ORIENTATION TO OUR ONCOLOGY R&D OVERVIEW

Focused Oncology R&D Strategy
- Building on foundational expertise in hematologic malignancies and a growing portfolio in lung cancer

Novel Discovery Strategy in Immuno-Oncology (I/O) and Advance in Cell Therapies
- Pursuing novel I/O targets and next-generation platforms with world class external partners
- Next-generation cell therapies will bring transformative potential to patients with cancer

Near Term Inflections
- FY2018-FY2020 will be highlighted by several submissions, approvals, pivotal trial starts, and novel assets entering clinical trials
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WE ASPIRE TO CURE CANCER

OUR MISSION
We endeavor to deliver novel medicines to patients with cancer worldwide through our commitment to science, breakthrough innovation, and passion for improving the lives of patients.

HEMATOLOGIC MALIGNANCIES

LUNG CANCER

IMMUNO-ONCOLOGY (I/O)
BUILDING ON THE TAKEDA ONCOLOGY FOUNDATION IN HEMATOLOGIC MALIGNANCIES

GROWING LEADERSHIP POSITION IN HEMATOLOGIC MALIGNANCIES

MDS
Phase 3
pevonedistat

AML
Phase 3
alisertib

Lymphoma
Chronic Myeloid Leukemia

Improving Patient Outcomes in Multiple Myeloma

Next Generation I/O TAK-573 TAK-981

RECENT PROGRESS AND NEXT STEPS

Current Status
Approved in 59 countries for Relapsed/Refractory Multiple Myeloma
First Phase 3 maintenance readout (post-transplant)

Looking Forward
2019 Data Inflections:
MM2 (newly diagnosed)
MM4 (non-transplant maintenance)
AL1 (amyloidosis)
Evolution of real world evidence

Ideal Maintenance Therapies in Multiple Myeloma:
Easy to administer
Minimal toxicity
Maintain response
ADVANCE CD38 BIOLOGY FOR REFRACTORY MULTIPLE MYELOMA

**TAK-079**
- A fully human, anti-CD38 cytolytic IgG1 lambda antibody
- Potent and selective reduction of plasmablasts and NK cells
- Potential for convenient subcutaneous delivery
- Currently in Phase 1 for refractory multiple myeloma

**TAK-573**
- Novel immuno-cytokine approach
- Potential to overcome toxicity of unmodified interferon α and realize the true benefit in oncology
- Compelling pre-clinical data; Phase 1 enrolling for patients with refractory multiple myeloma

**TAK-169**
- 2nd generation Molecular Templates platform
- pM activity against CD38+ cells plus activity in daratumumab-resistant cells
- IND planned in 2019

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TAK-079: IMPROVING UPON FIRST GENERATION ANTI-CD38 mAb FOR REFRACTORY MULTIPLE MYELOMA PATIENTS

A potent anti-CD38 mAb administered as a low volume subcutaneous (SC) injection

**Plasmablast depletion**
- After a single SC injection of 0.6 mg/kg into healthy volunteers (n=6)

**NK cell depletion**
- Novel pharmacokinetic properties enhance potency and enable convenient administration
BRINGING NOVEL THERAPIES TO MDS AND AML

PEVONEDISTAT IN HR-MDS

Unmet Need
1 in 3 MDS patients will progress to AML

Clinical Status
Overall survival 1-1.5 years in the relapse setting

Next Steps
Potential accelerated filing based upon Phase II data in 2019

ALISERTIB IN AML

ALM: Current 5 year survival ~30%

Transplant remains only curative option

American Society of Hematology
ASH 2018: Phase 2 Data Submitted

• Alisertib is a novel, first in class mechanism for front-line AML in combination with chemotherapy

• Exploring initiation of Phase 3 registration enabling study in frontline AML in 2019

DUAL STRATEGY IN LUNG CANCER: TARGETING DRIVER MUTATIONS AND NEXT-GENERATION I/O

Molecularly-Targeted Precision Therapy

CURRENT PORTFOLIO

Sapanisertib (TAK-228)

Next-generation kinase inhibitors

EMERGING ASSETS

TAK-788

NEXT GENERATION TARGETS AND PLATFORM

ALUNBRIG ALTA 1L— POTENTIAL BEST-IN-CLASS PROFILE IN ALK+ NSCLC

Camidge R., WCLC 2018

- Clear superiority to crizotinib and early separation in PFS curve
- Primary endpoint (PFS) hazard ratio is 0.49
- Risk/benefit profile consistent with the expectations of a best-in-class therapy

TAK-788: ADDRESSING UNMET NEED IN EGFR EXON20 MUTATIONS

Overall survival <6 months for exon 20 insertions
Current therapies ineffective for these mutations

Robichaux et al., WCLC 2016

Expected to begin registration-enabling Phase 2 trial in FY2018

Neal et al., WCLC 2018
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WORLD CLASS PARTNERS FUELING THE I/O PIPELINE

- Re-directed immunity
  - NOILE-IMMUNE BIOTECH
  - Haemalogix
  - GAMMA DELTA
  - MAVERICK THERAPEUTICS

- Key Academic Collaborations in CAR-T

- Targeted payloads
  - Heidelberg PHARMA
  - Mersana

- Tumor micro-environment
  - Crescendo Biologics
  - Teva

- 2016
  - Gamma Delta Therapeutics
  - Maverick Therapeutics
  - Teva
  - Crescendo Biologics
  - Mersana Therapeutics

