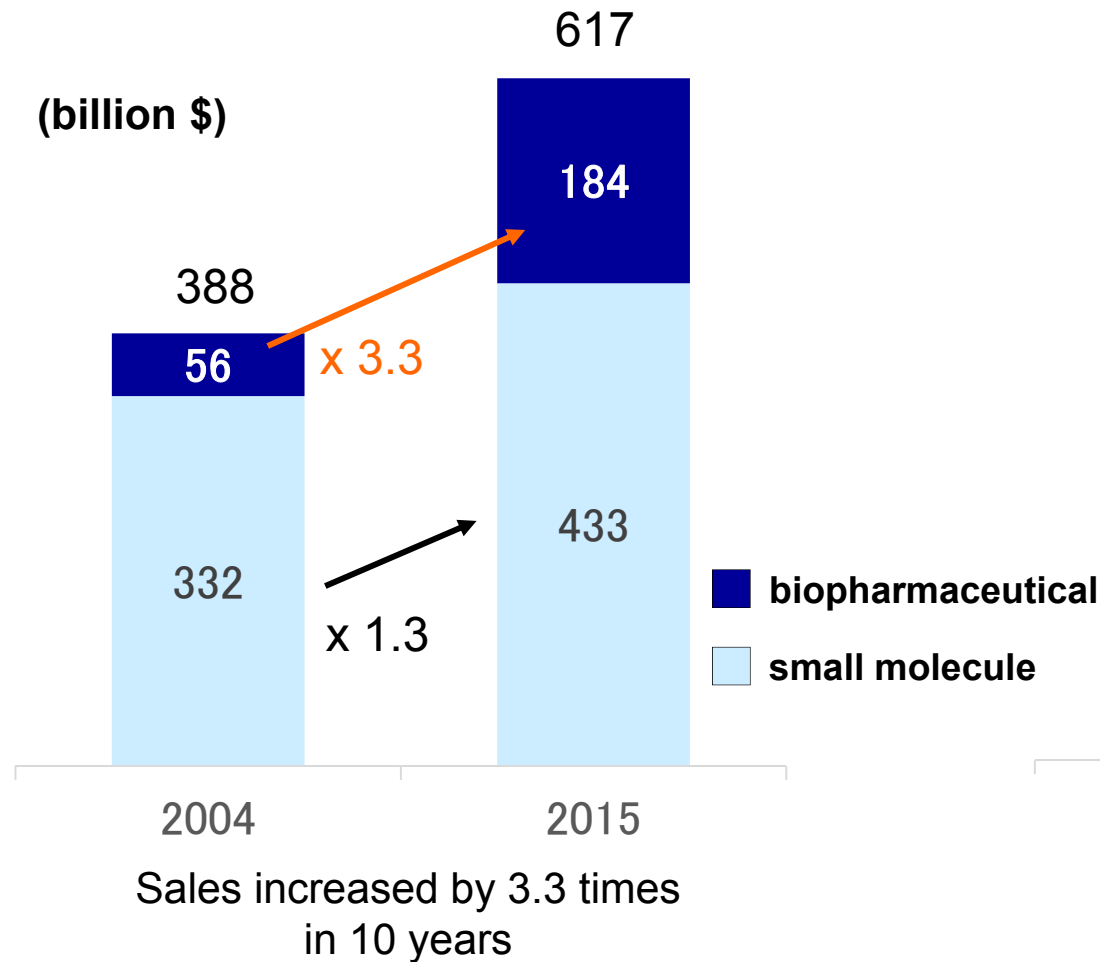
: Biopharmaceuticals Red: New drugs originated in Japan

The above tables include the world's top 10 medicines and new medicines developed in Japan outside the top 10.

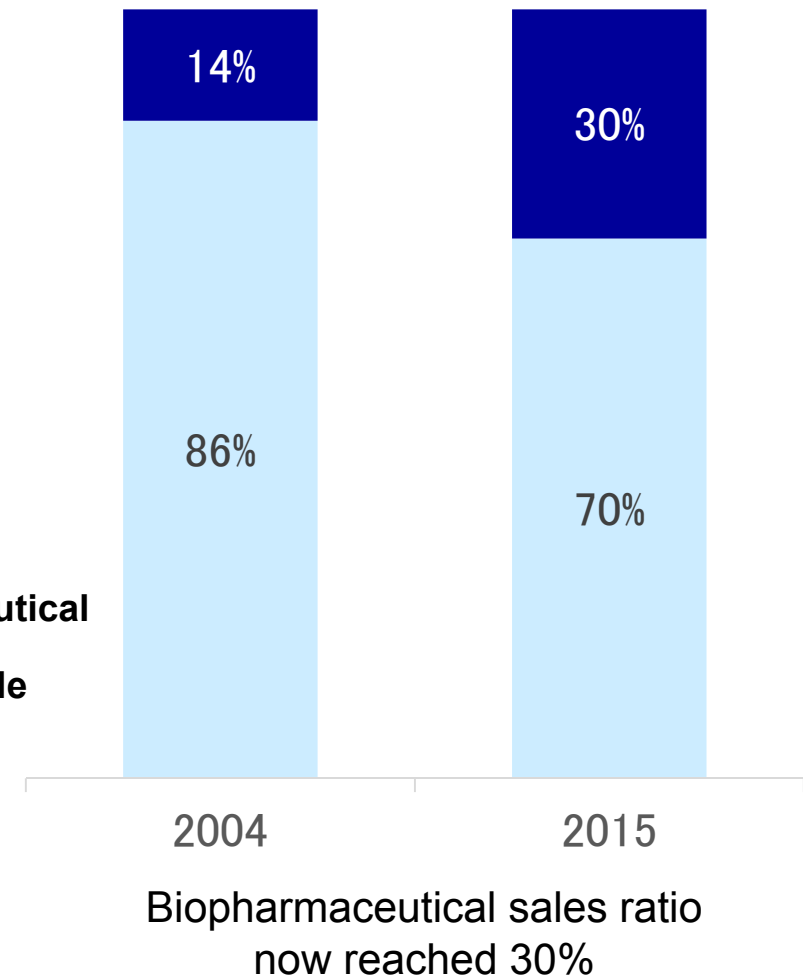
Global Growth of Biopharmaceuticals



Sales of biopharmaceuticals



Sales ratio of biopharmaceuticals





Today's Agenda

1. Overview of the Japanese Market
2. Transition of Drug Discovery
- 3. Challenges Facing Japan's Pharmaceutical Industry and Orientation of the Solution**
4. Chugai's Strategy



R&D Cost in Genomic Drug Discovery Era

- R&D costs per product until approval was 2,558 million USD from 2000s to early 2010s, increased by 2.45 times compared to the previous decade

