

FY2014 2Q Consolidated Financial Overview (IFRS based)

CHUGAI PHARMACEUTICAL CO., LTD.
Executive Vice President CFO
Yoshio Itaya

July 24/25, 2014



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.

Note: Amounts shown in this report are rounded to the nearest 0.1 billion yen

Variance and % are calculated based on the amounts shown



Summary

■ Revenues: 222.0 billion JPY (+10.4% YoY)

- Domestic sales excl. Tamiflu (+8.8%): increase due to steady growth of mainstay products and new products
- Overseas sales (+28.4%): increase due to growth in Actemra export and weak yen
- Royalties and other operating income (+13.9%): increase due to growth of milestone income and Actemra-related income

■ Cost of sales / Operating expenses

- Cost of sales: the ratio to sales worsened due primarily to yen depreciation
- Operating expenses: 2.4% increase on a core basis in total expenses due to yen depreciation, an increase in research and development resulting primarily from progress in in-house projects and increased activities of CPR, etc

■ Profits

- IFRS results: operating profit 43.1 billion JPY (+13.1%),
net income 29.4 billion JPY (+16.2%)
- Core results: operating profit 43.7 billion JPY (+12.9%)
- Core EPS: 53.66 JPY (+16.5%)



IFRS and Core Results Jan – Jun

(Billion JPY)	IFRS results	Non-core items		Core results
	2014 Jan - Jun	Intangible assets and Business combinations	Other eliminated items	2014 Jan - Jun
Revenues	222.0			222.0
Sales	208.1			208.1
Royalties and other operating income	13.9			13.9
Cost of sales	-102.6	+0.5		-102.1
Gross profit	119.4	+0.5		119.9
Operating expenses	-76.3	+0.0	+0.1	-76.2
Marketing and distribution	-34.3	+0.0		-34.3
Research and development	-36.7	+0.0	+0.1	-36.6
General and administration	-5.2		+0.0	-5.2
Operating profit	43.1	+0.6	+0.1	43.7
Financing costs	-0.0			-0.0
Other financial income (expense)	0.3			0.3
Profit before taxes	43.4	+0.6	+0.1	44.1
Income taxes	-14.0	-0.2	-0.0	-14.2
Net income	29.4	+0.3	+0.0	29.8
Chugai shareholders	28.9	+0.3	+0.0	29.3
Non-controlling interests	0.5			0.5

Non-Core items

- Intangible/Business combinations
Amortization of intangible assets: +0.6bn JPY
No business combinations
- Other eliminated items
Restructuring expenses: +0.1bn JPY

(Billion JPY)

Core net income
attributable to Chugai
shareholders 29.3

(Millions of shares)

Weighted average
number of shares
and equity securities
in issue used to
calculate diluted
earnings per share 546

(JPY)

Core EPS 53.66

Year on Year (Core)

Financial Overview Jan – Jun



(Billion JPY)	2013 Jan - Jun vs. Rev*.		2014 Jan - Jun vs. Rev*.		Growth	
Revenues	201.0		222.0		+21.0	+10.4%
Sales	188.8		208.1		+19.3	+10.2%
excl. Tamiflu	179.8		201.0		+21.2	+11.8%
Domestic	152.0		165.3		+13.3	+8.8%
Export to Roche	18.4		26.3		+7.9	+42.9%
Other overseas	9.4		9.5		+0.1	+1.1%
Tamiflu	9.0		7.1		-1.9	-21.1%
Ordinary	8.2		7.0		-1.2	-14.6%
Stockpiling	0.8		0.1		-0.7	-87.5%
Royalties and other operating income	12.2		13.9		+1.7	+13.9%
Cost of sales	-87.9	43.7%	-102.1	46.0%	-14.2	+16.2%
Gross profit	113.1	56.3%	119.9	54.0%	+6.8	+6.0%
Operating expenses	-74.4	37.0%	-76.2	34.3%	-1.8	+2.4%
Operating profit	38.7	19.3%	43.7	19.7%	+5.0	+12.9%
Financing costs	-0.0		-0.0		+0.0	0.0%
Other financial income (expense)	-1.2		0.3		+1.5	-
Income taxes	-11.9		-14.2		-2.3	+19.3%
Net income	25.6	12.7%	29.8	13.4%	+4.2	+16.4%
EPS (JPY)	46.06		53.66		+7.60	+16.5%

(Billion JPY)

Royalties and other operating income +1.7

Milestone income and Actemra-related income increased

Other financial income (exp.) +1.5

Exchange gains/losses +3.6

Gains/Losses on derivatives -2.2

Cost of sales ratio vs. Sales

2013 Jan– Jun	2014 Jan–Jun
46.6%	49.1%

Average exchange rate (JPY)

