

# Comparative Effectiveness Research (CER) and Pharmaceutical Companies

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Eli Lilly and Company

# CER represents:

1. The next logical step in the progression of more rigorous information about new healthcare technologies
2. A necessary input for a value-driven healthcare system

# History of Pharmaceutical R&D

## CLINICAL PRACTICE

### ■ Early 20<sup>th</sup> Century

- Flexner Report led to dominance of biomedical model of medical care in the US (Education, Research, Practice)

### ■ Mid-Late 20<sup>th</sup> Century

- Rapid growth in biomedical science and new technologies
- Physicians primary decision makers
  - Lack of coherent synthesis of knowledge enables practice variation
    - Wennberg/Dartmouth Atlas

## PHARMACEUTICAL R&D

### ■ Early 20<sup>th</sup> Century

- Little Regulation
- Few Effective Medicines

### ■ Mid-Late 20<sup>th</sup> Century

- Growth of Modern Pharmaceutical Industry
- Regulation of Pharmaceutical Marketing & Sales
  - Safety & Efficacy – RCTs
- Limited barriers to market access
  - MD as learned intermediary

# End of 20<sup>th</sup> Century

## CLINICAL PRACTICE

- Emergence of Evidence-based Medicine
  - Cochrane Collaboration
  - AHCPR → AHRQ
  - NCQA, USPSTF
- Appearance of Practice Guidelines and Performance Metrics (downward pressure on practice variation)
  - Pay-for-Performance
- Exploding Health Care Costs
  - Health Technology Assessment to permit greater restriction on coverage and reimbursement
    - Australia, Ontario
    - UK (NICE)

## PHARMACEUTICAL R&D

- More information required by regulatory bodies on the efficacy and safety of new products
- New tools for R&D
- Outcomes Research Studies & Health Economic Models provide additional information on value and therapeutic role for new technology
- Disease Management tools & programs to ensure that providers and payers obtain value from new technologies

# The 21<sup>st</sup> Century

- Mitigating the continued rise of healthcare costs is now a public priority
  - The pharmaceutical industry is being asked to be part of the solution in US Healthcare Reform
  - Payers and providers are “managing” access to new and expensive technologies through a variety of methods that will increase downward pressure on industry ROI
    - HTA is widely adopted by payers
      - Europe, Growing in Asia
      - Managed Care in US
      - MedCAC
    - Tiered Formularies and Benefits
    - Coverage with evidence development
    - Risk sharing Contracts

# Early Efforts in the US in the Application of CER to Health Policy decisions

- **MMA**
  - Comparative effectiveness (e.g., EBM) – Section 1013 (AHRQ)
- **CMS**
  - CMS endorsement of HECON in MMA formulary design
  - Coverage with Evidence Development
  - Coverage with Conditions
- **DERP (17 State Consortium - Medicaid)**
  - Evidence-based Drug Class Reviews
- **AHRQ**
  - Centers for Research & Education in Therapeutics (CERTs)
  - Evidence-based Practice Centers (EPCs)
  - Effectiveness Health Care Program
    - Comparative Effectiveness (EPCs and DeCIDE)
    - Network of Research Centers (DEcIDE)
    - Eisenberg Center for Clinical Decisions and Communications (Oregon)

# How will the Pharmaceutical Industry Adapt?

- Some (“enlightened”) companies will develop new strategies for:
  - Research & Development
  - Commercialization
  - Industry Policy Initiatives

**ENHANCE VALUE  
DERIVED BY PATIENTS,  
PROVIDERS, & PAYERS**

# The Evolving Paradigm of Drug Development

- Basic Science
  - Clinical Research
  - Outcomes Research
  - Disease Management
- } Traditional
- } 1990's
- Value-based Development
    - Sub-populations that benefit most
    - Stratified / Personalized Medicine
      - Biomarker / Genetic Diagnostics to Target Treatments
- } 2007 & Beyond

# Strategy for Traditional Drug Discovery

## ■ MICRO Considerations

- Understand the molecular basis of the disease
- Select a therapeutic target
- Link the therapeutic target to a defined mechanism of action
- Discover a lead compound that is safe, effective, and novel
- Always have backup compounds with structural diversity

