Focused World Class R&D
New approaches to innovation

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Takeda Pharmaceutical Company Limited

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Our mission is to serve patients

Takeda is a patient-centric, science-driven company

We do more than develop medicines
We strive towards better health and a brighter future for people worldwide

Focused world class R&D is a vital component of our strategic roadmap

VALUES
Takeda-ism
Patient → Trust → Reputation → Business

PEOPLE
Patient and customer centricity
Agile global organization
Fostering talent

R&D
Focused world class R&D
New approaches to innovation

BUSINESS PERFORMANCE
Sustaining sales growth
GI, Oncology, CNS and Emerging Markets
Sustaining profit growth
Cost discipline
Our strategy for focused world class R&D involves four major components:

1. Focus our Therapeutic Areas
2. Optimize our Pipeline
3. Enhance our Capabilities
4. Transform our Culture

**R&D Strategy**
*Patient-centric Science-driven*

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**Agenda**

**Building on our heritage**
Recognizing increasing demand for innovation

Four major components in our strategy for focused world class R&D
- Focus our Therapeutic Areas
- Optimize our Pipeline
- Enhance our Capabilities
- Transform our Culture

Therapeutic area R&D strategy highlights
- Oncology
- Gastroenterology (GI)
- Central Nervous System (CNS)
- Vaccines

Summary
Takeda has a 235 year heritage of successful, sustained innovation translating science into life-changing medicines.

**GLOBAL PORTFOLIO**
- **PREVACID** - Acid reflux disease
- **LUPRON** - Prostate cancer (Lupron Depot launched 1989)
- **actos** - Pioglitazone HCI, Type 2 diabetes
- **VELCADE** - Multiple myeloma (launched 2003, acquired 2008)
- **Entyvio** - Vedolizumab, Ulcerative colitis, Crohn's disease
- **NINLARO** - (xerobrom) capsules, R/R multiple myeloma

**REGIONAL PORTFOLIO**
- Origins in herbal medicine
- Pioneering role in anti-virals, antibiotics, pediatric vaccines, etc.

**Partnering for global launches**


**Products tailored to individual market needs, in-license deals leveraging regional strengths**

**Maximizing the potential of our marketed portfolio is key to near- and mid-term success**

Takeda will invest ~50% of FY16 and FY17 development budget to maximizing these assets.

**Oncology**
- **Phase 1**
  - ENTYVIO®: Hematologic monoclonal antibody against IL-6 receptor (CD26)
  - ENTYVIO®: Hematologic monoclonal antibody against IL-6 receptor
  - TAKECAB®: Potassium competitive acid blocker

- **Phase 2**
  - TAKECAB®: Potassium competitive acid blocker

**GI**
- **Phase 1**
  - ENTYVIO®: Hematologic monoclonal antibody against IL-6 receptor (CD26)

- **Phase 2**
  - ENTYVIO®: Hematologic monoclonal antibody against IL-6 receptor
  - AMITIZA®: Cholecystokinin activator

**CNS**
- TRINTELLIX™: Multimodal antidepressant (NCE LPS)

**Vaccines**
- AZILVA®: FDC with Methylprednisolone (HCTZ) (JP, AR, ABB, Argentina)

**Other**
- BENET™: Bone receptor activator (JP, Asia-Pac, Europe)

**Filed**
- NINLARO®: R Raf inhibitor (EU & Emerging Markets)
- ADCETRIS®: CD30 ADC (EML)
- AZILECT®: MAOI (JP, AR, Argentina)
- TRINTELLIX™: Multimodal antidepressant (NCE LPS, India, China, Korea)
- ULORIC®: Non-potential XA inhibitor, XR formulation (JP, AR, ABB, Argentina)

This slide includes ongoing studies and planned studies starting this year. See appendix for list of abbreviations.

* AZILECT is brand name in Tova territories.

Takeda Pharmaceutical Company Limited
Agenda

Building on our heritage

Recognizing increasing demand for innovation

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- Vaccines

Summary

The explosion of new modalities offers the potential to treat diseases in new ways

1. E.g., nanotechnologies, bioelectronics, virus particles
2. Currently ~60% of global clinical pipeline
Truly differentiated medicines based on these new modalities are being developed increasingly by biotechs.

Origination of Global Top 100 Products

Worldwide Sales, Global Top 100 Products

- **2007**: $226 B
  - Pharma: 48% (73%)
  - Biotech, non-profit/academia: 21% (27%)
  - Other Pharma: 6%

- **2015**: $270 B
  - Pharma: 29% (48%)
  - Biotech, non-profit/academia: 45% (54%)
  - Other Pharma: 9%

Breakthroughs in science and medicine have led to increasing demand for innovation.

- Payers set a high bar for differentiated medicines
- Patients need new advances in medicine to address significant global unmet medical needs

Takeda will address this demand with a patient-centric, science-based strategy for world class R&D.
Agenda

Building on our heritage
Recognizing increasing demand for innovation

**Four major components in our strategy for focused world class R&D**

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- Optimize our Pipeline
- Enhance our Capabilities
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Therapeutic area R&D strategy highlights

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- Vaccines

Summary

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Our strategy for focused world class R&D involves four major components

1. Focus our Therapeutic Areas
2. Optimize our Pipeline
3. Enhance our Capabilities
4. Transform our Culture

R&D Strategy

Patient-centric
Science-driven
Focus Therapeutic Areas

We know that companies with narrower therapeutic area focus outperform their peers

% Probability From Phase I To Launch For All Drugs In A Given Category¹ (1996 - 2013)

- Industry average
- Best-in-class specialist company³

<table>
<thead>
<tr>
<th>Category</th>
<th>Industry average</th>
<th>Best-in-class specialist company</th>
</tr>
</thead>
<tbody>
<tr>
<td>CNS</td>
<td>7%</td>
<td>25%</td>
</tr>
<tr>
<td>Oncology</td>
<td>11%</td>
<td>22%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>17%</td>
<td>31%</td>
</tr>
<tr>
<td>Virology</td>
<td>8%</td>
<td>44%</td>
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<tr>
<td>Enzyme replacement</td>
<td>37%</td>
<td>86%</td>
</tr>
</tbody>
</table>

¹ Category definitions: Central Nervous System (CNS) as main therapy class; Cancer as primary indication group; Diabetes as primary indication group; HIV/AIDS infection as primary indication; Enzyme replacement = Recombinant protein AND Endocrine as main therapy classes, includes reformulated drugs.
² Total number of phase transitions included in each calculation. Includes reformulations.
³ Companies with very high success rates in R&D in the respective Therapeutic Areas based on Takeda analysis.