	2013 Jan–Jun	2014 Jan–Jun
CHF	101.94	115.04
EUR	125.33	140.51

*Revenues

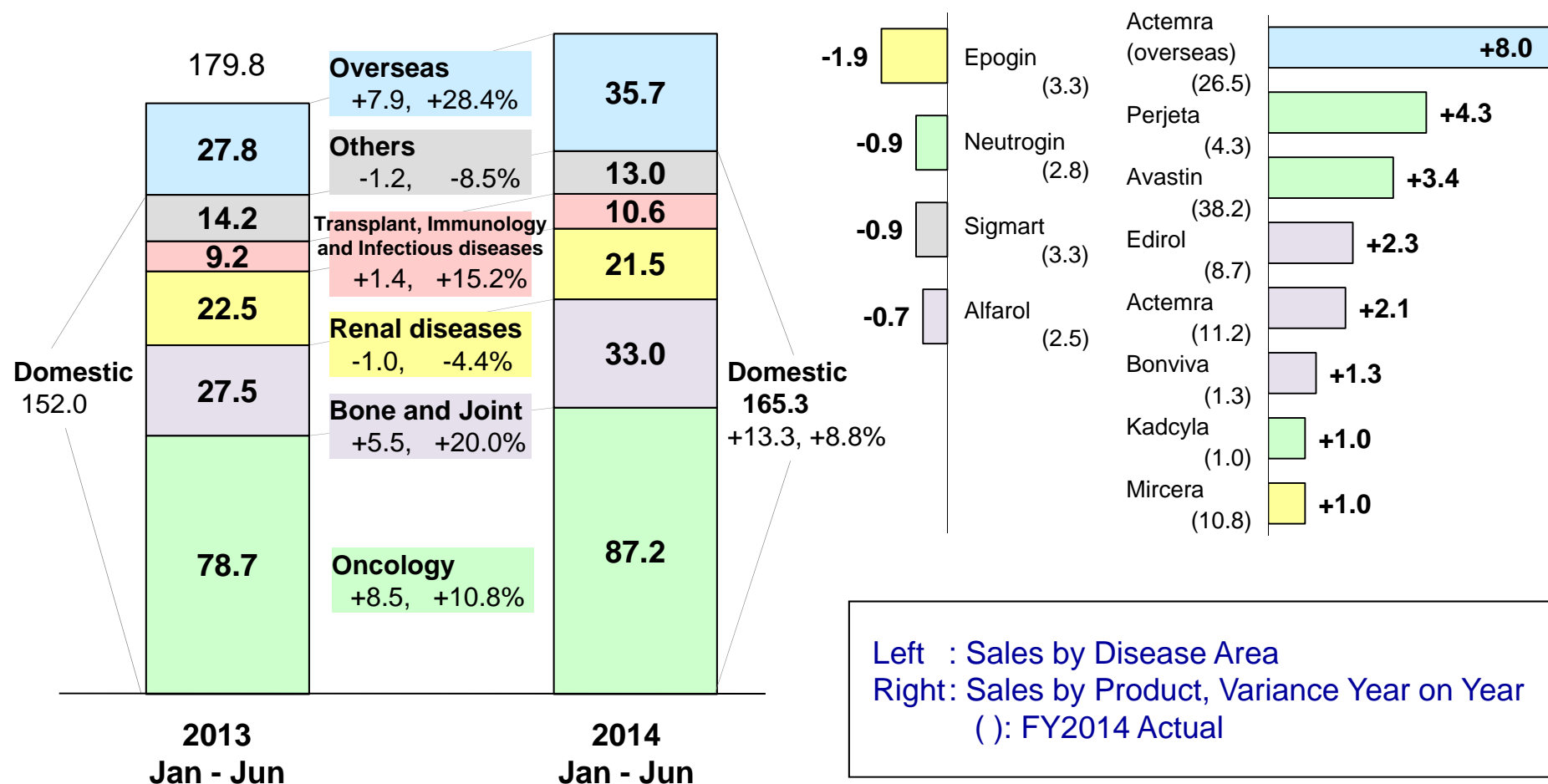
Year on Year

Sales (excl. Tamiflu) Jan – Jun



(Billion JPY)

Sales excl. Tamiflu
201.0 (+21.2, +11.8%)





Tamiflu Sales Performance

(Billion JPY)		Fiscal Term Sales												Forecast	
		FY2009.12		FY2010.12		FY2011.12		FY2012.12		FY2013.12		FY2014.12		Seasonal Sales	Cases per sentinel* (millions)
		Jan-Jun	Jul-Dec	Jan-Jun	Jul-Dec	Jan-Jun	Jul-Dec	Jan-Jun	Jul-Dec	Jan-Jun	Jul-Dec	Jan-Jun	Jul-Dec		
Ordinary	2008-09	11.0												16.7	1.27
	2009-10		25.2	1.4										26.6	2.02
	2010-11				0.2	4.1								4.3	1.26
	2011-12						1.3	7.8						9.1	1.63
	2012-13								2.4	8.2				10.6	1.11
	2013-14										1.9	7.0		9.0	1.44
	2014-15												1.7	-	-
Ordinary		36.2	(+29.1)	1.6	(-34.6)	5.4	(+3.8)	10.2	(+4.8)	10.1	(-0.1)	8.8	(-1.3)		
Govt. Stockpile etc.	2008-09	14.4												15.5	
	2009-10		25.6	10.6										36.2	
	2010-11				5.9	0.5								6.4	
	2011-12						2.8	0.4						3.2	
	2012-13								1.5	0.8				2.3	
	2013-14										0.1	0.1		0.2	
	2014-15												0.0	-	
Govt. Stockpile etc.		40.0	(+38.7)	16.6	(-23.4)	3.3	(-13.3)	1.9	(-1.4)	0.9	(-1.0)	0.1	(-0.8)		
Total		25.4	50.8	12.0	6.1	4.6	4.1	8.1	3.9	9.0	2.0	7.1	1.7		
		76.2	(+67.8)	18.2	(-58.0)	8.7	(-9.5)	12.0	(+3.3)	11.0	(-1.0)	8.8	(-2.2)		

*Total patient number of the controlled samples in the "Infectious Diseases Weekly Report", period between late October and mid-April (between early July 2009 and mid-March 2010 for 2009/2010), published by Japan's National Institute of Infectious Diseases.

