

## Forging a Path From Companion Diagnostics to Holistic Decision Support

L.E.K. Consulting is a strong believer in personalized medicine and its promise to improve patient outcomes and reduce healthcare costs. While still in its relative infancy, we see personalized medicine as enabling the healthcare community to tailor screening and prevention programs, identify and dose the most effective treatments, and customize disease monitoring and management programs.

Companion diagnostics<sup>1</sup> (and their companion therapies) are critical building blocks in personalized medicine as they typically enable the identification of likely responders to therapies that work in patients with a specific molecular profile. Companion diagnostics have also enabled access to novel therapies that may otherwise have not been approved or reimbursed in all-comers by demonstrating strong efficacy signals in enriched patient populations.

While companion diagnostics enable personalized medicine, they tend to only answer a targeted drug-specific question and may not address other important clinical decision needs. As an example, HER2 testing informs Herceptin candidacy but does not provide insights on therapeutic intervention for non-candidates. Furthermore, landscape trends suggest companion diagnostic tests in their current “one-test/one-drug” embodiment will not adequately cover future decision support

needs as the number of validated biomarkers overwhelms available sample amounts for testing (especially with tumor biopsies) and physicians become inundated with more biomarker data (likely to be interrelated, nuanced and at times even contradictory).

### Identifying the Building Blocks for Holistic Decision Support Solutions

While L.E.K. expects that companion diagnostics will continue to propel advances in personalized medicine by providing highly validated biomarkers linked to approved therapies, we also expect to see the emergence of more holistic decision support tests that interrogate multiple biomarkers (e.g., panels of companion diagnostics and other validated biomarkers/signatures) as well as more holistic decision support solutions that consider a broader range of inputs (e.g., test data, imaging data, clinical trial activity, outcomes data, patient EMR data, reimbursement and coverage data) to inform patient management. While a comprehensive decision support solution that considers all available data to support patient management is likely decades away, we are already seeing leaders in personalized medicine begin to pursue more holistic models and lay the groundwork for future participation.

<sup>1</sup> Diagnostic tests typically used to predict responsiveness / determine candidacy for a particular therapy often included in drug labels as either required or recommended testing prior to therapy initiation.

*Forging a Path From Companion Diagnostics to Holistic Decision Support* was written by **Alexander Vadas**, Ph.D., Vice President; **Sue St. Sure**, Vice President; and **Brian Baranick**, Ph.D., Manager, of L.E.K. Consulting. Please contact L.E.K. at [lifesciences@lek.com](mailto:lifesciences@lek.com) for additional information.

L.E.K. believes the evolution to more holistic models will have a broad impact across healthcare stakeholders, creating opportunities for new businesses as well as challenges to the current “one drug/one test” companion diagnostic model. To better understand how the evolution to holistic models is taking shape – and its potential impact on healthcare stakeholders – L.E.K. examined today’s treatment decision support testing landscape, personalized medicine partnership activity, and also leveraged insights from its global Biopharma & Life Sciences practice.

Our findings confirm that more holistic decision support tests and solutions are coming and will require stakeholders to think differently about how they establish themselves through a broad network of partners and strategic initiatives.

## Surveying the Decision Support Testing Landscape

As a starting point, L.E.K. characterized the landscape of available tests in the U.S. that inform treatment decisions compiled from ~50 leading diagnostics companies<sup>2</sup> operating in the U.S. between 2004-2011. L.E.K. identified more than 200 decision support tests that we classified by test purpose, and more specifically, whether tests inform treatment decisions for a single drug/class (e.g., companion diagnostics) vs. more holistic treatment decisions across multiple drugs/classes (i.e., multi-agent response tests). (see Figure 1.)

**Figure 1**  
Example Treatment Decision Support Tests

Test Purpose	Description <sup>3</sup>	Test Name	Company	Decision Informed	
Companion Diagnostics	Predict response/safety or guide dosing of a single drug or class	HercepTest	Dako	Determines HER2 protein overexpression for Herceptin treatment selection	Single drug/class  Increasingly holistic tests  Multiple drugs/classes
		Vysis ALK Break Apart FISH	Abbott Labs	Predicts the NSCLC patient response to Xalkori	
Other Decision Support	Provide prognostic and predictive information on the benefit of treatment	Oncotype Dx	Genomic Health, Inc.	Predicts both recurrence of breast cancer and potential patient benefit to chemotherapy regimens	
		PML-RAR $\alpha$	Clariant, Inc.	Predicts response to all-trans retinoic acid (ATRA) and other chemotherapy agents	
		TRUGENE	Siemens	Measures resistance to multiple HIV-1 anti-retroviral agents	
Multi-Agent Response	Inform targeted therapy class selection by interrogating a panel of biomarkers	Target Now	Caris Life Sciences	Examines tumor’s molecular profile to tailor treatment options	
		ResponseDX: Lung	Response Genetics, Inc.	Examines multiple biomarkers to guide therapeutic treatment decisions for NSCLC patients	

