Market Access Evidence Roadmaps: Maximizing Asset Value Through Evidence Generation Planning
Presenters

Anne Heyes, MBA
Vice President, Head Market Access and Outcomes Strategy, Europe

Kati Copley-Merriman, MBA
Vice President, Market Access and Outcomes Strategy

Sorrel Wolowacz, PHD
Head, European Health Economics

Alan Hutton, Director, Business Development
Learning Objectives

When should you develop a Roadmap and why?

What is an evidence planning Roadmap?

What can the Roadmap do for your asset?
## Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
<th>Slide Number(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>EMA</td>
<td>European Medicines Agency</td>
<td>6, 23</td>
</tr>
<tr>
<td>FDA</td>
<td>Food and Drug Administration</td>
<td>6, 23</td>
</tr>
<tr>
<td>HTA</td>
<td>Health Technology Assessment</td>
<td>6, 7, 13, 19, 23, 28, 29</td>
</tr>
<tr>
<td>QUALY</td>
<td>quality-adjusted life-years</td>
<td>8, 25, 27</td>
</tr>
<tr>
<td>EQ-5D</td>
<td>EuroQOL-5 Dimension Questionnaire</td>
<td>8, 14</td>
</tr>
<tr>
<td>HEOR</td>
<td>health economics and outcomes research</td>
<td>10, 18</td>
</tr>
<tr>
<td>UK</td>
<td>United Kingdom</td>
<td>14, 19</td>
</tr>
<tr>
<td>P</td>
<td>payer</td>
<td>14</td>
</tr>
<tr>
<td>S</td>
<td>societal</td>
<td>14</td>
</tr>
<tr>
<td>CUA</td>
<td>cost-utility analysis</td>
<td>14</td>
</tr>
<tr>
<td>CEA</td>
<td>cost-effectiveness analysis</td>
<td>14</td>
</tr>
<tr>
<td>SF-36</td>
<td>36-Item Short Form Survey</td>
<td>14</td>
</tr>
<tr>
<td>US</td>
<td>United States</td>
<td>19</td>
</tr>
<tr>
<td>SLR</td>
<td>systematic literature review</td>
<td>20</td>
</tr>
<tr>
<td>Tx</td>
<td>treatment</td>
<td>20</td>
</tr>
<tr>
<td>TPP</td>
<td>total product price</td>
<td>24</td>
</tr>
<tr>
<td>CE</td>
<td>cost-effectiveness</td>
<td>25, 27, 28</td>
</tr>
<tr>
<td>HRQoL</td>
<td>health-related quality of life</td>
<td>26</td>
</tr>
</tbody>
</table>
Introduction to why you Need a Roadmap

Anne Heyes
Vice President,
Head Market Access and Outcomes Strategy, Europe
Journey to Market Access Success

- EMA submission
- FDA submission
- Regulatory approval
- HTA submissions
- Reimbursement
Maximising Value in the Market Place: Considerations for Reimbursement

CLINICAL EFFECTIVENESS

1. Effectiveness
2. Safety
3. Quality of life
4. Compelling evidence of benefit vs. relevant comparators

VALUE FOR MONEY

2. Cost-effectiveness vs. comparators
3. Value-based price

AFFORDABILITY

3. Budget impact
4. Size of patient population / budget impact can influence which HTA process applies
Quality-Adjusted Life-Years

Single, payer-relevant measure of patient health benefit, capturing differences in survival and quality of life, in all health conditions.

A QALY is the product of the length of time spent in a particular health state and the utility weight (1 = full health; 0 = dead).

Utility can be measured in a variety of ways, the most common is the EQ-5D instrument.
What is an Evidence Planning Roadmap?

Kati Copley-Merriman
Vice President, Market Access and Outcomes Strategy
HEOR Roadmap Timing

• For products that might be approved based on phase 2 data, the HEOR Roadmap should start prior to beginning phase 2 trials.

