A CURATIVE-INTENT IMMUNO-ONCOLOGY PIPELINE IS TAKING SHAPE

WAVE 1
NMEs that complement our global brands

- **Hematologic Malignancies**
  - TAK-924
    - FY21 target approval
  - TAK-007
    - FY23 target approval
  - TAK-788
    - FY21 target approval

- **Lung Cancer & Solid Tumors**

WAVE 2
Leading platforms in immuno-oncology and cell therapies

- **Immuno-Oncology**
- **Hematologic Malignancies**
- **Lung Cancer & Solid Tumors**
PARTNERSHIPS DRIVE OUR DIFFERENTIATED EARLY CLINICAL PIPELINE

Unique Partnership Model

- Innovative, disruptive platforms
- Agility in ‘open lab’ model

Differentiated Portfolio

- Harness innate immunity
- Eye towards solid tumors

THE FIRST BREAKTHROUGHS IN CANCER IMMUNOTHERAPY TARGET T CELLS

T CELL CHECKPOINT INHIBITORS

- PD-1
- CTLA-4

FIRST-GEN CAR-Ts

Adapted from Chen & Mellman, Immunity 2013
OUR FOCUS IS ON NOVEL MECHANISMS IN THE CANCER-IMMUNITY CYCLE

1. Innate immunomodulation
   - Novel-scaffold immune checkpoint platforms
   - Next-gen cell therapy & immune engager platforms

2. Cancer cell death

3. Systemic therapies leveraging innate immunity to enhance response breadth, depth & durability

EMERGING STRENGTH IN TARGETED INNATE IMMUNE MODULATION

<table>
<thead>
<tr>
<th>PLATFORM</th>
<th>PARTNER</th>
<th>MECHANISM-OF-ACTION</th>
<th>PROGRAMS</th>
<th>PRE-CLINICAL</th>
<th>PH 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>STING agonism</td>
<td>CURADEV</td>
<td>Innate-to-adaptive priming</td>
<td>TAK-676 (STING agonist)</td>
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<tr>
<td>Attenukine™</td>
<td>teva</td>
<td>Targeted attenuated IFN-α</td>
<td>TAK-573 (CD38-Attenukine™)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Next-gen Attenukine™</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

ADCC = Antibody-dependent cellular cytotoxicity

= first-in-class
ATTENUKINE™ PLATFORM ELICITS BOTH DIRECT TUMOR KILL AND IMMUNE ACTIVATION

TARGETED ATTENUATED TYPE I IFN PAYLOAD

TAK-573
Binds CD38
Human IgG4 Fc
Attenuated IFNα2b

Immunomodulation in preclinical models
Includes CD8+ T cell migration / activation

NEXT-GEN ATTENUKINE™
Binds innate immune target
Attenuated IFNα2b

TAK-573 POM IN ONGOING PHASE 1 R/R MM STUDY

Activation of CD8+ T cells in bone marrow

Baseline 7.3%
Cycle 1 Day 16 18.4%
Cycle 2 Day 2 28.8%

Activation Marker (CD69+)

EXPECTED MILESTONES (FY)

2019 2020
Ph1 FPI in solid tumors
Ph1b MM (incl. combinations)

TARGETED ATTENUATED TYPE I IFN PAYLOAD

FPI = first patient in  R/R MM = Relapsed / refractory multiple myeloma  POM = proof-of-mechanism

NOVEL SCAFFOLD NEXT-GENERATION CHECKPOINT MODULATORS

HIGH UNMET NEED
Current checkpoint modulators fail to improve overall survival in majority of patients

OUR DIFFERENTIATED APPROACH
New classes of checkpoint inhibitors designed to increase breadth and depth of responses

PLATFORM PARTNER MECHANISM-OF-ACTION PROGRAMS PRE-CLINICAL PH 1
Humabody Vh Crescendo Biologicals
• Unique pharmacology Concept 1
Concept 2
Agonist redirected checkpoints Shattuck
• Co-inhibition & co-stimulation TAK-252 / SL-279352 (PD1-Fc-OX40L)
TAK-254 / SL-115154 (CSF1R-Fc-CD40L)

Vh = Variable heavy domain

= first-in-class
BRINGING 5 NOVEL CELL THERAPY PLATFORMS TO THE CLINIC BY THE END OF FY20

Current CAR-T therapies have significant challenges & fail to address solid tumors

Leverage novel cell platforms & engineering to address shortcomings in liquid & solid tumors

INNATE IMMUNE PLATFORMS

- Multiple mechanisms of tumor killing
- ‘Off-the-shelf’
- Utility in solid tumors

NK = Natural killer

A NETWORK OF TOP INNOVATORS IS FUELING TAKEDA’S CELL THERAPY ENGINE

CUTTING-EDGE ENGINEERING & CELL PLATFORMS

IPSC expertise

γδ T cell platform

Armored CAR-Ts

Next-gen CARs

IPSC CAR-Ts

CAR-NK platform

Dec 2015

May 2017

Sept 2017

July 2018

April 2019

Nov 2019

Takeda Cell Therapy Translational Engine

First Development-Stage Partnership

NK = Natural killer

Dr. Sadelain is a co-inventor on patents relative to next-gen CARs, intellectual property that MSK has licensed to Takeda. As a result of these licensing arrangements, Dr. Sadelain and MSK have financial interests related to these research efforts.
TAKEDA IS EMBARKING ON A TRANSFORMATIVE CAR-NK PARTNERSHIP THAT COULD ENTER PIVOTAL TRIALS IN 2021

NK CAR Platform

Multiple mechanisms of tumor killing
Potentiation of innate & adaptive immunity

PATIENT VALUE PROPOSITION

Rapid and deep responses with a short-time-to-treatment, safe, off-the-shelf CAR-NK available in outpatient & community settings

<table>
<thead>
<tr>
<th>PLATFORM</th>
<th>PARTNER</th>
<th>MECHANISM-OF-ACTION</th>
<th>PROGRAMS</th>
<th>PRECLINICAL</th>
<th>PH 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAR-NK (allo cord blood)</td>
<td>MD Anderson Cancer Center Dr. Katy Rezvani</td>
<td><em>Non-autologous NK cell therapy</em></td>
<td>TAK-007 (CD19 CAR-NK) BCMA CAR-NK Platform expansion</td>
<td>= first-in-class</td>
<td></td>
</tr>
</tbody>
</table>

FOUR NOVEL, OFF-THE-SHELF CAR-NK THERAPIES IN DEVELOPMENT

PLATFORM VALUE INFLECTIONS

<table>
<thead>
<tr>
<th>FY</th>
<th>2H 2020</th>
<th>2021</th>
<th>2023</th>
<th>BLA filing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ongoing maturation of clinical data: Efficacious dose, durability, partial vs. full allo, cryopreserved product Manufacturing process complete Pivotal trials in r/r DLBCL / CLL / Indolent NHL</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Initial opportunity in G7 countries (CD19)*

| 3L+ DLBCL | ~8,000 |
| 3L+ CLL | ~5,000 |
| 3L+ NHL | ~6,000 |

Potential to move into earlier lines of therapy

CLL = Chronic lymphocytic leukemia  
DLBCL = Diffuse large B-cell lymphoma  
iNHL = Indolent non-Hodgkin's lymphoma

*Estimated number of patients projected to be initially eligible for treatment in G7 markets, subject to regulatory approval

= first-in-class
DRAMATIC COMPLETE RESPONSE IN FIRST PATIENT TREATED

47-YEAR OLD MALE WITH RELAPSED TRANSFORMED DOUBLE-HIT (C-MYC / BCL-2) DLBCL

Baseline scan  Day 30 post CAR19-NK

Data from Dr. Katy Rezvani, MD Anderson Cancer Center

KINETICS OF CAR-NK VERSUS ENDOGENOUS T AND B CELLS IN PERIPHERAL BLOOD

CAR-NK cells

Days post-CAR-NK infusion

T cells

B cells

307  312
308  312

Baseline scan  Day 30 post CAR19-NK

IMPRESSIVE RESPONSES IN OTHER HEAVILY PRETREATED PATIENTS

61-YEAR OLD MALE CLL/RICHTER’S TRANSFORMATION (5 PRIOR LINES OF THERAPY)

Baseline scan  Day 30 post CAR19-NK

CLL = Chronic lymphocytic leukemia  CR = Complete response  SD = Stable disease

Data from Dr. Katy Rezvani, MD Anderson Cancer Center

60-YEAR OLD FEMALE WITH CLL / ACCELERATED CLL (5 PRIOR LINES OF THERAPY)

Baseline scan  Day 30 post CAR19-NK

CR in Richter’s; SD in CLL
CAR-NK CELLS PERSIST IN PATIENTS AND DO NOT TRIGGER CYTOKINE RELEASE SYNDROME (CRS)

CAR-NK CELLS PERSIST UP TO 4 MONTHS POST INFUSION

IL-6 LEVELS POST CAR-NK INFUSION DO NOT INDICATE CRS

---

**CAR-NK EFFICACY & TOXICITY TREATING MULTIPLE DIAGNOSES**

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Lines of Treatment</th>
<th>HLA Match</th>
<th>CRS / Neurotox</th>
<th>Complete Response</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dose Level 1</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DLBCL - Relapsed transformed double-hit</td>
<td>3 Incl. ASCT</td>
<td>Partial match</td>
<td>None</td>
<td>✓</td>
</tr>
<tr>
<td>DLBCL - Refractory</td>
<td>7</td>
<td>Partial match</td>
<td>None</td>
<td>PD</td>
</tr>
<tr>
<td>CLL</td>
<td>4 Incl. ibrutinib &amp; venetoclax</td>
<td>Partial match</td>
<td>None</td>
<td>✓</td>
</tr>
<tr>
<td><strong>Dose Level 2</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CLL</td>
<td>4 Incl. ibrutinib</td>
<td>Partial match</td>
<td>None</td>
<td>PD</td>
</tr>
<tr>
<td>CLL/Richter’s transformation</td>
<td>5 Incl. ibrutinib</td>
<td>Partial match</td>
<td>None</td>
<td>✓, *Richter’s</td>
</tr>
<tr>
<td>CLL/Accelerated CLL</td>
<td>5 Incl. ibrutinib &amp; venetoclax</td>
<td>Partial match</td>
<td>None</td>
<td>✓</td>
</tr>
<tr>
<td>CLL</td>
<td>4 Incl. ibrutinib</td>
<td>Partial match</td>
<td>None</td>
<td>✓</td>
</tr>
<tr>
<td><strong>Dose Level 3</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DLBCL - Refractory</td>
<td>11 Incl. ASCT</td>
<td>Partial match</td>
<td>None</td>
<td>✓</td>
</tr>
<tr>
<td>DLBCL - Relapsed transformed double-hit</td>
<td>4 Incl. ASCT</td>
<td>Partial match</td>
<td>None</td>
<td>✓</td>
</tr>
<tr>
<td>Follicular lymphoma - Relapsed</td>
<td>4 Incl. ASCT</td>
<td>Mismatch</td>
<td>None</td>
<td>PD</td>
</tr>
<tr>
<td>Follicular lymphoma - Relapsed</td>
<td>4 Mismatch</td>
<td>None</td>
<td>✓</td>
<td></td>
</tr>
</tbody>
</table>

