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Agenda

Overview of Takeda Oncology

ADCETRIS (brentuximab vedotin)
NINLARO (ixazomib)
  NINLARO development
  Multiple myeloma treatment paradigm
  NINLARO action plan

Summary

The Takeda Oncology team here today

Christophe Bianchi, M.D.
President, Global Oncology Business Unit

Brian DeSchuytner
Global Head, NINLARO

Helgi Van De Velde, M.D., Ph.D.
VP, Oncology Clinical Research

Kelly Page
Global Head, ADCETRIS

Tsudoi Miyoshi
Head of Japan Oncology Business Unit

Liviu Niclescu, M.D., Ph.D.
VP, Global and U.S. Oncology Medical Affairs
Takeda Oncology

Our Vision
WE ASPIRE TO CURE CANCER

Our Mission
To deliver extraordinary medicines for people with cancer worldwide through our science, innovation and passion.

Oncology is a key growth driver for Takeda

- >2,000 Employees dedicated against cancer
- >70 Countries operating in oncology
- >$1B Overall annual investment in oncology R&D
- 6 Marketed oncology products

<table>
<thead>
<tr>
<th></th>
<th>FY14 (billion JPY)</th>
<th>FY15 (billion JPY)</th>
<th>Underlying growth of Oncology excl. VELCADE royalties</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oncology</td>
<td>333.0</td>
<td>336.4</td>
<td>+4.4%</td>
</tr>
</tbody>
</table>
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
Our aspiration is to be a top 10 oncology company in 2025 and rank top 5 in hematological malignancies.

### Global Oncology sales, USD $B

<table>
<thead>
<tr>
<th>Company</th>
<th>2015 (current)</th>
<th>2025 (forecasted)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Roche</td>
<td>25.5</td>
<td>27.2</td>
</tr>
<tr>
<td>Novartis</td>
<td>10.9</td>
<td>Bristol Myers Squibb</td>
</tr>
<tr>
<td>Celgene</td>
<td>8.6</td>
<td>Novartis</td>
</tr>
<tr>
<td>Amgen</td>
<td>6.9</td>
<td>Abbvie</td>
</tr>
<tr>
<td>Bristol Myers Squibb</td>
<td>4.4</td>
<td>Celgene</td>
</tr>
<tr>
<td>Johnson &amp; Johnson</td>
<td>4.2</td>
<td>Johnson &amp; Johnson</td>
</tr>
<tr>
<td>Pfizer</td>
<td>3.3</td>
<td>AstraZeneca</td>
</tr>
<tr>
<td>Lilly</td>
<td>3.0</td>
<td>Takeda</td>
</tr>
<tr>
<td>AstraZeneca</td>
<td>2.7</td>
<td>Merck</td>
</tr>
<tr>
<td>Astellas</td>
<td>2.3</td>
<td>Lilly</td>
</tr>
<tr>
<td><strong>Takeda</strong></td>
<td><strong>2.0</strong></td>
<td><strong>6.5</strong> (Analysts forecast $4.3B)**</td>
</tr>
</tbody>
</table>

1. Includes immunosuppressants, immunostimulants, and interferons, with indications in oncology.
2. 2015 sales reported in EvaluatePharma® 2016.
3. From Takeda’s internal base case projection.

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The 6 brands of our oncology portfolio are transforming the market and the lives of patients.

#### Solid Tumors

<table>
<thead>
<tr>
<th>Brand</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>ENANTONE</td>
<td>A foundational hormonal treatment in prostate cancer</td>
</tr>
<tr>
<td>Vectibix</td>
<td>First fully human anti-EGFR mAb in colorectal cancer</td>
</tr>
<tr>
<td>Mepact</td>
<td>First-in-class immuno-modulator for non-metastatic osteosarcoma</td>
</tr>
<tr>
<td>VELCADE</td>
<td>First ever proteasome inhibitor, for multiple myeloma and mantle cell lymphoma</td>
</tr>
<tr>
<td>Ad cetris</td>
<td>First-in-class CD30-directed antibody-drug conjugate in Hodgkin lymphoma and systemic ALCL</td>
</tr>
<tr>
<td>NINLARO</td>
<td>First and only oral proteasome inhibitor; Transformative in multiple myeloma</td>
</tr>
</tbody>
</table>

#### Hematologic Malignancies

<table>
<thead>
<tr>
<th>Brand</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>ENANTONE</td>
<td>Japan and select countries in Asia and EU</td>
</tr>
<tr>
<td>Vectibix</td>
<td>Japan</td>
</tr>
<tr>
<td>Mepact</td>
<td>EU EM expansions</td>
</tr>
<tr>
<td>VELCADE</td>
<td>U.S.</td>
</tr>
<tr>
<td>Ad cetris</td>
<td>Global Outside U.S. and Canada</td>
</tr>
<tr>
<td>NINLARO</td>
<td>Global</td>
</tr>
</tbody>
</table>

**Takeda Territories**

- **First Launch**
  - ENANTONE: 1985 (U.S.)
  - Vectibix: 2010 (Japan)
  - Mepact: 2010 (EU)
  - VELCADE: 2003 (U.S.)
  - Ad cetris: 2012 (EU)
  - NINLARO: 2015 (U.S.)

