



## R&D Activities in FY2012 and R&D Initiatives in the Mid-Range Growth Strategy

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Takeda Pharmaceutical Company Limited

## Takeda R&D Value & Mission

### Value

Takeda is a pharmaceutical company committed to the discovery and development of innovative solutions addressing unmet medical needs of patients through R&D investment

### Mission

- Meet the future promise of Takeda as a leader in the pharmaceutical industry by providing solutions to patients with unmet medical needs
- Transform the R&D organization to be an engine of growth that is an industry leader in R&D productivity

## Looking Back on FY2012

## Looking Back on FY2012 Approval and Filing Achievements

				Ph-1	Ph-2	Ph-3	Filing	Approval
SYR-322 SYR-322/PIO <sup>1</sup> SYR-322/MET <sup>2</sup>	NESINA® OSEN® KAZANO®	Diabetes mellitus	US					
SGN-35	ADCETRIS®	Relapsed/Refractory Hodgkin lymphoma Relapsed/Refractory sALCL	EU					
ferumoxytol	RIENSO®	Iron deficiency anaemia in adult patients with chronic kidney disease	EU					
TAK-085	LOTIRIGA®	Hyperlipidemia	JP					
risedronate	BENET®	Osteoporosis (once-monthly formulation)	JP					
AG-1749	TAKEPRON®	H. Pylori gastritis (triple therapy)	JP					
Lu AA21004	BRINTELLIX®	Major depressive disorder	US					
naltrexone SR/ bupropion SR	CONTRACE®	Obesity	US					Preparing to file soon
MLN0002		Ulcerative colitis, Crohn's disease	US					Preparing to file soon
MLN0002		Ulcerative colitis, Crohn's disease	EU					
SYR-322 SYR-322/PIO <sup>1</sup> SYR-322/MET <sup>2</sup>		Diabetes mellitus	EU					
lurasidone		Schizophrenia	EU					
ATL-962		Obesity	JP					
AG-1749	TAKEPRON®	FDC with low-dose aspirin	JP					
BLB-750		Prevention of pandemic influenza	JP					
SGN-35		Relapsed/Refractory Hodgkin lymphoma Relapsed/Refractory sALCL	JP					

## Looking Back on FY2012 Major Ongoing Ph-3 Programs



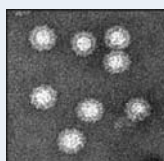
<b>TAK-875</b> <fasiglifam>	Diabetes mellitus	Ongoing Ph-3 studies include head-to-head with sitagliptin, concomitant use trials (with metformin, SU and DPP4 inhibitor), and CV outcomes study.	<b>Global</b>
<b>TAK-700</b> <orteroneI>	Prostate cancer	Ongoing Ph-3 studies include pre-chemo and post-chemo in metastatic, castration-resistant patients. Ph-2 without steroid in non-metastatic, castration resistant patients has been completed, Ph-3 to begin in FY2013.	<b>Global</b>
<b>MLN9708</b> <ixazomib>	Multiple myeloma Relapsed/Refractory AL amyloidosis	Ongoing Ph-3 in multiple myeloma in combination with Revlimid/Dexamethasone for all-oral regimen.	<b>Global</b>
<b>MLN8237</b> <alisertib>	Relapsed/Refractory peripheral T-cell lymphoma	Earlier stage trials also ongoing in variety of hematological malignancies and solid tumors.	<b>US/EU</b>
<b>ADCETRIS®</b> <brentuximab vedotin>	Post-transplant Hodgkin lymphoma Relapsed cutaneous T-cell lymphoma Front line Hodgkin lymphoma Front line mature T-cell lymphoma	Collaboration with Ventana Medical Systems using companion diagnostic test to identify CD30 expression in patients in Ph-3 studies for CTCL and MTCL.	<b>EU</b>
<b>SYR-472</b> <trelagliptin>	Diabetes mellitus	Ongoing Ph-3 studies of once-weekly SYR-472 compared to a once-daily DPP4 inhibitor.	<b>JP</b>
<b>TAK-438</b> <vonoprazan>	Acid-related diseases (GERD, Peptic ulcer, etc.)	Ongoing Ph-3 studies include head-to-head studies with lansoprazole.	<b>JP</b>

## Looking Back on FY2012 Partnerships & Business Development



### LigoCyte (now Takeda Vaccine (Montana) Inc.)

- Only clinical-stage norovirus vaccine in the world
- Pre-clinical pipeline including vaccines for rotavirus, RSV virus and influenza
- Virus-Like Particle (VLP) technology



LigoCyte's norovirus VLP

### Envoy Therapeutics

- bacTRAP technology to identify proteins produced by specific cell types
- Pre-clinical pipeline including innovative programs for Parkinson's disease, schizophrenia, etc.



