Growth Strategy: Evidence Based Reimbursement & Commercialization Strategies for Innovators & Investors

January 25, 2011

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Panelists

- **Anita Chawla**, Ph.D., Vice President, *Analysis Group*
- **Antoun Nabhan**, J.D., Senior Director, Corporate Development, *Onyx Pharmaceuticals*
- **Antoinette Konski**, Partner and member, Chemical, Biotechnology & Pharmaceutical Practice, *Foley & Lardner LLP*
- **Judy Waltz**, Partner and Co-Chair, Life Sciences Industry Team, *Foley & Lardner LLP*

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Road Map

- Legal overview of recent developments in product coverage (Judy)
- Proper planning for product coverage and reimbursement (Anita)
- Working towards payer expectations (Antoun)

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Comparative Effectiveness

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2010 Affordable Care Act (ACA)

- Patient Protection and Affordability Act and Health Care and Education Reconciliation Act (Pub.L. 111-148, a/k/a H.R. 3590, and Pub. L. 111-152, a/k/a H.R. 4872) – finalized by President Obama's signatures on March 23 and 30, 2010
- Consolidated language compiled by the House Legislative Counsel now available at http://www.premierinc.com/about/advocacy/issues/10/healthcarereform/PPACA-CONSOLIDATED.pdf

Foley.com/HCReform (resource site)

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"Comparative Effectiveness Research is out; Patient Centered Outcomes Research is in."

As congressional debate on creating a public/private entity to conduct such research was heating up, Senate Finance Committee Chairman Max Baucus (D-Mt.) Baucus decided that the term "comparative effectiveness research" was becoming too much of a lightning rod for controversy and changed the term in health care reform legislation to "patient-centered outcomes research."

Gregory Twachtman, The RPM Report, "*What's In a Name? The Semantics of CER*" (September 10, 2010)

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Comparative Effectiveness Research

- Comparative effectiveness research is designed to inform health-care decisions by providing evidence on the effectiveness, benefits, and harms of different treatment options. The evidence is generated from research studies that compare drugs, medical devices, tests, surgeries, or ways to deliver health care.

- There are two ways that this evidence is found:
  - Researchers look at all of the available evidence about the benefits and harms of each choice for different groups of people from **existing** clinical trials, clinical studies, and other research. These are called research reviews, because they are systematic reviews of existing evidence.
  - Researchers conduct studies that generate **new** evidence of effectiveness or comparative effectiveness of a test, treatment, procedure, or health-care service.

http://effectivehealthcare.ahrq.gov/index.cfm/what-is-comparative-effectiveness-research1/

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Comparative Effectiveness Research

- Seven steps are involved in conducting this research and in ensuring continued development of the research infrastructure to sustain and advance these efforts:
  - Identify new and emerging clinical interventions.
  - Review and synthesize current medical research.
  - Identify gaps between existing medical research and the needs of clinical practice.
  - Promote and generate new scientific evidence and analytic tools.
  - Train and develop clinical researchers.
  - Translate and disseminate research findings to diverse stakeholders.
  - Reach out to stakeholders via a citizens forum.

AHRQ website

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Patient-Centered Outcomes Research Institute (PCORI)

- ACA Section 6301,
- Nonprofit corporation
- Will identify national priorities for research,
- Will assist in the analysis of health outcomes and the clinical effectiveness, risks, and benefits of more medical treatments such as therapies, diagnostic tools, and pharmaceuticals (e.g., drugs and biologics).
- The research funded must take into account, as appropriate, the potential for differences in the effectiveness of health care treatments in various subpopulations; for example, individuals with different genetic and molecular sub-types.
- Results of the studies are to be published in a format that is comprehensible to patients and providers, with safeguards to protect patient privacy and confidentiality of study subjects.

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AARA Funds PCORI

- AARA (aka Stimulus Bill) signed by President Barack Obama in February 2009, authorized $1.1 billion for research on what medical treatments work best for which people. (AARA split funding between the Agency for Healthcare Research and Quality (AHRQ); National Institute for Health (NIH), and HHS
- $17 million of ARRA funds will be used to establish a network of PCOR centers. PCOR stands for "patient-centered outcomes research," also known as "comparative effectiveness research."
- "Patient-centered outcomes research can improve health outcomes by developing and disseminating evidence-based information to patients, providers and decision-makers about the effectiveness of different treatments," said HHS Secretary Kathleen Sebelius.