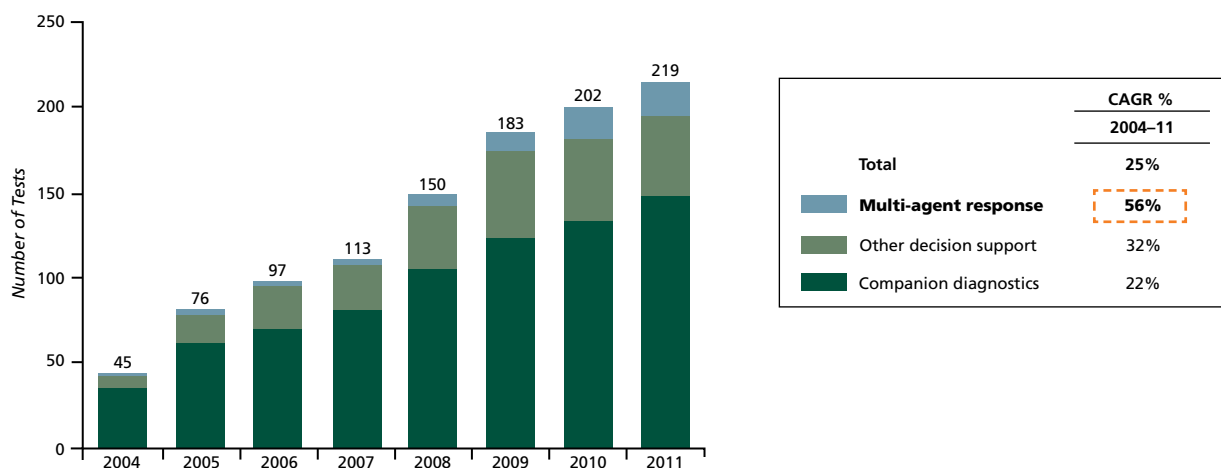
Source: L.E.K. Analysis

<sup>2</sup> Includes IVD and LDT tests from top-15 IVD test suppliers, top-four large reference labs, top-five AP labs, and top-20 specialty reference labs.

<sup>3</sup> For descriptive purposes only, may not map to exact regulatory labeling.

Figure 2

Cumulative Number of U.S. Treatment Decision Support Tests by Purpose and CAGR % (2004 – 2011)



Source: Company websites, SEC filings, GenomeWeb, L.E.K. analysis

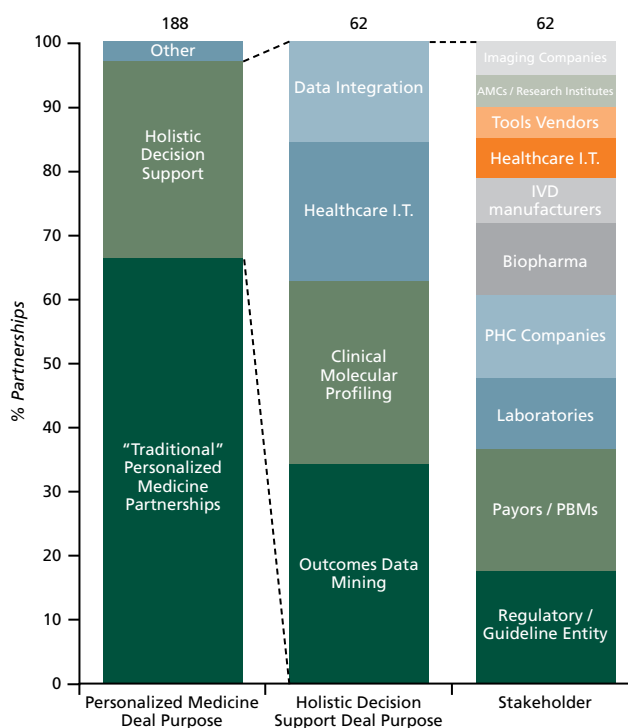
Our findings highlight that most tests are companion diagnostics and other decision support tests that provide guidance on single drug/class therapy decisions. However, holistic decision support tests (e.g., multi-agent response) are growing the fastest at 56% CAGR (see Figure 2). The emergence of multi-agent response tests suggests diagnostics companies are already seeing the need to aggregate individual tests (e.g., companion diagnostics) into panels of appropriate markers addressing a given clinical decision need. L.E.K. believes this trend is likely to continue as increasing numbers of biomarkers become validated for diseases and multiplexing tools enabling the aggregation of multiple biomarker interrogations into a single test become deployed in the clinic.