**Takeda Revenues (FY2015)**

- ENANTONE: 124.4B ¥
- Vectibix: 18.4B ¥
- Mepact: 2.7B ¥
- VELCADE: 162.0B ¥ (US Sales >$1B for past 2 years)
- Ad cetris: 27.6B ¥
- NINLARO: 4.0B ¥
NINLARO key markets summary

- U.S. Launch proceeding ahead of expectations with excellent demand ramp up and positive feedback from the community
- Japan submission timelines under discussion
- European CHMP issued a negative opinion on May 27
  - Exact scientific grounds for that opinion are being analyzed but we believe it is only a temporary setback and stand by the clinical profile of NINLARO as do other stakeholders:
    - U.S. FDA record time approval and the initial experience from doctors and patients after launch
    - New England Journal of Medicine publication of pivotal study
    - Many European myeloma experts expressing strong support
  - We have filed a request for re-examination which should take about 6 months

Takeda has a legacy in the fight against myeloma with VELCADE, an important clinical and commercial benchmark

- VELCADE positively impacted survival of myeloma patients across lines of treatment and established proteasome inhibition as the standard of care
- VELCADE has achieved great commercial success treating about 70,000 patients per year resulting in global sales of $2.7B*
Injectable proteasome inhibitors have limitations preventing them from achieving higher impact

- Twice weekly injections requiring frequent clinic/hospital visits
- A side effect profile including either:
  - A clinically meaningful rate of peripheral neuropathy
  - Unpredictable and potentially life threatening cardiovascular events
- Real-life duration of treatment of only 6 months
  - Much shorter than clinical trial experience
  - Often shorter than required to optimize patient outcomes

Oral NINLARO builds on the legacy of injectable proteasome inhibitors

- Efficacy of proteasome inhibition
- Oral
- Low overall peripheral neuropathy
- No cardiovascular safety signals
Takeda Oncology

- Cambridge, MA USA headquarters
  - Well situated for Business Development activities, innovation network, academic collaborations and attracting talent
- Dedicated to delivering best-in-class medicines with the goal of significantly improving the treatment of cancer worldwide
- Oncology Business Unit: an agile model balancing the local needs of the cancer community and global alignment
  - Strong cohesion among Commercial, Medical Affairs and R&D
  - Ability to respond quickly to emerging data and patient needs
  - Strong commercial infrastructure in hematological malignancies in key markets
- Two potential future blockbusters, ADCETRIS and NINLARO, will position Takeda Oncology in a strong leadership position

Patient Video
Agenda

Overview of Takeda Oncology

**ADCETRIS (brentuximab vedotin)**

Presented by Kelly Page

NINLARO (ixazomib)

  - NINLARO development
  - Multiple myeloma treatment paradigm
  - NINLARO action plan

Summary

ADCETRIS: Designed with the patient in mind

Antibody-Drug Conjugate

- Anti-CD30 monoclonal antibody
- Protease-cleavable linker
- Monomethyl auristatin E (MMAE), microtubule-disrupting agent

Moving beyond chemotherapy to a highly targeted approach to deliver a cytotoxin directly to tumor cells
ADCETRIS: Transforming patient care
Approved in 64 countries with over 27,000 patients treated

ADCETRIS is becoming a global standard of care
FY15 revenues up 21% from FY14

ADCETRIS Sales (¥B)

- ADCETRIS is approved for use in:
  - Relapsed or refractory (R/R) Hodgkin lymphoma (HL)
    - Following autologous stem cell transplant
    - Patients ineligible for transplant that have failed two prior chemotherapy regimens
  - R/R systemic anaplastic large cell lymphoma (sALCL)
- In early launch countries (DE, FR, UK, JP), greater than 60% of R/R HL patients have received ADCETRIS and continues to grow in other parts of the world
- Similarly, share in R/R sALCL is reaching 60% in these countries

Source: KPI Tracking Research, H2 FY15
Unprecedented outcomes with ADCETRIS in R/R HL

41% Overall Survival at 5 years in Relapsed or Refractory Hodgkin Lymphoma

- First new agent approved in R/R HL in over 30 years
- Estimated 5 yr OS = 41%
  (95% CI: 31%, 51%; range: 1.8-72.9+)
- Median PFS = 9.3 months
  (95% CI: 7.1, 12.2)
- Median overall survival (OS) and progression free survival (PFS) not reached in patients with a complete response
- The most frequent adverse events were peripheral sensory neuropathy, fatigue, nausea, diarrhea, neutropenia, vomiting, cough, pyrexia, and upper respiratory tract infection

Unprecedented outcomes with ADCETRIS in R/R sALCL

64% Overall Survival at 4 years in Relapsed or Refractory Systemic Anaplastic Large Cell Lymphoma (sALCL)

- First agent ever approved specifically for sALCL
- Estimated 4 yr OS = 64%
  (95% CI: 51%, 76%)
- Median PFS per investigator = 20.0 months (95% CI: 9.4, -)
- 19 of 38 patients with a complete response remained progression free at the time of this analysis
- The safety profile was similar to that reported for R/R HL
Success of the Phase 3 AETHERA study may lead to a new treatment paradigm in Hodgkin lymphoma

Consolidation treatment following ASCT in HL patients showed an 18.8 month benefit over the comparator

- At 2 years, early consolidation with ADCETRIS demonstrated improved PFS in HL patients at increased risk of relapse or progression (HR=0.57, P=0.001)
- 2-year PFS rates per investigator of 65% and 45% on the ADCETRIS and placebo arms, respectively
  - Difference was sustained at the 3 year follow-up (shown)
- Safety was similar to that of previous single agent studies, however a higher rate of peripheral neuropathy was seen

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Redefining treatment of frontline HL

Frontline Advanced Hodgkin Lymphoma

<table>
<thead>
<tr>
<th>Phase 1 ADCETRIS+AVD (N=26)</th>
<th>Historical Results with ABVD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete remission (CR)</td>
<td>CR rate in advanced HL</td>
</tr>
<tr>
<td></td>
<td>96%</td>
</tr>
<tr>
<td>Pulmonary toxicity (any event)</td>
<td>0%</td>
</tr>
<tr>
<td>3-year failure-free survival</td>
<td>Rate of pulmonary toxicity</td>
</tr>
<tr>
<td></td>
<td>92%</td>
</tr>
<tr>
<td>3-year overall survival</td>
<td>up to 25%</td>
</tr>
<tr>
<td></td>
<td>100%</td>
</tr>
<tr>
<td></td>
<td>70-80%</td>
</tr>
</tbody>
</table>

