# Molecular Diagnostics and their Evolving Influence on the Healthcare System

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FROM **BOARDROOM TO BENCH**



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# Agenda

- **The Role of MDx in Personalized Medicine**
  - » Recent Industry Trends
  - » Evolution of Business Models
- Public Policy Considerations
- Future Directions


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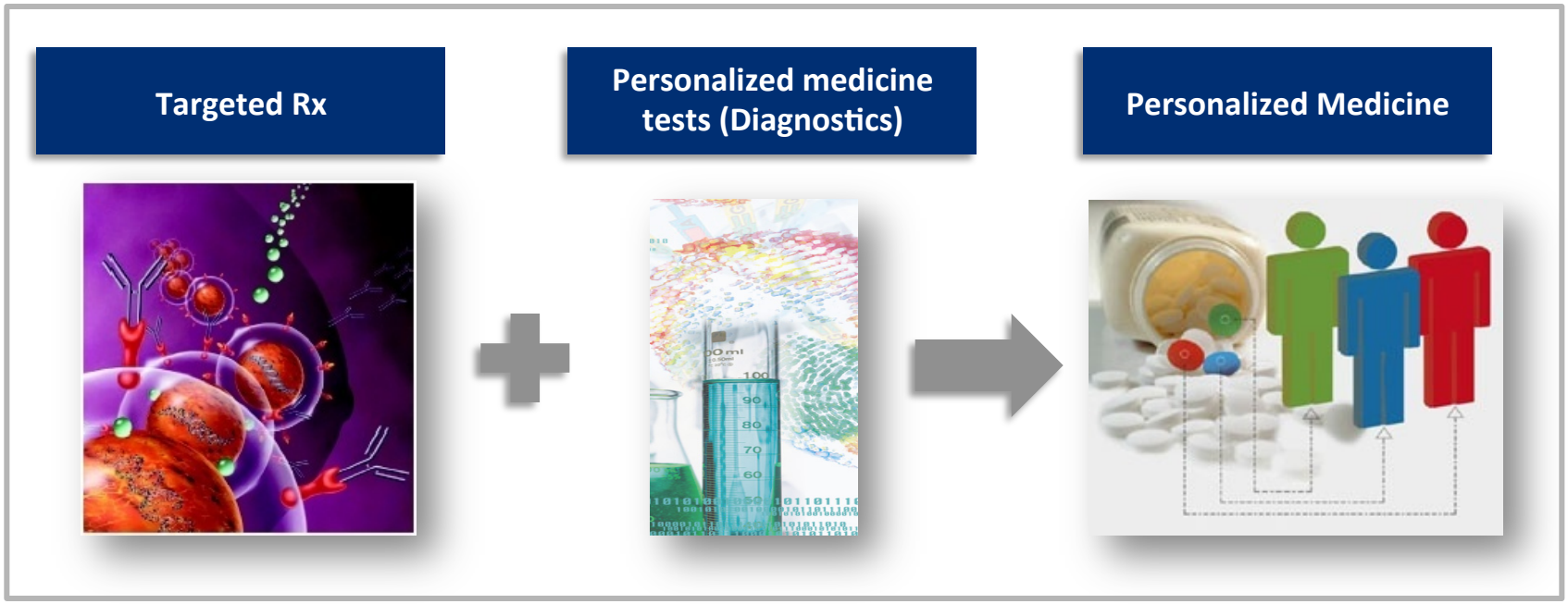
# What is Personalized Medicine (PM)?

The Right Therapy for the Right Patient, at the Right Time, with the Right Dose

Best responders to therapy are identified using Personalized Medicine Tests and then given the Targeted therapy at the right time to maximize efficacy and minimize adverse reaction




Source: Scientia Analysis



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# World of Healthcare is Changing -Healthcare stakeholders are increasingly interested in more personalized delivery medicine, creating a great catalyst not just for pharma …


## REGULATORS

- Greater integration of Rx and Dx for more efficient and safer clinical trials (e.g. critical path initiative)
- Increased vigilance on drug approvals
- Increased approval of tests that influence safety & efficacy of

## DIAGNOSTIC & PHARMA COMPANIES

- Research advances in biomarker discovery and systems biology is translating into more Dx tests
- Enables focused trials – smaller groups for shorter periods with better results
- Dx facilitates better Rx sales by enabling better market penetration and expansion

## PAYORS

- Payment for performance
- Payors are pushing for Rx-Dx integration, especially diagnostics that reduce healthcare expenditure e.g. Oncotype Dx

## PATIENTS & PHYSICIANS

- Increasing influence of patient advocacy groups
- Personalized medicine reduces unnecessary therapies, leading to fewer side effects

Source: Scientia Analysis



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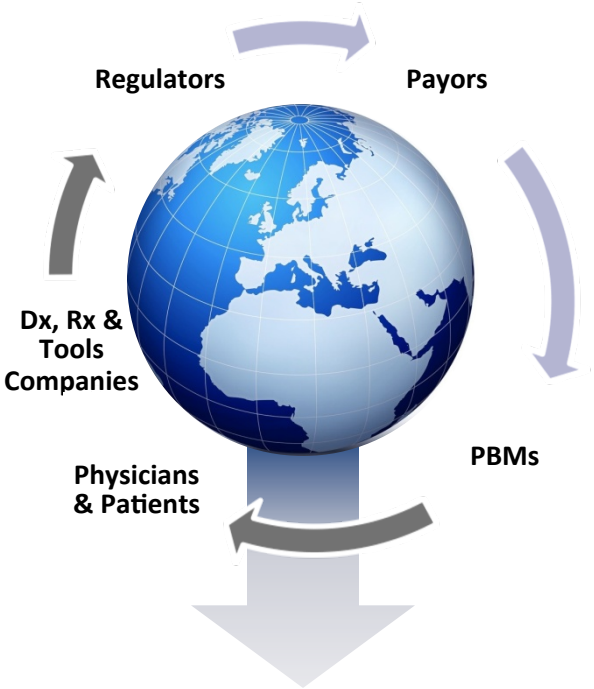
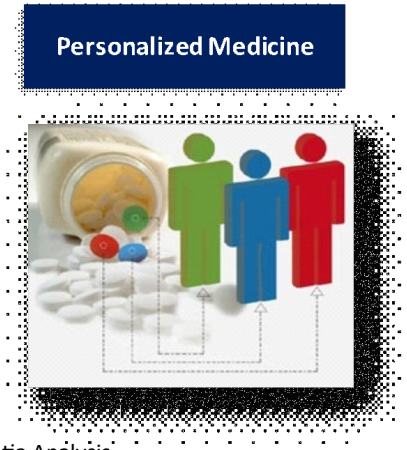
# … but also for hospitals and PBMs such that all the stakeholders are taking initiatives to capitalize on applications of MDx technologies




## HOSPITALS

- Actively adopting PM measures to obtain better outcomes
- Developing CDSS to control prescription behavior
- Employing whole genome sequencing to direct clinical decisions

## PHARMACY BENEFIT MANAGERS

- Increased involvement in the personalized medicine revolution
- Establishing themselves as a control point for clinical information
- Will have a significant impact on physician prescription decisions

## LIFE SCIENCE TOOLS COMPANIES

- Whole genome sequencing - Developing next generation sequencing platforms promise large clinical utility with whole genome sequencing for personalized medicine such as
  - Identifying new biomarkers & genetic targets
  - Simplifying technology for diagnosing genetic biomarkers

Source: Scientia Analysis



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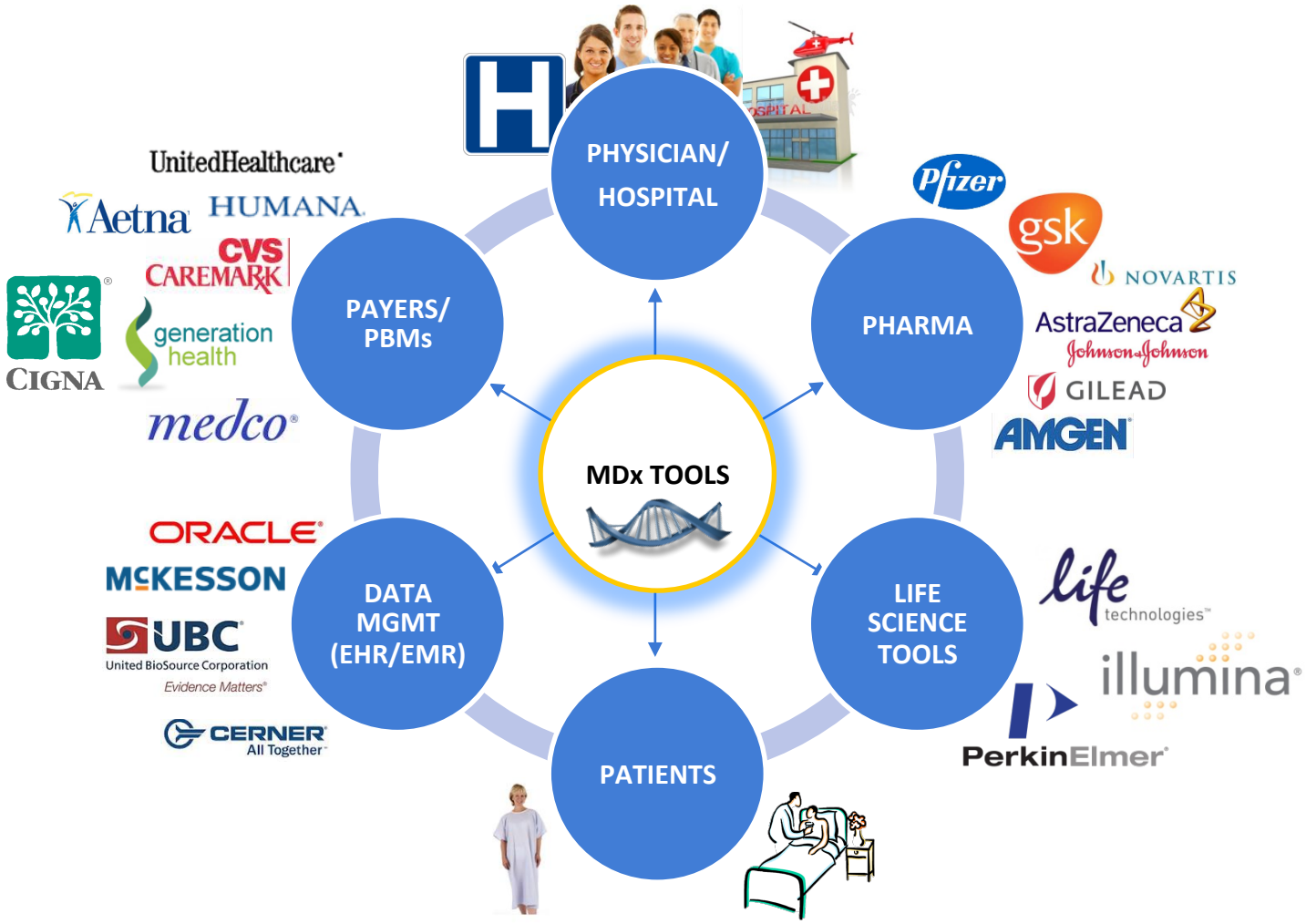
# Healthcare business models and partnerships are evolving among the major stakeholders as a result of newfound applications of MDx technologies across the healthcare spectrum

## MOLECULAR DIAGNOSTICS IS FACILITATING PERSONALIZED MEDICINE FOR ALL STAKEHOLDERS

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# Molecular Diagnostics (MDx) are clinical tests based on measurements of nucleic acids (e.g., DNA or RNA)

## MOLECULAR DIAGNOSTICS (MDx)*:

Molecular diagnostics is the detection of DNA/RNA and its variation with the intent to diagnose disease, determine a patient's susceptibility to disease, evaluate response to therapy or establish the condition's prognosis

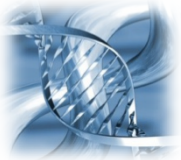
### MDx TESTING & INFORMATION …

- Gene sequencing
- Micorarrays
- Signal amplification
- Strand Displacement Amplification (SDA)
- Transcription Mediated Amplification (TMA)
- pPCR

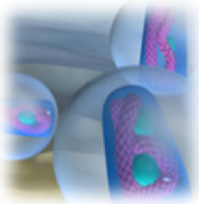
… ENABLES …

### … PERSONALIZED HEALTHCARE

- Oncology
- Genetic diseases
- Blood screening
- Infectious diseases
- Other





Sources: Scientia analysis, FDA, CDC; * Includes analyte specific reagents and revenue from CLIA^ certified labs that supply their own IVD product that is an analyte specific reagent or approved by a regulatory body (e.g. Genomic Health)



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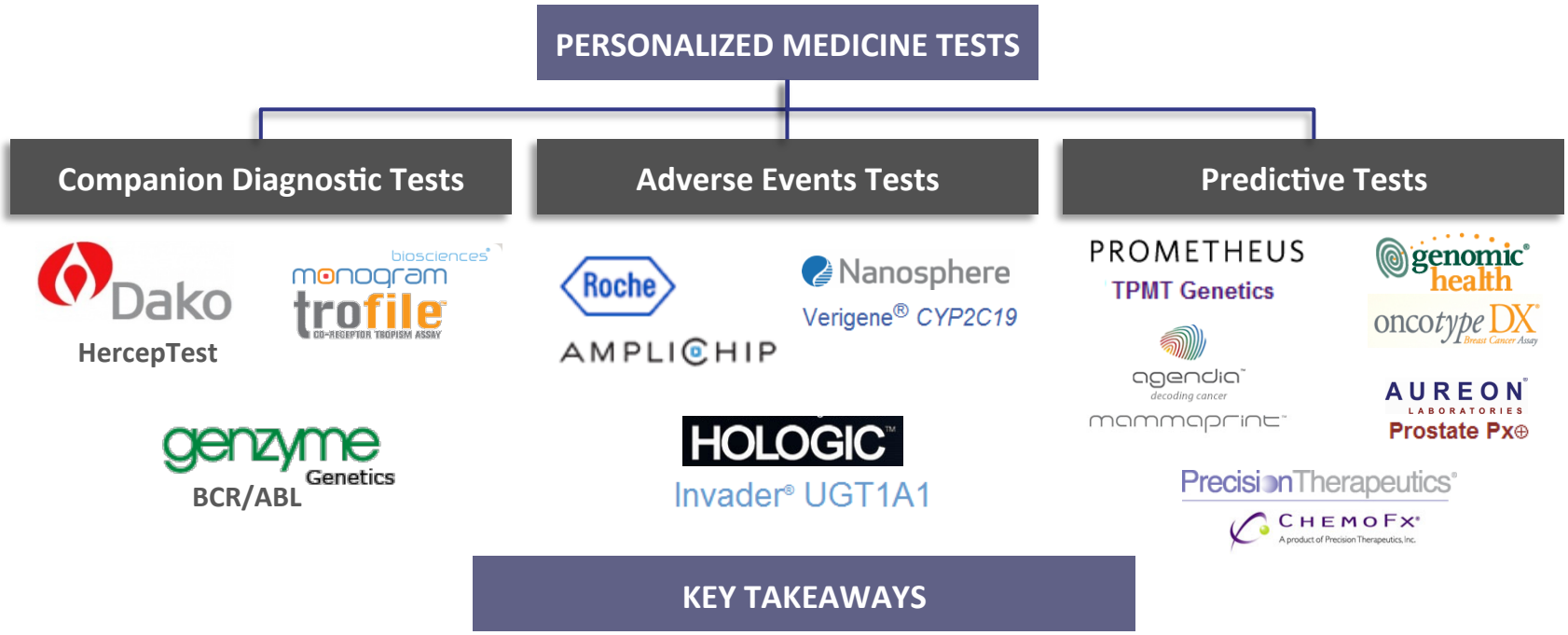
# Diagnostic companies have made significant strides in advancing personalized medicine; now with the cooperation of pharma, we expect rapid growth in tests




## KEY TAKEAWAYS

- Diagnostics are having a large role in personalized medicine due to its ability to
  - » Identify suitable patient subsets for targeted therapies
  - » Identify patients who may have significant adverse effects
  - » Identify patients who will respond to classes of drugs
- Diagnostics in personalized medicine used to be focused on drugs already on the market such as Amplichip and Verigene CYP2C19, now many diagnostic companies have forged relationships with pharma in hopes of developing companion diagnostic tests for drugs in the pipeline such as DxS's (Qiagen) collaborations with Boehringer Ingelheim's (NSCLC) and Pfizer's (Brain Cancer) drug candidates

Sources: Scientia Analysis, company websites



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# As result, unlike in the past, applications of MDx technologies have expanded beyond finding one customized treatment for each patient

