G2 INTELLIGENCE

Diagnostic Testing & Technology Report

Competitive Intelligence & Analysis for an Expanding Global Market

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Foundation Medicine Closes Expanded Round of Financing, Gains Strategic Investors

Foundation Medicine (Cambridge, Mass.), developer of a comprehensive, next-generation sequencing-based cancer test, announced that the company closed an expanded $33.5 million Series A financing round in late October. In addition to founding investor Third Rock Ventures (Boston), this financing includes new investors Kleiner Perkins Caufield & Byers (KPCB) and Google Ventures. As part of the terms of the investment, Brook Byers, partner, KPCB, and Krishna Yeshwant, M.D., partner, Google Ventures, will join Foundation Medicine's board of directors.

Calling the financiers "strategic," Foundation Medicine CEO Michael Pellini, M.D., says the investors will be helpful as the company readies for the 2012 launch of its pan-cancer test that analyzes for more than 200 clinically actionable genes.

"KPCB has a tremendous track record for building valued diagnostic companies and they bring a thorough understanding of the regulatory and reimbursement components of our business," said Michael Pellini, M.D., CEO of Foundation Medicine in a statement. "Google Ventures brings deep insights into the areas of informatics, storage and user interface, as well as strong knowledge on how to work with large amounts of data to leverage and build a scalable business."

For more on the planned 2012 launch of Foundation Medicine's pan-cancer test, see *Inside the Diagnostic Industry* on page 5.

Unmet Need for Bioinformatics Attracts New Investments, Bolsters Partnerships

The inability to apply clinical significance to the vast amounts of genomic data is recognized as one of the rate-limiting factors affecting the adoption of next-generation sequencing technologies. The bioinformatics piece of the sequencing puzzle attracts less investment interest than instrument makers and service providers do. But experts see the ability of two bioinformatics companies to close financing rounds with strategic investors as a sign that the importance of bioinformatics is gaining recognition.

At the end of October GenoLogics (Victoria, British Columbia) announced it raised $8 million in a "strategic" financing round led by Illumina (San Diego). GenoLogics is a developer of laboratory information management system (LIMS) software specifically designed for next-generation genomics labs delivering

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end-to-end management of genomics laboratory samples, tests, and results. The company said the capital will be used to accelerate product development for new desktop sequencing systems, as well as for an expansion of sales and marketing capabilities. GenoLogics and Illumina had previously partnered together. In February 2011 GenoLogics and Illumina entered into a worldwide coselling agreement for the GenoLogics LIMS. In September, GenoLogics released the GenoLogics LIMS preconfigured package for Illumina next-generation sequencing.

"It would be a human genome project-sized effort. … There is 250 years' worth of work to move this information into real products."

—Harold Garner, Ph.D.

DNAnexus (Mountain View, Calif.), a developer of DNA data management and analysis platforms for genomic researchers and sequence service providers, announced in mid-October that it raised $15 million with a lead investment from Google Ventures. The company will use the funds to expand hiring and accelerate product development aimed at cloud-based hosting and collaborative data-management technologies.

"The truth is the world's best bioinformatics company may make a few million dollars, whereas the world's worst pharmaceutical company will make a few hundred million dollars in a year," Harold Garner, Ph.D., executive director, Virginia Bioinformatics Institute at Virginia Tech, tells *DTTR*. "There is an upswing in the number of bioinformatics companies, but it is lost [in comparison to the size of the bigger biotech industry]. Investments in bioinformatics companies are still very small for the most part."

The demand to sequence biological samples is expected to rise as the price of genome sequencing falls. The resulting data is overwhelming researchers while the industry simultaneously grapples with shortages of trained bioinformaticists needed to make sense of the clinical meaning of genetic variants.

"Only one-third to one-half of the genes are known . . . It would be a human genome project-sized effort to understand the functionality of all of those genes," says Garner. "There is 250 years' worth of work to move this information into real products."

