Data-driven Medicine in the Age of Genomics

Overcoming the Challenge With Advanced Molecular Analytics

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Safe Harbor Statement

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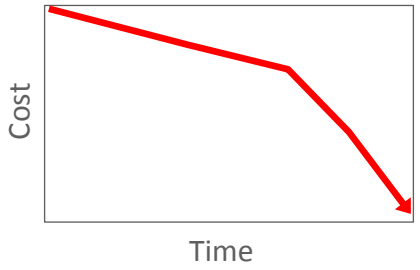
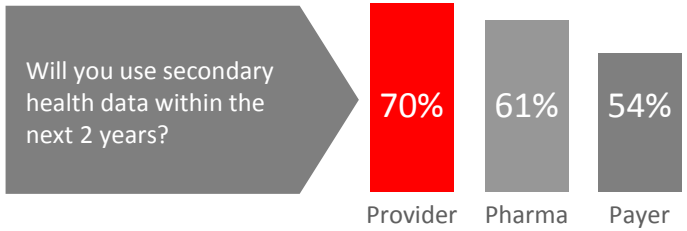
Where is the need and the opportunity?

Industry Trends

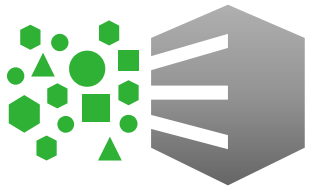
Significant reduction in cost of genome sequencing



Increase in real-world data



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

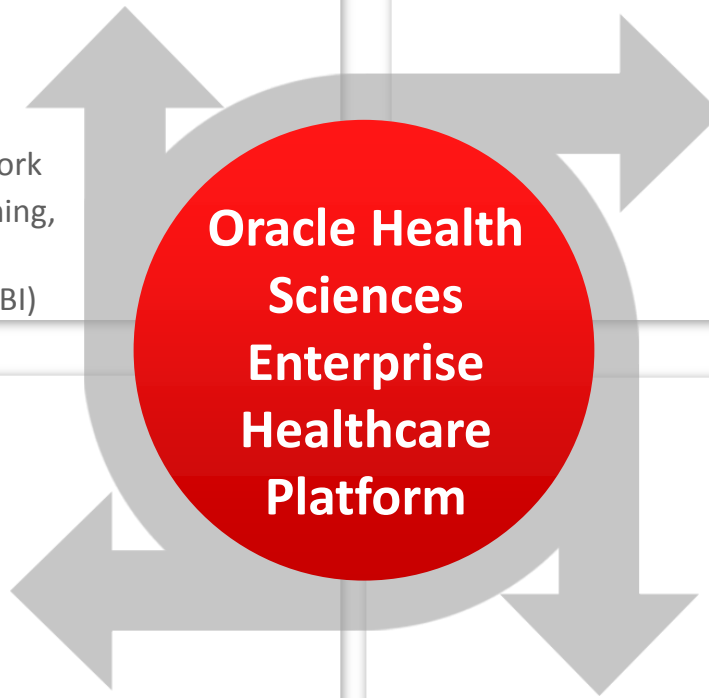
Same data, different context

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

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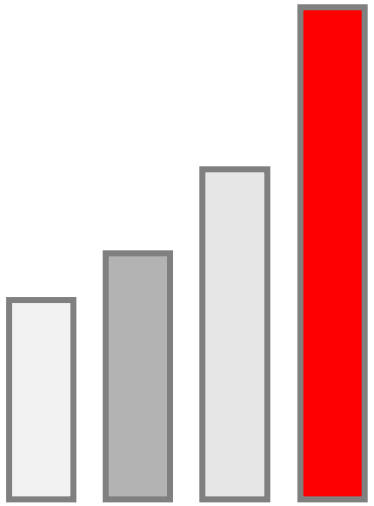
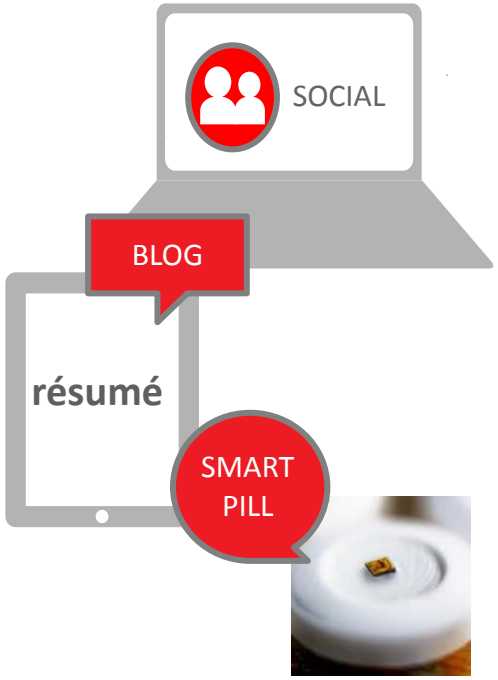
Big Data Intensifies the Challenges…



