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HIGHLIGHTS

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Invitae Greatly Expands Testing Panels, Introduces Pricing for Uninsured

San Francisco-based startup laboratory Invitae has dramatically expanded its menu of test offerings and is also offering significant discounts to uninsured patients. The company said it was providing testing for more than 60 rare pediatric diseases, including severe combined immunodeficiency and periodic fever syndromes. It was also offering screening for metabolic diseases for newborns. Additionally, Invitae announced that it was expanding its offerings of neurological tests to more than 30 disorders, including muscular dystrophies, myopathies and congenital myasthenic syndrome.

"We are proud to now offer more comprehensive testing panels for patients who may be suffering from a variety of disorders, including neuromuscular, pediatric, and a host of rare conditions. We're also now

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Quest Sells Much of Focus Affiliate to Italian Laboratory

Quest Diagnostics has engaged in a rare shedding of assets, selling a portion of its California-based Focus Diagnostics affiliate to an Italian laboratory. DiaSorin S.p.A. will pay $300 million in cash for Focus' immunodiagnostics and molecular diagnostics business, further globalizing the U.S. laboratory sector. DiaSorin will operate Focus through a new U.S. subsidiary. The deal is expected to close in the second quarter of this year. Excluded from the deal are Focus' diagnostic information service laboratory, which primarily serves the biopharmaceutical sector.

Focus had total revenue of about $80 million in 2015, up a double-digit percentage from 2014, according to Quest. Revenue for the portions being sold to DiaSorin were not broken out. Focus is known primarily for its Simplexa molecular tests, serology, IFA and ELISA assays.

"The combination of DiaSorin and Focus products will create a unique portfolio of specialty products, especially in the clinical area of infectious disease, which will continue to strengthen the leadership

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Quest Sells Much of Focus Affiliate to Italian Laboratory, *from page 1*

of DiaSorin in this segment that today already represents over half of DiaSorin revenues," said company Chief Executive Officer Carlo Rosa.

DiaSorin has its own line of molecular products it markets under the brand name Liaison. However, Focus has about 200 hospital clients in the U.S., a business base coveted by DiaSorin, which is trying to make inroads into the American market. It has a goal of locating half of its test volume in the U.S. in the coming years, the company said.

"As a leader in diagnostic products, DiaSorin is well positioned to build on the Focus platform of innovation to deliver continuing value to Focus' employees, customers and patients," said Quest Chief Executive Officer Steve Rusckowski. "This transaction reflects our ongoing commitment to refocusing on Quest's core diagnostic information services business. We remain committed to delivering disciplined capital deployment, the fifth element of our five-point strategy. We return the majority of our free cash flow to investors in the form of dividends and share repurchases, and also have been investing in the business through strategically aligned acquisitions."

Takeaway: As Quest makes a rare move to sell off one of its assets, it contributes to the ongoing globalization of the U.S. laboratory sector.

Aurora Breaks Into Pacific Northwest Market With Pathology Practice Acquisition

Aurora Diagnostics has entered the Pacific Northwest market, acquiring Pacific Pathology Associates. Based in Salem, Ore., about 50 miles south of Portland, Pacific has eight pathologists in practice and 25 employees in total. There are no layoffs planned post-transaction, according to Bruce Walton, Aurora's Chief Operations Officer. Terms of the deal were not disclosed.

"Joining the Aurora Diagnostics team provides Pacific Pathology Associates with additional resources and new capabilities to serve our community," said Clark McDonald, M.D., who leads the Pacific Pathology Associates ownership group. "Aurora has a reputation for affiliating with high quality labs that maintain strong local relationships. This, together with our excellent team and unique role in serving this community, will help make this a successful relationship for our clients."

The deal makes Pacific the fifth lab or pathology practice acquired by the Palm Beach Gardens, Fla.,-based Aurora since 2013. It now operates 25 labs in total in 17 states, primarily in the South, Southwest, and New England. The only other locales it has remotely near Oregon are three sites in Nevada and Arizona.