The shortage of skilled bioinformaticists is so profound that on the home page of DNAnexus there is an offer for $20,000 plus a full genome sequencing if you refer (and the company hires) software engineers with theoretical algorithm, machine learning, and computational genomics skills.

More Large-Scale Projects Taking Shape

Despite the daunting nature of the amount of work yet to be done, it is an exciting time in the field as more large-scale bioinformatics projects aimed at improving access to datasets and enhancing analytic collaboration are taking shape.

DNAnexus in October announced a technology collaboration with Google to provide free access to a cloud-based "mirror" version of the Sequence Read Archive (SRA) with enhanced search and analysis tools. The public SRA database houses all primary sequence data for National Institutes of Health-sponsored next-generation sequencing projects, but its future has been uncertain given possible federal funding cuts. Google said the database (nearly 400 terabytes) is one of the largest ever put into its storage service.

Also in October the Dana-Farber Cancer Institute and Brigham and Women's Hospital announced the launch of Profile, a large-scale cancer research program and com-

prehensive genomic database. All cancer patients at the institutions can have their tumor tissue scanned and analyzed for hundreds of genetic mutations. A second, linked database will contain medical record information on the disease's progression, response to treatment, relapse, and side effects. Taken together, the Profile database will expand discovery of cancer-related mutations, speed research for treatments that are most effective against individual tumors, and lead to the development of more screening technologies.

Natriuretic Peptide Levels Key to Reducing Risk, Guided Therapy in Heart Failure Patients

Monitoring levels of amino-terminal pro–B-type natriuretic peptides (NT-proBNPs) and keeping them below a certain threshold with guided therapy proved to be more beneficial for heart failure (HF) patients than the standard of care, according to results of a new study. The findings suggest potential applications for personalized medicine in the management of HF patients.

Results of the Pro-BNP Outpatient Tailored Chronic Heart Failure Therapy (PROTECT) study, published in October in the *Journal of the American College of Cardiology,* found that tailored therapy to keep NT-proBNP values suppressed below 1,000 pg/mL led to significant reductions in adverse outcomes in a population of HF patients.

Elevated values of natriuretic peptides are known to predict adverse outcomes with rising values indicating an increasing risk for adverse outcomes. But managing medication dosage in HF patients to keep levels in check is notoriously difficult, say the authors of the study, who note "ascertainment of clinical stability and volume status in chronic heart failure can be challenging in inexperienced hands."

During a mean 10 months of follow-up, those patients in the NT-proBNP monitoring arm had significantly fewer cardiovascular events (58 versus 100) and a longer duration before their first event than those who received standard care. NT-proBNP monitoring was well tolerated and those in the interventional group also reported higher quality-of-life scores.

The researchers need to replicate their findings in a larger multicenter randomized trial. But given the promising early results, research is reportedly beginning on developing a home-based finger-prick NT-proBNP test. This study was funded in part by Roche Diagnostics.

Legionella Testing Underutilized in Endemic Areas

New findings suggest that testing guidelines underestimate the number of cases of community-acquired pneumonia caused by Legionella. In an article published online in *BMC Infectious Disease*, researchers say more widespread Legionella testing in endemic areas should be considered to catch undiagnosed cases and to improve anti-microbial therapy selection.

In a retrospective study researchers found that a diagnostic workup for Legionella (urine antigen testing or culture of respiratory specimens) was performed in about 35 percent of discharged patients with pneumonia from Rhode Island Hospital (Providence, R.I.), an endemic region for the bacteria. If Legionella testing was limited to testing that followed the recommendations in the Infectious Diseases Society of

America/American Thoracic Society (IDSA/ATS) community-acquired pneumonia guidelines, the diagnosis of Legionella pneumonia would have been missed more than 40 percent of the time.

Legionella pneumophila urine antigen testing is recommended for patients with severe pneumonia requiring intensive care unit (ICU) admission, failure of outpatient antibiotics, active alcohol abuse, history of travel within the previous two weeks, or pleural effusion.

