Japan Healthcare Market Entry—Opportunity & Challenges

Rob Claar: rob@vorpaltechnologies.com  Toshi Yoshioka: toshi@vorpaltechnologies.com
Japan is the world’s second largest single country market with roughly 10% of worldwide healthcare markets

**Pharmaceuticals ($1,174.3B)**

- North America: 38%
- Latin America: 12%
- Japan: 13%
- EU: 22%
- ROW: 16%

2016 Projected Revenue (Source: IMS Health, 2015)

**Medical Devices ($388B)**

- North America: 41%
- Europe: 31%
- ROW: 19%
- Japan: 9%

2014 Manufacturer Sales (Source: Espicom, Eucomed, 2015)
Japan’s healthcare market offers a tremendous opportunity for innovators

- Highly advanced infrastructure
- The most general hospitals of any Western country
- Universal access and high utilization of healthcare services
- Among the world’s highest adult life expectancies
- Premium pricing available for healthcare innovations
- Japan’s contribution to worldwide profit can be 2x its worldwide sales contribution
However, many companies leave their Japan strategy for later

- Japan has a lingering reputation for being a difficult market to enter
  - Slow and expensive regulatory process
  - Difficulty recruiting effective local management
  - Difficulty finding good distribution partners
- The conventional strategy for medical start-ups is to think about Japan only after focusing on Europe and the US
- Many drugs and devices are delayed in coming to Japan by 3-5 years or never make it here
The reality is that Japan’s environment is improving

• Japan’s approval process is getting faster and is now roughly equivalent to the US

• Reimbursement prices can be high

• Japan has reduced regulatory timelines and introduced a number of favorable initiatives for fast tracking and premium price acquisition

• Now, Japan should be a higher priority
  - US FDA approval process is slowing
  - European pricing is low
Due to growth in the number of reviewers and internal targeting, PMDA review time for drugs is shrinking.
Medical device PMDA review time is also shrinking

**New Device Review Time**

- New priority device avg. & target
- New standard device avg. & target

**Improved Device Review Time**

- Improved device (with clinical data) avg. & target
- Improved device (without clinical data) avg. & target
Japan has a number of fast-tracking programs which overseas companies can utilize to further reduce timelines

- **High Medical Needs Program**
  - Medical society initiates petition to the MHLW for fast approval of a product category approved in a similar overseas market

- **Orphan Designation**
  - Therapies targeting fewer than 50,000 patients
  - Benefits include faster review and longer data exclusivity

- **Highly Advanced Medical Treatment (HAMT) Program**
  - Doctors at accredited institutions apply
  - Enables early use of an unapproved therapy partly using patient self-pay

- **Regenerative Medicine Law**
  - Provides for fast conditional approval based on safety with minor efficacy data
Japan is open for business!

- Japan is a large and potentially profitable market
- The environment for market entry is improving
- New entrants need to carefully consider their strategies for:
  - Regulatory approval
  - Reimbursement pricing
  - Commercialization
What could go wrong? Let’s review some examples:

- Wrong Business Model
- Commercial Partner Selection or Timing Missteps
- Clinical Trial Management Difficulties
- Regulatory Program Management Difficulties
- Reimbursement Pricing Failure
Wrong Business Model: Direct Entry Too Early

- The Case: Company set up a direct office in Japan with all regulatory infrastructure to be their own marketing authorization holder (MAH) to launch a single, limited product line
  - Company business was unable to support the high investment level
  - Company closed business and went to a distributor model
  - Company ended up unhappy with distributor and wanted to get rights back and improve business results
- The Solution: Consider using a reliable designated marketing authorization holder (D-MAH) and maintaining a small rep office for commercial support of distributor
Wrong Business Model: Selected Commercial Partner Too Early

• The Case: Company licensed asset but became dissatisfied with the transparency of communication and business results after launch
  - Company hired a retiree to be their on-the-ground rep, but costs went up without improved results and the rep office was closed

