Data-driven Medicine in the Age of Genomics

Overcoming the Challenge With Advanced Molecular Analytics

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Life and Health Sciences Strategic Development
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Safe Harbor Statement

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Where is the need and the opportunity?
Industry Trends

**Significant reduction in cost of genome sequencing**

**Increase in real-world data**

- Will you use secondary health data within the next 2 years?
  - Provider: 70%
  - Pharma: 61%
  - Payer: 54%

**Aggregation and analysis of Big Data**

**More than half of clinical trials** already have a molecular biomarker component

**Patient stratification** to identify population subsets most likely to respond to a therapy

**Cloud technologies** are enhancing R&D collaboration
Effective Use of Healthcare Data

Same data, different context

Enterprise Healthcare Analytics
- Healthcare Data Warehouse Foundation (HDWF)
- Oracle Healthcare Analytics Data Integration
  - Source-friendly interface
  - MDM
  - Data quality and business rules framework
  - Late-arriving data management, versioning, etc.
- Application Toolkit (data mart and self service BI)

Translational Research Center/InForm AMA
- Cohort Explorer
  - Patient Cohort ID & Selection
  - Statistical & Scientific Analysis
  - Biomarker Discovery
- OMICS Data Bank
- Precision Medicine
- Inform AMA

Health Information Exchange
- Master Person Index (OHMPI)
- Healthcare Data Repository
- HIG
- HIM
- Care & Disease Management
- Utilization Management
- Performance Measurement

Health Sciences Network
- Protocol Validation & Recruitment
- Safety & Pharmacovigilance
- Comparative Effectiveness Research
- Provider-Pharma Convergence
- Cloud Platform
Big Data Intensifies the Challenges...

VOLUME  VELOCITY  VARIETY  VALUE
Today’s Research & Development Process
Linear: Focus on Optimization and Analytical Insights

<table>
<thead>
<tr>
<th>Discover</th>
<th>Develop</th>
<th>Post Marketing</th>
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</thead>
<tbody>
<tr>
<td>Plan</td>
<td>Study Setup</td>
<td>Study Conduct</td>
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<tr>
<td>Reduced cycle times</td>
<td>Traceability and compliance</td>
<td>Solution simplification</td>
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</table>
Effectiveness of Most Drugs

<table>
<thead>
<tr>
<th>Major Drug</th>
<th>Drug Effectiveness</th>
<th>Cost of Ineffectiveness to Healthcare System</th>
</tr>
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<tbody>
<tr>
<td>Hypertension Drugs</td>
<td>10-30%</td>
<td>$390 million – $1.2 billion</td>
</tr>
<tr>
<td>Heart Failure Drugs</td>
<td>15-25%</td>
<td>$345 million – $575 million</td>
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<tr>
<td>Anti Depressant Drugs</td>
<td>20-50%</td>
<td>$2.3 billion – $5.8 billion</td>
</tr>
<tr>
<td>Cholesterol Drugs</td>
<td>30-70%</td>
<td>$3.8 billion – $8.8 billion</td>
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<tr>
<td>Asthma Drugs</td>
<td>40-70%</td>
<td>$560 million – $1.0 billion</td>
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Source: The Personalized Medicine Coalition
Transformative R&D Process from Linear to Continuous

Data Access and Utilization Across the Lifecycle

- Targeted treatments
- More effective trials
- Faster time to market
- Improved safety
- Dramatically lower costs
# Accelerated Drug Discovery Through Biomarkers

<table>
<thead>
<tr>
<th><strong>Formulated To</strong></th>
<th><strong>Results</strong></th>
<th><strong>Targets</strong></th>
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</thead>
<tbody>
<tr>
<td><strong>Imatinib (Gleevec)</strong></td>
<td>First in class targeted cancer therapeutic</td>
<td>Targets the BCR-ABL protein only occurring in Chronic Myelogenous Leukemia (CML)</td>
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<td></td>
<td>Now considered <strong>standard of care</strong> for Myelogenous Leukemia (CML)</td>
<td>Indication expanded to Gastrointestinal Stromal Tumors (GIST) with KIT mutations</td>
</tr>
<tr>
<td><strong>Crizotinib (Xalkori)</strong></td>
<td>Targets ALK protein, mutated in 7% of lung cancers</td>
<td>FDA approved from a trial of only 255 patients with the biomarker</td>
</tr>
<tr>
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<td><strong>3 years</strong> from biomarker mutation discovery to approval</td>
<td></td>
</tr>
<tr>
<td><strong>Ivacaftor (Kalydeco)</strong></td>
<td>Targets CFTR G551D mutation, present in 5% of cystic fibrosis patients</td>
<td>Phase-III trial approval based on 161 subjects</td>
</tr>
<tr>
<td></td>
<td><strong>10.5% mean improvement</strong> in lung function</td>
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Biomarkers are Critical for Achieving Success

82% of projects with an efficacy biomarker were active or successful in Phase IIa
- compared to 30% of projects without such biomarkers

85% of all projects now include a “personalized healthcare strategy”
- initial analysis shows a 400% increase in success rate

Source: Nature Reviews | Drug Discovery, Lessons learned from the fate of AstraZeneca’s drug pipeline: a five-dimensional framework May 16, 2014

Right Target
- Strong link between target and disease
- Differentiated efficacy
- Available and predictive biomarkers

Right Tissue
- Adequate bioavailability and tissue exposure
- Definition of PD biomarkers
- Clear understanding of preclinical and clinical PK/PD
- Understanding of target liability

