Comparative Effectiveness Research (CER) and Pharmaceutical Companies

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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 20th Century
  - Flexner Report led to dominance of biomedical model of medical care in the US (Education, Research, Practice)
- Mid-Late 20th 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 20th Century
  - Little Regulation
  - Few Effective Medicines
- Mid-Late 20th 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 20th 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 21st 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

} Traditional

- Outcomes Research
- Disease Management

} 1990's

- Value-based Development
  - Sub-populations that benefit most
  - Stratified / Personalized Medicine
    - Biomarker / Genetic Diagnostics to Target Treatments

} 2007 & Beyond

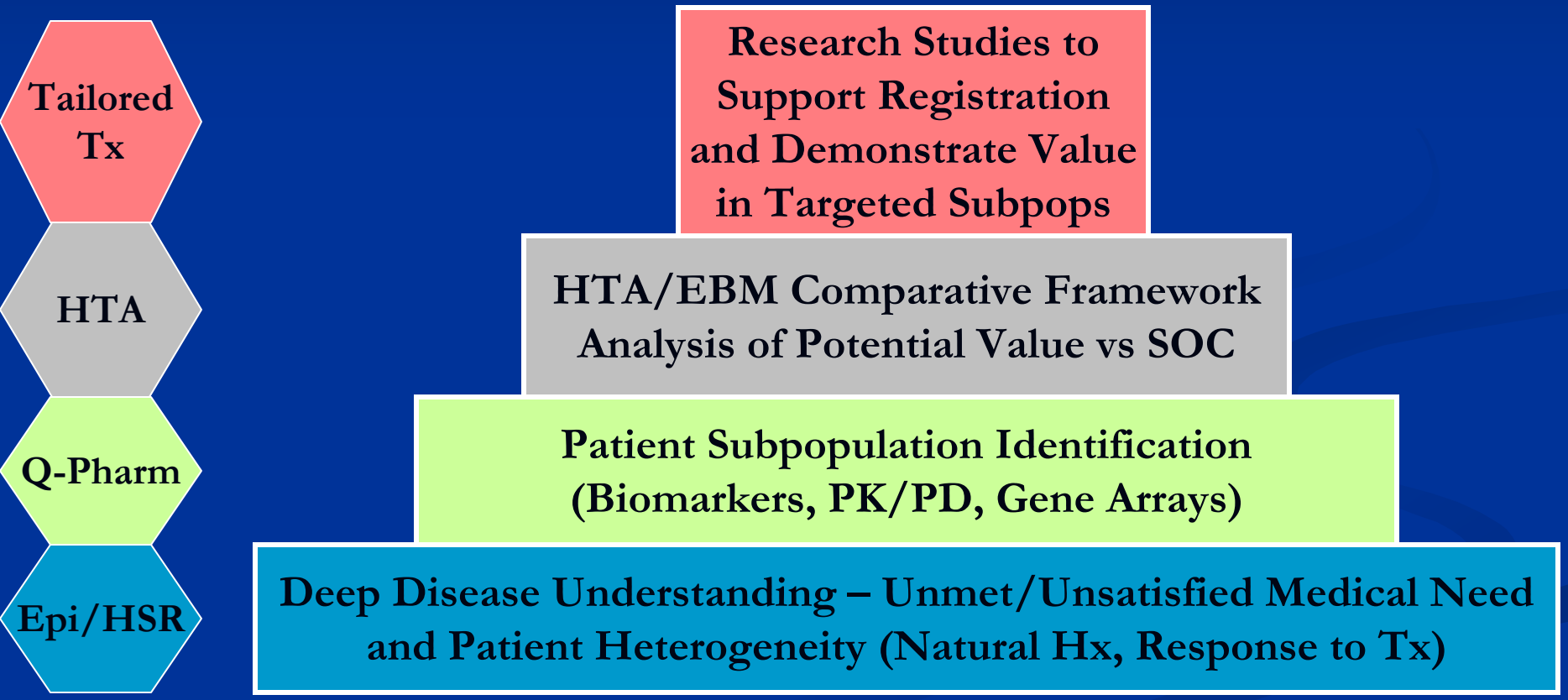
Strategy for Traditional Drug Discovery

- **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

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

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

- 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 <u>individual</u> patient outcomes and health outcome predictability through <u>tailoring</u> of treatment.**