**Data from Dr. Katy Rezvani, MD Anderson Cancer Center**
FAST-TO-CLINIC CELL THERAPY ENGINE WILL MAXIMIZE LEARNINGS ON MULTIPLE ‘DISRUPTIVE’ PLATFORMS

5 CLINICAL-STAGE PROGRAMS EXPECTED BY END OF FY20

<table>
<thead>
<tr>
<th>FY19</th>
<th>FY20</th>
</tr>
</thead>
<tbody>
<tr>
<td>TAK-007</td>
<td>TAK-102</td>
</tr>
</tbody>
</table>

TAK-007: Other cell therapy candidates

CD19 1XX-CAR-T: Next-gen CART signaling domain

GDX012: Gamma-delta T cells

GCC CAR-T: Colorectal Cancer

A RICH AND POTENTIALLY TRANSFORMATIVE EARLY CLINICAL ONCOLOGY PIPELINE

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<td>Agonist-redirected checkpoints</td>
<td>SHATTUCK</td>
<td>Co-inhibition &amp; co-stimulation</td>
<td>TAK-252 / SL-279535, TAK-254 / SL-115154</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shiga-like toxin A</td>
<td>avanti</td>
<td>Novel cytotoxic payload</td>
<td>TAK-169 (CD38-SLTA)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IGN toxin</td>
<td>IMMUN-GEN</td>
<td>Solid tumor-targeted ADC</td>
<td>TAK-164 (GCC-ADC)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Conditional T cell engagers</td>
<td>MAVERICK</td>
<td>Novel solid tumor platform</td>
<td>MVC-101 (EGFR COBRA™)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cell therapy platforms</td>
<td>MD Anderson Cancer Center</td>
<td>Off-the-shelf cell therapies</td>
<td>TAK-007 (CD19 CAR-NK)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

UNDISCLOSED TARGETS

- Cressoendo (CBOK)
- ImmuneX (IMX)
- MD Anderson Cancer Center
- TAK-254 / SL-115154
- MVC-101 (EGFR COBRA™)

5 cell therapies expected in clinic by end of FY20

= first-in-class
NME MILESTONES ACHIEVED IN FY19 AND LOOKING AHEAD TO OTHER POTENTIAL MILESTONES¹ THROUGH FY20

PIVOTAL STUDY STARTS, APPROVALS

KEY DATA READOUTS

1. Potential key milestone dates as of November 14, 2019. The dates included herein are estimates based on current data and are subject to change
2. Potentially registration enabling

SUMMARY

1. Total transformation of preclinical & early clinical pipeline

2. Differentiated opportunities in IO leveraging innate immunity & cell therapies

3. Multiple near-term catalysts informing momentum towards solid tumors
# R&D Day Agenda – Tokyo, November 21, 2019

<table>
<thead>
<tr>
<th>Time</th>
<th>Agenda</th>
</tr>
</thead>
<tbody>
<tr>
<td>11:00 – 11:05</td>
<td>Welcome and Introduction of Presenters</td>
</tr>
<tr>
<td>11:05 – 11:45</td>
<td>Realizing the Potential of Plasma-derived Therapies</td>
</tr>
<tr>
<td></td>
<td>Julie Kim, President, Plasma-Derived Therapies Business Unit</td>
</tr>
<tr>
<td>11:45 – 12:15</td>
<td>A New Dedicated Focus on Innovative, Sustainable Solutions for Plasma-Derived Therapies</td>
</tr>
<tr>
<td></td>
<td>Christopher Morabito, M.D., Head of R&amp;D, Plasma-Derived Therapies</td>
</tr>
<tr>
<td>12:15 – 12:45</td>
<td>Q&amp;A session</td>
</tr>
<tr>
<td>12:45 – 13:25</td>
<td>Lunch Break</td>
</tr>
<tr>
<td>13:25 – 13:35</td>
<td>Welcome back and Introduction of Presenters</td>
</tr>
<tr>
<td></td>
<td>Ayako Iwamura, Investor Relations, Global Finance</td>
</tr>
<tr>
<td>13:35 – 13:45</td>
<td>Takeda: A Global Values-Based, R&amp;D-Driven Biopharmaceutical Leader</td>
</tr>
<tr>
<td></td>
<td>Christophe Weber, President &amp; CEO Takeda</td>
</tr>
<tr>
<td>13:45 – 14:15</td>
<td>Translating Science into Highly Innovative, Life-changing Medicines</td>
</tr>
<tr>
<td></td>
<td>Andy Plump, President R&amp;D</td>
</tr>
<tr>
<td>14:15 – 14:40</td>
<td>Oncology and Cell Therapies with Spotlight on CAR-NK</td>
</tr>
<tr>
<td></td>
<td>Chris Arendt, Head Oncology Drug Discovery Unit</td>
</tr>
<tr>
<td>14:40 – 15:00</td>
<td>Spotlight on Oncology Opportunities</td>
</tr>
<tr>
<td></td>
<td>• TAK-788: Rachael Brake, Global Program Lead</td>
</tr>
<tr>
<td></td>
<td>• Pevonedistat: Phil Rowlands, Head Oncology Therapeutic Area Unit</td>
</tr>
<tr>
<td>15:00 – 15:20</td>
<td>Break</td>
</tr>
<tr>
<td>15:20 – 15:45</td>
<td>Rare Diseases &amp; Gene Therapy</td>
</tr>
<tr>
<td></td>
<td>Dan Curran, Head Rare Disease Therapeutic Area Unit</td>
</tr>
<tr>
<td>15:45 – 16:00</td>
<td>Spotlight on Orexin2R agonists</td>
</tr>
<tr>
<td></td>
<td>Deborah Hartman, Global Program Lead</td>
</tr>
<tr>
<td>16:00 – 16:20</td>
<td>Therapeutic Area Focus in GI with Spotlight on Celiac Disease</td>
</tr>
<tr>
<td></td>
<td>Aat Parkh, Head GI Therapeutic Area Unit</td>
</tr>
<tr>
<td>16:20 – 17:00</td>
<td>Panel Q&amp;A Session</td>
</tr>
<tr>
<td>17:00</td>
<td>Drinks reception</td>
</tr>
</tbody>
</table>

## TAK-788: Pursuing a Fast-to-Patient Strategy for NSCLC Patients with EGFR Exon 20 Insertions

Rachael L Brake, PhD  
Global Program Leader, Oncology  
Takeda Pharmaceutical Company Limited  
Tokyo  
November 21, 2019
1. American Cancer Society; Cancer facts and figures 2019
2. Office for National Statistics UK (www.ons.gov.uk)

**THE SIZE OF THE LUNG CANCER CHALLENGE IS VAST**

228,000¹
New Lung cancer cases / year

143,000¹
Lung cancer deaths/ yr
More than breast, colon, and prostate cancer combined

Survival of Lung cancer is amongst the lowest of all cancers

Male 10% survival
Female 13% survival

5 yr survival estimates among adults diagnosed with lung cancer between 2007-2011²

---

**EXON 20 INSERTIONS ARE A RARE SUBSET OF EGFR MUTANT NSCLC**


Non-Sq NSCLC 200,000 pts/yr¹

EGFR Exon 20 Insertions 2,000 pts/yr²

Insertion variants

1. V769_D770insASV (=20%)
2. D770_N771insSVD (=19%)
3. H773_V774insH (=8%)
4. A763_Y764insFQEA (=7%)
5. H773_V774insPHE (=5%)
6. H773_V774insNPH (=4%)
7. N771_P772insN (=3%)
8. H773_V774insAH (=3%)
9. Other (=31%)

---

¹ Estimated US annual incidence of non-squamous NSCLC
² Represents annual incidence of the US addressable patient population
PATIENTS WITH EGFR EXON 20 INSERTIONS HAVE NO EFFECTIVE THERAPY

EGFR exon 20 insertions do not demonstrate significant PFS benefit with 1st and 2nd gen EGFR TKIs

Hazard ratio = 12.3 (p<0.0001)

<table>
<thead>
<tr>
<th>Group</th>
<th>Median PFS (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>EGFR exon 20 ins (n=9)</td>
<td>2.0</td>
</tr>
<tr>
<td>Classical EGFR mut (n=129)</td>
<td>12.0</td>
</tr>
</tbody>
</table>

EGFR exon 20 ins patients demonstrate limited benefit to anti PD-1 directed therapy

<table>
<thead>
<tr>
<th>Group</th>
<th>Median PFS (months)</th>
<th>PDL-1 expression ≥1%</th>
</tr>
</thead>
<tbody>
<tr>
<td>EGFR exon 20 ins (n=20)</td>
<td>2.7 (1.7-3.8)</td>
<td>40%</td>
</tr>
<tr>
<td>Classical EGFR mut (n=22)</td>
<td>1.8 (1.2-2.4)</td>
<td>25%</td>
</tr>
</tbody>
</table>

1. Robichaux et al., WCLC 2016
2. Adapted from Negrao et al., WCLC 2019

OVERCOMING THE DRUG DEVELOPMENT CHALLENGE IN EXON 20 INSERTIONS

EGFR exon 20 insertion mutations have a similar structure and similar affinity for ATP to wild type EGFR

L858R EGFR mutation
Significantly alter both structure and affinity for ATP compared to wild type EGFR

Source. TAK-788 bound to EGFR kinase domain containing D770 ins NPG, crystal structure (data on file)
TAK-788 PROOF OF CONCEPT DATA IN EGFR EXON 20 INSERTIONS

- Confirmed ORR: 12/28 patients: 43% (24.5-62.8%)
- Median PFS: 7.3 months (4.4 mo - NR)

![Graph showing antitumor activity in EGFR Exon 20 ins at 160 mg daily](image)

**SAFETY SUMMARY IN PATIENTS TREATED WITH TAK-788**

<table>
<thead>
<tr>
<th>N (%)</th>
<th>All Patients 160 mg qd (n=72)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade ≥3</td>
<td>29 (40)</td>
</tr>
<tr>
<td>Dose reduction due to AE</td>
<td>18 (25)</td>
</tr>
<tr>
<td>Dose interruption due to AE</td>
<td>36 (50)</td>
</tr>
<tr>
<td>Discontinuation due to treatment-related AE</td>
<td>10 (14)</td>
</tr>
</tbody>
</table>

TAK-788 has not been approved for the use or indications under investigation in the clinical trials (and there is no guarantee it will be approved for such use or indication). Claims of safety and effectiveness can only be made after regulatory review of the data and approval of the labeled claims.