- 2017
  - Noile-Immune Biotech
  - Shattuck Labs
  - Heidelberg Pharma

- 2018
  - Memorial Sloan Kettering Cancer Center
  - Haemalogix

2016
- 2017
- 2018
**TAK-573: BRINGING A NOVEL IMMUNO-CYTOKINE APPROACH TO MULTIPLE MYELOMA**

Targeted delivery of attenuated interferon α to CD38 - a known target in multiple myeloma

- Binds to CD38
- Human IgG4 Fc
- Attenuated IFNα2b with 2 point mutations

Highly compelling pre-clinical data with TAK-573 in a core area of our clinical development expertise in multiple myeloma

Ph 1 currently enrolling for patients with refractory multiple myeloma

Pogue et al. PLOS ONE 2016

**TAKEDA ONCOLOGY AIMS TO BECOME A LEADER IN CELL THERAPIES**

TRANSFORMATIVE POTENTIAL UTILIZING NEXT GENERATION CELL THERAPY PLATFORMS

- GAMMADELTA
- NOILE-IMMUNE BIOTECH

**Key Academic Collaborations in CAR-T**

- FY2019: Differentiated CAR-Ts in Phase I
- FY2020+: Other Hematologic Malignancy and Solid Tumor CAR-Ts

(Takeda-CiRA) Joint Program Framework
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AN INNOVATIVE PIPELINE ENHANCED WITH EXTERNAL PARTNERSHIPS

Discovery/preclinical* | Phase 1 | Phase 2 | Phase 3 | Approved**
---|---|---|---|---
Hematologic Malignancies | TAK-510 CD38 SLTA | TAK-655 Lymphoma | Panobinostat HR-MDS/ANLM, NEDD 8 Small Molecule | NINJARO Amyloidosis, ND MM, R/R MM data corredo, R/R MM Niflumixider, Maint. MM post-SCT PROTEASOME Small Molecule
---|---|---|---|---
Lung Cancer | TAK-079 RR MM, SLE CD18 mAb | Sapanisertib Small Molecule Lung Cancer mTORC1/2 Small Molecule | ALUNBRIG 2L post-previous ALK+NSCLC (EU, JP), FL ALK+ NSCLC ALK Small Molecule
---|---|---|---|---
Immuono-Oncology | TAK-788 NSCLC | Sapanisertib Endometrial Cancer Lung Cancer mTORC1/2 Small Molecule | ALUNBRIG 2L post-previous ALK+NSCLC (EU, JP), FL ALK+ NSCLC ALK Small Molecule
---|---|---|---|---
Solid Tumors | TAK-373 RR MM CD18 Attenualone mAb Fusion Protein | TAK-931 Solid Tumors CD17 Small Molecule | cabozantinib*** 1L/BRC, 2L RCC Multi-RTK Small Molecule
---|---|---|---|---
Maiorana | TAK-675 STING | TAK-4675 Solid Tumors HER2 Small Molecule | niraparib*** Duodenal Cancer, 1L/2/3 Small Molecule | TESARO
---|---|---|---|---
Teva | TAK-373 RR MM CD18 Attenualone mAb Fusion Protein | TAK-931 Solid Tumors CD17 Small Molecule | cabozantinib*** 1L/BRC, 2L RCC Multi-RTK Small Molecule | Exelixis
---|---|---|---|---
Mersana | TAK-322 Solid Tumors HER2 mAb ADC | TAK-322 Solid Tumors HER2 mAb ADC | MIOVANT Prostate Cancer (JP) Griflin antagonist Small Molecule | MIOVANT
---|---|---|---|---

Pipeline as of September 23, 2018. * Assets shown in discovery/preclinical and Phases 1-3 explicitly refer to new molecular entities
** Some with active development seeking new or supplemental indications, or approvals in new territories
*** To pivotal trial for Japan approval

Note: Takeda holds the right to develop and commercialize Adcetris in Japan. For Ninlaro and Cabozantinib, Takeda holds the right to develop and commercialize in Japan and selected Emerging Markets.
EXPECTED KEY ONCOLOGY PORTFOLIO INFLECTION AND MILESTONES

Dates in fiscal year (FY) starting April 1st

ALUNBRIG EU APPROVAL (2L)
ADCRETIS EU/JP APPROVAL (FL)
NINLARO maintenance post-transplant
US APPROVAL
ALUNBRIG US APPROVAL (1L)

ALUNBRIG JP APPROVAL
NINLARO non-transplant maintenance
US APPROVAL
NINLARO newly diagnosed US/EU
APPROVAL
Pevonedistat US APPROVAL
Niraparib JP APPROVAL
Cabozantinib JP APPROVAL

ICLUSIG – Ph+ ALL pivotal start
TAK-788 – EGFR Exon 20 pivotal start
ALUNBRIG 2L Head-to-Head pivotal start
ALUNBRIG 2L Post-2nd Generation TKI pivotal start
Cabozantinib 2L HCC pivotal start (JP)
Cabozantinib 1L RCC pivotal start (JP)
Niraparib Ovarian Cancer pivotal start (JP)

Projected timelines as of September 23, 2018, subject to change

CONCLUSION

1. Focused on delivering the next approvals for NINLARO, ALUNBRIG, and pevonedistat
2. Expanding transformative treatment options in our focus areas of hematologic malignancies and lung cancer with alisertib, TAK-788 and novel CD38 targeted mechanisms
3. Harnessing the power of external innovation with a diverse set of world-class partnerships, accelerating novel therapies into the clinic