• Ideally for all other products, the HEOR Roadmap would begin prior to phase 3, in time to influence the study design.
Market Access Evidence Plan Creation Process Overview

- Conduct a literature review to understand the disease burden, unmet need, and disease data gaps (e.g., utility data)
- **Product SWOT** (Strengths / Weaknesses / Opportunities / Threats)
- Evaluate key country HTA requirements
- Identify and review evidence base for key comparators (current treatments)
- **Conduct a literature review** to understand the disease burden, unmet need, and disease data gaps (e.g., utility data)
- Create value story
Market Access Evidence Plan Creation Process Overview

1. Review existing data to support value story
2. Conduct payer research to assess perceptions of unmet need, payer evidence needs, and price expectations
3. Conduct a gap analysis for evidence to support the value story
4. Create market access evidence plan

Review existing data to support value story
Elements of HTA / Pricing & Reimbursement Submission (Reflecting the Value Story)

- Targeted & Systematic Reviews
  - Burden of illness, clinical literature, utility, and economic literature

- Network Meta-Analysis
  - Bayesian & frequentist methods

- Cost-Effectiveness Analysis

- Budget-Impact Analysis

- Utility Research
  - and resource use / cost estimates

- Key Stakeholder Validation

HTA Submission Strategy & Dossier Development
### Country-Specific HTA Requirements in Europe

<table>
<thead>
<tr>
<th>Assessment Criteria / Tools</th>
<th>Germany</th>
<th>UK</th>
<th>France</th>
<th>Italy</th>
<th>Spain</th>
<th>Netherlands</th>
<th>Nordic Countries¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assessment of therapeutic benefit</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Assessment of patient benefit</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Perspective</td>
<td>P</td>
<td>P</td>
<td>P</td>
<td>S/P</td>
<td>S/P</td>
<td>S</td>
<td>S</td>
</tr>
<tr>
<td>Cost-effectiveness model</td>
<td>—</td>
<td>CUA</td>
<td>CUA</td>
<td>CEA, CUA</td>
<td>CEA, CUA</td>
<td>CEA, CUA</td>
<td>CEA, CUA</td>
</tr>
<tr>
<td>Budget-impact model</td>
<td>Cost calculation</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>Cost calculation</td>
</tr>
<tr>
<td>Therapeutic alternatives</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>—</td>
<td>—</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Systematic literature reviews</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Quality-of-life evaluation</td>
<td>—</td>
<td>EQ-5D</td>
<td>EQ-5D</td>
<td>EQ-5D</td>
<td>EQ-5D / SF-36</td>
<td>EQ-5D</td>
<td>EQ-5D</td>
</tr>
<tr>
<td>Dossier required</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Reference pricing required in dossier</td>
<td>Supportive information</td>
<td>No</td>
<td>Main criterion</td>
<td>Supportive information</td>
<td>Supportive information</td>
<td>Main criterion</td>
<td>Sweden: no Denmark, Finland, Norway: yes</td>
</tr>
<tr>
<td>Time from submission to reimbursement</td>
<td>0 (12-month free pricing)</td>
<td>180-250 days</td>
<td>180-250 days</td>
<td>180-250 days</td>
<td>180-400 days</td>
<td>90-400 days</td>
<td>180 days</td>
</tr>
</tbody>
</table>

¹ The Nordic countries include Denmark, Finland, Norway, and Sweden.
SWOT Analysis: Example

**Strengths**
- PRODUCT X is durable and has relatively quick onset and high response rate.
- PRODUCT X has a good safety profile similar to placebo.
- Phase 3 randomized trial with long-term follow-up.

**Weaknesses**
- PRODUCT X is rare and not well understood by payers.
- Epidemiology is not well studied and is affected by misdiagnosis.
- Natural history is not well understood.
- Economic burden had been studied in a few studies, but data are limited.

**Opportunities**
- There is high unmet need.
- PRODUCT X will be the first approved treatment.
- Current treatment is a complex risky procedure.

**Threats**
- PRODUCT X competitor has started phase 3 trials.
- PRODUCT X competitor is a once-daily oral tablet; PRODUCT X is intravenous administration.
- European markets have tougher reimbursement environments.
### Value Messages: Example

#### Efficacy Messages
- The percentage of responders is higher after 2 weeks, 3 months, and 6 months of treatment with PRODUCT X, compared with placebo.
- Total body fat mass in overweight / obese patients is reduced after 3 and 6 months of treatment with PRODUCT X, compared with placebo, and is maintained for at least X months.