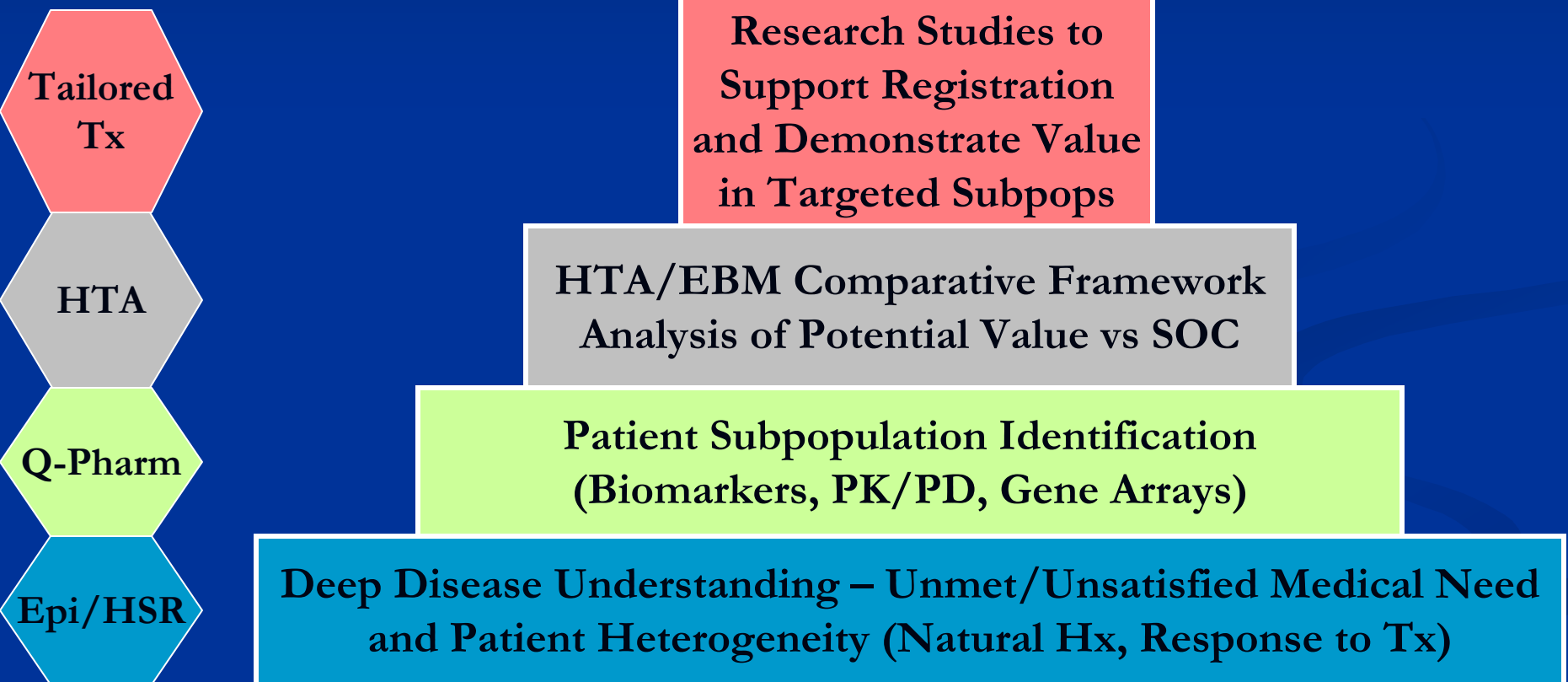
## ■ MACRO Considerations

- Target Populations
  - Prevalence / Incidence
  - Unmet medical need
- Economic Considerations
  - Willingness-to-pay
  - Competitiveness of market environment in disease area

# New R&D Paradigm Goals

- **Enhanced Efficiency**
  - **Decrease Cycle Time**
    - Adaptive Clinical Trials
  - **Decrease Late Stage Failures**
- **Enhanced perception of value to payers, providers and patients**
  - **Greater product differentiation**
    - Biomarkers, Outcomes
  - **Stratified / Personalized Medicine**
    - Targeting of therapy to those patients who will benefit most
      - Biomarkers, Diagnostics (responders/non-responders)
    - Decrease toxicity

# Building Blocks of R&D Strategy



# Strategies for the New Paradigm

## Early Development

- Greater reliance on biomarkers including genomics combined with modeling for predictive efficacy and toxicity
- Combine dose-finding and POC studies

## Late Development

- Simulated clinical trials
- Adaptive clinical trial designs
- Large simple trials
- Stratified Phase III development
- Parallel timelines
- Active comparators in Phase III studies

## Life Cycle Development

- Effectiveness Studies
- Treatment Registries
- Novel reimbursement and contracting strategies