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ECHELON-1: Phase 3 Study of ADCETRIS+AVD in Treatment Naïve, Advanced HL

- Treatment naïve, Advanced HL N=1334
- Primary Endpoint: modified PFS
- Study is fully enrolled and expected to readout between 2017 to mid-2018

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2. ABVD historical data: Younes et al., Lancet Vol 14 December 2013; Daggan DB et al., JCO 2000;21(4):967-14; Johnson et al., JCO 2005; 23 (30)
The ADCETRIS opportunity

ADCETRIS has the potential to be the foundation of care for CD30-expressing lymphomas

- **2012**: ADCETRIS approved in Europe
- **2013**: First full year EU sales; start global expansion JPY 13.6 B
- **2014**: Takeda Sales of JPY 22.9 B
- **2015**: Takeda Sales of JPY 27.6 B
- **2016**: Phase 3 AETHERA approval in HL
- **2017 – 2019**: Phase 3 CTCL ALCANZA
- **Phase 3 Frontline HL ECHELON-1 ~ Phase 3 Frontline MTCL ECHELON-2**

Continued data generation in other CD30-expressing indications and combinations

Assuming success in ongoing studies ~4-fold expansion of addressable patient population possible

<table>
<thead>
<tr>
<th>Year of First Major Approval</th>
<th>2016</th>
<th>2017</th>
<th>2018</th>
<th>2019</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current Indications</td>
<td>11,200</td>
<td>13,300</td>
<td>17,200</td>
<td>55,900</td>
</tr>
<tr>
<td>HL Consolidation</td>
<td>3,000</td>
<td>2,100</td>
<td>3,900</td>
<td>6,100</td>
</tr>
<tr>
<td>CD30+ R/R CTCL</td>
<td></td>
<td></td>
<td>49,800</td>
<td></td>
</tr>
<tr>
<td>ASCT ineligible HL</td>
<td></td>
<td></td>
<td>26,600</td>
<td></td>
</tr>
<tr>
<td>CD30+ Frontline MTCL</td>
<td></td>
<td></td>
<td>6,000</td>
<td></td>
</tr>
</tbody>
</table>

Takelon epidemiology flow models (2014-2015)
Numbers of patients not adjusted for lack of access, represents ex-North America treatable patients

Takeda Pharmaceutical Company Limited
ADCETRIS is well positioned for global success

- Demonstrated long-term overall survival in both R/R sALCL and R/R Hodgkin lymphoma
- Approval of retreatment in both R/R sALCL and R/R Hodgkin lymphoma
- Combination studies with PD-1 agents
- Potential approval of earlier line indications, particularly frontline Hodgkin lymphoma
- Proven global commercial infrastructure and resources
- Commitment to our vision and to the patient community
  - Access to Medicine Initiative providing opportunities to bring ADCETRIS to additional EM countries, such as Kenya, and increasing access in other places, such as Brazil

Agenda

Overview of Takeda Oncology
ADCETRIS (brentuximab vedotin)
NINLARO (ixazomib)

NINLARO development

- Multiple myeloma treatment paradigm
- NINLARO action plan

Summary
Patients face many treatment and disease burdens

**TYPICAL R/R MM PATIENT**

**PATIENT DEMOGRAPHICS**
- >70 years, failed 1-3 therapies
- Most likely polypharmacy for other conditions, prophylaxis, and treatment-related adverse reactions

**PREVIOUS TREATMENTS**
- Bortezomib (VELCADE), lenalidomide, and oral steroids
- Alkylating agents for transplant patients (eg, melphalan)

**STANDARDS OF CARE**
- Current: bortezomib or lenalidomide plus dexamethasone
- Potential future: treating to progression with triplet therapy and/or combinations of monoclonal antibodies, proteasome inhibitors, and immunomodulators

**POTENTIAL ADVERSE REACTIONS/COMORBIDITIES**
- Disease-related: renal impairment, bone pain, fractures, and fatigue
- Treatment-related: peripheral neuropathy, deep vein thrombosis, or secondary malignancies
- Other: Cardiovascular complications, bone disease, metabolic, and other conditions that must be treated

**UNMET MEDICAL AND PERSONAL NEEDS:**
- Avoiding relapse and extending life
- Safer treatment (fewer toxicities)
- Simpler treatment (minimizing the impact of treatment/clinical concerns on daily life)
Patients with adverse prognostic characteristics have a particularly high unmet need

**High ISS stage**

- ISS Stage 1
- ISS Stage 2
- ISS Stage 3

**High-risk cytogenetics**

- Standard risk FISH
- High risk FISH

**Multiple prior relapses**

- First
- Second
- Third
- Fourth
- Fifth
- Sixth

**Poor renal function**

- % Events
- G-Cr ≥40 ml/min = 943
- G-Cr <40 ml/min = 395 (42%)
- Median: 122 months
- Median: 43 months

**Elderly**

- Age at diagnosis
- Survival proportion

- Median adjusted for relative survival
- <40: 3.1 years
- 40-49: 5.3 years
- 50-59: 4.6 years
- 60-69: 3.6 years
- 70-79: 3.1 years
- >80: 2.6 years

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**NINLARO mechanism of action**

1. NINLARO temporarily blocks proteasomes from breaking down proteins.
2. This causes a buildup of proteins in the cell.
3. The buildup of proteins can result in cell death.
The TOURMALINE-MM1 Study is the first of a most comprehensive myeloma development program.

Number of patients

- Frontline SCT induction
- Post-SCT maintenance
- Frontline indution
- No SCT extended therapy

Time since diagnosis/duration of therapy

- TOURMALINE-MM3
  - NINLARO 24 months vs pbo
  - Filing target: FY2018

- TOURMALINE-MM2
  - NINLARO + Rd vs Rd to progression
  - Filing target: FY2017

- TOURMALINE-MM4
  - NINLARO 24 months vs pbo
  - Filing target: FY2019

- 2nd line
  - POSITIVE RESULTS
  - TOURMALINE-MM1
    - NINLARO + Rd vs Rd to progression
    - Approved (US): FY2015
    - Filed (EU): FY2015
    - Filing target (JP): FY2016
    - Filing in EM: FY2015 onwards

- 3rd line +

Our myeloma expertise drove excellent R&D execution and allowed rapid progress.