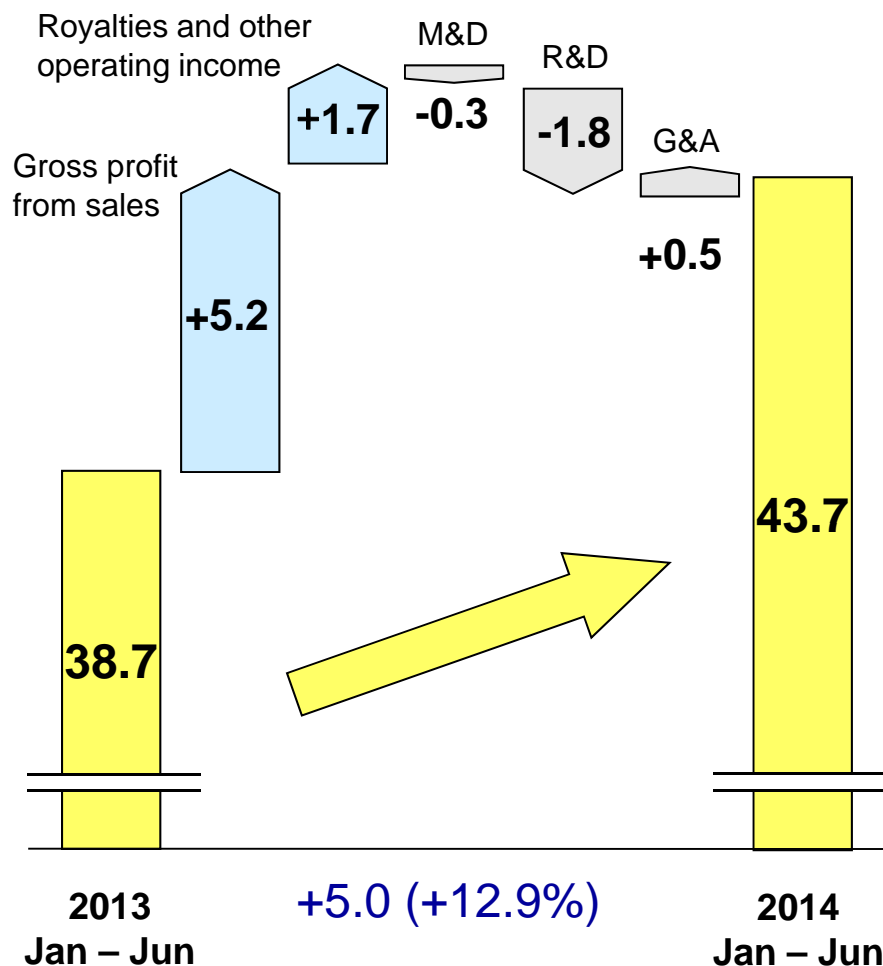
Company forecast
() Year on year

Year on Year (Core)



Operating Profit Jan – Jun

(Billion JPY)



(Billion JPY)	2013 Jan - Jun	2014 Jan - Jun	Growth
Revenues	201.0	222.0	+21.0
Cost of sales	-87.9	-102.1	-14.2
Gross profit	113.1	119.9	+6.8
of which Sales	100.9	106.1	+5.2
Royalties, etc.	12.2	13.9	+1.7
Marketing and distribution	-34.0	-34.3	-0.3
Research and development	-34.8	-36.6	-1.8
General and administration	-5.7	-5.2	+0.5
Operating profit	38.7	43.7	+5.0

Increase in gross profit from sales	+5.2
Increase in mainstay products, new products and Actemra overseas	
Increase in royalties and other operating income	+1.7
Increase in marketing and distribution	-0.3
Negative foreign exchange impact on expenses of overseas sales subsidiaries, etc	
Increase in research and development	-1.8
Negative foreign exchange impact, progress in in-house projects, increased activities of CPR*, etc	
Decrease in general and administration	+0.5
Various expenses decreased	

Year on Year (Core)



Financial Overview Apr – Jun

(Billion JPY)		2013 Apr - Jun vs. Rev*.		2014 Apr - Jun vs. Rev*.		Growth		(Billion JPY)	
Revenues		110.6		98.0		-12.6	-11.4%	Royalties and other operating income -4.7	
Sales		101.8		93.9		-7.9	-7.8%	Milestone income decreased	
excl. Tamiflu		101.1		93.7		-7.4	-7.3%		
Domestic		83.2		80.1		-3.1	-3.7%	Operating expenses +0.7	
Export to Roche		13.3		9.3		-4.0	-30.1%		
Other overseas		4.6		4.3		-0.3	-6.5%	Marketing and distribution +0.3	
Tamiflu		0.7		0.2		-0.5	-71.4%	Research and development -0.0	
Ordinary		0.7		0.2		-0.5	-71.4%		
Stockpiling		-		-		-	-	General and administration +0.6	
Royalties and other operating income		8.8		4.1		-4.7	-53.4%	Various expenses decreased	
Cost of sales		-47.3	42.8%	-46.8	47.8%	+0.5	-1.1%		
Gross profit		63.3	57.2%	51.1	52.1%	-12.2	-19.3%		
Operating expenses		-39.6	35.8%	-38.9	39.7%	+0.7	-1.8%		
Operating profit		23.6	21.3%	12.3	12.6%	-11.3	-47.9%	Cost of sales ratio vs. Sales	
Financing costs		0.0		0.0		+0.0	0.0%		
Other financial income (expense)		-0.2		0.1		+0.3	-		
Income taxes		-7.3		-1.9		+5.4	-74.0%		
Net income		16.2	14.6%	10.5	10.7%	-5.7	-35.2%		
EPS (JPY)		29.23		18.85		-10.38	-35.5%		