Ongoing Consultation with Regulatory Authorities and Payers

# Commercialization Opportunities

- Increased consultation with scientific and payer thought-leaders during development can create true champions to enhance the “pull” in the market at launch
- Better differentiation of the value of new products will mitigate downward pressure on price
  - Need to develop value story tailored to payers that enable payers to “do the right thing” and provide access
  - Understanding value story across sub-populations opens the door to novel contracting and pricing strategies
    - Risk Sharing
    - Benefit-based coverage

# Enhancing the Value Proposition for the Patient and Payer

**Goal:** Improve individual patient outcomes and health outcome predictability through tailoring of treatment.

One size fits all

*Degree of Tailoring*

Targeted Therapy

*Lower predictability of health outcomes*

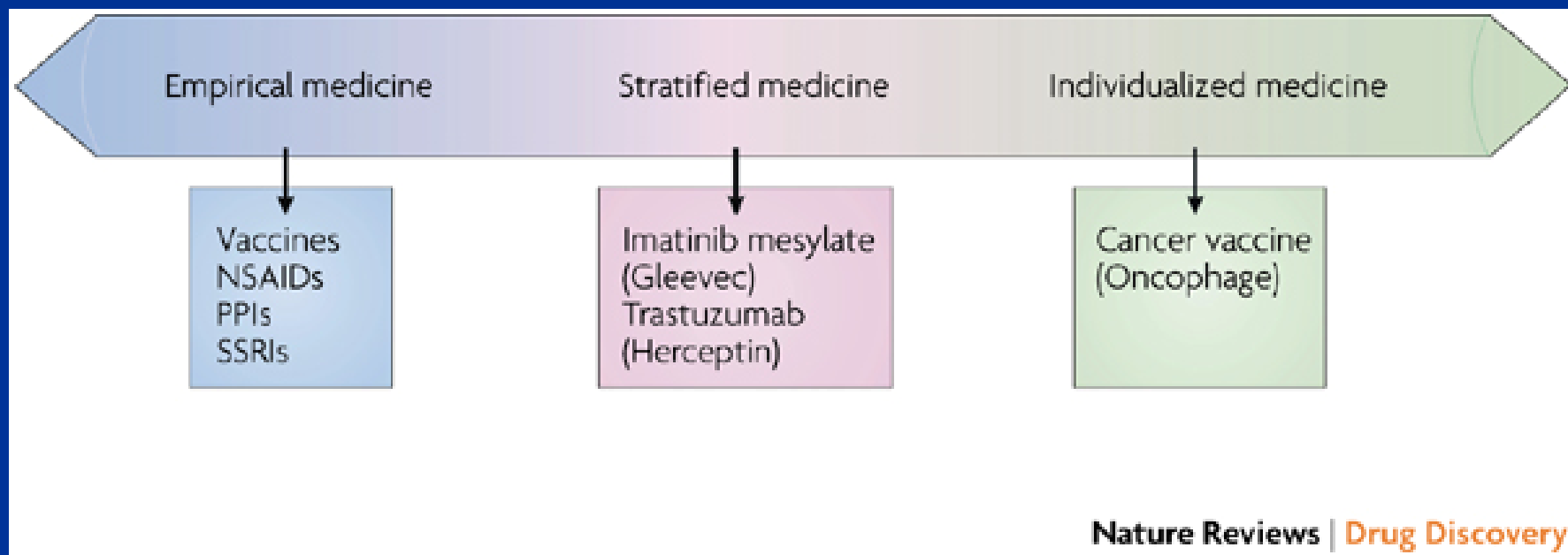
*(e.g. most pharma products today)*

*Assess spectrum of patient response to therapy;  
Stratify patient populations;  
Optimize benefit / risk based upon biomarkers including Imaging, Clinical Observation, Patient Self-report.*