### Surveying Personalized Medicine Partnerships

L.E.K. also completed an assessment of publicly available personalized medicine partnership activity from 2009-2011 for ~150 leading organizations operating in the U.S.<sup>4</sup> to look at broader decision support trends and emergence of more holistic solutions beyond diagnostic tests (see Figure 3). Across the sample we identified 189 publicly announced partnerships of which ~65% focused on more traditional areas such as

Figure 3

U.S. Personalized Medicine Partnerships (2009 – 2011)



Source: Company websites, GenomeWeb, L.E.K. analysis

<sup>4</sup>Survey of partnerships deals was conducted for top-10 academic medical centers research institutions, top-25 biopharma, top-four healthcare IT companies, top-three healthcare imaging companies, top-20 IVD manufacturers, top-20 laboratories, top-10 payers / PBMs, top-15 personalized healthcare companies, top-10 regulatory/guideline entities, and top-20 tools vendors for the period of 01/01/2009 – 12/31/2011.

**Figure 4**  
**Example Partnerships Including Holistic Decision Support Elements**

Holistic Decision Support Focus	Partners		Holistic Decision Support Activities
	Technology Provider	Stakeholder Deploying the Solution	
<b>Molecular Profiling</b>	Life Technologies	TGEN/US Oncology	Sequencing of triple-negative breast cancer patients to identify potential treatment strategies
	Foundation Medicine	Novartis	Deployment of cancer genomics analysis platform to support Novartis clinical research efforts
	Clariant, Inc. (GE Healthcare)	Acorn Research	Biomarker profiling of patients within Acorn's network of providers to support clinical research efforts
	GenomeQuest	Beth Israel Deaconess Medical Center	Whole genome analysis and predictive genomics to guide patient management
<b>Outcomes Data Mining</b>	AstraZeneca	WellPoint	Evaluate comparative effectiveness of selected marketed therapies
	23andMe	NIH	Leverage self-reported information to understand the link between drug response and CYP2C9/CYP2C19 variation
	Pfizer	Medco	Leverage patient genotype, phenotype and outcome to assist in treatment decisions and target therapeutics
<b>Healthcare IT Infrastructure</b>	IBM	WellPoint	Deployment of IBM's Watson-based solution to support evidence-based health care decision making
	Oracle	Moffitt Cancer Center	Deployment of Oracle's informatics platform to store and manage patient medical information
<b>Data Integration</b>	Siemens	Susquehanna Health	Integration of imaging and laboratory diagnostics
	Cernostics	Geisinger Health	Integration of advanced tissue diagnostics, digital pathology, annotated biorepository and EMR to create next-generation treatment decision support solutions
	CardioDx	GE Healthcare	Integration of genomics with imaging data in cardiovascular disease

Source: L.E.K. Analysis

biomarker discovery, companion diagnostics and targeted therapies. However, a significant portion (~30%) included elements geared towards creating more holistic decision support models.

Partnerships categorized as holistic decision support by L.E.K. were focused on mining large patient datasets (e.g., from payers or providers), molecular profiling (e.g., deploying next-generation sequencing), creating information technology (IT) infrastructure needed to enable holistic decision support

models and integrating various datasets to create richer decision support solutions. Interestingly, holistic decision support partnerships often included stakeholders outside of biopharma and diagnostics such as research tools, payers/PBMs, healthcare IT companies as well as emerging personalized healthcare (PHC) companies (e.g., Knome, Foundation Medicine and 23andMe). This finding suggests that these new stakeholders will be increasingly important in influencing care decisions going forward.

## Implications

L.E.K. believes the likely holistic decision support debate won't center on whether this advance will be realized, but rather how long it will take, and which models and companies will prevail. Although it will take time to achieve this capability, there are signs that the industry is already moving along the continuum from companion diagnostics to a truly holistic capability. Of course the mainstay of personalized medicine today (e.g., companion diagnostics) will continue to play an important role in validating content, but we believe they will become integrated and enhanced by other data.

