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LABORATORY INDUSTRY REPORT™

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HIGHLIGHTS

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Upcoming G2 Events

Lab Institute

October 14-16, 2015

Hyatt Regency Washington DC on Capitol Hill

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Theranos, Cleveland Clinic Enter Into Strategic Relationship

Theranos, the California-based company whose revolutionary method for collecting blood for specimens has so far been confined to a handful of retail clinics in Arizona and California, inked its first big deal with a major provider earlier this month. The pact with the Cleveland Clinic includes having the big Midwestern health system run trials toward using the Theranos system for its own laboratory services as well as expanding the nascent lab's relatively small test menu.

Cleveland Clinic officials said the agreement, which they described as a strategic alliance, came as a result of top-level negotiations between the health care system's CEO, Toby Cosgrove, M.D., and Theranos CEO Elizabeth Holmes.

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ACMG, CAP, AMP Develop Gene Variant Diagnostic Guidelines

Working in tandem with two other major laboratory lobbying groups, the American College of Medical Genetics and Genomics (ACMG) earlier this month released guidelines to better determine the disease-causing potential of specific DNA sequence variations.

The guidelines, which were released by ACMG with the College of American Pathologists, and the Association for Molecular Pathology, are intended to create a more uniform system of classifying genetic variants and their potential to cause harm.

The new system took some 24 months to develop, ACMG officials said, and included not only a working group but a variety of public forums at ACMG and other group events.

Such updates were required given the wide variability in how genetic makeup can create or influence a particular genetic condition. As a result, clinicians are often challenged juggling the genetic variants in tandem with their clinical validity and the actions required to address any health care issues. Indeed, the new guidelines only cover inherited

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ACMG, CAP, AMP Develop Gene Variant Diagnostic Guidelines, *from page 1*

variants, not those that may occur within cells of a cancer tumor, which create treatment challenges of their own. The new guidelines include five different classifications: "pathogenic," "likely pathogenic," "uncertain significance," "likely benign," and "benign," along with standard definitions for each term.

That still may not be enough for the medical community to wrap its arms around all the gene variants and their impact on health care. The variants that can lead to sickle cell disease are contained in everyone's genetic makeup. But among the CFTR gene that is linked to cystic fibrosis, ACMG officials said there are more than 150 variants that can have an impact on how that gene functions, and more than 1,000 others where the impact is still uncertain.

"These updated guidelines provide a systematic and sound way to classify genomic variants so that when Lab A on the east coast and Lab B on the west coast are reporting results, they are using the same method to classify that variant," said Sue Richards, who chaired the workgroup that developed the guidelines, in a press release. She serves as medical director of the Knight Diagnostic Laboratories, and is a professor of molecular and medical genetics at Oregon Health & Science University in Portland.

Some laboratories have been sharing the genetic variations and accompanying data through a public domain database known as ClinVar, but it is relatively new and not all laboratories are posting data.

"In the past, standard terms such as 'pathogenic' and a consistent strategy for classifying variants have been lacking, leading to wide variation in how laboratories classify individual differences in DNA sequence," Richards said in the release.

However, the ACMG cautioned that making a diagnosis should not be done with the molecular data alone. For example, a classification of "likely pathogenic" would provide enough evidence for a physician to act if it's combined with prenatal ultrasound, enzyme assays, physical findings or imaging studies.

Takeaway: The laboratory and pathology communities believe the advances in sequencing technology require commensurate updates in classifications of genetic variants.

BioReference, Foundation Medicine Report Strong Sales Growth

BioReference Laboratory and Foundation Medicine, a larger and mid-level player in the laboratory sector, both reported strong growth for their respective fiscal and year-end quarters, but the latter continues to report steep losses.

The New Jersey-based BioReference reported a 15 percent rise in revenue for its fiscal first quarter ending Jan. 31, reaching $209 million. That compares with $181.3 million for the first quarter of fiscal 2014. Net income more than doubled, to $6.6 million from $3 million, although the company noted that severe weather conditions during the winter of 2014 shaved more than 30 percent off its net earnings in the year-ago quarter and should be taken into account.

Nevertheless, BioReference missed the earnings predictions of analysts. Their consensus was that the company would report revenue of $216.3 million.

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However, the company reported other strong fundamentals. Revenue per patient rose 8 percent during the quarter, to more than $88, as the company's pricey esoteric assays provided 70 percent of revenue, up from 66 percent a year ago. According to William Blair & Co., that represents a 22 percent growth in esoteric testing over the past year.

"Commercial execution and growth rates were strong across both our clinical and pharma customers in the fourth quarter, highlighting the broad adoption of our comprehensive genomic profiling approach."

