Opportunities and Challenges in the Development of Companion Diagnostics

E. Patrick Groody, Ph.D.
Divisional Vice President Research and Development
Abbott Molecular



Abbott Molecular

Agenda

- Value of Personalized Medicine
  - Herceptin/PathVysion
  - Xalkori/Vysis Alk
- Challenges and Uncertainties
  - Development
  - Regulatory
  - Commercialization
  - Reimbursement
- Elements of a Successful Partnership

Abbott Molecular is a Division of Abbott Laboratories

- Independent Operating division of Abbott
- State-of-the-art molecular diagnostics facility in Des Plaines, Illinois, U.S.A
- 1000+ employees (300+ scientists and engineers)
- $400+ million sales

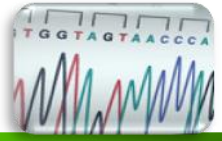
- Multiple Products: 510K, PMA, CE, SFDA
- Sun-Times Innovation Award
  - ✓PathVysion (2005)
  - ✓m2000/HIV (2007)
- WSJ Technology Innovation Gold Medal
  - T5000®/PLEX-ID (2009)

Abbott Molecular

Abbott Molecular products use a variety of Technology Platforms….

RealTime PCR
Infectious Disease
NSCLC
Melanoma
CRC

FISH
Bladder Cancer
Breast Cancer
Chromosome Enumeration
Genetics
Hematology
Oncology
Solid Tumors



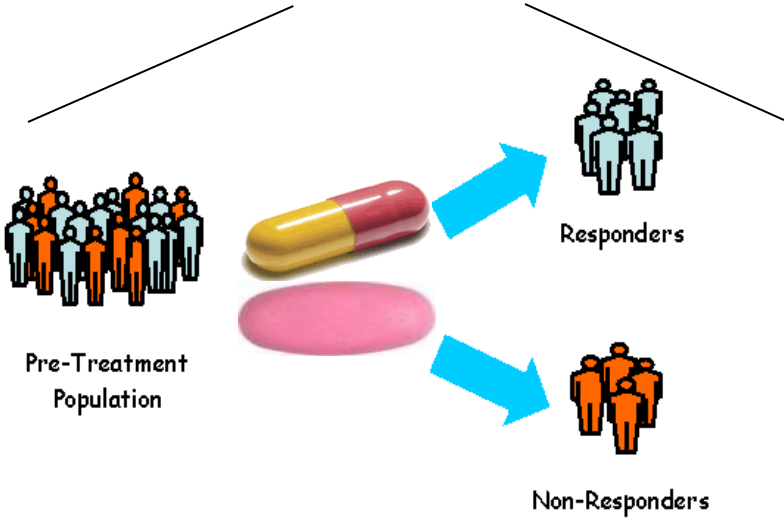
Sequencing Bead Array
Genetics
Respiratory
Infectious Disease

Bioidentification
Applied Research
Bio-preparedness
Bio-Pharm
Clinical Research
Food Safety
Forensics
Surveillance Public Health