VOLUME

VELOCITY

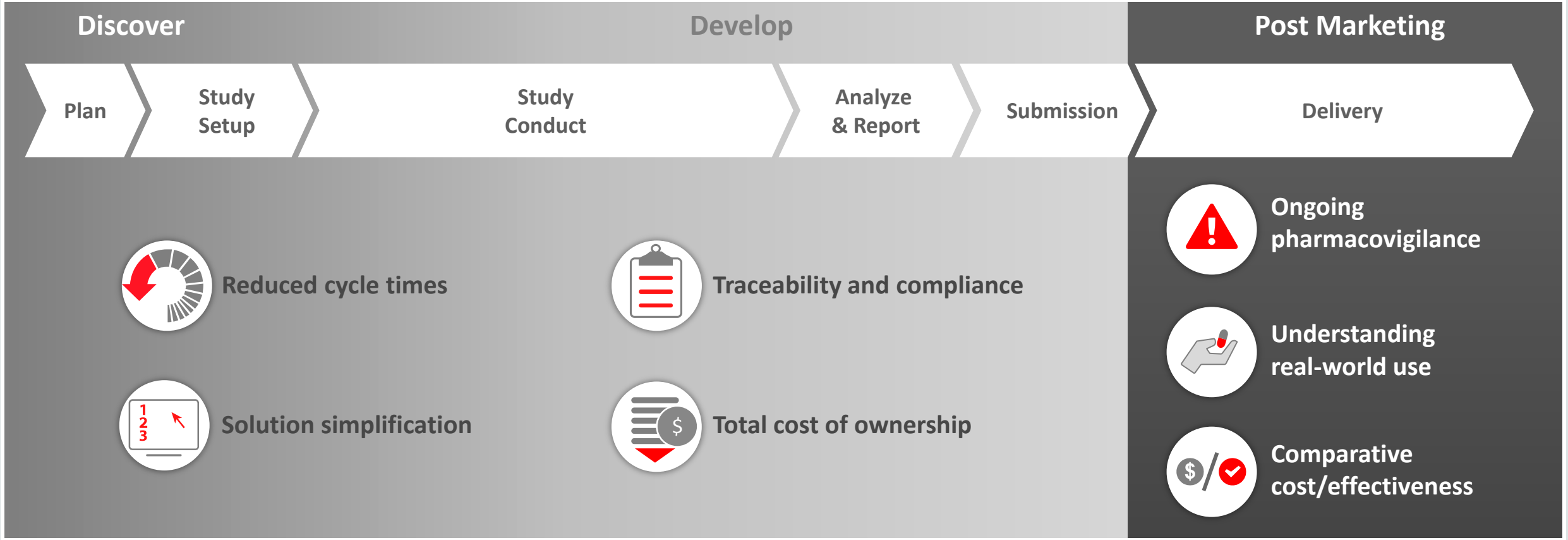


VARIETY

VALUE

Today's Research & Development Process

Linear: Focus on Optimization and Analytical Insights



Effectiveness of Most Drugs

Major Drug	Drug Effectiveness	Cost of Ineffectiveness to Healthcare System
Hypertension Drugs ACE Inhibitors	10-30% 	$390 million – $1.2 billion
Heart Failure Drugs Beta Blockers	15-25% 	$345 million – $575 million
Anti Depressant Drugs SSRIs	20-50% 	$2.3 billion – $5.8 billion
Cholesterol Drugs Statins	30-70% 	$3.8 billion – $8.8 billion
Asthma Drugs Beta-2-agonists	40-70% 	$560 million – $1.0 billion

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

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Accelerated Drug Discovery Through Biomarkers

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

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 verses future standard of care
- Focus on market access, payer, and provider
- Personalized healthcare strategy, including diagnostic and biomarkers

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But Significant Technology Challenges Exist

