Acquisition of Tolero Pharmaceuticals, Inc.

December 21, 2016
Sumitomo Dainippon Pharma Co., Ltd.
Acquisition of Tolero Pharmaceuticals, Inc.

Significance of the Acquisition

✓ Acquire attractive compounds with potential to treat hematological disorders
✓ Obtain outstanding expertise in drug discovery capabilities for kinase inhibitors and other drug targets
✓ Contribute to business growth after LATUDA LOE

Reinforce pipeline in oncology area (Expand into hematologic malignancy area)

Company profile

<table>
<thead>
<tr>
<th>Name</th>
<th>Tolero Pharmaceuticals, Inc.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Established</td>
<td>June 2011</td>
</tr>
<tr>
<td>Headquarters</td>
<td>Lehi, UT, United States</td>
</tr>
<tr>
<td>Number of Employees</td>
<td>23 (As of October 31, 2016)</td>
</tr>
</tbody>
</table>

Executive management

<table>
<thead>
<tr>
<th>Name</th>
<th>Position</th>
</tr>
</thead>
<tbody>
<tr>
<td>David J. Bearss, Ph.D.</td>
<td>Chief Executive Officer</td>
</tr>
<tr>
<td>Dallin M. Anderson</td>
<td>Chairman and President</td>
</tr>
<tr>
<td>David W. Sampson</td>
<td>Chief Financial Officer</td>
</tr>
<tr>
<td>Steven D. Weitman, M.D., Ph.D.</td>
<td>Chief Medical Officer</td>
</tr>
<tr>
<td>Michael V. McCullar, Ph.D.</td>
<td>Chief Operating Officer</td>
</tr>
<tr>
<td>Steven L. Warner, Ph.D.</td>
<td>Vice President, Drug Discovery and Development</td>
</tr>
<tr>
<td>Michael A. Bernstein, M.P.H.</td>
<td>Vice President, Regulatory Affairs</td>
</tr>
</tbody>
</table>
### Development products

<table>
<thead>
<tr>
<th>Development code</th>
<th>Generic name</th>
<th>Mechanism of action</th>
<th>Target indication</th>
<th>Development location</th>
<th>Development stage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alvocidib</td>
<td>CDK9 inhibitor</td>
<td>Acute myeloid leukemia</td>
<td>U.S.</td>
<td>Phase 2 (Completed)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Acute myeloid leukemia (Biomarker)</td>
<td>U.S.</td>
<td>Phase 2</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Myelodysplastic syndromes</td>
<td>U.S.</td>
<td>Preclinical</td>
<td></td>
</tr>
<tr>
<td>TP-0903</td>
<td>TBD</td>
<td>AXL receptor tyrosine kinase inhibitor</td>
<td>Solid tumors, Hematologic malignancies</td>
<td>U.S.</td>
<td>Phase 1</td>
</tr>
<tr>
<td>TP-1287</td>
<td>TBD</td>
<td>CDK9 inhibitor</td>
<td>TBD</td>
<td>U.S.</td>
<td>Preclinical</td>
</tr>
<tr>
<td>TP-0184</td>
<td>TBD</td>
<td>ALK2 inhibitor</td>
<td>TBD</td>
<td>U.S.</td>
<td>Preclinical</td>
</tr>
</tbody>
</table>

* In addition to the above list, Tolero possesses two compounds in the preclinical stage.

### Drug discovery capabilities

- Experienced personnel who have been involved in drug discovery and clinical development targeting kinases for more than 10 years.
- Unique evaluation system that assesses disease relevance and in-silico platform to discover disease-related kinases.

Select target indication, such as hematologic malignancies, most relevant to targeted kinase.
Profile of Alvocidib

- **Mechanism of action**: Cyclin-dependent kinase 9 inhibitor (injection)
  * Cyclin-dependent kinase 9 (CDK9): A member of the cyclin-dependent kinase family, which activates transcription of cancer-related genes

- **Target indications**: Acute myeloid leukemia (AML), myelodysplastic syndrome (MDS), etc.

