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

Dr. Tadataka Yamada
Director and Chief Medical & Scientific Officer

May 9, 2013

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<br>SYR-322/PIO[1]<br>SYR-322/MET[2] | NESINA®<br>OSENI®<br>KAZANO® | Diabetes mellitus | US | | | | | |
| SGN-35 | ADCETRIS® | Relapsed/Refractory Hodgkin lymphoma<br>Relapsed/Refractory sALCL | EU | | | | | |
| ferumoxytol | RIENSO® | Iron deficiency anaemia in adult patients with chronic kidney disease | EU | | | | | |
| TAK-085 | LOTRIGA® | 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/<br>bupropion SR | CONTRAVE® | 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<br>SYR-322/PIO[1]<br>SYR-322/MET[2] | | 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<br>Relapsed/Refractory sALCL | JP | | | | | |

[1] Pioglitazone (Actos), [2] Metformin

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

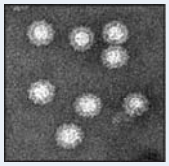
| | | | |
|---|---|---|---|
| **TAK-875** <fasiglifam> | Diabetes mellitus | Ongoing Ph-3 studies include head-to-head with sitagliptin, concomitant use trials (with metformin, SU and DPP4 inhibitor), and CV outcomes study. | **Global** |
| **TAK-700** <orteronel> | Prostate cancer | Ongoing Ph-3 studies 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. | **Global** |
| **MLN9708** <ixazomib> | Multiple myeloma<br>Relapsed/Refractory AL amyloidosis | Ongoing Ph-3 in multiple myeloma in combination with Revlimid/Dexamethasone for all-oral regimen. | **Global** |
| **MLN8237** <alisertib> | Relapsed/Refractory peripheral T-cell lymphoma | Earlier stage trials also ongoing in variety of hematological malignancies and solid tumors. | **US/EU** |
| **ADCETRIS®** <brentuximab vedotin> | Post-transplant Hodgkin lymphoma<br>Relapsed cutaneous T-cell lymphoma<br>Front line Hodgkin lymphoma<br>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. | **EU** |
| **SYR-472** <trelagliptin> | Diabetes mellitus | Ongoing Ph-3 studies of once-weekly SYR-472 compared to a once-daily DPP4 inhibitor. | **JP** |
| **TAK-438** <vonoprazan> | Acid-related diseases (GERD, Peptic ulcer, etc.) | Ongoing Ph-3 studies include head-to-head studies with lansoprazole. | **JP** |



# 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

BC Cancer Agency CARE + RESEARCH

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

ADVINUS

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

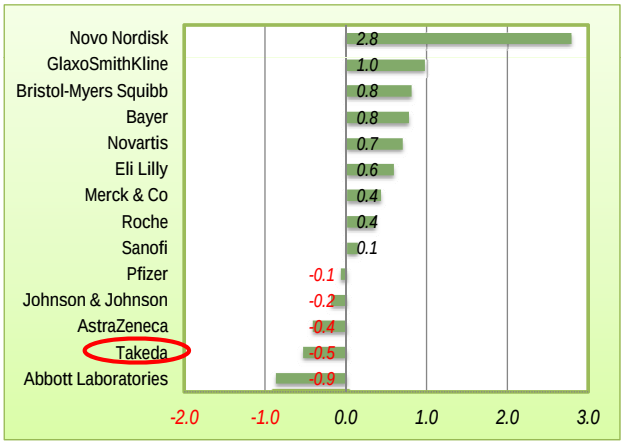
Resolve THERAPEUTICS

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

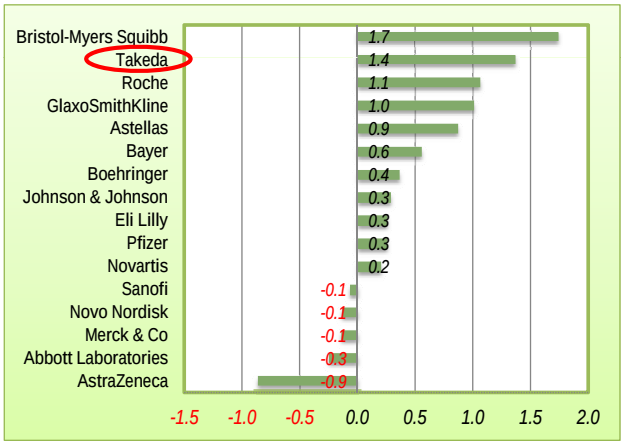
2 year period from '08 year end – '10 year end
data as of Aug 23, 2011,
Source: Parexel Biopharmaceutical statistical Sourcebook, Evaluate Pharma




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

## 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 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 | 1.9-fold | 2.2-fold | 2.2-fold |
|---|---|---|---|
| NDA/MAA approvals | POC&C achievements | Ph-2 Stage-up | 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
- lurasidone
- 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