- First Myeloma Trial: Oct. 2009
- Initiation of Phase 3 Rd Combo in R/R MM: Aug 2012
- FDA Submission: July 2015
- FDA Approval: Nov 2015

6 years from 1st patient enrolled to approval

133 days from submission to approval

NINLARO (ixazomib) capsules

33 Rd = Revlimid (lenalidomide) + dexamethasone
pbo = placebo

Takeda Pharmaceutical Company Limited
**TOURMALINE-MM1: Phase 3 study of weekly oral ixazomib + lenalidomide + dexamethasone**

**Global, double-blind, randomized, placebo-controlled study design**

- **N = 722**
- **Randomization**
  - 1:1

**Ixazomib + Lenalidomide + Dexamethasone**
- Ixazomib: 4 mg on days 1, 8, and 15
- Lenalidomide: 25 mg* on days 1-21
- Dexamethasone: 40 mg on days 1, 8, 15, 22

**Placebo + Lenalidomide + Dexamethasone**
- Placebo on days 1, 8, and 15
- Lenalidomide: 25 mg* on days 1-21
- Dexamethasone: 40 mg on days 1, 8, 15, 22

**Stratification:**
- Prior therapy: 1 vs 2 or 3
- ISS: I or II vs III
- PI exposure: yes vs no

**Primary endpoint:**
- PFS

**Key secondary endpoints:**
- OS
- OS in patients with del(17p)

**Response and progression** (IMWG 2011 criteria) assessed by an independent review committee (IRC) blinded to both treatment and investigator assessment.

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**TOURMALINE-MM1 is a rigorous Phase 3 trial with populations representative of real-world patients**

<table>
<thead>
<tr>
<th>TRIAL</th>
<th>TOURMALINE-MM1 ixazomib</th>
<th>ELOQUENT-1 elotuzumab</th>
<th>ASPIRE carfilzomib</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blinded, Placebo Control</td>
<td>⬤</td>
<td></td>
<td>⬤</td>
</tr>
<tr>
<td>Primary Refractory Patients Allowed</td>
<td>⬤</td>
<td></td>
<td>⬤</td>
</tr>
<tr>
<td>Free Light Chain Only Disease Allowed</td>
<td>⬤</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Creatinine Clearance &lt; 50 mL/min</td>
<td>⬤</td>
<td>⬤</td>
<td>⬤</td>
</tr>
<tr>
<td>Serum M-Protein cut-off ≥ 1 g/dL</td>
<td>⬤</td>
<td>⬤</td>
<td></td>
</tr>
<tr>
<td>Global Enrollment Including Asia</td>
<td>⬤</td>
<td>⬤</td>
<td></td>
</tr>
<tr>
<td>del(17) cut-off &gt; 60%</td>
<td>⬤</td>
<td>⬤</td>
<td></td>
</tr>
<tr>
<td>Response rates co-primary endpoint</td>
<td>⬤</td>
<td></td>
<td>⬤</td>
</tr>
</tbody>
</table>
Ixazomib, the first oral proteasome inhibitor, significantly extends PFS in TOURMALINE-MM1

- TOURMALINE-MM1 is a uniquely robust placebo-controlled study of IRd compared to Rd
  - This data was recently published in the *New England Journal of Medicine* and demonstrated a significant extension in progression-free survival and a favorable benefit-risk profile for patients with relapsed and/or refractory multiple myeloma (R/R MM)
- IRd provided patients with relapsed and/or refractory MM with:
  - A significant and clinically meaningful improvement in PFS
  - Significantly improved time to progression (TTP) and response rates
  - Improved PFS in high-risk patients
- Ixazomib added limited additional toxicity to the placebo regimen
  - Low rates of peripheral neuropathy and no cardiovascular, pulmonary, or renal signals
  - Patient-reported quality of life was maintained
- The all-oral regimen of IRd provides an additional therapeutic option for patients with R/R MM

IRd = NINLARO (ixazomib) + Revlimid (lenalidomide) + dexamethasone
Rd = Revlimid (lenalidomide) + dexamethasone

TOURMALINE-MM1: Significant 35% improvement in progression-free survival (PFS) with IRd

Median PFS:
Ixazomib+Rd 20.6 months, Placebo+Rd 14.7 months

Log-rank test p=0.012
Hazard ratio (95% CI): 0.742 (0.587, 0.939)

Median follow-up:
Ixazomib+Rd 14.8 months
Placebo+Rd 14.6 months
TOURMALINE-MM1: Consistent PFS benefit across pre-specified patient subgroups

