IS IT TIME FOR A NEW DRUG DEVELOPMENT PARADIGM?

PREPARING THE PHARMACEUTICAL INDUSTRY FOR 2020

19th Annual Meeting of the International Society for Pharmacoeconomics and Outcomes Research
Montreal, Canada
Penny Mohr, Senior Vice President, Program Development
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OBJECTIVES

- Produce a vision of what the demand for and capacity to produce CER/RE will look like in the United States and Europe by 2020

- Develop a New Drug Development Paradigm (NDDP) that takes into account the need for efficient strategies for evidence development
PRIMARY QUESTIONS ADDRESSED

- What type of CER/RE will drug companies need to invest in by 2020, at what stage of drug development?
- What type of CER/RE will external entities (e.g., federal, HTA bodies, health plans) be investing in or expecting by 2020 that will impact the business model for drug development?
- What are the key drivers for this change, and how likely are each of the three alternative scenarios of change?
- What type of NDDP can enable drug companies to efficiently meet the evidentiary requirements of these scenarios?

THE OLD STYLE PARADIGM

2030 The future of Medicine - Avoiding a Medical Meltdown
Dr. Richard Barker, MA, FRSM

Current medicines development path
- 8 - 10 years
- First in Man
- Proof of Concept
- Regulatory Submission
- Approval
- Pricing Launch

Key Characteristics of current model
- Inflexible processes and methods
- Expensive, increasing data demands
- Lack of early alignment between key parties
- Segmented input & decision making
- Access needs not designed in
- Patient perspective not fully addressed

External activities
Sponsor activities
FUTURE SCENARIOS APPROACH

- Parallel US and EU Processes
  - Initial Key Factor Generation: Literature review, internal expert review, and refinement
  - Investigate Factors and Future Outcomes: Key Informant Interviews
  - Rank Factors and Vote on Possible Outcomes: Expert panel questionnaire
  - Build and Refine Scenarios: In-person meeting; voting during and after meeting

Interface with coordinating project teams for characterizing US and EU current drug development practices, current and future payer requirements

**Modified Delphi technique**

MOVEMENT TOWARD INTEGRATION OF HEALTH SYSTEM IN THE US

- Most Likely Scenario
  - Increasing data systems ability to produce quality measures
  - ACA and private payers driving investment in ACOs
  - Risk-based payments move towards capitation
  - Federal investments to improve research infrastructure/methods/processes
  - Changing locus of decision-making providing opportunities for new partnerships

- Most Conducive To CER Scenario
  - Increasing willingness and ability to invest in EHRs and desire to reduce system costs
MOVEMENT TOWARD HARMONIZATION IN EU

Most Likely Scenario

Coordination across HTA bodies in P-L studies, often linked to CED, P4P schemes

Greater HTA and EMA coordination pre-launch

Post-authorisation efficacy studies

PAES implemented

Al applied to a variety of drugs
Joint HTA and EMA coordination for pre-and post-launch

Collaborations across large registries
Full use of EHRs
Good progress in methods
Public-private partnerships have a major role

Most Conducive To RE Scenario

COMMONALITIES BETWEEN US AND EU

MOST LIKELY SCENARIOS FOR CER AND RE

• Payers/HTA bodies will still require RCTs for initial market access
• Payers/HTA bodies will impose greater demands on CER/RE for market access, specifically:
  – How does this work in my population?
  – How does this compare with existing alternatives?
• Payers/HTA bodies will impose greater demands on CER/RE for preferential tier placement/favorable pricing
  – How does this affect resource use and cost?
• Data rich environment in the US, but conducive for conduct of RCTs in only select systems, largely for observational research
• Progress on the development of patient/disease registries and on cross country registries in the EU
### DIFFERENCES BETWEEN US AND EU MOST LIKELY SCENARIOS FOR CER AND RE