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

"This is the first quarter in several years where we believe that one can make valid year over year quarterly comparison given the reset attributable to both the reimbursement changes we have seen as an industry as well as our investment in our own infrastructure, both of which occurred in 2013," said Marc Grodman, M.D., BioReference's chief executive officer, in a press release. The latter is a reference to a more than 50 percent reduction in payments for the technical component of CPT code 88305, a move by the Centers for Medicare & Medicaid Services that had a profound impact on the finances of pathology practices throughout the U.S.

BioReference appears to have gotten over that hump, as Grodman reiterated 2015 guidance of 10 percent growth in revenue and 20 percent growth in earnings during a recent call with analysts. William Blair reported that sales are expected to reach $945 million during fiscal 2015, and top the $1 billion mark next year.

Meanwhile, the Massachusetts-based Foundation Medicine reported revenue of $18.7 million for the fourth quarter ending Dec. 31, up 93 percent from the $9.7 million reported for the fourth quarter of 2013. For the entire year, revenue reached $61.1 million, more than doubling the $29 million reported in 2013.

Company officials said test volumes increased 93 percent in the fourth quarter and 167 percent for calendar 2014. The company focuses on esoteric tests, primarily for cancer companion diagnostics. Revenue averaged about $3,600 per test in the fourth quarter, according to Jason Ryan, Foundation's senior vice president of finance.

"Commercial execution and growth rates were strong across both our clinical and pharma customers in the fourth quarter, highlighting the broad adoption of our comprehensive genomic profiling approach," said Foundation Medicine Chief Executive Officer Michael Pellini, M.D., in a press release. "We're also pleased with the achievement of many strategic and operational milestones that culminated in the announcement of a broad collaboration agreement with Roche, which we expect will strengthen all aspects of our business."

Foundation and Roche entered into a strategic research and commercialization collaboration last January that included the drug giant making a $250 million investment in Foundation. However, Foundation has continued to operate deep in the red. It reported a loss of $13.3 million in the fourth quarter of 2014, up from $13 million a year ago. For calendar 2014, it reported a loss of $52.2 million, up from $42.9 million in 2013.

The company's 2015 revenue guidance is in the range of $105 million to $115 million, of which $10 to $12 million will be derived from the Roche relationship.

Takeaway: Aggressive growth is continuing at some of the other major laboratories in the U.S. G2

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Inside The Lab Industry

Does Quest's New CDC Pact Signal Bigger Shift Toward Public-Private Health Initiatives?

Hepatitis has been a disease whose progression in the United States has been difficult to pin down.

According to data from the U.S. Centers for Disease Control and Prevention (CDC), the etiology of the disease tends to differ with the viral strain. Cases of hepatitis A have generally been declining for 20 years. Reported cases of hepatitis B dropped by nearly two-thirds from 2000 to 2012.

However, the hepatitis B trends may be misleading, as a large number of patients exhibit no symptoms at all, sometimes for decades, while their livers are slowly destroyed. And cases of hepatitis C appear to be in an epidemic mode. The number of reported cases increased 75 percent between 2010 and 2012 alone, with many more Americans still undiagnosed.

The often stealth manner of hepatitis tends to impact the cost of treating it. If hepatitis is undetected for a long period of time, the options may dwindle to a liver transplant that can cost $500,000 or more, or a regimen of drugs that can approach $100,000. That has prompted the CDC to take a different tack on monitoring the progression of hepatitis and ways to treat it. And laboratory giant Quest Diagnostics has been a beneficiary of that change.

"The innovative collaboration with Quest Diagnostics will allow us to use data analytics to better monitor the implementation of CDC's testing guidelines and progress toward reducing deaths from hepatitis."

— John W. Ward, M.D.

In late January, Quest announced that it received a contract from the CDC to provide data analytics to the agency through its Health Trends database. It contains 20 billion de-identified test results compiled by the New Jersey-based national laboratory over the last decade, including reams of de-identified hepatitis data. All of it has been collected through the testing services performed by Quest, and company officials say it is the largest repository of such data ever compiled by a health care organization.

"That data will help the CDC look at the general epidemiology (of hepatitis) across the country," said Rick L. Pesano, M.D., a Quest vice president who serves as medical director of its infectious disease division.

The $500,000 pact is minuscule for a company with annual revenue approaching $8 billion, and Quest has entered into similar deals with accountable care organizations and pharmaceutical firms seeking diagnostic expertise. But it's the first-ever fee-based contract of any kind for hepatitis research awarded by the CDC to a diagnostic information services company.