<table>
<thead>
<tr>
<th>Variable</th>
<th>Subgroup</th>
<th>Median PFS (months)</th>
<th>HR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Placebo-Rd</td>
<td>IRd</td>
</tr>
<tr>
<td>All patients</td>
<td>ALL</td>
<td>362</td>
<td>360</td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>≤65</td>
<td>176</td>
<td>168</td>
</tr>
<tr>
<td></td>
<td>&gt;65-75</td>
<td>125</td>
<td>145</td>
</tr>
<tr>
<td></td>
<td>&gt;75</td>
<td>61</td>
<td>47</td>
</tr>
<tr>
<td>ISS stage (stratification factor)</td>
<td>I or II</td>
<td>318</td>
<td>314</td>
</tr>
<tr>
<td></td>
<td>III</td>
<td>44</td>
<td>46</td>
</tr>
<tr>
<td>Cytogenetic risk</td>
<td>Standard-risk</td>
<td>216</td>
<td>199</td>
</tr>
<tr>
<td></td>
<td>High-risk</td>
<td>62</td>
<td>75</td>
</tr>
<tr>
<td>Number of prior therapies</td>
<td>1</td>
<td>217</td>
<td>224</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>111</td>
<td>97</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>34</td>
<td>39</td>
</tr>
<tr>
<td>Proteasome inhibitor</td>
<td>Exposed</td>
<td>253</td>
<td>250</td>
</tr>
<tr>
<td></td>
<td>Naive</td>
<td>109</td>
<td>110</td>
</tr>
<tr>
<td>Prior IMID therapy</td>
<td>Exposed</td>
<td>204</td>
<td>193</td>
</tr>
<tr>
<td></td>
<td>Naive</td>
<td>158</td>
<td>167</td>
</tr>
<tr>
<td>Refractory to last prior therapy</td>
<td>Yes</td>
<td>55</td>
<td>59</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>397</td>
<td>301</td>
</tr>
<tr>
<td>Relapsed or refractory</td>
<td>Relapsed</td>
<td>280</td>
<td>276</td>
</tr>
<tr>
<td></td>
<td>Refractory</td>
<td>40</td>
<td>42</td>
</tr>
<tr>
<td></td>
<td>Ref &amp; rel</td>
<td>42</td>
<td>41</td>
</tr>
</tbody>
</table>

TOURMALINE-MM1: Improved response rates, durable responses, and improved time to progression (TTP) with IRd

<table>
<thead>
<tr>
<th>Response rates</th>
<th>IRd (N=360)</th>
<th>Placebo-Rd (N=362)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Confirmed ORR (≥PR), %</td>
<td>78.3</td>
<td>71.5</td>
<td>p=0.035</td>
</tr>
<tr>
<td>CR+VGPR, %</td>
<td>48.1</td>
<td>39.0</td>
<td>p=0.014</td>
</tr>
</tbody>
</table>

Response categories

| CR, %   | 11.7 | 6.6 | p=0.019 |
| PR, %   | 66.7 | 64.9 | – |
| VGPR, % | 36.4 | 32.3 | – |
| Median time to response, mos | 1.1 | 1.9 | – |
| Median duration of response, mos | 20.5 | 15.0 | – |
| Median TTP, mos | 21.4 | 15.7 | HR 0.712 p=0.007 |
TOURMALINE-MM1: Ixazomib adds limited additional toxicity to Rd upon prolonged exposure

- At 23 months, median number of treatment cycles: 17 (range 1–34) for IRd, and 15 (1–34) for placebo-Rd
  - 48% and 43% of patients had received ≥18 cycles, respectively

<table>
<thead>
<tr>
<th>Adverse event (AE)</th>
<th>IRd (N=361), %</th>
<th>Placebo-Rd (N=359), %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any AE</td>
<td>98</td>
<td>99</td>
</tr>
<tr>
<td>Any grade ≥3 AE</td>
<td>74</td>
<td>69</td>
</tr>
<tr>
<td>Any serious AE</td>
<td>47</td>
<td>49</td>
</tr>
<tr>
<td>AE resulting in discontinuation of study regimen</td>
<td>17</td>
<td>14</td>
</tr>
<tr>
<td>On-study death (death within 30 days of last dose)</td>
<td>4</td>
<td>6</td>
</tr>
</tbody>
</table>

- Higher frequency of grade ≥3 AE, primarily due to thrombocytopenia
- Rates of serious AEs, AEs resulting in discontinuation or on-study death were similar between the two arms
- Peripheral neuropathy: no difference in high grade events
- No cardiac, thrombovascular, renal or pulmonary signals

IRd = NINLARID (ixazomib) + Revlimid (lenalidomide) + dexamethasone
Rd = Revlimid (lenalidomide) + dexamethasone

AEs after median follow-up of 23 months: Increased rates with IRd driven by low-grade events

<table>
<thead>
<tr>
<th>Preferred terms</th>
<th>IRd (N=361), %</th>
<th>Placebo-Rd (N=359), %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All-grade</td>
<td>Grade 3</td>
</tr>
<tr>
<td><strong>AEs overlapping with lenalidomide</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>45</td>
<td>6</td>
</tr>
<tr>
<td>Constipation</td>
<td>35</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Nausea</td>
<td>29</td>
<td>2</td>
</tr>
<tr>
<td>Vomiting</td>
<td>23</td>
<td>1</td>
</tr>
<tr>
<td>Rash*</td>
<td>36</td>
<td>5</td>
</tr>
<tr>
<td>Back pain</td>
<td>24</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>23</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>31</td>
<td>12</td>
</tr>
<tr>
<td><strong>AEs with proteasome inhibitors</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peripheral neuropathy*</td>
<td>27</td>
<td>2</td>
</tr>
<tr>
<td>Peripheral edema</td>
<td>28</td>
<td>2</td>
</tr>
<tr>
<td><strong>AEs with lenalidomide</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thromboembolism*</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td>Neutropenia*</td>
<td>33</td>
<td>18</td>
</tr>
</tbody>
</table>

*Represents multiple MedDRA preferred terms.
Other infrequent AEs of any grade (median follow-up of 23 months)

<table>
<thead>
<tr>
<th>AE</th>
<th>IRd (N=361), %</th>
<th>Placebo-Rd (N=359), %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arrhythmias*</td>
<td>16</td>
<td>15</td>
</tr>
<tr>
<td>Hypertension</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>Hypertension crisis</td>
<td>&lt;1</td>
<td>0</td>
</tr>
<tr>
<td>Hypotension*</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Heart failure*</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Myocardial infarction*</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Acute renal failure*</td>
<td>9</td>
<td>11</td>
</tr>
<tr>
<td>Liver impairment*</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td>Interstitial lung disease*</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Encephalopathy*</td>
<td>&lt;1</td>
<td>1</td>
</tr>
</tbody>
</table>

Events of special interest

New primary malignancy*†

<table>
<thead>
<tr>
<th></th>
<th>IRd</th>
<th>Placebo-Rd</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>5</td>
<td>4</td>
</tr>
</tbody>
</table>

*Represents multiple MedDRA preferred terms.
†Includes treatment-emergent AEs and new primary malignancies reported during follow-up period.