"This is a new market footprint in which we hope to expand," Walton said. Altogether, Aurora now serves 85 hospitals and has 150 physicians on staff. Pacific uses a 3,500-square-foot laboratory it operates in space leased from Salem Hospital, to which it provides services. It also has an outreach business in gastrointestinal, genitourinary pathology and women's health in a roughly 50-mile radius around Salem.

"As the only pathology group of its kind in the region, Pacific Pathology Associates is relied upon to provide exceptional pathology services. We will help the group

reach out to new clients and maintain its reputation for premier inpatient and outpatient pathology services," said Aurora CEO Daniel D. Crowley in a statement.

Aurora said it would upgrade Pacific Pathology's services and infrastructure, although Walton declined to provide any specifics. He did note that the company would continue to seek opportunities to grow. "We are actively looking to add to our team, including through acquisitions," he said

Takeaway: Aurora has continued on its transaction roll, breaking into a new market and region as a result.

Bill Would Strip California of Its Authority to Regulate Laboratories

A bill is pending in the California Legislature that would take the licensing and inspection of clinical laboratories away from state regulators if signed into law.

Authored by Assemblywoman Susan Bonilla, a Democrat from the Northern California city of Concord, the bill would strip laboratory licensing from the California Department of Public Health (CDPH), the primary regulator in the state for both hospitals and laboratories. Licensure is required from that agency if a lab is performing tests that are considered moderate or high complexity. The CDPH also collects fees for various inspections, which range from $25 for a clinical laboratory scientist's license renewal to $5,260 to relicense a lab that is performing more than one million tests annually. Bonilla's office did not respond to a request seeking comment on the bill.

The CDPH has come under scrutiny in recent years for personnel shortages, particularly in its hospital division.

If the bill becomes law, the duties for inspection and enforcement would likely be transferred to the Centers for Medicare & Medicaid Services (CMS), which was given the authority under the Clinical Laboratory Improvement Amendments (CLIA) passed in the 1980s.

The CDPH has come under scrutiny in recent years for personnel shortages, particularly in its hospital division. Fines and administrative penalties against acute care facilities have dropped in recent years, although the agency has recently made new hires of dozens of inspectors in Los Angeles County, the state's most populous county by a wide margin, CDPH officials said. CDPH also recently approved the use of private non-profit organizations to approve a lab's ongoing deemed status after their initial licensure.

The state's primary lobbying group for laboratories has yet to take a position on the bill, which was introduced last month. Michael Arnold, executive director of the California Clinical Laboratory Association, said it is currently in a "watch position" on the measure, and that its position would evolve after an initial public hearing.

"We are working with the author. There are amendments being discussed," Arnold said. He added that "there is considerable opposition (to the bill) from employee organizations representing clinical lab scientists and others." The bill's first committee hearing is scheduled for April 19.

Takeaway: California could take actions to delegate laboratory licensure and inspections back to the federal government.

Inside The Lab Industry

Theranos Continues to Confront Thunderheads Regarding Accuracy of Its Testing Platform

Whether or not in its uncertain future it manages to survive or even thrive, Theranos will at least receive credit for never being boring.

The Theranos saga has just entered its most critical state, as the Centers for Medicare & Medicaid Services (CMS) recommended the company's CLIA certification be revoked for its California lab only days after its scathing inspection report was made public. Meanwhile, a group of researchers from one of the most prestigious teaching hospitals in the nation questioned the validity of Theranos' testing platform.

Theranos responded by deflecting the former while attacking the latter, all the while appointing a new scientific and advisory board jam-packed with health care luminaries. Promising to allow low-cost lab testing with just a few drops of blood that can be drawn without needles, Theranos was valued at $9 billion just a few months ago. But as a deal to install testing facilities at Walgreens pharmacies throughout the country is placed on hold, it is experiencing a storm of criticism all but unprecedented for a laboratory.