How to …

- **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

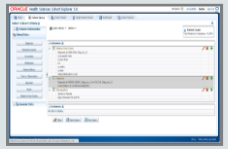
(Genomics, Reference Data Sets…)

Data Integration, MDM & Other Services

Security

Platform for a Pharma/Healthcare Research Database

Cohort Exploration



Cohort Analytics

Customer/ Partner Custom Analytic Apps

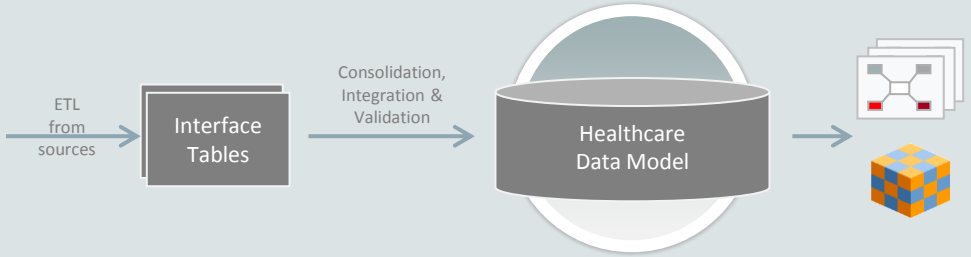
Statistical Apps(eg Survival Analysis)

World-wide Researcher Collaboration (HSN)