#### Economic Value Messages
- PRODUCT X is cost-effective compared with placebo (no treatment).
- PRODUCT X has a low budget impact because the disease is rare.

#### Safety Messages
- Treatment with PRODUCT X over 12 months shows no clinically significant findings in adverse events, compared with placebo.
- Treatment with PRODUCT X is well tolerated, and adverse events are mild.

#### HRQOL Improvement Messages
- Clinically meaningful improvement in quality of life has been shown after x weeks of treatment with PRODUCT X vs. a worsening with placebo.
- Time to deterioration is longer with PRODUCT X vs. placebo.
• Some epidemiology data are available but vary by study, possibly due to misdiagnosis; size of the population in different regions is uncertain

• Clinical burden is well established in the literature, but natural history and economic burden has not been well studied over time

• Longitudinal phase 2 / 3 trial design is robust, with several endpoints for reduction of primary disease and comorbidities, patient quality of life, and safety; utility values for economic models is unavailable

• Competitive trials designs are similar but have additional endpoints
Objectives of Payer / Stakeholder Research

• In parallel to the outputs of the HEOR evidence plan for Product X, assess evidence-generation tactics and price expectations for key markets

• Stakeholder research can address key topics:
  – Market access considerations for the disease in target markets
  – Perceptions of disease burden and unmet need in target disease
  – Importance of clinical trial design endpoints for Product X
  – Pricing expectations based on target product profile
  – Evidence weaknesses and information gaps
## HEOR Plan Recommended Projects: Example

<table>
<thead>
<tr>
<th>Statements / Evidence Needed</th>
<th>Data Source</th>
<th>Country</th>
<th>Start Date / Study Length / Price Estimate</th>
<th>Strategy Objective Addressed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early HTA advice</td>
<td>Letter of intent 3 months prior to building economic models</td>
<td>Europe</td>
<td>Q3, 2020 6-8 months $XX,XXX</td>
<td>Gain strategic input from country HTAs</td>
</tr>
<tr>
<td>Real-world burden of disease and treatment patterns</td>
<td>Database study or disease registry / partner with disease associations</td>
<td>US, UK, and others</td>
<td>Q3, 2020 $XX,XXX</td>
<td>Understand the burden of disease and current treatments</td>
</tr>
<tr>
<td>Early economic model</td>
<td>Economic model</td>
<td>US</td>
<td>Q4, 2020 $XX,XXX</td>
<td>Understand model data gaps and pricing implications</td>
</tr>
<tr>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
</tbody>
</table>
### Timeline of Activities for the HEOR Plan: Example

#### Phase 2b

<table>
<thead>
<tr>
<th>Year 1</th>
<th>Year 2</th>
<th>Year 3</th>
<th>Year 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q3</td>
<td>Q1</td>
<td>Q1</td>
<td>Q1</td>
</tr>
<tr>
<td>Q4</td>
<td>Q2</td>
<td>Q2</td>
<td>Q2</td>
</tr>
<tr>
<td></td>
<td>Q3</td>
<td>Q3</td>
<td>Q3</td>
</tr>
<tr>
<td></td>
<td>Q4</td>
<td>Q4</td>
<td>Q4</td>
</tr>
</tbody>
</table>

- **Burden of illness literature review**
- **Early economic model**

#### Phase 3

<table>
<thead>
<tr>
<th></th>
<th>Year 3</th>
<th></th>
<th>Year 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q1</td>
<td>Q1</td>
<td></td>
<td>Q1</td>
</tr>
<tr>
<td>Q2</td>
<td>Q2</td>
<td></td>
<td>Q2</td>
</tr>
<tr>
<td>Q3</td>
<td>Q3</td>
<td></td>
<td>Q3</td>
</tr>
<tr>
<td>Q4</td>
<td>Q4</td>
<td></td>
<td>Q4</td>
</tr>
</tbody>
</table>

- **SLRs for clinical evidence and economic models**
- **Economic models (BIM/CEM)**
- **Global value dossier**
- **AMCP Dossier**

#### Launch

- **RWD Strategy**
- **Value Message Development**
- **Reimbursement submissions**
- **Real-world disease burden and Tx patterns**
- **ICER Strategy**
- **Preference Study (Patient/Caregiver/Physician)**
- **Publications and presentations**

---

Example for illustrative purposes only. Actual HEOR Plan will vary by asset and development program.
Market Access Pitfalls and the Value of a Roadmap.