**MOLECULAR DIAGNOSTICS TOOLS & TECHNOLOGIES**

**In the past, MDx technologies were mainly targeted towards the final goal of personalized medicine - 1 treatment customized per patient …**

**… however, now, MDx technologies are being targeted to various different aspects of clinical development to improve R&D & patient care**

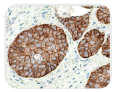
**Custom Treatment**

**1 Person**

**Optimizing drug discovery for a subset of patients**

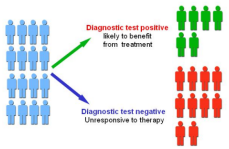
**Pharma introducing diagnostics earlier in the drug trial process**

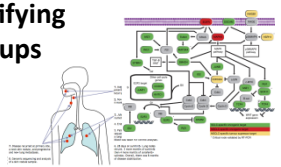
(MetMab + Tarceva)



**Whole Genome Sequencing - diagnostic tool for specific patient's cancer pathway & therapy selection**

**Acute Care – identifying patient sub-groups**



**Chronic Care – Early detection & Prevention**

**Rx/Dx**

**Studies with IVD companies (CPT Coding Program)**

CVS CAREMARK | generation health | PGxL laboratories

*Non-exhaustive list of MDx applications for clinical development & patient care*

Source: Scientia Analysis



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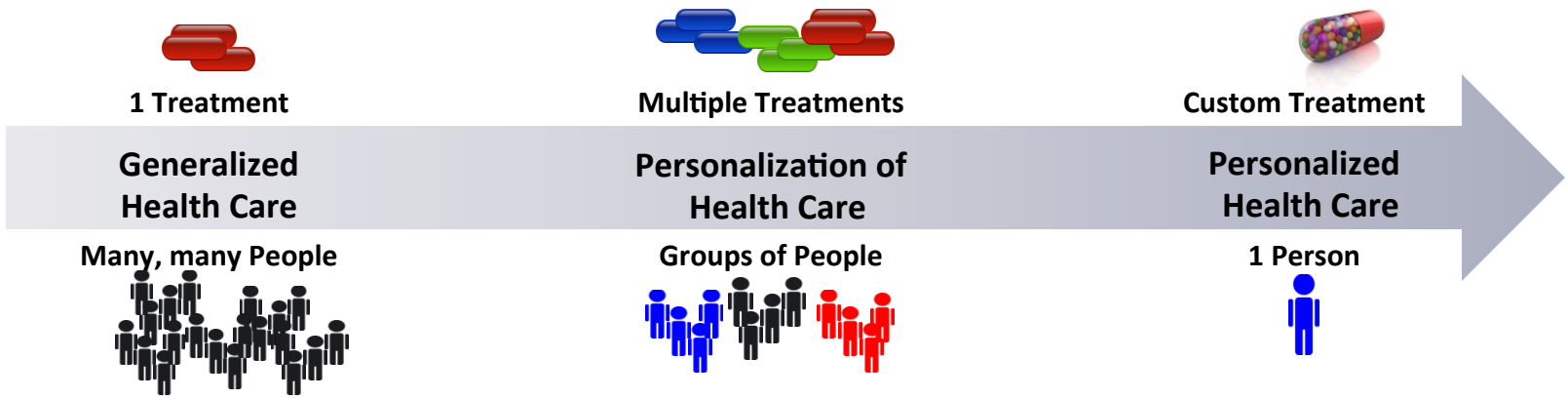
# Even though advances in MDx has paved the way for personalized medicine, healthcare is still evolving from generalized care to personalized care

## PERSONALIZED HEALTHCARE:

Personalized Healthcare is the custom design and implementation of health care for every individual. This would include personalized solutions across the health spectrum, from health & wellness, to chronic disease management, to acute care

- Personalized Healthcare is a function of:
  1. ***Upfront information*** that can segment populations by health status into an ever increasing number of sub-categories
  2. ***Direction of Therapy***: An increasing number of therapeutic (or preventative) options downstream that can specifically treat ever more specific sub-categories

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# Healthcare business models and partnerships are evolving as a result of newfound applications of MDx technologies across the healthcare spectrum

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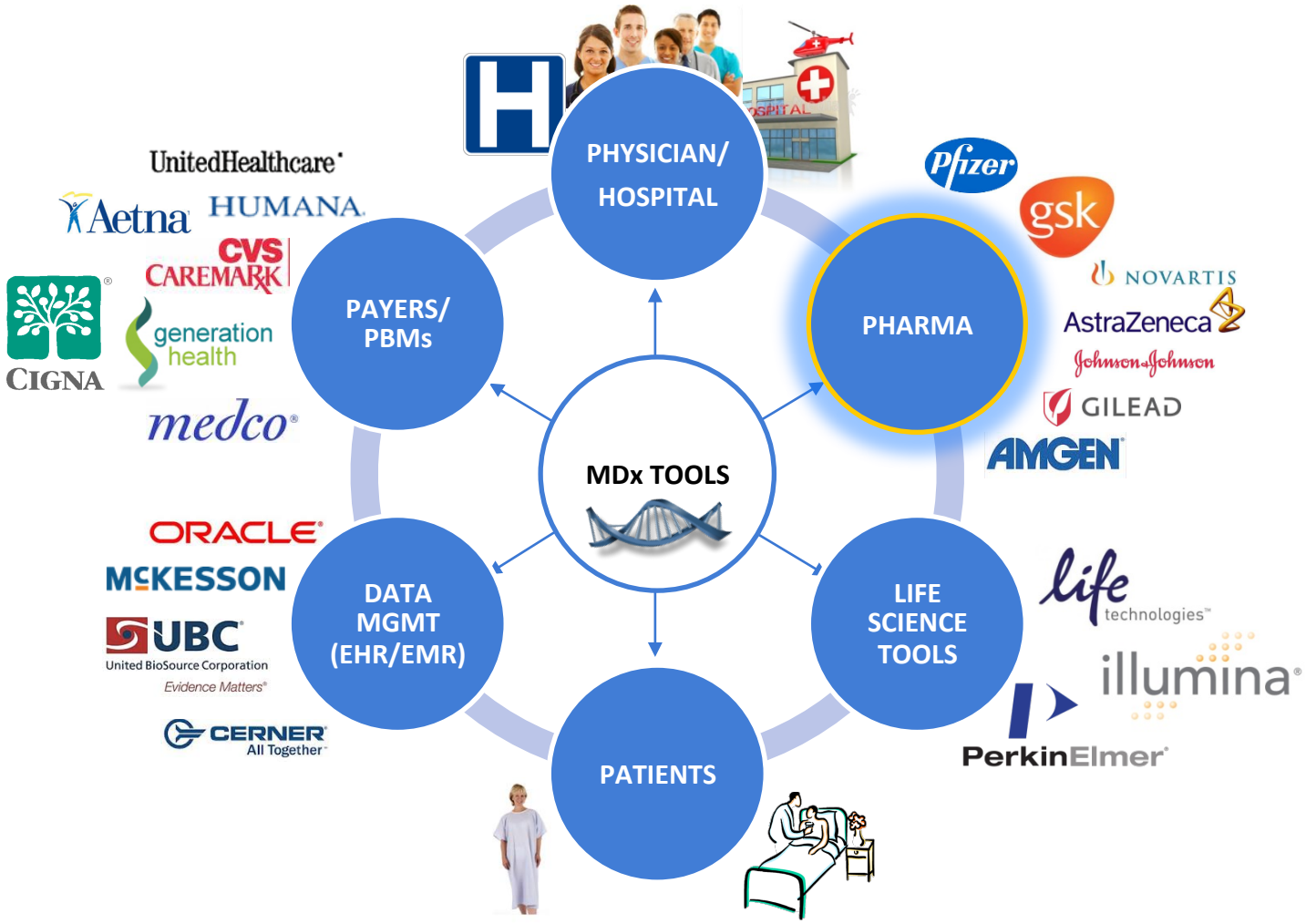


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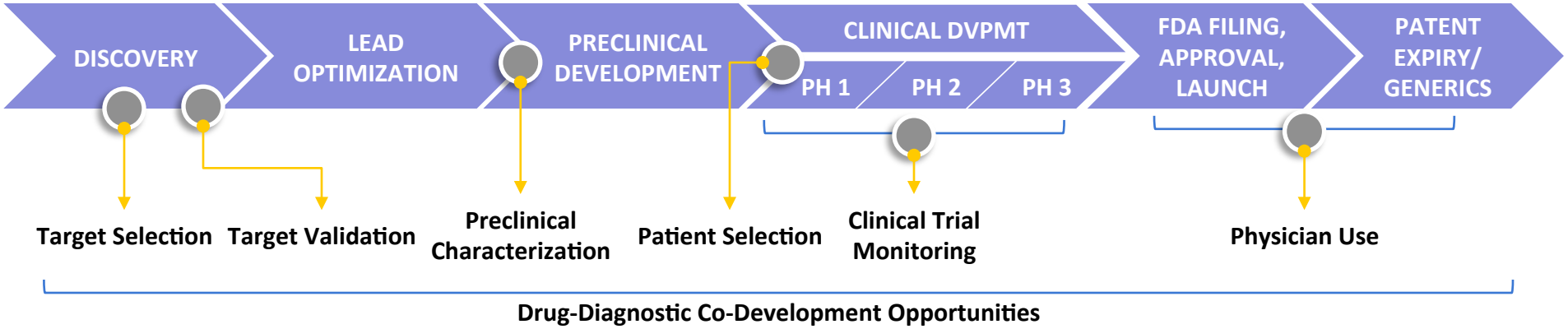
# Changes to the drug discovery & clinical trial process is key to securing pharma's future in personalized medicine

## Personalized Medicine approaches impacts the pharmaceutical development process at almost every stage of a drugs lifespan




***Personalized medicine approaches have the potential to de-risk development projects, shorten development timeframes, accelerate new product adoption, and generate additional revenue streams***

- Increased partnering & collaborative efforts to reduce risk
- Shorter timelines and cost for increased efficiency and broader portfolios
- Targeted clinical trials with smaller cohorts, potentially reducing cost and time
- Pricing based on smaller target population
- Consideration of the diagnostic into the process of drug pricing
- Pricing with clinical comparative effectiveness & health economic data

Source: Scientia Analysis



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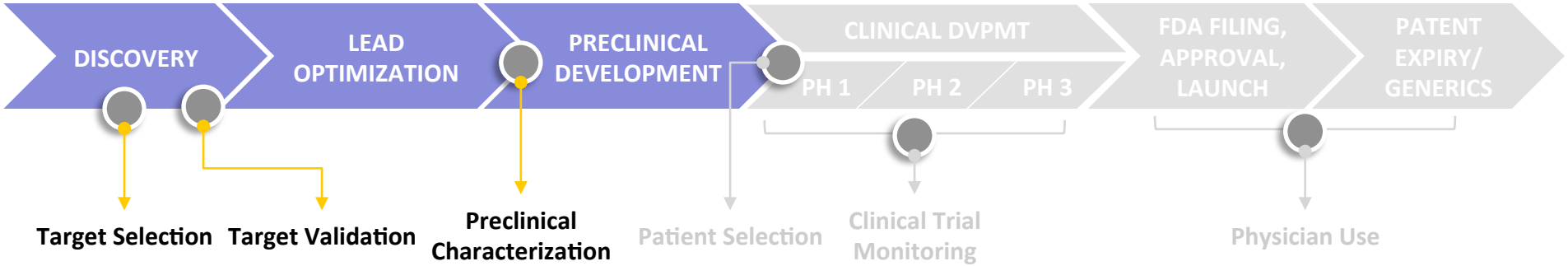
# Several collaborations have recently been established where diagnostics are used to aid in the discovery process and identify disease-specific targets




**NOTABLE ACTIVITY**

- **Genentech Partners with Xenon Pharmaceuticals in $646M Pain Pact (Jan 2012)**
  - » Xenon's strategic alliance with Genentech to discover and develop compounds and companion diagnostics for the potential treatment of pain
  - » Xenon's discovery and development efforts focus on development of small-molecule therapies based on the genetic causes of metabolic, neurological, and cardiovascular disease
- **GlaskoSmithKline enters into companion program with diaDexus for heart disease drug**

  LpPLA2 immunoassay, developed by diaDexus and approved for predicting the risk of heart disease and ischemic stroke
  - » GlaxoSmithKline is developing a small molecule designed to inhibit this enzyme, thus reducing the risk of adverse cardiovascular events

Sources: Scientia Analysis; Company literature and press releases



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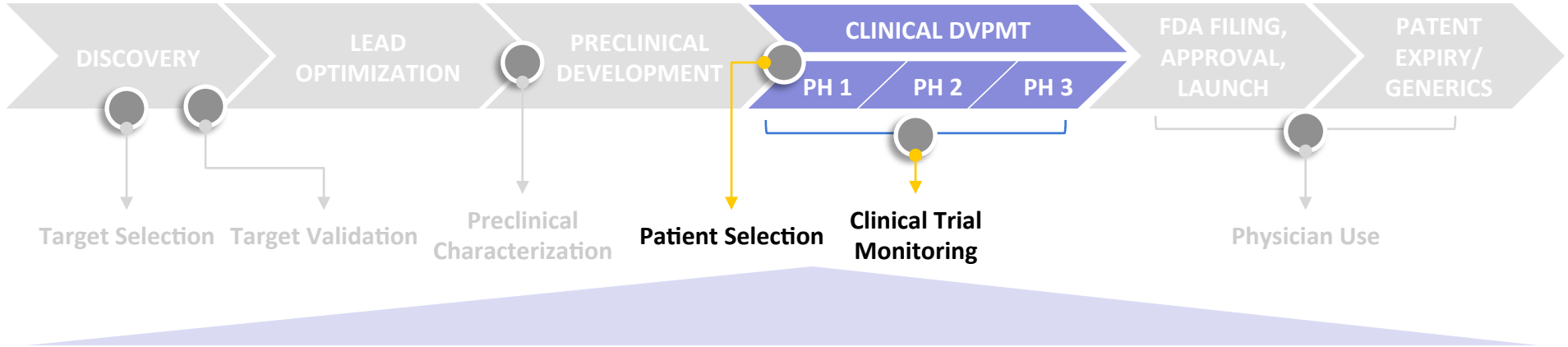
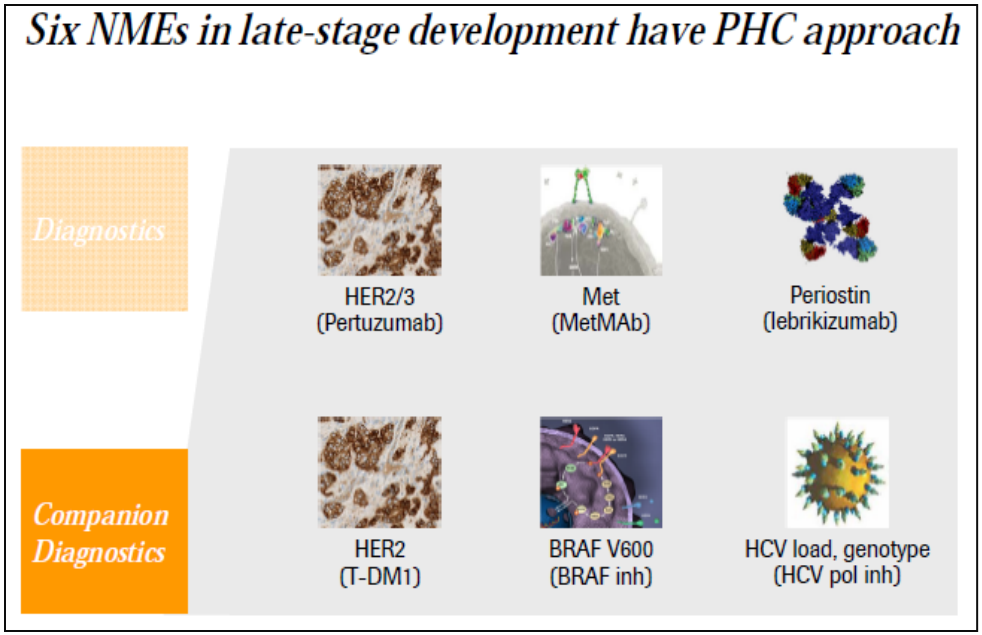
# Molecular diagnostics are also increasingly being used to refine patient populations for optimization of clinical studies …




**Personalized Healthcare approach which includes collaboration of Diagnostics and Pharma as early as Phase II**

**MetMab + Tarceva**

- Collaboration began in Phase II studies
- Roche cMET assay identified candidate metastatic NSCLC patients
- Trials showed that for patients with high Met, a combination use of MetMAB and Tarceva extended overall survival