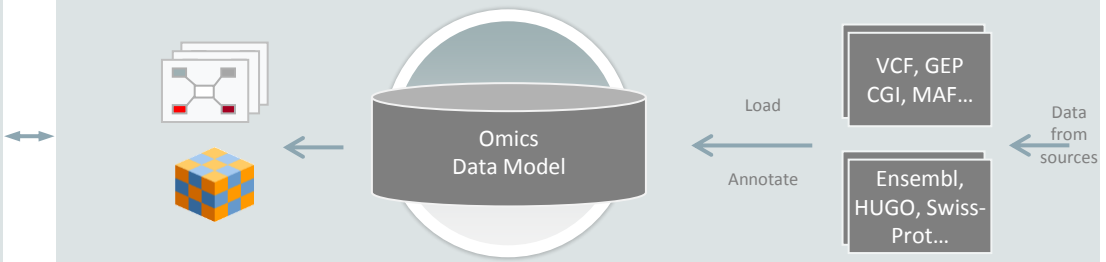
Analytics Applications

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

Analytics Tools



Healthcare Data



Omics Data

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

Data Integration, Master Data Management & Other Services

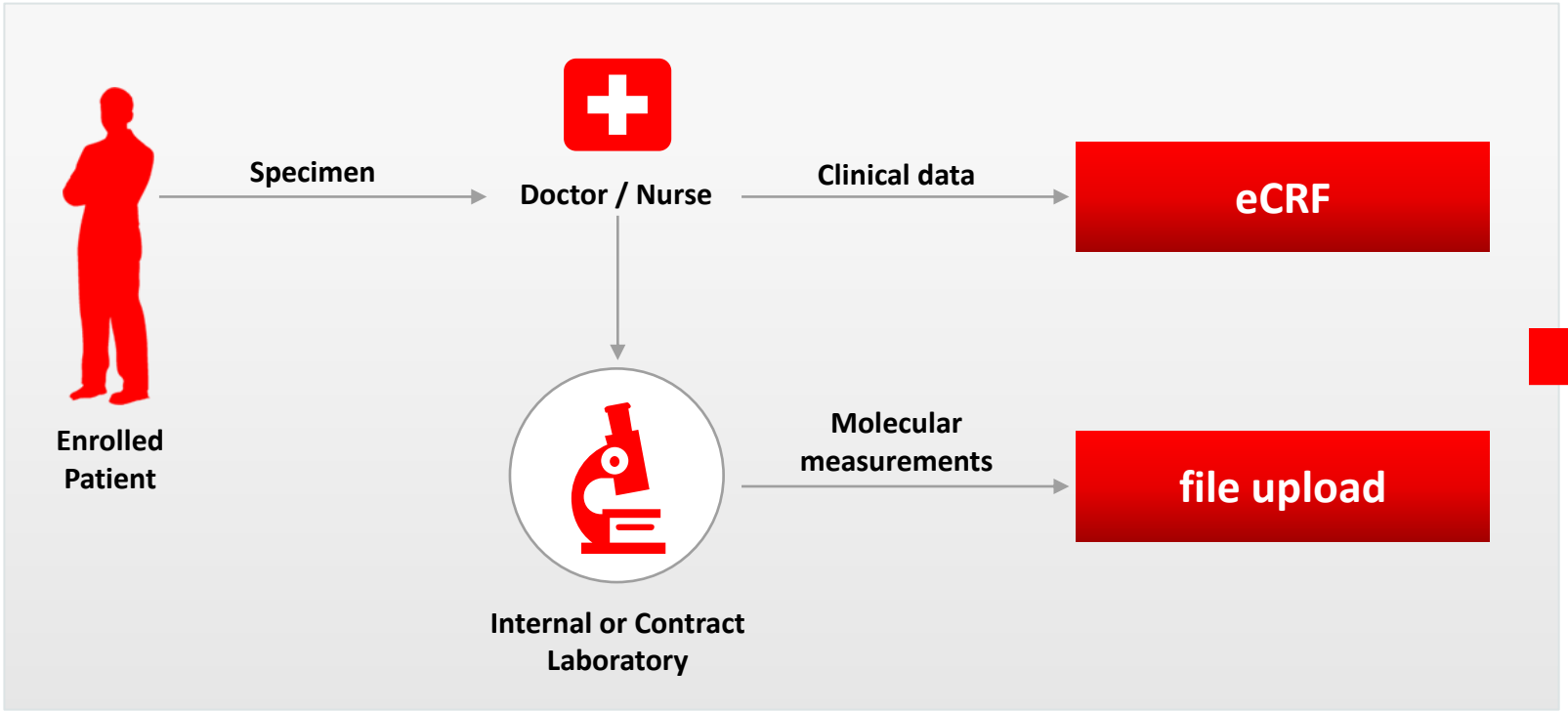
Security