The companies that ultimately succeed will be able to capture vast amounts of information and synthesize it for personalized

care. Holistic models will be powered by increasingly larger datasets, sophisticated decision-making algorithms and intuitive reporting mechanisms. This will likely require the participation of an increasingly broad range of stakeholders to provide the science, technologies, infrastructure and tools necessary for deployment. It will also be important for payers and regulators to support this evolution by adapting their policies as the approach to patient care evolves dramatically.

Below we have identified a small number of the issues that stakeholders will need to address as the shift to holistic decision support takes place:

Stakeholders	Questions to Consider
<b>Medical Products Companies (e.g., Pharmaceuticals, Medical Devices)</b>	<ul style="list-style-type: none"> <li>• How will holistic decision support impact the landscape (e.g., treatment /testing algorithms, decision making, clinical trials)?</li> <li>• How proactively should product companies play in holistic decision support over time?               <ul style="list-style-type: none"> <li>– Can holistic decision support be leveraged as a differentiator?</li> <li>– Are there situations where not being part of a holistic decision support solution could adversely impact a product opportunity?</li> </ul> </li> <li>• How will the move to holistic decision support impact life cycle planning (e.g., companion diagnostics) and commercial models?</li> <li>• What partnering strategies need to be considered to ensure products are part of the holistic decision support solution?</li> </ul>
<b>Holistic Decision Support Enablers (e.g., Diagnostics, Research Tools, IT, Payers, PBMs)</b>	<ul style="list-style-type: none"> <li>• In what spaces (therapeutic areas, provider segments) should holistic solutions be deployed?</li> <li>• What components will be required to build out holistic solutions?               <ul style="list-style-type: none"> <li>– Testing technologies</li> <li>– Information (e.g., associations, outcomes, trial databases, records)</li> <li>– IT infrastructure for data integration and management, simulation and reporting</li> </ul> </li> <li>• How can various components be brought together to build seamless holistic decision support solutions?</li> <li>• How might solutions be tailored for provider segments and regions?</li> <li>• How can holistic decision support solutions be effectively monetized?               <ul style="list-style-type: none"> <li>– Are there models beyond selling infrastructure and components?</li> <li>– Can information be monetized?</li> </ul> </li> <li>• What partnerships will be required to build out holistic solutions?</li> </ul>
<b>Providers and Payers</b>	<ul style="list-style-type: none"> <li>• How can providers and payers leverage holistic decision support models to improve outcomes for their patients while improving healthcare efficiency?</li> <li>• In which areas should models be deployed over time? Where are clinical and economic arguments most compelling?</li> <li>• Where should providers and payers consider funding initiatives?</li> </ul>

L.E.K. Consulting is a global management consulting firm that uses deep industry expertise and analytical rigor to help clients solve their most critical business problems. Founded nearly 30 years ago, L.E.K. employs more than 900 professionals in 20 offices across Europe, the Americas and Asia-Pacific. L.E.K. advises and supports global companies that are leaders in their industries – including the largest private and public sector organizations, private equity firms and emerging entrepreneurial businesses. L.E.K. helps business leaders consistently make better decisions, deliver improved business performance and create greater shareholder returns.

**For further information contact:**

**Boston**

75 State Street  
19th Floor  
Boston, MA 02109  
Telephone: 617.951.9500  
Facsimile: 617.951.9392

**Chicago**

One North Wacker Drive  
39th Floor  
Chicago, IL 60606  
Telephone: 312.913.6400  
Facsimile: 312.782.4583

**Los Angeles**

1100 Glendon Avenue  
21st Floor  
Los Angeles, CA 90024  
Telephone: 310.209.9800  
Facsimile: 310.209.9125

**New York**

1133 Sixth Avenue  
29th Floor  
New York, NY 10036  
Telephone: 646.652.1900  
Facsimile: 212.582.8505

**San Francisco**

100 Pine Street  
Suite 2000  
San Francisco, CA 94111  
Telephone: 415.676.5500  
Facsimile: 415.627.9071

**International Offices:**

*Auckland*  
*Bangkok*  
*Beijing*  
*London*  
*Melbourne*  
*Milan*  
*Mumbai*  
*Munich*  
*New Delhi*  
*Paris*  
*Shanghai*  
*Singapore*  
*Sydney*  
*Tokyo*  
*Wroclaw*

L.E.K. Consulting is a registered trademark of L.E.K. Consulting LLC. All other products and brands mentioned in this document are properties of their respective owners.