Adapted from Riley et al. ASCO. 2019

ENCOURAGING EFFICACY AND SAFETY HAS BEEN OBSERVED WITH TAK-788

<table>
<thead>
<tr>
<th>Clinical feature</th>
<th>TAK-788 1 n=28</th>
<th>Poziotinib 2 n=50</th>
<th>Afatinib 3 n=23</th>
<th>Osimertinib 4 n=15</th>
</tr>
</thead>
<tbody>
<tr>
<td>ITT confirmed ORR (%)</td>
<td>43%</td>
<td>NR</td>
<td>8.7%</td>
<td>0%</td>
</tr>
<tr>
<td>Evaluable confirmed ORR (%)</td>
<td>NR</td>
<td>43%</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>ITT median PFS (months)</td>
<td>7.3</td>
<td>5.5</td>
<td>2.7</td>
<td>3.5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Grade ≥ 3 Adverse event</th>
<th>TAK-788 1 n=72</th>
<th>Poziotinib 2 n=63</th>
<th>Afatinib 3 n=229</th>
<th>Osimertinib 4 n=279</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhea ≥ Gr3</td>
<td>18%</td>
<td>17.5%</td>
<td>14%</td>
<td>1%</td>
</tr>
<tr>
<td>Rash ≥ Gr3</td>
<td>1%</td>
<td>35%</td>
<td>16%</td>
<td>1%</td>
</tr>
<tr>
<td>Paronychia ≥ Gr3</td>
<td>0%</td>
<td>9.5%</td>
<td>11%</td>
<td>0%</td>
</tr>
</tbody>
</table>

Total dose reduction rates

| AE related dose reductions (%) | 25% | 60% | 52% | 2.9% |

Direct cross-trial comparison cannot be made between TAK-788 and other treatments due to different studies with different designs.

ITT = Intention to treat, ORR = Overall response rate, PFS = progression free survival, NR = Not reported.

Average time on TAK-788
7.9 months

<table>
<thead>
<tr>
<th>Diarrhea</th>
<th>Time on Treatment (Mo)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 3</td>
<td>4.6</td>
</tr>
<tr>
<td>Grade 2</td>
<td>9.8</td>
</tr>
<tr>
<td>Grade 1</td>
<td>12.7</td>
</tr>
<tr>
<td>No diarrhea</td>
<td>12.1</td>
</tr>
</tbody>
</table>

WE HAVE MODIFIED OUR APPROACH TO GI ADVERSE EVENT MANAGEMENT WITH THE AIM TO IMPROVE EFFICACY

Source. TAK-788 Clinical trial database (data on file)

2021: EXPECTED FIRST APPROVAL IN EGFR EXON 20 INSERTIONS

- Single arm Phase 2 trial
- Refractory EGFR Exon 20 insertion patients

- Previously treated, ≤2 systemic anticancer chemotherapy
- Locally advanced or metastatic
- NSCLC harboring EGFR exon 20 insertion

RWE will be used to assess the benefit of conventional standard of care (SOC) agents in patients with EGFR Exon 20 insertions

EMR claims databases and Medical Chart Review

Chemo +/- VEGFR - Immunotherapy - Other

1. Overall Response Rate
2. Duration of Response
3. Median Progression Free Survival
4. Duration of Response
5. Overall survival

NEW ACTIVATION: A TRIAL FOR NEWLY DIAGNOSED PATIENTS

- Randomized, controlled, Phase 3 trial
- Treatment-naïve EGFR exon 20 insertion patients

- Advanced or metastatic
- Treatment-naïve patients diagnosed with NSCLC harboring EGFR exon 20 insertion mutations

TAK-788 at 160 mg qd  Platinum doublet

1. Median Progression Free Survival
2. Overall Response Rate
3. Duration of Response
4. Overall survival

Electronic patient reported outcomes

- ACTIVELY ENROLLING
- US, EU, LATIN AMERICA AND ASIA-PACIFIC

2 year enrollment
Anticipated approval 2023

SUMMARY

1. NSCLC patients with EGFR Exon 20 insertions are underserved with the current available therapies
2. TAK-788 is the first purposely designed inhibitor and clinical proof-of-concept has demonstrated efficacy
3. The EXCLAIM trial in refractory patients could lead to the first approval of TAK-788 by 2021

Source: https://clinicaltrials.gov/ct2/show/NCT04125502
PEVONEDISTAT (TAK-924): A POTENTIAL NEW TREATMENT FOR HR-MDS AND AML

Phil Rowlands, PhD
Head Oncology Therapeutic Area Unit
Takeda Pharmaceutical Company Limited
Tokyo
November 21, 2019

BUILDING ON THE TAKEDA ONCOLOGY FOUNDATION IN HEMATOLOGIC MALIGNANCIES
HIGH RISK MYELODYSPLASTIC SYNDROME (HR-MDS) AND ACUTE MYELOID LEUKEMIA (AML) HAVE LIMITED TREATMENT OPTIONS

CONTINUUM OF HR-MDS AND AML

- HR-MDS and AML are both rare bone marrow-related cancers that share foundational biology, clinical features, and genetic mutations*
- Incidence highest in elderly (>70 years old)
- Overall survival several months to a few years, depending on risk category

* 30% of HR-MDS patients progress to AML

CLINICAL TREATMENT

BM failure → cytopenias
- Fatigue (anemia)
- Infection (neutropenia)
- Bleeding (thrombocytopenia)

Clinical treatment goals:
- Alleviate cytopenias
- Improve patient quality of life
- Improve survival

Fit Patients
- Younger
- Fewer co-morbidities
- Better performance status

Unfit Patients
- Older
- Unfit for intensive chemotherapy and/or stem cell transplant

Intensive Chemotherapy

Stem Cell Transplant
(Only curative treatment)
≤ 10% HR-MDS, ~45% AML

Chemotherapy
- Azacitidine
- Decitabine
- Low dose ara-c

Targeted therapies
(AML only)
- BCL2
- IDH1/2
- FLT3

CURRENT STANDARD OF CARE IS INADEQUATE FOR HR-MDS PATIENTS

No new treatments have been approved for MDS in over a decade

Transplant ineligible patients treated with first line therapy:
- Median OS = 15mo; 2yr OS rate 35%

Economic burden is substantial - hospitalizations are common among patients and many are transfusion dependent

MDS SURVIVAL BY PROGNOSTIC RISK

Median survival ~6 months to 5 years

Schanz et al., J Clin Oncol. 2012, 30:820-829
PEVONEDISTAT: A UNIQUE FIRST-IN-CLASS NAE INHIBITOR

- Pevonedistat is a small molecule inhibitor of NAE (NEDD-8 activating enzyme), a protein involved in the ubiquitin-proteasome system
- NAE acts upstream of the proteasome and catalyzes the first step in the neddylation pathway

ENCOURAGING RESPONSES IN AML PATIENTS TREATED WITH PEVONEDISTAT + AZACITIDINE

60% ORR with a trend towards improved survival in secondary AML

Response rates not influenced by AML genetic risk or leukemia burden

Initial data drove interest to move to registration
A PHASE 2 STUDY IN HR-MDS TO CONFIRM THE RISK / BENEFIT PROFILE OBSERVED IN AML

Phase 2, Randomized, Open-label, Global, Multicenter Study Comparing Pevonedistat Plus Azacitidine vs. Azacitidine in Patients with Higher-Risk MDS, CMML, or Low-Blast AML

- Mature OS data will be available in November
- Data will be presented in upcoming congress
- Potential approval in FY21*

THE PHASE 3 PANTHER STUDY WAS INITIATED AT RISK TO ACCELERATE DEVELOPMENT

Phase 3, Randomized controlled trial of Pevonedistat Plus Azacitidine Versus Single-Agent Azacitidine as First-Line Treatment for Patients with Higher-risk-MDS/CMML, or Low-blast AML

- Completed global enrollment 10 months earlier than originally projected*
- Indicative of demand for new innovative therapies

* Closed to global enrollment; Open for extended enrollment in China
EXPANDING PATIENT-CENTRIC DEVELOPMENT OF PEVONEDISTAT

Continuum of disease

HR-MDS

Ph2 (P2001)
Potential approval in FY21*

Ph3 (P3001)

NEW STUDIES IN UNFIT AML

Ph3 PEVOLAM
pevo + aza vs. aza
Currently enrolling patients

Utilizing partnership (PETHEMA) for efficient development

Ph2 (P2002) Combo
pevo + venetoclax + aza vs. venetoclax + aza
Study will open in 2020

Unique MOA and biologic hypothesis to support combination

* Projected approval date assumes filing on Phase 2 data

SUMMARY

1. Unmet need in High-risk MDS and AML remain high with few treatment options

2. Pevonedistat is a selective first-in-class inhibitor with potential to be first new therapy in over a decade for HR-MDS