*Revenues

vs. Forecast (Core)



Financial Overview Jan – Jun

(Billion JPY)	Actual	Forecast on Jan 30		2013
	2014 Jan - Jun	2014 Jan - Dec	Progress	Progress*
Revenues	222.0	451.0	49.2%	47.4%
Sales	208.1	427.0	48.7%	47.0%
excl. Tamiflu	201.0	418.2	48.1%	46.1%
Domestic	165.3	335.7	49.2%	46.2%
Export to Roche	26.3	64.6	40.7%	42.9%
Other overseas	9.5	17.9	53.1%	51.9%
Tamiflu	7.1	8.8	80.7%	81.8%
Royalties and other operating income	13.9	24.0	57.9%	54.5%
Cost of sales	-102.1	-213.0	47.9%	47.2%
Gross profit	119.9	238.0	50.4%	47.6%
Operating expenses	-76.2	-167.0	45.6%	47.2%
Operating profit	43.7	71.0	61.5%	48.4%
EPS (JPY)	53.66	82.62	64.9%	48.6%

*Jan - Jun progress versus Jan - Dec

vs. Forecast (Core)



Domestic Sales (excl. Tamiflu) Jan – Jun

(Billion JPY)	Actual	Forecast on Jan 30		2013
	2014 Jan - Jun	2014 Jan - Dec	Progress	Progress*
Domestic sales excl. Tamiflu	165.3	335.7	49.2%	46.2%
Oncology	87.2	178.9	48.7%	45.6%
Avastin	38.2	81.2	47.0%	46.2%
Herceptin	14.9	30.0	49.7%	46.6%
Tarceva	5.6	11.3	49.6%	44.2%
Xeloda	5.0	10.8	46.3%	48.7%
Perjeta	4.3	4.7	91.5%	-
Kadcyla	1.0	1.9	52.6%	-
Bone and Joint	33.0	67.3	49.0%	45.4%
Actemra	11.2	22.4	50.0%	44.6%
Edirol	8.7	17.6	49.4%	42.7%
Bonviva	1.3	3.9	33.3%	-
Renal	21.5	45.8	46.9%	46.0%
Mircera	10.8	24.6	43.9%	43.6%
Epogin	3.3	6.7	49.3%	49.5%
Transp., Immun., Infectious	10.6	17.3	61.3%	48.9%
Pegasys	3.7	5.1	72.5%	50.9%
Copegus	1.7	1.8	94.4%	53.8%
Others	13.0	26.3	49.4%	49.7%

*Jan - Jun progress versus Jan - Dec. Forecast for Kadcyla as disclosed on Apr. 24

vs. Forecast (Core)

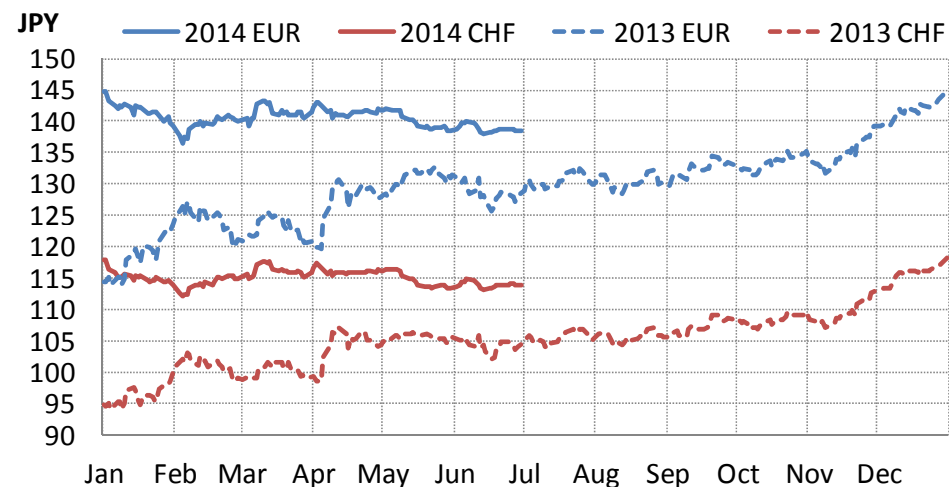


Impact from Foreign Exchange

(Billion JPY)	FX impact Jan - Jun (vs. Forecast on Jan. 30)	
Revenues	-0.4	
	Sales	-0.3
	Royalties and other operating income	-0.0
Cost of sales	Cost of sales	+0.2
Operating expenses	Expenses	+0.1
Operating profit	-0.1	

FX rate to the JPY*	Assumption Jan - Dec (as of Jan. 30)	Actual Jan - Jun avg.	Reference Actual Jan - Jun avg. (2013)
1CHF	116.00	115.04	101.94
1EUR	142.00	140.51	125.33