Sorrel Wolowacz
Head, European Health Economics
How can a Market Access Evidence Plan Support the Value of a Pipeline Product?

“If you fail to plan, you are planning to fail!”

BENJAMIN FRANKLIN
The Value of an Evidence Roadmap

- **Phase 2**
  - FDA submission
  - HTA submissions
  - Reimbursement
  - Regulatory approval

- **Phase 3**
  - EMA submission
  - HTA submissions
  - Reimbursement

- **Assets**
  - Asset acquisition negotiations
  - Net present valuation for shareholder value
  - Venture capital investor valuations
The Value of an Evidence Roadmap

- Asset acquisition negotiations
- Net present valuation for shareholder value
- Venture capital investor valuations

TPP target markets

Price expectation
The Value of an Evidence Roadmap

Phase 3

Target indication

- Added value (QALYs), value-based price, and market size differ by, e.g. indication, line of treatment, precise patient subgroup
- Pitfall example: phase 3 trial population currently treated with generic → Price restriction as very little data in target positioning (after generic) undermined credibility of clinical evidence
- With a Roadmap, will have identified optimum indication / positioning, and informed price expectation (from early CE model)

Highest added patient benefit = best price & reimbursement
The Value of an Evidence Roadmap

**Phase 2**

- Control treatment and study endpoints
  - Convincing evidence of comparative effectiveness (direct or indirect) vs. all relevant comparators and HRQoL benefit
  - Pitfall examples: single-arm trial, endpoints misaligned → Cost more in additional studies to create “synthetic” control arm; price restriction due to uncertainty in comparative effectiveness
  - With a Roadmap, will understand comparator trials, have indirect comparisons planned and HRQoL measurement optimized

**Phase 3**

- Clinical benefit vs. payer-relevant comparators
The Value of an Evidence Roadmap

Utility measurement

- Opportunity to collect utility estimates for the CE model
- Pitfall example: trial didn't provide data for model health states → Cost more money for additional utility study; price restriction as payer-relevant value (QALY gain) was uncertain
- With a Roadmap, will have optimized trial and other studies to provide utility estimates required

Poor utility data can undermine price
The Value of an Evidence Roadmap

HTA research

• Systematic literature review, network meta-analysis, CE model, budget-impact model
• Pitfall example: utility and natural history data gap recognized too late
• With a Roadmap, will have research in good time for submissions
Key Take-Home Messages

What is a market access evidence Roadmap?

A plan for generation of **payer-relevant** evidence to support HTA, pricing, and reimbursement
Key Take-Home Messages

How can a market access evidence plan support the value of a pipeline product?

- Ensures **payer-relevant** evidence is generated demonstrating clinical effectiveness, quality-of-life benefit, cost-effectiveness, and budget impact
- Develops evidence package in parallel with and throughout product development process, so it is available to **support acquisitions, licensing, and/or asset valuations**
- Identifies opportunities for **highest value-added patient benefit** = best price & reimbursement opportunity
Key Take-Home Messages

When should a Roadmap be developed?

- Ideally start during phase 2 trials
- Still useful in early phase 3
- Update over time to adapt for any changes in the product profile / competitive landscape
Anne Heyes  
Vice President, Head Market Access and Outcomes Strategy, Europe  
Email: aheyes@rti.org

Kati Copley-Merriman  
Vice President, Market Access and Outcomes Strategy  
Email: kcmerriman@rti.org

Sorrel Wolowacz  
Head, European Health Economics  
Email: swolowacz@rti.org

Alan Hutton  
Director, Business Development  
Email: ahutton@rti.org