Astellas Oncology Day
-Research-

July 11, 2012
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Senior Vice President,
Drug Discovery Research
Astellas Pharma Inc.
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This material includes forward-looking statements based on assumptions and beliefs in light of the information currently available to management and subject to significant risks and uncertainties. Actual financial results may differ materially depending on a number of factors including adverse economic conditions, currency exchange rate fluctuations, adverse legislative and regulatory developments, delays in new product launch, pricing and product initiatives of competitors, the inability of the company to market existing and new products effectively, interruptions in production, infringements of the company’s intellectual property rights and the adverse outcome of material litigation.

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Oncology R&D Global Strategy
Mission of Drug Discovery Research

Business Model of Astellas
Establish a competitive edge as a Global Category Leader (GCL)

Delivery of innovative medicine from our drug discovery research is the driving force for establishment of GCL status
Establish a GCL model in the five focused therapeutic areas utilizing multiple NME platforms, Oncology chosen as the third.

Current GCL areas:
- Urology
- Transplantation
- Immunology & Infectious Diseases

Future GCL candidates:
- Oncology
- Neuroscience
- DM Complications & Kidney Diseases

NME platform:
- Small molecule synthesis
- Fermentation
- Antibody
- Protein

NME: New Molecular Entity
Reinforcement of Oncology Business Base

2006  Select “oncology” as a focus therapeutic area

Promote in-house research system

Mar. 2007  Regeneron: VeloclImmune

Dec. 2007  Acquisition of Agenys

Jan. 2006  Degarelix (Prostate cancer: Japan)

Oct. 2009  Enzalutamide (Prostate cancer)

Dec. 2009  Quizartinib (AML)

Feb. 2011  Tivozanib (RCC etc.)

May/Jun. 2012  Filed NDA in US  Filed MAA in EU

Jun. 2012  Approval in Japan

Tarceva revenues (OSI)  $426M (FY2011)

Eligard sales  €127M (FY2011)

NDA: New drug application  MAA: Marketing authorization application
Astellas’ Worldwide R&D Network

EU Development Research
(Leiderdorp/the Netherlands)
Development research

Tsukuba Research Center
(Ibaraki)
Exploratory research
Optimization research
Development research

OSI Pharmaceuticals, LLC
(Farmingdale/New York)
Oncology research
(Small molecule)

Astellas Pharma Global Development
(Leiderdorp/the Netherlands)

Kashima R&D Center
(Osaka)
Development research

Urogenix, Inc.
(Durham/North Carolina)
Urology research

Astellas Pharma Global Development
(Tokyo)

Astellas Pharma Global Development
(APGD)(Northbrook/Illinois)
HQ for APGD

Perseid Therapeutics LLC
(Redwood City/California)
Immunology and transplantation research (protein drugs)

ARIA: Astellas Research Institute of America LLC
(Skokie/Illinois)
Target discovery in the immunology and CNS area

AVM: Astellas Venture Management LLC
(Menlo Park/California)
Investment and partnering in bio-ventures

Agensys, Inc.
(Santa Monica/California)
Oncology research
(Antibody drugs)
Early development
Cross-functional Management of Oncology Therapeutic Area

- **STAR (Strategy Team for Therapeutic Area Reinforcement)**
  - Create and implement individual therapeutic area (TA) strategy encompassing research, development, and marketing
  - Build and strengthen intra-TA knowledge

- **Oncology STAR**
  - An international team led by Wayne Klohs, Ph.D. (SVP, APGD)
  - Review activities of three research sites (Tsukuba, OSI, Agensys) to improve programs at each site and to promote cross-site collaboration