* Actual: average exchange rate for the period of Jan - Jun



vs. 2013 Year End

Balance Sheet Items



< Assets, Liabilities, and Net Assets >

(Billion JPY)	2013 Dec	2014 Jun	Change
Trade accounts receivable	111.1	106.6	- 4.5
Inventories	128.5	141.8	+ 13.3
Trade accounts payable	-35.9	-42.9	- 7.0
Other net working capital	-26.6	-21.1	+ 5.5
Net working capital	177.1	184.4	+ 7.3
Property, plant and equipment	140.4	140.0	- 0.4
Intangible assets	9.5	9.6	+ 0.1
Other long-term assets - net	-1.8	-1.6	+ 0.2
Long-term net operating assets	148.1	147.9	- 0.2
Net operating assets	325.2	332.3	+ 7.1
Debt	-0.2	-0.2	+ 0.0
Marketable securities	119.6	115.1	- 4.5
Cash and cash equivalents	115.1	128.8	+ 13.7
Net cash	234.4	243.6	+ 9.2
Other non-operating assets - net	13.6	9.5	- 4.1
Net non-operating assets	248.0	253.1	+ 5.1
Total net assets	573.2	585.4	+ 12.2

Total net assets	573.2	585.4	+ 12.2
Total assets	697.2	708.2	+ 11.0
Total liabilities	-124.0	-122.8	+ 1.2

Other net working capital: accrued receivable, accrued payable, accrued expenses, etc

Other long-term assets - net: long term prepaid expenses, long-term provisions, etc

Other non-operating assets - net: deferred income tax assets, accrued corporate tax, etc

Net working capital	+7.3
Trade accounts receivable	-4.5
Mainly seasonal change	
Inventories	+13.3
Launch of new product, increased demand for new product, increase in safety stocks to ensure stable supply, etc	
Trade accounts payable	-7.0
Other net working capital	+5.5
Long-term net operating assets	-0.2
Net cash	+9.2
Other non-operating assets – net	-4.1

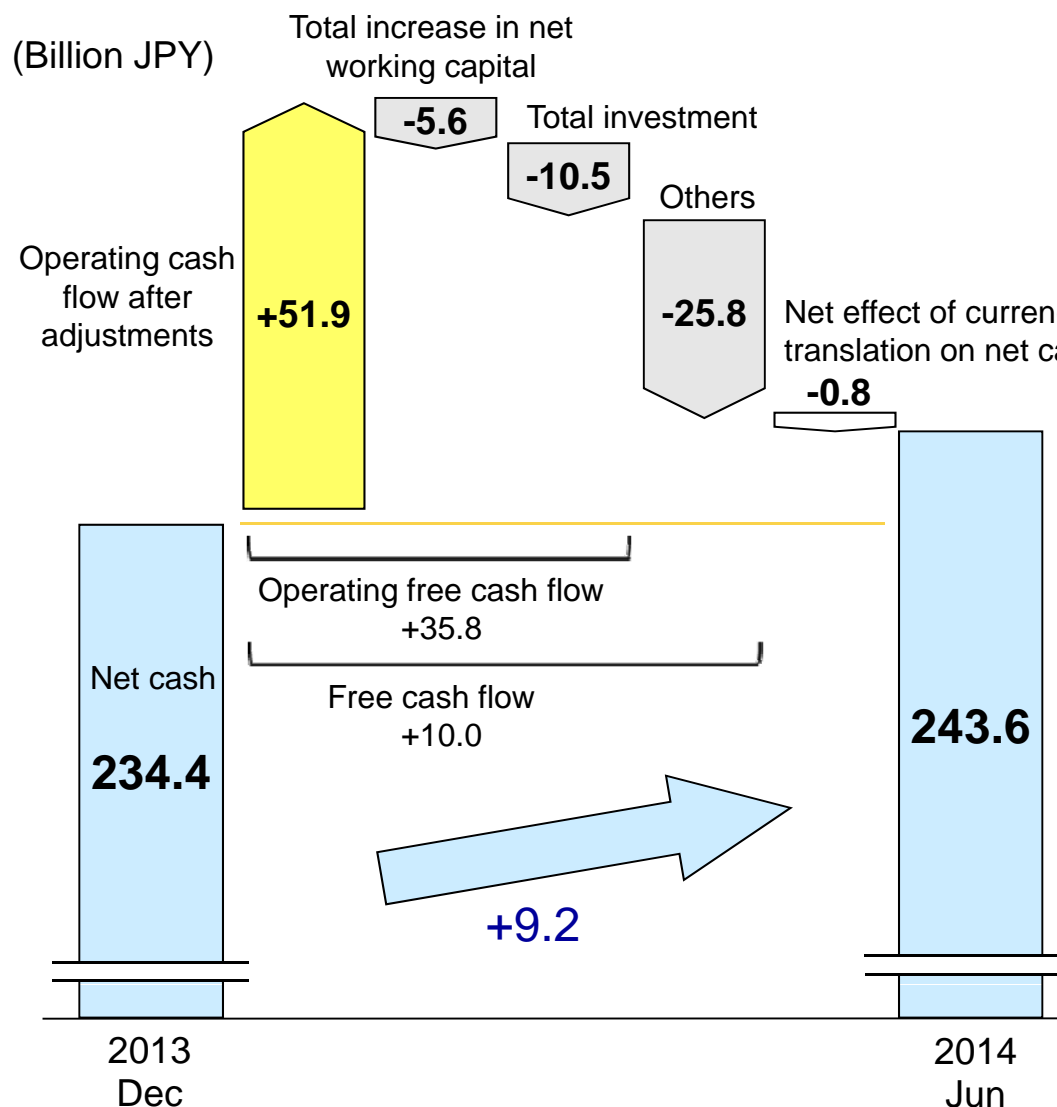
Equity ratio attributable to Chugai shareholders
+0.5%pts