Focus Therapeutic Areas

We are focusing our efforts in the therapeutic areas where we want to be at the cutting edge of innovation

Core focus

- Oncology
- Gastroenterology (GI)
- Central Nervous System (CNS)
- Vaccines
- Specialty CV

We are focusing our innovation in three core therapeutic areas where we have:
- Track record of recent successes
- Deep scientific expertise
- High unmet patient need

We are committed to global public health through our Vaccines portfolio

Targeted approach to specific assets

- Autoimmune Diseases (such as psoriasis, RA)¹
- Respiratory
- Nephrology
- Metabolism
- Women's Health and General Medicine²

¹ Ongoing discovery platform to support autoimmune diseases, GI inflammation and CNS inflammation interests
² Genitourinary, pain, others (e.g., sepsis)
Optimizing our R&D pipeline requires discipline and rigorous decision-making

1. Focus our Therapeutic Areas
2. Optimize our Pipeline
3. Enhance our Capabilities
4. Transform our Culture

R&D Strategy
Patient-centric
Science-driven

Optimize Pipeline

A look back: Our FY2013 pipeline of NMEs had many assets in late-stage development

<table>
<thead>
<tr>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3 / Filed</th>
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<tbody>
<tr>
<td><strong>Oncology</strong></td>
<td></td>
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</tr>
<tr>
<td>TAK-117 (MLN117)</td>
<td>TAK-226 (MLN180)</td>
<td>alisertib (MLN235)</td>
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<td>TAK-243 (MLN248)</td>
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<td>orteronel (MLN201)</td>
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<td>TAK-264 (MLN264)</td>
<td>TAK-580 (MLN580)</td>
<td>NINLARO (MLN708)</td>
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<td>TAK-659</td>
<td>TAK-733</td>
<td>motesanib (diphosphate)</td>
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<tr>
<td></td>
<td></td>
<td>trebananib (JP) (AMG 280)</td>
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<tr>
<td></td>
<td>pvenonistat (MLN482 / TAK-324)</td>
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</tr>
<tr>
<td><strong>GI/General Medicine</strong></td>
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<tr>
<td>TAK-233</td>
<td>TAK-114</td>
<td>ENTMYO (IN N0002)</td>
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<tr>
<td></td>
<td>relugolix (TAK-280)</td>
<td>OMTOMYS (pegrotodar)</td>
</tr>
<tr>
<td><strong>CNS</strong></td>
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<td>TAKECAB (TAK-438)</td>
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<tr>
<td>LU AA24530</td>
<td>TAK-483</td>
<td>FOMEPZOLE (JP)</td>
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<td>ITI-214</td>
<td>TAK-137</td>
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<td>AD-4833 TOMM40</td>
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<td></td>
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<td>LATUDA (US) (loradone)</td>
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<tr>
<td><strong>Vaccines</strong></td>
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<td>TAK-021</td>
<td>TAK-003</td>
<td>VaxemM1 (JP) (TAK-016)</td>
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<td>Other</td>
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<tr>
<td>TAK-272</td>
<td>namilumab (MI260)</td>
<td>CONTRAVE (US)</td>
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<tr>
<td>AMG 403</td>
<td>fasigimim (TAK-275)</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>ZAFATEK (EUR-2/2)</td>
</tr>
</tbody>
</table>

Source: Pipeline as of Takeda's FY2013 Q4 earnings materials, May 8th 2014 (also includes fasigimim, terminated Dec. 2013)
## Optimize Pipeline

**Since 2013 we have achieved several key NME approvals**

<table>
<thead>
<tr>
<th>Phase 1</th>
<th>Phase 2</th>
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<td>TAK-102</td>
<td>TAK-154</td>
<td>NINLARO (ME, NR)</td>
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<tr>
<td><strong>GI/General Medicine</strong></td>
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<tr>
<td>TAK-233</td>
<td>TAK-154</td>
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<tr>
<td><strong>CNS</strong></td>
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<td>LU-004260</td>
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<td>TAK-152</td>
<td>TAK-137</td>
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<tr>
<td></td>
<td></td>
<td>AD-4215 TOMMAOD</td>
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<tr>
<td></td>
<td></td>
<td>LATUDA (EU)</td>
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<tr>
<td></td>
<td></td>
<td>CONTRAVE (US)</td>
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<tr>
<td></td>
<td></td>
<td>fasiglumab (TP, EU)</td>
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<tr>
<td><strong>Vaccines</strong></td>
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<tr>
<td>TAK-021</td>
<td>TAK-903</td>
<td>VaxemHib (JP)</td>
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<td></td>
<td>TAK-214</td>
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<tr>
<td></td>
<td>TAK-650 (JP)</td>
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<tr>
<td></td>
<td>TAK-301B (JP)</td>
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<tr>
<td></td>
<td></td>
<td>ZAFATEK (OYR-472)</td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td></td>
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</tr>
<tr>
<td>TAK-272</td>
<td>nemilumab (MT/EU)</td>
<td>CONTRAVE (US)</td>
</tr>
<tr>
<td>AMG-403</td>
<td></td>
<td>fasiglumab (TP, EU)</td>
</tr>
</tbody>
</table>

Note: Does not highlight products that were approved but subsequently divested, returned, or withdrawn from the market.

## Optimize Pipeline

We have divested or returned to partners 4 NMEs that no longer fit with our strategic focus
## Optimize Pipeline

We have terminated programs and discontinued 10 NMEs

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<thead>
<tr>
<th>Phase 1</th>
<th>Phase 2</th>
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<tbody>
<tr>
<td><strong>Oncology</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TAK-264 (MLN0264)</td>
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<td>allisertib (MLN0277)</td>
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<td>motesanib (AMG208)</td>
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<tr>
<td><strong>GI/General Medicine</strong></td>
<td>TAK-114</td>
<td>OMONTYTS (pegylated)</td>
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<tr>
<td>LU A24530</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>CNS</strong></td>
<td>TAK-903</td>
<td>AD-4633 TOMM40</td>
</tr>
<tr>
<td>TAK-137</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Vaccines</strong></td>
<td>TAK-214</td>
<td></td>
</tr>
<tr>
<td>TAK-950</td>
<td>TAK-3615 (Lg)</td>
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<tr>
<td><strong>Other</strong></td>
<td>nemilumab (MT300)</td>
<td>fasigilgam (TAK-879)</td>
</tr>
<tr>
<td>TAK-272</td>
<td></td>
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<tr>
<td>AMG 403</td>
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</tbody>
</table>

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### Optimization Pipeline

In our core focus areas, we have added 10 innovative early-stage NMEs

<table>
<thead>
<tr>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3 / Filed</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Oncology</strong></td>
<td></td>
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</tr>
<tr>
<td>TAK-243 UNC inhibitor Solid Tumors</td>
<td>TAK-589 Pan-HMG kinase inhibitor Solid Tumors</td>
<td>pevonedistat (TAK-592) NAC inhibitor Metastatic Renal Cancer</td>
</tr>
<tr>
<td>XMT-1522 GPR85 agonist colorectal cancer</td>
<td>TAK-831 OX22 antagonist Solid Tumors</td>
<td>TAK-117 Phase III doublet inhibitor Small Cell Lung Cancer</td>
</tr>
<tr>
<td>TAK-202 CCR2 antagonist</td>
<td></td>
<td>trebananib (Lg) Angiogenesis inhibitor Pancreatic Cancer</td>
</tr>
<tr>
<td><strong>GI</strong></td>
<td></td>
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</tr>
<tr>
<td>TAK-328 RhoQ1 activator Crohn’s Disease</td>
<td>TAK-041 SHT3 receptor antagonist GI/AD</td>
<td>TAK-228 st-519 inhibitor Stomach Cancer</td>
</tr>
<tr>
<td><strong>CNS</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TAK-058 5-HT3 receptor antagonist GI/AD</td>
<td>TAK-071 BTK-PHI LBD-AD</td>
<td>TAK-057 CAG-358 inhibitor Schizophrenia, anxiety</td>
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<tr>
<td>TAK-953 AMPA receptor potentiator Treat resistant depression</td>
<td>TAK-831 DCA inhibitor LBD-AD</td>
<td>TAK-083 AD-4633 TOMM40 Microglial agonist inhibitor Delay of M1</td>
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<tr>
<td>TAK-355 ORAU1 inhibitor Epilepsy</td>
<td>TAK-915 PDE4A inhibitor CB-839</td>
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<tr>
<td><strong>Vaccines</strong></td>
<td></td>
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</tr>
<tr>
<td>TAK-214 Dengue</td>
<td>TAK-850 (Lg) Influenza</td>
<td></td>
</tr>
<tr>
<td><strong>Specialty CV</strong></td>
<td></td>
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</tr>
<tr>
<td>TAK-372 Direct renin inhibitor Diabetic nephropathy</td>
<td></td>
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<tr>
<td><strong>Other</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AMG 403 human monoclonal antibody against tumor HGF</td>
<td>TAK-202 Repositioned to oncology from CV/Metabolic</td>
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<tr>
<td>TAK-359 Direct renin inhibitor Rheumatoid arthritis</td>
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<tr>
<td>TAK-879 Anti-CGR8 only Rheumatoid arthritis</td>
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<td></td>
</tr>
<tr>
<td>nemilumab (MT300) GPCR 56 monoclonal antibody Promises 6 &amp; 8</td>
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</tr>
</tbody>
</table>