HHS Press Release, "*HHS Awards $17 Million for Patient-Centered Outcomes Research*" (Sept. 1, 2010).

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HHS Awards $475 Million in Patient-Centered Outcomes Research Funding

- AHRQ announced the award of $473 million in grants and contracts for a portfolio of coordinated projects designed to support patient-centered outcomes research, also known as comparative effectiveness research, which will help people make health care decisions based on the best evidence of effectiveness. The funding covers all of AHRQ's allocation and $173 million administered for the HHS Secretary by AHRQ. The awards are part of the investments made under the American Recovery and Reinvestment Act of 2009, (which included $1.1 billion to support patient-centered outcomes research. Of that total, $300 million was designated to AHRQ and $400 million was designated to be allocated at the discretion of the HHS Secretary for a variety of patient-centered outcomes research and related activities. An additional $400 million was directed to the National Institutes of Health.

AHRQ Electronic Newsletter, No. 296 (Oct. 1, 2010)

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PCORI Parameters

- PCORI may not mandate coverage, reimbursement, or policy recommendations
- HHS is prohibited from denying coverage based solely on PCORI research
- HHS may not use PCORI research in a way that treats extending the life of elderly, disabled, or terminally ill patients as of lower value than for a person who is younger, non-disabled or not terminally ill
- The institute is prevented from developing or using "a dollars-per-quality adjusted life year (or similar measure that discounts the value of a life because of an individual's disability) as a threshold to establish what type of health care is cost effective or recommended."

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Medicare – Historical Approach

- Coverage with Evidence-Based Development
- Least Costly Alternative
- Trend towards focus on "outcomes" as part of the quality initiative
- FDA/CMS Sentinel Initiative – shared information about the Medicare population
  - 2011 Budget Justification – focus on increased sophistication of data collection/use so as to be a leader in comparative effectiveness

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Roadblocks to CER/PCO approach

- Who pays for the clinical trial to gather comparative data?
- Co-pay differentials encourage patient choices among drugs tested
- How do you bill for an unknown drug, and get to unidentified claims on patient EOBs?
- Statutory authority for alternative payment mechanisms under Medicare, but not implemented

Martin, McGuire and Fine, "*Roadblocks to Comparative-Effectiveness Research,*" N. Engl. J. Med. 363;2 (July 8, 2010)

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Demands associated with evidence based reimbursement and commercialization have created a new environment

2000	2011
Clinical Utility	**Clinical Utility**
▪ Primary focus on clinical safety & efficacy (inc. surrogate endpoints)	▪ Primary focus on clinical safety & efficacy around patient outcomes
▪ Most likely placebo comparator	▪ Increasing instance of active comparator
Eligible Patients	**Eligible Patients**
▪ Blockbuster orientation toward broad patient populations	▪ Patient selection a critical variable for outcomes and value proposition
Market Access	**Market Access**
▪ Generally assumed if safety and efficacy meet regulatory hurdle	▪ ***Access not a "given" in most areas, regardless of regulatory outcome***
Commercial Potential	**Commercial Potential**
▪ Focus on market share as a function of clinical comparison to SOC	▪ ***Economic value vs. competition plays a more important role in access and share gained***

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Drivers for evidence will impact drug, device, and diagnostic—new criteria are emerging

- Global economic conditions increase pressure for cost containment
- Increasingly competitive global markets with more payer scrutiny will demand stronger evidence packages
  - Impact on **outcomes** rather than just intermediate or surrogate measures
  - **Implications for changing clinical practice—clinical utility**
- Compelling evidence of value for must be generated for multiple stakeholders—physicians, patients, and payers

Large firms
- Commercialize products
- Licensees or acquirers of products developed by smaller firms

Smaller firms
- Compete for scarce funding
- License or sell assets

Investors
- Must be prepared to evaluate strength of an asset's value proposition, particularly in the context of reimbursement