2014 Jun	82.5%
2013 Dec	82.0%

FX rate to the JPY (end of period)	2013 Dec	2014 Jun	Change
CHF	118.42	113.79	-4.63
EUR	145.16	138.37	-6.79
USD	105.16	101.38	-3.78

vs. 2013 Year End

Net Cash



Operating cash flow after adjustments	+51.9
Operating profit	+43.1
Depreciation and amortization, etc	+8.8
Total increase in net working capital	-5.6
Decrease in trade accounts receivable	+4.5
Increase in inventories	-14.3
Increase in trade accounts payable	+7.0
Increase in other net working capital	-2.8
Total investment	-10.5
Investment in PPE	-9.2
Mainly maintenance expenditures for R&D equipment and plant production machinery	
Investment in intangible assets	-1.3
Operating free cash flow	+35.8
Others	-25.8
Tax paid	-13.3
Dividends paid	-12.9
Free cash flow	+10.0

* Net effect of currency translation on net cash, etc: Transaction in own equity instruments + Net effect of currency translation on net cash

Year on Year

Free Cash Flow Jan - Jun



(Billion JPY)	2013 Jan-Jun	2014 Jan-Jun	Change	
Operating profit - IFRS basis	38.1	43.1	+5.0	
Depreciation and impairment of Property, plant and equipment	7.2	6.8	-0.4	
Amortization and impairment of intangible assets	0.5	0.6	+0.1	
Other cash adjustment on operating profit	1.3	1.4	+0.1	
Operating profit, net of operating cash adjustments	47.2	51.9	+4.7	Operating profit, net of operating cash adjustments +4.7
Increase (-) / decrease in trade accounts receivable	6.8	4.5	-2.3	Increase in revenues
Increase (-) / decrease in inventories	-6.1	-14.3	-8.2	
Increase / decrease (-) in trade accounts payable	-8.4	7.0	+15.4	Total increase (-) / decrease in net working capital +4.1
Other change in net working capital	-1.9	-2.8	-0.9	
Total increase (-) / decrease in net working capital	-9.7	-5.6	+4.1	
Investment in Property, plant and equipment	-6.5	-9.2	-2.7	Increase (-) / decrease in trade accounts receivable -2.3
Investment in intangible assets	-0.4	-1.3	-0.9	Increase (-) / decrease in inventories -8.2
Total investment	-6.9	-10.5	-3.6	Increase / decrease (-) in trade accounts payable +15.4
Operating free cash flow	30.6	35.8	+5.2	Total investment -3.6
as % of revenues	15.2%	16.1%	+0.9%pts	Operating free cash flow +5.2
Treasury activities	0.5	0.4	-0.1	
Tax paid	-11.9	-13.3	-1.4	Increase in operating profit, net operating cash adjustments, increase in investment was offset by lower increase of net working capital compared with the same period of the previous year
Dividends paid	-11.4	-12.9	-1.5	
Free cash flow	7.8	10.0	+2.2	
Transaction in own equity instruments	0.6	0.5	-0.1	
Net effect of currency translation on net cash	3.1	-1.3	-4.4	
Net change in net cash	11.5	9.2	-2.3	
Average exchange rate (JPY)				Operating free cash flow as % of revenues +0.9%pts
CHF	101.94	115.04	+13.10	
EUR	125.33	140.51	+15.18	Revenues +21.0
USD	95.43	102.49	+7.06	

* Net effect of currency translation on net cash, etc: Transaction in own equity instruments + Net effect of currency translation on net cash

Overview of Development Pipeline

CHUGAI PHARMACEUTICAL CO., LTD.
Executive Vice President
Head of Project & Lifecycle Management Unit
Yutaka Tanaka

July 24/25, 2014

Oncology Field

Projects under Development (as of 24 July, 2014)



	Phase I	Phase II	Phase III	Filed
Oncology	CKI27 / RG7304 (Japan / overseas) - solid tumors RG7321 / pictilisib -solid tumors RG7596 / polatuzumab vedotin ★ - NHL	GC33 / RG7686 - HCC RG340 / Xeloda - aGC AF802 (RG7853) / alectinib (overseas) - NSCLC (PI/II)	RG1273 / Perjeta -aBC -GC -RG3502 / Kadcyla - GC (PII/III) - aBC GA101 (RG7159) / obinutuzumab - NHL RG7446 / MPDL3280A - NSCLC	RG7204 / vemurafenib - melanoma

Letters in orange: in-house projects

★: Projects with advances in stages since 24 April, 2014

Primary Field Projects under Development (as of 24 July, 2014)



	Phase I	Phase II	Phase III	Filed
Bone & Joint			RG484 / Bonviva (oral) - osteoporosis NRD101 / Suvenyl - enthesopathy	
Autoimmune		MRA / Actemra (overseas) - systemic sclerosis	MRA / Actemra (overseas) - giant cell arteritis SA237 ★ - neuromyelitis optica	
CNS	RG1577 - Alzheimer's disease RG1662 ★ - improvement of intellectual ability in individuals with Down syndrome	RG7090 - major depressive disorder	RG1678 / bitopertin - schizophrenia RG1450 / gantenerumab ★ - Alzheimer's disease	
Others	URC102 (Overseas) - gout	CIM331 ★ - atopic dermatitis ACE910 - hemophilia A (PI/II)	RG3637 / lebrikizumab - asthma	

Letters in orange: in-house projects

★: Projects with advances in stages since 24 April, 2014

★: Global study managed by Chugai



Development Status: Oncology, Bone & Joint

In-house

AF802 / Alecensa® :