• The Solution: Explore ways to improve or dissolve the commercial relationship
  - Build co-promotion options into the contract
  - Bring the marketing authorization back in house if possible
Partnering Misstep: Poor Pharma Licensee Execution

• The Case: Company licensed asset but became dissatisfied with the development progress
  - Company discovered later that the partner had a disincentive to develop due to conflicting portfolio issues
• The Solution: Company terminated the contract
  - Company brought the rights back in house during the development period using an in-country clinical caretaker (ICCC)
  - Development is progressing after a 3-year time loss
Partnering Misstep: Poor Device Distributor Performance

- **The Case:** Company assigned device marketing rights to a distributor but became dissatisfied with commercial performance 2 years after launch
  - Poor communication on top of suboptimal commercial performance led to growing frustration

- **The Solution:** Explore ways to improve or dissolve the partnership
  - Sometimes companies have to buy their way out of contracts or wait for a contract to expire
  - Maintaining approvals in your own name using a designated marketing authorization holder (D-MAH) enables you to make changes later
Clinical Trial Management Challenges

• The Case: Clinical trial management from afar is a huge challenge
  - Common problems include lack of transparent communication, timeline slippage and budget overruns

• The Solution: Maintain better direct control of your clinical program in Japan
  - Using a 3rd party in-country clinical caretaker (ICCC), independent from your distributor and separate from your monitoring CRO can be a good solution
  - Posting your own clinical staff to Japan can also be a very effective solution
Having your own staff and an in-country clinical caretaker enables best transparency and accountability.
Regulatory Program Management Challenges

• The Case: Company lost confidence in the ability of their distributor to achieve regulatory approval
  - Communication problems among the PMDA, company and distributor can lead to lengthy Q&A delays, additional testing requirements or a narrow indication

• The Solution: Maintain better direct control of your regulatory program in Japan
  - Using a 3rd party designated marketing authorization holder (D-MAH) puts you in control to make changes as needed
  - A good D-MAH will be your virtual team throughout the regulatory process
Reimbursement Pricing Failure

• The Case: Company failed to get premium pricing for their new category device
  - In one case, Company used their regulatory CRO to file their pricing petition. The CRO had no pricing expertise
  - In another case, Company handled their pricing submission through their Japan rep office, but they didn’t start the process until they were near regulatory approval, which was too late

• The Solution: Start your reimbursement program at the same time as your regulatory program, and before deciding on your commercial strategy
  - Using experts and starting early is the only way to succeed
Influencing reimbursement involves broad-based data development and consensus building.

**Client Data Review**
- Review client overseas cost data
- Review client pricing and reimbursement data
- Review client health economic studies
- Set strategy hypothesis

**Consensus Building**
- Assess stakeholder support/resistance
- Generate KOL understanding & support for strategy & target price
- Discuss with Economic Affairs Division
- Align with medical associations
- Facilitate timely submission of proposals from associations to Medical Economics Division

**Market Access Research**
- Identify stakeholders
- Define current treatment landscape
- Quantify & define patient segments
- Review analogous pricing cases
- Meet with KOLs & Payors
- Identify unmet needs
- Evaluate usefulness and innovation
- Collect Japanese inputs for HEM
- Set pricing strategy

**Report Development**
- Generate Japan health economic report
- Develop Japan specific cost data
- Develop reimbursement application
- Submission
- Acceptance

Best Reimbursement Price
Successful reimbursement requires starting early!