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*TAK-202 repositioned to oncology from CV/Metabolic, **XMT-1522 is still pre-clinical, INH expected in 2016*
2. **Optimize Pipeline**

Our pipeline today is strategically focused with exciting early assets; we must continue to optimize for sustainability.

### Oncology

- **Phase 1**
  - TAK-202 (GCY-717, Immunomodulator)
  - TAK-243 (anti-TGF-b, Monoclonal Antibody)
  - TAK-699 (anti-VEGF, Monoclonal Antibody)
  - TAK-608 (anti-VEGF, Monoclonal Antibody)
  - TAK-831 (anti-VEGF, Monoclonal Antibody)

- **Phase 2**
  - Pembrolizumab (Anti-PD-1, Monoclonal Antibody)
  - Nivolumab (Anti-PD-1, Monoclonal Antibody)
  - pembrolizumab (anti-PD-1, Monoclonal Antibody)

- **Phase 3**
  - trebananib (PTP, Anti-angiogenic Factor)

### GI

- TAK-628 (anti-angiogenic factor)

### CNS

- TAK-295 (anti-angiogenic factor)
- TAK-63 (anti-angiogenic factor)
- TAK-393 (anti-angiogenic factor)

### Vaccines

- TAK-201 (Vaccines)
- TAK-805 (Vaccines)
- TAK-814 (Vaccines)

### Specialty CV

- AMG 403 (anti-angiogenic factor)
- TAK-272 (anti-angiogenic factor)
- TAK-379 (anti-angiogenic factor)

### Other

- TAK-021 (Vaccines)
- TAK-805 (Vaccines)
- TAK-806 (Vaccines)

Note: this slide does not represent the entire pipeline.

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3. **Enhance Capabilities**

To optimize our pipeline using cutting-edge science and technology, we need enhanced capabilities in key areas.

1. **Focus our Therapeutic Areas**
2. **Optimize our Pipeline**
3. **Enhance our Capabilities**
4. **Transform our Culture**
3 Enhance Capabilities
We are strengthening essential capabilities through further focus on external innovation

A robust innovation network is the core of our future
3 Enhance Capabilities

We are building a network through innovative models to become among the best partners in the industry.

Takeda Innovation Network

- Bill & Melinda Gates Foundation: Grant for polio vaccine development
- Kyoto University: T-CiRA collaboration
- Tri-I TDI: Collaborative drug discovery
- Mersana: Next generation ADCs
- Theravance: Novel agent for gastrointestinal motility disorders
- Enterome: Microbiome for GI
- Prosetta: Neurodegenerative disease therapies
- ImmunoGen: Oncology, ADC
- enGene: GI therapies
- Cour: Celiac disease, GI therapies
- Seattle Genetics
- ImmunoGen
- Mersana Therapeutics
- MacroGenics
- T-CiRA

We are currently working in a variety of new modalities through our innovation network.

Monoclonal antibodies/ADCs

- Seattle Genetics
- ImmunoGen
- Mersana Therapeutics
- MacroGenics

Gene therapy

- enGene

Nano-biotechnology

- Cour

RNA-binding proteins

- Keio University
- Niigata University

Enterome

Microbiome-derived agents

Recombinant proteins (non-mAb)

Cell and tissue therapies

RNA-binding proteins

Monoclonal antibodies

Peptides
3 Enhance Capabilities
Our T-CiRA partnership creates new modality opportunities across our therapeutic areas

- Groundbreaking Takeda partnership with Center for iPS Cell Research and Application (CiRA), Kyoto University
- Collaboration led by Nobel laureate Prof. Shinya Yamanaka
- iPS cells can differentiate into any type of cell in the body, making them very promising for regenerative medicine, as well as drug discovery for a wide range of conditions including rare and intractable diseases
- Takeda hosts the joint collaboration to develop innovative treatments from iPS technology at our Shonan site
- Takeda is playing a unique role, fostering important medical innovation in Japan

4 Transform Culture
We are transforming our culture to drive progress on our strategy

- Focus our Therapeutic Areas
- Optimize our Pipeline
- Enhance our Capabilities
- Transform our Culture

This transformation requires... leadership, agility and a culture of actively seeking connection with partners and trends in the external landscape
This focus permeates our R&D culture, reinforced by our investments and decisions

- Simplified leadership with clear accountability
  - Seasoned leadership team spanning Research, TAUs, externalization
  - Key enabling capabilities embedded in leadership structure
  - Building next generation of leaders in partnership with Massachusetts Institute of Technology

- Agile structure to implement strategy, seize opportunities and act swiftly
  - Key governance committee co-chaired with Commercial
  - Other decisions devolved to teams

- Streamlined external business development structure to build and maintain critical linkages with external partners
  - One leader (D. Curran) accountable for driving externalization across all Takeda R&D business development

We are rapidly becoming a focused, world class R&D organization

1. Focus our Therapeutic Areas
2. Optimize our Pipeline
3. Enhance our Capabilities
4. Transform our Culture

R&D Strategy
Patient-centric
Science-driven
We are rapidly becoming a focused, world class R&D organization

- Oncology
- GI
- CNS
- Vaccines

- LCM
- Prioritize, Accelerate
- Innovation network

R&D Strategy
Patient-centric
Science-driven

- Modality
- Diversification
- Translational Medicine
- Genomics & Big Data
- Innovation network

- Leadership
- Agility
- External mindset

Agenda

Building on our heritage
Recognizing increasing demand for innovation
Four major components in our strategy for focused world class R&D
- Focus our Therapeutic Areas
- Optimize our Pipeline
- Enhance our Capabilities
- Transform our Culture

Therapeutic area R&D strategy highlights

Presented by Andy Plump

- Oncology
- Gastroenterology (GI)
- Central Nervous System (CNS)
- Vaccines

Summary
Our oncology strategy builds on current pipeline success and strengthens new capabilities through partnerships.