Sources: Scientia Analysis; Company literature and press releases



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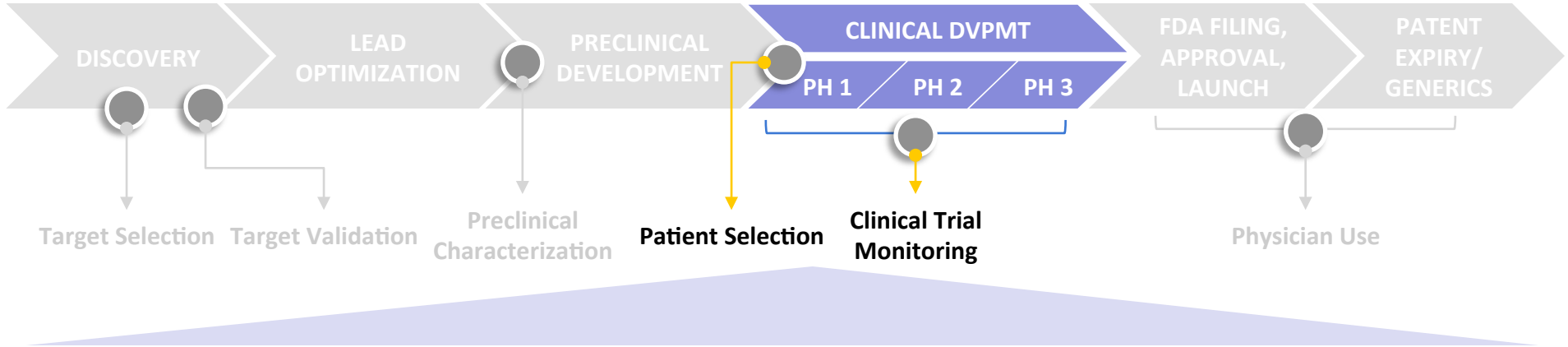
# …with additional collaborations occurring more frequently




**NOTABLE ACTIVITY**

Abbott
A Promise for Life

MERCK

NOVARTIS

FOUNDATION MEDICINE

- **Abbott and Merck Collaborate to Develop Companion Diagnostic Test for Investigational Cancer Therapy (March 2012)**
  - » Collaboration to evaluate the use of a FISH-based companion diagnostic test to aid in the development of a Merck investigational cancer therapy
  - » Abbott will develop a test to identify deletions of the TP53 gene in cancer patients and evaluated in clinical trials to help identify patients more likely to respond favorably to Merck's investigational cancer therapy

- **Foundation Medicine, Novartis Ink New Deal for Clinical Oncology Programs (June 2012)**
  - » The use of Foundation Medicine's molecular information platform will be used across many of Novartis' Phase 1 and Phase 2 oncology clinical programs
  - » Tumor genomic profiling has become an important part of Novartis' clinical trials

Sources: Scientia Analysis; Company literature and press releases



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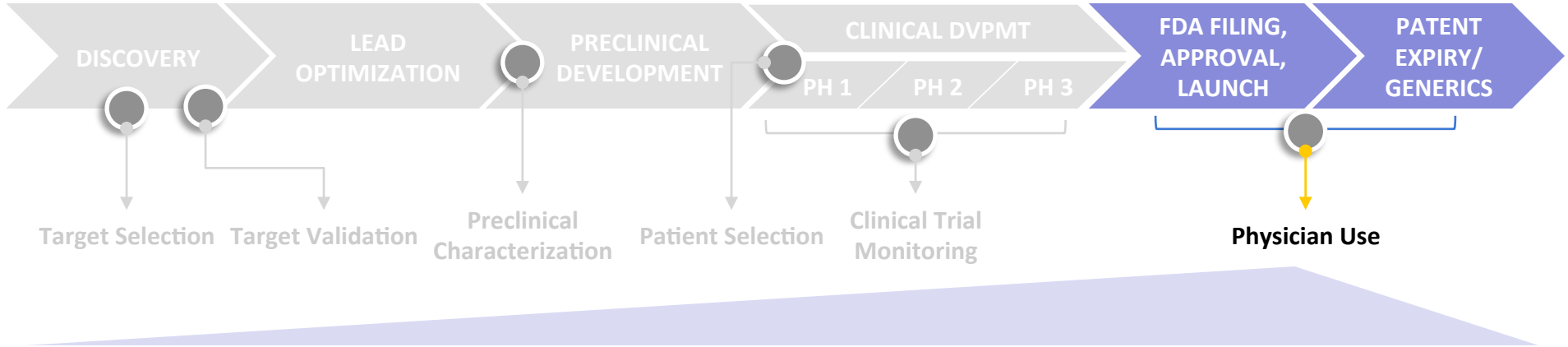
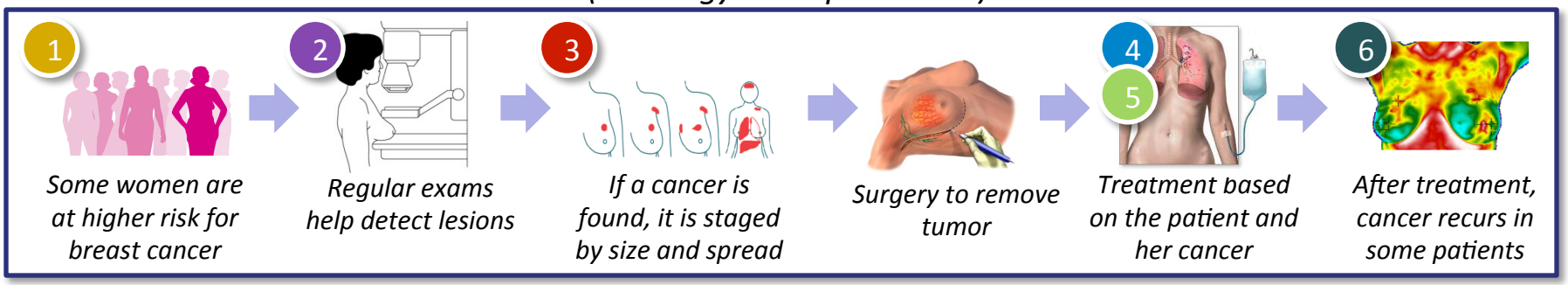
# Several Rx/Dx approaches exist for targeted patient treatment




***Personalized medicine approaches are being used across all stages of the patient care cycle***

*(oncology example shown)*




1 **PREDISPOSITION**

2 **SCREENING & DETECTION**

3 **DIAGNOSIS/STAGING/ CLASSIFICATION**

4 **THERANOSTIC**

5 **PROGNOSIS/PREDICTION**

6 **MONITORING**

Sources: Scientia Analysis; Company literature and press releases



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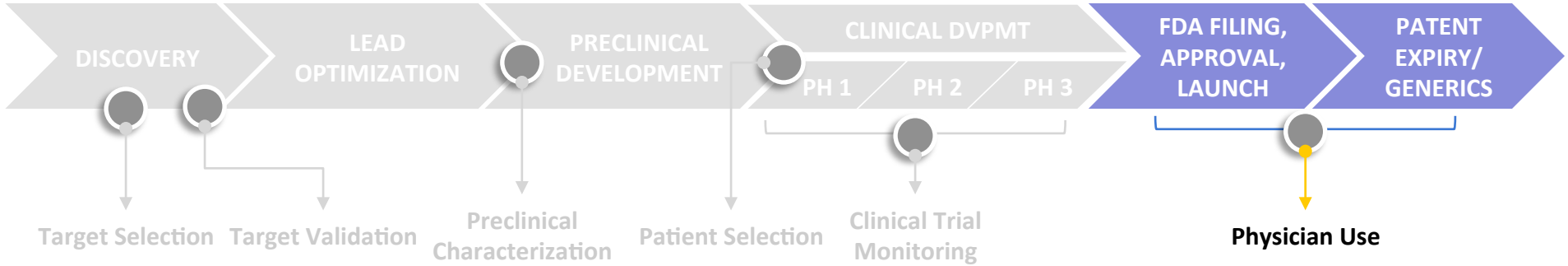
# Case studies of recently approved Rx/Dx exemplify how co-development can maximize value for the pharmaceutical companies




| | Vectibix® (panitumumab) + AMGEN + Dako + DxS Diagnostic Innovations |
|---|---|
| **Partnership Type** | Amgen initially had a partnership with Dako to usepharmDx™ EGFR as a companion diagnostic |
| **Value capture** | **Diagnostic: Low**<br>TheraScreen® is inexpensive compared to other genomic based tests<br>**Therapy: High**<br>Vectibix® would not have had EU approval without KRAS data |

| | XALKORI® CAPSULES CRIZOTINIB + Pfizer + Abbott Molecular |
|---|---|
| **Partnership Type** | **Co-development:** Pfizer and Abbott collaborated for the simultaneous approval of Rx and Dx |
| **Value capture** | **Diagnostic: High**<br>Vysis ALK Break Apart FISH Probe Kit: $1,500<br>**Therapy: High**<br>Highly effective, orphan drug: $115,200 per year |

Sources: Scientia Analysis; Company literature and press releases



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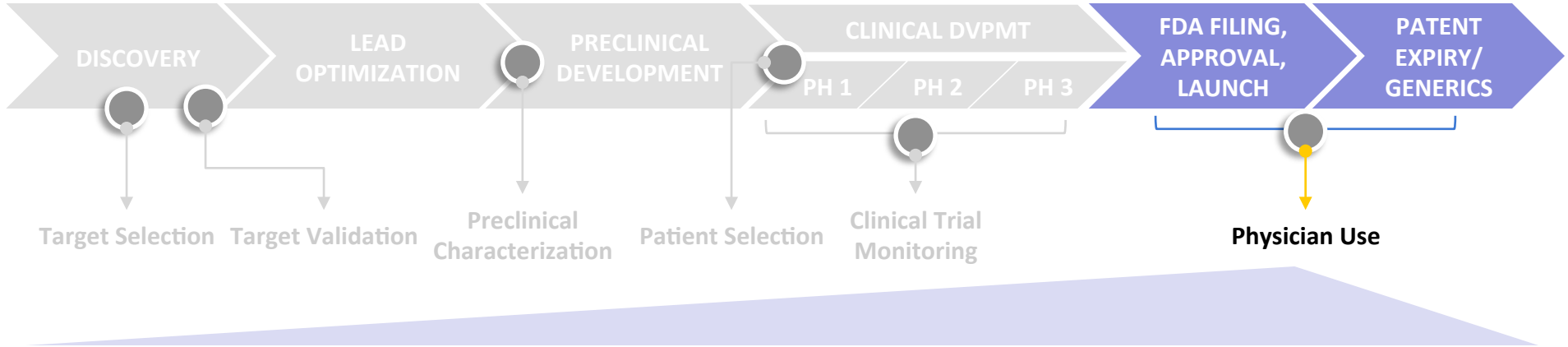
# Several other partnerships are being established between pharma and diagnostic companies for companion diagnostics initiatives




**NOTABLE ACTIVITY**

- **MDxHealth, Merck KGaA Partner to Develop Companion Dx for Glioblastoma Drug (July 2012)**
- **Eli Lilly collaborates with PrimeraDx for Companion Diagnostics Development (June 2012)**
- **Ventana to Collaborate with Bayer on Companion Diagnostic Test for new cancer biological cancer therapy (Jan 20120**
- **Takeda and Zinfandel Pharmaceuticals Sign Licensing Agreement for Alzheimer's Disease Biomarker in Combination with Pioglitazone (Jan 2011)**

Sources: Scientia Analysis; Company literature and press releases



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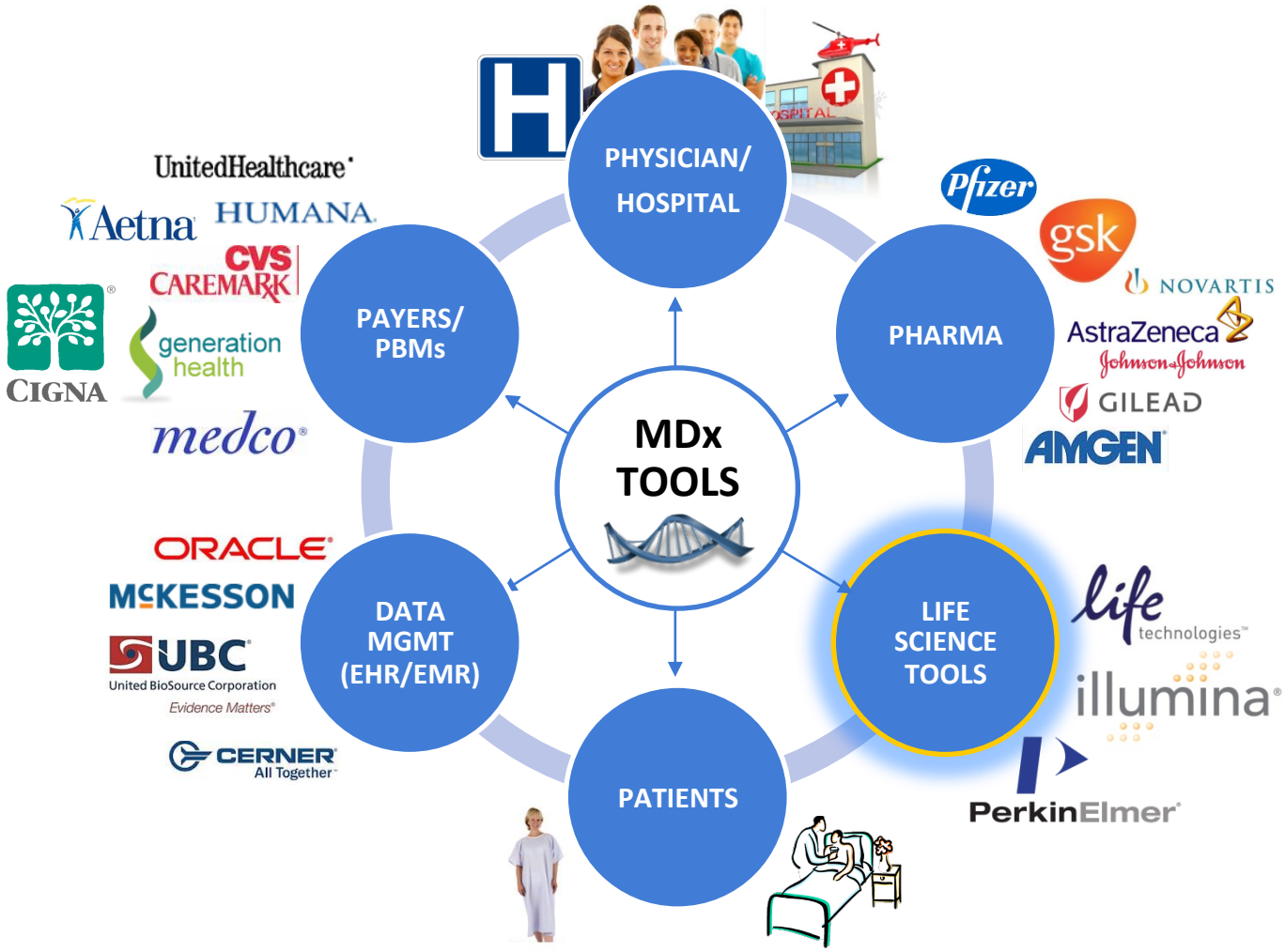
# Healthcare business models and partnerships are evolving as a result of newfound applications of MDx technologies across the healthcare spectrum

## MOLECULAR DIAGNOSTICS IS FACILITATING PERSONALIZED MEDICINE FOR ALL STAKEHOLDERS




Source: Scientia Analysis



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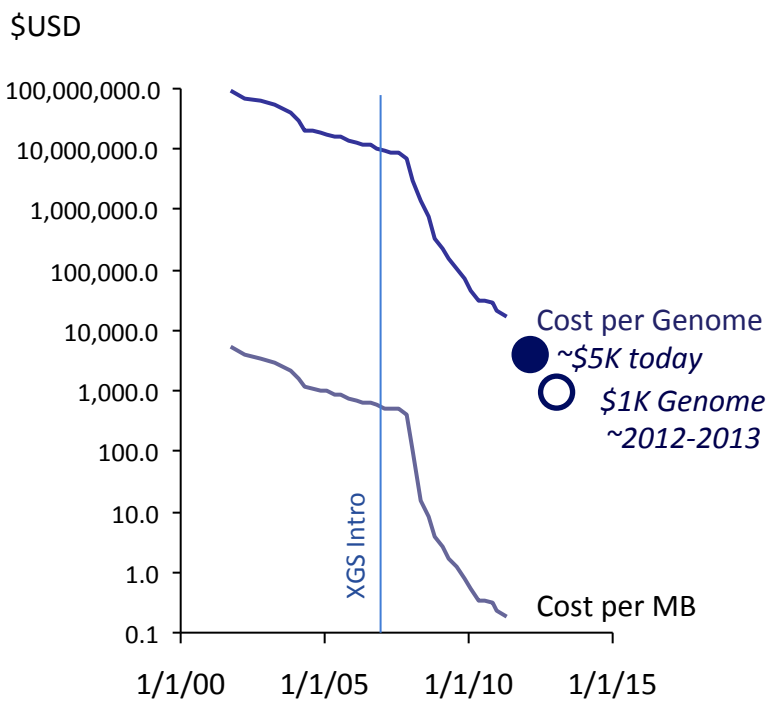
# As the average cost of sequencing declines, several opportunities emerge for life science tools companies to provide enabling technologies for personalized medicine