- **Development stage**:
  - Newly diagnosed AML (poor-risk patients): Phase 2 completed
  - Relapsed or refractory AML: Phase 2 completed
  - Relapsed or refractory AML (biomarker positive patients): Phase 2 ongoing

- **Expected Characteristics**:
  - Induce apoptosis in various types of cancer cells through suppressing MCL-1 expression by inhibiting CDK9

Apoptosis of cancer cells

- MCL-1 (anti-apoptosis)
- Myc (oncogene)

RNA Pol II

CDK9

Cyclin T1 BRD4

mRNA

Suppression of anti-apoptosis factor, MCL-1
Phase 2 Study Results of Alvocidib (efficacy)  
(Conducted by NCI)

- ACM regimen (alvocidib combination therapy) demonstrated a statistically significant improvement compared to control therapy
  - **Newly diagnosed poor-risk AML patients**
    - Complete Remission (CR) rate
      - ACM (n=109) 70%  
      - 7+3 (n=56) 46%  

- **Relapsed or refractory AML patients**
  - Complete Remission (CR) rate
    - ACM (n=36) 28%  
    - CT (n=35) 14%  
    - Sirolimus+MEC (n=20) 15%  
Phase 2 Study Results of Alvocidib (safety) (Conducted by NCI)

- ACM regimen (alvocidib combination therapy) demonstrated tolerability similar to that of the control therapy

- Newly diagnosed poor-risk AML patients

<table>
<thead>
<tr>
<th>Grade ≥3 toxicity</th>
<th>ACM (n=109)</th>
<th>7+3 (n=56)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumor lysis syndrome</td>
<td>9 (8%)</td>
<td>4 (7%)</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Myocardial dysfunction</td>
<td>8 (7%)</td>
<td>3 (5%)</td>
<td>0.75</td>
</tr>
<tr>
<td>GI toxicity</td>
<td>12 (11%)</td>
<td>5 (9%)</td>
<td>0.79</td>
</tr>
<tr>
<td>Hepatic dysfunction</td>
<td>23 (21%)</td>
<td>13 (23%)</td>
<td>0.84</td>
</tr>
<tr>
<td>Infection</td>
<td>38 (35%)</td>
<td>21 (38%)</td>
<td>0.74</td>
</tr>
<tr>
<td>Pulmonary toxicity</td>
<td>8 (7%)</td>
<td>4 (7%)</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Renal toxicity</td>
<td>3 (3%)</td>
<td>1 (2%)</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Thromboembolic events</td>
<td>3 (3%)</td>
<td>1 (2%)</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Febrile neutropenia events</td>
<td>52 (48%)</td>
<td>25 (45%)</td>
<td>0.74</td>
</tr>
</tbody>
</table>


- NCI completed 9 studies of Phase 1 and Phase 2 for AML (Total number of patients: about 600)
Clinical Development Plan of Alvocidib

➢ Development Strategy:
  • Prioritize global studies with biomarker-positive population, aiming for early approval
  • To be positioned as one of the standard regimens in induction therapy in AML
  • Indication subsequently to be expanded to maintenance therapy by oral drug (TP-1287)

➢ Target Indication:
  • Relapsed or refractory AML ⇒ Expand to newly diagnosed AML
  • Additional indication for MDS

➢ Expected Peak Sales: About 50 billion yen

(Reference) Number of AML patients in the U.S.
  • Estimated New Cases in 2016: 19,950
  • Estimated Deaths in 2016: 10,430
  • Percent Surviving 5 Years (2006～2012): 26.6 %

National Cancer Institute; SEET Stat Fact Sheets: Acute Myeloid Leukemia (AML) Created in 2016
Phase 2 Study Design of Alvocidib (Biomarker)