Device Reimbursement Dossier Pre-submission Workflow

<table>
<thead>
<tr>
<th>Month</th>
<th>1M</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>11</th>
<th>12</th>
<th>13</th>
<th>14</th>
<th>15</th>
<th>16</th>
<th>17</th>
</tr>
</thead>
<tbody>
<tr>
<td>Action</td>
<td></td>
<td>KOL / Academia Engagement &amp; Support Development</td>
<td></td>
<td>Dossier Preparation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Post-submission Workflow

<table>
<thead>
<tr>
<th>Month</th>
<th>18</th>
<th>19</th>
<th>20</th>
<th>21</th>
<th>22</th>
<th>23</th>
<th>24</th>
<th>M</th>
</tr>
</thead>
<tbody>
<tr>
<td>Action</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Shonin Approval</td>
</tr>
</tbody>
</table>


Dossier Preparation

- Collect Data & Evidence, Create Strategy
- Preparation for Pre-meeting
- Consult
- Preparation for Presentation
- Q&A
- Preparation of Draft Dossier & Submission
- Finalize

Preparation for Presentation

- Pre-Meeting
- Consult
- Presentation
- Q&A
- Review Draft, Q&A

Post-Meeting

- Q&A
- Review Draft, Q&A
- Finalize

Preparation of Draft Dossier & Submission

- Pre-Meeting
- Consult
- Presentation
- Q&A
- Review Draft, Q&A
- Finalize

Collect Data & Evidence, Create Strategy

- Preparation for Pre-meeting
- Consult
- Preparation for Presentation
- Q&A
- Preparation of Draft Dossier & Submission
- Finalize

KOL / Academia Engagement & Support Development

- Device Reimbursement Dossier Pre-submission Workflow
- Post-submission Workflow

Shonin Submission

Shonin Approval

Dossier submission

Approval

Unofficial Announcement Agree or Disagree

Price Plan Examination

Agreement

Confirmation

Keizai-ka
MHLW Economic Affairs

Iryo-ka
MHLW Economics Division

MEO
Medical Equipment Organization

Chuikyo
Central Social Insurance Medical Council

January 21, 2016
Conclusion

• Japan is a great opportunity
• Many overseas companies decide to avoid Japan and do not capitalize on the opportunity
• Others encounter difficulties and disappointments
• New ways are needed to get in to Japan with gradual investment, flexibility and tangible results
Vorpal offers integrated services for success in Japan on your own terms

Innovation Research & Development
- Joint Development with Clinicians
- Intellectual Property Strategy
- Technology Transfer
- Biomedical Design
- Prototype Development
- Usability Confirmation
- Regulatory Compliance Confirmation

Clinical Development
- Clinical Trial Design
- In-Country Clinical Caretaker (ICCC) Services
- KOL Engagement & Site Selection
- Clinical Operations & CRO Management
- GCP Compliance Assessments
- Post-Marketing Surveillance (PMS)
- Clinical Research Support

Regulatory Development
- Regulatory Strategy Formulation
- PMDA & MHLW Engagement
- KOL & Medical Society Engagement
- High Medical Needs & HBD Program Listing
- Orphan Drug / Device Designation
- Regulatory File Submission
- Q&A to Approval

Opportunity Validation
- Patient Population Definition
- KOL Identification & Influence Mapping
- Treatment Landscape Clarification
- Product Evaluation
- Pricing Assessment
- Opportunity Sizing

Market Access
- Reimbursement Strategy Formulation
- Medical Society Engagement
- Patient Group Engagement
- Treatment Guideline Influencing
- MHLW Engagement
- HTA & Health Economic Analysis
- Reimbursement Application Submission
- Q&A to Acceptance

Quality & Operations
- QMS Development & Maintenance
- Designated Marketing Authorization Holder (D-MAH) Services
- Importation & Trade Finance
- Labeling & Repackaging Services
- Warehousing & Logistics Services
- Vigilance Management & Reporting

Commercial Development
- Marketing & Business Strategy Development
- KOL & Rising KOL Engagement
- Advisory Board Establishment
- Congress Strategy & Implementation
- Clinical Education Program Development
- Clinical Research & Publication Support
- Distribution Partner Selection & Engagement
- Business Incubation & Acceleration
- Sales & Distribution