These results suggest that available methodologies to diagnose Legionella may be underutilized in endemic areas such as the eastern United States, where pretest probability is higher. National data suggest an increasing incidence of Legionnaires' disease from 1990 to 2005, with the most pronounced rise in noted in the northeastern United States. Given the number of Legionella pneumonia cases that did not meet the IDSA/ATS criteria for testing, the proportion of pneumonia cases that are currently being tested for Legionnaires' disease, and the possibility of rising incidence there may be a need to extend urine Legionella antigen testing recommendations. The cost-effectiveness of screening all cases of community-acquired pneumonia requiring hospital admission in endemic locales needs to be assessed. Such a testing program would likely identify more Legionella pneumonia cases, thereby focusing anti-microbial therapy.

Oral Microbe Markers May Stratify Patients at Risk for HCAP

Oral bacteria profiles may signal which patients are likely to develop health care-associated pneumonia (HCAP) according to findings presented at the Infectious Diseases Society of America's annual meeting in Boston in October. The results suggest sequencing oral microbes in patients at risk for HCAP may be useful in stratifying patients for targeted prevention efforts.

In pyrosequencing oral microbiota of 37 subjects (community dwellers, nursing home residents, and mechanically ventilated intensive care unit (ICU) patients), the researchers found oral microbial profiles differ in community-dwelling adults compared to those in health care settings at high risk for pneumonia. Streptococcaceae was the dominant microbe found within the oral cavities, but as the risk of pneumonia increased among the groups, certain baseline bacteria levels decreased. In the three patients who developed HCAP, Streptococcaceae represented a smaller average proportion of oral bacteria (7 percent), compared with 49 percent Streptococcacaceae load for the other five ventilated ICU patients. The proportions of three other microbe groups—Enterococcaceae, Micrococcaceae, and Mycoplasmataceae—rose sharply in the HCAP patients. The researchers concluded that if larger studies confirm these results, oral microbes may be used as markers of impending disease.

"Our discovery may lead to new and improved ways that we can prevent pneumonia by maintaining the composition of oral bacteria which live inside our mouths or maintaining our local immune defense mechanisms," explains Samit Joshi, D.O., fellow in infectious diseases at Yale School of Medicine. "If future research confirms our preliminary findings and the cost of pyrosequencing continues to decrease, then there may be opportunities in the future for the use of innovative technologies, such as pyrosequencing, to identify patients at high risk for HCAP."

G2 INTELLIGENCE Inside the Diagnostics Industry

Foundation Medicine Preparing for Launch of Next-Generation Cancer Test

Michael Pellini, M.D., CEO, Foundation Medicine

Foundation Medicine (Cambridge, Mass.) is closing the year with huge success. The creator of a next-generation sequencing-based diagnostic test recently announced that it closed an expanded first round of financing totaling $33.5 million. The company is using information garnered from its clinical trials and collaborations with four pharmaceutical companies to ready itself for its mid-2012 national launch of its comprehensive, pan-cancer diagnostic test. The lab-developed test (LDT) will aid oncologists in directing treatment decisions in newly diagnosed patients based on the analysis of more than 200 cancer-related genes. Foundation Medicine CEO Michael Pellini, M.D., who joined the company in May 2011, recently spoke with *DTTR* about the drivers behind the company's recent achievements as well as how the company is positioning itself for the evolution of next-generation sequencing technologies into clinical practice.

Foundation Medicine is nearing commercialization of a comprehensive diagnostic test. What differentiates Foundation Medicine's test?

In essence we apply next-generation sequencing to cancer diagnosis. We sequence approximately 200 clinically actionable genes, which is an important point. We are not arbitrarily sequencing the whole genome or exome. We focus on genes and pathways that have been shown to have some clinical application. We view this as the "sweet spot" between conventional hot spot testing that is most common today and whole genome/exome.