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<th>US</th>
<th>EU</th>
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<tr>
<td>• Focus on increased capacity to conduct CER</td>
<td>• Focus on differences between national HTA bodies’ requirements</td>
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<td>• FDA looks favourably on active comparators, but may still require placebo control (when endpoints are subjective and it is ethical)</td>
<td>• EMA and HTA bodies demanding active comparators</td>
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<td>• Payers/providers will do some of their own research</td>
<td>• Requirements to develop RWE is pushed to industry</td>
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<td>• Focus on patient-centered research prominent</td>
<td>• Will EMA allow observational data for post-authorization efficacy (PAES) studies?</td>
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<td>• Will US observational data on resource use be useful in the EU market?</td>
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### CHARACTERISTICS OF THE “MOST LIKELY” SCENARIO

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<tr>
<td>• Patients in integrated delivery systems have doubled</td>
<td>• PAES implemented by EMA, putting regulatory post-launch requirements ahead of HTA body requests</td>
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<td>• EHR interoperability between a few large players; EHR quality for most systems not reliable for CER</td>
<td>• Some harmonization of evidence standards for reimbursement between individual member states; however, individual decisions still made nationally or regionally</td>
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<td>• Data mining produces few new insights</td>
<td>• Some alignment of pre-launch study requirements by HTA bodies and regulators</td>
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<td>• Growing high-quality infrastructure for distributed data networks</td>
<td>• Increased use of disease registries in some countries; some limited development of non-experimental methods and limited increase in their acceptability to payers</td>
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<td>• Highly active patient groups participating in patient-powered networks</td>
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PRODUCT ARCHETYPE # 1
BREAKTHROUGH DRUG

A new drug that is a breakthrough for treating patients who suffer from a common disease, but has been studied only in a small population that has a specific predictive biomarker identified by a companion diagnostic test.

Example:
Lipid-lowering drug studied in patients with familial hyperlipidemia
Ultimate potential use would be statin users in the general population

NEW DRUG DEVELOPMENT PARADIGM FOR 2020:
MOST LIKELY SCENARIO FOR CER/RE

Archetype 1: Breakthrough drug studied only in small population with biomarker

New Seamless Framework

Patient/Payer Engagement

Exploratory Research

Confirmatory Trials

Pivotal Trials

Sequential Cohort Studies

Key Features
- Patient/payer engagement early to ensure outcomes reflect those of importance to them
- Smaller targeted trial brings drug to market earlier
- Bayesian/adaptive designs to improve efficiency of trial development throughout the life cycle with clear decision points after each round of evidence development
- Second trial in broader population is large simple trial with focused question
- EMA requirements for post-authorization efficacy studies can be built into the second trial
- Sequential cohort studies initially used to track off-label use, data used to design second trial
### QUESTIONS FOR ALL PANELISTS

- The IOM has commented that “Although there is a great deal of interest and activity surrounding [CER]..., the aggregate research capacity is very thin, and the products fall substantially short of the need.” We paint a view of the future where there is substantial progress towards a learning healthcare system by 2020 that could facilitate this research.

  - Do you believe this progress will occur by 2020? Why or why not?

### QUESTIONS FOR INDUSTRY PERSPECTIVE

- Given the high focus on meeting the needs of regulators and the fact that in the US most payers cover drugs that are FDA approved and have little control over off-label use, do you think the incentives are changing enough to call for a radical new drug development paradigm? Has the clinical development side of industry bought into this belief?

- Does this view of the world represent a paradigmatic shift in drug development, or just an incremental shift beyond what companies are already doing?

- What is industry’s role in helping to ensure this vision of the future is realized?

- Is industry likely to invest in LSTs that take advantage of this infrastructure if it had made the progress we depict? Why or why not?

- How does your thinking about the way events are unfolding in the EU versus the US change the way you would approach evidence development in 2020?
QUESTIONS FOR PAYER PERSPECTIVE

• What are the most important changes, if any, in the payer community that will be changing incentives for industry to embrace a new drug development paradigm in the future?

• What is the role of the payer community in making the vision of the learning healthcare system a reality in the future?

• One aspect of this vision is there will be greater incentives for the data-rich payer or health system community to embrace partnerships with industry to track on-label use of targeted drugs, and to provide access to data to help them design trials that would better meet our needs for coverage, improved formulary placement, or expanded indications. Is that likely to happen?

• Would payers likely help industry fund or design an LST to better meet their needs if this could be completed in a timely and efficient manner with an improved research infrastructure?