TOURMALINE-MM1: Quality of life maintained with IRd vs placebo-Rd

**EORTC-QLQ-C30**
Mean global health status score

**MY-20**
Mean side effects of treatment score
Ixazomib, the first oral proteasome inhibitor, significantly extends PFS in TOURMALINE-MM1

- TOURMALINE-MM1 is a uniquely robust placebo-controlled study of IRd compared to Rd
  - This data was recently published in the *New England Journal of Medicine* and demonstrated a significant extension in progression-free survival and a favorable benefit-risk profile for patients with relapsed and/or refractory multiple myeloma (R/R MM)
- IRd provided patients with relapsed and/or refractory MM with:
  - A significant and clinically meaningful improvement in PFS
  - Significantly improved time to progression (TTP) and response rates
  - Improved PFS in high-risk patients
- Ixazomib added limited additional toxicity to the placebo regimen
  - Low rates of peripheral neuropathy and no cardiovascular, pulmonary, or renal signals
  - Patient-reported quality of life was maintained
- The all-oral regimen of IRd provides an additional therapeutic option for patients with R/R MM

\[\text{IRd} = \text{NINLARO (ixazomib)} + \text{Revlimid (lenalidomide)} + \text{dexamethasone}\]
\[\text{Rd} = \text{Revlimid (lenalidomide)} + \text{dexamethasone}\]

**TOURMALINE-MM1 China continuation**

- Same randomized study design of IRd versus placebo-Rd
- Same eligibility criteria and methodology
- N = 115 (China only)
- Significant improvement in PFS
  - Supported by secondary endpoint improvement in TTP and response
- Ixazomib added limited additional toxicity to placebo regimen
- Conclusion: consistent positive treatment effect in Chinese patients
The relapsing nature of myeloma is reflected in distinct treatment settings representing up to 3 million patient months primarily in developed markets.

The Global Myeloma Market Map

**Myeloma Market**
- 3M patient months primarily derived from developed markets due to under-diagnosis in emerging markets
- Pursuing aggressive NINLARO registrations in emerging markets to grow this opportunity further

**Source:** Leadzyme epidemiology and chart reviews

**NSCT** = no stem cell transplant; **R/R MM** = relapsed/refractory multiple myeloma; **SCT** = stem cell transplant.
However, even in developed markets only 1.5 million patient months of treatment are delivered due to limitations of current therapy.

The Global Myeloma Market Map

- **Frontline SCT**
- **NSCT**
- **Post-SCT maintenance**
- **NSCT extended therapy/maintenance**
- **2nd line (R/R MM)**
- **3rd line + (R/R MM)**

Duration of therapy/time since diagnosis:
- Few options
- Several options
- Many options
- No treatment

NSCT = no stem cell transplant; R/R MM = relapsed/refractory multiple myeloma; SCT = stem cell transplant.

Source: Lexityme epidemiology and chart reviews

So what do MM patients need?

**SAFER**
- Minimal toxicities, especially peripheral neuropathy, cardiovascular events, secondary malignancies

**SIMPLER**
- Limit burden on patients and caregivers
- Infrequent dosing

**SUSTAINABLE**
- Ability to stay on therapy
- Maintain quality of life

**MORE EFFECTIVE**
- Improve PFS (and ultimately OS)
- Especially in high-risk and difficult-to-treat patients
Continuous treatment has shown improved overall survival vs. fixed-duration treatment

\[ \text{HR} = 0.69 \quad (95\% \text{ CI, 0.54 to 0.88}; P = 0.003) \]

But continuous treatment is difficult to achieve with current proteasome inhibitors

**VELCADE in the US: Duration of Therapy**

- Pivotal trial VISTA: 11.5 months
- Real-world (US) use*: 6.5 months

Patients have trouble staying on VELCADE in the real world

Reasons for discontinuation include:
- Peripheral neuropathy
- Inconvenience
- Treatment fatigue

NINLARO can deliver sustainable treatment for multiple myeloma patients

**UNIQUE**
- The 1st and only oral proteasome inhibitor

**EFFECTIVE**
- ~6 month PFS improvement in a real-world representative population
- Efficacy in high risk patients

**MANAGEABLE SAFETY**
- Low neuropathy and mostly low grade
- No cardiovascular safety signal

**SIMPLE**
- Replace twice weekly injections at hospital with one capsule, once weekly at home

**COMPETITIVELY PRICED**
- Competitive vs. newly introduced agents
- Access solutions

Sustainable efficacy from a proteasome inhibitor can offer new opportunities

**Today**

- ~ 6 months PI therapy
- Premature discontinuation of therapy due to fatigue from office visits or side effects

**Tomorrow**

- Improved duration of therapy ~ 12+ months PI therapy
- New settings of care
  - Where earlier generation PIs are not currently used
  - An alternative PI option
  - After treatment with another PI
  - As a combination partner for novel agents

= More benefits for more myeloma patients
Overview of Takeda Oncology

ADCETRIS (brentuximab vedotin)

NINLARO (ixazomib)

NINLARO development

Multiple myeloma treatment paradigm

NINLARO action plan

Summary

The current myeloma market is approaching $10B

<table>
<thead>
<tr>
<th>Global Myeloma Market ($M)</th>
<th>Growth drivers</th>
</tr>
</thead>
<tbody>
<tr>
<td>2013: 6,704</td>
<td>Introduction of novel therapies</td>
</tr>
<tr>
<td>2014: 7,683</td>
<td>Longer treatment durations that can result in improved efficacy</td>
</tr>
<tr>
<td>2015: 8,598</td>
<td>Newer treatment paradigms (e.g., maintenance therapy)</td>
</tr>
<tr>
<td></td>
<td>Treatment combinations with novel agents (e.g., triplet therapy)</td>
</tr>
</tbody>
</table>