- Biomarker-driven Phase 2 AML Study:
  - Two-stage Phase 2 study; Open-label, randomized study to assess the clinical response to ACM compared to AM treatment in relapsed or refractory AML patients (18-65 years) with patients with high MCL-1 expression
    - MCL-1 positive patients: Method of measuring using biomarker
  - Primary endpoint: Complete remission rate
  - Secondary endpoint: Overall Survival Rate, etc.
  - Study Start Date: December 2015

Stage 1
Alvocidib + Cytarabine + Mitoxantrone (ACM)

Stage 2
Alvocidib + Cytarabine + Mitoxantrone (ACM)
Cytarabine + Mitoxantrone (CM)

NDA to the FDA in FY2018 at the earliest (utilize accelerated approval*)
* Plan to consult with the FDA

ClinicalTrials.gov, NCT02520011
## Rate of Patients with High MCL-1 Expression

<table>
<thead>
<tr>
<th>Type</th>
<th>Cancer type</th>
<th>Patients rate with high MCL-1 expression</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hematologic malignancy</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute myeloid leukemia</td>
<td>middle</td>
<td></td>
<td>Data of Tolero</td>
</tr>
<tr>
<td>Myelodysplastic syndromes</td>
<td>high</td>
<td></td>
<td>Data of Tolero</td>
</tr>
<tr>
<td>Chronic lymphocytic leukemia</td>
<td>21 %</td>
<td></td>
<td>J Clin Oncol 2014;32:5s</td>
</tr>
<tr>
<td><strong>Solid tumors</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non small cell lung cancer</td>
<td>33 %</td>
<td></td>
<td>Cell Death Differ. 2015;22:2098</td>
</tr>
<tr>
<td>Breast cancer (triple negative)</td>
<td>53 %</td>
<td></td>
<td>Cell Death Differ. 2015;22:2098</td>
</tr>
<tr>
<td>Non-Hodgkin's lymphoma</td>
<td>53 %</td>
<td></td>
<td>Blood Cancer J. 2015;5:e368</td>
</tr>
<tr>
<td>Prostate cancer</td>
<td>81 %</td>
<td></td>
<td>Am J Pathol. 1996;148:1567</td>
</tr>
</tbody>
</table>
Profile of TP-0903

- **Mechanism of action**: AXL receptor tyrosine kinase inhibitor (oral)
  *AXL receptor tyrosine kinase: a member of the receptor tyrosine kinase family, involved in cell proliferation, migration, aggregation, and anti-inflammation*

- **Target Indication**: Solid tumors and hematologic malignancies

- **Development Stage**: Phase 1 (US)

- **Expected Characteristics**:
  - Reduction of EMT
  - Synergistic effect with EGFR inhibitors
  - Suppression of metastasis and resensitization to drug resistance
  *EMT (Epithelial-Mesenchymal Transition): Process by which epithelial cells lose their cell polarity and cellular adhesion function, and gain migratory and infiltrative properties to become mesenchymal stem cells*

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AXL kinase

**Acquisition of migration and infiltration capacity**

**Mesenchymal Phenotype**

Epithelial Cell → TP-0903
Profile of TP-0184

**Mechanism of action**: ALK2 inhibitor (oral)
*ALK2 (activin receptor-like kinase-2) : a member of the bone morphogenetic protein (BMP) Receptor*

**Development Stage**: Preclinical (Treated experience to patients)

**Expected Characteristics**:
- ALK2 mutations in diffuse intrinsic pontine glioma (DIPG, one of pediatric brain tumors) are identified. TP-0184 is expected for a potential treatment to pediatric brain tumors
- Suppression of hepcidin (regulator of iron metabolism)
- Potential treatment to associated with chronic inflammation and cancer-related anemia

<Anemia associated with chronic inflammation>
- BMP6 production by inflammation
- Activation of BMPR signaling by BMP6
- Induction of hepcidin gene
- Suppression of iron metabolism by hepcidin
- Anemia caused by deficiency of iron, which is needed in hematopoietic lineage
Transaction Summary and Financial Impact