There is a lot of noise in the marketplace about whole-genome sequencing or applying broad-based next-generation sequencing to clinical diagnostics. But what most people do not understand is how challenging it is to actually apply this technology to cancer diagnostics. . . . When you couple the fact that cancer tends to be a very heterogeneous disease with the fact that many of the alterations that are clinically actionable are found at very low frequencies, the challenges of using this technology go up exponentially—especially doing this in FFPE [formalin-fixed paraffin-embedded], which adds to the challenge significantly. Foundation Medicine has spent the past year and half working through these challenges. We now have a clinical-grade test that applies next-generation sequencing to cancer diagnostics and are able to perform the test in an efficient way in terms of the type of sample and amount of tumor sample that we need as well as the cost of performing the test. Our lab has recently started accepting specimens from most states. However, our broad commercialization efforts won't come until 2012.

While your test takes a comprehensive approach, are there subspecialties within oncology that will be targeted as part of the launch?

The test was developed as a pan-cancer test. While it makes sense medically going to the market with a pan-cancer test [as opposed to a targeted test], it might not be the best approach from a regulatory and/or reimbursement standpoint, so we are still working through some of these complexities. . . . In 12 months or so, a newly diagnosed patient with non-small cell lung carcinoma is probably going to have anywhere from 10 to 15 molecular assays performed on their biopsy. That

fact may represent an enormous cost burden to the health care system and in most cases, there will just not be enough tissue to run all of those tests. Biopsies are too small and the expense is too great. So, from that scenario, lung cancer is an area ripe for a targeted approach using Foundation Medicine's test.

The test will launch next year as a lab-developed test. Do you have any plans to have it approved by the U.S. Food and Drug Administration (FDA)?

As you stated, it will be launched as a laboratory-developed test, however, we certainly do want to work closely with the FDA on the regulatory path and we have already engaged the FDA in discussions. The good news is that the FDA appears to be very open to working with companies like Foundation Medicine on bringing next-generation sequencing through the regulatory process. I think they do understand that long-term this type of approach is very important for cancer care and it can also ultimately save the health care system a significant number of dollars if we approach it correctly.

How is Foundation Medicine readying for the national launch and what are the company's pricing and reimbursement plans?

We are receiving specimens right now from pharmaceutical companies, academic medical centers, and early users, but the national launch will be towards the middle of 2012. . . . On the operations side, the laboratory is able to process a fair number of samples every week and turn results around in approximately 14 days. Having the broader launch in another six months or so allows us time to pressure test our processes and adequately ramp up the commercial side of the organization.

Foundation Medicine by the Numbers

Year Launched: 2010

Employees: 50

Financing: $33.5M expanded Series A round

Partners: Four pharmaceutical collaborations

Test: Uses approximately 200 genes

Capacity: 250 samples per week, with doubling of capacity by mid-2012

What is powerful about the test from a pricing standpoint is that for the price of running four, five, or six individual molecular assays, not only can you have the information on those four, five, or six markers, but you can also have complete information on 200 additional genes. . . . We are in the final stages of locking down the pricing, but it is safe to say it will be close to the aggregate price of testing for a half dozen molecular assays.

We have already initiated discussions with third-party payers and we have had our first conversation with CMS [the Centers for Medicare and Medicaid Services] as well. Like with any new test, we do believe it will take time and appropriate clinical studies to convince payers this is the right approach long-term. We are a data- and market-driven organization and we ultimately will have a dozen or so clinical trials to support the commercialization of our test. The trials are being put in place to demonstrate the clinical utility of this test, as well as the health economics of this test.

Foundation Medicine recently announced its fourth pharmaceutical collaboration. How does Foundation Medicine's new partnership with Johnson & Johnson differ from the previously announced pharmaceutical deals?

There is a common thread to each of these collaborations. Our test is being used to better understand the molecular basis of their clinical trials' participants'

cancer. The information may allow them to better stratify patients, to seek out better ways to identify responders and nonresponders, to identify why certain patients might have adverse reactions. It is all driving towards providing pharmaceutical companies with a tool to conduct clinical trials more quickly and efficiently.

