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
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
   - SUMOylation MECHANISM-OF-ACTION PROGRAMS
   - Attenukine™ PARTNER

3. Phonetic reading: = first-in-class

---

**EMERGING STRENGTH IN TARGETED INNATE IMMUNE MODULATION**

**HIGH UNMET NEED**
- Patients refractory/ unresponsive to current immunotherapies

**OUR DIFFERENTIATED APPROACH**
- Systemic therapies leveraging innate immunity to enhance response breadth, depth & durability

<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>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Targeted STING agonist</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SUMOylation</td>
<td></td>
<td>Innate immune enhancer</td>
<td>TAK-981</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>TAK-981 (ADCC combo)</td>
<td></td>
<td></td>
</tr>
<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
1. **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%

**EXPECTED MILESTONES (FY)**
- 2019: Ph1 FPI in solid tumors
- 2020: Ph1b MM (incl. combinations)

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

2. **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**
---|---|---|---|---|---
Humbody Vh | Crescendo Biosciences | • Unique pharmacology | Concept 1 | | |
| | | | Concept 2 | | |
Agonist-directed checkpoints | Shattuck Biopharma | • 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

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

OUR DIFFERENTIATED APPROACH
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 & γδT cells
Innate tumor sensors & effectors
Engineered CAR
Fc-mediated killing

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

CUTTING-EDGE ENGINEERING & CELL PLATFORMS

IPSC expertise
γδT cell platform
Armored CAR-Ts
Next-gen CARs
IPSC CAR-Ts
CAR-NK platform

2016 2017 2018 2019

Takeda Cell Therapy Translational Engine
First Development-Stage Partnership

IPSC = Induced pluripotent stem cell  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

![Cancer cell diagram](#)

**PLATFORM VALUE INFLECTIONS**

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

<table>
<thead>
<tr>
<th>PATIENT VALUE PROPOSITION</th>
<th>PLATFORM VALUE INFLECTIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rapid and deep responses with a short-time-to-treatment, safe, off-the-shelf CAR-NK available in outpatient &amp; community settings</td>
<td><strong>FY</strong></td>
</tr>
<tr>
<td>Initial opportunity in G7 countries (CD19)*</td>
<td>2H 2020</td>
</tr>
<tr>
<td>3L+ DLBCL</td>
<td>~8,000</td>
</tr>
<tr>
<td>3L+ CLL</td>
<td>~5,000</td>
</tr>
<tr>
<td>3L+ iNHL</td>
<td>~6,000</td>
</tr>
<tr>
<td>Potential to move into earlier lines of therapy</td>
<td>2021</td>
</tr>
<tr>
<td>Ongoing maturation of clinical data: Efficacious dose, durability, partial vs. full allo, cryopreserved product</td>
<td>2023</td>
</tr>
<tr>
<td>Manufacturing process complete</td>
<td>BLA filing</td>
</tr>
<tr>
<td>Pivotal trials in r/r DLBCL / CLL / Indolent NHL</td>
<td></td>
</tr>
<tr>
<td>BLA filing</td>
<td></td>
</tr>
</tbody>
</table>

**PLATFROM VALUE INFLECTIONS**

<table>
<thead>
<tr>
<th>CAR-NK (allo cord blood)</th>
<th>MD Anderson Cancer Center</th>
<th>Dr. Katy Rezvani</th>
<th>Non-autologous NK cell therapy</th>
<th>TAK-007 (CD19 CAR-NK)</th>
<th>BCMA CAR-NK</th>
<th>Platform expansion</th>
</tr>
</thead>
</table>

**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**

![Graph showing time vs. percentage of CAR-NK, T, and B cells](image)

**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

CR in Richter’s; SD in CLL

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

Data from Dr. Katy Rezvani, MD Anderson Cancer Center
### 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>

CLL = Chronic lymphocytic leukemia  
CRS = Cytokine release syndrome  
DLBCL = Diffuse large B-cell lymphoma  
ASCT = Autologous stem cell transplant  
HLA = Human leukocyte antigen  
PD = Progressive disease  
*Complete response for Richter’s  

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

FY19

FY20

FY21+: Other cell therapy candidates

TAK-007

Off-the-shelf CAR-NK product

TAK-102

Cytokine + chemokine armed CAR-T

CD19 1XX-CAR-T

Next-gen CART signaling domain

GDX012

Gamma-delta T cells

GCC CAR-T

Colorectal Cancer

5 CLINICAL-_STAGE PROGRAMS EXPECTED BY END OF FY20

TAK-007

MD Anderson Cancer Center

TAK-102

NOILE-IMMUNE BIOTECH

CD19 1XX-CAR-T

Memorial Sloan Kettering Cancer Center

GDX012

GAMMADELTA THERAPEUTICS

GCC CAR-T

Takeda

A RICH AND POTENTIALLY TRANSFORMATIVE EARLY CLINICAL ONCOLOGY PIPELINE

PLAT FORM

PARTNER(S)

MECHANISM-OF-ACTION

PROGRAMS

PRECLINICAL

PH1

STING agonism

CURADEV

• Innate-to-adaptive priming

TAK-676 (STING agonist)

Targeted STING agonist

SUMOylation

• Innate immune enhancer

TAK-981

TAK-981 (ADCC combo)

Attenukine™

teva

• Targeted attenuated IFN-α

TAK-573 (CD38-Attenukine™)

Agnost-directed checkpoints

SHATTUCK

Co-inhibition & co-stimulation

TAK-252 / SL-279353

TAK-254 / SL-115154

Shiga-like toxin A

tem

Novel cytotoxic payload

TAK-169 (CD38-SLTA)

IGN toxin

immunogen

Solid tumor-targeted ADC

TAK-164 (GCC-ADC)

Conditional T cell engagers

MAVERICK

Novel solid tumor platform

MVC-101 (EGFR COBRA™)

Cell therapy platforms

GAMMADELTA

Off-the-shelf cell therapies

TAK-007 (CD19 CAR-NK)

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**

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

---

**KEY DATA READOUTS**

- Denotes milestones that have been achieved.
# R&D Day Agenda – New York, November 14, 2019

<table>
<thead>
<tr>
<th>TIME</th>
<th>AGENDA</th>
</tr>
</thead>
</table>
| 12:30 – 12:35 | Welcome and Opening Remarks  
Sheelagh Cowley-Knopf, Head R&D Global Portfolio Strategy |
| 12:35 – 12:45 | Takeda: A Global Values-Based, R&D-Driven Biopharmaceutical Leader  
Christophe Weber, President & CEO Takeda |
| 12:45 – 13:20 | Translating Science into Highly Innovative, Life-changing Medicines  
Andy Plump, President R&D |
| 13:20 – 13:45 | Oncology and Cell Therapies with Spotlight on CAR-NK  
Chris Arendt, Head Oncology Drug Discovery Unit |
| 13:45 – 14:05 | Spotlight on Oncology Opportunities  
• TAK-788: Rachael Brake, Global Program Lead  
• Pevonedistat: Phil Rowlands, Head Oncology Therapeutic Area Unit |
| 14:05 – 14:20 | Break |
| 14:20 – 14:45 | Rare Diseases & Gene Therapy  
Dan Curran, Head Rare Disease Therapeutic Area Unit |
| 14:45 – 15:00 | Spotlight on Orexin2R agonists  
Deborah Hartman, Global Program Lead |
| 15:00 – 15:20 | Therapeutic Area Focus in GI with Spotlight on Celiac Disease  
Asit Parikh, Head GI Therapeutic Area Unit |
| 15:20 – 16:00 | Panel Q&A Session |
| 16:00 | Drinks reception |