Stained protein on mouse brain tissue



Research collaboration with **BC Cancer Agency** to explore new drug targets based on gene analysis



Discovery collaboration with **Advinus Therapeutics** focused on novel targets in inflammation, CNS and metabolic diseases



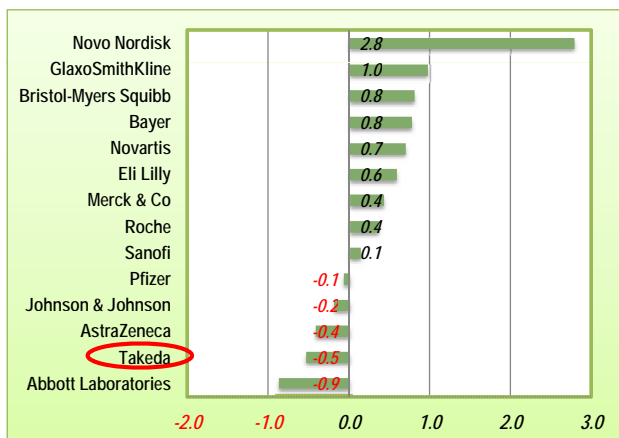
Partnership with **Resolve Therapeutics** to develop compounds for the treatment of Systemic Lupus Erythematosus (SLE) and other autoimmune diseases

## Looking Back on FY2012 R&D Productivity



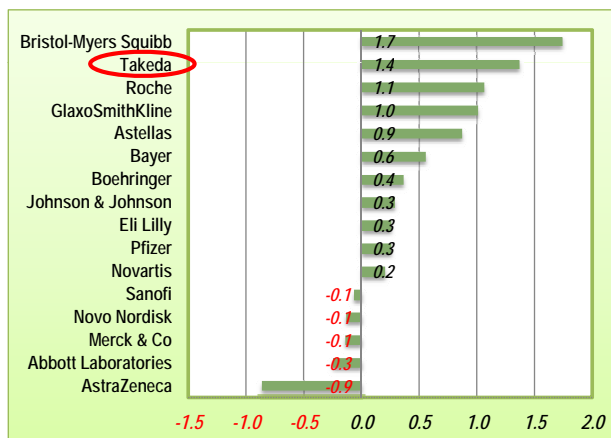
### Criteria to Assess R&D Productivity

2 year period from '08 year end – '10 year end  
data as of Aug 23, 2011,  
Source: Parexel Biopharmaceutical statistical Sourcebook, Evaluate Pharma



### Criteria to Assess R&D Productivity

2 year period from '09 year end – '11 year end  
data as of Nov 14, 2012,  
Source: Parexel Biopharmaceutical statistical Sourcebook, Evaluate Pharma



Note: Methodology; Expected NPV (eNPV) of products at clinical stage (Phase 1 or later) is used. eNPV at the end of year 2008 is subtracted from eNPV at the end of 2010, followed by addition of NVP of products launched in 2009-2010. The delta eNPV is the divided by the total R&D expenditure of 2009-2010

Note: Methodology; Expected NPV (eNPV) of products at clinical stage (Phase 1 or later) is used. eNPV at the end of year 2009 is subtracted from eNPV at the end of 2011, followed by addition of NVP of products launched in 2010-2011. The delta eNPV is the divided by the total R&D expenditure of 2010-2011

## Looking Back on FY2012 R&D Productivity



**R&D Productivity significantly improved in FY2012**

**1.8-fold**

**NDA/MAA  
approvals**

**1.9-fold**

**POC&C  
achievements**

**2.2-fold**

**Ph-2  
Stage-up**

**2.2-fold**

**IND filings**

Calculated by value creation (expected peak year sales) compared to the value goals set at the beginning of FY2012

## R&D Initiatives in the Mid-Range Growth Strategy

## Continued Focus on 6 Therapeutic Areas

### Pipeline Assets in Ph-2 or Beyond

#### Cardiovascular & Metabolic

- NESINA
- OSENI (LIOVEL)
- KAZANO
- CONTRAVE
- ATL-962
- TAK-875
- SYR-472
- BLOPRESS/CCB\*
- EDARBI
- EDARBYCLOR
- AZILVA/CCB\*
- LOTRIGA
- TAK-428