January 21, 2016
About Vorpal - Who We Are
Board of Directors

• André Ulmann, M.D., Ph.D., Chairman
  - André Ulmann is internationally recognized as an expert in reproductive health. He has been instrumental in the conception and development of a number of highly successful pharmaceutical products and companies, including HRA Pharma where he is currently Chairman

• Robert E. Claar, President & CEO
  - Rob Claar has over 20 years experience in global healthcare innovation management, opportunity assessment, strategy development and implementation. He is passionate about developing solutions alongside inventors, authorities and companies to enable expanded access to healthcare innovations worldwide. Rob is the founder of Junicon, a global healthcare consultancy

• Mark T. Campbell, Director & CFO
  - Mark is a venture capital & private equity professional with extensive skills in healthcare related to transfer pricing and U.S. and international tax. For several years, Mark was named by International Tax Review as one of the "World’s Leading Tax Advisors" and one of the "World’s Leading Transfer Pricing Advisors". He has authored or co-authored several books and articles on international taxation. Mark has fourteen years of business operations experience in Japan
Vorpal Management

• **Toshiharu Yoshioka, General Manager of Regulatory Research Development & Quality Management**
  - Toshi’s regulatory affairs career spans over 20 years and exceeds 100 approvals with companies including Lotte, Sterling Winthrop, Johnson & Johnson, Medtronic, B. Braun Aesculap, Mölnlycke and Japan MDM. Areas of specialty include:
    - Medical Devices (Class I-IV): Orthopaedics, Neurosurgery, General Surgery, Wound Care, Cardiac Surgery, Interventional Cardiology, Absorbable Sutures
    - Pharmaceuticals: Cardiology, Endocrinology, OB/GYN, Diagnostic Imaging Agents, High Level Disinfectants

• **Benjamin D. Pratt, General Manager of Innovation Commercialization**
  - Ben has expertise in strategy development, marketing and operations, and has commercialized and marketed best-in-class medical devices for over a decade with Edwards Lifesciences in the US and Japan
  - Before joining Vorpal, Ben was Director of Strategic Planning & Operations for Edwards’ Transcatheter Heart Valve business in Japan, overseeing the clinical education program and team development through successful product launch
  - His forte and personal mission is creating new businesses in Japan for the betterment of patient care
The Vorpal Vision

- Vorpal unlocks the Japan opportunity for healthcare innovators through expert regulatory, clinical and commercial solutions
- There is a tremendous opportunity for innovative companies that can mobilize local knowledge, expertise and networks
- However, many companies have less than satisfactory results with Japanese commercialization partners
- Japanese partnering missteps will reduce the innovator’s equity value
- Innovators that control their own destiny in Japan will command premium equity valuations
- Vorpal offers a transparent and reliable process for entering Japan
- We are confident that our end-to-end solutions offer your best opportunity for success in the world’s second largest healthcare market
Vorpal Strengths

- Our medical device regulatory team has a collective century of experience with a track record of 100+ approvals including first-in-class and High Medical Needs products in therapeutic areas including Orthopedics, Neurosurgery, General Surgery, Thoracic Surgery, Wound Care, Interventional Cardiology & Interventional Neuroradiology

- Our pharma regulatory team has a collective century of experience with a track record of 25+ new drug approvals in therapeutic areas including Cancer, Immunology, CNS, Cardiology, Endocrinology, GI, Respiratory Disease, OB/GYN & Infectious Disease

- Our expertise in regulatory and reimbursement strategy gives novel drug and device innovators their best opportunity for optimal reimbursement acceptance

- Our commercial team enables innovative companies to stage their Japan entry and right-size their investment every step of the way while maintaining control of marketing authorizations

- Vorpal’s Advisory Board Members are prominent veterans in healthcare innovation and commercialization, opening new doors for Vorpal clients

- Vorpal offers expertise, creativity and a sensitive yet tenacious approach to building your business in Japan
Thank you very much!

Rob Claar: rob@vorpaltechnologies.com   Toshi Yoshioka: toshi@vorpaltechnologies.com