Right Safety
- Differentiated and clear safety margins
- Understanding of secondary pharmacology risk
- Understanding of reactive metabolites, genotoxicity, drug-drug interactions
- Understanding of target liability

Right Patients
- Identification of the most responsive population
- Definition of risk-benefit for given population

Right Commercial Potential
- Differentiated value proposition versus future standard of care
- Focus on market access, payer, and provider
- Personalized healthcare strategy, including diagnostic and biomarkers
But Significant Technology Challenges Exist

- Acquire, normalize, and combine clinical trial, OMICS, and other real-world data
- Operate across studies and silos of information
- Manage petabytes of OMICS data and ensure real-time information queries
- Maintain interoperability between open source and enterprise software
- Collaborate in the cloud while ensuring HIPAA compliance
How can Technology help?
Normalized, Standardized and Integrated Platform for a Pharma/Healthcare Research Database

Source Systems
- Clinical/EHR
- Study/EDC
- Omics
- Biobank
- Operations
- Financial
- Public Domain
- Claims

Analytics Applications

Analytics Tools
(Visualisation, Query Engines, Statistical Languages ...)

Healthcare Data
(Administrative, Clinical, Financial...)

Omics Data
(Genomics, Reference Data Sets...)

Data Integration, MDM & Other Services

Security
Platform for a Pharma/Healthcare Research Database

Analytics Applications
- Cohort Exploration
- Cohort Analytics
- Customer/Partner Custom Analytic Apps
- Statistical Apps (e.g., Survival Analysis)
- World-wide Researcher Collaboration (HSN)

Analytics Tools
- Reporting
- Dashboards
- Ad Hoc Queries
- Strategy Management
- R Statistical Language
- Big Data / Hadoop
- Mobile Analytics
- Information Discovery
- Data Mining
- Scorecard
- Real Time Decisions
- Unstructured Data Analysis
- Bring your own
- Spatial

Healthcare Data
- Interface Tables
- Consolidation, Integration & Validation
- Healthcare Data Model
- ETL from sources

Omics Data
- Omics Data Model
- Load
- Annotate
- VCF, GEP, CGI, MAF...
- Ensemble, HUGO, Swiss-Prot...

Data Integration, Master Data Management & Other Services
- De-Identification
- Terminology Services
- Unit of Measures
- Secure Files
- Data Quality
- Data Quality Governance
- In memory analysis
- Re-Identification
- Patient Linkage
- NLP
- Job Scheduling
- ETL
- End to End Data Lineage
- HW SW Integration
Clinical Development Integrated With Advanced Molecular Analytics

- Must be fully HIPAA compliant
- Need to integrate ePRO, EDC, CTMS data
- Single study and cross-study analysis of biomarkers
- Systematic way to manage genomic data generated in a clinical trial
- Genomic profile and analysis reporting
- Integrates with well-established public domain/RWD data for joint analysis with your own data

Enabling Organizations to Incorporate Genomic Data into Clinical R&D for Targeted, Biomarker-Driven Clinical Trials
Potential Workflow During a Study

- Genomic profiling
- Molecular data analysis for statisticians
- FDA submission
Potential Workflow Post-Study

Study 1

Study 2

Study N

- New biomarkers
- Drug repurposing idea
- Combination therapies
- Understanding why a trial failed
Pharma: Driving More Efficient and Effective Trials and Submissions

**Phase Ia Study**
- Genetic Analysis Data
- Experimental Group
- Control Group
- Integrated Data Analysis
- Responders
- Non-Responders
- Clean Signature Responders
- Muddy Signature Responders
- Muddy Signature Non-Responders
- Clean Signature Non-Responders

**Integrated Data Analysis**
- Phase Ia Clinical Study Design #1
- Phase Ia Clinical Study Design #2
- Phase Ia Clinical Study Design #n
- Integrated Data Analysis Approach

**Refined/Proposed Genetic Screening Criteria**
- Suspected Efficacy Biomarker Defined
- Efficacy Biomarker Confirmed

**Multi-Study/Program Integrated Analysis Approach**
- End Phase Ila Go/No-Go Decision
- NDA

**Public Domain Genetic Database**
- Internal Pre-Clinical Genomic Database

**Pharma: Driving More Efficient and Effective Trials and Submissions**
Translational Medicine Analytics Platform

Source Systems
- Clinical/EHR
- Study/EDC
- Omics
- Biobank
- Public Domain
- RWD
- Claims

Oracle Platform
- Data Integration
- Oracle Database
- OMICS Data Bank
- Healthcare Data Model

Analytics Application Ready
- Biomarker Discovery
- Protocol Validation & Patient Recruitment
- Patient Stratification
- Clinical & Molecular Data Collection for Trials
- Comparative Effectiveness
- Structured & Unstructured Data Analysis

Oracle
- OHMPI * NLP * Terminology Services
- Big Data Appliance & Exadata

Partner
- Spotfire
- Thomson Reuters

Open Source & Custom
- transSMART Foundation
- R

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Summary

• The “Old” model of clinical development is no longer sustainable
• The entire therapeutic discovery, development, use and reimbursement paradigm is rapidly evolving
  – Linear → Iterative feedback loop
• The volume of data is overwhelming, and is growing
• The pace of technology development is accelerating
• Healthcare policy, process and practice drastically changing:
  – No Outcome = No Income
• The challenges have never been harder and our ability to make a positive impact has never been greater