Identification to Implementation: Partnering with Your Laboratory Through Biomarker and Companion Diagnostic Development

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Chief Scientific Officer

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Focus on CDx

An industry trend establishing permanent strongholds in pharma and IVD sectors

Promise and potential:

- Improve probability of approval
- Accelerate the approval of new drugs
- Increase therapeutic benefit by ensuring: Right drug, Right patient, @ Right time
- Economic benefit, both short and long-term
- Market growth

Source: Personalized Medicine- The Path Forward, McKinsey & Company 2013
CDx Adoption in Oncology and Beyond

Biomarker-driven drug development is driving CDx strategy across therapeutic areas

• Led by oncology, CDx expanding broadly into other therapeutic areas
• 22% of the Rx in pivotal trials are developed in a biomarker-defined patient population*
• Between 2012-2015, 58% of the 189 oncology Rx under development have an associated biomarker*
• By 2017, 20 out of the 34 oncology Rx expected to launch will be targeted to biomarkers*
• 500+ clinically relevant biomarkers
• >85 CDx assays on-market

Source: Pharmgenomics Pers Med. 2015; 8: 99–110
According to recent data from McKesson Specialty Health/US Oncology Network (MSH)

US FDA-approved companion diagnostic drugs (2012)
Key Factors For Successful Development Of CDx

- Not every drug will benefit from or require a CDx
- CDx is only as strong as the underlying science
- Biomarker analysis drives critical decision-making for CDx development
- Good knowledge of the biology of the biomarkers
- Fit-for-Purpose assay development and analytical validation
- Clear strategy for deployment in trials and intended use
- Defined scoring/reporting rules
- CHANGE CONTROL
- Solid understanding of the use of CDx and assay format in clinical space
## Building Better CDx Together:

*Develop a clinically and commercially viable CDx strategy*

<table>
<thead>
<tr>
<th>Build a solid biomarker foundation</th>
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<tbody>
<tr>
<td>• Establish a strategy for identification of candidate biomarkers</td>
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<tr>
<td>• Confirm and validate using orthogonal methods, engaging external expertise as needed</td>
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<th>Develop a clinically viable CDx strategy</th>
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<td>• Demonstrated assay robustness and clinical utility</td>
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<tr>
<td>• Ease to use: consider real-world feasibility, including platform, sample type/collection device, pre-analytics, stability, throughput, practicality, % of test repeats and generation of unambiguous results</td>
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<th>Engage all partners earlier</th>
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<td>• Leverage partner expertise during each stage of development</td>
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<td>• Constant communication between Rx, Dx, and CRO is invaluable for risk mitigation</td>
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Q² Solutions: Bringing Biomarkers to the Clinic
A biomarker-focused central laboratory combining clinical and diagnostics expertise

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Consulting
Portfolio & Strategy Planning
Clinical Trial Execution

Laboratories

Real World and Late Phase
Technology Solutions
Patient and Provider
Engagement
Product Marketing and Sales

Diagnostic Testing
Diagnostic Products
Healthcare IT
Wellness and Risk Management
Employer Health

Drug Screening
Informatics

Clinical Trials

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Clinical Trials
**CDx Conventional IVD Manufacturer-Lab Partnership**

Roles and responsibilities for 2-party CDx development (lab + IVD vendor)

**Pre-study**
- Install, validate & operate Dx platform
- Perform Dx assay transfer, proficiency training & testing
- Develop study specific SOPs
- Distribute collection device and sample handling instructions

**In-study**
- Provide technical, medical
- Monitor laboratory & sample QC
- Adhere to CDx assay protocol
- Monitor sites, logistics, pre-analytics
- Receive and process samples
- Test and report
- Collect data

**IVD Vendor**
- Technology Development
- Assay Design/R&D
- Regulatory (PMA/510k)

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CDx conventional Pharma-Lab Partnership

Roles and responsibilities for 2-party CDx development (lab + pharma)

Pharma
- Drug Development
- Early Biomarker/R&D
- Protocol Development
- Regulatory (IND)

Test Oversight Study Execution

Drug Biologic

Pre-study
- Assess feasibility of clinical assay*
- Select methodology and platform*
- Provide CDx strategy/regulatory support
- Validate and deploy the assay
- Develop study specific SOPs
- Distribute collection device and sample handling instructions

Laboratory

In-study
- Provide technical, medical and regulatory support
- Adhere to CDx assay protocol
- Monitor sites, logistics, pre-analytics
- Receive and process samples
- Test and report
- Monitor laboratory & sample QC
- Collect data

*LDT prototype to lockdown assay

Q² Solutions
**CDx Tripartite Partnership Model**

Integrated partnering to support optimized CDx development and commercial success

**Pharma**
- Drug Development
- Early Biomarker/R&D
- Protocol Development
- Regulatory (IND)

**IVD Vendor**
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**Study Execution**

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**In-study**
CRO laboratories as CDx “test kitchens”
Labs promote IVD partner success by providing real-world perspective for assay optimization

- Are sites able to perform the sample acquisition and pre-analytical steps?
- Will the sample type & collection device allow for minimal test rejection?
- Is the analyte stable enough to support consistent valid test results?
- Is the assay robust enough to support consistent valid test results?
- Is the assay complexity manageable for specialty labs? Reference labs?
- Is the instrument/platform user-friendly (ex: automation, test reporting)?
- Will test generate unambiguous results?
- Will the test result be subject to technician/pathologist subjectivity?
- Will the test provide a clear medical decision enabler?

