The Future of Companion Diagnostics

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This slide presentation contains forward-looking statements which are subject to change based on various important factors, including without limitation, competitive actions in the marketplace and adverse actions of governmental and other third-party payors.

Actual results could differ materially from those suggested by these forward-looking statements. Further information on potential factors that could affect the Company’s financial results is included in the Company’s Form 10-K for the year ended December 31, 2010, and subsequent SEC filings.

The opinions expressed in this presentation are those of the presenter and do not necessarily reflect the opinions of LabCorp.
Economics

The science of explaining tomorrow why the predictions you made yesterday didn't come true today.
Background

Why Pharma must change

Realities and challenges of Personalized Medicine

A view of the future
Companion Diagnostics

• Biomarker:
  – An analyte measurable in a biologic matrix, stable in a control group, that changes in response to disease or treatment

• Companion Diagnostic:
  – A diagnostic test intended to help select or monitor therapy
    → Facilitate precision medicine by selecting the right drug for the right person at the right dose
LabCorp is leading an independent clinical laboratory

LabCorp’s Platform
220,000 customers  31,000 employees
1,500 patient centers  440,000 samples per day
40 years

Our mission is to be a leading provider of high science laboratory services that support clinical decision-making, enhance the management of
Labcorp is a leading provider of laboratory testing for clinical trials

Central Labs

Esoteric Testing
- Dedicated labs for clinical trials
- Cranford, NJ
- Mechelen, Belgium
- Beijing, China
- Singapore
- Broad, validated test menu
- Test method harmonization
- 8 Centers of Excellence
  - Covering: Coagulation, Endocrinology, Oncology, Infectious disease, Anatomic pathology, Molecular pathology, Flow cytometry

Bioanalytical Labs
- Small and large molecule
- Method development and validation
- LC/MS/MS
- Non-GLP discovery services
- Cell-based assays
- Discovery and development
- GLP biomarker services
- MS-based assays
- Global expertise: Cranford, NJ, Mechelen, Belgium, San Diego, CA, West Trenton, NJ

Biomarker Discovery
- Discovery, development, commercialization
- FDA experience
- IVD Trial Participation
- Successful PMA submission
- 40,000 ft² biorepository

CDX

Commitment to Quality

Integrated Data Management

Dedicated Project Management
Labcorp has unique qualifications to support clinical trials

<table>
<thead>
<tr>
<th>Scientific Expertise</th>
<th>Global Scale and Logistics</th>
<th>Relevant Experience</th>
<th>Near Patient Testing</th>
<th>Data Analytics</th>
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</thead>
<tbody>
<tr>
<td>Comprehensive test menu</td>
<td>27 sites on 5 continents</td>
<td>7,300 studies</td>
<td>1,500 patient centers</td>
<td>Data mart with over 1.2MM clinical results daily</td>
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<tr>
<td>8 Centers of Excellence</td>
<td>Clearstone acquisition provides wholly owned labs in China and Singapore</td>
<td>1200 international studies</td>
<td>Large courier network</td>
<td>Biomarker co-prevalence</td>
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<td>Dedicated development and validation resources</td>
<td>Able to cost effectively deliver a sample globally</td>
<td>725 active trials</td>
<td>Economies of scale</td>
<td>Protocol design</td>
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<td>PBMC networks</td>
<td>49,000 sites</td>
<td>Standardization of analytics and IT systems</td>
<td>Identification of investigators</td>
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<td>25 years CT experience</td>
<td>Unique model for Ph I/II and Ph IIIb/IV studies</td>
<td>Patient recruitment</td>
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<td>Companion diagnostic co-development</td>
<td>Scientific data queries</td>
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Reflections on the pharma industry

...or why Pharma must change
Global pharma market is large
>70% growth from emerging markets

57% of prescriptions

$62B

OTC 11%

Generic

($44B)

Higher approval rates

Ethical Biologic

Ethical Conventions

North America: 50% of spend

$353B

100% = $513 B
R&D spend is increasing - 6% CAGR
R&D cost/drug are increasing
New Drug Approvals Are Not Keeping Pace with Rising R&D Spending

R&D expenditures are adjusted for inflation
Source: Tufts CSDD Approved NCE Database, PhRMA, 2005
Pharma Industry Sales are Generally Keeping Pace with R&D Spending

Source: PhRMA, Tufts CSDD Analysis, 2005
NME Approvals are Declining – Biologics are Filling the Void

NME/BLA Approvals

NME Approvals
BLAs Approvals

Source: FDA
1990’s
5% of new drug approvals were biologics

2006
36% of new drug approvals were biologics

Accelerating Demand for Biologics
Shift to MABs

- Preclinical: Mostly MABs
  - MABs: 66%
  - Non-MABs: 34%

- Clinical Trials: Shift to MABs
  - MABs: 66%
  - Non-MABs: 34%

- Marketed Products: Mostly Non-MABs
  - MABs: 22%
  - Non-MABs: 78%
Therapeutic areas for MABs

- Cancer: 45%
- Infectious Diseases: 15%
- Cardiovascular: 11%
- Autoimmune: 9%
- Other: 20%