**MAXIMIZE**
NINLARO & ADCETRIS

**PRIORITIZE**
FOCUS ON KEY PIPELINE ASSETS WITH TRANSFORMATIVE POTENTIAL

**COLLABORATE**
ANTIBODY DRUG CONJUGATES & PARTNERING IN IMMUNO-ONCOLOGY

Deliver to broader patient populations  Set high barriers to differentiate, sourcing from internal and external expertise  Bringing internal expertise in discovering and developing targeted therapies together with external cutting-edge platforms and capabilities

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We are maximizing the clinical potential of our recently launched medicines NINLARO and ADCETRIS

<table>
<thead>
<tr>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Solid Tumors</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TAK-243 UAB inhibitor Solid Tumors</td>
<td>TAK-202 CDC20 chemokine antagonist Solid Tumors</td>
<td>alisertib (MLN8237) Aurora A kinase inhibitor Small Cell Lung Cancer</td>
</tr>
<tr>
<td>TAK-500 Pan-RAP kinase inhibitor Solid Tumors</td>
<td>TAK-831 CDC7 inhibitor Solid Tumors</td>
<td>relugolix (TAK-385) LH-RH antagonist Prostate Cancer</td>
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<tr>
<td>XMT-1522* anti-HER2 ADC Solid Tumors</td>
<td></td>
<td>TAK-117 PI3Kα/PI3Kδ inhibitor Non-small Cell Lung Cancer</td>
</tr>
<tr>
<td><strong>Hematological Malignancies</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TAK-659 SYK inhibitor Hematologic malignancies</td>
<td>pevonedistat (TAK-554) NAE inhibitor HR Myelodysplastic Syndromes</td>
<td></td>
</tr>
</tbody>
</table>

**ADCETRIS**
CD30 ADC Front Line Hodgkin Lymphoma Front Line Mantle T-cell Lymphoma Relapsed cutaneous T-cell Lymphoma

**NINLARO**
Proteasome inhibitor Front Line Multiple Myeloma Maintenance Multiple Myeloma post-Stem Cell Transplant Maintenance Multiple Myeloma without Stem Cell Transplant R/R AL Amyloidosis

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**Earlier clinical stage assets enrich the scope of our oncology pipeline**

<table>
<thead>
<tr>
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<tbody>
<tr>
<td><strong>Solid Tumors</strong></td>
<td><strong>Hematological Malignancies</strong></td>
<td><strong>AMG386</strong></td>
</tr>
<tr>
<td>TAK-243 UAE inhibitor</td>
<td>alisertib (MLN8237)</td>
<td>Anti-angiopetin peptide (tirapazamine) Ovarian Cancer</td>
</tr>
<tr>
<td>Solid Tumors</td>
<td>Aurora A kinase inhibitor</td>
<td>Small Cell Lung Cancer</td>
</tr>
<tr>
<td>TAK-202 CCR2 chemokine antagonist</td>
<td>TAK-228 mTORC1/2 inhibitor</td>
<td>Renal Cell Carcinoma Breast Cancer Endometrial Cancer</td>
</tr>
<tr>
<td>Solid Tumors</td>
<td>relugolix** (TAK-388)</td>
<td>LH-RH antagonist Prostate Cancer</td>
</tr>
<tr>
<td>TAK-500 Pan-RAF kinase inhibitor</td>
<td>TAK-117 PI3Kα/δ isoform inhibitor</td>
<td>Non-small Cell Lung Cancer*****</td>
</tr>
<tr>
<td>Solid Tumors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>XMT-1522* anti-HER2 ADC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Solid Tumors</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*TMT-1522 is still pre-clinical, IND expected in 2016

**Also in Phase 3 for uterine leiomyomata, Phase 2 for endometriosis. Takeda has granted Myovant an exclusive, worldwide license to relugolix, excluding Japan and certain other Asian countries.

***Also in Gastric cancer in Phase 1, ****Also in Solid Tumors in Phase 1,

---

**TAK-659 is a SYK/FLT-3 dual inhibitor that is a potential innovative oral medicine for hematological malignancies**

**BCR Clinical Precedence Established**
- BTK: Ibrutinib (CLL, MCL, WM)
- PI3Kδ: Idelalisib (CLL, FL, SLL)

**TAK-659 SYK Inhibitor**
- Unique SYK inhibitor with good pharmaceutical properties
- SYK signaling is critical for B-cell and myeloid malignancies

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**Source:** Trends in Immunology December 2013, Vol. 34, No. 12

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Takeda Pharmaceutical Company Limited

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CLL: chronic lymphocytic leukemia; MCL: mantle cell lymphoma; WM: Waldenstrom's macroglobulinaemia; Fl: follicular lymphoma; SLL: small lymphocytic lymphoma
We are pursuing three distinct hypotheses for TAK-659 based on evolving science and emerging data.

**Differentiated Opportunities**

**BCR Hypothesis**
*Non-Hodgkin Lymphoma (NHL)*
- Ongoing Ph1 expansion in NHL
- Early efficacy data show: 8/21 DLBCL and 3/3 FL responders

**BTK Resistance**
*BTK resistance: CLL and MCL*
- Ongoing Ph1 study in ibrutinib relapse/refractory CLL/MCL patients

**Immuno-Oncology**
*Initiate PD-1 Combination Study*
- Evolving science on the diverse roles of SYK in immunological functions

**Partial Response in a patient with DLBCL**
- Ann Arbor Stage III, GCB subtype; heavily pretreated flu auto-HSCT
- Baseline vs. End of Cycle 2 (60 mg)

**Overview of immune system components which could be targeted by IO therapies**

- **T-cell**
- **NK cell**
- **Dendritic cell**
- **Macrophage**
- **B-cell**
- **NKT-cell**
- **Local mediators**
- **Myeloid-derived suppressor cell**
- **T-reg (regulatory T-cell)**

**Recent IO products have transformed patient outcomes, but only a portion of the immune system is currently harnessed.**

**Approved Drug**
- **Ipilimumab**
- **Pembrolizumab**
- **Nivolumab**
- **Blinatumomab**

*There is still a broad range of targets for IO mechanisms beyond the approach of currently approved products.*
Takeda’s immuno-oncology R&D strategy focuses on identifying IO entry points beyond T-cell checkpoints

ADCs
- Seattle Genetics
- ImmunoGen
- Mersana

Tumor targeted
- Directly target tumor cell antigens

Bi-specific T-cell engagers
- Tumor targeted immuno-modulators (e.g. STING agonists)

Novel combination with PD-1 inhibitors
- TAK-202 – anti-CCR2 mAb
- TAK-659 – Syk inhibitor
- TAK-580 – pan-Raf inhibitor
- Entyvio

Innate Immune targeted
- Target innate immunocytes

MDSC targets
- Fc-engineered Abs

We will expand cornerstone hematology presence and build in ADCs and IO

Long-Term

Near / Mid-Term

End of FY18

NINLARO & ADCETRIS
- New indications in MM and amyloidosis
- New indications in FLHL and TCLs
- Maintenance platform in MM
- Cornerstone in CD30+ malignancies

Pipeline
- Leverage protein quality control and ADC expertise to drive new programs
- Accelerate current high priority programs
- Modality-diverse sustainable pipeline of early and late-stage programs with transformative potential

ADCs
- Leverage expertise from development of ADCETRIS
- Advance next wave of ADCs utilizing new technologies (e.g. Mersana, Immunogen)
- Seek novel technology to advance targeted delivery beyond ADC constructs