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**Oncology**

<table>
<thead>
<tr>
<th>Research</th>
<th>Development</th>
<th>Product Strategy</th>
<th>Marketing</th>
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<tr>
<td>Oncology STAR</td>
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<tr>
<td>Urology</td>
<td>Uro STAR</td>
<td>Immuno STAR</td>
<td>Immunology (Transplantation) &amp; Infectious Diseases</td>
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<tr>
<td>Immunology (Transplantation) &amp; Infectious Diseases</td>
<td>Tx STAR / I&amp;I STAR / ID STAR</td>
<td>Neuroscience</td>
<td>CNS STAR / Pain STAR</td>
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<tr>
<td>Neuroscience</td>
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<td>DMK STAR</td>
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<td>DM Complications &amp; Kidney Diseases</td>
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”STAR (Strategy Team for Therapeutic Area Reinforcement)”

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**Oncology STAR**

- An international team led by Wayne Klohs, Ph.D. (SVP, APGD)
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Astellas aims to establish a leading position in Precision Medicine by leveraging Translational Science. Oncology is our focus of this approach.

**Precision Medicine**

- Right drug for right patient
- Drug targeting causal molecule for disease
- Companion diagnostic to identify right patients

Precision Medicine offers highly effective therapeutics:
- Higher efficacy and fewer side effects
- Smaller-scale clinical trials targeting specific population of patients
- Pharmacoeconomical advantages by prescribing for responders only

Partnering with diagnostics company
### Precision Medicine Approach Candidates

<table>
<thead>
<tr>
<th>Project</th>
<th>Target cancer</th>
<th>Companion Diagnostics</th>
<th>Mechanism of action</th>
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</thead>
<tbody>
<tr>
<td>Enzalutamide MDV3100</td>
<td>Prostate cancer, Breast cancer</td>
<td>Development ongoing</td>
<td></td>
</tr>
<tr>
<td>Tivozanib ASP4130</td>
<td>Renal cell carcinoma, Colorectal cancer, Breast cancer</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quizartinib AC220</td>
<td>Acute myeloid leukemia</td>
<td>✔</td>
<td>✔</td>
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<tr>
<td>Degarelix (Gonax)</td>
<td>Prostate cancer</td>
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<tr>
<td>Sepantronium YM155</td>
<td>Breast cancer, Non-Hodgkin's lymphoma</td>
<td></td>
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<tr>
<td>ASP1707</td>
<td>Prostate cancer</td>
<td></td>
<td></td>
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<tr>
<td>ASP3026</td>
<td>Cancer</td>
<td>✔</td>
<td>✔</td>
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<tr>
<td>ASP9521</td>
<td>Prostate cancer</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ASP9603</td>
<td>Prostate cancer</td>
<td></td>
<td></td>
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<tr>
<td>Erlotinib (Tarceva)</td>
<td>NSCLC (1st line for patients with EGFR mutation, adjuvant), HCC, Colorectal cancer, Pediatric ependymoma</td>
<td>✔</td>
<td>✔</td>
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<tr>
<td>Linsitinib ASP7487 (OSI-906)</td>
<td>Ovarian cancer, NSCLC</td>
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<tr>
<td>OSI-027</td>
<td>Renal cell cancer</td>
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<td></td>
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<tr>
<td>AGS-1C4D4</td>
<td>Pancreatic cancer</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>AGS-16M8F/AGS-16C3F</td>
<td>Renal cancer</td>
<td>✔</td>
<td></td>
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<tr>
<td>ASG-5ME</td>
<td>Prostate cancer, Pancreatic cancer</td>
<td>✔</td>
<td></td>
</tr>
<tr>
<td>ASG-22ME</td>
<td>Solid tumors</td>
<td>✔</td>
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NSCLC: Non-small cell lung cancer, HCC: Hepatocellular carcinoma
“Multi-Track R&D” (Open Innovation) in Oncology

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**Academic institutions**
Collaborations on target discovery for precision medicine (Tsukuba)

**AVEO**
Novel target molecules and animal models (OSI)

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**Regeneron**
VeloclImmune® antibody technology (Tsukuba & Agensys)

**KEK**
Priority access to X-ray beam line purposely built for drug discovery (Tsukuba)

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**Seattle Genetics**
ADC platform Co-development of ADCs (Agensys)

**BioWa**
Potelligent® antibody technology platform (Agensys)

**ImaginAb**
Antibody-based bio-imaging (Tsukuba & Agensys)

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**Alliances with external research organizations**