Lower predictability of health outcomes

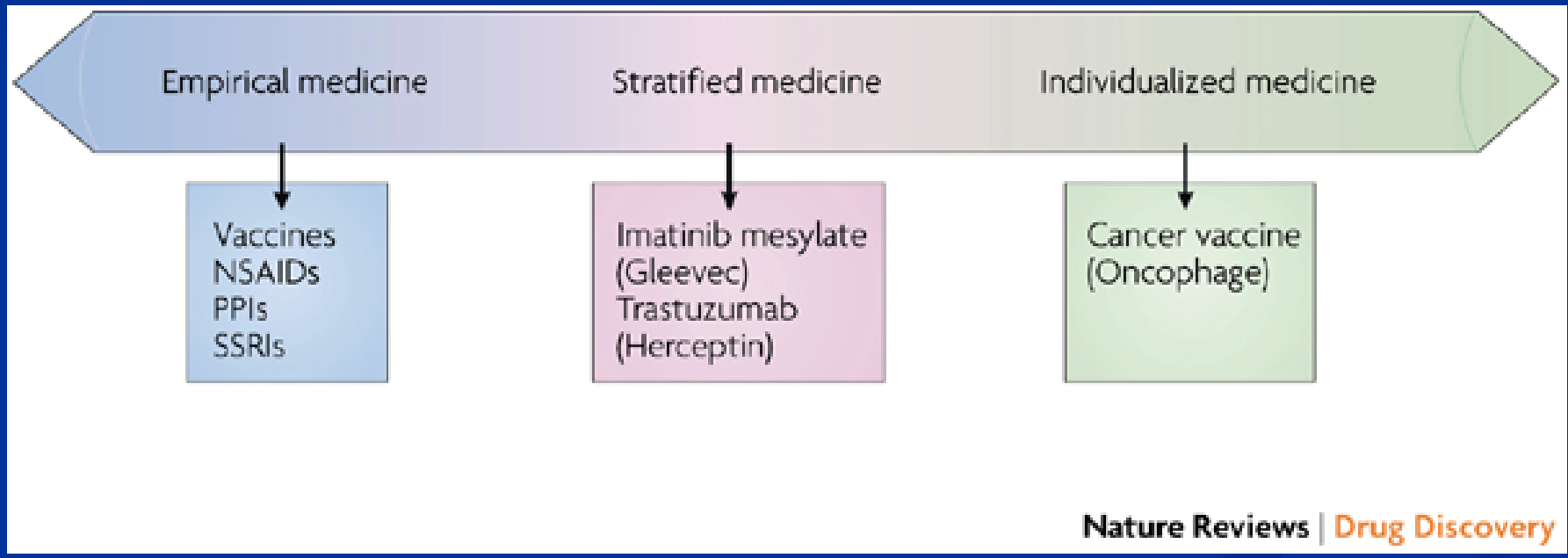
(e.g. most pharma products today)

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

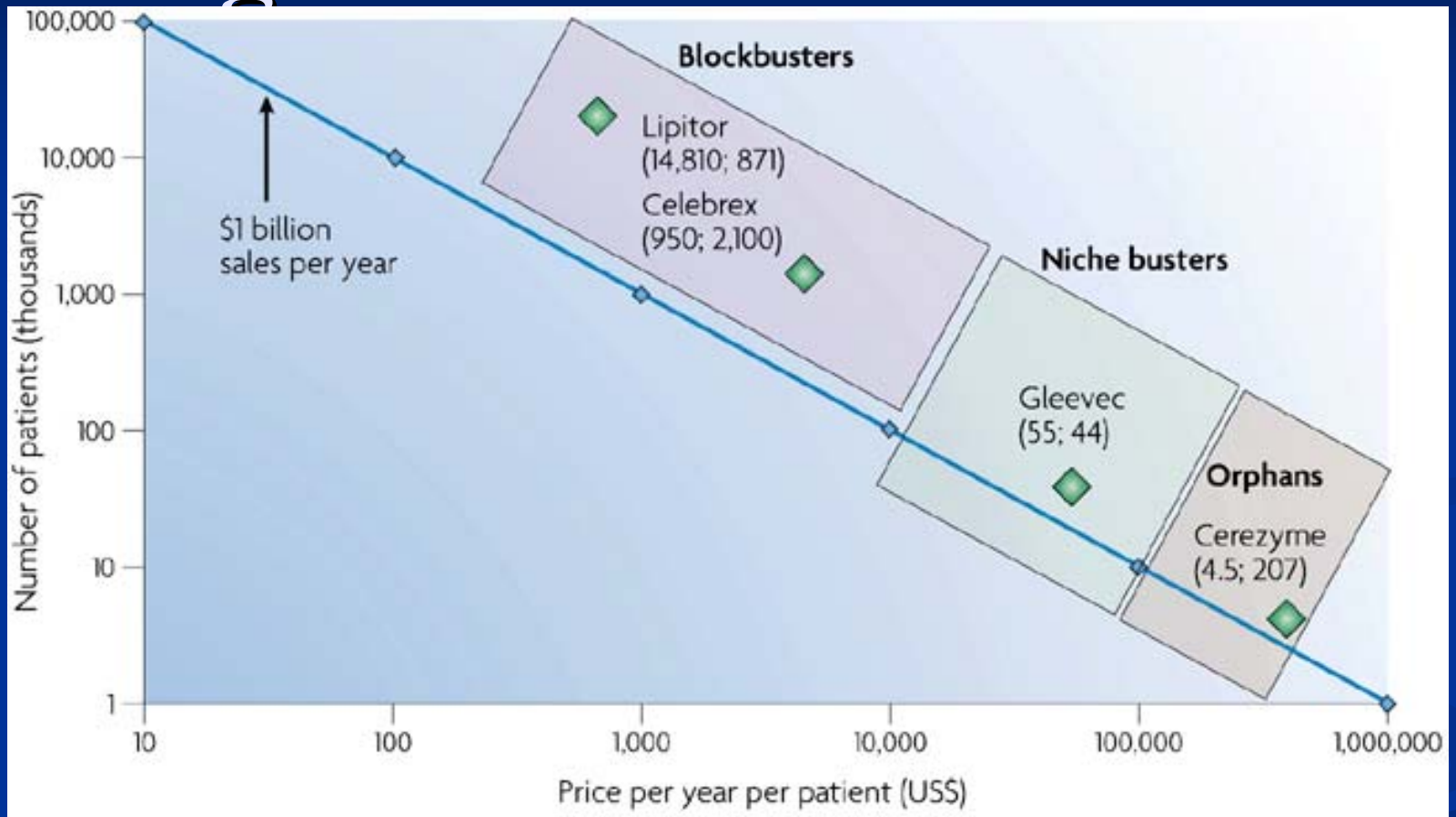
(e.g. oncology products comprising drug and companion diagnostic)

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)