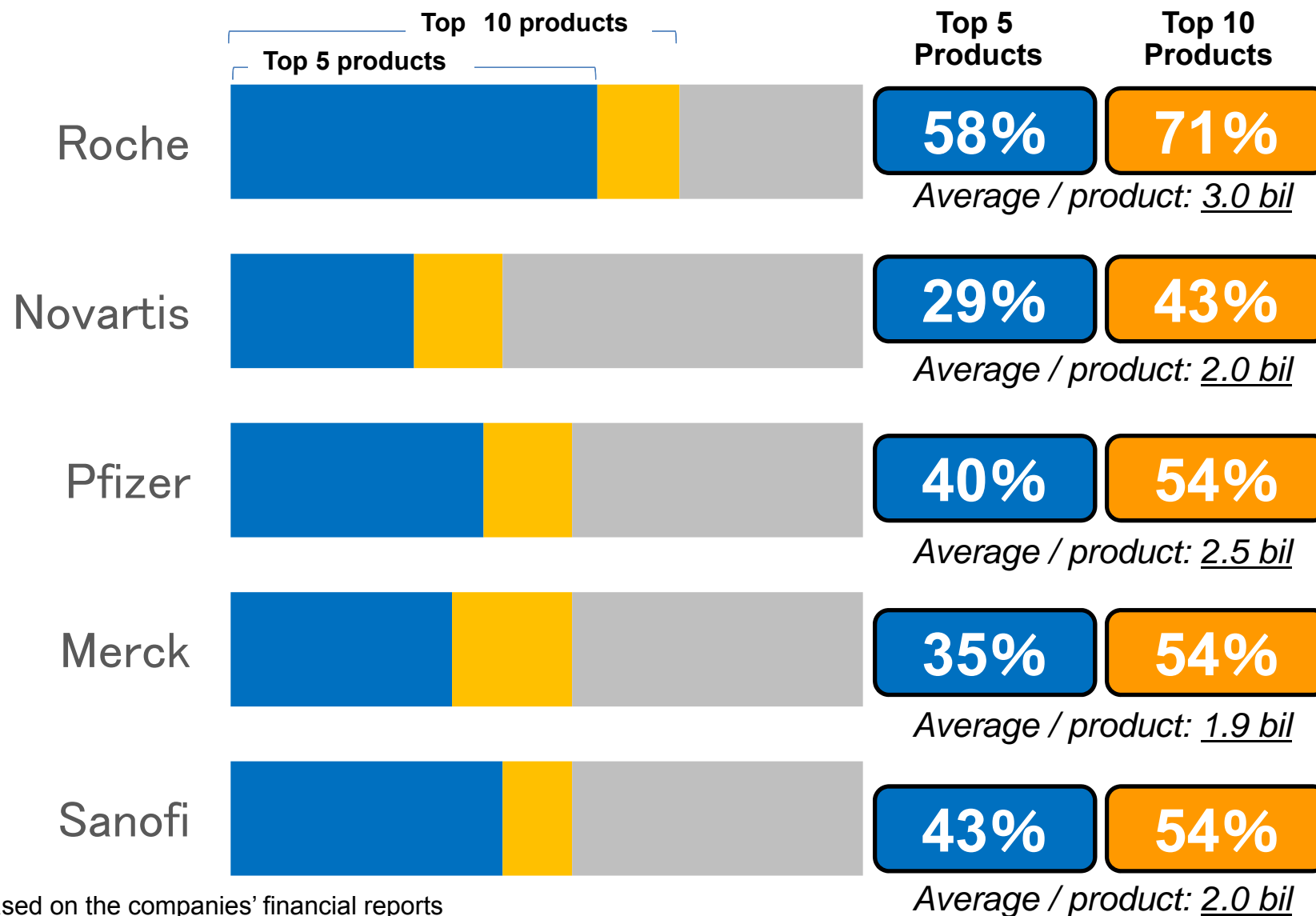
(mil. US \$)

	1970s	1980s	1990s – early 2000s	2000s – early 2010s
Pre-human	109	278	436	1,098 x 2.52
Clinical	70	135	608	1,460 x 2.40
Total	179	413	1,044	2,558 x 2.45

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

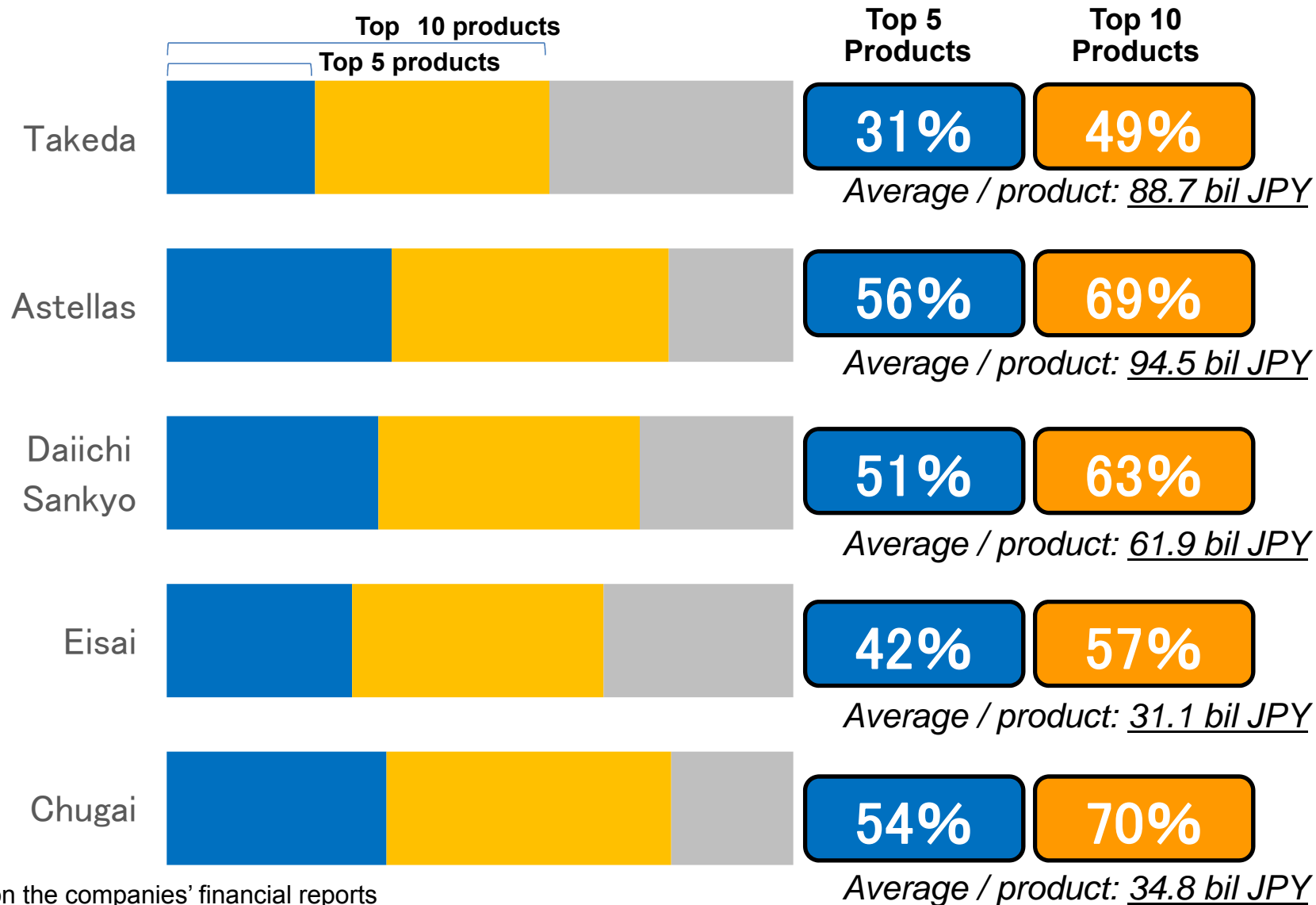


Major Pharma Companies Rely Heavily on Top Sellers





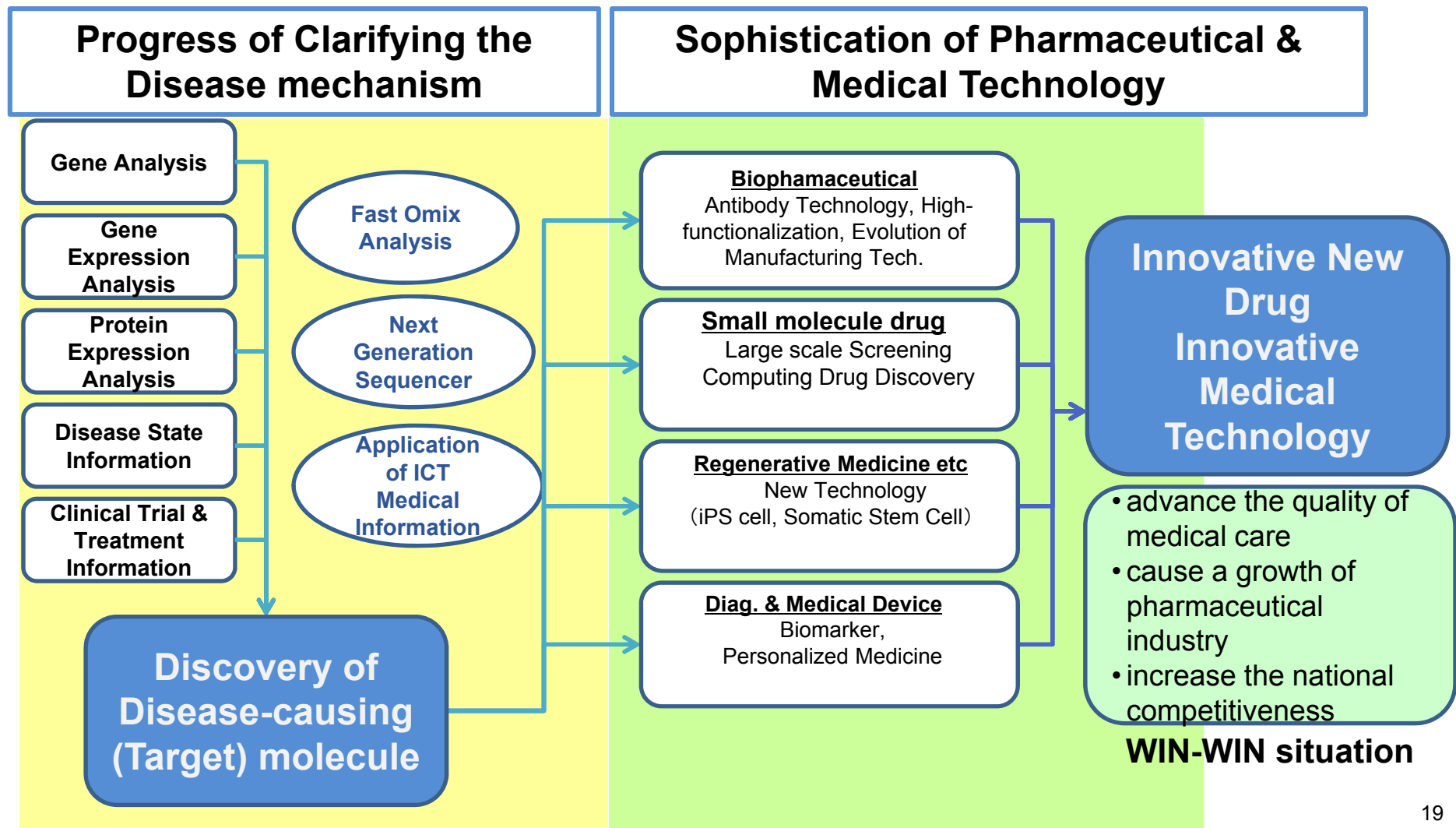
Sales Breakdown of Major Japanese Pharmaceutical Companies