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Earlier planning increases degrees of freedom and ROI

Phase 1 — Phase 2 (early) — Phase 2 (late) — Phase 3 — Launch

Typical Early-Phase Issues

- Trial design, optimal set of metrics to support market access and physician choice
- Patient sub-groups most likely to benefit
- Indication sequencing
- Prioritization of development resources, go/no go decision making

Value Planning and Payer Research

- Early pricing and market landscape assessment
- Assess evidence based review of analogues
- Test positioning with stakeholders
- Health outcomes simulation modeling

Typical Late-Phase Issues

- Optimal gross/net pricing
- Refined stakeholder value propositions, positioning, and messaging
- Post-marketing study planning
- Identification of resources required for launch (manufacturing, sales, etc.)

Value Planning and Payer Research

- Quantitative pricing analysis
- Market access and contracting strategy

Early planning for coverage and reimbursement also demonstrates this issue has been addressed in the clinical development plan

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General Approach to Planning for Evidence Based Reimbursement and Commercialization

Landscape and Stakeholder Assessment → **Gap Assessment and Value Strategy** → **Planning**

Assess market landscape and stake-holder perspectives

Characterize context and performance requirements for successful product

Evaluate gaps between product profile, anticipated or available evidence, and stakeholder expectations

Set value objectives and strategy

Develop functional tactical plans, with defined accountability

Specify planned activities and deliverables to fulfill value strategy

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Planning should include strategy for evidence review, generally, and eventually comparative effectiveness

- To inform planning, manufacturers can use information such as WellPoint's guidelines on how it will use CER to make formulary decisions
- NCCN's approach for their Comparative Therapeutic Index™ also provides information on how new therapies will be evaluated
- Coverage policies for devices and diagnostics may reveal specific criteria that should be addressed in planning for evidence generation

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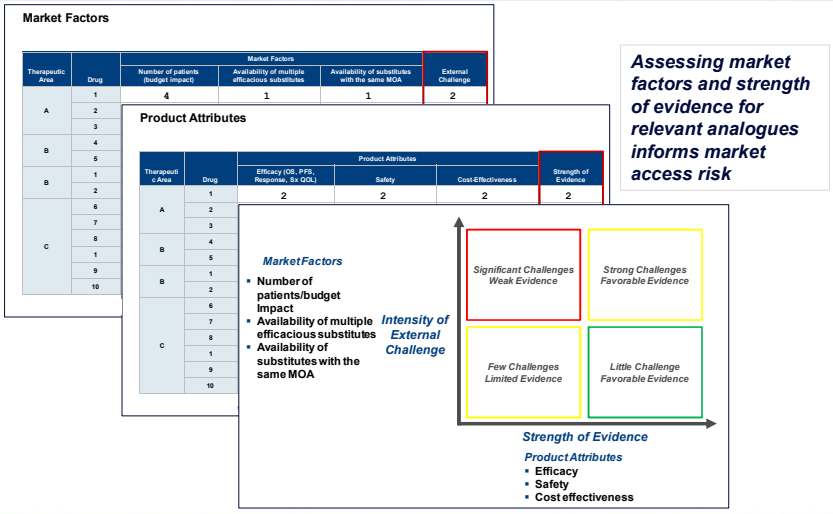
Systematically characterizing context and performance requirements for a successful product should also inform planning for evidence generation



Assessing market factors and strength of evidence for relevant analogues informs market access risk