Transaction Summary

- **Form**: Implemented by way of a merger between Tolero and a special purpose company which has been established under Dainippon Sumitomo Pharma America America Holdings, Inc. (Tolero will be the surviving company)
- **Consideration**:
  - Upfront payment: US$200 million
  - Development milestones: up to US$430 million
  - Sales milestones: up to US$150 million
- **Closing (Planned)**: February 2017

Financial Impact

- **Accounting Treatment (USGAAP)**
  - The consideration will be allocated to assets and liabilities, and the difference between the net asset and total consideration will be recorded as goodwill.
  - (Contingent consideration related to each milestone is recorded in liabilities by its fair value. Change of the fair value is recognized as expense.)

- **Impact to P/L**
  - Details of purchase price allocation and amortization of intangible assets / goodwill will be announced after the transaction completed.

- **Funding of Acquisition**
  - Own fund and debt loan
R&D System of Oncology Area after Deal Closing

- Sumitomo Dainippon Pharma, Boston Biomedical and Tolero Pharmaceuticals to collaborate in drug discovery activities
- Continually create innovative products

U.S. business chart on April 2017 (planned)

Sumitomo Dainippon Pharma Co., Ltd. (Japan)

Dainippon Sumitomo Pharma America Holdings, Inc. (U.S.)

Sunovion Pharmaceuticals Inc. (U.S.)

Boston Biomedical, Inc.* (U.S.)

Tolero Pharmaceuticals, Inc. (U.S.)

DSP Cancer Institute / Oncology Clinical Development Unit (Japan)

Global Oncology Office (Japan) promote to cooperation

Global oncology

* As of April 1, 2017, Boston Biomedical, Inc. planned to merge with Boston Biomedical Pharma, Inc.
Appendix

Results of Past Clinical Studies of alvocidib (AML)

- Clinical studies of ACM with newly diagnosed non-favorable risk AML (6 studies, 256 total patients)

<table>
<thead>
<tr>
<th>Type of Clinical study</th>
<th>CR rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase 1 and pharmacokinetic study</td>
<td>50 %</td>
</tr>
<tr>
<td>Phase 1 and pharmacokinetic study</td>
<td>40 %</td>
</tr>
<tr>
<td>Phase 2 study</td>
<td>75 %</td>
</tr>
<tr>
<td>Phase 2 study</td>
<td>67 %</td>
</tr>
<tr>
<td>Phase 2 study</td>
<td>62 %</td>
</tr>
<tr>
<td>Phase 2 study</td>
<td>74 %</td>
</tr>
<tr>
<td>Phase 2 study</td>
<td>70 %</td>
</tr>
<tr>
<td>Total</td>
<td>68 %</td>
</tr>
</tbody>
</table>

- Clinical studies of ACM with relapsed or refractory ATM (4 studies, 149 total patients)

<table>
<thead>
<tr>
<th>Type of Clinical study</th>
<th>CR rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase 1 and pharmacokinetic study</td>
<td>18 %</td>
</tr>
<tr>
<td>Phase 1 and pharmacokinetic study</td>
<td>39 %</td>
</tr>
<tr>
<td>Phase 2 study</td>
<td>43 %</td>
</tr>
<tr>
<td>Phase 2 study</td>
<td>28 %</td>
</tr>
<tr>
<td>Total</td>
<td>36 %</td>
</tr>
</tbody>
</table>

AML Treatment Methods

- **Induction therapy**
- **Post-induction therapy**
  - **Consolidation therapy**
  - **Maintenance / intensification therapy**

**Number of leukemia cells**
- Cure: All leukemia cells killed
- Relapsed: Leukemia cells reproduce again
- Refractory: Repeat treatment even after relapsed

**Course of treatment**
- Remission
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Sumitomo Dainippon Pharma

Innovation today, healthier tomorrows