Genomic Drug Discovery Approach and Soaring Costs

- Various technologies and multiple discovery approaches require high costs



Sales Ranking of Pharmaceutical Companies and R&D expenditure

Innovation all for the patients



Roche A member of the Roche group

- R&D expenses of Japanese companies are far below 5 billion USD, the required level for global growth

Pharma Rx Sales Ranking		Company	US \$ Million			Pharma Rx Sales Growth Rate	R&D Expenditure % to Total Sales
2015	2014		Pharma Rx Sales	Total Sales	R&D Expenditure		
1	2	Pfizer	44,547	48,851	7,690	-2.5%	15.7%
2	1	Novartis	43,415	49,414	8,426	-7.8%	17.1%
3	3	Roche	41,071	50,124	8,711	1.2%	17.4%
4	4	Sanofi	34,804	38,324	5,638	9.4%	14.7%
5	5	Merck	34,782	39,498	7,180	-3.5%	18.2%
6	9	Gilead	32,639	32,639	3,014	31.1%	9.2%
7	6	J&J	31,430	70,074	6,821	-2.7%	9.7%
8	7	GSK	27,754	36,578	4,339	-4.4%	11.9%
9	8	AstraZeneca	24,708	24,708	5,997	-5.3%	24.3%
10	11	AbbVie	22,859	22,859	4,285	14.5%	18.7%
17	17	Takeda	13,681	14,998	2,870	2.1%	19.1%
19	19	Astellas	11,391	11,391	1,873	10.1%	16.4%
24	21	Otsuka HD	8,612	11,992	1,668	-9.1%	13.9%
25	24	Daiichi Sankyo	7,742	8,185	1,732	7.0%	21.2%
36	33	Eisai	4,263	4,546	1,424	1.0%	31.3%
37	36	Chugai	4,139	4,139	680	8.2%	16.4%
41	38	Mitsubishi Tanabe	3,551	3,582	625	4.2%	17.4%
45	41	Sumitomo Dainippon	2,996	3,346	673	9.2%	20.1%

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

Innovation all for the patients



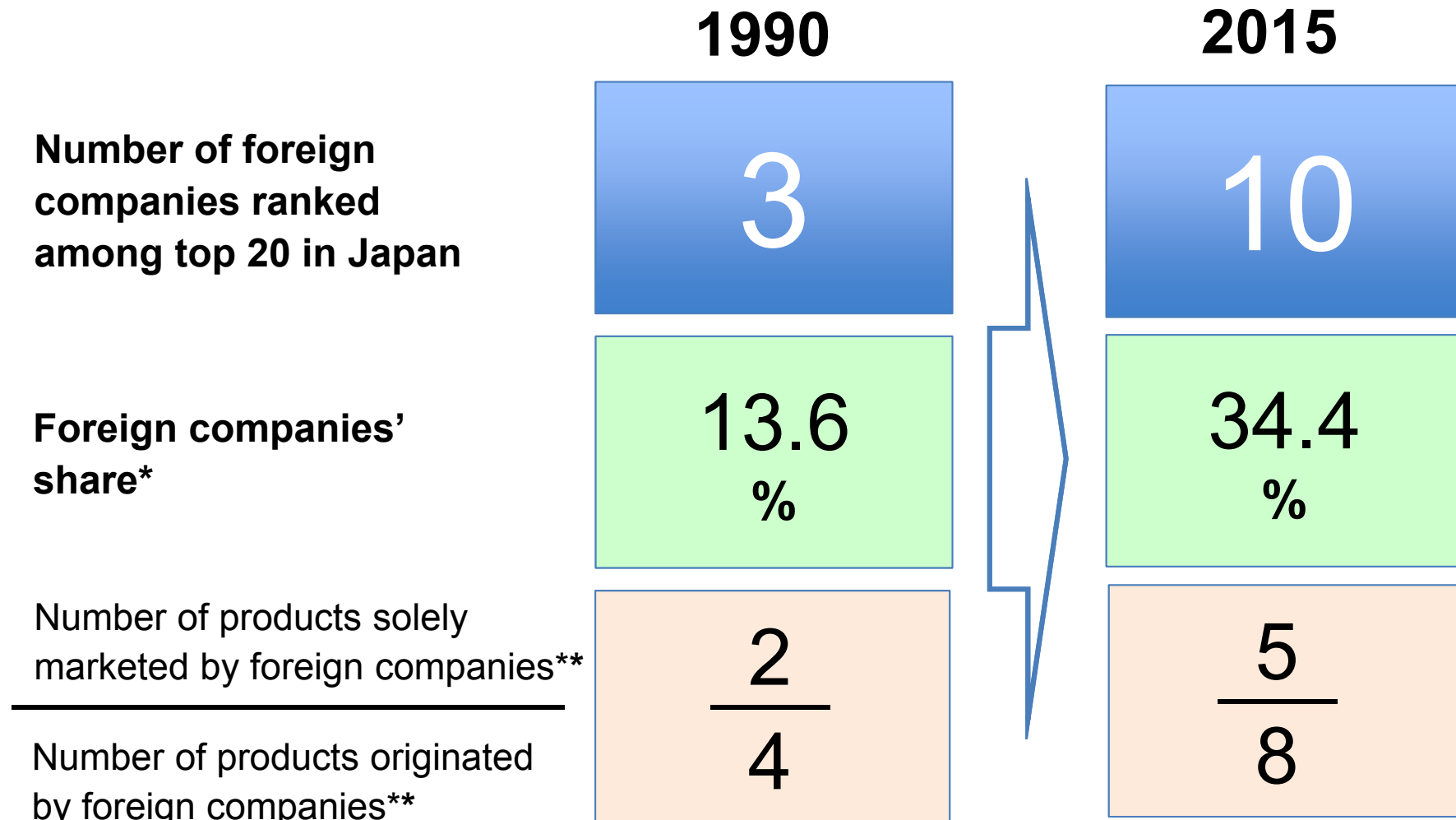
Roche A member of the Roche group

- 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 to 10 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%)



Increasing Presence of Foreign Companies in the Japanese Market



*Total share of foreign companies ranked among top 100 in the Japanese market

**Number of products ranked among top 10 in Japanese market



Closure of R&D Base in Japan by Foreign Companies

2004	Bayer closed Kyoto Research Center
2006	Merck & Co. closed research centers for synthesis and formulation
2007	Bayer Schering closed Kobe Research Center
2008	Novartis closed Tsukuba Research Center Merck & Co. closed Tsukuba Research Center
2009	GSK closed Tsukuba Research Center Pfizer closed research center

Newly established R&D base in Asia

- ◆ GSK: Singapore (2005), Shanghai (2007)
- ◆ Novartis: Singapore (2005), Shanghai (2007)
- ◆ AstraZeneca: India (2003), Shanghai (2009)
- ◆ Roche: Shanghai (2004)
- ◆ Bayer Schering: Beijing (2009)



Foreign Companies Taking Seeds of Drugs in Japan

Eli Lilly

Efforts	Achievements
Holding the matching event "Innovation Day Japan" for Japanese academia (Sept. 2015, Sept. 2016) for joint discovery research	<ul style="list-style-type: none"> ➤ Joint research with National Cancer Center (Progressive stomach cancer) ➤ Joint research with Kanazawa Medical University (Intractable stomach cancer) ➤ Joint research with Osaka University (Obesity prevention)
Evaluation of Japanese drug seeds (Effectiveness / Safety) via the Web	<ul style="list-style-type: none"> ➤ Developed data discussions with 15 universities (Parkinson's Disease, etc.)