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Inside The Lab Industry

The need for data analytics appears urgent. According to Quest, the company's annual revenue for performing hepatitis C testing is around $100 million—more than 1 percent of overall revenue—and is growing at a double-digit clip.

"The innovative collaboration with Quest Diagnostics will allow us to use data analytics to better monitor the implementation of CDC's testing guidelines and progress toward reducing deaths from hepatitis," said John W. Ward, M.D., director of the CDC's viral hepatitis division, in a press release announcing the contract. "Increased testing is critical to ensure that those who are infected with hepatitis receive life-saving care and treatment."

The contract's tiny size may be more than overshadowed by the implication that laboratories such as Quest and the testing data they have aggregated over the years may play a significant role in combating expensive to treat and ultimately deadly diseases such as hepatitis. It's a sort of public health-private data partnership that had not really existed in the past.

The need for data analytics appears urgent. According to Quest, the company's annual revenue for performing hepatitis C testing is around $100 million—more than 1 percent of overall revenue—and is growing at a double-digit clip.

Quest spokesperson Wendy Bost attributed the growth in part to the recent development of a group of antiretroviral drugs known as direct-acting agents, which are distributed in the U.S. by Gilead under the Harvoni brand and AbbVie as Viekira.

Both provide cure rates at above 90 percent, remarkably more effective than the traditional treatment with Interferon, which is able to slow the damage wrought by the virus but not keep it at bay. And while the pharmaceutical firms have come under fire for pricing their products at around $1,000 a pill, that treatment is still a fraction of the cost of a liver transplant. The testing Quest performs can help expedite the start of the drug treatment. And the data Quest is gathering from its testing can help with monitoring how the disease is progressing in the U.S.

Under the terms of the pact, the CDC and Quest will scour the latter's national database for hepatitis A, B, C and E viral infection in American adults. The analysis will extend to screening and confirmatory tests, treatment-guiding genotyping and viral load tests classified by a variety of demographics. These include gender, age group, geography and type of physician. The data will then be used to identify patterns in disease prevalence and help direct the clinical management of patients.

The CDC's Ward approached Quest on this venture, according to Pesano. The company had been developing algorithms to better analyze hepatitis cases, while the agency had recently developed new testing guidelines with the U.S.

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> *"Nearly three million Americans are infected with hepatitis C, and at least half don't know it. We believe that everyone living with hepatitis C should know their status and have access to effective care and discuss with their provider whether treatment using new therapies is right for them. Through innovative public-private partnerships, we are improving the efficiency and effectiveness of surveillance by incorporating electronic data from large commercial labs into our viral hepatitis surveillance efforts."*
>
> *— John W. Ward, M.D.*

Preventive Services Task Force that recommended one-time screenings to pretty much the entire Baby Boomer population.

"Nearly three million Americans are infected with hepatitis C, and at least half don't know it," Ward said in a statement. "We believe that everyone living with hepatitis C should know their status and have access to effective care and discuss with their provider whether treatment using new therapies is right for them. Through innovative public-private partnerships, we are improving the efficiency and effectiveness of surveillance by incorporating electronic data from large commercial labs into our viral hepatitis surveillance efforts."

Pesano also noted that the incidences of hepatitis B are also likely far higher than diagnosed, and this collaboration could help pinpoint where cases are more likely to crop up.

Heather Creran, an Atlanta-based health care consultant with a focus on the laboratory sector, said she expected more such arrangements with public agencies "and really all areas of health care, as our nation works to improve the system and reduce costs." She added that if performed well, "these collaborations could be very powerful."

The CDC is not working solely with Quest on its hepatitis efforts. Ward said in a statement that the agency is also working with LabCorp to make the surveillance of hepatitis A, B and C more timely. And it is working with ARUP Laboratories in Utah and the Mayo Clinic in Minnesota to promote the addition of pregnancy status to requests for hepatitis B testing to help public health authorities provide prevention services to newborns of mothers infected with the virus.

Pesano, who noted that he is a clinician at the core, thinks such collaborations can go a long way toward controlling a disease that often flies under the radar in the U.S.

I see this as a public health risk for the country," he said. "Ultimately, it affords an opportunity for people to get tested and get their diagnosis confirmed, match it against (actionable) data and do something about it."

Takeaway: Quest's contract with the CDC could be the start of a wave of contracts with labs to assist in public health monitoring efforts.