*Higher predictability of health outcomes*

*(e.g. oncology products comprising drug and companion diagnostic)*

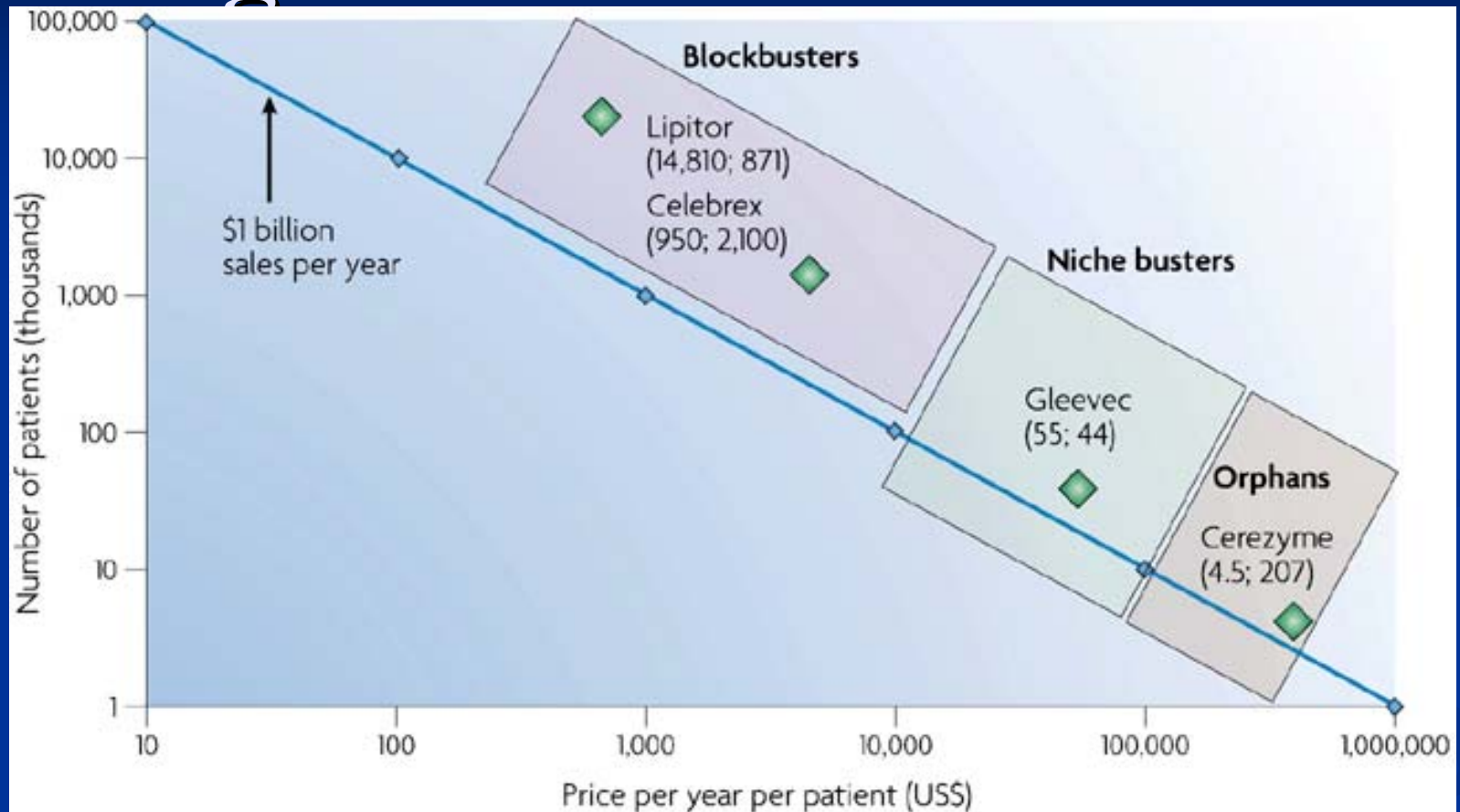
# The Patient Therapeutic Continuum



Mark R. Trusheim, M.S., Ernst R. Berndt, Ph.D., and Frank L. Douglas, Ph.D., M.D.,

“Stratified Medicine: Strategic and Economic Implications of Combining Drugs and Clinical Biomarkers”,  
*Nature Reviews: Drug Discovery*, 6:4, April 2007:287-293.

# One view: Large Revenues Are Possible



(thousands of patients, average yearly price in \$thousands)

Trusheim et al.

Nature Reviews | Drug Discovery

# My view: Substantial ROI is Possible

- Greater value may translate into:
  - Some price premium
  - More rapid access and uptake
  - Better adherence and compliance
- This can offset decreases in revenues associated with smaller target populations

# Industry Transformation: A New and Sustainable Business Model

- More Valued Treatments
- More Efficient Development
- Stronger Partnership with Payers and Providers
  
- Restructuring to provide greater flexibility to manage R&D risk
  - Fully Integrated Pharmaceutical Network (FIPNET)

# Challenges

- Industry needs consistent “rules of the road” to succeed in its transformation
  - CER
    - Transparency, Reproducibility, Limitations of Bias
    - How are gaps in evidence handled → translation into policy
- CER can both assist healthcare improvement and appropriately shape the evolution of pharmaceutical R&D
  - Broad stakeholder involvement (ex patients, industry)
  - Broad scope (not just focus on drugs)
  - Explicitly address patient heterogeneity
  - Translation of into health policy decisions should be put into appropriate context (ex. uncertainty, unmet medical need)