Immuno-oncology
- Explore rational combinations of current pipeline with PD-1 therapy
- Identify new entry points in IO through strategic partnerships
- Invest in emerging transformative sciences
Today's R&D presenters

- Asit Parikh, M.D., Ph.D.
  Head of GI Therapeutic Area Unit
- Emiliangelo Ratti, Ph.D.
  Head of CNS Therapeutic Area Unit
- Rajeev Venkayya, M.D.
  President, Global Vaccines Business Unit

Agenda

- Building on our heritage
- Recognizing increasing demand for innovation
- Four major components in our strategy for focused world class R&D
  - Focus our Therapeutic Areas
  - Optimize our Pipeline
  - Enhance our Capabilities
  - Transform our Culture

Therapeutic area R&D strategy highlights

- Oncology
- **Gastroenterology (GI)**
  - Central Nervous System (CNS)
  - Vaccines

Summary
We seek to become the global GI leader via an R&D engine that maximizes a diverse portfolio with ENTYVIO as a cornerstone.

**MAXIMIZE**
- CURRENT GI PORTFOLIO

**PRIORITIZE**
- INNOVATIVE SCIENCE

**COLLABORATE**
- TO BUILD A COMPelling EARLY STAGE PIPELINE

- Inflammatory bowel disease (IBD)
- Acid related disease
- Constipation

- ENTYVIO for oncology-related disease
- Next generation IBD
- GI drug discovery unit

- Motility disorders
- Liver disease
- Celiac disease
- Microbiome

---

We have a robust GI portfolio with which we are exploring ways to maximize value.

<table>
<thead>
<tr>
<th>IBD/IBD-Related</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>ENTYVIO</td>
<td>Humanized monoclonal antibody against α4β7 integrin</td>
<td>TAK-825</td>
<td>ENTYVIO</td>
</tr>
<tr>
<td></td>
<td>IBD. CPTt1</td>
<td>ROC/ryl Inverse against Crohn’s Disease</td>
<td>Humanized monoclonal antibody against α4β7 integrin</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>GI Motility Disorders</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
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<tbody>
<tr>
<td>TD-4954</td>
<td>Selective T4H4 Integrin agonist</td>
<td>ENTYVIO</td>
<td>AMITIZA</td>
</tr>
<tr>
<td></td>
<td>Enteral Feeding Improvement</td>
<td>UCCD JP</td>
<td>Chloride channel activator</td>
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</table>

<table>
<thead>
<tr>
<th>Acid Disorders</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>TAKECAB</td>
<td>Potassium competitive acid blocker</td>
<td>TAK-825</td>
<td>TAK-825</td>
</tr>
<tr>
<td></td>
<td>TPI Partial Responders</td>
<td>ROC/ryl Inverse against Crohn’s Disease</td>
<td>ROC/ryl Inverse against Crohn’s Disease</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Other</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>ENTYVIO</td>
<td>Humanized monoclonal antibody against α4β7 integrin</td>
<td>ENTYVIO</td>
<td>ENTYVIO</td>
</tr>
<tr>
<td></td>
<td>CPTt1</td>
<td>GIHD</td>
<td>UCCD</td>
</tr>
</tbody>
</table>

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Takeda Pharmaceutical Company Limited
ENTYVIO’s specific binding action inhibits lymphocyte trafficking to the inflamed gut, reducing inflammation.

- ENTYVIO selectively inhibits the movement of a discrete subset of T lymphocytes that preferentially migrate into inflamed GI tissue.
- ENTYVIO does not bind to or inhibit function of the α4β1 or αβ7 integrins.

ENTYVIO’s current clinical development programs help create significant potential for treatment of IBD.

- Nearly 40,000 patients treated
- Increasing use as first-line biologic
- Approved in 50 countries*
- Global submissions ongoing
- Long-term safety data published in *Gut*
- Long-term efficacy data presented at ECCO/DDW
- AGA / ECCO recommended as a first-line biologic in UC

**European Crohn’s and Colitis Organisation (ECCO)**
Congress 2016, March 16-19, 2016
Amsterdam, The Netherlands

- 12 Takeda abstracts
- 10 Independent ENTYVIO abstracts

**Digestive Disease Week (DDW)**
May 21-24, 2016
San Diego, California, USA

- 13 Takeda abstracts
- 18 Independent ENTYVIO abstracts
A robust life cycle program will further ENTYVIO’s knowledge base in IBD

**Mucosal Healing in Crohn’s Disease**

- Increasingly considered goal of Crohn’s disease therapy since it is associated with improved outcomes¹
- Aligns ENTYVIO dataset with expectations for biologics
- Endoscopic remission readout expected in H1 FY2017

**Head to Head in Ulcerative Colitis**

**52w Clinical Remission in UC**

- Landmark study to establish superiority vs anti-TNF
- Data could establish ENTYVIO as standard of care for moderate to severe UC
- Clinical remission readout expected in H1 FY2018

---

1. De Cruz et al, Inflamm Bowel Dis. 2013; 19:429-44

---

**Japan Development**

- IV formulation pivotal studies for UC and Crohn’s
- Increasing prevalence of IBD across Japan, especially for Crohn’s¹
- Clinical remission readout expected in H1 FY2017

**Subcutaneous (SC) Formulation**

- Patients prefer convenience of SC injection, especially when in remission following IV induction
- Randomized placebo controlled studies include Japan
- Clinical remission readout expected in H2 FY2018

---

¹. Ng, Wong, and Ng. Inter Res. 2016; 14:111-119

Note: all data readout projections are current estimates and subject to change.
A robust life cycle program will further ENTYVIO’s knowledge base in IBD

**Primary Sclerosing Cholangitis (PSC)**

- Significant liver disease often seen alongside UC
- $\alpha_4\beta_7$ mediated trafficking is proposed to cause hepatic complications
- Histology readout expected in FY2021

**Real World Evidence Generation**

<table>
<thead>
<tr>
<th>Corticosteroid use</th>
<th>ENTYVIO Persistence at 6 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>79%</td>
<td>81%</td>
</tr>
<tr>
<td>20%</td>
<td>62%</td>
</tr>
<tr>
<td>0%</td>
<td>0%</td>
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</tbody>
</table>

Reflects real world experience to address important scientific questions about ENTYVIO use for IBD

>6,000 patients currently being studied

**ENTYVIO’s mechanism of action could have use in oncology for intestinal graft-versus-host disease (GvHD)**

**Rationale**

- $\alpha_4\beta_7$ plays an essential role in T trafficking that leads to intestinal acute graft versus host disease (GvHD)

**Evidence to date**

- Increase of $\alpha_4\beta_7$ on peripheral T cells and intestinal infiltrate in intestinal GvHD
- Small open-label case series in steroid refractory patients suggests activity

---

ENTYVIO could also play a role in supportive care for immuno-oncology (IO) therapy related colitis

Reducing immune related GI toxicities
• IO biologic treatment results in significant overall survival benefit¹
• Immune-related adverse events such as diarrhea and colitis limit treatment duration
• Addressing GI symptoms offers potential for completing therapy and, possibly, increasing survival

Proof of concept in advanced melanoma
• First patient in during H1 FY2016

IO Adverse Events²

![Image showing IO adverse events]