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Theranos, Cleveland Clinic Enter Into Strategic Relationship, *from page 1*

"Health care innovation is essential to making care more accessible, affordable and timely for patients. This relationship could open up new opportunities for both patients and physicians to be part of high-quality, low-cost healthcare," Cosgrove said in a statement. "We're excited to begin exploring new initiatives that can offer improved care for our patient's health care dollar."

Theranos's blood collection system does not require any needles. Blood is drawn through the capillaries in the fingertips of patients using a nearly microscopic lancet. The company requires only a few drops of blood to perform a wide variety of tests. Theranos' test menu is also priced at about 50 percent below Medicare rates, with assays such as a lipid panel costing less than $3.

The company was founded by Holmes as a teenager when she dropped out of Stanford University. Holmes and Theranos were the subject of a lengthy New Yorker magazine profile last year. Her firm was recently valued by Forbes magazine at $9 billion.

Until the Cleveland Clinic deal, Theranos's primary business relationship had been with the consumer drugstore chain Walgreens, where it provided testing services in 40 locations in the Phoenix area and one in California near its Palo Alto headquarters. This new alliance suggests the company may play a major role in revamping laboratory technology at major clinical providers throughout the U.S.

"This alliance with a world-renowned health system like Cleveland Clinic furthers our mission, and is another step in our work to bring access to high-quality, affordable lab testing to everyone and help improve the quality and cost of care," Holmes said in a statement.

The full scope of the relationship between Theranos and the Cleveland Clinic will be developed in a series of incremental steps, according to Kandice Kottke-Marchant, M.D., who heads Cleveland Clinic's Pathology and Laboratory Medicine Institute.

The first step will be to scrutinize the compatibility of the Theranos technology through a series of clinical studies that will involve specific Cleveland Clinic patients, Kottke-Marchant said. Those studies are still in the development stage, although she added that they would likely focus on fairly routine chemistry and hematology tests, with draws and testing performed using Theranos's equipment. The resulting data might also be published in peer-reviewed journals. "As an academic institution, we'd like to have that published," Kottke-Marchant said.

In addition to that facet of the agreement, the Cleveland Clinic's pathologists will also perform interpretive testing on behalf of Theranos patients. "Since they only do a subset of tests, Theranos will seek to utilize our reference lab," Kottke-Marchant said. Currently, Theranos's test menu has about 250 assays, compared to more than 1,200 performed by the Cleveland Clinic, according to Kottke-Marchant.

Kottke-Marchant declined to disclose the financial terms of the relationship. Theranos, which has a reputation for secrecy, did not respond to a request seeking comment.

Takeaway: Theranos has entered into its first significant agreement with a clinical institution regarding the use of its draw and testing technologies. G2

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INDUSTRY BUZZ

Case Western, University Hospitals Collaborate With British Firm on HIV Drug Resistance Test

Population Genetics Technologies Ltd. has struck a deal with Case Western Reserve University and the University Hospitals health care system to help develop a test that would provide a better gauge of drug resistance in patients with the HIV virus.

Patients with HIV, which can cause AIDS, have been successfully treated with a cocktail of antiretroviral drugs since the mid-1990s. However, the World Health Organization reported last year that as much as 10 percent of the population with HIV is resistant to the front-line drugs. Resistance is the leading reason why antiretroviral treatments fail. Those patients require alternative treatments, and they are potentially placed at risk of developing resistance to all antiretroviral medications if their condition is not diagnosed in a timely manner.

"Detection of the development of resistance at the earliest possible time is critical for optimal clinical management of HIV infection," said Miguel Quiñones-Mateu, M.D., in a press release. He is the scientific director of the University Hospitals translational laboratory and a Case Western pathology professor and will be leading the collaboration with Population Genetics.

The United Kingdom-based Population Genetics has been using next generation sequencing (NGS) for its test development. The current standard assays detect drug resistance about 20 percent of the time; NGS can provide 95 percent accuracy. Population Genetics wants to combine NGS with a proprietary system that would provide accuracy of up to 99.9 percent, meaning virtually every mutation that could lead to drug resistance would be detected. The two parties intend to develop a companion diagnostic that can be used in the long-term treatment and management of HIV in patients.

"We are delighted to have access to the expertise of Dr. Miguel Quiñones-Mateu, who brings enormous technical expertise and success in the development and validation of infectious disease diagnostics to our organization," said Alan Schafer, Population Genetics' chief executive officer, in the release announcing the arrangement. "His skills and knowledge will add greatly to the capabilities of the company, and enable us to accelerate our product development program."

Takeaway: Laboratories are on the frontline of developing assays to better assist in treating HIV patients through antiretroviral drugs.

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American College of Medical Genetics and Genomics
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Association of Molecular Pathology
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