Predictive Diagnostic Tests: Improving the Benefit/Risk Ratio of Pharmaceuticals

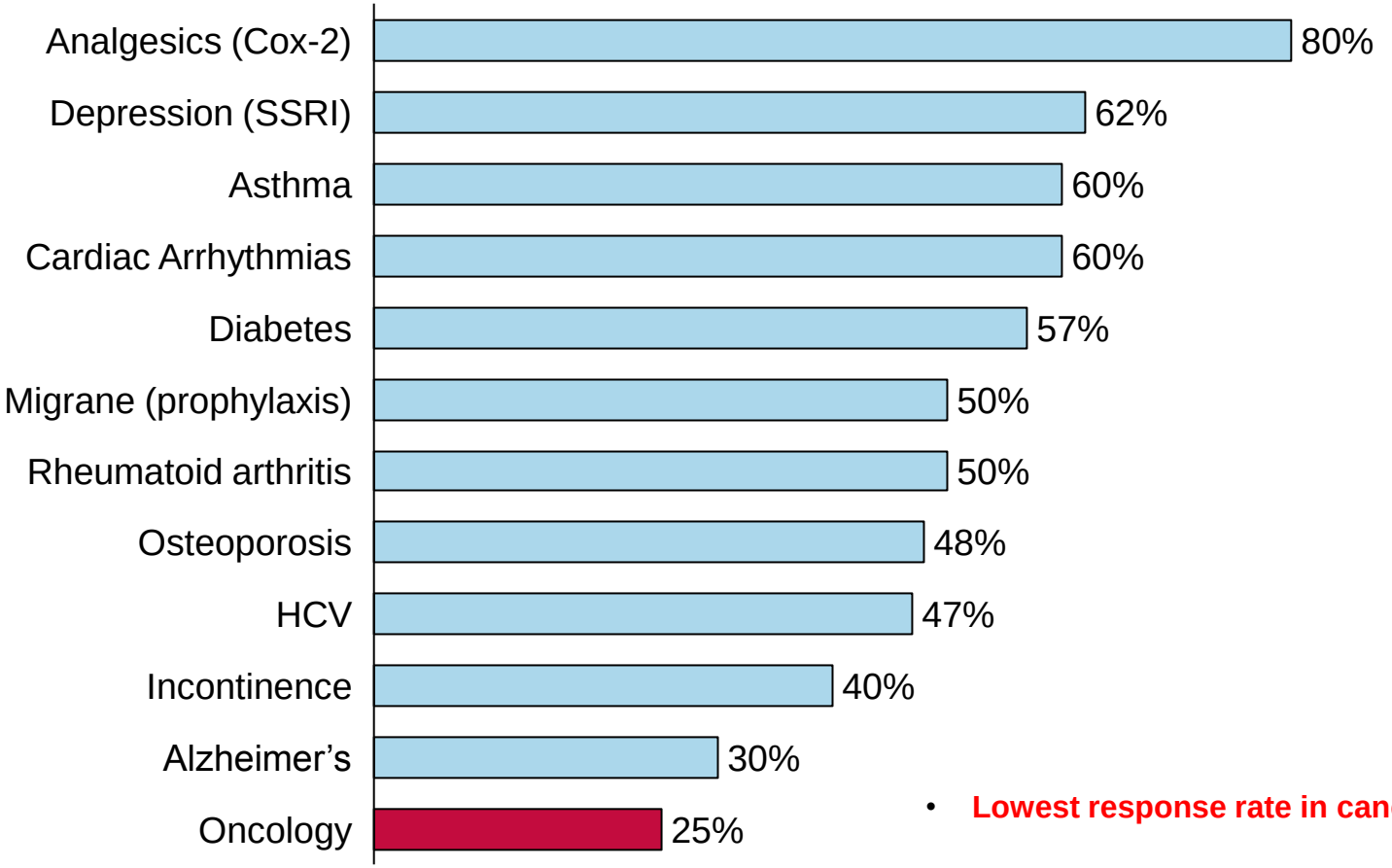
Asymptomatic population		Symptomatic population		Diagnosed population			
predisposition	screening	risk assessment (benign to cancer)	differential diagnosis	staging	prognosis	**prediction**	monitoring

- **Personalized Medicine:** the **ability to predict** which therapeutic intervention will be the most **efficacious and safe based on a test.**



Current Therapies Result in Poor Efficacy Rates

- **Therapeutic Response Rate**



- **Lowest response rate in cancer, 25%**

Source: Spear et al., Trends Molecular Medicine 2001;7;201-4.

Abbott Molecular

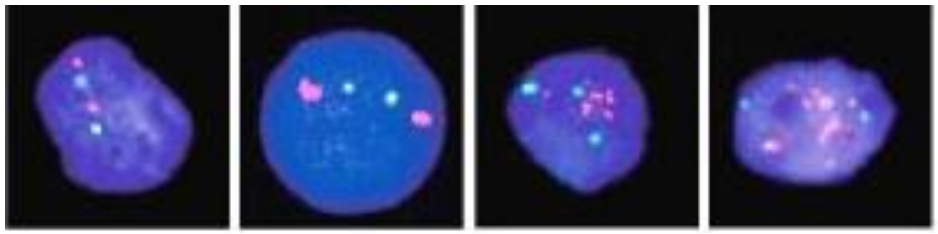
Personalized Medicine Benefits All Key Stakeholders

Physicians	• Prescribe the most effective therapeutic for the disease indication
Patients	• Receive the optimal treatment in the minimum amount of time
Payors	• Allocate treatment resources in a targeted manner to improve the overall cost effectiveness
Regulatory Bodies	• Increase safety and efficacy of prescribed drugs and reduce adverse events
Pharma Companies	• Increase R&D productivity and improve efficacy claims with CDx test,
Diagnostic Companies	• Demonstrate the value of diagnostic test, broaden product portfolio