IO Treatment Discontinuation³

![Image showing IO treatment discontinuation]

¹ Poslow et al. AACR Meeting 2016, Abstract CT002
² Mellman et al., Nature 2011; 480:480-89
³ Larkin et al., New Eng J Med. 2015; 373:23-34

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TAKECAB is expanding its ability to address patient needs for acid related diseases

Current approvals
• Rapid, long-lasting acid neutralization resulted in approval for 7 indications in Japan

Future clinical studies
• Data on superior symptom control in severe GERP patients only partially responsive to PPI expected FY2017
• Healing and prevention of relapse in erosive esophagitis (EE) in China/Asia expected to finish in H2 FY2018

TAKECAB pH Profile¹

![Image showing TAKECAB pH profile]

EE recurrence rate at week 24²

![Image showing EE recurrence rate]

¹ Sakurai et al., Aliment Pharmacol Ther. 2015; 42:719-30
² Umezaki et al., Gastro. 2014; 146 S736

Takeda Pharmaceutical Company Limited
We are building an early stage GI portfolio in which we are prioritizing high science and unmet medical need

<table>
<thead>
<tr>
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<td><strong>AMITIZA</strong></td>
</tr>
<tr>
<td>Humanized monoclonal antibody against α4β7 integrin</td>
<td>Humanized monoclonal antibody against α4β7 integrin</td>
<td>Oral cholesteryl esters cholesterol lowering pediatric formulation, pediatric constipation</td>
</tr>
<tr>
<td><strong>ENTYVIO</strong></td>
<td><strong>TD-8954</strong></td>
<td><strong>ENTYVIO</strong></td>
</tr>
<tr>
<td>RORγt inverse agonist</td>
<td>Selective δ-14 receptor antagonist</td>
<td>Enteral feeding intolerance</td>
</tr>
<tr>
<td><strong>ENTYVIO</strong></td>
<td><strong>TAKECAB</strong></td>
<td><strong>ENTYVIO</strong></td>
</tr>
<tr>
<td>Humanized monoclonal antibody against α4β7 integrin</td>
<td>Proton pump inhibitor and blocker</td>
<td>Humanized monoclonal antibody against α4β7 integrin</td>
</tr>
<tr>
<td><strong>TD-8954</strong></td>
<td><strong>TAKECAB</strong></td>
<td><strong>TD-8954</strong></td>
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</table>

**GI Motility Disorders**

**Acid Disorders**

**Other**

Takeda Pharmaceutical Company Limited

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TAK-828 is a first in class molecule for IBD that offers potential to restore immune balance

**TAK-828 Rationale**
- RORγt plays a critical role in TH17 cell driven immunity via IL17, IL23
- Clinical proof of concept in psoriasis

**2016 Milestones**
- Phase 1 Single Dose completed
- Initiation of Ph1b Multiple Dose Study in H1 FY2016

---

Takeda Pharmaceutical Company Limited
As part of Takeda’s R&D strategy, GI has built an externally facing Drug Discovery Unit to accelerate promising programs.

- Newly created, highly matrixed drug discovery unit with a strong external focus
- Prioritizes collaboration over infrastructure
- Broad base conducive to new target ID and access to state of the art technology
- Emphasizes modality diversification

>75% of Takeda GI discovery investment is external facing

---

Exciting partnerships established in FY2015 are providing access to cutting-edge modality diversification.

- **University of Melbourne**
  State of the art institute on disorders of GI motility

- **University of Nevada, Reno**
  World leading basic GI biology unit

- **enGene**
  A unique, nucleotide-based, gut-targeted therapeutic for the treatment of Inflammatory Bowel Disease

- **Cour**
  A unique immune modifying approach to celiac disease

- **Takeda Innovation Network**
  Early Innovation

- **Theravance**
  Novel agent for gastrointestinal motility disorders

- **Pipeline Innovation**

- **Enterome**
  Using the microbiome to discover new targets for the treatment of GI diseases
Agenda

Building on our heritage
Recognizing increasing demand for innovation
Four major components in our strategy for focused world class R&D
Focus our Therapeutic Areas
Optimize our Pipeline
Enhance our Capabilities
Transform our Culture

Therapeutic area R&D strategy highlights
Oncology
Gastroenterology (GI)
Central Nervous System (CNS)
Vaccines

Summary

Our focus in CNS is on patients with neuropsychiatric disorders who have no adequate treatments

Our current pipeline focuses on:

Schizophrenia
Cognitive Impairment Associated with Schizophrenia (CIAS) & Negative Symptoms

Depression
Treatment Resistant Depression (TRD)

Selected Neurological Diseases
Assets primarily progressed through external partnerships
We are addressing past R&D challenges in CNS

- Targets with high association to the disease pathophysiology
- Poor disease biology understanding
- Operational challenges (failed trials)
- Heterogeneous patient populations
- Low precision of clinical endpoints
- Sub-domain specific endpoints based on deconstruction of complex diseases

Our approach to developing new medicines is deeply rooted in translational science and precise clinical assessment

PATIENT SUBPOPULATIONS
SUBDOMAIN APPROACH
BIOLOGICAL MARKERS
DIGITAL HEALTH MEASURES

Precise Clinical Assessment

CLINICAL OBSERVATIONS
DISEASE GENETICS
PATIENT iPSC
BIOINFORMATICS

High Quality Targets

Clinical Biomarkers
Target Occupancy

Optimal Therapeutic Molecule

Effective Medicine

Therapies & Biomarkers

Target

Disease Mechanism

Patient
We will build on TRINTELLIX® and leverage internal and external innovation to accelerate our CNS early pipeline.

**MAXIMIZE**
- Strengthen position in MDD
- Further establish cognitive benefit in MDD and beyond

**PRIORITIZE**
- Prioritize the best science
- Leverage human patient data
- Robust translational package
- De-risk early pipeline in selected subpopulations

**COLLABORATE**
- Capture external innovation
- Accelerate CNS pipeline development

---

**Our near-term focus is on maximizing TRINTELLIX and expanding our CNS presence in Japan with AZILECT**

<table>
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<tr>
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<tbody>
<tr>
<td><strong>Psychiatry</strong></td>
<td><strong>Neurology</strong></td>
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</tr>
<tr>
<td>TAK-931</td>
<td>TAK-971</td>
<td>AD-4533 TOMM40</td>
</tr>
<tr>
<td>GSK: NGF Symptosis, B2C, More</td>
<td>ML-PAK</td>
<td>Mitochondrial growth stimulator, Delay of MO</td>
</tr>
<tr>
<td>TR-958</td>
<td>TAK-971</td>
<td>MAOB inhibitor</td>
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<td>5-HT3 receptor antagonist</td>
<td>PD-0329</td>
<td>Parkinson's Disease - JP</td>
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<tr>
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<td>GABAergic EC</td>
</tr>
</tbody>
</table>

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1 TRINTELLIX was formerly known as BRINTELLIX. Co-developed with H. Lundbeck A/S
TRINELLIX is an effective antidepressant with demonstrated cognitive benefit

**Differentiated Mechanism**
- SSRI + direct effect on serotonin receptors
- Modulates a range of neurotransmitter systems implicated in cognitive processing

**Cognitive Dysfunction in Depression – Major Unmet Need**
- Typically inadequately addressed/treated by standard therapies for depression
- ~2/3 of depressed patients – associated with disability in functioning, greater severity of illness and increased disease burden