## Key Pricing Trends

### AS COST OF SEQUENCING DECLINES…




**XGS:** High Throughput Sequencing (*i.e.* NGS, 3GS, etc.)
**MB:** Megabase (1MM nucleotide bases)

### …OPPORTUNITIES WILL EMERGE FOR LST COMPANIES

| | |
|---|---|
| **TECHNOLOGY** | • Accuracy<br>• Read length<br>• Turnaroundtime |
| **ANALYSIS AND EXPERTISE** | • Proprietary analysis pipeline<br>• Specialized scientific staff<br>• Data handling |
| **LOGISTICS** | • Courier service<br>• Turnaroundtime<br>• Cloud-based access/delivery and tools |
| **REGULATORY STANDING AND EXPERTISE** | • cGMP<br>• cGLP<br>• CLIA accreditation / ISO |

Sources: Scientia analysis; Wetterstrand KA. DNA Sequencing Costs: Data from the NHGRI Large-Scale Genome Sequencing Program



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# For example, next-gen sequencers are increasingly being adopted for oncology MDx as price per base pair drops and throughput increases

## VALUE PROPOSITION OF NGS IN ONCOLOGY

| | Planar Array | Bead-Array | RT-PCR | Sanger Seq'n | Next-Gen Seq'n |
|---|---|---|---|---|---|
| **ATTRIBUTES** | | | | | |
| Flexibility for custom content | -- | + | ++ | -- | |
| Robustness of fixed content | | + | + | - | |
| Accuracy / Reproducibility | - | ++ | ++ | ++ | ++ |
| Throughput: # GT's sample | + | ++ | - | -- | ++ |
| Throughput: Samples / Study | -- | | + | -- | + |
| Per Genotype Cost | + | ++ | - | -- | - |
| Per Sample Cost | - | ++ | ++ | - | - |
| **APPLICATIONS SUITABILITY** | | | | | |
| Clinical diagnostics | - | ++ | + | -- | + |

***In the near term , NGS is expected to move into areas of MDx that currently use Sanger sequencing, such as the analysis of K-Ras mutations. In the long term, NGS will be used in many areas where RT-PCR is currently being used.***

## SEQUENCING PLAYERS

life technologies™

illumina

Helicos BioSciences Corporation

SEQUENOM INDUSTRIAL GENOMICS

## KEY TAKEAWAYS

- Sales of next-gen sequencing (NGS) equipment are experiencing explosive growth with increasing use in MDx
- IVD companies must assess the NGS opportunity and development strategy :
  - » *How attractive are clinical applications for next-gen sequencers market?*
  - » *Whether to partner with NGS companies, or have their own NGS technology?*

Sources: Scientia Analysis; Company literature and press releases



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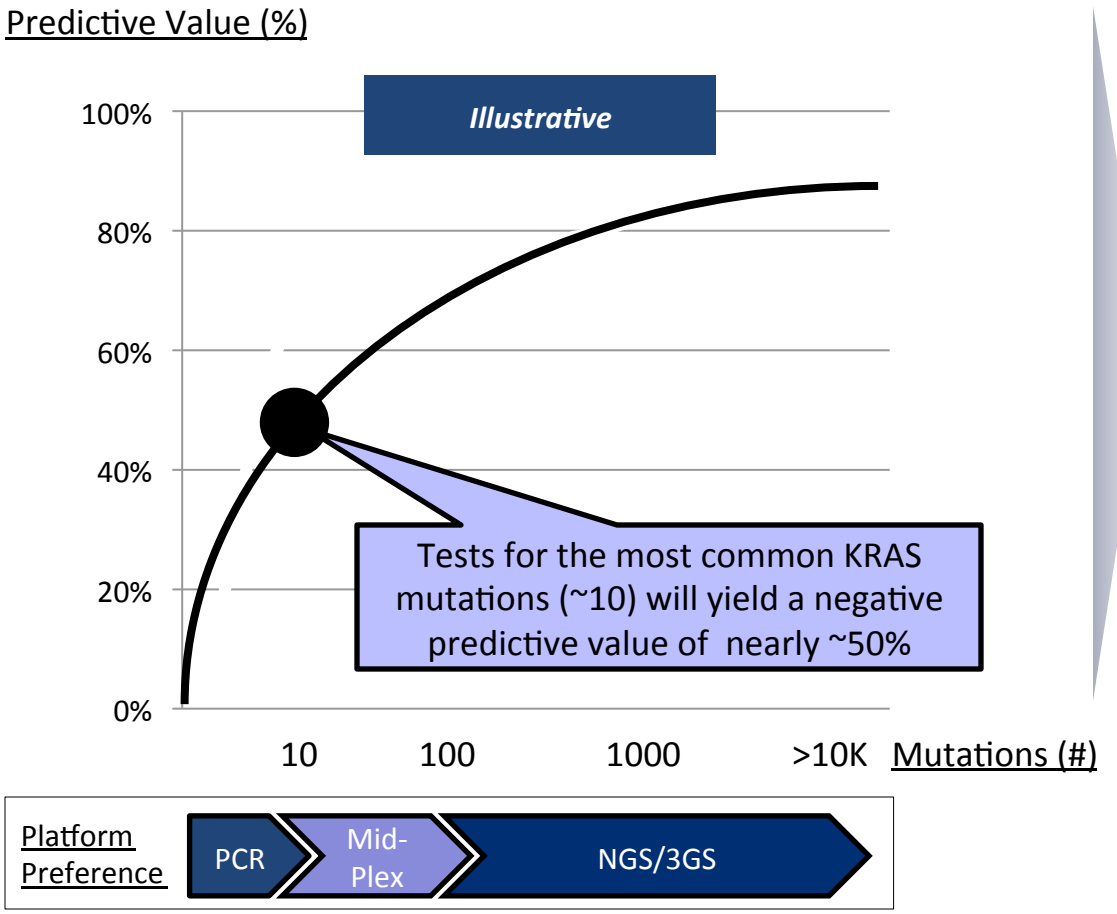
# Post-2014, NGS/3GS technologies are likely predominate in oncology theranostics because of the need for higher predictive values

## Number of Markers vs. Predictive Value in Oncology Theranostics




## Key Takeaways

- In many situations a small number of markers will provide predictive values of less than 50%
- While this may represent a substantial improvement to the *status quo* upon introduction, competition amongst service providers drives demand for more comprehensive testing
- As the number of validated theranostic markers eclipses 100 (next 2-5 years), NGS/3GS platforms are expected to begin taking share

"The quality metrics have not been well established for the newer technology. That is ok in a research setting but can't be tolerated in a clinical setting. As costs come down in the future, new technology could provide greater depth by running the same sample in multiple lanes." – *Oncologist, Weill Cornell Medical College*

Sources: Scientia Analysis; ScientiaNET (KOL interviews)



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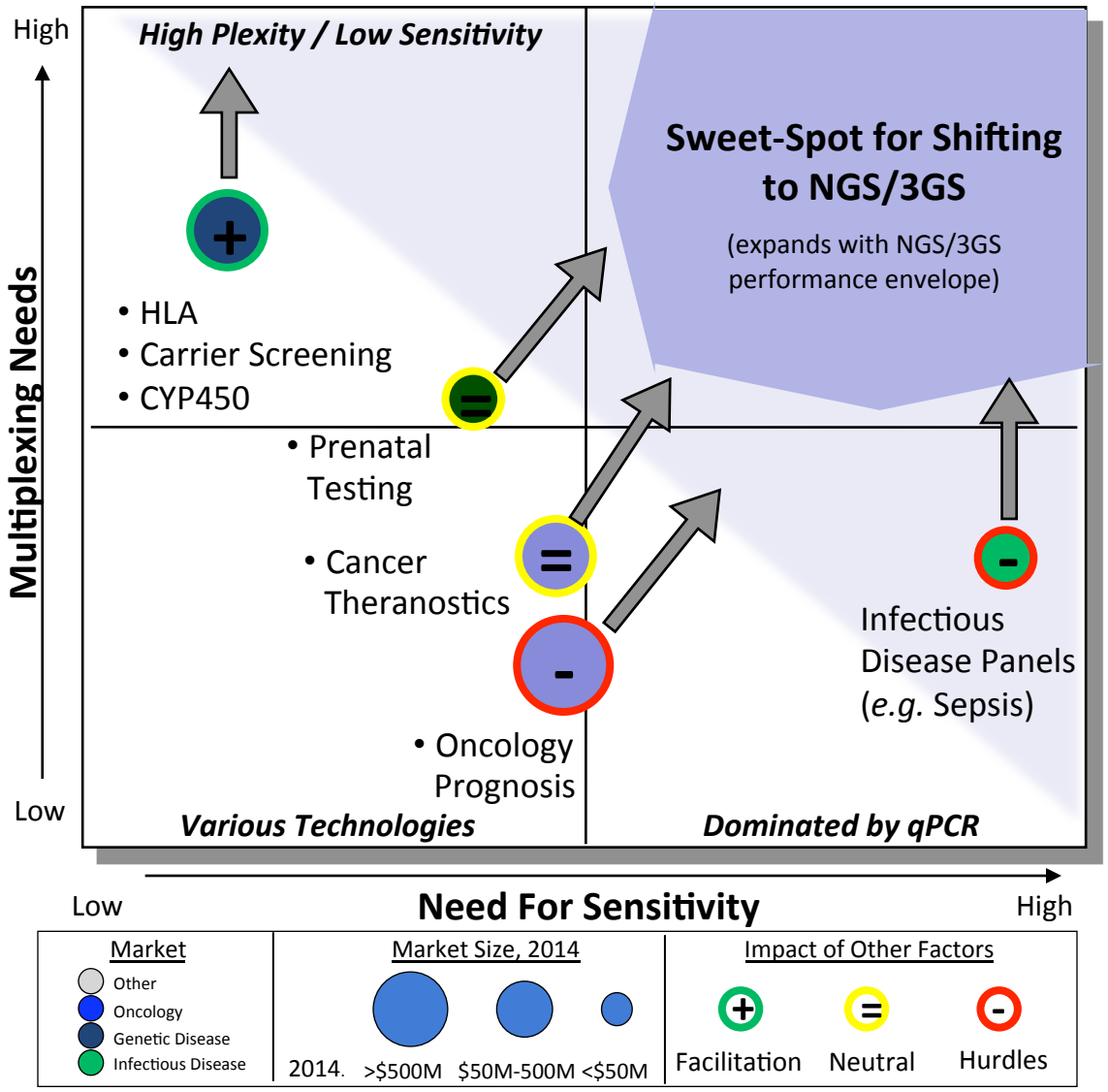
# In addition to oncology, several other markets will be shifting towards greater use of sequencing technologies in the future




## KEY TAKEAWAYS

- As users needs for multiplexing and sensitivity becomes greater, there will be a transition to NGS/ 3GS technology
- The shift within genetic testing is supported by competition among labs to provide the most comprehensive panels
- The shift within sepsis and oncology prognosis have somewhat higher barriers to entry:
  - » Sepsis requires < 6hr TaT and ease of use before considerable adoption
  - » Oncology prognosis requires clinical trials, health economics and overcoming the early mover (GHDX)

Note: In the near term (2014) technology shifts to NGS/ 3GS are likely to see adoption rates similar to that of array comparative genomic hybridization (aCGH) for developmental delay observed over the past decade (~35% penetration a decade after introduction)

Sources: Scientia Analysis; ScientiaNET (KOL interviews)



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# As a result, Life Science Tools companies are expanding their capabilities and offerings in order to play a greater role in personalized medicine

## Life Science Tools activity

**NOTABLE ACTIVITY**

- **Life Technologies to follow Navigenics buy with more acquisitions as it builds MDx portfolio (July 2012)**

- **PerkinElmer to open new Personalized Medicine Center (June 2012)**
  - The mission of the Center will be to create new enabling technologies for scientists developing and commercializing new diagnostic and therapeutic products

- **GE Healthcare moves to develop lung cancer Dx (May 2012)**
- **GE to buy Personalized Medicine Company, SeqWright (April 2012)**
- **GE to Buy Clarient to Expand in Cancer Diagnostics (Oct 2010)**

Sources: Scientia Analysis; Company literature and press releases



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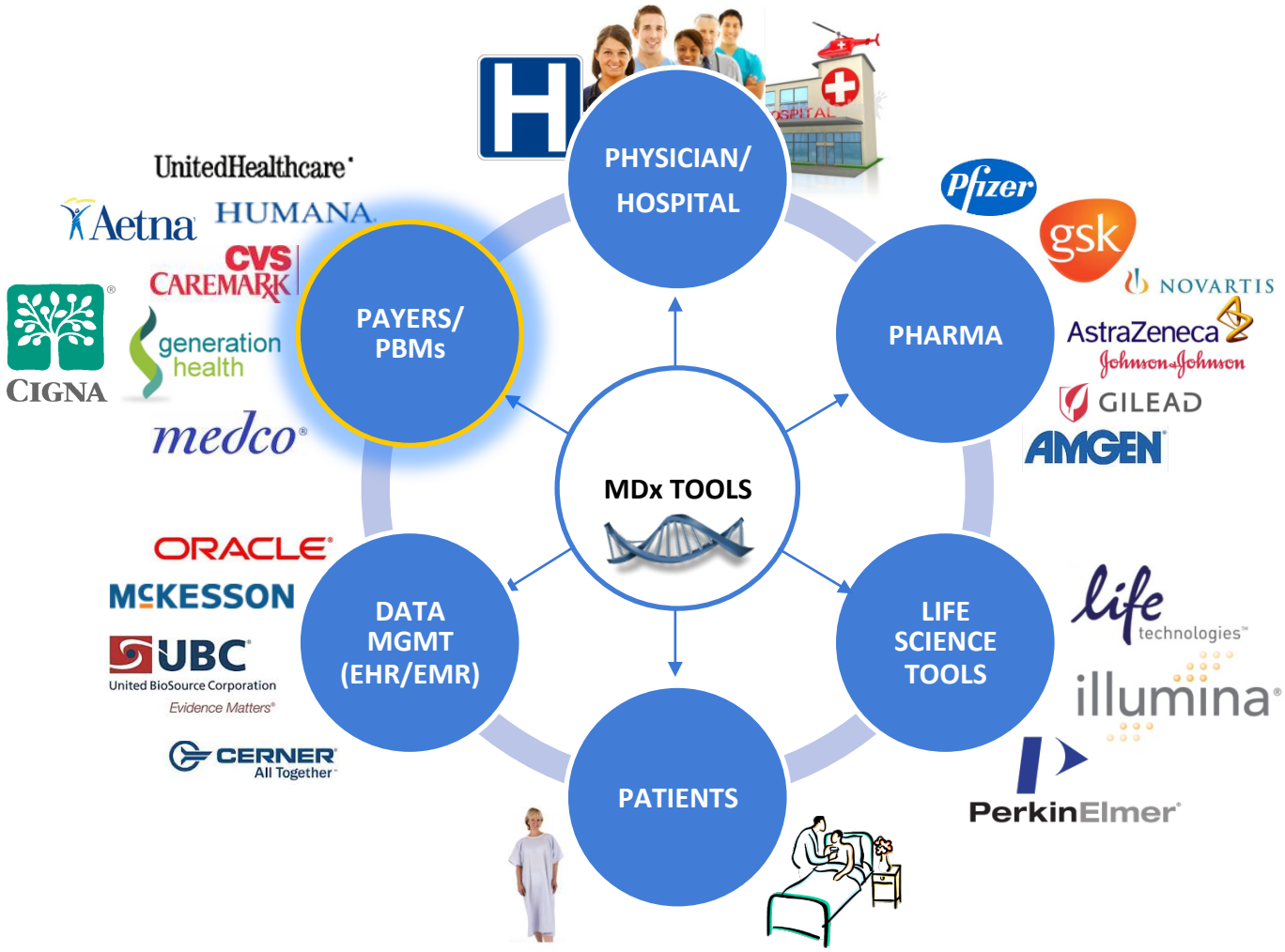
# Healthcare business models and partnerships are evolving as a result of newfound applications of MDx technologies across the healthcare spectrum