Bayer

Efforts	Achievements
Establishment of Open Innovation Center in Japan (June 2014), strengthening networks with academia, etc.	<ul style="list-style-type: none"> ➤ Joint research with Kyoto University (Drug discovery in major therapeutic areas)
Establishment of a Japanese version of publicly recruited research grant program	<ul style="list-style-type: none"> ➤ Adoption of research project from Kobe University (July 2015)

Other Companies and Major Joint Research Partners

- ✓ **Boehringer Ingelheim Japan** : Kyoto University CiRA (From Mar. 2014)
- ✓ **GlaxoSmithKline** : Tokyo Metropolitan Geriatric Hospital (From Jan. 2015)
- ✓ **Pfizer** : National Cancer Center (From Mar. 2015)
- ✓ **MSD** : National Cancer Center (From Jun. 2015)

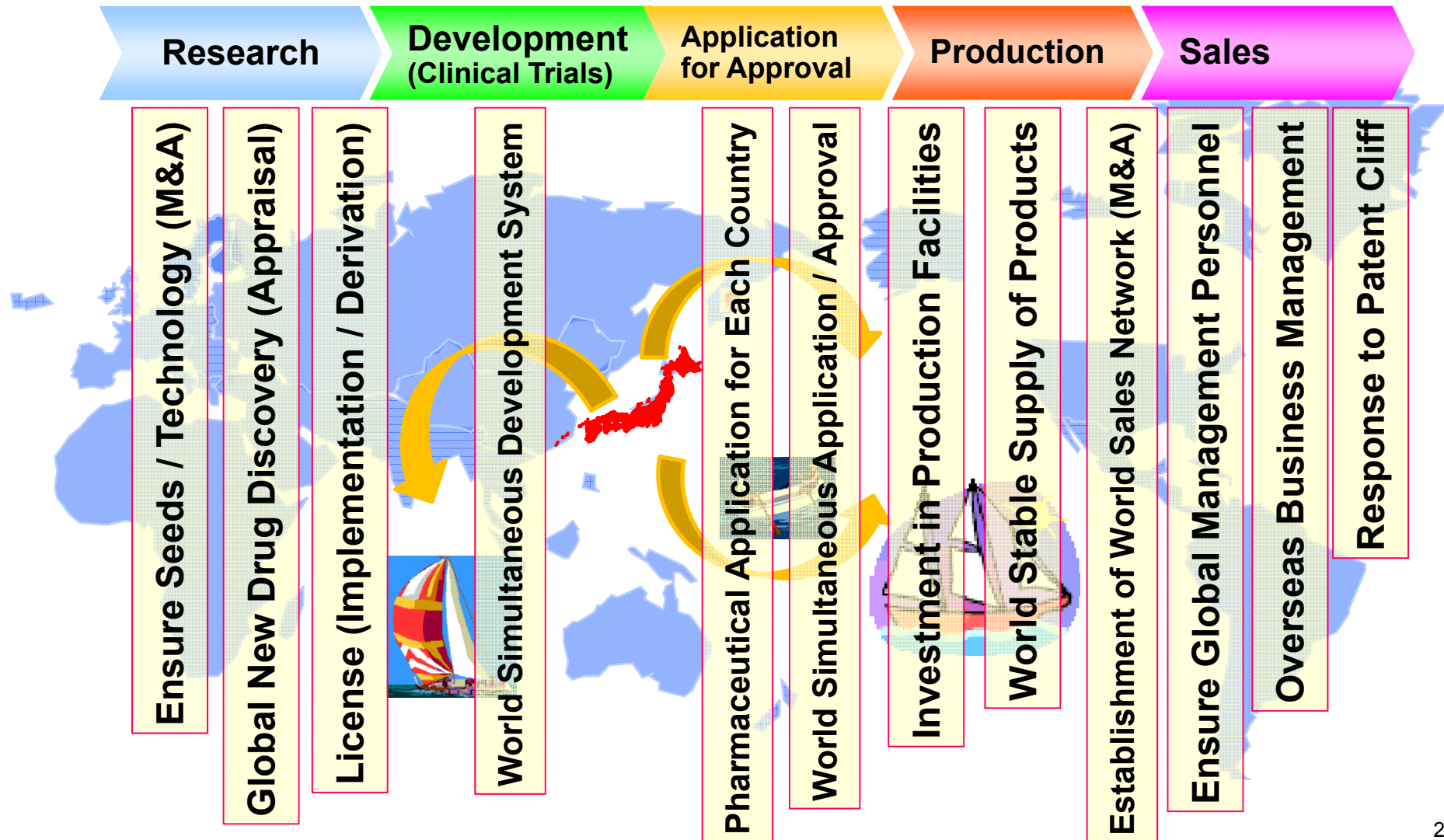
Challenges for Japanese Pharma to Keep Growing in the Future



- **Minimize the gap with global companies**
- **Get out from conventional drug discovery (implementation of biopharmaceutical drug discovery technologies, etc.)**
- **Activate open innovation to germinate drug seeds into practical use**
- **Foster bio-ventures**
- **Incentives for innovation creation**



Challenges to Establish Business Structure Comparable to Global Peers



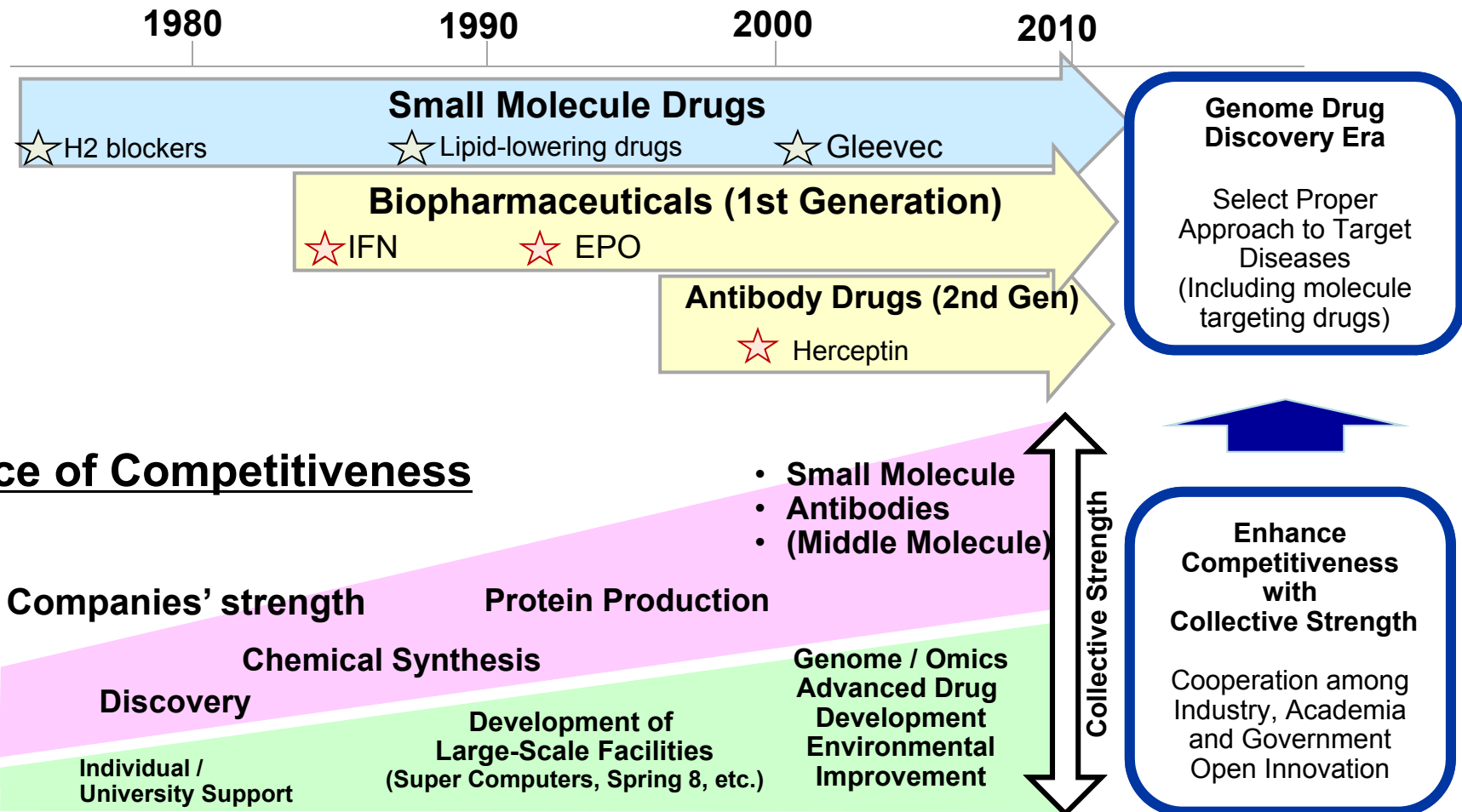
Enhance Collective Strength to Achieve Further Competitiveness