LabCorp
Laboratory Corporation of America
Growing Percentage of NME Approvals are from Small/Mid-Tier Pharma Firms

Source: Ventiv Health, 2005
Market Exclusivity for First-in-Class has Declined: Mean Time to First Follow-on Approval

Impact on LabCorp: Fast followers are good for our business; a biomarker developed for one client is likely to be useful for another

Source: DiMasi, Paquette, Pharmacoeconomics 2004;22(Suppl 2):1-14
Generics share of U.S. prescriptions increasing

- 1984: 19%
- 1987: 27%
- 1990: 33%
- 1993: 40%
- 1996: 43%
- 1999: 47%
- 2002: 51%
- 2005: 57%
Major Threats to Pharmaceutical Innovation

• Industry productivity and output
  ▪ Rapidly rising R&D costs
  ▪ Increasing size of clinical trials
  ▪ Increasing regulatory pressure

• Political threat of price controls in US
  ▪ Rising global healthcare costs
  ▪ Global price disparities

• Public discontent
  ▪ Safety of prescription drugs
  ▪ Regulatory agency accountability
  ▪ Industry Rx marketing practices
Drivers of Rising Clinical Costs

- Chronic and complex indications
- Clinical trial size
- Patient recruitment/retention
- Regulatory demands
- R&D inefficiency
- Market oriented studies
Adverse Drug Reactions

• >2.2 million ADR*
• >100,000 deaths*
• Majority preventable
  • polypharmacy
  • drug metabolism
  • individual variations
• Cost to treat ADR est. between $1.5 and $5.6 billion annually

*Annually in US.
Source: CDC and www.ahrq.gov/qual/aderia/aderia.htm
Current medical practice leads to inefficient treatment

- Limited efficacy/response of drugs currently on the market
  - ACE-Inhibitors: 10-30%
  - Beta Blockers: 15-35%
  - SSRIs: 10-25%
  - Tricyclic Anit-Depressants: 20-50%
  - Statins: 10-60%

- Only 30% of breast cancer patients benefit from the anticancer drug Herceptin

Source: JAMA 1998 279:1200
Companion Diagnostics
Individual Response to Hypothetical New Drug

Promise of Personalized Medicine

Study Population

60% Response
35% No Response
5% Toxicity
Goal: To re-engineer patient management using predictive diagnostics

From “trial and error” “one schedule fits all patients”

To tailored therapy selection based on individual molecular response profiles

- RR → 100%
- increased survival rates
- improved quality of life
- cost savings (reduced morbidity and mortality)
KRAS mutation predicts response to cetuximab treatment in colorectal cancer

Overall survival according to KRAS mutation

Percent survival

- non mutated KRAS
- mutated KRAS

p=0.016

Lievre A, Bachet JB, Le Corre D, et al. KRAS mutation status in predictive of response to cetuximab therapy in...
Oncology – Mutation, FISH and Protein Expression

- EGFR
- Kras
- Braf
- Jak-2

- EGFR
- Her-2
- ATM
- Bcr-abl

- EGFR
- Her-2
- ER/PR
- pERK
Examples of Companion Diagnostics in Oncology

- Her-2 test for Herceptin treatment of Her2+ breast cancer patients
  - Patient with Her2 positive respond to Herceptin
- K-ras mutation status and cetuximab response in CRC
  - Patients with a tumor bearing wild-type K-ras benefit from cetuximab
  - Patients with a colorectal tumor bearing mutated K-ras do not benefit from cetuximab
- OncotypeDx
  - 21-genes, validated in multiple studies, ~4000 patients
  - Utility: estimate patient’s likelihood of chemotherapy benefit and recurrence in early-stage breast cancer
    - Less than 10% of node negative ER+ breast cancer patients benefit from the cytotoxic chemotherapy
    - Patients with node negative ER+ and low risk of recurrence will be on tamoxifen alone, spared from the cytotoxic chemotherapy
But...let’s not get ahead of ourselves

- Access to clean water
- Serum test improving drug safety
- Complex genetic test predicting slightly enhanced response to therapy
- Whole genome sequencing with supportive informatics used in all Rx

More

Scale

Innovate

Stop

Benefit

Cost
Realities and Challenges we face in Personalized Medicine
Technical Challenges

• Hypothesis, mechanism and study design efficacy and response rate
• Nature of test, platforms and analytical performance
• Clinical specimen, availability, representation, variation/confounding factors
• Clinical validation, power, performance, success of drug trial
• Synchronization of biomarker and drug development in timing and application
• Analytical or clinical poor performance
• Clinical utility not well demonstrated
• Limited availability of well annotated samples
Regulatory Challenges

• Current regulatory framework is being outpaced by technological advancement
• One test- one intended use structure
• Whole genome sequencing, multiplex assays present challenges
• Interpretation of complex tests and multiplatform panels
• Use of preexisting lab data for downstream diagnostic purposes
• Integrated regulatory requirements and guidelines for biomarker and drug
• Product to product and market to market differences in regulatory and reimbursement standards, US, European Union, and Japan
Commercial Challenges