#### Oncology

- VELCADE
- LUPRON
- ADCETRIS
- MLN9708
- MLN8237
- TAK-700
- motesanib
- AMG 386

#### CNS

- BRINTELLIX
- Iurasidone
- AD-4833/TOMM40
- TAK-375SL
- SOVRIMA

#### Immunology & Respiratory

- DAXAS
- DAXAS combo
- veltuzumab

#### General Medicine

- TAKEPRON
- TAKEPRON/LDA\*\*
- DEXILANT
- RIENSO
- AMITIZA
- BENET
- MLN0002
- TAK-438
- TAK-385

#### Vaccine

- BLB-750
- TAK-816
- TAK-361S
- Norovirus vaccine

\*Calcium Channel Blocker  
\*\* Low-dose aspirin

## Focus for Mid-Range Growth Strategy Special Initiatives



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## Improving R&D Productivity



Short term: Leverage our advantage of a rich late-stage pipeline

### Successful Programs Toward Approvals

Lu AA21004  
(vortioxetine)

Contrave

MLN0002  
(vedolizumab)

Iurasidone

### Focus Attentions on Ph-3 Programs

TAK-875  
(fasiglifam)

TAK-438  
(vonoprazan)

MLN9708  
(ixazomib)

TAK-700  
(orteronel)

### Progress Valuable Late-stage Assets

AD-4833/TOMM40

Norovirus Vaccine

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## Mid term: Fill the Gap in the Mid-stage Portfolio with 3 Strategies

### Push Forward Promising Preclinical & Clinical Assets

**TAK-385**

**MLN8237**

**MLN4924**

- AMPA potentiator
- CD38 receptor antibody

### Mono-oki Project: Explore additional uses for existing compounds

Looking at possible indications such as in diabetes, NASH, asthma, Idiopathic pulmonary fibrosis, schizophrenia etc.

### Business Development

Focus on assets that are ready for a POC&C experiment

## Takeda acquires Inviragen

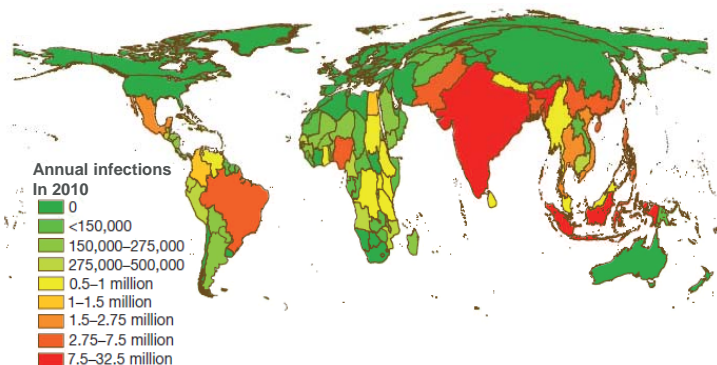
And its vaccine against Dengue, which threatens half of the world's population

### Expands pipeline with vaccines that are high priority in EMs

- Dengue (Ph 2)
- Enterovirus 71 (Ph 1)<sup>1</sup>
- Chikungunya (Preclinical)

### Extends Takeda's vaccine R&D capabilities to inactivated and live viral vaccines, building upon LigoCyte's capabilities

Dengue is “the most important mosquito-borne viral disease in the world” affecting populations across Asia, Latin America and Africa<sup>2</sup>



### Estimated annual global burden of Dengue

- 400 million people infected
- 100 million develop clinical illness
- 500 thousand hospitalized
- 20 thousand deaths, mostly in children



**inviragen**

<sup>1</sup>Hand, foot and mouth disease caused by Enterovirus 71 (EV71)

<sup>2</sup> <http://www.who.int/csr/disease/dengue/impact/en/>

Source of graphic: Bhatt, S et al. *Nature* Vol. 496, 504-507 (2013)

## Long term: Strengthen Research Competitiveness & Productivity

Great Progress in FY12 to bridge the gap in Productivity  
required for optimum competitiveness