Authentication | Provisioning | Role Based Security | Authorization | Row level security | Directories

Clinical Development Integrated With Advanced Molecular Analytics

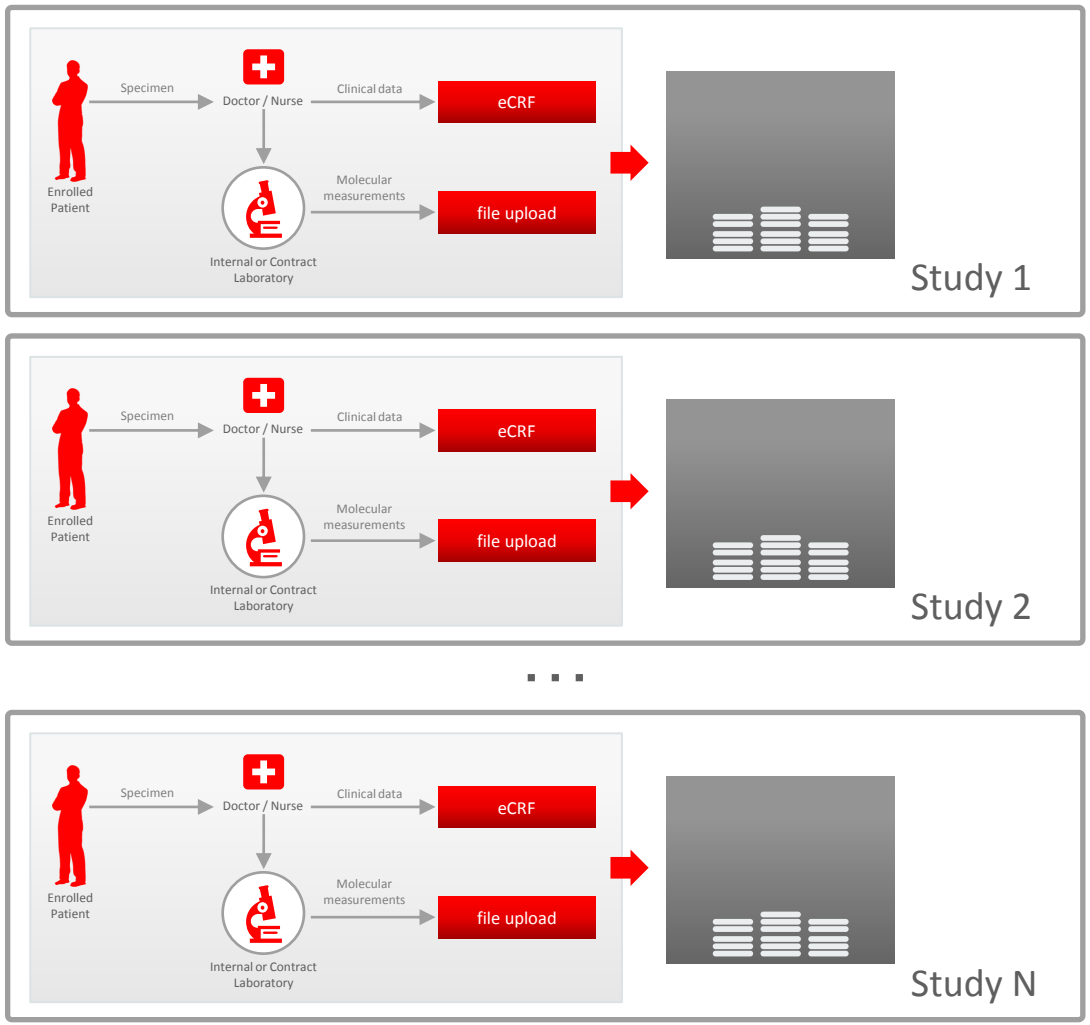
Enabling Organizations to Incorporate Genomic Data into Clinical R&D for Targeted, Biomarker-Driven Clinical Trials