3. The Ph2 HR-MDS trial has reached the updated OS endpoint data readout and the PANTHER Ph3 trial has completed global enrollment
<table>
<thead>
<tr>
<th>TIME</th>
<th>AGENDA</th>
</tr>
</thead>
<tbody>
<tr>
<td>11:00 – 11:05</td>
<td>Welcome and Introduction of Presenters</td>
</tr>
<tr>
<td></td>
<td>Ayako Iwamuro, Investor Relations, Global Finance</td>
</tr>
<tr>
<td>11:05 – 11:45</td>
<td>Realizing the Potential of Plasma-derived Therapies</td>
</tr>
<tr>
<td></td>
<td>Julie Kim, President, Plasma-Derived Therapies Business Unit</td>
</tr>
<tr>
<td>11:45 – 12:15</td>
<td>A New Dedicated Focus on Innovative, Sustainable Solutions for Plasma-Derived Therapies</td>
</tr>
<tr>
<td></td>
<td>Christopher Morabito, M.D., Head of R&amp;D, Plasma-Derived Therapies</td>
</tr>
<tr>
<td>12:15 – 12:45</td>
<td>Q&amp;A session</td>
</tr>
<tr>
<td>12:45 – 13:25</td>
<td>Lunch Break</td>
</tr>
<tr>
<td>13:25 – 13:35</td>
<td>Welcome back and Introduction of Presenters</td>
</tr>
<tr>
<td></td>
<td>Ayako Iwamuro, Investor Relations, Global Finance</td>
</tr>
<tr>
<td>13:35 – 13:45</td>
<td>Takeda: A Global Values-Based, R&amp;D-Driven Biopharmaceutical Leader</td>
</tr>
<tr>
<td></td>
<td>Christophe Weber, President &amp; CEO Takeda</td>
</tr>
<tr>
<td>13:45 – 14:15</td>
<td>Translating Science into Highly Innovative, Life-changing Medicines</td>
</tr>
<tr>
<td></td>
<td>Andy Plump, President R&amp;D</td>
</tr>
<tr>
<td>14:15 – 14:40</td>
<td>Oncology and Cell Therapies with Spotlight on CAR-NK</td>
</tr>
<tr>
<td></td>
<td>Chris Arendt, Head Oncology Drug Discovery Unit</td>
</tr>
<tr>
<td>14:40 – 15:00</td>
<td>Spotlight on Oncology Opportunities</td>
</tr>
<tr>
<td></td>
<td>• TA-K-788: Rachel Brake, Global Program Lead</td>
</tr>
<tr>
<td></td>
<td>• Pevonedistat: Phil Rawlands, Head Oncology Therapeutic Area Unit</td>
</tr>
<tr>
<td>15:00 – 15:20</td>
<td>Break</td>
</tr>
<tr>
<td>15:20 – 15:45</td>
<td>Rare Diseases &amp; Gene Therapy</td>
</tr>
<tr>
<td></td>
<td>Dan Curran, Head Rare Disease Therapeutic Area Unit</td>
</tr>
<tr>
<td>15:45 – 16:00</td>
<td>Spotlight on Orexin2R agonists</td>
</tr>
<tr>
<td></td>
<td>Deborah Hartman, Global Program Lead</td>
</tr>
<tr>
<td>16:00 – 16:20</td>
<td>Therapeutic Area Focus in GI with Spotlight on Celiac Disease</td>
</tr>
<tr>
<td></td>
<td>Aat Parikh, Head GI Therapeutic Area Unit</td>
</tr>
<tr>
<td>16:20 – 17:00</td>
<td>Panel Q&amp;A Session</td>
</tr>
<tr>
<td>17:00</td>
<td>Drinks reception</td>
</tr>
</tbody>
</table>

**RARE DISEASES & GENE THERAPY**

Dan Curran, MD  
Head Rare Diseases Therapeutic Area Unit  
Takeda Pharmaceutical Company Limited  
Tokyo  
November 21, 2019
RARE DISEASES: AN OPPORTUNITY TO TRANSFORM TREATMENT

HIGH UNMET NEED

<table>
<thead>
<tr>
<th>7,000</th>
<th>Distinct rare diseases(^1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>350 million</td>
<td>Patients worldwide</td>
</tr>
<tr>
<td>95%</td>
<td>Diseases have no FDA-approved treatment</td>
</tr>
</tbody>
</table>

SCIENTIFIC AND REGULATORY ADVANCES

- 80% Diseases are genetic in origin
- 95%\(^2\) Transformative therapies
- 80% Diseases are genetic in origin
- 70% Orphan drug approvals benefited from expedited review

1. Rare diseases defined by prevalence in line with regulatory agencies (US: <7 in 10,000, EU: <5 in 10,000 and JPN: <4 in 10,000), Global Genes, NIH National Human Genome Research Institute; 2. Comprises four pathways in US: Accelerated approval, breakthrough therapy designation, fast track designation, priority review designation; 3. Three pathways in JPN: Priority review, Sakigake designation and conditional approval, CIRS R&D Briefing 70, New drug approvals in six major authorities 2009-2018

---

RARE DISEASE MARKET IS EXPECTED TO DOUBLE IN SIZE

GLOBAL ORPHAN DRUG\(^{1}\) SALES EXCLUDING ONCOLOGY\(^{2}\), USD BN

- Orphan drugs expected to make up ~17% of global branded Rx sales by 2024
- Growth driven by advances in new modalities and new indications
- Orphan cell and gene therapies estimated at ~$20 bn by 2024, up from ~$2 bn in 2018

1. Orphan drugs generally used as synonyms for rare diseases due to lack of uniform definition, including also non-rare, but neglected diseases lacking therapy (e.g., tropical infectious diseases); 2. EvaluatePharma (03 June 2019)
TAKEDA IS THE LEADER IN RARE DISEASES

PATIENT IMPACT

• Foundation of >30 year history of leadership in rare diseases
• Leading portfolio of rare disease therapies: 11 out of 14 global brands spanning Hematology, Metabolic, GI and Immunology

SCIENCE & INNOVATION

• Multiple opportunities for transformational therapies across therapeutic areas
• Emerging, cutting edge platforms to drive high-impact pipeline
• Investments in technologies to accelerate diagnosis

CAPABILITIES AND SCALE

• Engagement with key stakeholders within the ecosystem e.g. patient groups, regulators
• Pioneering regulatory pathways
• Global footprint

OUR STRATEGY IS TO TRANSFORM AND CURE RARE DISEASES

As the global leader in Rare Diseases, we aspire to provide transformative and curative treatments to our patients

Transformative

Programs with transformative potential in devastating disorders with limited or no treatment options today

Curative

Emerging early pipeline of AAV gene therapies to redefine treatment paradigm in monogenic rare diseases
1. Projected timing of approvals depending on data read-outs; some of these Wave 1 target approval dates assume accelerated approval. 2. Some Wave 2 assets could be accelerated into Wave 1 if they have breakthrough data; 3. Projected approval date assumes filing on Phase 2 data; 4. TAK-079 to be developed in Rare Diseases indications; 5. Currently in a non-pivotal Phase 2 study; planning underway to include interim stage gates that can advance the program into a pivotal trial.

WE ARE POSITIONED TO DELIVER NEAR-TERM & SUSTAINED GROWTH

Potentially Approved Transformative Therapies

<table>
<thead>
<tr>
<th>Wave 1</th>
<th>Target Approval</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>TAK-721</td>
<td>Eosinophilic Esophagitis (EoE)</td>
<td>FY 2020</td>
</tr>
<tr>
<td>TAK-620</td>
<td>Cytomegalovirus (CMV) infection in transplant</td>
<td>FY 2022</td>
</tr>
<tr>
<td>TAK-755</td>
<td>Congenital Thrombotic Thrombocytopenic Purpura (cTTP)</td>
<td>FY 2023</td>
</tr>
<tr>
<td>TAK-611</td>
<td>Metachromatic Leukodystrophy (MLD)</td>
<td>FY 2023</td>
</tr>
<tr>
<td>TAK-935</td>
<td>Developmental and Epileptic Encephalopathies (DEE)</td>
<td>FY 2023</td>
</tr>
<tr>
<td>Orexin2R-ag</td>
<td>Narcolepsy Type 1 (NT1)</td>
<td>FY 2023</td>
</tr>
<tr>
<td>TAK-607</td>
<td>Complications of Prematurity</td>
<td>FY 2023</td>
</tr>
</tbody>
</table>

1. Projected timing of approvals depending on data read-outs; some Wave 1 target approval dates assume accelerated approval. 2. Currently in a non-pivotal Phase 2 study; planning underway to include interim stage gates that can advance the program into a pivotal trial.
3. Estimated number of patients projected to be eligible for treatment, in markets where the product is anticipated to be commercialized, subject to regulatory approval.
4. For TAK-620 and TAK-607, the addressable population represents annual incidence.

TARGET APPROVAL

- FY 2020: ~150k/Under evaluation
- FY 2021: ~7 - 15k/25 - 45k
- FY 2023: ~500/2 - 6k
- FY 2023: ~350/~1 - 2k
- FY 2023: ~50k/~70 - 90k
- FY 2024: 70 - 140k/300k - 1.2M
- Possible Wave 1 Approval: ~25k/~80 - 90k

Estimated dates as of November 14, 2019.
SELECTED TRANSFORMATIVE PROGRAMS

**TAK-620**
Potential first treatment of CMV infection in transplant patients in over 10 years. Inhibitor of protein kinase UL97.

**TAK-755**

**TAK-607**
Potential first pharmacologic therapy in >20 years to prevent complications of prematurity. Recombinant IGF-1 growth factor.

---

**TAK-620: POTENTIAL BEST IN CLASS TREATMENT FOR POST-TRANSPLANT CMV INFECTION**

**BURDEN OF CMV INFECTION IN TRANSPLANT RECIPIENTS**

CMV infection is the most common post-transplant viral infection\(^1\)

- Affects >25% of transplants

CMV infection can be fatal\(^2,3\)

- Higher rates of graft failure: 2.3X and mortality: 2.6X

Current therapies have significant toxicities and resistance\(^4,5,6,7\)

- Incidence of neutropenia >20% and renal toxicity >50%

---

**TAK-620: NOVEL MOA TARGETING PROTEIN KINASE UL97**

TAK-620 ADDRESSES UNMET NEED IN BOTH FIRST-LINE AND RESISTANT / REFRACTORY SETTING

Transplant treatment

CMV Viremia

First-Line: Newly diagnosed CMV

Failure First-Line

Resistant/Refractory (R/R) CMV

Solid organ transplant (SOT) patients1,2:

~100K

First-Line: Newly diagnosed CMV

~30K

Resistant/Refractory (R/R) CMV

~5K

Hematopoietic Stem Cell Transplants (HSCT) patients1,2:

~90K

~15K

~5K

TAK-620: Ph 3 Study 302

TAK-620: Ph 3 Study 303


TAK-620 DEMONSTRATED SIMILAR EFFICACY AND BETTER SAFETY VERSUS SOC IN A PHASE 2 STUDY IN FIRST-LINE PATIENTS

TAK-620: Dose 400, 800 or 1200 mg BID2

VGV (N=40)

All Doses (N=119)