Innovation all for the patients



Roche A member of the Roche group

- Approach target diseases by utilizing biotechnology
- Need to reinforce collective strength utilizing industry-academia-government collaboration and open innovation

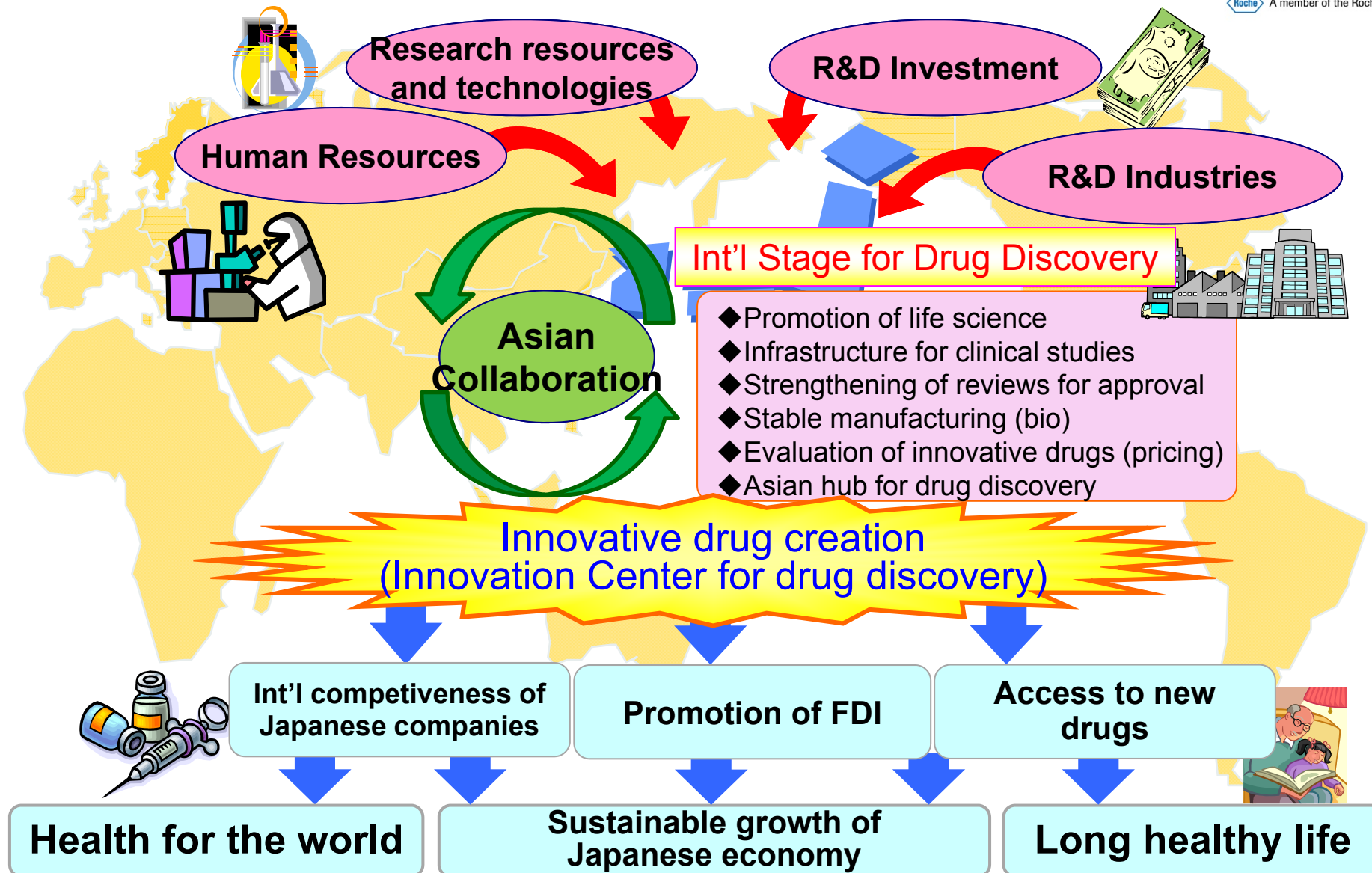


Japan as International Arena for Drug Discovery and Development

Innovation all for the patients



Roche A member of the Roche group





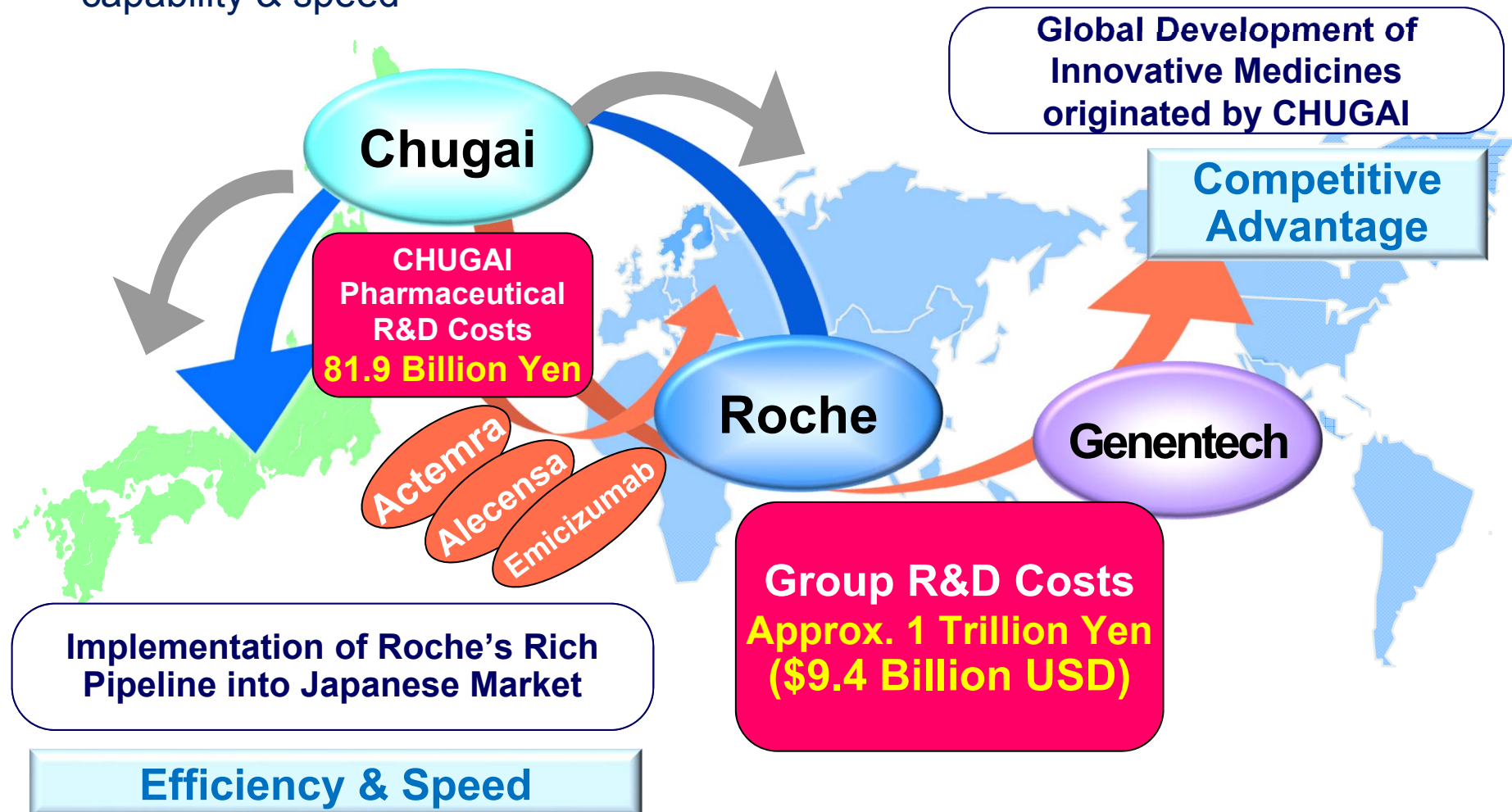
Today's Agenda

1. Overview of the Japanese Market
2. Transition of Drug Discovery
3. Challenges Facing Japan's Pharmaceutical Industry and Orientation of the Solution
- 4. Chugai's Strategy**