**In-house research**

**POC study**

**In-house development**

Alliances in early development stages

Alliances in advanced development stages

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*POC: Proof of Concept*

Website for Astellas’ open innovation

Website to promote collaborative research with universities or public research facilities in Japan
Tsukuba Research Center

Tsukuba, Ibaraki, Japan
Tsukuba: History and Achievements

- **Pre-2005** Drug discovery by former Fujisawa & Yamanouchi
  - Focus on hormonal therapy and natural products
- **2005** Launch of Astellas
- **2006** Initiation of Astellas’ oncology drug discovery
  - Selection of Oncology as the area for the third GCL
  - Focus on precision medicine based on VISION 2015
- **2009** Enhancement of technology platform
  - Priority access to X-ray beam line at KEK
  - Establishment of Bioimaging Laboratories
- **2012** 4 compounds advanced to clinical development
  - ASP1707, ASP9521, ASP9603, ASP3026
  - Four additional clinical development candidates
Tsukuba: Focus & Core Competency

- Focus on precision medicine for gene alterations in tumor
  - Discover target molecules essential for growth or survival of tumor cells derived from gene alterations
  - Create first-in-class small-molecule inhibitors for such target molecules leveraging our drug discovery platform
  - Leverage such target molecules as predictive biomarkers to identify right patients

- Core competency
  - Proprietary “Omics” technologies and bioinformatics leveraged for discovery of novel oncogenic proteins and translational research
  - Protein structure elucidation by X-ray (priority access to a beam line in the Photon Factory, Tsukuba)
  - Proprietary Bio-imaging technology
Proprietary “Omics” Technologies Drive Astellas’ Oncology Drug Discovery

- Discovery of KIF5B-RET
  - A novel oncogenic protein for lung cancer
  - Discovered by our genomics team
  - International patent application published on February 2, 2012
  - Scientific papers by three groups published on February 12, 2012

- Award-winning proteomics research
  - The 2011 R&D Award of Japan Human Proteome Organization (JHUPO) given to Astellas’ proteomics research team
  - First winner as a private company

Nature Medicine 18, 375 (2012)
Nature Medicine 18, 382 (2012)

The 9th JHUPO conference at Niigata, July 29th 2011
Translational Research Led by Cutting-Edge Imaging Technology

● Bioimaging Research Laboratories
  ➢ The first in-house research facilities specializing imaging technologies among Japanese pharmaceutical industries
  ➢ Real-time monitoring of drug in the living body fully utilizing positron emission tomography (PET), magnetic resonance imaging (MRI) and X-ray computer tomography (CT)
  ➢ State-of-the-art facilities and proprietary key technologies

PET scanner for large animals co-developed with Hamamatsu Photonics K.K.

Best Presented Image of the Year at World Molecular Imaging Conference 2011 (San Diego, USA)
OSI Pharmaceuticals, LLC
Farmingdale, New York, USA
OSI: History and Achievements

- **1983** Founded from NIH and Cold Spring Harbor Labs
- **2004** Tarceva NSCLC 2nd line approval
- **2005** Linsitinib (OSI-906) dual IGF1R/IR inhibitor
  - Tarceva & Linsitinib (OSI-906) response linked to epithelial-mesenchymal transition (EMT) status of tumors
- **2006-2009** EMT drug discovery & translational research platform development
  - Collaboration with AVEO
- **2010** Acquired by Astellas
  - Full technology platform for low molecular drug discovery
  - In-license core tumor model, biomarker & bioinformatics technologies from AVEO
- **2012** 3 compounds under clinical development
  - Erlotinib (Tarceva), Linsitinib (OSI-906), OSI-027
  - Two additional clinical development candidates
OSI: Focus & Core Competency

- **Focus on precision medicine for refractory and resistant tumors**
  - Small molecules that inhibit survival and growth of refractory type of tumor cells (mesenchymal-type tumor cells or cancer stem cell-like cells)
  - Small molecules that inhibit resistance mechanisms against standard of care
  - Proprietary predictive biomarkers to identify right patients, such as multi-gene signature and resistance-related proteins