Confirmed undetectable plasma CMV DNA within 6 weeks

79%

67%

Neutropenia that occurred or worsened during treatment through week 12

5%

18%

1. Confirmed undetectable CMV DNA in plasma was defined as two consecutive CMV DNA polymerase-chain-reaction assay values measure during treatment that were below the level of quantitation (i.e., <200 copies per millimeter according to the central laboratory) separated by at least 5 days. For the primary analyses of confirmed undetectable CMV DNA within 3 weeks and 6 weeks, data were missing for 3 patients: 1 each in the 400-mg TAK-620 group, the 1200-mg TAK-620 group and the valganciclovir group

2. N Engl J Med 2019; 381:1136-47. Overall risk ratio (95% CI) relative to the Valganciclovir reference was 1.20 (0.95-1.51)
TAK-620: GRANTED BREAKTHROUGH DESIGNATION IN RESISTANT OR REFRACTORY CMV INFECTION

1. Efficacy in seriously ill R/R CMV in SOT and HSCT recipients with multiple risk factors predictive of poor outcomes

**TAK-620 Dose: 400 mg, 800 mg, 1200 mg BID**

<table>
<thead>
<tr>
<th>Primary efficacy endpoint</th>
<th>All doses (Total N = 120)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with confirmed undetectable plasma CMV DNA within 6 weeks in ITT² population</td>
<td>80 (66.7%)</td>
</tr>
</tbody>
</table>

2. Superior renal safety profile - did not result in treatment discontinuations

Historical outcomes: High (~50%) failure rates / relapse rates³,⁴,⁵

Renal impairment is the primary reason for discontinuation with SOC (Foscarnet, Cidovir); nephrotoxicity is > 50%⁶

---

TAK-620: TWO ONGOING PIVOTAL STUDIES; EXPECT FIRST APPROVAL IN RESISTANT OR REFRACTORY CMV IN 2021

**TAK-620 PHASE 3 STUDY 303**

Resistant/Refractory CMV Patients with SOT or HSCT

- 2:1 Randomization
- TAK-620 400mg BID (N=234)
- Investigator's choice (N=117)

Primary Endpoint: Viremia @ 8 wks of Rx

**EXPECTED MILESTONES (FY)**

- 2020: 2H 2020: Ph 3 Readout
- 2021: Ph 3 US Approval
- 2022: EU Approval

**TAK-620 PHASE 3 STUDY 302**

HSCT Recipients With First CMV Infection

- 1:1 Randomization
- TAK-620 400mg BID (N=275)
- 900mg BID VGV (N=275)

Primary Endpoint: Viremia @ 8 wks of Rx

**EXPECTED MILESTONES (FY)**

- 2021: 1H 2021: Ph 3 Readout
- 2021: US Approval
- 2022: EU Approval

---

### SELECTED TRANSFORMATIVE PROGRAMS

<table>
<thead>
<tr>
<th>TAK-620</th>
<th>Potential first treatment of CMV infection in transplant patients in over 10 years. Inhibitor of protein kinase UL97.</th>
</tr>
</thead>
<tbody>
<tr>
<td>TAK-607</td>
<td>Potential first pharmacologic therapy in &gt;20 years to prevent complications of prematurity. Recombinant IGF-1 growth factor.</td>
</tr>
</tbody>
</table>

### CONGENITAL AND IMMUNE TTP HAVE SUBSTANTIAL MORTALITY AND MORBIDITY BURDEN DUE TO INADEQUATE SOC

#### CONGENITAL TTP (cTTP)
- Sub-therapeutic dose with plasma infusions
- Patients still experience ischemic injury of brain, kidneys and heart
- Poor long-term outcomes

#### IMMUNE TTP (iTTP)
- ~30% relapse rate with plasma exchange (PEX)
- New market entrant reduces relapse rate, but has significant limitations\(^3,4\)
  - Enhanced risk of bleeding:
    - Gingival bleeding 18% vs. 1% placebo
    - Epistaxis 32% vs. 3% placebo

### ADDRESSABLE POPULATION (WW)\(^1,2\)

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>cTTP</td>
<td>2,000 – 6,000</td>
</tr>
<tr>
<td>iTTP</td>
<td>5,000 – 18,000</td>
</tr>
</tbody>
</table>

TAK-755 DIRECTLY ADDRESSES UNDERLYING CAUSE OF TTP

TAK-755 REPLACES ADAMTS13, DEFICIENCY OF WHICH LEADS TO TTP

**ADAMTS13:**
Cleaves VWF multimers that mediate platelet aggregation and clotting

**TTP**
Formation of microthrombi due to accumulation of large VWF multimers

TAK-755: POTENTIAL TRANSFORMATIVE THERAPY FOR TTP

**TAK-755 PHASE I, OPEN-LABEL, DOSE ESCALATION STUDY IN cTTP**

- Administered as a single dose in 15 cTTP patients
- TAK-755 was well tolerated
- No anti-ADAMTS13 antibodies detected

**TAK-755 PK PROFILE AND PD EFFECT ON VWF CLEAVAGE AT 40 IU/KG**

TAK-755: ONGOING PHASE 3 CONGENITAL TTP STUDY

TAK-755 PHASE 3 PROPHYLAXIS STUDY

- All patients roll over to a 6 month TAK-755 extension
- Phase 3 study has a cohort of acute cTTP patients who receive TAK755. Patients are eligible to enter the prophylaxis study upon completion of acute treatment

Primary Endpoint: Incidence of acute TTP episodes

- 1:1 Randomization

TAK-755 PHASE 3 PROPHYLAXIS STUDY

- cTTP patients (N = 26 – 42)
- Tx duration: 6 months

SOC

TAK-755 40 IU/kg Every other week

TAK-755 40 IU/kg Every other week

SOC

Primary Endpoint: Incidence of acute TTP episodes

EXPECTED MILESTONES (FY)

2019
1H: Ph 3 initiated

2021
2H: Ph 3 Readout

2023
US Approval

2025
EU Approval

1. A single dose modification to 1x/week may be mandated based on clinical outcomes; 2. Plan to seek deferral of pediatric data requirement in EU for initial filing, which would enable possible approval in EU in 2023

TAK-755 IMMUNE TTP PHASE 2 STUDY DESIGN

Primary or relapse acute iTTP episode (N=30)

PEX Day 1

1:1:1 Randomization

Placebo + SOC

TAK-755 Low dose + SOC

TAK-755 High dose + SOC

Remission Phase
Placebo or TAK-755

Primary endpoints: PK/PD

EXPECTED MILESTONES (FY)

2020
2H: Ph 2 Readout

2021
2H: Ph 3 Start

2023
2H: Ph3 Readout

2025
US/EU Approval
SELECTED TRANSFORMATIVE PROGRAMS

**TAK-620**
Potential first treatment of CMV infection in transplant patients in over 10 years. Inhibitor of protein kinase UL97.

**TAK-755**

**TAK-607**
Potential first pharmacologic therapy in >20 years to prevent complications of prematurity. Recombinant IGF-1 growth factor.

EXTREMELY PREMATURE INFANTS EXPERIENCE CONSIDERABLE MORBIDITY

- **Morbidity (%) by birth year, US data**
  - Bronchopulmonary dysplasia (BPD)
  - Severe intraventricular hemorrhage (IVH)

- ~80,000-90,000 Extremely preterm babies (<28 wks gestational age) born
- ~40% have lung complications in addition to morbidities in brain, eye that adversely impact development and learning
- ~$200,000 hospitalization costs per infant

TAK-607 REPLENISHES IGF-1, A FETAL GROWTH FACTOR THAT IS DECREASED IN PRETERM INFANTS

TAK-607: IGF-1 / IGFBP-3\(^1\) COMPLEX

- IGF-1 is an important fetal growth factor supplied by the mother that is involved in the development of multiple organs
- IGF-1 is low or absent in premature infants born before 28 weeks\(^2\)
- TAK-607 demonstrated beneficial effects in lung development and brain vasculature in preclinical models\(^3,4\)

IGF-1 LEVELS ARE LOW IN PRETERM INFANTS\(^2\)

![Graph showing IGF-1 levels in normal in utero fetus and preterm infants](image)

4. Ley D et al. JENS 2019

TAK-607: PHASE 2 STUDY INFORMED DOSE AND ENDPOINT SELECTION

ROP-2008-01: RANDOMIZED, CONTROLLED PHASE 2 STUDY OF TAK-607

- Pre-term infants with a gestational age (GA) <28 weeks (N = 120)
- Assessed outcomes in ITT and “evaluable” sets (40% patients who achieved target exposure of IGF-1 levels)\(^1\)
  - Primary endpoint: ROP not met
  - Pre-specified secondary endpoints: Bronchopulmonary Dysplasia (BPD) was reduced and Intra-Ventricular Hemorrhage (IVH) showed a positive trend
- Granted FDA fast-track designation

TAK-607 IMPACTED BPD AND IVH\(^2\)

![Bar graph showing impact of IGF-1/IGFBP-3 on BPD and IVH](image)

1. Evaluable set: ≥70% IGF-1 measurements within targeted intrauterine range (28–109 µg/L) AND ≥70% intended duration of treatment
2. Ley D, J Pediatrics, 2018

ROP – retinopathy of prematurity
TAK-607: FOOTPRINTS STUDY DESIGNED TO DEMONSTRATE REDUCTION IN THE COMPLICATIONS OF PREMATURETY

**Primary endpoint:** Duration of supplemental oxygen use through 1 year corrected age

**MILESTONES (FY)**
- 1H: Ph 2b initiated
- 1H: Ph 2b Readout

**Treatment** (2-7 wks based on GA)
- Rx: Day 1
- Rx End: 29 wk + 6 d PMA

**Post Treatment Follow-up period**
- Primary endpoint: 12 months corrected age
- Outpatient: Respiratory morbidity assessments/week

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1. Supplemental oxygen use defined by one of the following: a) Any fraction of inspired oxygen (FiO2) >21%, b) Non-invasive respiratory support delivered via a nasal interface (e.g., continuous positive airway pressure [CPAP], nasal cannula, etc.), c) Invasive respiratory support (mechanical ventilation) via an endotracheal tube or tracheostomy

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NME MILESTONES ACHIEVED IN FY19 AND LOOKING AHEAD TO OTHER POTENTIAL MILESTONES THROUGH FY20