## MOLECULAR DIAGNOSTICS IS FACILITATING PERSONALIZED MEDICINE FOR ALL STAKEHOLDERS




Source: Scientia Analysis



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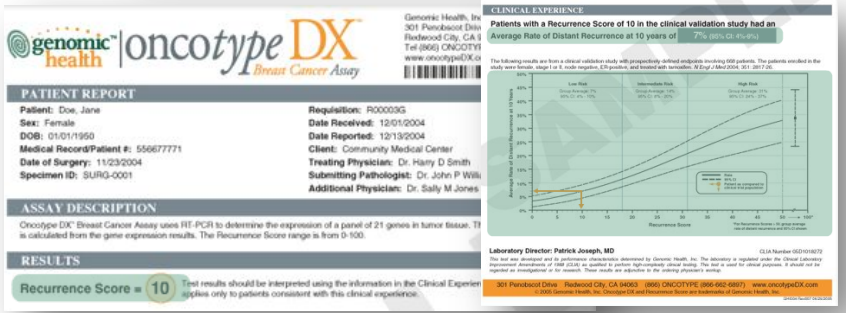
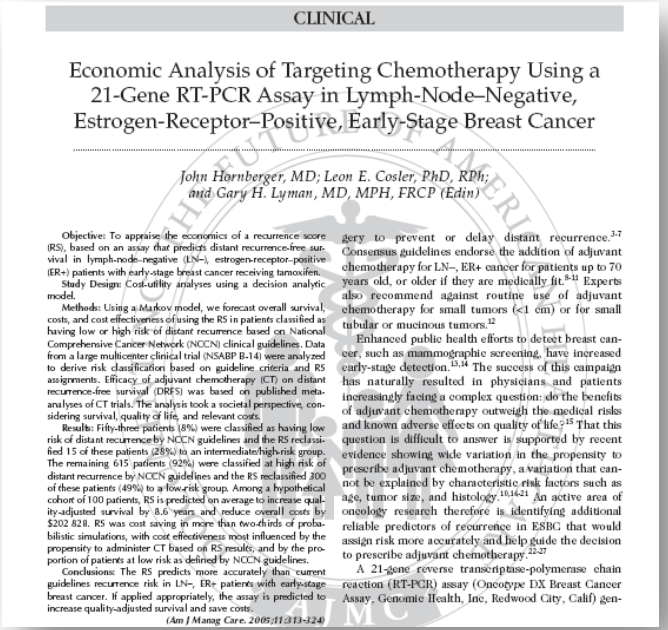
# Payors are pushing for Rx-Dx integration; OncotypeDx has received increasing adoption and reimbursement since launch in 2004

## Payors reimburse Genomic Health's OncoType Dx assay for breast cancer recurrence


- Predicts likelihood of recurrence and benefit of chemotherapy for early stage (N- ER+) breast cancer
- Test based on algorithm and proprietary 21-gene panel using quantitative RT-PCR

## KEY TAKEAWAYS



CLINICAL

Economic Analysis of Targeting Chemotherapy Using a 21-Gene RT-PCR Assay in Lymph-Node–Negative, Estrogen-Receptor–Positive, Early-Stage Breast Cancer

*John Hornberger, MD; Leon E. Cosler, PhD, RPh; and Gary H. Lyman, MD, MPH, FRCP (Edin)*

**Objective:** To appraise the economics of a recurrence score (RS), based on an assay that predicts distant recurrence-free survival in lymph-node–negative (LN–), estrogen-receptor–positive (ER+) patients with early-stage breast cancer receiving tamoxifen.

**Study Design:** Cost-utility analyses using a decision analytic model.

**Methods:** Using a Markov model, we forecast overall survival, costs, and cost effectiveness of using the RS in patients classified as having low or high risk of distant recurrence based on National Comprehensive Cancer Network (NCCN) clinical guidelines. Data from a large multicenter clinical trial (NSABP B-14) were analyzed to derive risk classification based on guideline criteria and RS assignments. Efficacy of adjuvant chemotherapy (CT) on distant recurrence-free survival (DRFS) was based on published meta-analyses of CT trials. The analysis took a societal perspective, considering survival, quality of life, and relevant costs.

**Results:** Fifty-three patients (8%) were classified as having low risk of distant recurrence by NCCN guidelines and the RS reclassified 15 of these patients (28%) to an intermediate/high-risk group. The remaining 615 patients (92%) were classified at high risk of distant recurrence by NCCN guidelines and the RS reclassified 300 of these patients (49%) to a low-risk group. Among a hypothetical cohort of 100 patients, RS is predicted on average to increase quality-adjusted survival by 8.6 years and reduce overall costs by $202 828. RS was cost saving in more than two-thirds of probabilistic simulations, with cost effectiveness most influenced by the propensity to administer CT based on RS results, and by the proportion of patients at low risk as defined by NCCN guidelines.

**Conclusions:** The RS predicts more accurately than current guidelines recurrence risk in LN–, ER+ patients with early-stage breast cancer. If applied appropriately, the assay is predicted to increase quality-adjusted survival and save costs.

*(Am J Manag Care. 2005;11:313-324)*

gery to prevent or delay distant recurrence.[3-7] Consensus guidelines endorse the addition of adjuvant chemotherapy for LN–, ER+ cancer for patients up to 70 years old, or older if they are medically fit.[8-11] Experts also recommend against routine use of adjuvant chemotherapy for small tumors (<1 cm) or for small tubular or mucinous tumors.[12]

Enhanced public health efforts to detect breast cancer, such as mammographic screening, have increased early-stage detection.[13,14] The success of this campaign has naturally resulted in physicians and patients increasingly facing a complex question: do the benefits of adjuvant chemotherapy outweigh the medical risks and known adverse effects on quality of life?[15] That this question is difficult to answer is supported by recent evidence showing wide variation in the propensity to prescribe adjuvant chemotherapy, a variation that cannot be explained by characteristic risk factors such as age, tumor size, and histology.[10,16-21] An active area of oncology research therefore is identifying additional reliable predictors of recurrence in ESBC that would assign risk more accurately and help guide the decision to prescribe adjuvant chemotherapy.[22-27]

A 21-gene reverse transcriptase-polymerase chain reaction (RT-PCR) assay (Oncotype DX Breast Cancer Assay, Genomic Health, Inc, Redwood City, Calif) gen-

- Increasing adoption and reimbursement
  - » Over 27,000 tests have been ordered by over 5,500 physicians since 2004
  - » Approximately 80% of the population is covered for the test

^ Other breast cancer prognosis tests provided by Agendia, ABT-CRA, Ipsogen, Exagen, Aviara; with Veridex (JnJ) and Roche entering the market in the future

Sources: Scientia Analysis; Genomic Health company website



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# Even PBMs like CVS Caremark is entering Personalized Medicine with promises of expanding PGx testing to improve patient health outcomes and cost

**CVS Caremark, Generation Health to Expand PGx Testing to Millions** "CVS Caremark…has decided to expand pharmacogenomic testing…for certain drugs as of the second quarter of 2010" – *GenomeWeb, Nov 10, 2009*

**Generation Health contracts PGXL to be preferred MDx lab** **"**PGXL is a CLIA certified lab providing many PGx tests such as KRAS, CYP tests, Warfarin, Factor II, V & MTHFR and therapy monitoring tests." - *June 2010*

## KEY TAKEAWAYS

- Pharmacy Benefit Management companies like CVS Caremark are getting more involved in the personalized medicine revolution, looking to get establish themselves as a control point for information
  - » In the past, Medco has run many studies to gather clinical data for PGx tests, such as KIF6 with Celera, in their "Genetics for Generics" program, as well as, launching their new TRC-AOS program to help educate and guide physicians regarding the right choices in testing, prescribing drugs, and monitoring for adverse events
  - » CVS have developed relationships with sole service PGx test providers for access to lab testing capabilities
- Their move into personalized medicine will have a significant impact on drug prescription decisions, particularly to limit the use of branded drugs vs. generics

Sources: Scientia Analysis; Genomeweb



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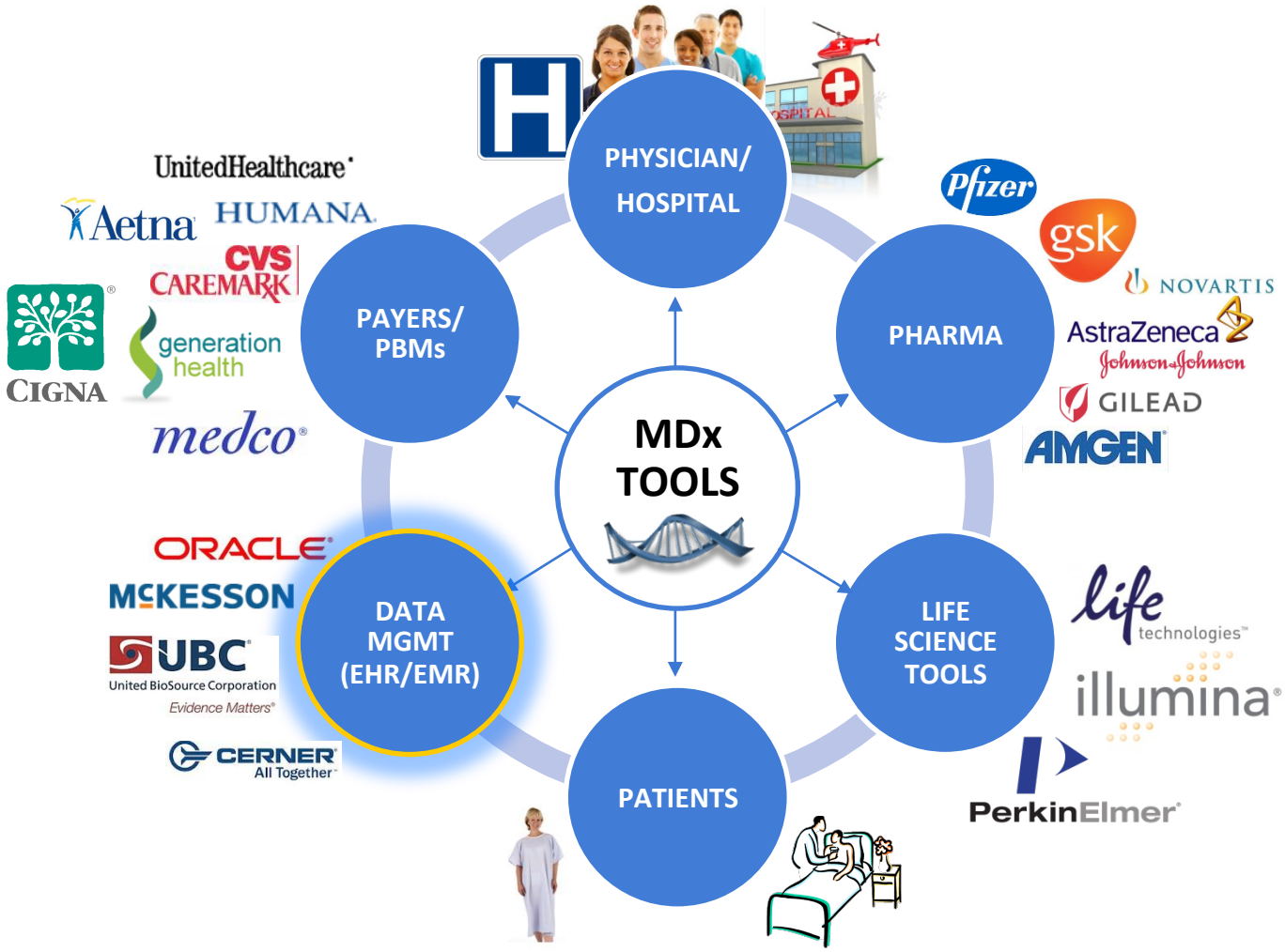


Source: Scientia Analysis



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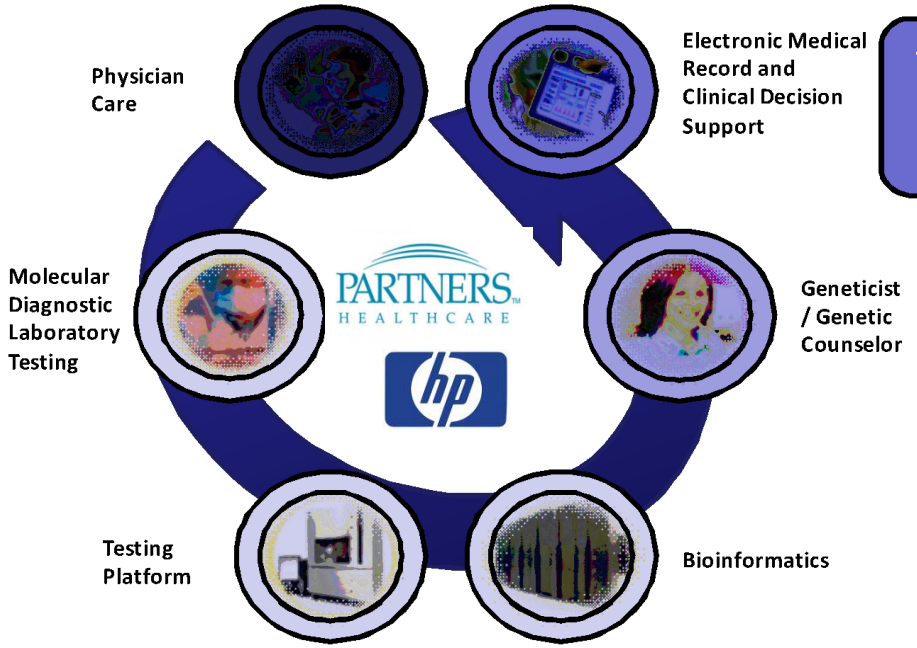
# Premier hospitals such as MGH are actively enforcing personalized medicine to enable better outcomes by taking knowledge management initiatives for data stored in EMRs and CDSS




**EMR and CDSS:** *Manage the storage and security of structured data, and alert physician of important gene interpretations*

**Knowledge Management:** *"GVIE" and GeneInsight accelerate the interpretation of test results*

**Advanced LIS:** *"GIGPAD" manages the physical aspects of the testing process*

## IMPLICATIONS TO PERSONALIZED MEDICINE

- This portal has revolutionary potential to translate the promise of personalized medicine into reality
- The portal when expanded into an enterprise wide application across several labs/hospitals can be used to educate physicians, increase awareness of emerging high value MDx tests and accelerate adoption of these tests
- IVD/MDx companies can use this portal to streamline their internal biomarker mining efforts to identify biomarkers with most clinical validity and utility for physician

Sources: Scientia analysis, the Harvard Medical School Partners Healthcare Center for Genetics and Genomics



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# Health IT companies are actively getting involved in PM by collaborating with payors to ensure accurate prescription of drugs

McKESSON Empowering Healthcare

InterQual® access a higher intelligence.