Growth drivers:

- Introduction of novel therapies
- Longer treatment durations that can result in improved efficacy
- Newer treatment paradigms (e.g., maintenance therapy)
- Treatment combinations with novel agents (e.g., triplet therapy)
We can capture this market opportunity by focusing on three segments of the market:

- **Market for Proteasome Inhibitors in Myeloma**: Total $2.7 B
  - As an oral and sustainable alternative to earlier generation PIs

- **Market for Immunomodulators in Myeloma**: Total $5.9 B
  - As a triplet alternative to lenalidomide doublets

- **Market for Early Discontinuation / Mid-treatment Addition**: Total $8.5 B
  - As a way to sustain therapy despite efficacy, toxicity, or convenience issues encountered with other agents

Note: Proteasome inhibitors and immunomodulators have indications outside of myeloma so global sales of products are higher than the global myeloma market.

---

**NINLARO** is off to a great start in the U.S. since December launch:

- **U.S. NINLARO Net Sales ($M)**
  - December: 5, January: 6, February: 10, March: 13, April: 18, May: 25

- **NINLARO Weekly Demand Units (4 Week Moving Average)**
  - Current new starts share:
    - 6% 1st Line**
    - 16% 2nd Line
    - 11% 3rd+ Line

* Intrinsiq, IntellView April 2016; **unpromoted
To achieve the equivalent of $1B of VELCADE revenues, NINLARO in the U.S. must only achieve half of current VELCADE share

<table>
<thead>
<tr>
<th></th>
<th>U.S. New Patient Starts</th>
<th>Share of Patients</th>
<th>Patients Treated</th>
<th>Length of Therapy (Months)</th>
<th>Patient Months Delivered</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>VELCADE</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1st Line</td>
<td>26,000</td>
<td>60%</td>
<td>15,600</td>
<td>6</td>
<td>93,600</td>
</tr>
<tr>
<td>2nd Line</td>
<td>17,000</td>
<td>40%</td>
<td>6,800</td>
<td>6</td>
<td>40,800</td>
</tr>
<tr>
<td>3rd Line +</td>
<td>16,000</td>
<td>20%</td>
<td>3,200</td>
<td>6</td>
<td>19,200</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>59,000</td>
<td>43%</td>
<td>25,600</td>
<td>6</td>
<td>153,600</td>
</tr>
<tr>
<td><strong>NINLARO</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1st Line</td>
<td>26,000</td>
<td>10%</td>
<td>2,600</td>
<td>18</td>
<td>46,800</td>
</tr>
<tr>
<td>2nd Line</td>
<td>17,000</td>
<td>30%</td>
<td>5,100</td>
<td>12</td>
<td>61,200</td>
</tr>
<tr>
<td>3rd Line +</td>
<td>16,000</td>
<td>25%</td>
<td>4,000</td>
<td>12</td>
<td>48,000</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>59,000</td>
<td>20%</td>
<td>11,700</td>
<td>13</td>
<td>156,000</td>
</tr>
</tbody>
</table>

Growth of NINLARO and the end of amortization of intangible assets related to VELCADE is expected to offset the VELCADE US API patent expiry

Additional expected events include NINLARO approval in newly diagnosed MM and NINLARO approval in maintenance settings not accessible with VELCADE

---

NINLARO is simple and practical and can give more time to patients and their families

**Minimum number of hospital visits required for administration/collection of multiple myeloma treatments over 18 cycles**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Visits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rd</td>
<td>18</td>
</tr>
<tr>
<td>NINLARO + Rd</td>
<td>18</td>
</tr>
<tr>
<td>Carfilzomib + Rd</td>
<td>96</td>
</tr>
</tbody>
</table>

Based on the Carfilzomib U.S. Prescribing Information.
Within our indication we know which patients NINLARO can help

- **Working Patients (15%)**
  - NINLARO offers administration profile that allows continued work

- **Logistically Challenged Patients (20%)**
  - NINLARO offers administration profile that avoids cumbersome additional clinic visits

- **Co-Morbid Patients (20-30%)**
  - NINLARO offers safety profile manageable for patients with renal and cardiovascular issues

- **High Cytogenetic Risk Patients (20-40%)**
  - NINLARO offers compelling efficacy

- **Multiple Relapse Patients (50%)**
  - NINLARO offers compelling efficacy

Compared to other agents, we have priced NINLARO so as not to increase the overall monthly cost

**U.S. PUBLISHED GROSS PRICES PER 28-DAY (USD, April 2016)**

- NINLARO: $8,670
- VELCADE: $8,597
- CARFILZOMIB: 20 to 27mg/m2 Price: $18,944
- ELOTUZUMAB: 56mg/m2 Price: $22,992
- DARATUMUMAB: After induction price: $23,400
- POMALIDOMIDE: After induction price: $13,058
- LENALIDOMIDE: $11,274

Our pricing approach is based on:

- Understanding of patient need
- Removing barriers to adoption and facilitating conversion to NINLARO
- Confidence in NINLARO’s potential as continuous therapy
NINLARO global footprint: 15 submissions/approvals to date using an ASAP/As-Wide-As-Possible strategy

As of June 2016
- Approved
- Submitted
- Submissions FY2016
- Submissions FY2017

We will commercialize using:
- U.S. infrastructure built for VELCADE
- Enhanced European infrastructure built for ADCETRIS (all planned new headcounts hired and on board promoting ADCETRIS today)
- Japan infrastructure promoting Leuprolin, VECTIBIX, VELCADE and ADCETRIS

Ixazomib Named Patient Program (NPP) has provided early access to 328 patients across 17 countries to date*

NPP is an unsolicited program that provides access for patients with an unmet need before local commercial availability