Will companion diagnostic products likely emerge from these collaborations?
Yes. We are generating a significant amount of content and uncovering new information as we run samples through our laboratory. With that information we will pursue two avenues. One path will allow us to use this information to enhance the value of our comprehensive test, while the other path recognizes the benefit of having an IVD [in vitro diagnostic] strategy due to some of the potential reimbursement and regulatory challenges early on.

"Having the right complementary cancer biology skillset, as well as the IT infrastructure to sort through all of this data in a timely fashion, is something we still have to focus on as an industry. To allow for a clinically useful test, we have to simplify this complex information so that it is actionable."

–Michael Pellini, M.D., CEO, Foundation Medicine

How will the clinical relevance of sequencing evolve in the next five years?
The advancement of [this] technology certainly means one thing, namely there will be more and more data out there that has to be managed. One of the rate-limiting steps from the broad-based application of this technology to cancer diagnostics is the number of well-trained clinically focused computational biologists is not yet sufficient to do this on a broad-scale basis. Having the right complementary cancer biology skillset, as well as the IT infrastructure to sort through all of this data in a timely fashion, is something we still have to focus on as an industry. To allow for a clinically useful test, we have to simplify this complex information so that it is actionable. That is something Foundation Medicine already does well.

How will Foundation Medicine evolve in the next three to five years?
In some ways it is straightforward. Our aim is to have our comprehensive, fully informative genomic profile used up front in a high percentage of newly diagnosed cancer patients . . . not only throughout the United States but internationally. There are potentially profound medical and economic advantages of moving in this direction.

As we get insight into the additional genes, we do have the ability to add them to our test. Within the next year or two I would envision that maybe once or twice a year we would come out with a new version of our test that expands the number of genes sequenced.

Longer term, the question of whole-exome sequencing and whole-genome sequencing certainly surfaces. We have already done the internal proof of concept for whole-exome sequencing and whole-genome sequencing, so it is not as much of a technical hurdle as it is really a question of whether all of that information is necessary. Is it clinically actionable? . . . I do think whole-genome sequencing will be used more broadly in cancer diagnostics. But still 90 percent of tests, even in five years, will be much more targeted than whole-genome sequencing.

Antibodies to Known Ovarian Cancer Antigen Found in High-Risk Women, May Lead to Screening Test

Researchers may be one step closer to identifying a biomarker that can be used in the development of a screening test for ovarian cancer, according to a study, which appeared in September in *Cancer Epidemiology, Biomarkers & Prevention*. The findings show that women with infertility, a known risk factor for ovarian cancer, have significantly increased levels of circulating antibodies to mesothelin, an established ovarian cancer antigen.

"Instead of investigating molecules specific to ovarian cancer alone, we asked what molecules women with a risk of ovarian cancer and those with ovarian cancer had in common," said Judith Luborsky, Ph.D., professor of clinical laboratory science and obstetrics and gynecology at Rush University Medical Center (Chicago) and lead author of the study. "The point is this is a brand new approach. The principle is that we took defined high-risk women and found an antibody already shown to shed from tumors."

> ***"Instead of investigating molecules specific to ovarian cancer alone, we asked what molecules women with a risk of ovarian cancer and those with ovarian cancer had in common. … With the discovery of the mesothelin antibody, we now have what appears to be a biomarker that can potentially be used in screening tests to help us conquer ovarian cancer."***
>
> ***—Judith Luborsky, Ph.D., Rush University***

Mesothelin expression is elevated in ovarian tumors but low in normal tissue. Circulating mesothelin has relatively high specificity for ovarian cancer. Researchers tested for mesothelin antibodies in the bloodstream of 109 women who were infertile, 28 women diagnosed with ovarian cancer, 24 women with benign ovarian tumors or cysts, and 152 healthy women. Significant levels of mesothelin antibodies were found in women with infertility as well as in women with ovarian cancer, but not in healthy women or women with benign disease.