**PIVOTAL STUDY STARTS, APPROVALS**

**1H FY 2019**
- TAK-611 MOC Ph 2 start
- TAK-705

**2H FY 2019**
- PEVONEDISTAT TAK-148
- TAK-788 2L NSCLC Ph 2 start

**1H FY 2020**
- TAK-788 2L NSCLC Ph 3 start
- TAK-573 R/R MM, Solid Tumor POC

**2H FY 2020**
- TAK-788 1L NSCLC Ph 3 start
- PEVONEDISTAT TAK-148

---

**1H FY 2020**
- TAK-788 2L NSCLC Ph 2 Pivotal
- TAK-721 EoE Ph 3 data
- TAK-573 R/R MM, Solid Tumor POC

**2H FY 2020**
- TAK-788 1L NSCLC Ph 3 start
- PEVONEDISTAT TAK-148

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**KEY DATA READOUTS**

1. Potential key milestone dates as of November 14, 2019. The dates included herein are estimates based on current data and are subject to change.
2. Potentially registration enabling.
WE AIM TO PROVIDE CURATIVE THERAPY

As the global leader in Rare Diseases, we aspire to provide transformative and curative treatments to our patients

Transformative

Programs with transformative potential in devastating disorders with limited or no treatment options today

Curative

Emerging early pipeline of AAV gene therapies to redefine treatment paradigm in monogenic rare diseases

BUILDING A WORLD CLASS GENE THERAPY ‘ENGINE’

TOP TIER GMP MANUFACTURING

GENE THERAPY AAV^1 PLATFORM

GENE THERAPY PIPELINE

TAKEDA THERAPEUTIC AREAS

Liver expression

- Strong capabilities in liver expression
- Emerging capabilities in CNS expression

3+ Research Candidates | NextGen Hem A | TAK-748 Hem B | TAK-754 Hem A

CNS expression

StrideBio Research Candidate | StrideBio Friedreich Ataxia | TAK-686 Huntington’s Disease
WE WILL APPLY OUR CELL THERAPY PLAYBOOK AND UNIFYING CAPABILITIES TO BUILD A GENE THERAPY PIPELINE

Select Cell Therapy Partnerships/Acquisitions

Cell To Gene Therapy
Unifying Capabilities
- Viral expertise
- Manufacturing

Focus of Future Gene Therapy Partnerships
1. Enable re-dosing
2. Lower dose and enhance biodistribution
3. Develop alternative gene delivery vehicles

Gene Therapy Platform

Deliver protective or regenerative factors to hepatocytes
Capsids to enhance biodistribution in CNS
AAV tool box and manufacturing platform

SUMMARY

1. Takeda has the capabilities, scale, and innovative platforms to extend our leadership in Rare Diseases

2. We have a leading late stage portfolio of transformative programs that will establish or re-define the standard of care for highly underserved patients

3. We are building cutting-edge capabilities in gene therapy that aim to deliver ‘cures’ in monogenic rare diseases
R&D DAY AGENDA – TOKYO, NOVEMBER 21, 2019

<table>
<thead>
<tr>
<th>TIME</th>
<th>AGENDA</th>
</tr>
</thead>
</table>
| 11:00 – 11:05 | Welcome and Introduction of Presenters  
Ayako Iwamuro, Investor Relations, Global Finance |
| 11:05 – 11:45 | Realizing the Potential of Plasma-derived Therapies  
Julie Kim, President, Plasma-Derived Therapies Business Unit |
| 11:45 – 12:15 | A New Dedicated Focus on Innovative, Sustainable Solutions for Plasma-Derived Therapies  
Christopher Morabito, M.D., Head of R&D, Plasma-Derived Therapies |
| 12:15 – 12:45 | Q&A session |
| 12:45 – 13:25 | Lunch Break |
| 13:25 – 13:35 | Welcome back and Introduction of Presenters  
Ayako Iwamuro, Investor Relations, Global Finance |
| 13:35 – 13:45 | Takeda: A Global Values-Based, R&D-Driven Biopharmaceutical Leader  
Christophe Weber, President & CEO Takeda |
| 13:45 – 14:15 | Translating Science into Highly Innovative, Life-changing Medicines  
Andy Plump, President R&D |
| 14:15 – 14:40 | Oncology and Cell Therapies with Spotlight on CAR-NK  
Chris Arendt, Head Oncology Drug Discovery Unit |
| 14:40 – 15:00 | Spotlight on Oncology Opportunities  
• TAK-788: Rachel Brake, Global Program Lead  
• Pevonedistat: Phil Rowlands, Head Oncology Therapeutic Area Unit |
| 15:00 – 15:20 | Break |
| 15:20 – 15:45 | Rare Diseases & Gene Therapy  
Dan Curran, Head Rare Disease Therapeutic Area Unit |
| 15:45 – 16:00 | Spotlight on Orexin2R agonists  
Deborah Hartman, Global Program Lead |
| 16:00 – 16:20 | Therapeutic Area Focus in GI with Spotlight on Celiac Disease  
Asit Parikh, Head GI Therapeutic Area Unit |
| 16:20 – 17:00 | Panel Q&A Session |
| 17:00 | Drinks reception |

OX2R AGONISTS FOR THE TREATMENT OF NARCOLEPSY TYPE 1

Deborah Hartman, PhD  
Global Program Leader, Neuroscience  
Takeda Pharmaceutical Company Limited  
Tokyo  
November 21, 2019
NARCOLEPSY TYPE 1 IS A RARE, ACQUIRED CHRONIC NEUROLOGICAL DISORDER

- Psychosocially devastating effects
- Current treatments are only partially effective
- Polypharmacy is common

When I’m awake, sleep is constantly intruding on that part of my life. And when I’m asleep, wakefulness is constantly intruding on that part of my life. It’s frustrating because no matter how well you regulate your narcolepsy, you’re always tired. You’re exhausted.

- Charlie, adviser with NT1

NARCOLEPSY TYPE 1 IS DISTINGUISHED BY THE PRESENCE OF CATAPLEXY AND LOW OREXIN LEVELS

It’s not just about sleep, it’s about quality of wakefulness... it’s really about partnership with your extended family, your spouse, taking care of your children... it limits my ability to play with my kids.

-Sara, adviser with NT1

CSF: Cerebral spinal fluid; Orexin also referred to as hypocretin
1. Individuals with Obstructive Sleep Apnea who are compliant with use of continuous positive airway pressure at night
NARCOLEPSY TYPE I IS CAUSED BY PROFOUND LOSS OF OREXIN-PRODUCING NEURONS

OREXIN mRNA LABELLING OF POSTMORTEM HYPOTHALAMIC SECTIONS

Healthy control  Narcolepsy Type 1

• Individuals with NT1 have >85% less orexin neurons than control, which are located in the hypothalamus.

ACTIVATION OF OREXIN 2 RECEPTOR (OX2R) LEADS TO AROUSAL AND PROMOTES WAKEFULNESS

Orexin neuropeptides A and B  Post-synaptic neurons with orexin 2 receptors  Downstream signalling promoting wakefulness

THE OREXIN HYPOTHESIS IN NARCOLEPSY TYPE I

An orexin 2 receptor agonist may replace the missing endogenous orexin peptide, addressing the underlying orexin deficiency of Narcolepsy Type 1 and reduce disease specific symptoms.

TAK-925, A SELECTIVE OX2R AGONIST, REDUCES NARCOLEPSY-LIKE SYMPTOMS IN AN OREXIN-DEFICIENT MOUSE MODEL

TAK-925 FULLY RESTORED WAKEFULNESS

Wakefulness time of NT1 mouse model in active phase for one hour

TAK-925 ELIMINATED SLEEP / WAKE TRANSITIONS

Hypnogram of sleep/wake transitions in NT1 mouse model

TAK-925 ABOLISHED CATAPLEXY-LIKE EPISODES

Cataplexy-like episodes in NT1 mouse model for three hours after chocolate

---

TAK-925 SHOWED PROMISING ABILITY TO MAINTAIN WAKEFULNESS IN AN EARLY PROOF OF CONCEPT STUDY IN NT1 PATIENTS

SLEEP LATENCY IN THE MAINTENANCE OF WAKEFULNESS TEST (MWT): CURRENT TREATMENTS

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Placebo-adjusted change from baseline (minutes, 95% CI)</th>
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</thead>
<tbody>
<tr>
<td>Pitolisant</td>
<td>NR</td>
</tr>
<tr>
<td>Modafinil</td>
<td>3.0</td>
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<tr>
<td>Sodium oxybate</td>
<td>3.3</td>
</tr>
<tr>
<td>Armodafinil</td>
<td>3.8</td>
</tr>
<tr>
<td>Solriamfetol</td>
<td>7.7</td>
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</tbody>
</table>

TAK-925 (N=14)

SLEEP LATENCY IN THE MAINTENANCE OF WAKEFULNESS TEST (MWT):
(single dose nine hour continuous IV infusion during the day)

<table>
<thead>
<tr>
<th>TAK-925 5 mg (n=6)</th>
<th>Placebo-adjusted observed value (minutes, 95% CI)</th>
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</thead>
<tbody>
<tr>
<td>18.8</td>
<td></td>
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</tbody>
</table>

| TAK-925 11.2 mg (n=4) | 36.1 |
| TAK-925 44.8 mg (n=4) | 36.7 |

*** P value <0.001

- TAK-925 was well-tolerated; most AEs were mild and no SAEs were observed
- In this TAK-925-1001 study, four 40 minute MWTs were conducted per period
- Direct cross-study comparison cannot be made between TAK-925 and treatments due to different studies with different designs


TAK-925 ALSO REDUCED SUBJECTIVE SLEEPINESS IN THIS EARLY PROOF OF CONCEPT STUDY IN NT1

KAROLINSKA SLEEPINESS SCALE VALUES DURING AND AFTER ADMINISTRATION OF TAK-925

1. TAK-925 effective plasma half-life <2 hours

TAK-925 MAINTAINED WAKEFULNESS IN SLEEP-DEPRIVED HEALTHY ADULTS IN A SECOND PHASE 1 STUDY

SLEEP LATENCY IN THE MAINTENANCE OF WAKEFULNESS TEST (MWT) IN SLEEP-DEPRIVED HEALTHY ADULTS

Results suggest potential therapeutic use of TAK-925 in other hypersomnia disorders not associated with orexin deficiency

Average minutes (least squares means, 95% CI)

- Placebo (n=20) 9
- TAK-925 44.8mg (n=18) 25
- TAK-925 112mg (n=18) 39

***: p-value <0.001 relative to placebo

TAK-925 was well-tolerated; most AEs were mild and no SAEs were observed


WE ARE COMMITTED TO LEADING INNOVATION IN OREXIN BIOLOGY AND EXPANDING THERAPEUTIC INDICATIONS FOR OX2R AGONISTS

- TAK-925-1003 for Narcolepsy Type 2 (NCT03748979)
- SPARKLE 2001 study for Residual EDS in Obstructive Sleep Apnea (NCT04091425)
- SPARKLE 2002 study for Idiopathic Hypersomnia (NCT04091438)