MVP HEALTH CARE

BlueCross of Idaho

**Payors Adopt McKesson's Automated InterQual Molecular Dx System to Avoid Inaccurate Coverage Decisions**

*- Pharmacogenomics Reporter – November 18, 2009*

McKESSON

Aetna, Medicare, PacifiCare, CIGNA, Prudential, HUMANA, DELTA Health Systems, UniCare, UnitedHealth Group

**McKesson Aims to Help Health Plans Navigate MDx, Genetic Testing Space** "… McKesson is seeking to capitalize on the growing demand from health plans for help with MDx tests, and announced that 3 new health plans had joined its burgeoning list of clients using its products to help navigate the MDx space …" *Press Release, July, 2011*

## KEY TAKEAWAYS

- Although McKesson's initial use of Molecular Dx in their InterQual CDSS is to manage the appropriate use of diagnostic testing, the likely next step will be to use diagnostic tests to guide therapeutic and prescription decisions and to manage coverage based on evidence
- CDSS systems offered by health IT companies will have a significant impact on drug prescription decisions, particularly to limit the use of branded drugs vs. generics
- McKesson's goal is to provide them with enough data and information to make informed decisions and not to tell health plans which of the ~2,000 MDx tests they should cover
- In the US, health IT is gaining in importance as Obama's healthcare reform mandates the implementation of electronic health records

Sources: Scientia Analysis; Genomeweb



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# Small and large health IT companies are also actively getting involved in PM by collaborating with providers to ensure accurate prescription of drugs

**Dana-Farber Informatics Team Launches GenoSpace to Link Genomic and Clinical Data via the Cloud**
"…GenoSpace, a Cambridge, Mass.-based informatics startup, has teamed with DFCI and launched a cloud-based platform intended to provide access to a variety of 'omic and phenotype data." – *Press Release, June, 2012*

**DNAnexus Raises $15 Million, Teams With Google To Host Massive DNA Database** "… raised funds from Google Ventures and TPG Biotech to help help scientists and genome-related services host and manage this data… announced a key partnership with Google to give long-term home to the Short/Sequence Read Archive (SRA) database which spans 400 terabytes at this point, includes publically available whole-genome sequences that scientists can use for research purposes…." – *Press Release, Oct, 2010*

**N-of-One Announces Agreement with Foundation Medicine to Provide the First Patient-Specific Genomic Diagnostic Solution for Precision Oncology**
"… provider of Diagnostic Strategy Roadmaps™ & Treatment Strategy Roadmaps™ for personalized cancer care, announced a strategic collaboration with Foundation Medicine, Inc. to support the development of its fully informative molecular cancer profiles that can be used to guide individualized patient treatment strategies…" – *Press Release, May, 2012*

## KEY TAKEAWAYS

- Health IT companies are developing "roadmaps" to drive informed clinical decision-making by linking data about the molecular variations in each patient's cancer cells with leading-edge diagnostics, treatments, and technologies relevant to the tumor type
- In addition to providing a general data access portal, GenoSpace works with clients to build customized research portals to enable them to ask particular research questions
  - Example - a user might want to locate candidates in a disease cohort that have a particular mutational profile required for a clinical trial
- Besides disease foundations, CROs, and pathology departments, other likely clients for GenoSpace and other such health IT vendors include pharmaceutical companies and information vendors

Sources: Scientia Analysis; Company literature and press releases



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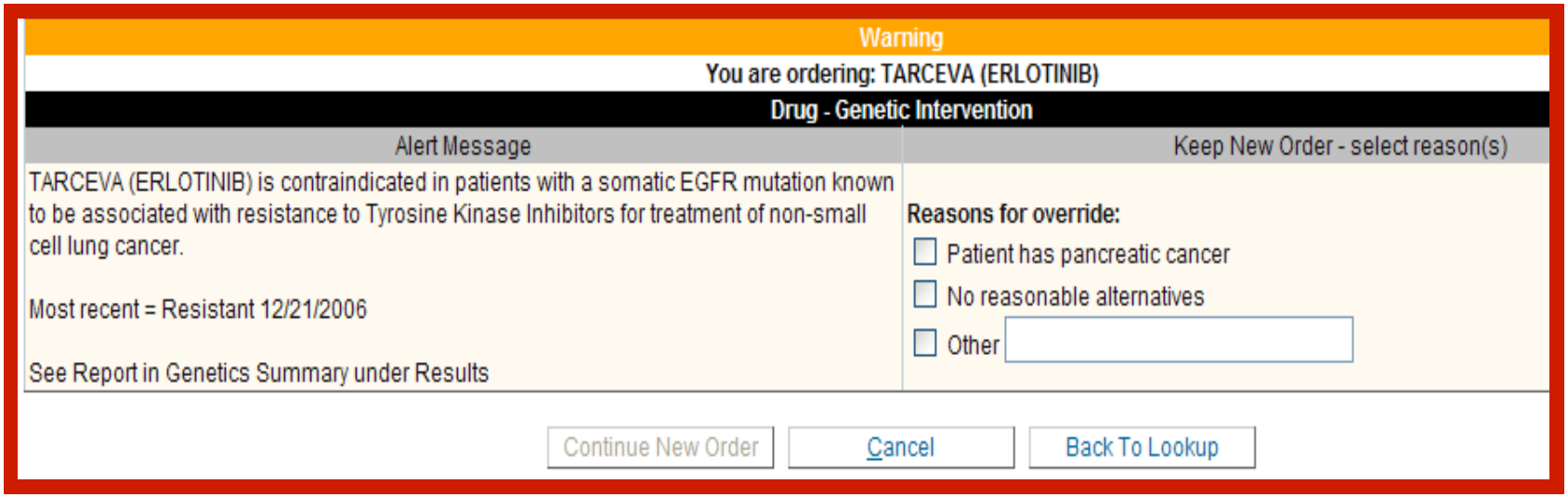
# Such partnerships for genetic data collection, integration and analysis will enable PM CDSS rules that will remind physicians of a contraindications between drugs and certain mutations

## EXAMPLE PM CLINICAL DECISION SUPPORT RULE

***Partners Healthcare's EHR contains a PM CDSS component which will remind a physician of a contraindication between TARCEVA and certain genetic mutations when the physician tries to prescribe this drug to a patient with the mutation***




## KEY TAKEAWAYS

- By reminding physicians of "easy to learn, easy to forget" information, CDSS tools can decrease variation in the use of various tests and interventions
- A CDSS will also be able to suggest options of published or guideline suggested therapeutic options allowing physicians to stay on top of the latest research and guideline changes

Sources: Scientia analysis, ScientiaNet, Partners' Healthcare



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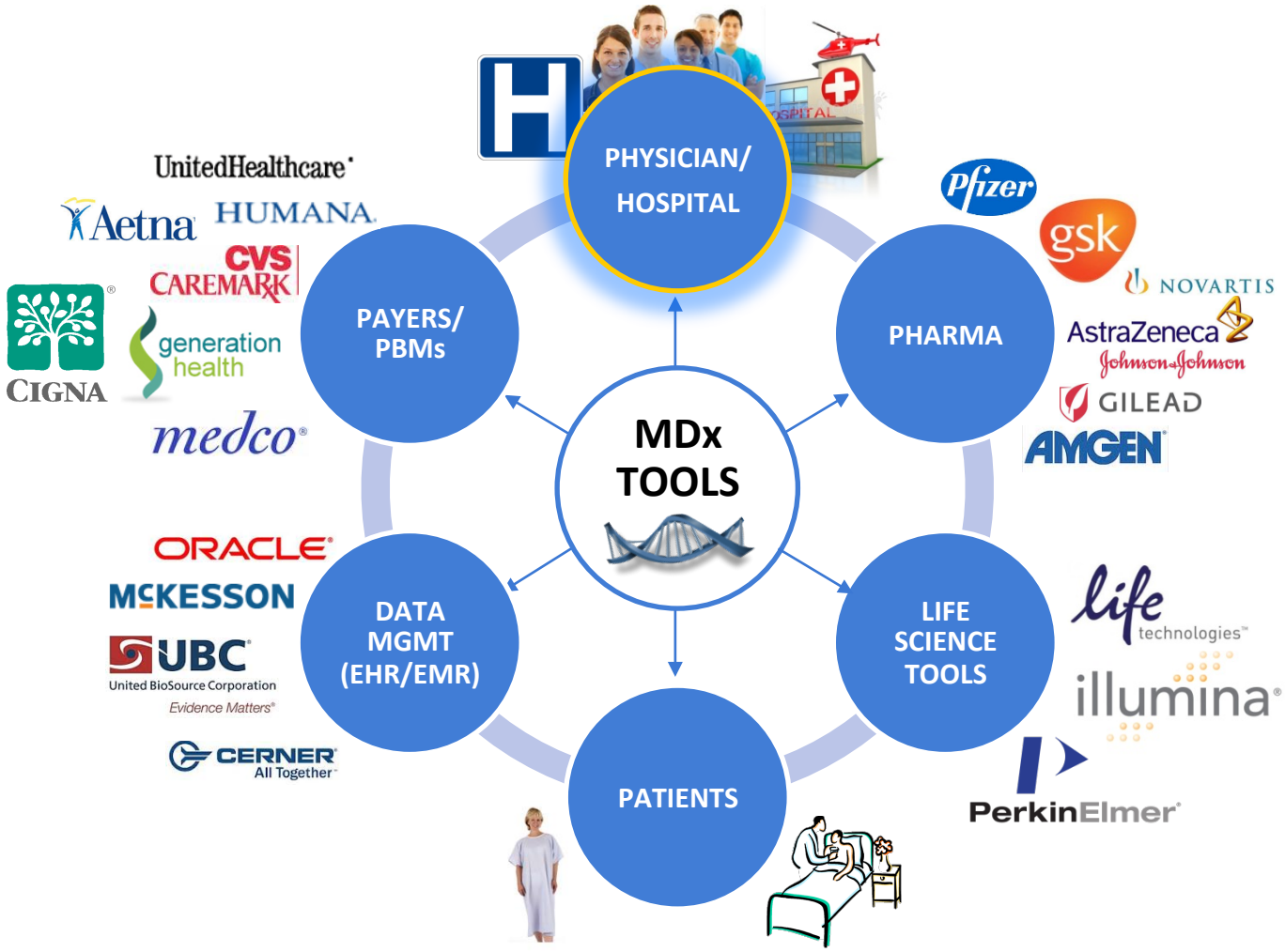


Source: Scientia Analysis



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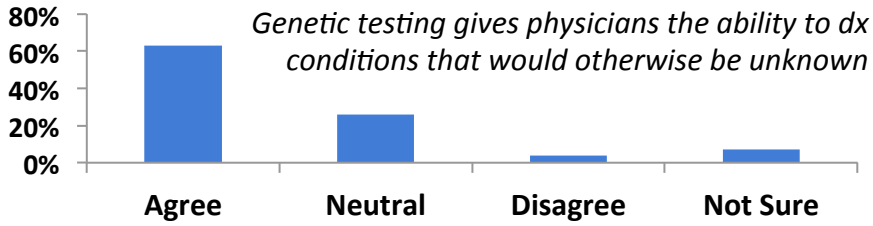
# Physician interest in personalized medicine is high but adoption of PM genetic testing will increase after physicians gain education and comfort with the tests

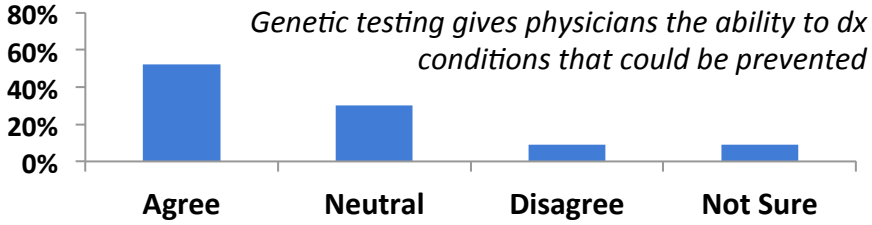
## NEED FOR PHYSICIAN EDUCATION

- ***United Healthcare survey*** *in 2012 reported that 75% of the physicians believe that there are patients in their practice who have not yet had a genetic test but would benefit from having one*
- ***Medco/American Medical Association survey*** *in 2009 reported that while* ***98%*** *of physicians understand the value of PGx, they don't feel they have the sufficient knowledge to comfortably order such tests*

## UNITED HEALTHCARE: CENTER FOR HEALTH REFORM & MODERNIZATION SURVEY

## (US estimates 2012 - % Physicians)




## KEY TAKEAWAYS

- In a Medco/AMA survey, almost all physicians indicated a lack of knowledge and comfort-level regarding personalized medicine tests currently available on the market today
- The education of physicians on correct use and applicability of the results of a PM test will greatly accelerate the adoption of that test
- Only ~400 out of 1300 molecular diagnostic tests have evidence based guidelines
  - To empower physicians, there is a need for a mechanism to move information from 'bench' to 'point of care'
- There is increasing need for genetic counselors and cross-training of physicians in genomics and bioinformatics
- The Wideroff study published in 2003 found that test usage went up significantly when patients asked physicians about the tests

Sources: Scientia analysis; United Healthcare Working Paper – March 2012; Wideroff, L, *et al.* (2003) Cancer Epidemiology, 12:295; GenomeWeb



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# Besides increasing physicians' education and comfort, physician payment models may see modifications in order to promote MDx based approach to treating diseases

## - EVOLUTION OF CANCER TREATMENT PARADIGM -

**Unlike the traditional approach …**

- Type of cancer?
- Stage of cancer?

**… MDx tools & information enable …**

- Type of cancer?
- Genetic variation?
- Epigenetic factors?
- Genetic resistence to therapy?

**… a targted approach in the future**

- Predisposition/Prognostic Dx/Rx?
- Diagnosis/Staging Dx/Rx?
- Theranostic Dx/Rx?
- Monitoring Dx/Rx?

## UnitedHealthcare Report Recommends Adopting New Cancer Care Payment Model to Reward Physicians for Health Outcomes

*Health Affairs article examines current cancer care payment system and alternative strategies to reduce costs and improve health outcomes for patients*

**MINNETONKA, Minn.** (April 16, 2012) – A new report from UnitedHealthcare examines the current cancer care payment system and considers alternative

*According to Dr. Newcomer, 'Paying physicians for a total treatment cycle promotes better care and eliminates the incentive to prescribe costly drugs that may not be the most effective treatment option.'*

Examples : Newly proposed physician payment models being evaluated include ….

- **OPTION A:** Treating oncologist can choose the least expensive clinical pathway approach OR choose an alternative if patient displays drug resistance
  - Oncologists rewarded for compliance with the clinical pathway through higher fee schedules, bonus programs, or other forms of incentives
- **OPTION B:** a "bundled payment" or an "episode payment," reimburses medical oncologists upfront for an entire cancer treatment program vs. using the current "fee-for-service" approach that rewards volume regardless of health outcomes
  - Payment based on the expected cost of a standard treatment regimen for the specific condition, as predetermined by the oncologists

Sources: Scientia analysis; United Healthcare Working paper



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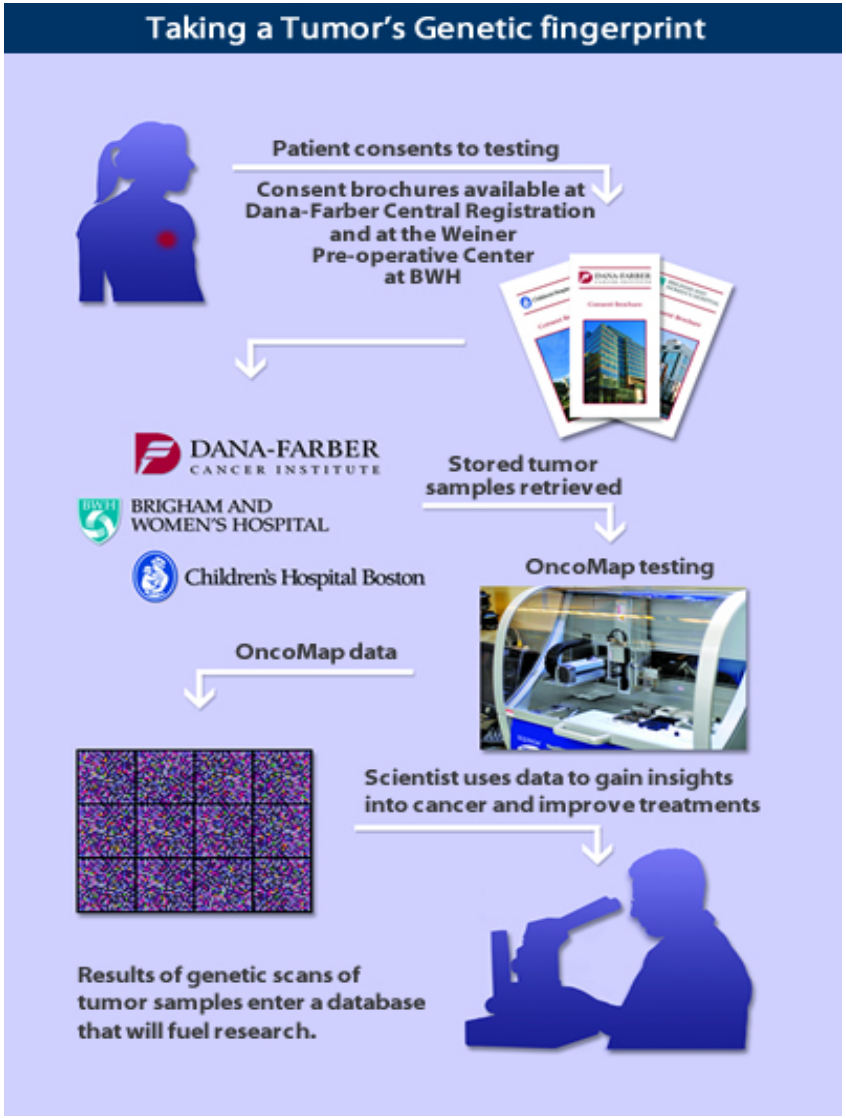
# As a result, providers like Dana-Farber and Brigham & Women's Hospital join to launch PROFILE for genetic research, one of the most extensive national level research projects in cancer genomics yet

**Dana-Farber, Brigham and Women's launch PROFILE, a large-scale research program to scan tumors for mutations, establish extensive genomic database (Oct 2011)**

- Goal of PROFILE
  - To leverage access to patients' tumor samples and genetic testing tools to scan tumor tissue for hundreds of gene mutations linked to cancer
- Advantages of PROFILE
  - Enable clinicians to treat more cancers with mutation-specific targeted therapies in the future
  - Expand with the discovery of additional cancer-related mutations
  - Develop more advanced screening technologies
  - Patient eligibility for clinical trials




