Life Sciences Consortium
Task Force Report to The National Cancer Policy Forum Workshop

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U.S. Medical Science Lead, Emerging Products
AstraZeneca - Oncology
Outcome: CEOs agreed to ask and answer one important question:

“What are we doing in our own companies with respect to cancer awareness, prevention, early diagnosis and optimal treatment?”
What is the LSC?

• **Membership:** Representatives from CEO-RT Companies Involved in Health Research

• **Mandate:** Accomplish Together What No Single Company Might Consider Alone

• **Methods:** Engage Academic Centers, NCI and Others as “Safe Harbors” in Shared Areas of Mutual Interest

*Be Bold And Venturesome*
What Makes LSC Unique?

Consortium of Industry Oncology Programs Seeking Collaborative Accomplishments

Viewed as Collaborative by the DoJ
LSC Priorities

Provide Safe & Effective New Medicines … Faster

- *Decrease* the Time for Patients to Enter Cancer Clinical Trials
- *Develop* a Pool of Pre-Competitive Intellectual Property for Biomarkers
- *Diminish* the Regulatory Burden of New Cancer Drug Approval
Product Development Time Comparisons

Decreasing the Time to Enter Trials

- *What* is the rate-limiting factor for opening a clinical trial?
  - *What researchers thought:* processing by Institutional Review Board (IRB)
  - *What the data showed:* contracting & budgeting!
Does time make a difference?

• Yes, for three reasons:
  1. ~$1M of sales is lost every day a drug is not in the market
  2. Every day, there are ~3,800 new cancer diagnoses and ~1,500 cancer deaths
  3. Each day of delay is more likely a study will fail to achieve its goal
Importance of Time

- **64%** the critical Phase III clinical trials “never finish” i.e., did not enroll enough patients to answer a scientific question
- **29%** of oncology trials started result in **zero** patients
AMC Contract Execution Cycle Time 2008

Days to contract execution

Of the 18% of Sites with greater than 120+ Days AMCs sites make up > 90%
Contract Negotiation:
A Key Bottleneck to Starting Clinical Trials

• Collaboration Between LSC Companies (11), Cancer Centers (14), and Cooperative Groups (5)
• *Hogan & Hartson* Reviewed Redacted Final Agreements (49) and Agreement Templates (29)
• *Hogan & Hartson* Obtained Letter from the DOJ
• Finding: Two-thirds of the Language in the Approved Agreements Converged

• Results: the “START” Clauses
“START- II”

Pre-Clinical Trial Contracts

• Use the Same Methods to Expand *START Clauses* to Studies of New Industry Drugs with Academic Collaborators in the Laboratory
  - Intellectual Property Risk is Greater
  - The Potential Results of Early Partnering with Academic Centers of Excellence Could Be Considerable
  - There are Currently No Standards Governing the Important Areas Covered in the *Clinical START Clauses*
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Create a Pre-Competitive Pool of IP For Drug Development

• Biomarkers

• Potential Approach: LSC Companies Present Programs *Under Confidentiality* to NCI
  - NCI Selects Most Promising Markers for Co-Investment and Collaboration
  - NCI Invests in “Gaps”

• Validated Marker Enters Public Domain
## Biopsy Assays

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<th>Concept</th>
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<tr>
<td>Target</td>
<td>Application</td>
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<td>Feasibility</td>
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<td>γ-H2AX Protein (tumor)</td>
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<td>ELISA</td>
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<td>Top 1 Protein</td>
<td>TOPO Inhibitors</td>
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<td>MET TK domain and Grb2 Docking Site</td>
<td>Kinase Inhibitors</td>
<td>IFA Commercial Reagents</td>
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<td>PARG mRNA</td>
<td>PARP Inhibitors</td>
<td>RT-qPCR</td>
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<td>RT-qPCR</td>
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<td>PARP 1,2 Activity (PAR levels)</td>
<td>PARP Inhibitors</td>
<td>IA</td>
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<td>PARP 2 mRNA</td>
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<tr>
<td>Stem Cell Proteins -ALDH 1A1 -OCT 3/4 -NANOG -CD44v6</td>
<td>Tumor Stem Cell Inhibitors</td>
<td>IFA</td>
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**KEY:**
- **P** Completed
- **X** Dropped
- **CA** Commercially Available
- **NA/UIN** Not Applicable or Uninformative
- **R** Ready
- **H** On Hold
- **In Progress**
- **Delayed**
- **Technical Difficulty**
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<td>Tyrosinase mRNA Melanoma Marker</td>
<td>Melanoma Drugs</td>
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**Normalization (Denominator) Assays**

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<th>Beckman Coulter ACT</th>
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<td>Number of PBMCs (%)</td>
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<td>Number of PBMCs (cell #)</td>
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Accelerating NCI’s Timeline to Personalized Medicine in Cancer Treatment

Pre-Clinical START Clauses

- Development of biomarker assays
- Pharmacology, Toxicology, Formulation
- First-in-Human Clinical Trials
- Prospective biomarker validation clinical trial

Clinical START Clauses

- Discovery, pre-clinical efficacy
- Parallel track imaging agent development
- Early combination & combined modality trials

'10 '11 '12 '13 '14 '15

FDA
No Pharmacodynamic Marker: Phase III Trial Where 25% Patients Show Treatment Effect

N = 400 patients total
25% eligible pts Rx effective
50 with median OS 27 mo
150 median OS 22 mo
200 placebo median OS 22 mo
Effect of Trastuzumab in HER 2 Positive Breast Cancer

Overall Survival

N = 469  
RR = 0.76  
p = 0.025

Probability Alive

- H + CT
- CT

Months 5 15 25 35 45

25.4 mo (∆25%)  
20.3 mo
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• Decrease the Time for Patients to Enter Cancer Clinical Trials
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Improving the “Critical Path” for New Cancer Therapies

- **Collaborative initiative convened by Brookings and Friends of Cancer Research**
  - Supported by ASCO, AACR, Susan G. Komen, and Lance Armstrong Foundation
  - With full participation from FDA, NCI, patient advocates, and life sciences industry

- **Conference on Clinical Cancer Research**
  - September 14, 2009; Washington, DC
    - Data Submission Standards
    - Auditing PFS Endpoints
    - Targeted Therapies and Companion Diagnostics
    - Evaluating Two Investigational Agents in Combination
Optimizing Data Submissions

- The amount of data collected in Phase III trials for supplemental approvals is excessive. *Is there a more effective approach?*
  - Grades 1 or 2 *Adverse Events*
  - *Adverse Events* start/stop dates
  - Concomitant meds

- **ASCO formed the** *Data Optimization Working Group*
  (8 trials from CALGB, GSK, Eli Lilly, Novartis, and Genentech)

- **Recommendations (for qualified supplemental trials):**
  - *Adverse Events* data collection in subsets of patients
  - No collection of concomitant meds or start/stop dates for *Adverse Events* except by cycle
  - Guidance from FDA
What Makes LSC Unique?

Engages 3rd parties as “Safe Harbors”