- **Core Competency**
  - Full technology platform for small molecule drug discovery
  - Proprietary knowledge on EMT and pathway biology
  - Unique target molecules and *in vitro/in vivo* tumor models derived from collaboration with AVEO
  - Translational research platform cultivated in Tarceva R&D
OSI Research Platform – *In vitro* Models

- **EMT platform**
  - Industry-leading knowledge in cancer EMT
  - Elucidation of EMT-related growth and survival targets/pathways
  - EMT models for discovery of novel targets and biomarkers

- **Pathway biology platform**
  - Elucidation of alternative signaling mechanism causing resistance to standard of care
  - Novel targets & combination strategies

**EMT model**

E (epithelial) type tumor cells

M (mesenchymal) type tumor cells

**Alternative signaling**

E (epithelial) type to M (mesenchymal) type

E (epithelial) type

M (mesenchymal) type

**Signaling pathways**

- MET
- RON
- IGF1R
- IR
- EGFR
- PDGFR
- AXL
- FGFR
- TGFβR
- WNT
OSI Research Platform – *In vivo* Models

- Translational research platform
  - Based on collaboration with AVEO
  - Proprietary tumor archives mimicking variety of tumor cells in a tumor tissue
  - Industry-leading knowledge in composite biomarker discovery & development

Generation of tumor archive  Testing of drug efficacy  Identification of response biomarkers

Index score

-1  0  1  2

astellas
Leading Light for Life
Agensys: History & Achievements

- 1997  Founded as Urogenesys
- 2007  In-licensing of ADC (Antibody Drug Conjugate) technology from Seattle Genetics
- 2007  Acquired by Astellas
  - An integrated unit specializing oncology antibody discovery, early development and early CMC
- 2009  Expansion of ADC agreement with Seattle Genetics
- 2010  Extension of license agreement with Regeneron on VelocImmune® antibody technology (V-mice)
  (original agreement in 2007 between Regeneron and Astellas)
- 2012  3 ADCs advanced to clinical development
  - AGS-16M8F/AGS-16C3F, ASG-5ME, ASG-22ME
  - Three additional clinical development candidates
Agensys: Focus & Core Competency

- Focus on precision medicine using naked Antibody and ADC accompanied by companion diagnostics
  - Functional human antibody targeting cancer specific antigen
  - ADC using Seattle Genetics’ technology or other technologies
  - Translational research to identify biomarkers to select right patients

- Core competency
  - An integrated unit specializing oncology antibody discovery, early clinical development and early CMC
  - Proprietary tumor panel leveraging patient-derived xenograft models
  - Fully humanized antibody technology using V-mice
  - ADC technology including new technology development
  - Rapid access to novel antibody-related technologies
Agensys: ASG-22ME, our third ADC

- An antibody drug conjugate that delivers monomethyl auristatin E (MMAE), a tubulin polymerization inhibitor, to tumor cells expressing cell surface protein, Nectin 4
- Pronounced anti-tumor effect in patient-derived xenograft models
- Co-development with Seattle Genetics ongoing

Structure of ASG-22ME

Staining of Nectin-4 in AG-B1, a patient-derived xenograft model

Efficacy of ASG-22ME in the AG-B1 model

Adopted from the 102th AACR Meeting (2011), Abstract #2832
Summary

Integrated strategy to deliver innovative drugs through Precision Medicine approach

Tsukuba

Gene Alteration

Right Drug for Right Patients

Translational Research

Drug Discovery

Target Discovery

Antibody ADC

EMT

OSI

Agensys
Our goal is to deliver innovative and reliable pharmaceutical products to cancer patients for whom no effective treatments exist.

We are implementing a globally and cross-functionally integrated strategy of Precision Medicine in our drug discovery which is carried out at three research sites fully leveraging research platform and research style of each site.

We are increasing our productivity by extension of external research network leveraging multi-track approach (open innovation) and by internal optimization of product pipeline through prioritization of R&D programs.