Patients Enrolled: 328
Countries: 17

*as of May, 2016
The TOURMALINE-MM1 Study is the first of a most comprehensive myeloma development program

IISR program with a global footprint explores the benefit of NINLARO to patients

- >80 active and approved studies, planned to enroll over 7,000 patients over next five years
- Including 14 countries and key research groups such as ALLIANCE, IFM, EMN, HOVON, PETHEMA, MMRF, etc
- Researching NINLARO in MM in various combinations and patient populations and in additional indications besides MM
- Publications from IISRs:
  - Kumar et al, Blood Cancer Journal
  - ASH 2015: 4 presentations (1 oral)
  - ASCO 2016: 2 oral presentations on ixazomib in non revlimid combinations
Impactful scientific presence

Published April 2016

- The New England Journal of Medicine

Congresses

- ASH 2015: 15 presentations, 4 orals, 11 posters
- ASCO 2016: 8 abstracts accepted, 2 oral presentations
- EHA 2016: 14 abstracts accepted

Manuscripts already available in:

- Blood
- The Lancet Oncology

INSIGHT MM:
Investigation of the global outcomes of multiple myeloma

- Treatment complexity in MM is increasing with more available drugs and exponentially more combinations. In this environment, data on real life outcomes across the world, currently very limited, are needed by MM community
- Target accrual – 5000 patients worldwide, in 15 countries
  - Brazil, France, Germany, UK, U.S., Belgium, Greece, Israel, Italy, Spain, China, Colombia, Mexico, Taiwan, Turkey
- Global Steering Committee (12 U.S. & 12 global representatives)
- Collaborative approach with Steering Committee Members, Investigators and the larger MM Community
  - Steering Committee to drive data analysis and publications
  - Open access to larger MM community after embargo period
  - Potential collaborations with medical societies including Japan Hematology
- Patient Focused
  - Patient member of the Steering Committee
  - Engagement with Patient Opinion Leaders
    - Optimize study experience for patient participants through the communication and return of information they consider valuable
NINLARO can deliver sustainable treatment for multiple myeloma patients

**UNIQUE**
- The 1st and only oral proteasome inhibitor

**EFFECTIVE**
- ~6 month PFS improvement in a real-world representative population
- Efficacy in high risk patients

**MANAGEABLE SAFETY**
- Low neuropathy and mostly low grade
- No cardiovascular safety signal

**SIMPLE**
- Replace twice weekly injections at hospital with one capsule, once weekly at home

**COMPETITIVELY PRICED**
- Competitive vs. newly introduced agents
- Access solutions

NINLARO is transformative for myeloma patients and for Takeda

<table>
<thead>
<tr>
<th>VELCADE Peak Global Revenues</th>
<th>$2.7B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Price versus VELCADE (per month)</td>
<td>x about parity</td>
</tr>
<tr>
<td>Length of therapy from 5 - 6 months to 12+ months</td>
<td>x 2 to 3</td>
</tr>
<tr>
<td>Relative share to current VELCADE share</td>
<td>x 0.5</td>
</tr>
<tr>
<td>Maintenance</td>
<td>+$1B</td>
</tr>
<tr>
<td>NINLARO global potential</td>
<td>&gt;$3B</td>
</tr>
</tbody>
</table>
With modest penetration across treatment settings, NINLARO has potential greater than $3B

### An Illustrative >$3 B Scenario

<table>
<thead>
<tr>
<th>Launch Year</th>
<th>R/RMM 3rd+ Line</th>
<th>R/RMM 2nd Line</th>
<th>NDMM 1st Line</th>
<th>R/R Amyloidosis</th>
<th>Post-SCT Maint</th>
<th>Non-SCT Maint</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>FY2015</td>
<td>89,000</td>
<td>85,000</td>
<td>102,000</td>
<td>13,000</td>
<td>12,400</td>
<td>47,000</td>
<td></td>
</tr>
<tr>
<td>Patient share (%)</td>
<td>15%</td>
<td>15%</td>
<td>10%</td>
<td>15%</td>
<td>10%</td>
<td>0%</td>
<td></td>
</tr>
<tr>
<td>Total eligible patients</td>
<td>13,350</td>
<td>12,750</td>
<td>10,200</td>
<td>1,950</td>
<td>1,240</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Duration (Months)</td>
<td>10</td>
<td>12</td>
<td>18</td>
<td>10</td>
<td>18</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Patient months</td>
<td>133,500</td>
<td>153,000</td>
<td>183,600</td>
<td>19,500</td>
<td>22,320</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Net Sales Range ($M) from $694 to $926**
- $2,663
- $3,551

---

**Agenda**

- Overview of Takeda Oncology
- ADCETRIS (brentuximab vedotin)
- NINLARO (ixazomib)
  - NINLARO development
  - Multiple myeloma treatment paradigm
  - NINLARO action plan

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**Summary**
Our patients are at the center of everything we do

Takeda Oncology is well positioned for global success

- Committed to our vision and to the patient community with a well-defined MAXIMIZE-PRIORITIZE-COLLABORATE strategy
  - Proven global commercial infrastructure and resources
  - Global Oncology Business Unit balances global alignment and local needs for customer focus, increased agility and commitment.

- NINLARO and ADCETRIS are two future potential blockbusters
  - **NINLARO**
    - Unique profile to help transform myeloma into a chronic disease: it is actively being developed in a comprehensive global registration lifecycle plan supported by a robust set of IISRs including cooperative group studies
    - Off to a strong start in the U.S., and by 2017 will be approved or filed across most of the globe. We are confident in the data and we believe we will succeed after re-examination in Europe
  - **ADCETRIS**
    - Already a standard of care in its indications and has shown unprecedented survival outcomes
    - Actively developed in a comprehensive lifecycle plan which, we are hopeful, will demonstrate its curative potential and substantially increase its revenues
We Aspire to Cure Cancer