**Cognitive Dysfunction in Depression – Efficacy**
- TRINELLIX has demonstrated efficacy in cognitive dysfunction and functional capacity in patients with depression

---

TRINELLIX improves cognitive performance and functional capacity in depression

**Effect on DSST Cognitive Performance**

- **ELDERLY**
  - 5 mg
  - 10 mg
  - 20 mg
  - 10/20 mg (flex)

- **FOCUS**
  - 5 mg
  - 10 mg
  - 20 mg

- **CONNECT**
  - 5 mg
  - 10 mg

**UCSD Performance-Based Skills Assessment (UPSA)**

- **CONNECT**
  - Standardized Effect Size
  - Difference vs. Placebo in Composite Total Score

---


Takeda Pharmaceutical Company Limited
We are pioneering the understanding of cognitive dysfunction in depression with TRINTELLIX

An adequate case has not been made to view cognitive dysfunction as a distinct clinical target for drug development

Additional evidence is required to show that cognitive dysfunction in MDD is a widely accepted unmet need in the field

FDA Advisory Committee Voted 8-2 In Favor of Label Change

FDA now views cognitive dysfunction as a legitimate target for drug development

No Drugs Approved
No Regulatory Guidelines
Exploratory Cognitive Endpoints ELDERLY Study
Pivotal Study FOCUS & CONNECT
Cognition Congresses & Symposia
sNDA Submission
FDA Advisory Committee
Complete Response Letter
Follow up scheduled with FDA


Our CNS discovery engine has delivered an innovative early portfolio pipeline of NMEs

<table>
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<tr>
<td>TAK-831 DACO inhibitor</td>
<td>TAK-063 PDE10 inhibitor</td>
<td>AD-4833 TOMM40 Mitochondrial growth modulator</td>
</tr>
<tr>
<td>CIAS: Neg Symptoms SCZ; Ataxia</td>
<td>Schizophrenia</td>
<td>Delay of MCI</td>
</tr>
<tr>
<td>TAK-058 5-HT3 receptor antagonist</td>
<td>TRINTELLIX Multinodal anti-emergent AHD</td>
<td>TRINTELLIX Multinodal anti-depressant Major Depressive Disorder</td>
</tr>
<tr>
<td>CIAS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TAK-041 GPR139 agonist</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CIAS; Neg. Symptoms SCZ</td>
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<tr>
<td>TAK-953 AMPA receptor potentiator</td>
<td>TRINTELLIX Multinodal anti-emergent AHD</td>
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<tr>
<td>Treatment Resistant Depression</td>
<td></td>
<td></td>
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<tr>
<td>TAK-071 M1 PAM</td>
<td></td>
<td></td>
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<tr>
<td>LBD, AD</td>
<td></td>
<td></td>
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<tr>
<td>TAK-915 PDE2A inhibitor</td>
<td></td>
<td></td>
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<tr>
<td>LBD, AD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TAK-935 CH24H inhibitor</td>
<td></td>
<td></td>
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<tr>
<td>Epilepsy EE</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Takeda Pharmaceutical Company Limited
TAK-831, a D-Amino Acid Oxidase Inhibitor (DAOi), a potential innovative treatment for cognitive and negative symptoms in schizophrenia.
TAK-831 has a robust preclinical and translational biomarker package to support evaluation in patient sub-population.

TAK-831, potent and selective DAOi
- PK/PD of D-Serine Plasma and Brain levels
- Efficacy in a range of preclinical models of Schizophrenia

Translational Biomarker Package
- PK/PD of D-Serine Plasma and CSF levels
- PET Receptor Occupancy
- EEG (mismatch negativity)

Baseline vs Timepoint 1

PoC Study in biomarker-enriched Schizophrenia patient sub-population

We are committed to being a global player in CNS

Long-Term
- Innovation-driven growth

Near / Mid-Term
- Expand psychiatry/build neurology
- TRINTELLIX innovation

Psychiatry
- Expand TRINTELLIX
- Progress early psychiatry pipeline

Neurology
- Partnership/co-development
- Create anchor in Neurology
Agenda

Building on our heritage
Recognizing increasing demand for innovation
Four major components in our strategy for focused world class R&D
  Focus our Therapeutic Areas
  Optimize our Pipeline
  Enhance our Capabilities
  Transform our Culture

Therapeutic area R&D strategy highlights
  Oncology
  Gastroenterology (GI)
  Central Nervous System (CNS)

Vaccines

Summary

Our vaccine business is leveraging world-class capabilities to address important priorities in global public health

MAXIMIZE
WIN IN JAPAN
Maximize the potential of the only fully integrated vaccine business in Japan
  VaxemHib (TAK-816)
  Varicella
  Pandemic Influenza
  Seasonal Influenza (TAK-850)

PRIORITIZE
DELIVER PIPELINE
Advance one of the most exciting late-stage pipelines in the industry, targeting more than one billion infections/year
  Dengue (TAK-003)
  Norovirus (TAK-214)

COLLABORATE
ADDRESS GLOBAL NEEDS
Leverage manufacturing technologies to expand capacity and achieve impact in all regions
  Polio (TAK-195)
Our pipeline tackles high-impact infectious diseases

<table>
<thead>
<tr>
<th>Prophylactic Vaccines for Infectious Diseases</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dengue</td>
<td></td>
<td>TAK-003 Dengue</td>
<td></td>
</tr>
<tr>
<td>Norovirus</td>
<td></td>
<td>TAK-214 Norovirus</td>
<td></td>
</tr>
<tr>
<td>Seasonal Influenza</td>
<td></td>
<td>TAK-850 Influenza</td>
<td></td>
</tr>
<tr>
<td>Enterovirus 71</td>
<td></td>
<td>TAK-021 Enterovirus 71</td>
<td></td>
</tr>
</tbody>
</table>

Sabin-strain Inactivated Polio Vaccine  
TAK-195* sIPV  

* TAK-195 is still pre-clinical, Phase 1 start expected in Q4 FY2016

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Dengue: “The Most Important Mosquito-Borne Viral Disease”¹

TAK-003: Tetravalent Dengue Vaccine Candidate

**Stage**
- Phase 2 demonstrated safety & immunogenicity to all four serotypes in endemic and naïve populations
- Phase 3 to begin in 2016: pivotal efficacy trial in multiple countries across Latin America and Asia

**Profile**
- Aimed at prevention of dengue fever of any severity due to any serotype
- Injectable, live attenuated vaccine engineered to elicit broad protection against all four virus types

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3.9 billion at risk for dengue infection with 400 million infections each year
More than 40% of the world's population² in 128 countries are at risk

Growing Global Threat
Transmission is expanding in the US, Japan and Southern Europe. The Tokyo outbreak of 2014 was first in Japan since 1945

Demand for Vaccine
There remains a need for a vaccine that is safe and effective against all four strains of dengue, and in all populations³

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Takeda Pharmaceutical Company Limited
TAK-003 could address important unmet needs in dengue prevention

- All four vaccine strains in TAK-003 are based on the Dengue Type 2 virus
- TAK-003 induces sustained antibody responses to all four dengue strains, in both naïve and previously-exposed populations
- The dengue virus backbone induces cell-mediated immune responses to all dengue proteins, which could play a role in protection
- The proposed schedule (two doses over three months) would be suitable for all populations, including naïve travelers to dengue-endemic regions
- Thus far, TAK-003 has demonstrated an acceptable safety profile in all populations evaluated

TAK-003 induces a sustained antibody response to all strains of dengue in all populations, which persists for at least two years\(^1\)

Antibody responses in children and adults aged 18 months to 45 years

<table>
<thead>
<tr>
<th>Previously exposed to dengue</th>
<th>Never exposed to dengue (&quot;naïve&quot;)</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1" alt="Graph showing antibody responses" /></td>
<td><img src="image2" alt="Graph showing antibody responses" /></td>
</tr>
</tbody>
</table>

\(^1\) Wallace ASHM 2015, Oral presentation 1224
TAK-003 induces broad antibody responses in subjects after two doses administered over three months.