ALK fusion gene positive unresectable, recurrent / advanced non-small cell lung cancer

Approved in Japan in July 2014

In-licensed

RG7596 (Anti-CD79b ADC) :

Non-Hodgkin's lymphoma

Started P1 in July 2014

In-licensed

RG435 / Avastin® :

Breast cancer (Adjuvant)

Development discontinued in June 2014

In-house

NRD101 / Suvenyl® :

Enthesopathy

Primary endpoint not met

Next steps to be considered

ADC: antibody-drug conjugate



Development Status: Autoimmune Diseases

In-house

MRA / Actemra® :

New formulation (subcutaneous injection) for RA

April 2014: Approved in EU

June 2014: Started P3 for weekly dosage in Japan

Large-vessel vasculitis

June 2014: Orphan drug designation granted in Japan

In-house

SA237 (anti-IL-6R MAb) :

Neuromyelitis Optica

June 2014: Orphan drug designation granted in US

In-licensed

RG7415 (Anti-interferon alpha MAb) :

Systemic lupus erythematosus

April 2014: Development discontinued

RA: Rheumatoid Arthritis



Development Status: CNS, Others

CNS: Central Nervous System

In-
licensed

RG1662 (GABA_Aα5 receptor antagonist) :

Improvement of intellectual ability
in individuals with Down syndrome
May 2014: Started P1 in Japan

In-
licensed

RG1450 (Anti-amyloid-beta MAb) :

Alzheimer's disease
May 2014: Started multinational P3 (Marguerite Road study)

In-
licensed

RG1678 (Glycine reuptake inhibitor) :

Schizophrenia
Met primary endpoint in one of two dose groups in multinational
P3 (NightLyte study)

In-
licensed

RG7652 (Anti-PCSK9 MAb) :

Hyperlipidemia
July 2014: Development discontinued



Other Progress: Data Presentation

■ Data presentation at scientific meetings

In-house

World Federation of Hemophilia 2014 (May)

ACE910: presented preliminary data from P1 (hemophilia A)

- Safety and tolerability confirmed in healthy adults
- Efficacy to prevent bleeding was confirmed at the lowest dose, regardless of the presence or absence of factor VIII inhibitors

In-licensed

American Society of Clinical Oncology 2014 (June)

Avastin® + Tarceva®: presented Japanese P2 data on combination therapy (NSCLC)

- Clinical benefit superior to Tarceva monotherapy was suggested for patients with EGFR Mutation-positive NSCLC

In-house

GC33: presented multinational P2 data (Hepatocellular carcinoma)

- Did not meet primary endpoint

■ Upcoming events (Planned)

Alecensa®: Update on Japanese P1/2 to be presented at 2014 Chicago Multidisciplinary Symposium in Thoracic Oncology (October)

ACE910: Update on Japanese P1 to be presented at American Society of Hematology 2014 (December)



Other Progress: License in Europe

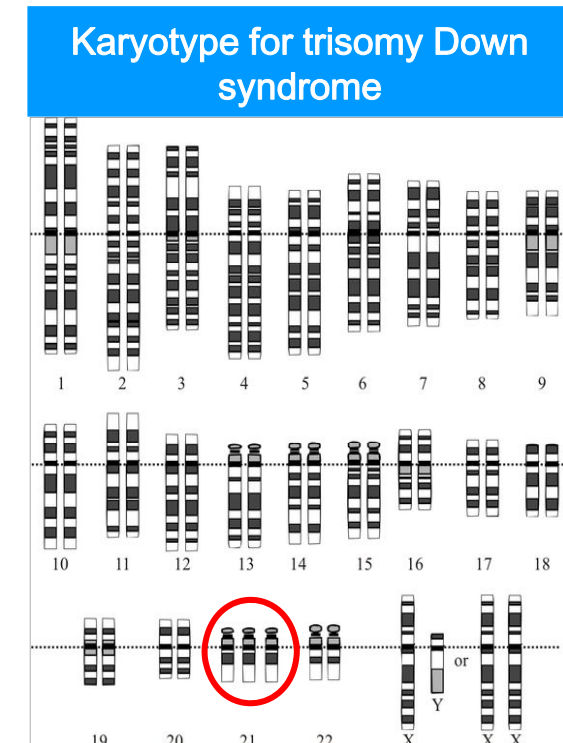
- Chugai Pharma Marketing obtained marketing license from two companies in Europe

PharmaMar	Plitidepsin / Aplidin®: Marketing rights granted for eight countries in Europe Multiple myeloma P3, filing in Europe planned in 4Q 2015
Helsinn	Netupitant-palonosetron (NEPA): Marketing rights granted for UK & Ireland Prevention of chemotherapy-induced nausea and vomiting (CINV) Filed in Europe and US
	Palonosetron / Aloxi®: Planned to start marketing in UK from January 2015 Prevention of CINV



Down Syndrome (DS)

- The most common chromosomal anomaly (trisomy of chromosome 21) with an incidence of one in 650 to 1,000 births¹⁾
- Associated with a delay in physical growth and intellectual disability in addition to various complications including congenital heart diseases
- Life expectancy of individuals with DS is increasing due to improvements in complication care, thus enabling more social participation of individuals with DS²⁾
- Lack of therapeutic options for intellectual disability prevents individuals with DS from achieving independent living



National Human Genome Research Institute (US)

- **RG1662 targets to improve intellectual ability in individuals with DS aged six to 30 years**
- **Both cognition and adaptive behavior* are to be assessed in clinical studies**