The Basis of Chugai's Strategy is the Alliance with Roche



- Global development of innovative medicines originated by Chugai
- Domestic development of Roche's pipeline with global-level development capability & speed



Business Performance Greatly Enhanced after Alliance with Roche

Innovation all for the patients



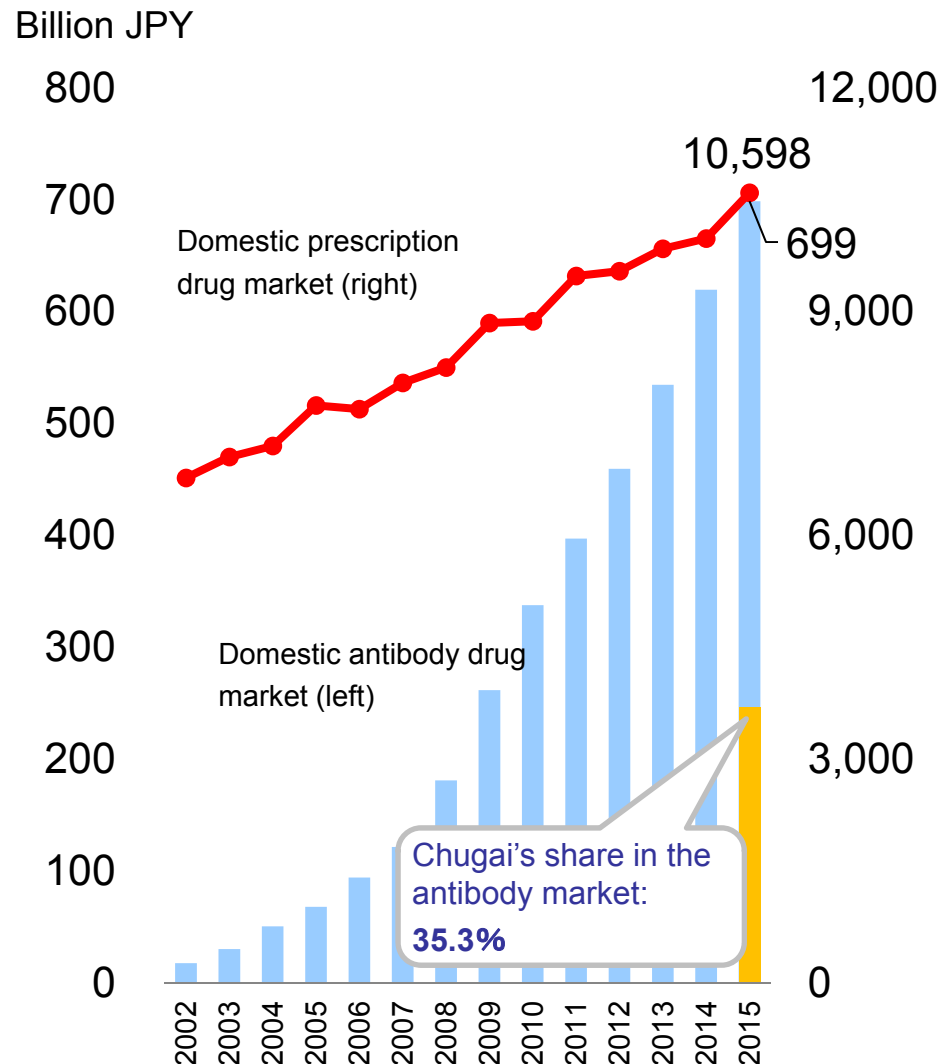
Roche A member of the Roche group

- Revenues doubled (Rx drug sales increased by 202%)
- Operating profit increased by 240%, R&D pipelines have been significantly enriched

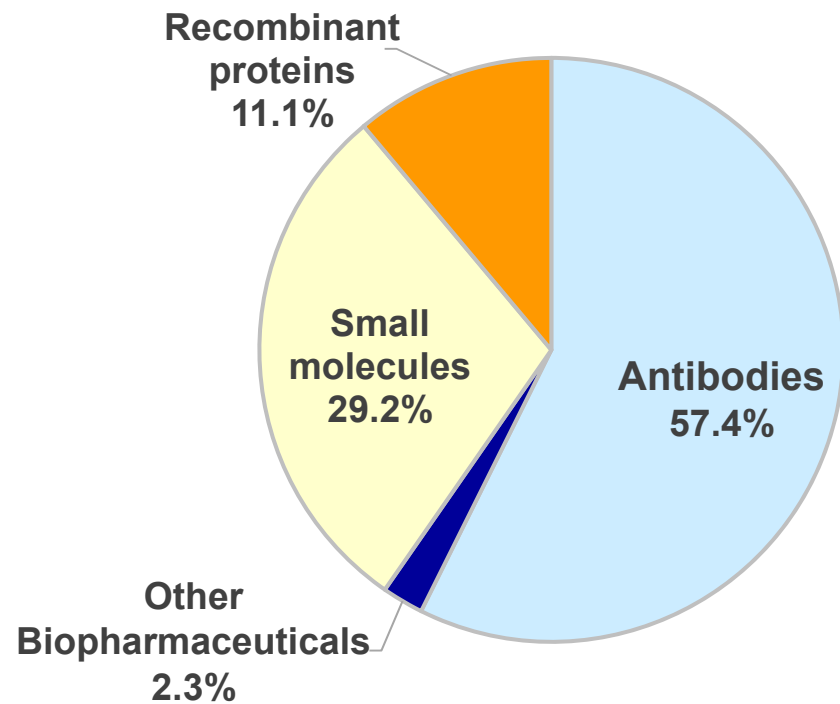
	FY2001		FY2015
Revenues	JPY 211.7 bil (JPY 165.1bil for Rx drugs)	+136%	JPY 498.8 bil
Core OP	JPY 26.7 bil	+202%	JPY 90.7 bil
Operating Margin	12.6%	+240%	JPY 90.7 bil
Pipelines under development (As of year end)	13	+5.6 pt.	18.2%
			34

2001: JGAAP, 2015: IFRS Core

Driving Growth of Japan's Pharmaceutical Market with Antibody Drugs



Sales composition in FY2015
(excluding Tamiflu)



Accelerate Creation of Next-generation Antibodies

Chugai Pharmabody Research Pte. Ltd (CPR)

Innovation all for the patients



Roche A member of the Roche group

【 Foundation 】

- Satellite Research Institute in Singapore
- Established in Jan 2012, operations initiated in July, 2012
- Headcount (including staff): approx. 100

【Mission】

- Focusing on R&D for creating new antibody drugs by using innovative antibody technologies



(CPR opening ceremony)

Innovative antibody technologies

SMART-Ig®: Recycling, sweeping antibody

ART-Ig®: Bispecific antibody

TRAB®: Cellular cytotoxicity antibodies by recruiting T-cell

ART-Fc®: ADCC activity enhancement

Created projects

SA237 (neuromyelitis optica, P3)

Emicizumab (hemophilia A, P3)

ERY974 (solid tumors, P1)