"We think that antibodies may arise in response to very early abnormal changes in ovarian tissue that may or may not progress to malignancy, depending on additional triggering events. Or, alternatively, antibodies may bind to normal cells in the ovary, causing dysfunction and leading to infertility—and, in a subpopulation of women, to the development of ovarian cancer," said Luborsky in a statement from Rush. "More important, with the discovery of the mesothelin antibody, we now have what appears to be a biomarker that can potentially be used in screening tests to help us conquer ovarian cancer."

"The next critical study is to get rare, repository samples, annual serial specimens that go back more than two years from diagnosis to see if [mesothelial antibodies] are useful in screening and diagnosis," Luborsky tells *DTTR*.

The study was funded in part by Fujirebio Diagnostics Inc. (Malvern, Pa.)

Genetic, Metabolic Screening Useful in Identifying Etiology of Developmental Delays in Children

Newer genetic and metabolic tests are increasingly able to provide an etiologic diagnosis for children with neurodevelopmental disabilities, according to a review by the American Academy of Neurology (AAN) Quality Standards Subcommittee and the Practice Committee of the Child Neurology Society. A new evidence report published in the October issue of the journal *Neurology* says that these higher diagnostic yields should be considered in the planning of laboratory evaluation of children with unexplained global developmental delay and/or intellectual disability (GDD/ID).

Major Commercial Tests for Development Abnormalities

MegAllele, Affymetrix (Santa Clara, Calif.)

MRX-Test, City of Hope Molecular Diagnostics Laboratory (Duarte, Calif.)

X-linked Mental Retardation (XLMR) panel, Ambry Genetics (Alisa Viejo, Calif.)

SLC9A6 Related Syndromatic Mental Retardation ARX, Partington X-Linked Mental Retardation Syndrome, X-Linked Infantile Spasm Syndrome, X-Linked Mental Retardation, Baylor College of Medicine-Medical Genetics Laboratories (Houston)

DNAarray, CombiMatrix Diagnostics (Irvine, Calif.)

One-Array, Phalanx Biotech Group (Belmont, Calif.)

CompGene, Combinational Genetic Services Inc. (Milwaukee)

BeadChip, BeadArray, Infinium, Illumina, (San Diego)

Source: Neurology Today

"Since the 2003 guidelines the field has changed so dramatically, and we expect and hope it continues to happen," says David Michelson, M.D., assistant professor of neurology and pediatrics at the Loma Linda University School of Medicine (Calif.) and an AAN subcommittee panelist. Michelson tells *DTTR* that the improved yields the committee found, which he called "a conservative" estimate, will increase the volume of genetic testing for these children, although he couldn't speculate on the quantity of increase.

Genomic microarray studies had the highest diagnostic yield—about 8 percent of all children with GDD/ID with 11 percent yields in children whose clinical evaluations were strongly suggestive of a genetic etiology. The researchers found G-banded karyotyping and subtelomeric fluorescence in situ hybridization testing have a lower sensitivity for abnormalities in similar populations of children. They found abnormalities in 4 percent and 3.5 percent of the children with GDD/ID studied, respectively. Karyotyping is usually reserved for patients having signs of a specific chromosomal syndrome (Down syndrome), a family history of a chromosomal rearrangement, or a parent with a history of multiple miscarriages. Tests for inborn errors of metabolism (IEM) have a yield of nearly 5 percent.

While an etiologic diagnosis for GDD/ID only occasionally leads to a specific therapy that improves the child's outcome (primarily with IEM), an etiologic diagnosis has psychological benefit to their families.

The committee members say more information is needed about the degree of delay necessary to justify testing children with mild GDD. Testing strategies (simultaneous

or sequential testing) should be assessed to help reduce unnecessary testing and more accurate diagnostic yields. The committee also suggests that the ability to rate diagnostic tests on factors other than diagnostic yield, such as the availability of effective treatment, would have a positive influence on clinical practice.

Marker Combination in Urine Test Predicts Clinically Significant Prostate Cancer

Researchers have developed a urine test capable of stratifying men at high risk for developing clinically significant prostate cancer and can help identify men who can delay or avoid a biopsy—an important step in improving the diagnosis and treatment of the disease. Planned commercialization of the test comes as pathologists and the urologic community wait to see how the U.S. Preventive Services Task Force's October controversial recommendation against using prostate-specific antigen (PSA) screening in healthy men will affect clinical practice.