- Top priority
- Other hypersomnia disorders
- Additional opportunities for expansion

- REM: Rapid eye movement
- Narcolepsy Type I
- Narcolepsy Type II
- REM disorders under evaluation
- Idiopathic Hypersomnia
- Rare primary hypersomnia disorders
- Shif Work Sleep Disorder
- Residual EDS in Obstructive Sleep Apnea
- EDS in other neurological & psychiatric disorders
- Metabolic disorders under evaluation
- Hypersomnia disorders secondary to other conditions

1. Individuals with Obstructive Sleep Apnea who are compliant with use of continuous positive airway pressure at night
**TAK-994 IS AN ORAL OX2R AGONIST PROGRESSING TO STUDIES IN NARCOLEPSY TYPE 1**

**TAK-994-1501 PROOF OF CONCEPT STUDY IN NARCOLEPSY TYPE 1**

- Multi-center, placebo-controlled trial in North America and Japan
- Enrollment target: 72 adults
- Duration of treatment: 28 days dosing
- Exploratory outcome measures include Maintenance of Wakefulness Test (MWT), Epworth Sleepiness Scale (ESS), and Weekly Cataplexy Rate (WCR)

---

**DIGITAL TECHNOLOGIES ARE ENHANCING THE DEVELOPMENT OF OX2R AGONISTS FOR SLEEP DISORDERS**

**TRADITIONAL CLINICAL INSTRUMENTS DO NOT FULLY MEASURE SYMPTOMS OF SLEEP DISORDERS**

**DIGITAL MEASURES WILL FURTHER CHARACTERIZE SLEEP ARCHITECTURE AND SUPPORT CLINICAL TRIAL ASSESSMENTS**

- Real-time data capture to understand disease burden and effects of treatment
- Non-invasive measures to optimize therapy
- Patient stratification using digital fingerprints

---

WE ASPIRE TO BRING A POTENTIALLY TRANSFORMATIVE OX2R ANAGONIST SOLUTION TO INDIVIDUALS WITH NARCOLEPSY TYPE 1

TAK-925

- Achieved early Proof of Concept for NT1
- Awarded Breakthrough Therapy Designation
- Awarded Sakigake Designation
- Launched formulation development activities

TAK-994

FY19
- TAK-994, first oral OX2R agonist, entered phase I

FY20
- Initiate SPARKLE-1501 Proof of Concept study in NT1

FY21
- Initiation of NT1 pivotal studies
- First approval targeted for 2024

Thank you to all the study participants who have enrolled in these early OX2R agonist clinical trials

SUMMARY

1. TAK-925 has achieved early Proof-of-Concept for OX2R agonists in Narcolepsy Type 1
2. TAK-925 has demonstrated potential of OX2R agonists for treatment of other sleep-related disorders
3. TAK-994 is an oral OX2R agonist progressing to studies in Narcolepsy Type 1
# R&D Day Agenda – Tokyo, November 21, 2019

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<td>Asit Parikh, Head GI Therapeutic Area Unit</td>
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<td>Panel Q&amp;A Session</td>
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<tr>
<td>17:00</td>
<td>Drinks reception</td>
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**Therapeutic Area Focus in GI with Spotlight on Celiac Disease**

Asit Parikh, MD, PhD  
Head Gastroenterology Therapeutic Area Unit  
Takeda Pharmaceutical Company Limited  
Tokyo  
November 21, 2019
WE TARGET UNMET NEEDS THAT ALIGN WITH OUR STRENGTHS

**AREAS OF FOCUS**

- High unmet medical need
- Potential to advance SoC through innovative science – by being first or best in class
- Fit with internal strengths
- Ability to create a commercially viable path

**GI WW RX SALES 2018 (USD BN)**

- Total = $57Bn

**TAKEDA GI DISEASE AREAS**

- GI inflammation
- GI motility
- Liver fibrosis
- Acid related diseases

**SOURCE:** Evaluate Pharma indication specific sales, accessed May 29, 2019. Other GI includes: pancreatic insufficiency, hepatic encephalopathy, diarrhea, bowel clearance, gallstones, hemorrhoids.

WE STRENGTHEN ENTYVIO BY CONTINUOUSLY IMPROVING VALUE FOR PATIENTS

**COMPETITIVE POSITIONING**

- **VARSITY:** 1st Head-to-Head study in IBD (UC)
  - Vedolizumab was superior to adalimumab on the primary endpoint of clinical remission at wk 52
  - Onset of action as rapid as anti-TNF

**EXPANDED PATIENT POPULATIONS**

- Entyvio Subcutaneous Development
  - Positive VISIBLE UC and CD trials
  - Subject to regulatory approval, on track to launch exclusive, digital, needle-free jet-injector by 2022

- **Gut GvHD prophylaxis**
  - Could transform SoC for cancer patients undergoing allo stem-cell transplants

**GEOGRAPHIC EXPANSION**

- **Envyvio IV**
  - Approved in 68 countries
  - Launched in Japan (UC: Nov 2018, CD: May 2019)

**EXPECTED MILESTONES (FY)**

- **2019**
  - Entyvio (SC UC) US approval
  - Entyvio (SC UC) EU, JP approval
  - Entyvio (IC) CN approval

- **2020**
  - Entyvio (SC UC) US, EU approval
  - Entyvio (SC UC) EU, JP approval

- **2021**
  - Entyvio GvHD Ph3 readout


IBD: Inflammatory Bowel Disease; UC: ulcerative colitis; CD: Crohn's Disease; IV=intravenous; SC= subcutaneous; TNF=tumour necrosis factor; SoC: standard of care; CN: China; JP: Japan; GvHD: graft versus host disease; Clinical remission: Complete Mayo score of 2 points and no individual subscore >2 point.

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135
## WE ARE POSITIONED TO DELIVER NEAR-TERM & SUSTAINED GROWTH ONCOLOGY

<table>
<thead>
<tr>
<th>Target Approval</th>
<th>FY20</th>
<th>FY21</th>
<th>FY22</th>
<th>FY23</th>
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<tbody>
<tr>
<td><strong>TAK-788</strong></td>
<td>HL NSCLC</td>
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<tr>
<td><strong>TAK-924</strong></td>
<td>HR-MDS</td>
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<tr>
<td><strong>TAK-788</strong></td>
<td>HL NSCLC</td>
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<tr>
<td><strong>TAK-611</strong></td>
<td>MLD (IT)</td>
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<td><strong>TAK-609</strong></td>
<td>Hunter (IT)</td>
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<tr>
<td><strong>TAK-755</strong></td>
<td>eTPP</td>
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## CLINICAL-STAGE NMEs

<table>
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<tr>
<th>Platforms</th>
<th>FY25 and Beyond</th>
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<tbody>
<tr>
<td><strong>Targeted Immune Engagers</strong></td>
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<tr>
<td><strong>Next-Gen Checkpoint Modulators</strong></td>
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<td><strong>Cell Therapy and Immune Modulation</strong></td>
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<td><strong>Gene Therapy</strong></td>
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<tr>
<td><strong>Other Platforms</strong></td>
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<tr>
<td><strong>RNA Modulation</strong></td>
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<td><strong>Antibody Transport</strong></td>
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<td><strong>Vehicle</strong></td>
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## RARE DISEASES

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<tr>
<td><strong>TAK-620</strong></td>
<td>CMV in transplant</td>
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<td><strong>TAK-609</strong></td>
<td>Hunter (IT)</td>
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<tr>
<td><strong>TAK-607</strong></td>
<td>Complications of paralytic ileus</td>
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## NEUROSCIENCE

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<tbody>
<tr>
<td><strong>TAK-341</strong></td>
<td>Parkinson’s Disease</td>
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<tr>
<td><strong>TAK-418</strong></td>
<td>Kabuki Syndrome</td>
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<tr>
<td><strong>TAK-754</strong></td>
<td>HemA</td>
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<tr>
<td><strong>TAK-755</strong></td>
<td>(ITP, SCD)</td>
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<tr>
<td><strong>TAK-531</strong></td>
<td>Hunter (IT)</td>
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## GASTROENTEROLOGY

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<tr>
<td><strong>TAK-721</strong></td>
<td>Eos</td>
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<tr>
<td><strong>TAK-003</strong></td>
<td>Dengue Vaccine</td>
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<tr>
<td><strong>TAK-214</strong></td>
<td>Nausea &amp; vomiting</td>
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## VACCINES

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<td><strong>TAK-003</strong></td>
<td>Dengue Vaccine</td>
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<tr>
<td><strong>TAK-214</strong></td>
<td>Nausea &amp; vomiting</td>
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## GENE THERAPY

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<tbody>
<tr>
<td><strong>TAK-535</strong></td>
<td></td>
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</table>

## MICROBIOME

<table>
<thead>
<tr>
<th>Target Approval</th>
<th>FY20</th>
<th>FY21</th>
<th>FY22</th>
<th>FY23</th>
<th>FY24</th>
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</thead>
<tbody>
<tr>
<td><strong>TAK-721</strong></td>
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</tbody>
</table>

## CELL THERAPY

<table>
<thead>
<tr>
<th>Target Approval</th>
<th>FY20</th>
<th>FY21</th>
<th>FY22</th>
<th>FY23</th>
<th>FY24</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>WAVE 11</strong></td>
<td></td>
<td></td>
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<tr>
<td><strong>WAVE 22</strong></td>
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</tbody>
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1. Projected timing of approvals depending on data read-outs; some of these WAVE 1 target approval dates assume accelerated approval
2. Some Wave 2 assets could be accelerated into Wave 1 if they have breakthrough data
3. Projected approval dates assume filing on Phase 2 data
4. TAK-079 to be developed in Rare Diseases indications myasthenia gravis (MG) and immune thrombocytopenic purpura (ITP) (FPI projected in each indication in 2H FY19)

---

## TAK-721: ON TRACK TO BE THE FIRST FDA APPROVED AGENT TO TREAT EOSINOPHILIC ESOPHAGITIS (EOE)

### ADDRESSES SIGNIFICANT UNMET NEED

- **Chronic, allergic, inflammatory condition of the esophagus that results in swallowing dysfunction**
- **Diagnosed prevalence is expected to increase significantly**

No approved US medication

SOC is food elimination, off-label use

TAK-721 granted breakthrough therapy designation by FDA in 2016

### INDUCTION DATA SHOWS SIGNIFICANT HISTOLOGIC AND SYMPTOM RESPONSE

**Results presented at presidential plenary at ACG, Texas, Oct 2019**

**Histologic Response at 12 Weeks**

- **Histologic Response at 12 Weeks (peak ≤ 6 eosinophils/hpf on biopsy)**
- **Proportion of patients (%)**
- **p < 0.001**
- **Placebo (n = 105)**
- **2 mg BID (n=213)**

<table>
<thead>
<tr>
<th>Proportion of patients (%)</th>
<th>2019</th>
<th>2020</th>
<th>2021</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.0%</td>
<td>53.1%</td>
<td>52.6%</td>
<td>39.1%</td>
</tr>
</tbody>
</table>

**Symptom Response at 12 Weeks**

- **Symptom Response at 12 Weeks (≥ 30% reduction in DSQ score)**
- **Proportion of patients (%)**
- **p = 0.024**

<table>
<thead>
<tr>
<th>Proportion of patients (%)</th>
<th>2019</th>
<th>2020</th>
<th>2021</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.0%</td>
<td>52.6%</td>
<td>51.7%</td>
<td>39.1%</td>
</tr>
</tbody>
</table>

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1. Swallowed use of glucocorticoids intended for asthma (e.g., home or compounded thickening of budesonide solution, or swallowing fluticasone aerosol).