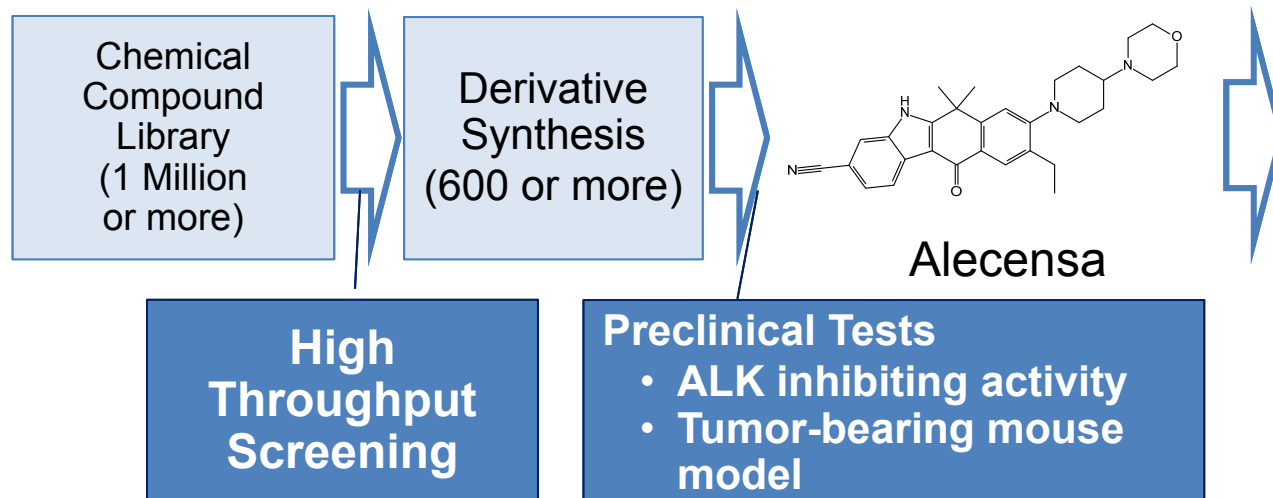
Innovative Small Molecule Drug Discovery Technologies & Next Generation Technologies

Innovation all for the patients



Roche A member of the Roche group

1. Small Molecule Drug Discovery (e.g. Alecensa)



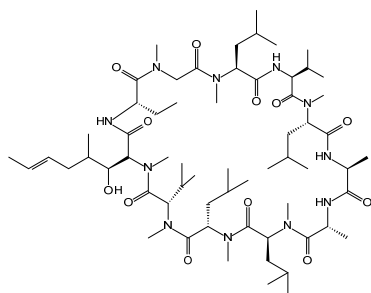
PI / II Study Results

Antitumor Effect	Subjects (Rate)
CR	9 (19.6%)
PR	34 (73.9%)
SD	1 (2.2%)
PD	0 (0%)
NE	2 (4.3%)*

NE: Not Evaluated

* Early discontinuation

2. Middle Molecule Drug Discovery (Next Generation Technologies)



Cyclic peptide, mw: $\sim \geq 1000$

- ✓ Has benefits of both small molecule drugs and antibodies
- ✓ Target:
 - Intracellular molecules
 - Protein / protein interaction
 - Protein / nucleic acid interaction

World-leading Drug Discovery Technologies

Innovation all for the patients



Roche A member of the Roche group

- Three products (five projects) have obtained the breakthrough therapy designation (BTD) by the US FDA

Number of BTD

Rank	Company	Number
1	Roche	14
2	Novartis	11
3	BMS	9
4	Merck	8
5	Pfizer	7
5	AbbVie	7

BTD for Roche Products

	Products	Company	Indication
2016	Actemra	Chugai/Roche	Giant Cell Arteritis
	Alecensa	Chugai/Roche	NSCLC 1 st line
	ocrelizumab	Genentech/Roche	multiple sclerosis
	Venetoclax	Abbvie/Roche	AML; combination
	Venetoclax	Abbvie/Roche	CLL
2015	Rituxan	Genentech/Roche	CLL
	ACE10	Chugai/Roche	Hemophilia A
	Actemra	Chugai/Roche	Systemic sclerosis
	Venetoclax	Abbvie/Roche	CLL
2014	Tecentriq	Genentech/Roche	NSCLC
	Lucentis	Genentech/Roche	DR
	Esbriet	InterMune/Roche	ICS
2013	Tecentriq	Genentech/Roche	Bladder cancer
	Alecensa	Chugai/Roche	NSCLC 2 nd line
	Gazyva	Genentech/Roche	CLL

Chugai origin

■ Breakthrough therapy designation system for innovative new drug

- System of FDA to accelerate development and review of investigational drugs

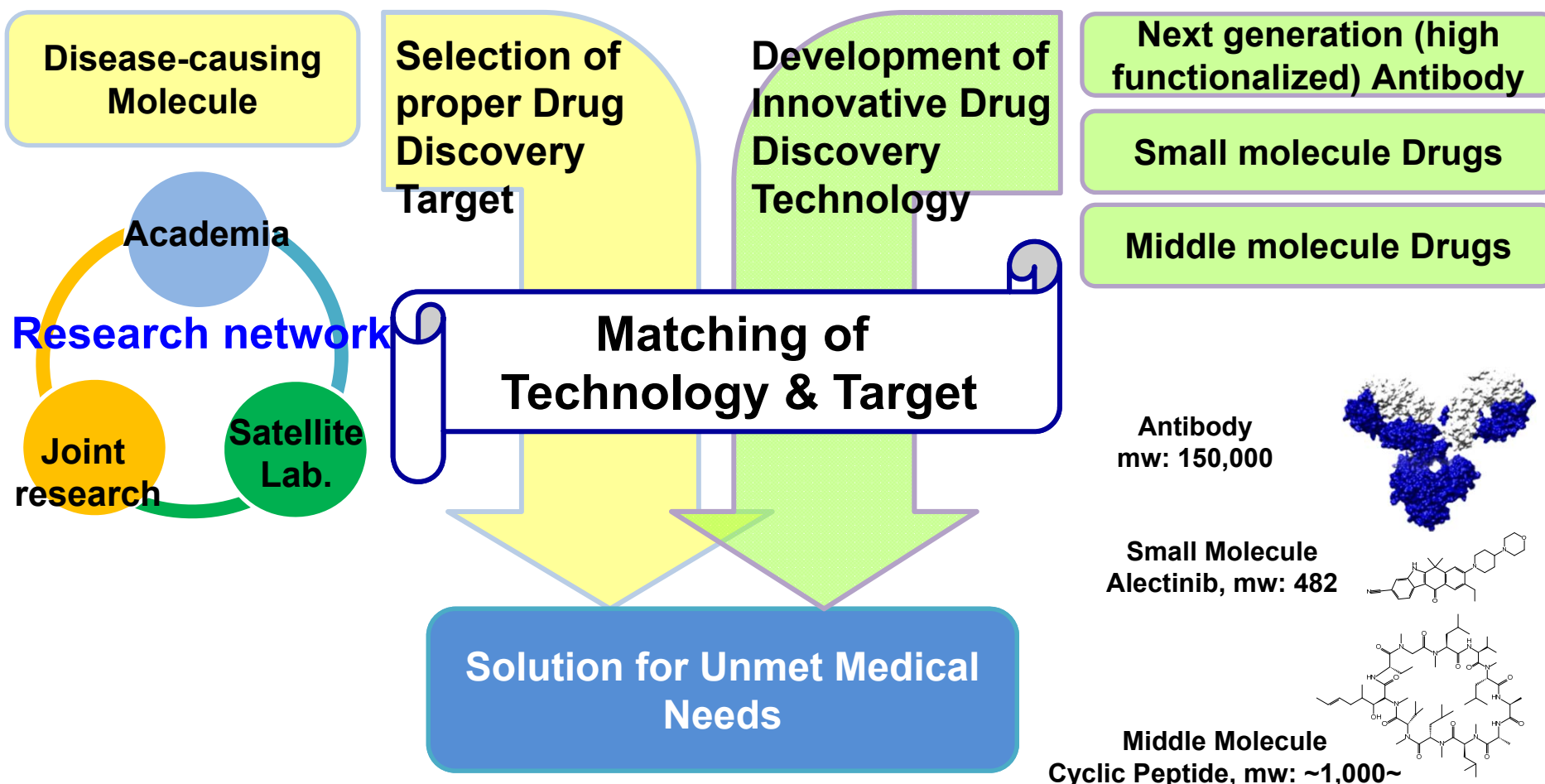
【Condition for designation】

- intended to treat a serious or life threatening disease or condition (monotherapy or combination)
- preliminary clinical evidence indicates a substantial improvement over existing therapies on one or more clinically significant endpoints