Results of a study using the transcription-mediated amplification assay in more than 1,300 men with elevated PSA levels was published in August in *Science Translational Medicine*. The test looks for a gene fusion (TMPRSS2:ERG) that is believed to cause prostate cancer. The urine TMPRSS2:ERG score was linked to the presence of cancer, tumor volume, and clinically significant cancer in patients.

While theTMPRSS2:ERG gene fusion almost always indicates cancer, it is present in only half of prostate cancer cases. When researchers added another marker, prostate cancer antigen 3 (PCA3), they found the combination was more predictive of cancer than either marker alone.

Given the uncertain clinical benefit of utilizing serum PSA for early prostate cancer detection, the expectation is that the new urine test will be used as an intermediate step as a means to individualize disease management in men with elevated PSA before getting a biopsy.

"What we found and the controversy over PSA highlights [is] this large gray zone if the PSA is slightly elevated. It is an area of clinical need to refine the biopsy decision," says lead author of the study Scott Tomlins, M.D., Ph.D., a pathology fellow at the University of Michigan Health System. "The negative things associated with PSA result from the treatment, not the test result. It is really a failure of the biomarker and how we are treating prostate cancer. In other countries there are lower levels of treatment for prostate cancer. They follow men at higher rates rather than the surgical treatment or radiation we do here."

Gen-Probe (San Diego) licensed the TMPRSS2:ERG fusion technology from the University of Michigan group and the PCA3 from a different group. The two assays are similar and can be run on the same specimen and the same platform. Tomlins expects that widespread commercialization of the combination test will be available around the fourth quarter of 2012.

G2 Index Rises 2%, Driven by Positive Quarterly Financial Reports

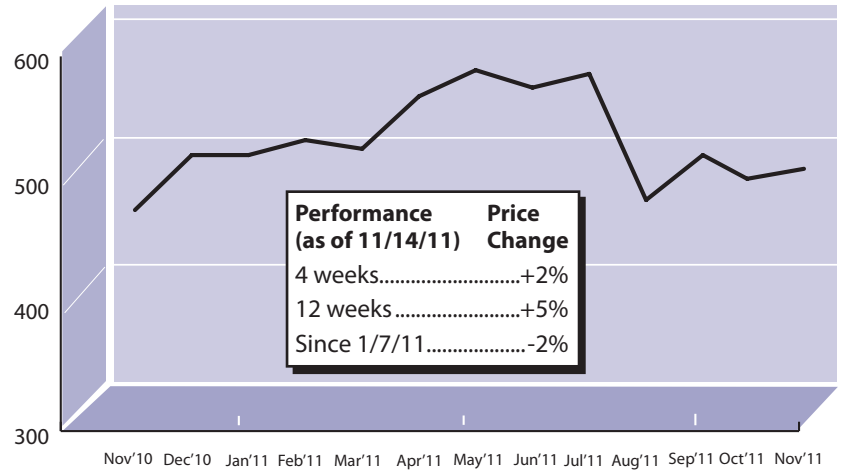
The G2 Diagnostic Stock Index was mixed for the four weeks ending Nov. 11. Despite 11 stocks that rose in value and one that remained unchanged, the index grew only by a modest 2 percent with three of the five declining stocks losing double-digit value. The Nasdaq and the S&P remained fairly flat over the same period, with the Nasdaq unchanged and the S&P gaining 3 percent.

One of the big gainers this period was **Abaxis** (Union City, Calif.), up 12 percent on strong second-quarter earnings. The maker of point-of-care blood analysis systems reported record quarterly revenue of $40 million, up 13 percent over the same quarter last year. Revenue was boosted by strong sales in the veterinary market, which saw an 18 percent increase. Total sales were up 40 percent internationally. The company's earnings per share of 15 cents also beat analyst expectations.