Laboratory feedback at each stage of CDx development can save time, cost, and drive protocol optimization
**Case Study: Gene-Based CDx Collaboration**

*3-party engagement development of prototype assay and central lab testing*

- Large pharma collaborated with Q² Solutions* to develop and perform tissue-based FISH biomarker assays for use in oncology clinical trials
- Through strong working relationship, Q² Solutions enlisted lead IVD company to co-develop FISH prototype assay for patient screening
- Analytical method transferred to global labs to support testing for CDx studies
- **Benefits for Rx/IVD partners:** Collaboration enabled reduced cost for pharma, submission-ready data, and reduced development timelines

*Q² Solutions refers to either legacy Quintiles or legacy Quest central laboratories*
Case Study: Pathologist Expertise for IHC CDx

Development of scoring methodology for Rx-sponsored study using Dx-provided assay

- Large pharma works with Dx company for IHC-based CDx for NSCLC/Melanoma
- Pharma/Dx approached Q² Solutions to develop scoring methodology for follow-on indications using proprietary Dx-provided assay for Phase I studies
- Pathologists engaged to define scoring and assay protocol for 6+ indications in collaboration with Rx pathologist and support from Dx
- Clinical sample testing underway at multiple sites; ongoing support for regulatory discussions with Dx and Rx sponsors in preparation for Phase II studies
- **Benefits for Rx/IVD partners:** External pathology expertise, familiarity with Dx partner CDx best-practices, strategic program-wide pricing

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Implementing ‘Innovative’ Biomarkers towards CDx

Central laboratory expertise can support transition from RUO to IVD

- Focus on clinical biomarker testing brings exposure to new platforms in a research setting.
- As these technologies and platforms come online as Dx, laboratories and scientists are equipped to transition quickly into “CDx mode”.
- Strong working relationships with Dx companies.
- Required laboratory scientists to have industry leadership experience/expertise with most cutting edge technologies and have good relationship with IVD manufacturers.

Thorough understanding of both inherent biomarker challenge and technology pros/cons are required to implement innovative solutions.
Case Study: PGx-Guided Program Optimization

Pharma sponsor enlists genomics laboratory for pharmacogenomics R&D

- Significant incidence of AEs observed in Phase III study
- Retrospective array-based profiling of banked blood samples by Q²Solutions|EA Genomics identified potential genetic biomarkers associated with AE
- Targeted sequencing panel developed with sponsor and Q²Solutions|EA Genomics to confirm specific germline mutations, predict response, and improve understanding of MOA

- **Benefits for Rx/potential IVD partners:** Robust data to support CDx strategy generated by lab familiar with key aspects of NGS CDx validation (e.g. analysis software, BFX pipelines, platforms, validation, etc.)
NGS Technologies are Transitioning From R&D to Clinic
A paradigm switch from retrospective patient screening to prospective matching of patients’ genomic profile and symptoms to known targeted therapy

NGS transition to clinic will require reducing TAT, costs, and complexity of data analysis, and more robust bioinformatics algorithms to link tumor genotype to targeted therapies

End to End Support for CDx Development and Commercial Success

Companion Diagnostic Pipeline

- **Biomarker ID & Assay Development**
- **Prototype Assay & Technical Feasibility**
- **Analytical Validation**
- **Clinical Validation**
- **Diagnostic (Drug) Registration**
- **Launch and Commercial Support**

**Goal**
- MOA & Population Studies
- Platform / Sample Strategies
- Assay Performance and Robustness
- Clinical Utility
- Regulatory Strategies (IVD/LDT)
- Adoption Strategies

**Complexity**
- Prognostic vs predictive biomarker?
- Rapidly changing technologies
- Interlab reproducibility
- Coordination with Rx development
- Changing regulatory guidance
- Multiple stakeholders in fragmented market

**Solutions**
- Scientific collaboration & R&D/genomics labs
- Multiple Dx company relationships & ADL’s
- Global harmonized labs
- Coordinated clinical and lab PM/DM
- Regulatory experts with regional knowledge
- HEOR and commercial consulting
**The Laboratory Partner: An ally in CDx development**

Key opportunities to leverage laboratory expertise from biomarker ID to CDx launch

1. Biomarker R&D services and CDx strategic consulting
2. Assay development expertise and Dx partnerships
3. Assay optimization/ Bridging study/ CLIA laboratory testing
4. Global study execution for pivotal CDx trials
5. Regulatory support, including BIMO/FDA inspection support
6. Commercial, diagnostic, and late-phase expertise

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**Flexible Support Across the CDx Life Cycle**

- **Rx**
  - Pre-Clinical
    - Phase I
  - Clinical
    - Phase II
    - Phase III
  - FDA Filing/Approval
  - Launch

- **Dx**
  - Research/ Biomarker ID
  - Develop Prototype
  - Analytical Validation
  - Clinical Validation
  - Drug-diagnostic Registration
  - Commercialization

- **CRO**

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Q² Solutions
Conclusion

The benefits of long-term Rx/Dx/CRO partnerships

- Rx and/or Dx standards and best practices
- Combined expertise and thought leadership
- Contracting and operational efficiencies
- Expert review of feasibility and methods
- Strategic pricing (central Lab/CDX testing)
- Early engagement for implementation of new technology
Thanks
Questions?