Chugai's Technology Driven Approach

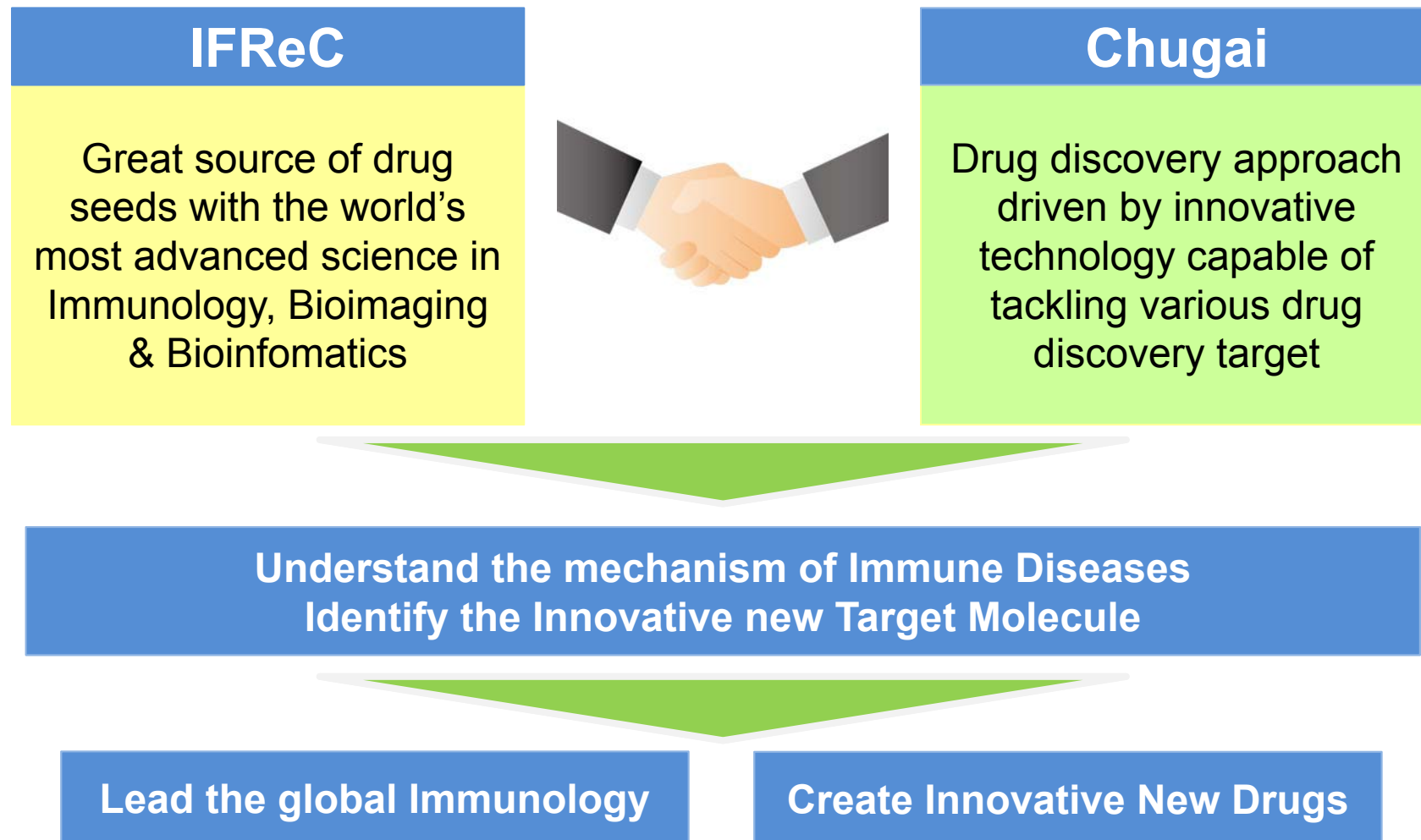
- Select best approach to target diseases with an arsenal of technologies including antibody engineering, small molecule and the next generation middle molecule
- Gain innovative drug seeds with enhanced research capabilities in oncology and immunology



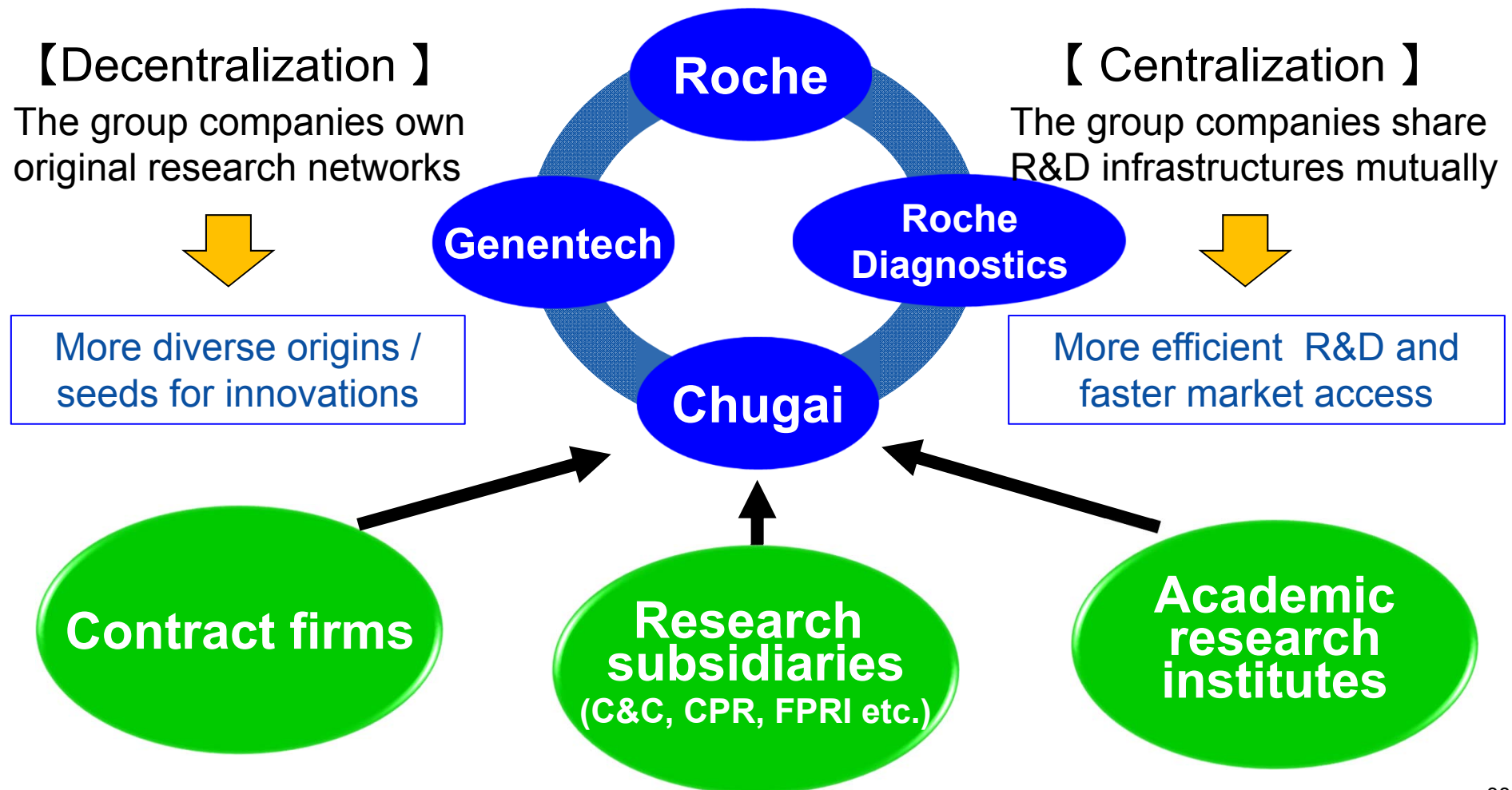
Value Generation through the IFReC - Chugai Collaboration



- 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



Drug Discovery Utilizing Global Networks and Satellite Labs



Innovation all for the patients



CHUGAI PHARMACEUTICAL CO., LTD.



A member of the Roche group

Contact:

Corporate Communications Department

Investor Relations Group

Tel: +81 (0)3-3273-0554 Fax: +81 (0)3-3281-6607

e-mail: ir@chugai-pharm.co.jp

Toshiya Sasai, Takayuki Sakurai,

Tomoko Shimizu, Tomoyuki Shimamura