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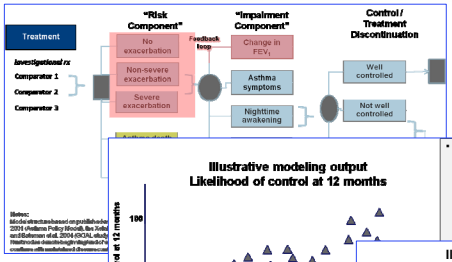
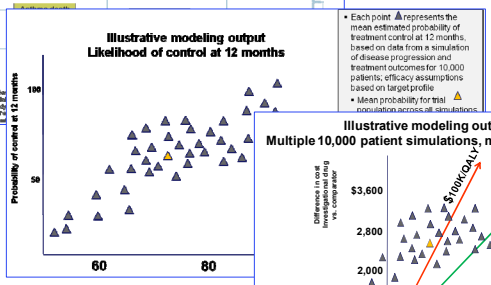
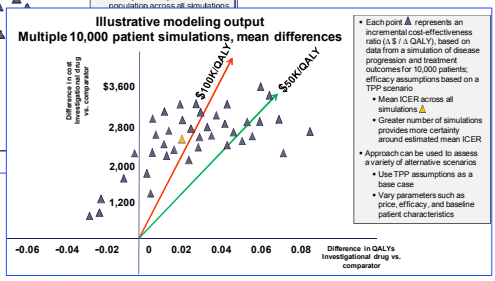
Modeling can help evaluate the likelihood that a product profile is *favorable*, *comparable*, or *unfavorable* compared to alternatives



Disease State Model



Assess probability of efficacy and economic outcomes



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Finally, a thorough evaluation of gaps between a product profile, anticipated or available evidence, and stakeholder expectations should be conducted as evidence strategy is refined

Issues	Key Points	Recommended Updates
Systematic review	▪ Few gaps due to broad sweep of literature ▪ Easily replicated to update with results from ongoing studies	▪ Narrow scope of search to focus on studies highly relevant to targeted indication ▪ Choose relevant comparator(s) and focus on evidence from trials of those treatments
Product description	▪ Current gap describing anticipated indication and product use	▪ Update indication accordingly
Target population & treatment	▪ Epidemiology should be expanded ▪ Value on the ability to target a specific subgroup of patients	▪ Develop more precise estimates of target population ▪ Include country-specific estimates of incidence and prevalence; ▪ Focus on subpopulation of responders
Summary of clinical evidence	▪ Broad sweep and summary of literature	▪ Narrow scope of evidence summarized in final formulary dossier and focus on comparators relevant to targeted indication ▪ Work with clinical teams to ensure there is more depth to support the clinical rationale and place in therapy argument
Cost-outcome assessment and product claims	▪ Early-phase framework is not based on a Monte Carlo Markov disease progression model ▪ Early-phase modeling effort will necessarily evolving with product planning and decisions regarding target population	▪ Differentiate patient-specific treatment histories and incorporate state transition probabilities through use of Markov modeling ▪ Incorporate other indications and additional clinical safety and efficacy evidence and refine assumptions ▪ Address uncertainty of estimates – communicate ranges of estimates to payers
System impact	▪ Calculate budget impact by modeling the penetration rate (market share)	▪ Refine market uptake assumptions

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Implications for R&D-Stage Companies

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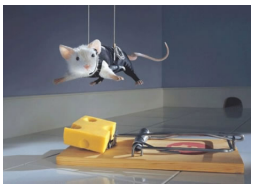
A Better Mousetrap? Better Bring Data!

- Now more difficult for R&D-stage companies to shift reimbursement risk
  - Acquisition comes at later stages
  - IPO market still "slushy," if not frozen



- Ex-U.S. regulatory processes incorporating comparative effectiveness thinking
  - Ex-US markets are an increasing share of your product value
- Your funders and buyers are making decisions based on this
  - "Can we sell it"?
  - "Can we sell it to companies who will sell it"?

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Implications for Partnering

- "Me too" drugs will be increasingly difficult to partner without randomized controlled study data vs. active comparator
- Early? Companion diagnostics & biomarker-driven trial strategies will be easier to partner
- Mgm't teams should anticipate deep diligence around reimbursability and comparative effectiveness → be prepared with research & data
- A higher bar for deals (maybe)...
  ... but deals that meet the bar will get improved economics than in the past

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Implications for Financing

- Investors know they will own companies for longer
- Partner / acquirer concerns central to investors also
  - Demand for innovation
  - Demand for biomarkers to compare to SOC
  - Demand that managers anticipate CE in clinical trial plans, etc.
- Expect a need to demonstrate more groundwork for reimbursement at Series B/C stages
  - Budget for pricing & reimbursement consulting
  - Speak to global launches & by-region value

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Questions?

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