# 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) | lurasidone |

**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 |

# Improving R&D Productivity

## 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<br>• 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

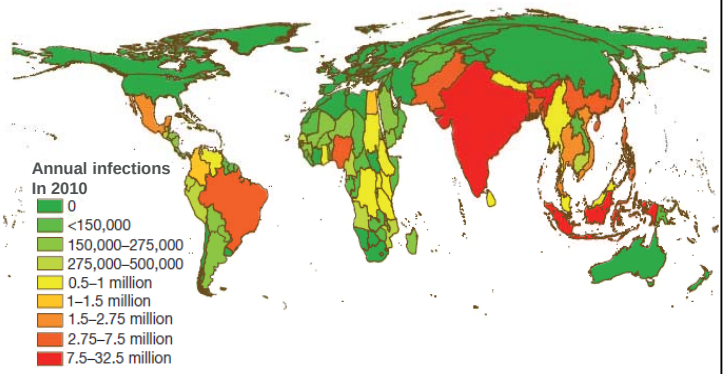
## And its vaccine against Dengue, which threatens half of the world's population

**Expands pipeline with vaccines that are high priority in EMs**
- Dengue (Ph 2)
- Enterovirus 71 (Ph 1)[1]
- Chikungunya (Preclinical)

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

inviragen

**Dengue is "the most important mosquito-borne viral disease in the world" affecting populations across Asia, Latin America and Africa[2]**




**Estimated annual global burden of Dengue**
- 400 million people infected
- 100 million develop clinical illness
- 500 thousand hospitalized
- 20 thousand deaths, mostly in children

[1]Hand, foot and mouth disease caused by Enterovirus 71 (EV71)
[2] http://www.who.int/csr/disease/dengue/impact/en/
Source of graphic: Bhatt, S et al. *Nature* Vol. 496, 504-507 (2013)

# Improving R&D Productivity

## Long term: Strengthen Research Competitiveness & Productivity

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

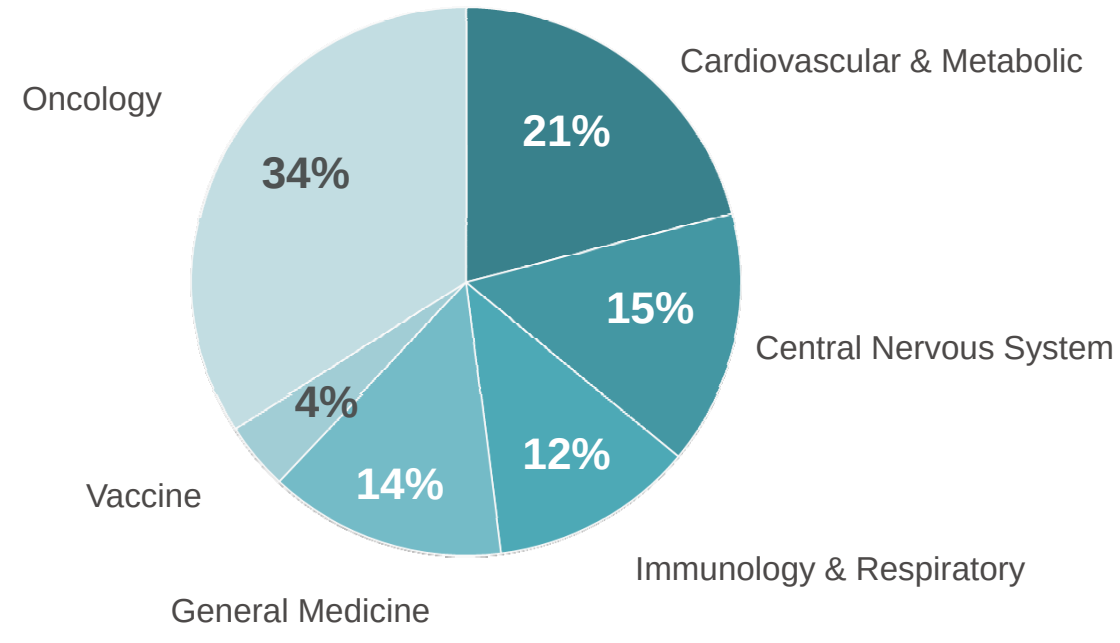
- Decreased research cost per candidate
- Fast to IND

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

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

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

In-house | In-license



# Forward-Looking Statements

This presentation contains forward-looking statements regarding the Company's plans, outlook, strategies, and results for the future.

All forward-looking statements are based on judgments derived from the information available to the Company at this time. Forward looking statements can sometimes be identified by the use of forward-looking words such as "may," "believe," "will," "expect," "project," "estimate," "should," "anticipate," "plan," "continue," "seek," "pro forma," "potential," "target, " "forecast," or "intend" or other similar words or expressions of the negative thereof.

Certain risks and uncertainties could cause the Company's actual results to differ materially from any forward looking statements contained in this presentation. These risks and uncertainties include, but are not limited to, (1) the economic circumstances surrounding the Company's business, including general economic conditions in the US and worldwide; (2) competitive pressures; (3) applicable laws and regulations; (4) the success or failure of product development programs; (5) decisions of regulatory authorities and the timing thereof; (6) changes in exchange rates; (7) claims or concerns regarding the safety or efficacy of marketed products or product candidates; and (8) integration activities with acquired companies.

We assume no obligation to update or revise any forward-looking statements or other information contained in this presentation, whether as a result of new information, future events, or otherwise.