Sources: Scientia Analysis; DFCI



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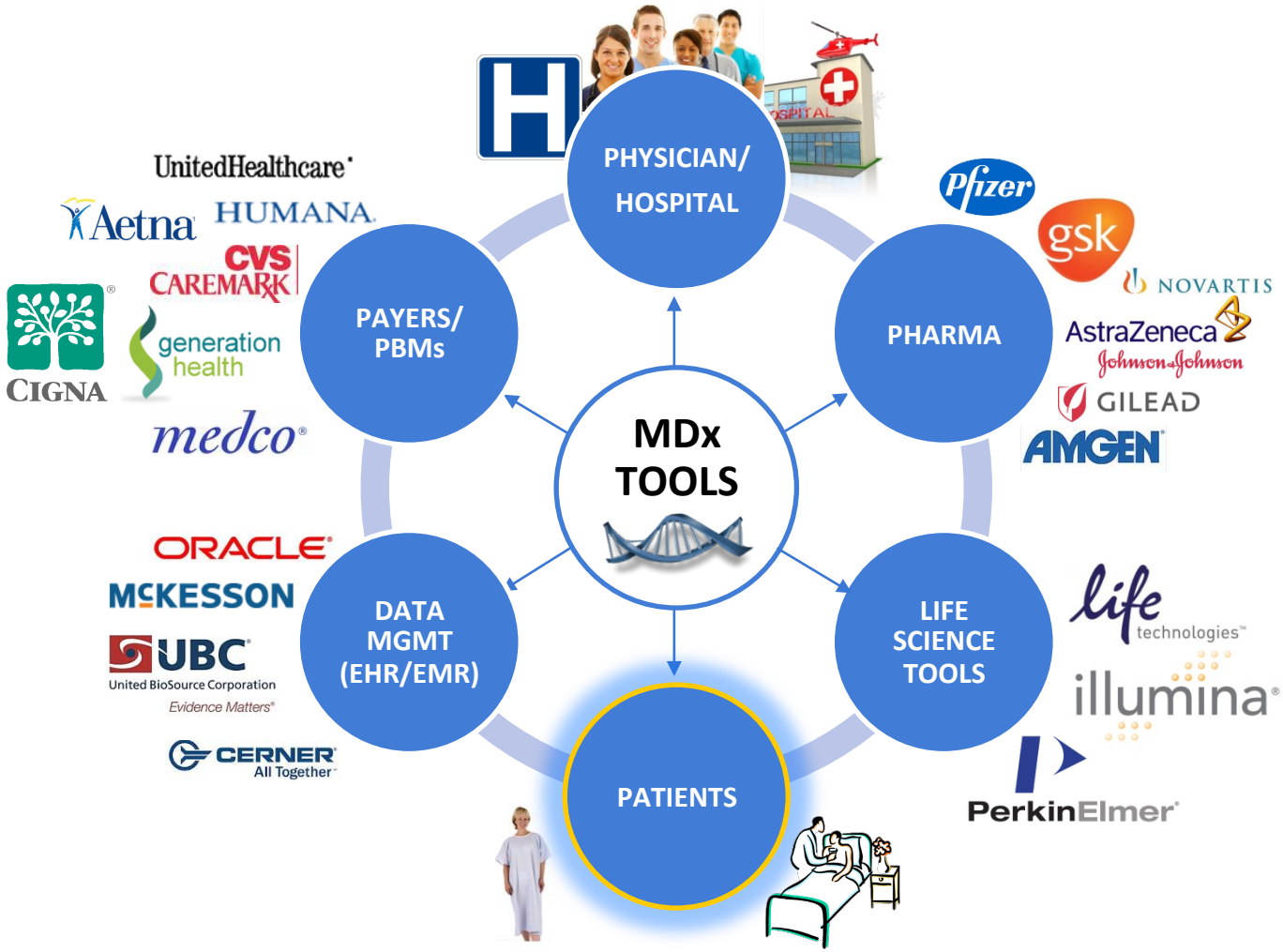


Source: Scientia Analysis



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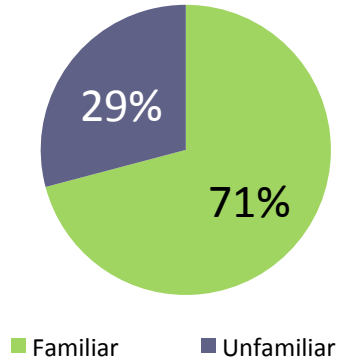
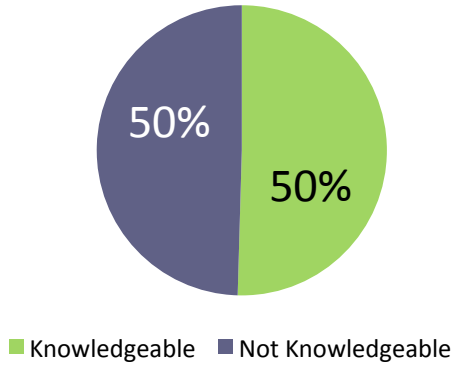
# As treatment becomes more personalized, patients believe they will have more options and view personalized medicine as a tool to improve healthcare

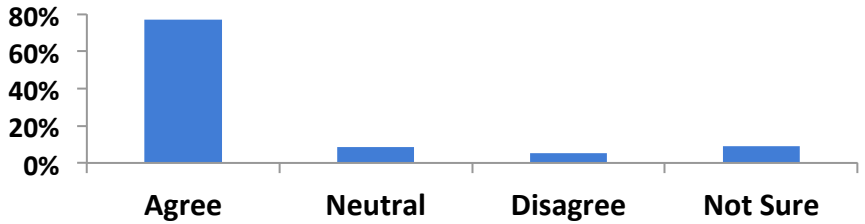
## How familiar are you with genetic testing?



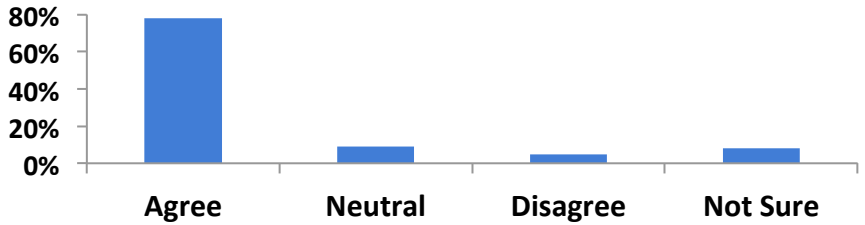

## How knowledgeable are you about genetic science?



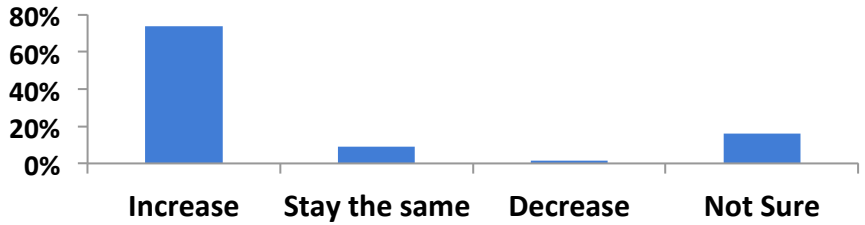

## Genetic testing allows for more personalized decisions.




## Genetic testing gives doctors the ability to diagnose conditions that can be prevented.




## 5 years from now, what do you think about the use of genetic testing of any kind in the US?




**UNITED HEALTHCARE: CENTER FOR HEALTH REFORM & MODERNIZATION SURVEY**
**(US estimates 2012 - % Consumers)**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# Patients are already becoming exposed to the possibilities of personalized medicine…

## PM THROUGH THE PROVIDER

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Genetic Gamble
*New Approaches to Fighting Cancer*

PART ONE A Race to Leukemia's Source
PART TWO Promise and Heartbreak
PART THREE What a Tumor Holds in Store

### In Treatment for Leukemia, Glimpses of the Future

**Second Chance:** Lukas Wartman, a leukemia doctor and researcher, developed the disease himself. As he faced death, his colleagues sequenced his cancer genome. The result was a totally unexpected treatment.

By GINA KOLATA
Published: July 7, 2012 | 304 Comments

ST. LOUIS — Genetics researchers at Washington University, one of the world's leading centers for work on the human genome, were devastated. Dr. Lukas Wartman, a young, talented and beloved colleague, had the very cancer he had devoted his career to studying. He was deteriorating fast. No known treatment could save him. And no one, to their knowledge, had ever investigated the complete genetic makeup of a cancer like his.

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## PM THROUGH DTC

TIME Specials
Best Inventions of 2008

*From a genetic testing service to an invisibility cloak to an ingenious public bike system to the world's first moving skyscraper — here are TIME's picks for the top innovations of 2008*

Invention of the Year

NEXT
View All

### 1. The Retail DNA Test

By ANITA HAMILTON Wednesday, Oct. 29, 2008

Before meeting with Anne Wojcicki, co-founder of a consumer gene-testing service called 23andMe, I know just three things about her: she's pregnant, she's married to Google's Sergey Brin, and she went to Yale. But after an hour chatting with her in the small office she shares with co-founder Linda Avey at 23andMe's headquarters in Mountain View, Calif., I know some things no Internet search could reveal: coffee makes her giddy, she has a fondness for sequined shoes and fresh-baked bread, and her unborn son has a 50% chance of inheriting a high risk for Parkinson's disease.

23andMe

Navigenics

RESPONSE GENETICS

Sources: Scientia Analysis; Industry news; Company literature and press releases



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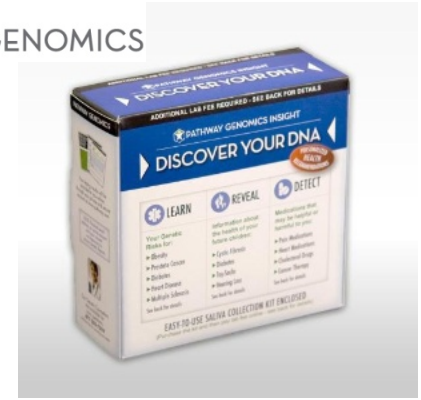
Scientia Advisors

# … however, until regulations are standardized, patients will experience the impact of personalized medicine primarily through approved channels

## Providing a DTC genetic test off-the-shelf …

PATHWAY GENOMICS




Walgreens
The Pharmacy America Trusts

## … received a negative reaction from the FDA

CNN Health

SEARCH

Politics | Justice | Entertainment | Tech | Health | Living | Travel | Opinion | iReport | Money | Sports

### Walgreens postpones plans to sell personal genetic tests

May 12, 2010 | By Madison Park, CNN

Share | Twitter | Email

Recommend | 480 people recommend this. Be the first of your friends.

Walgreens has postponed its plans to sell personal genetic test kits after the Food and Drug Administration intervened.

Genetic kits from Pathway Ge… nationwide drug stores startin… experts and the FDA, which w…

After the agency contacted th… on the sale of the kits.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
10903 New Hampshire Avenue
Document Mail Center - WO66-0609
Silver Spring, MD 20993-0002

James Plante
Founder and CEO
Pathway Genomics Corporation
4045 Sorrento Valley Blvd.
San Diego, CA 92121

MAY 10 2010

Dear Mr. Plante:

It has come to our attention that you are currently marketing the Pathway Genomics Genetic Health Report, a home-use saliva collection kit, intended to report customary and personal genetic health disposition results for more than 70 health conditions, including pharmacogenetics (prescription medication response), propensity for complex disease, and carrier status (pre-pregnancy health) information from which one can modify their health regime to live a healthier, longer life. The Genetic Health Report appears to meet the definition of a device as that term is defined in section 201(h) of the Federal Food Drug and Cosmetic Act.

We have conducted a review of our files, and have been unable to identify any Food and Drug Administration (FDA) clearance or approval number for the Genetic Health Report. We request that you provide us with the FDA clearance or approval number for the Genetic Health Report. If you do not believe that you are required to obtain FDA clearance or approval for the Genetic Health Report, please provide us with the basis for that determination.

The requested information should be submitted to:

James L. Woods
Deputy Director, Patient Safety and Product Quality
Office of *In Vitro* Diagnostic Device Evaluation and Safety
10903 New Hampshire Avenue
White Oak 66
Silver Spring, MD 20993

We would appreciate a response within 15 days from the date of this letter.
If you have any questions relating to this matter, please feel free to call Cecily Jones at 301-796-6172, or access our web site at http://www.fda.gov for general information relating to FDA's device requirements.

Sources: Scientia Analysis; Company literature and press releases



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Scientia Advisors

# Agenda

- The Role of MDx in Personalized Medicine
  - » Recent Industry Trends
  - » Evolution of Business Models
- **Public Policy Considerations**
- Future Directions


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# Government agencies are increasing their attention towards cost effectiveness and patient outcome measures that include the use of molecular or genetic tests

## GOVERNMENT INTEREST IN PERSONALIZED MEDICINE

**Several U.S. federal agencies are involved in personalized medicine**

CDC · FDA · National Institute of General Medical Sciences · CMS Centers for Medicare & Medicaid Services · National Institutes of Health – The Nation's Medical Research Agency · AHRQ Agency for Healthcare Research and Quality – Advancing Excellence in Health Care

**US Health Reform legislation includes the establishment of the Patient-Centered Outcomes Institute (PCOI)**

- Comparative Effectiveness Research (CER) will include primary research
- Will take into account individual and subpopulation differences, **including genetic and molecular subtypes**
- Experts appointed will include those in **genomics** and CER

…but proposed funding of $10-150 MM is inadequate

**The UK is increasing attention to in vitro diagnostic tests**

NHS National Institute for Health and Clinical Excellence

"New NICE programme to evaluate medical technologies established" – *NICE, Nov 16, 2009*

## KEY TAKEAWAYS

- The US has funded outcomes research via several agencies. Current legislation, if enacted, may establish an explicit agency responsible for effectiveness research, although effective funding is not yet clear.
- European Health Technology Assessment (HTA) agencies, such as the UK's NICE and Germany's IQWiG, have traditionally focused their outcomes and cost-effectiveness research on pharmaceuticals. They are now turning their attention to diagnostics and devices. Diagnostics that control drug costs are obvious winners.

Sources: Rugnetta and Kramer, "Paving the Way for Personalized Medicine"; Scientia research; press releases; BIVDA;



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# The FDA has been accelerating their involvement in development of molecular diagnostics and pharmaceuticals to enable personalized medicine

## PM DIAGNOSTICS ACTIVITY

### First PGx Test Approved

***Dec. 24 2004:*** *The FDA approved AmpliChip CYP450 test, the first FDA approved PGx test*

### FDA Approves Agendia's Mammaprint

***Feb. 6 2007:*** *The FDA approved Agendia's MammaPrint Dx for breast cancer recurrence, the first IVDMIA test*

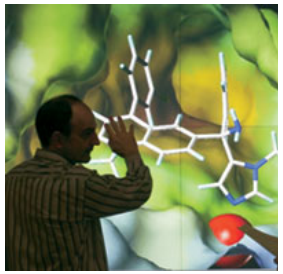

### FDA Simultaneously Approves Roche/ Plexxikon's Drug, Companion Dx for BRAF-Mutated Melanoma

***Aug. 17 2011:*** *The FDA* pproved Roche's personalized melanoma drug Zelboraf alongside a companion genetic test,


### FDA Clears Qiagen KRAS Test as CDx for Erbitux

***July 2012:*** *FDA cleared marketing of therascreen KRAS RGQ PCR Kit to be sold as a companion diagnostic test for Erbitux (cetuximab)*

## PM PHARMACEUTICAL ACTIVITY



### FDA Withheld Approval of Zarnestra

***May 2005:*** *Zarnestra was not approved by the FDA for AML because Johnson & Johnson did not have evidence in their trial that the drug was more effective than chemo. FDA's Oncologic Drug Advisory Committee on Zarnestra believed that the trials would have more effective if a diagnostic was utilized to determine patients that were not eligible for chemotherapy*

### FDA Updates Plavix Label

***May 2009:*** *The FDA updated Plavix label with with pharmacogenetic data informing doctors and patients of diminished response to the drug and increased risk of heart attack in patients with reduced CYP2C19 function*

### FDA Updates Vectibix and Erbitux Labels

***July 2009:*** *The FDA updated the "indication and usage" section of Amgen's Vectibix and BMS/ImClone's Erbitux to include "retrospective analyses of metastatic colorectal cancer trials have shown not shown a treatment benefit for the EGFR inhibitors in patients whose tumors had KRAS mutations in codon 12 or 13," and that the use of the drugs is not recommended for the treatment of CRC patients with these mutations*

Sources: Scientia Analysis; GenomeWeb



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# For example, the FDA released a guidance with recommendations on how to label RUO tests for their intended purposes …

## OVERVIEW OF FDA RUO GUIDANCE DOCUMENT

*FDA recently released a guidance document¥ reminding manufacturers of the requirements applicable to RUO and IUO IVDs. The aim is to control the clinical diagnostic use of IVDs in order to prevent the possibility of misinformed clinical decisions that may ultimately lead to adverse patient health consequences. The document is not legally enforceable; however, they represent current recommendations and suggestions on labeling and marketing these tests by the FDA.*


### GUIDANCE ON RUO/IUO LABELING

- Appropriate RUO labeling refers to IVD use strictly for research intended to evaluate the test itself or in non-clinical laboratory research. These tests are inappropriate for use in diagnostic procedures.
- Appropriate IUO labeling refers to the use of IVDs in an investigation, but it is not to be used for clinical diagnosis without confirmation from another established product or procedure.