Another company showing big gains was **Meridian Bioscience** (Cincinnati), closing the period up 10 percent. The company reported fourth-quarter net sales of $41.3 million and a record $159.7 million for the 2011 fiscal year, an annual increase of 12 percent. In the fourth quarter H. pylori business grew worldwide by 10 percent and 12 percent in the United States. Foodborne pathogen testing increased 27 percent in the quarter and 36 percent for the full fiscal year. C. difficile testing led growth on the company's illumigene molecular platform with a 24 percent worldwide increase in sales. The company also reaffirmed its fiscal 2012 guidance of diluted earnings per share of 85 cents to 89 cents (excluding plant consolidation costs of 1 cent to 2 cents) on net sales of $183 million to $192 million, an expected growth of over 15 percent in the coming year.

Despite the much-anticipated October launch of the MaterniT21 prenatal test and having reported improvements in its quarterly financials, **Sequenom's** (San Diego) third-quarter performance did not live up to market expectations and it saw its stock close the period down 22 percent. The company's diagnostic revenues increased 223 percent to $2.2 million for the third quarter over 2010, up from $687,000 for the same period in 2010. The increase was primarily from growth in cystic fibrosis testing.

G2 Diagnostic Stock Index



Source: The G2 Diagnostic Stock Index is tabulated weekly by *DTTR* from the average percentage change in the stock price of 17 IVD companies.

Up	Price	% Chg
Abbott Labs	$54.53	3%
Abaxis	27.03	12
Alere	26.08	21
Bio-Rad	101.06	7
Gen-Probe	61.88	7
Illumina	31.79	18
IRIS	9.24	1
Johnson & Johnson	65.25	1
Meridian	18.52	10
Qiagen	14.52	8
Quidel	17.41	7
Unchanged		
Beckman Coulter	74.12	0
Down		
Affymetrix	4.90	-10
Cepheid	34.69	-14
Luminex	20.50	-9
OraSure	8.77	-4
Sequenom	4.14	-22

Recontacting Patients as New Genetic Test Interpretations Emerge ... Genomic testing currently reveals data with unknown clinical significance. Patients may test negative for currently known disease-causing mutations, but future findings may emerge that reveal they do have a higher risk for a disease. Or current results may indicate "variants of unknown significance"—the primary finding in up to 30 percent of all gene-sequencing results. As both bioinformatics and sequencing technology evolve, current variants of unknown significance will become clinically understood, leaving clinicians with an ethical, legal, and practical conundrum.

In an October perspective piece in the *New England Journal of Medicine*, Reed Pyeritz, M.D., Ph.D., chief of medical genetics, University of Pennsylvania, says determining whether, when, and how to recontact patients must be addressed as the complexities inherent in genetic testing will expand markedly with more widespread use of whole-genome sequencing. Among the issues that must be considered:

- Whole-genome and whole-exome sequencing may yield pathologic alterations unrelated to the clinical indication that prompted the test. The number of potentially adverse findings will be overwhelming and the "incidentalomes" may be outside the ordering physician's expertise.
- It is unclear whose responsibility it would be to recontact patients. Entering a new interpretation of a previously ordered test into a chart may legally reestablish the relationship and failure to recontact could be considered abandonment.
- Bioinformatics systems that flag patients with updated interpretations will be essential.
- Patients may have different expectations regarding being recontacted. Changes in interpretation of test results may have implications for a patient's at-risk relatives, raising additional ethical considerations.
- If patients order and insert direct-to-consumer genetic test results into their own health records, are their physicians obligated to provide updates? G2

Company References

Abaxis 510-675-6500
Brigham and Women's Hospital 617-732-5500
Dana-Farber Cancer Institute 617-632-3000
DNAnexus 650-218-8222
Foundation Medicine 617-418-2200
Fujirebio Diagnostics 610-240-3800
GenoLogics 250-483-7011
Gen-Probe 858-410-8000
Google Ventures 650-253-0000
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