Decreased research cost  
per candidate

Fast to IND

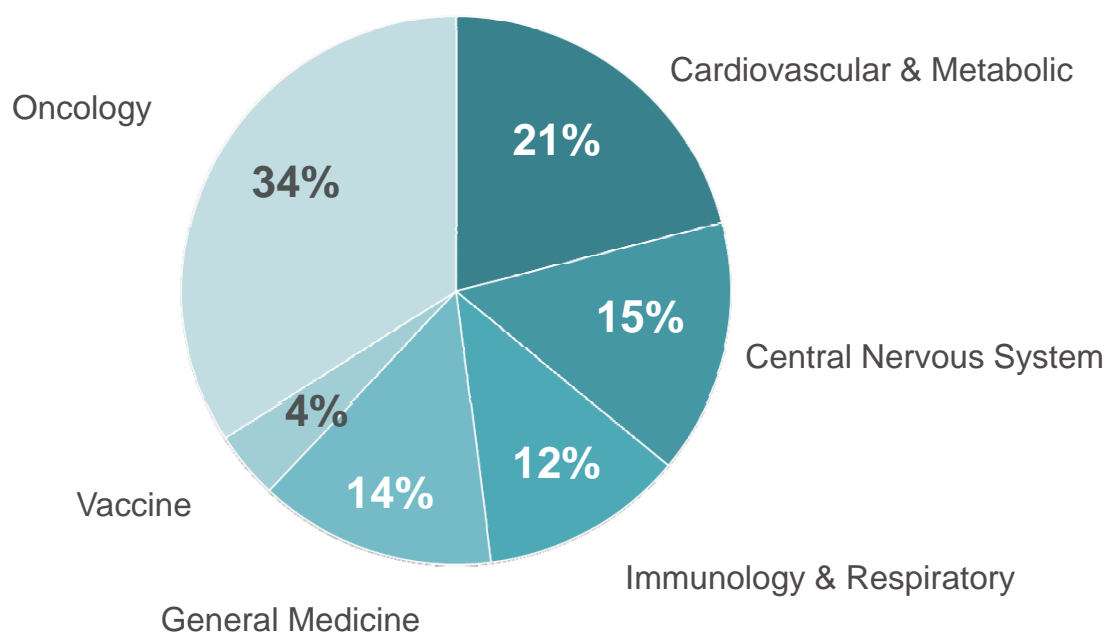
Key Initiatives undertaken in FY12 to be progressed to create an environment  
to enhance further greater competitiveness & productivity

Reinforced Drug  
Discovery Units  
(DDUs)

Elaboration of the  
potential of Envoy,  
Advinus, Resolve

Fast to Candidate

## R&D Budget in FY2013





# Ensuring Steady Pipeline Approval



	FY13	FY14	FY15	FY16 - FY17
<b>JP</b>	azilsartan (TAK-536) CCB <sup>1</sup> lansoprazole (AG-1749) LDA <sup>2</sup> cetilistat (ATL-962) influenza vaccine (BLB-750) brentuximab vedotin (SGN-35)	trelagliptin (SYR-472) vonoprazan (TAK-438) vortioxetine (Lu AA21004)	fasiglifam (TAK-875) ixazomib (MLN9708) orteronel (TAK-700) leuporelin 6M (TAP-144-SR) Hib vaccine (TAK-816)	relugolix (TAK-385) vedolizumab (MLN0002)
<b>US</b>	vortioxetine (Lu AA21004)	vedolizumab (MLN0002) orteronel (TAK-700)	ixazomib (MLN9708) alisertib (MLN8237)	fasiglifam (TAK-875) ramelteon (TAK-375) SL
<b>EU</b>	alogliptin (SYR-322) alogliptin MET <sup>3</sup> alogliptin PIO <sup>4</sup> dextansoprazole (TAK-390MR) lurasidone	azilsartan (TAK-491) CLD <sup>5</sup> vedolizumab (MLN0002)	ixazomib (MLN9708) orteronel (TAK-700)	fasiglifam (TAK-875)
<b>EM NA<sup>6</sup></b>	In emerging markets and North Asia, compounds including alogliptin, azilsartan, brentuximab vedotin, MEPACT, ramelteon, dextansoprazole, DAXAS will be launched consecutively.			

Please note that approval timing of several products, including certain in-licensed items, are not disclosed

<sup>1</sup> Calcium Channel Blocker (amlodipine), <sup>2</sup> Low Dose Aspirin, <sup>3</sup> Metformin, <sup>4</sup> Pioglitazone (ACTOS), <sup>5</sup> Chlorthalidone, <sup>6</sup> Emerging Market + North Asia,

In-house In-license

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