Antibody responses to all four strains of dengue, in children aged 2 to 18

- More than 90% of children (naïve or previously exposed to dengue) develop or get a boost to neutralizing antibody responses to all 4 dengue serotypes after 2 doses of TAK-003.
- Approximately 95% of naïve individuals develop responses to at least 3 of the 4 dengue serotypes after a single dose of TAK-003.

*seropositive = MNT ≥ titer > 10

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TAK-003 induces broad cellular immune responses due to the dengue virus backbone

- Cell-mediated immunity (CMI) may play a role in protection against dengue infection.
- TAK-003 stimulates CMI to all dengue proteins, due in part to the dengue backbone.
- TAK-003 induces cellular immune responses to at least one dengue protein in >95% subjects.

Responses to all dengue proteins

- C/M E NS1 NS2 NS3 NS4 NS5
- d0 0 0 0 3 3 3
- d28 0 45 52 65 65 65

Study conducted by Walter Reed Army Institute of Research (WRAIR)

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Norovirus: Leading Cause of Gastroenteritis Worldwide

TAK-214: Norovirus Vaccine Candidate

Stage
- Phase 2 studies have demonstrated safety, immunogenicity and potential for efficacy.
- Phase 2b field efficacy study to begin shortly, results expected in 2018.

Profile
- First-in-class vaccine candidate to protect against norovirus, the most advanced in clinical development
- Injectable formulation of proteins that mimic outer shell of virus, designed for protection across strains

Each year, norovirus causes more than 600 million cases of diarrheal illness, over 200,000 deaths and a global economic burden of more than $60 billion.\(^1,2\)

Leading Cause of Gastroenteritis Worldwide
Safe and effective vaccine is in demand by public health agencies.\(^3\)

Zero Vaccines
No vaccines are currently available, and Takeda’s vaccine is the only product in clinical trials.

Agenda

Building on our heritage
Recognizing increasing demand for innovation
Four major components in our strategy for focused world class R&D
- Focus our Therapeutic Areas
- Optimize our Pipeline
- Enhance our Capabilities
- Transform our Culture

Therapeutic area R&D strategy highlights
- Oncology
- Gastroenterology (GI)
- Central Nervous System (CNS)
- Vaccines

Summary
- We recognize the increasing demand for innovation to develop medicines that meet patient and payer needs.

- Our strategy for focused world class R&D is patient-centric and science-driven, as we focus our therapeutic areas, optimize our pipeline, enhance our capabilities and transform our culture.

- R&D success is a pillar of Takeda's strategic roadmap that will deliver the long-term aspiration to be recognized as best in class because of agility and innovation, qualities that help us build a steady pipeline and deliver growth.
<table>
<thead>
<tr>
<th>AD</th>
<th>Alzheimer's disease</th>
<th>HR</th>
<th>high risk myelodysplastic syndromes</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADC</td>
<td>antibody drug conjugate</td>
<td>IBD</td>
<td>inflammatory bowel disease</td>
</tr>
<tr>
<td>ADHD</td>
<td>attention deficit hyperactivity disorder</td>
<td>INHL</td>
<td>indolent non-Hodgkin lymphoma</td>
</tr>
<tr>
<td>ARD</td>
<td>acid-related diseases</td>
<td>IO</td>
<td>immuno-oncology</td>
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<tr>
<td>ASCT</td>
<td>autologous stem cell transplant</td>
<td>LBD</td>
<td>Lewy Body Dementia</td>
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<tr>
<td>BTK</td>
<td>Bruton's tyrosine kinase</td>
<td>mAb</td>
<td>monoclonal antibodies</td>
</tr>
<tr>
<td>CD</td>
<td>Crohn's disease</td>
<td>MAOB</td>
<td>monoamine oxidase B</td>
</tr>
<tr>
<td>CIAS</td>
<td>cognitive impairment associated with schizophrenia</td>
<td>MCI</td>
<td>mild cognitive impairment</td>
</tr>
<tr>
<td>CLL</td>
<td>chronic lymphocytic leukemia</td>
<td>MCL</td>
<td>mantle cell lymphoma</td>
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<tr>
<td>CNS</td>
<td>central nervous system</td>
<td>MDSC</td>
<td>myeloid-derived suppressor cells</td>
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<tr>
<td>COPD</td>
<td>chronic obstructive pulmonary disease</td>
<td>MM</td>
<td>multiple myeloma</td>
</tr>
<tr>
<td>CSF</td>
<td>cerebrospinal fluid</td>
<td>MS</td>
<td>multiple sclerosis</td>
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<tr>
<td>CTCL</td>
<td>cutaneous T Cell Lymphoma</td>
<td>MTCL</td>
<td>mature T-cell lymphoma</td>
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<tr>
<td>DLBCL</td>
<td>diffuse large B-cell lymphoma</td>
<td>Neg</td>
<td>negative</td>
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<tr>
<td>EEG</td>
<td>electroencephalogram</td>
<td>PD-1</td>
<td>programmed cell death protein 1</td>
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<tr>
<td>FLHL</td>
<td>front line Hodgkin's lymphoma</td>
<td>PET</td>
<td>positron emission tomography</td>
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<tr>
<td>GI</td>
<td>gastrointestinal</td>
<td>PPI</td>
<td>proton pump inhibitor</td>
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<tr>
<td>GvHD</td>
<td>graft versus host disease</td>
<td>PSC</td>
<td>primary sclerosing cholangitis</td>
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<td>H2H</td>
<td>head to head</td>
<td>PTLD</td>
<td>post transplant lymphoproliferative disorder</td>
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<td>HCTZ</td>
<td>hydrochlorothiazide</td>
<td>R/R</td>
<td>relapsed/refractory</td>
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<tr>
<td>HL</td>
<td>Hodgkin's lymphoma</td>
<td>RA</td>
<td>rheumatoid arthritis</td>
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<tr>
<td>RCC</td>
<td>renal cell cancer</td>
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<td>SCLC</td>
<td>small cell lung cancer</td>
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<td>SCT</td>
<td>stem cell transplant</td>
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<tr>
<td>SCZ</td>
<td>schizophrenia</td>
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<tr>
<td>sIPV</td>
<td>sabin inactivated polio vaccine</td>
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<td>Sjögren's syndrome</td>
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<td>SSRI</td>
<td>serotonin-specific reuptake inhibitors</td>
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<td>SubQ</td>
<td>subcutaneous formulation</td>
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<td>T2DM</td>
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<tr>
<td>UC</td>
<td>ulcerative colitis</td>
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