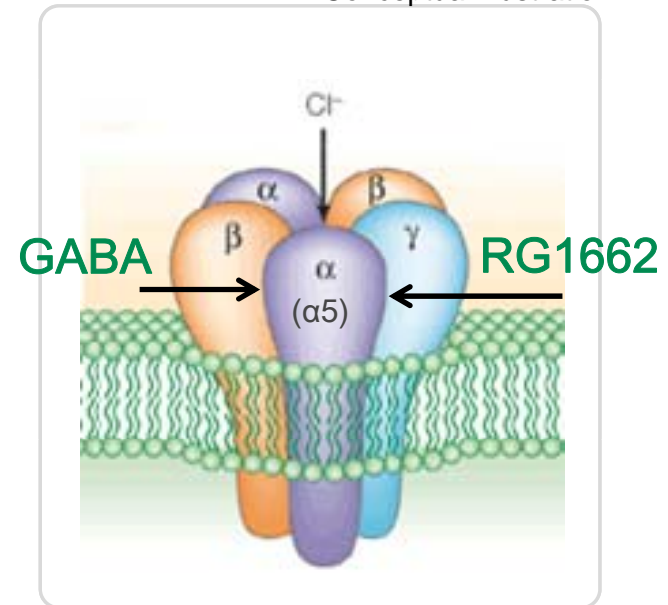
* Adaptive behavior: adaptive skills to meet demands of everyday living. For example, reading, writing, understanding of language, monetary concept, building personal relationships, dressing capability, etc.

RG1662 (GABA_Aα5 receptor antagonist): Mode of Action

- RG1662: a small-molecule GABA_Aα5 receptor antagonist created by Roche
- GABA is a representative inhibitory neurotransmitter
- GABAα5 receptor is widely expressed in the hippocampus and prefrontal cortex, which play important roles in cognition and memory
- Inhibitory neurotransmission mediated by GABA is superior in individuals with DS, which is considered a major barrier to effective learning and memory
- RG1662 is expected to inhibit GABA's excess activity and to enhance cognition and memory functions. By selectively binding to the GABA_Aα5 subunit, RG1662 weakens the binding affinity between the subunit and GABA.

Structure of GABA_A α5 receptor and binding site of RG1662

<Conceptual illustration>



Nature Reviews Neuroscience 6, 565-575. 2005

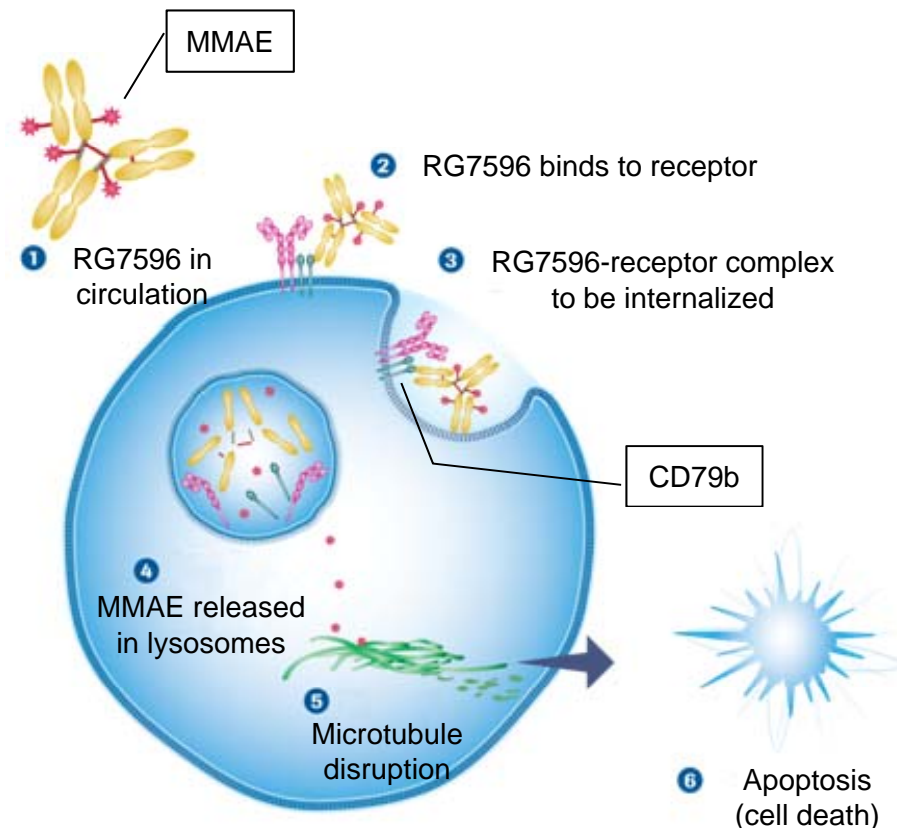
GABA : γ-amino butyric acid

GABA_Aα5 receptor : GABA subtype A receptors containing an α5 subunit

RG7596 (Anti-CD79b ADC) : Mode of Action

- RG7596 (polatuzumab vedotin) is an antibody-drug conjugate (ADC) created by Genentech utilizing ADC technology of Seattle Genetics
- Anti-CD79b monoclonal antibody is conjugated to the microtubule inhibitor MMAE via a linker
- CD79b is expressed in various B-cell malignancies including Non-Hodgkin's lymphoma, the target indication of RG7596
- By binding to CD79b, RG7596 is internalized in the cell and is considered to release MMAE, which exerts cytotoxic activity

MMAE = monomethyl auristatin E



<Conceptual illustration>
Created by Genentech

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