DSQ score: Dysphagia Symptom Questionnaire, patient reported outcome score, eos/hpf: peak eosinophils per high-powered field from endoscopic biopsies

Eos/hpf: eosinophils per high-power field; BID: Twice daily; SOC: Standard of care; NDA: new drug application

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CELIAC DISEASE IS AN EXAMPLE OF A HIGH UNMET NEED AREA WITH NO THERAPIES

- Overlooked disease, growing prevalence
- Chronic symptoms
- Higher risk of certain cancers
- High treatment burden affecting the whole family
- No current pharmacologic therapies

~1% Global population affected by celiac disease
~40% Patients still suffer from symptoms despite being on a gluten-free diet
~1M Estimated global, eligible patient population

Some of us are so extremely sensitive that one little crumb will make us extremely sick. I’m one of those people, and there is really nothing I can do about it.

– Delisi, Celiac disease patient

WE ARE FOCUSING ON THE NARROWEST POPULATION WITH HIGH UNMET NEED

Our focus:
- Niche patient segment with the highest unmet need
- Severe symptoms with villous atrophy
- Continue to suffer despite the GFD and are highly likely to take a therapy

40% Uncontrolled* on GFD
60% Controlled on Gluten Free Diet (GFD)
20% Moderate
18% Severe
4% Refractory

*Uncontrolled defined as ongoing chronic moderate to severe symptoms with villous atrophy
OUR APPROACH TO TREATING CELIAC DISEASE

TREATMENT OPPORTUNITIES FOR CELIAC DISEASE

1. Enzymatic digestion of gluten
2. Reduce intestinal permeability
3. Microbiome modulation
4. Cytokine inhibition
5. Transglutaminase inhibition
6. Promote Immune tolerance

Source: Green and Cellier, 2007

Kuma062 promises greatly increased enzymatic efficiency and improved formulation over predecessors

TAK-101 (TIMP-GLIA) has the potential to be a first in class, tolerizing immune therapy for celiac disease

KUMA062: A HIGHLY POTENT ORAL GLUTENASE THAT COULD CHANGE THE STANDARD OF CARE IN CELIAC DISEASE

ABOUT KUMA062

• Kuma062 is an oral, computationally-engineered super glutenase
• Enhanced catalytic activity compared to other glutenases

CLINICAL DATA SHOWS KUMA062 CAN DEGRADE >95% OF INGESTED GLUTEN

Gluten recovery in gastric contents aspirated 30mins after meal containing 3g of gluten

Optimal activity at the pH range of the stomach after a meal

Resistance to common digestive proteases

Specificity for peptides with immunogenic regions of gliadin

Eliminates ex vivo T cell response to all 3 major gliadin families

Gluten (mg)

Placebo (n=13) 900mg Kuma062 (n=12) 900mg Kuma062 + Nexium (n=13)

p = 0.001

>95% gluten degradation

Kuma well-tolerated, no identified safety concern
• Decision to acquire PVP Biologics expected Q3 FY2019
TAK-101: POTENTIAL BEST-IN-CLASS, INTRAVENOUS THERAPY FOR CELIAC DISEASE DESIGNED TO MODIFY T CELL RESPONSE

ABOUT TAK-101*

- Biodegradable polymer encapsulating antigen
- Designed to induce tolerance to gluten, reduce T cell responses to gliadin

**Expected to provide durable (3 months or longer) down regulation of T cell responses to immunogenic gliadin peptides**

TAKEDA ACQUIRED EXCLUSIVE GLOBAL LICENSE TO TAK-101

TAK-101 REDUCES IMMUNE ACTIVATION AFTER GLUTEN EXPOSURE

Interferon-gamma ELISPOT measurement of gluten-responsive T cells

Placebo
n=16

TIMP-GLIA
n=13

\[ p = 0.0056 \]

Treatment with TAK-101 reduced immune activation by >85%  

**TAKEDA ARE LEADING THE SCIENCE IN CELIAC DISEASE WITH A NEW AI - BASED TOOL AND INGESTIBLE DEVICE**

**PIONEERING AT BOUNDARIES OF CLINICAL MEDICINE**

- Innovative, non-invasive, patented method of measuring total burden of intestinal disease

**INNOVATIVE USE OF TECHNOLOGY**

- Ingestible high resolution camera pill
- Modern machine-learning/ AI based image processing

**PRECISION MEASUREMENT USING AI**

- Pioneering Automated Image assessment quantifies disease burden
TAKEDA IS THE BEST COMPANY TO BRING CELIAC THERAPIES TO PATIENTS

World-class, fully connected GI commercial infrastructure across 65+ countries that supports $6bn+ revenues

- Extensive GI clinical footprint
- Strong reputation for scientific excellence
- Lauded for calculated risk-taking by the GI community
- Experience with redefining guidelines and treatment paths

NME MILESTONES ACHIEVED IN FY19 AND LOOKING AHEAD TO OTHER POTENTIAL MILESTONES\(^1\) THROUGH FY20

PIVOTAL STUDY STARTS, APPROVALS

<table>
<thead>
<tr>
<th>1H FY 2019</th>
<th>2H FY 2019</th>
<th>1H FY 2020</th>
<th>2H FY 2020</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TAK-611</strong></td>
<td>MDZ Ph 3 start(^1)</td>
<td>TAK-328</td>
<td>Piv CML Ph 3 start</td>
</tr>
<tr>
<td><strong>TAK-765</strong></td>
<td>ITT Ph 2 start</td>
<td>TAK-788</td>
<td>EL MDSC Ph 3 start</td>
</tr>
<tr>
<td><strong>TAK-328</strong></td>
<td>Piv CML Ph 2 Overall Survival</td>
<td>TAK-788</td>
<td>Ph 3 start</td>
</tr>
<tr>
<td><strong>TAK-925</strong></td>
<td>Hem. Malignancies POC</td>
<td>TAK-721 EoE</td>
<td>Ph 3 data 2yr extension</td>
</tr>
<tr>
<td><strong>TAK-721</strong></td>
<td>EoE Ph 3 data (inclusion)</td>
<td>TAK-924</td>
<td>HR-MDS Ph 2 Overall Survival</td>
</tr>
<tr>
<td><strong>TAK-301</strong></td>
<td>Other Disease POC</td>
<td>TAK-721 EoE</td>
<td>Ph 3 data (maintenance)</td>
</tr>
</tbody>
</table>

**KEY DATA READOUTS**

1. Potential key milestone dates as of November 14, 2019. The dates included herein are estimates based on current data and are subject to change.
2. Potentially registration enabling.

Denotes milestones that have been achieved.

Oncology
Rare Disease
Neuroscience
Gastroenterology
SUMMARY

1
We have built an industry-leading portfolio rooted in unparalleled scientific excellence and outstanding global commercial strength

2
We are well positioned to bring the first therapies to celiac patients that could change the standard of care

3
We have multiple milestones, including expected key approvals in the next 2 years that will be transformative for patients

R&D DAY AGENDA – TOKYO, NOVEMBER 21, 2019

<table>
<thead>
<tr>
<th>TIME</th>
<th>AGENDA</th>
</tr>
</thead>
</table>
| 11:00 – 11:05 | Welcome and Introduction of Presenters  
Ayako Iwamuro, Investor Relations, Global Finance |
| 11:05 – 11:45 | Realizing the Potential of Plasma-derived Therapies  
Julie Kim, President, Plasma-Derived Therapies Business Unit |
| 11:45 – 12:15 | A New Dedicated Focus on Innovative, Sustainable Solutions for Plasma-Derived Therapies  
Christopher Morakito, M.D., Head of R&D, Plasma-Derived Therapies |
| 12:15 – 12:45 | Q&A session |
| 12:45 – 13:25 | Lunch Break |
| 13:25 – 13:35 | Welcome back and Introduction of Presenters  
Ayako Iwamuro, Investor Relations, Global Finance |
| 13:35 – 13:45 | Takeda: A Global Values-Based, R&D-Driven Biopharmaceutical Leader  
Christophe Weber, President & CEO Takeda |
| 13:45 – 14:15 | Translating Science into Highly Innovative, Life-changing Medicines  
Andy Plump, President R&D |
| 14:15 – 14:40 | Oncology and Cell Therapies with Spotlight on CAR-NK  
Chris Arendt, Head Oncology Drug Discovery Unit |
| 14:40 – 15:00 | Spotlight on Oncology Opportunities  
• TAK-788: Rachel Brake, Global Program Lead  
• Pevonedistat: Phil Rawlands, Head Oncology Therapeutic Area Unit |
| 15:00 – 15:20 | Break |
| 15:20 – 15:45 | Rare Diseases & Gene Therapy  
Dan Curran, Head Rare Disease Therapeutic Area Unit |
| 15:45 – 16:00 | Spotlight on Orexin2R agonists  
Deborah Hartman, Global Program Lead |
| 16:00 – 16:20 | Therapeutic Area Focus in GI with Spotlight on Celiac Disease  
Asit Parikh, Head GI Therapeutic Area Unit |
| 16:20 – 17:00 | Panel Q&A Session |
| 17:00 | Drinks reception |
Panel Q&A Session