Abbott Molecular's PathVysion HER-2 DNA Probe Kit

Herceptin and PathVysion

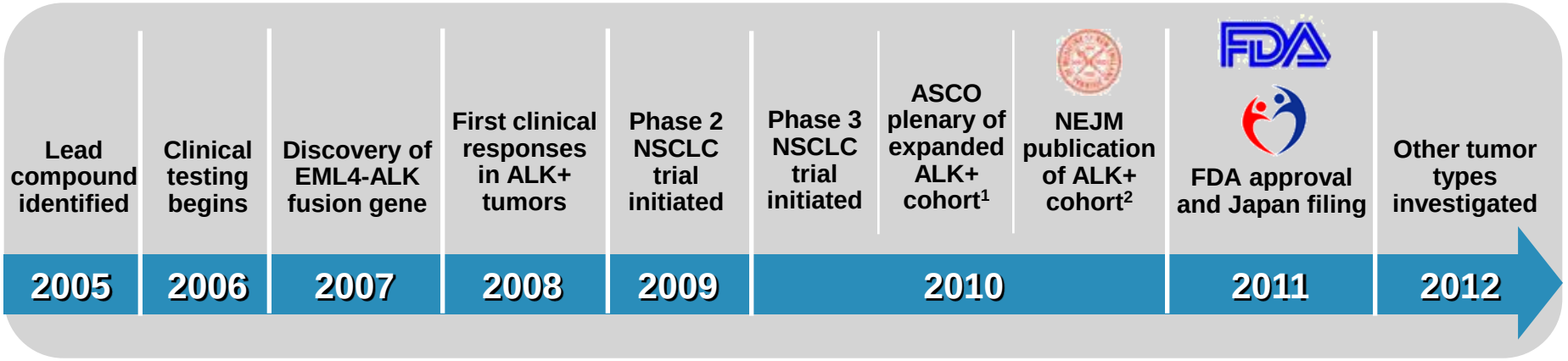
- Herceptin is a hallmark of personalized medicine for breast cancer patients and PathVysion serves to identify those that have the potential to respond positively
- PathVysion: The first FISH (gene-based) CDx product
  - Market acceptance of CDx requires clinical data, recognition by guidelines and appropriate reimbursement (payment) for the diagnostic
  - Herceptin was approved in 1998 and PathVysion sales grew mainly as a result of early clinical data



Abbott Molecular

Crizotinib: Pathway from Compound Identification to Discovery of ALK Target and Clinical Results

Crizotinib (PF-02341066) scientific breakthrough: Targeting the ALK fusion gene, a direct driver of oncogenesis



Rapid timeline from compound identification, target discovery and clinical results

Clinical results to date:

- Objective response rate = 61%[3]
- Disease control rate (CR+PR+SD) = 79% at 8 weeks[3]
- Median duration of response = 48 weeks[3]
- Median PFS = 10 months[3]

1. Bang JY et al. Oral presentation at ASCO, 2010.
2. Kwak et al. New Engl J Med. 2010;363:1693−03.
3. Camidge DR, oral presentation at ASCO 2011.

Abbott Molecular

Challenges and Uncertainties—CDx Development

- Biomarker selection and establishment of clinical utility
- Selection of diagnostic methodology
- Concordance with LDT's and other methods used in early phases of therapeutic development
- Dx/Rx trial timeline coordination
- Specimen availability/informed consent
- Geographically diverse patient cohorts

Abbott Molecular

Challenges and Uncertainties—Regulatory Approval

- Criteria that define risk for diagnostic tests
  - In the US, companion diagnostic tests require a PMA
- Standards for study design and product performance
  - What is sufficient compelling evidence?
  - What is appropriate correlation with LDT?
  - How can additional tests be launched once the initial clinical utility has been established?
- Coordination of submission and review process
- Coordination of requirements between FDA and other worldwide regulatory agencies
- Criteria and procedures for incorporating diagnostic in therapeutic product labeling

Challenges and Uncertainties—Commercialization

- CDx development has a higher risk profile than most diagnostic product investments
- Commercial strategy must be tailored to fit the scope and breadth of the opportunity
- Global coordination of efforts is key to overall success
- Extensive commercial investment required after the initial product launch

Challenges and Uncertainties—Commercialization

- Regulatory approval is no guarantee of coverage
- Lengthy process to establish coding, coverage and reimbursement
- Insurers are demanding more **evidence** in setting payment policy
- Insurance company goal is to reduce the cost burden
- Market development and adoption can be difficult and lengthy
- Budget impact, cost effectiveness, HEOR models may be required for drug-test combinations to ensure market access

Key Elements of a Strong Pharma-Diagnostic Partnership

- **Must have Business Incentives for Both Partners**
  - If small Dx revenue stream projected, Risk & ROI may not be sufficient enough for Dx company with traditional model. Pharma support may be needed.
  - Agree on success criteria early, consider performance-based incentives
  - Agreements must address how scope changes will be handled
- **Management and Flexibility**
  - Employ strong project management leadership to drive the project through the calm and stormy seas
  - Establish mechanisms for open communication
- **Leverage Core Competencies**
  - Pharma knows their market access and regulatory process
  - Diagnostic knows their market access and regulatory process
  - Identify interdependencies
  - Each partner must feel confident and trust the other will deliver

Thank you

Abbott Molecular