Potential Workflow During a Study



- Genomic profiling
- Molecular data analysis for statisticians
- FDA submission

Potential Workflow Post-Study



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THE CANCER GENOME ATLAS

COSMIC Cell Lines Project
Catalogue of somatic mutations in cancer

BROAD INSTITUTE
Cancer Cell Line Encyclopedia

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Ensembl

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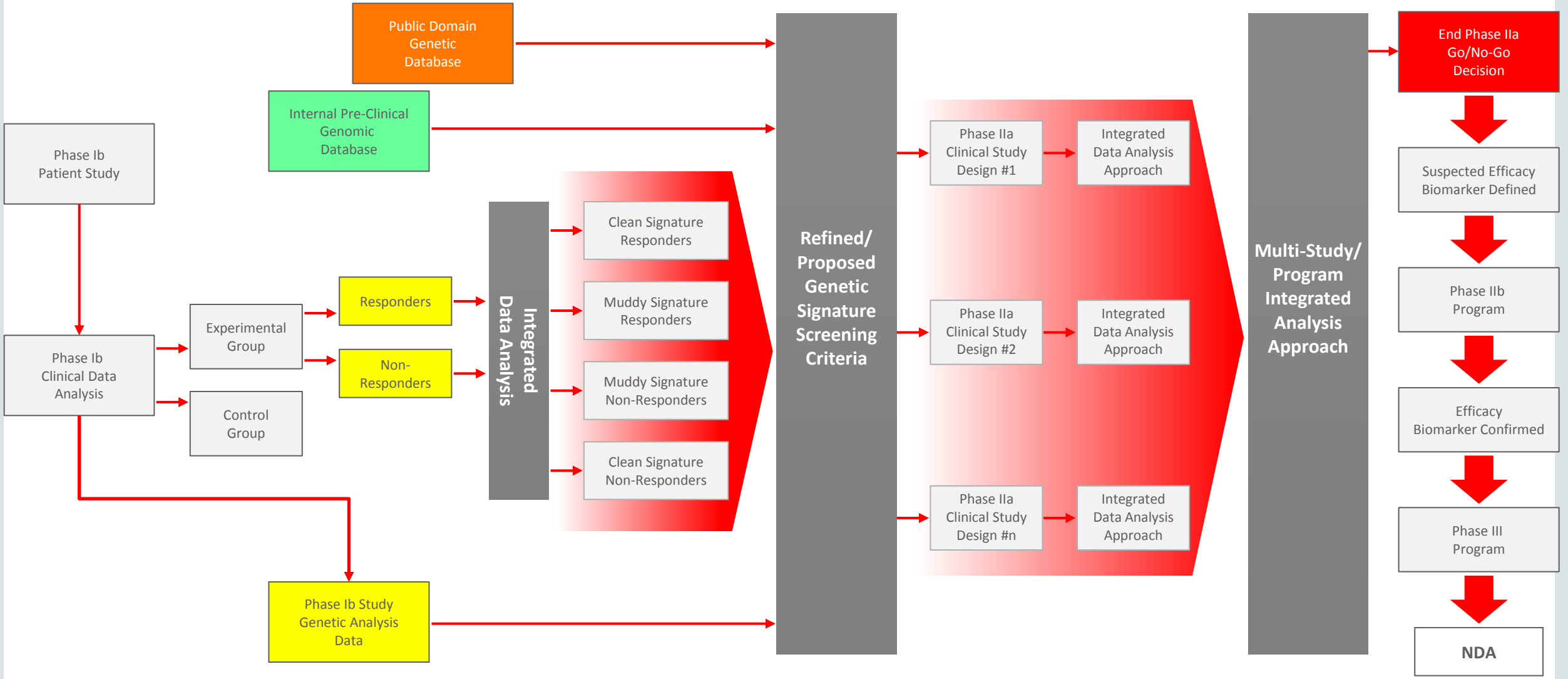
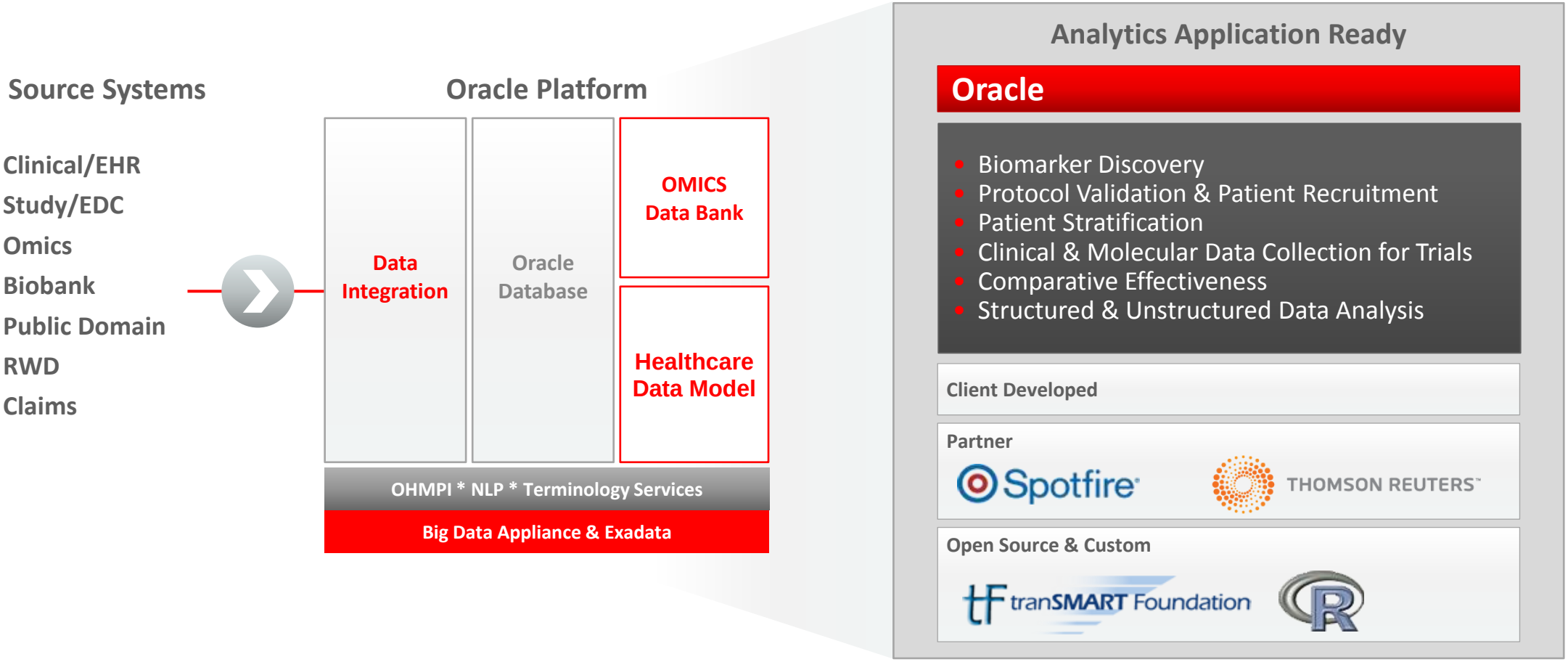
- New biomarkers
- Drug repurposing idea
- Combination therapies
- Understanding why a trial failed

Pharma: Driving More Efficient and Effective Trials and Submissions



Translational Medicine Analytics Platform



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

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