### GUIDANCE ON RUO/IUO MARKETING

- Advertising, promotion, support or sales of RUO IVD for use in clinical investigation, clinical diagnostic use, or for LDT development meant for clinical diagnosis conflicts with the intended use of an IVD labeled RUO
- Advertising, promotion, support, or sales of IUO IVD for use in non-investigational diagnosis, or use that is inconsistent with an exempt investigation conflicts with the intended use of an IVD labeled IUO

Notes: RUO- Research Use Only; IUO – Investigational Use Only; ¥Draft guidance released on June 1st, 2011 titled "Draft Guidance for Industry and FDA Staff - Commercially Distributed In Vitro Diagnostic Products Labeled for Research Use Only or Investigational Use Only: Frequently Asked Questions."

Sources: Scientia analysis; FDA Draft Guidance



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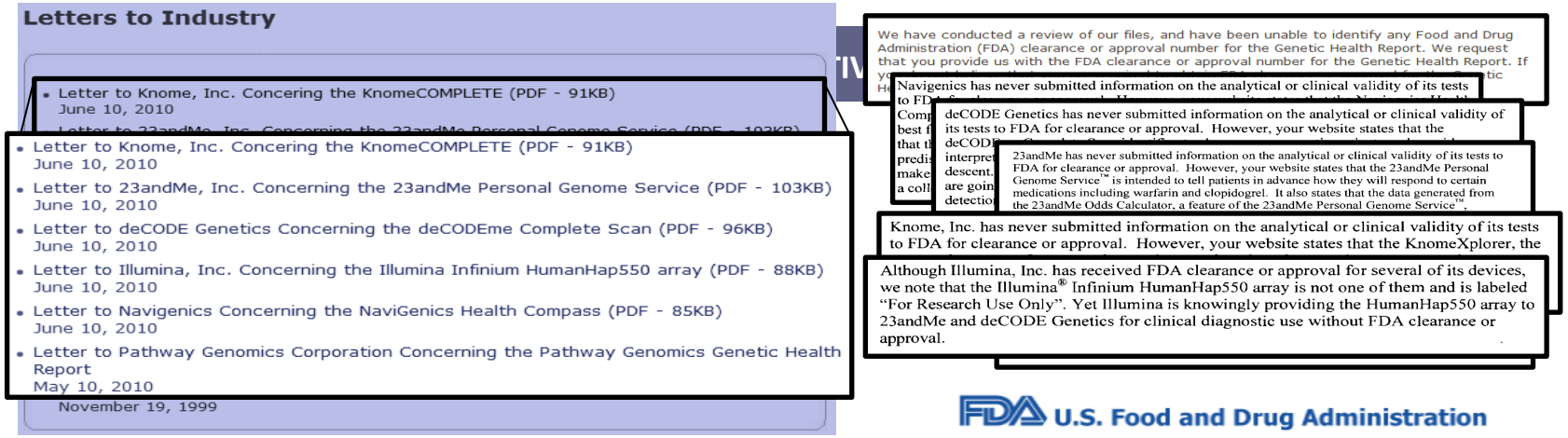
# … which may have stringent consequences on regulations surrounding Direct-to-Consumer (DTC) genetic and MDx testing and Laboratory Developed Tests (LDTs)




**On June 16, 2010, the U.S. Food and Drug Administration (FDA) announced its intention to dramatically expand its regulatory oversight of laboratory-developed tests (LDTs)**

*For years, the FDA had adopted a policy of "enforcement discretion" in declining to closely regulate LDTs. However, an expanding and changing LDT marketplace, along with heightened government and media scrutiny of certain LDTs, including high-complexity tests and tests marketed directly to consumers (DTC), has caused the FDA to reconsider its policy of enforcement discretion. FDA's has ongoing attempts and inititaies to develop a comprehensive system of oversight for LDTs*

- FDA issued 4 Letters to Knome, 23andMe, deCODE Genetics, and Navigenics requesting that their full genome testing service be submitted for FDA approval
- A similar letter sent to Pathway Genomics, coinciding with announcements of Walgreens' intent to stock the firm's Insight Saliva Collection Kit for genetic testing
- Illumina, who supplies 23andMe and deCode with the array for the genome test, was sent a letter taking issue with the RUO status of the array

Sources: FDA; Company literature and press releases

Sources: FDA; Genomics Law Report



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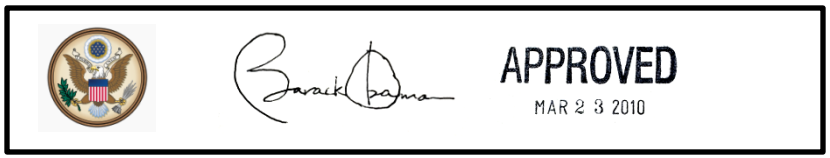
# Overall, government interests globally are increasing towards the incorporation of molecular or genetic profile information for improved patient care

## GOVERNMENT INTEREST IN PERSONALIZED MEDICINE

**Several U.S. federal agencies are involved in personalized medicine**




**Patient Protection and Affordable Care Act (Obamacare)**

- Includes provisions for allowing FDA approval for biologic drugs, increasing Medicaid drug rebate for brand name drugs, supporting comparative effectiveness research


**NICE OKs AstraZeneca Iressa For Lung Cancer After Cost Deal**

May 26, 2010 – NICE recommends the use of AstraZeneca drug Iressa for NSCLC patients after AstraZeneca offers the product to patients for free if treatment is less than 3 months. The drug was previously rejected for its cost efficiency and effectiveness.


**Italy Health Ministry pushes for greater use of low cost generics**

June 2010 – New package seeks to balance incentives to stimulate research with the need to lower overall drug bills

## KEY TAKEAWAYS

- President Obama's Patient Protection and Affordable Care Act, nicknamed Obamacare, will upon enactment authorized generic biologic FDA approvals, increase Medicaid drug rebate for brand names, and support comparative effectiveness research
- European Health Technology Assessment (HTA) agencies such as the UK's NICE and Germany's IQWiG have traditionally focused their outcomes and cost-effectiveness research on pharmaceuticals
  - » In Iressa's case, NICE recommended use of the drug for NSCLC only after AstraZenenca agreed to provide the drug to patients for free is use was below 3 months
- HTAs are now also turning their attention to diagnostics and devices. Diagnostics that control drug costs are obvious winners.
- Health Ministries in Europe including Italy, Germany and the Netherlands are also pushing for increased use generic drugs over branded to lower cost

Sources: Rugnetta and Kramer, "Paving the Way for Personalized Medicine"; Scientia research; press releases; BIVDA



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# Agenda

- The Role of MDx in Personalized Medicine
  - » Recent Industry Trends
  - » Evolution of Business Models
- Public Policy Considerations
- **Future Directions**


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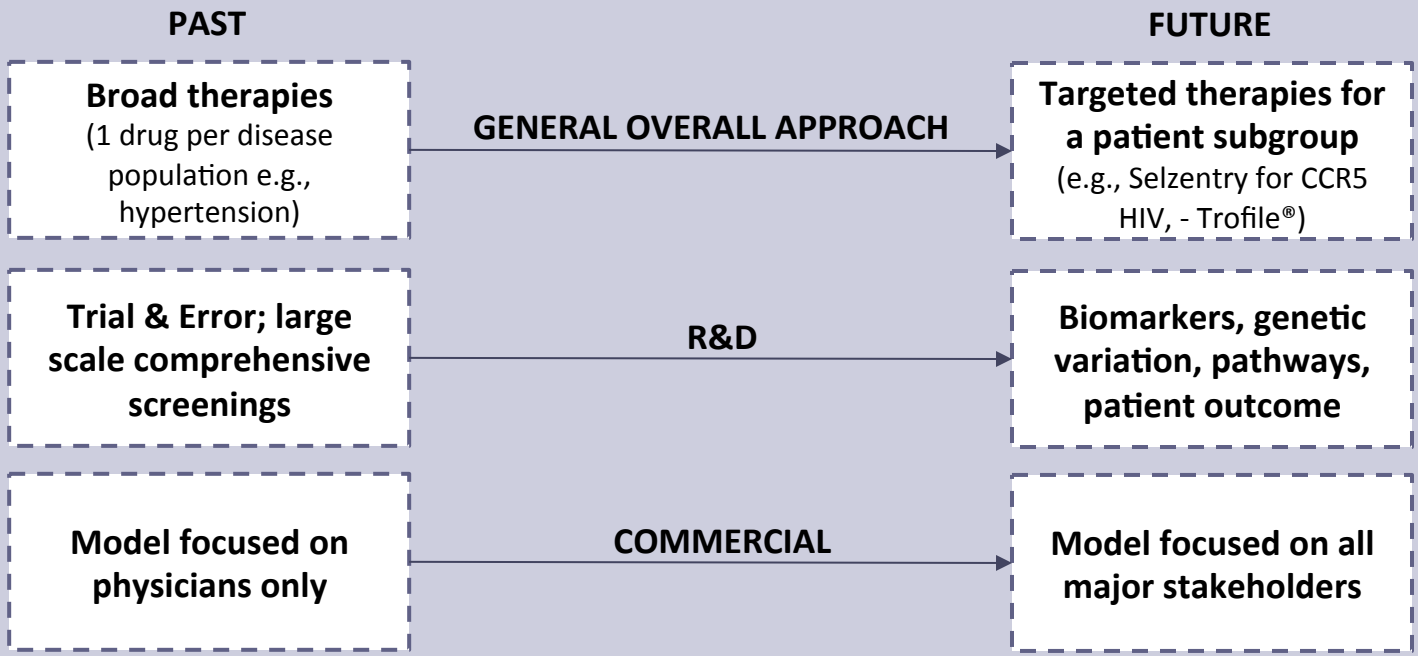
# In summary, it is imperative for stakeholders to focus on innovative business models to capitalize on molecular diagnostics and its evolving role healthcare thus, improving patient care cost-effectively

***- NEW APPROACH TO DURG DISCOVERY, DEVELOPMENT & COMMERCIALIZATION FOR OPTIMAL PATIENT CARE -***

***Shift in healthcare driven by MDx technologies and patient information***




Source: Scientia Analysis



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# Molecular diagnostics are driving personalized medicine, but the path to market is still filled with many hurdles

**Biomarker Development Issues**

- Discovery and validation of biomarkers can be expensive and who owns the IP?
- Technological hurdles of assay development
- Hurdles associated with manufacturing personalized therapies

**Coverage and Reimbursement Issues**

- Which tests specifically will save costs?
- The need for long-term results data
- Use of out-dated analysis models that do not factor in small, niche populations addressed by personalized medicine
- Price sustainability issues – how high will personalized medicine costs go?

**Business Model Considerations**

- Big pharma's commitment to biomarker investment
- How will the diagnostic be marketed as a kit or certified CLIA lab as is currently being done
- Regulatory hurdles as most assays are now central lab CLIA based
- Which assay platform should be used as that affects pricing and marketing
- Joint ventures vs partnerships due to the different goals of Rx and Dx companies


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# Key questions and strategic options for pharma companies

## KEY QUESTIONS

- Regional Regulatory Differences
  - » What exactly will EU and Asian countries require from a CDx?
- Regulatory Interactions
  - » What is the appropriate time for regulatory submissions and interactions?
- Non-Pivotal Prospective Trials
  - » For a non-pivotal study (e.g., Phase 2 or 1b), what are the regulatory requirements for patient stratification (e.g., neuregulin study)?
- Co-Development Timelines
  - » What are the co-development timelines for each potential CDx / drug program?
  - » Is it possible to proceed into a phase 3 trial without full analytical validation?
- Commercial Model
  - » What are the business model options?
- Pricing and Reimbursement
  - » What is the pricing and reimbursement landscape for companion diagnostics?
- IP
  - » What is the value of the IP? What is the key IP to have?
- Diagnostic Vendors
  - » Who are the potential diagnostic partners for each test / modality?

## STRATEGIC OPTIONS

1. PARTNER TO DEVELOP CDX UNDER PMA PATHWAY
2. USE CE-MARKED ROUTE
3. LEVERAGE PARALLEL LABELS
4. OTHERS?


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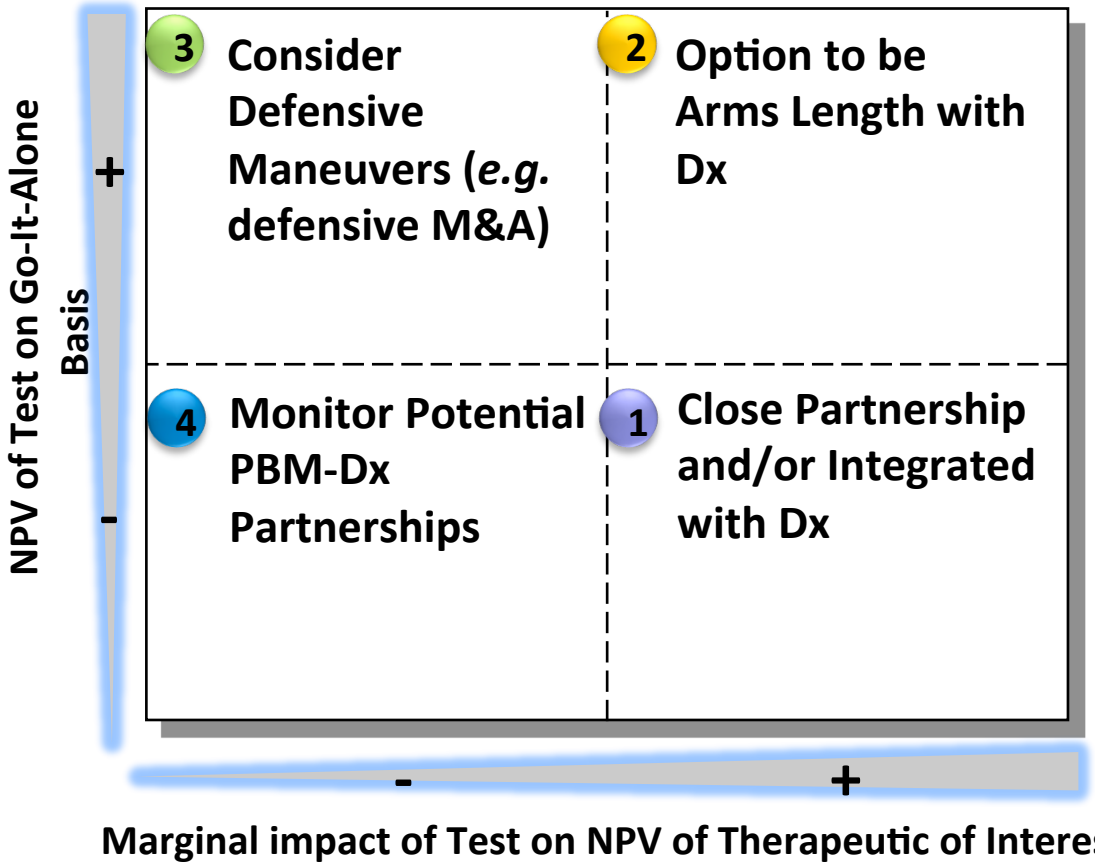
# Mapping Out Strategic Options (High-Level)

## Personalized Medicine Strategy Selection Framework




## Explanation

| | Quadrant | Details |
|---|---|---|
| 1 | Close Partnership with Dx Co. | • DxCo has no incentive to commercialize<br>• Pharma has interest in test commercialization<br>• **PharmaCo must subsidize commercialization** |
| 2 | Arms Length Relationship | • DxCo has incentive to commercialize<br>• PharmaCo also has interest in test<br>• **Deal is optional and may further increase NPV of Dx and Therapeutic** |
| 3 | Defensive Maneuvers | • DxCo has incentive to commercialize<br>• Pharma has incentive to limit uptake<br>• **Pharma should carefully assess risk mitigation ideas** |
| 4 | Monitor potential PBM relationships | • DxCo has no incentive to commercialize<br>• PBM has incentive to contain Rx cost<br>• **Pharma should consider the impact of potential Dx/PBM deals** |

Source: Scientia Advisors



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