• Different priority between stakeholders (drug makers and diagnostics etc)
• Risk and cost sharing, incentives, return on investment (this is a business after all)
• Intellectual property and product liability issues (who owns what and when)
• Market access and sharing, pricing, and reimbursement
• Laboratory testing, distribution, standardization and quality assurance
• Interpretation and physician Education
Stakeholder or Players in Companion Diagnostics

Pharmaceutical/Biotech
- Increase success rate, reduce time, cost and patients per NDA for new drug development by using biomarker to stratify patients
- Improve old drug or resurrect failed drugs for better efficacy in subpopulation
- Lack of expertise and experience in diagnostics development and commercialization
- Have incentive to share risk and cost with Diagnostics companies through co-development
- Even with diagnostics division, often limited interaction with pharma division in the same company

Major diagnostics companies (Quest Diagnostics, LabCorp, Roche Dx, Abbott Labs, Novartis Dx, J&J etc)
- Perceive personalized medicine as high margin business for future growth
- Have expertise in Dx development, regulatory and commercialization
- Established test infrastructure and distribution
- Have incentive to work with drug makers for companion Dx
- Keen to IP and position to capture future growth

Specialty Biomarker companies (Genomics Health, Myriad Genetics and many small companies)
- Specialized in a particular biomarker development
- Not sufficient in regulatory, central testing, distribution and reimbursement etc

Kit/reagent manufacture and technology company for test platform
- Provide test kit, reagent, device or technology, QS control and GMP
Stakeholders have divergent priorities
Commercializing a test is not easy!

Big IVD Co
- Test run on existing platform
- Test available in all major labs and hospitals
- High volume
- Proprietary content

Tools Co/ Small IVD Co
- Test run on new platform
- Test available POC everywhere
- Proprietary content
- High price

Laboratory
- Test run on a platform it already has or is broadly applicable
- Test available exclusively
- High volume
- Low cost reagents

Patient (at center)
- Low cost
- Meaningful result
Market Adoption of Test

Show of hands

Clinical Utility
- Is the test Standard of Care
- Existence/severity/utility of therapeutic options available
- Does the result affect patient care
- How often is an actionable result delivered
- TAT
- Reporting capabilities to client
- Availability of specialists for consult
- Ease of ordering test

Clinical Validity & Scientific Evidence
- Supporting publications seminal article in major journal
- Sensitivity and specificity; Reproducibility, precision
- Clinically reportable range; Reference intervals
- Specimen matrix, stability

Paradigm Shift?
- Economic: Impact on current economics of care
- Political: Physician ordering habits: is financial reward moved from one group to another?

Regulatory Acceptance
- CPT Coding
- FDA Approval
- Guidance from CMS

Advocacy
- Thought Leader involvement/acceptance
- Endorsement from advocacy groups
- Endorsement from that professional organization

Payor Adoption
- Managed Care contracts
- Edit Checks on claims
- Federal Government adoption
- State Government adoption

Promotional Efforts
- Price
- Size and structure of the target physician specialty
- Marketing focus and effort
- Sales comprehension, focus and effort
- Assistance from partner?
New Tests are adopted at the point of demonstrating clinical utility

New Test Adoption Curve

- Early Development: Typically >5 Years
- Test Acceptance: Clinical Utility Definitively Established
- Maturity: Test Ordering Stable

- Identification of Marker
- Early Data Demonstrating Utility
- Publications Supporting Application
- Test Becomes Accessible

Medicare and Payer Adoption
Professional Endorsement/Guideline Inclusion

Thought leader endorsement and multiple studies replicating the original finding.
A view of the future

“Here is my sequence”
• Ray Kurzweil: Analysis of history of technology shows that technological change is exponential.

• Faster, smaller, cheaper, better, easier
DNA Sequencing Cost and Data

courtesy R. Kurzweil
$200k in 1940’s
Evolution of Technology

$200k in 1940's
Nanotechnology will lead to convergence of diagnostic and therapeutics for some diseases.
Microfluidics and nanotechnology will lead to more near-patient testing with wireless result transmission

- QC
- Result interpretation
- Performance monitoring
• Patient empowered technologies will accelerate
• POC technologies for appropriate intended use and clinical utility (gap between need and market positioning)
• Near-patient testing increases as technologies are decentralized
Future of Companion Dgx

- Panels will consist of analytes across many platforms
  - Example: Oncology panel involving IHC, FISH, sequencing, expression flow cytometry and methylation
- Informatics and interpretation of test results increasingly important
- Fundamental changes to the way tests are reimbursed will be required to support growing need for informatics and interpretation
- Storage of high density medical data on the cloud
• Companion Diagnostics remain a key driver of diagnostic product, lab and tools company growth with meaningful patient impact

• Clinical usefulness is limited by market adoption, which is influenced by many factors

• Tests will increasingly rely on multiple platforms with the need for interpretive support

• Fundamental changes to test reimbursement and regulatory review are required to support delivery of companion diagnostics to patients
“More than any time in history, mankind faces a crossroads. One path leads to despair and utter hopelessness, the other to total extinction. Let us pray that we have the wisdom to choose correctly.”

- Woody Allen