The CMS' conclusions were the worst news. It recommended that Theranos lose its CLIA certification by May 17. That was based on an inspection that took place late last year where the agency determined Theranos' hematology testing, analytics and high-complexity testing were not accurate and posed an immediate danger to patients. CMS has concluded that the corrective actions taken by Theranos were not credible, pointing out numerous instances where Theranos plans were non-specific. Theranos can appeal the revocation if it is imposed. CMS also recommended limitations on the lab's performance of hematology assays that would take place almost immediately. Theranos faces a $10,000 daily fine for non-compliance. CMS has also requested a list of all providers who have used the lab since January to notify them of the ongoing issues at the facility.

CMS' 147-page inspection report charted a number of omissions and failures in the operation of the laboratory (Theranos' facility in Arizona was not included in this report). Among them:

- Preanalytic systems and relevant documentation when specimens were referred to other labs for testing failed.
- Corrective actions for chemistry quality control were not in place.
- The proper calibration of equipment failed.
- The laboratory director failed to sign off on mandated procedures or changes to procedures.

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- Appropriate temperature ranges were not maintained for freezers.
- Appropriate guidelines to maintain the integrity of quality control materials were not followed.
- The laboratory failed to notify a patient or patients of errors in their test results in a timely fashion.

There were some redactions to the report, including the annual test volume of the laboratory. According to a recent report by the *Wall Street Journal*, quality control efforts failed 22 to 87 percent of the time, depending on the kind of test being run.

"While most of the variability we found was within clinically accepted ranges, there were several cases where inaccurate results would have led to incorrect medical decisions."

— Joel Dudley

Theranos noted it had hired a new laboratory director to overhaul operations, and that it was retraining staff, along with taking other corrective actions CMS has since concluded were not satisfactory.

Just days before that correspondence was made public, a study appeared in the *Journal of Clinical Investigation*. Researchers from the Icahn School of Medicine at Mt. Sinai Hospital New York had 60 patients undergo common testing via Theranos' retail sites in Arizona last year, and compared the results against more traditional venipuncture testing at LabCorp and Quest Diagnostics. The study included more than 18,000 data points.

The results were not gratifying for Theranos: It flagged tests outside its normal range of results 1.6 times more often than Quest and LabCorp. Of the 22 lab measurements evaluated, 15 (68 percent) showed significant interservice variability. And 2.2 percent of Theranos' data results were missing, compared to 0.2 percent for LabCorp and no missing results for Quest.

"While most of the variability we found was within clinically accepted ranges, there were several cases where inaccurate results would have led to incorrect medical decisions," said Joel Dudley, the study's senior author and director of biomedical informatics at the Icahn School of Medicine at Mount Sinai Hospital in New York City, in a statement.

Theranos did report more precise results in leukocyte subsets, although the study's authors noted that that would not likely impact clinical decision-making. But the variances were stark enough in lipid panel testing that the study recommended Theranos be more transparent regarding how it calibrates its Edison testing platform.

Theranos expressed deep criticism not only of the test results, but of the integrity of some of the researchers behind the study. In a letter sent to the journal's editor and signed by its four laboratory managers, it questioned whether the researchers had contacted Theranos as they had purportedly claimed in media interviews; and

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noted that both Dudley and Schadt failed to disclose their participation in a Palo Alto, Calif.-based company called NuMedii, which uses some genomic testing to determine the efficacy of some pharmaceuticals under development (Theranos labeled NuMedii as a "potential competitor").

And Theranos also questioned the integrity of the study, including how the blood was collected. It noted that the larger draws of blood for the Quest and LabCorp testing could have caused blood flow issues that may have compromised the Theranos test results. It also raised questions because the study did not disclose which fingers of the patients had been pricked for collections.

"It is clear that Theranos has done what people thought was impossible."

— David Helfet, M.D.

"These fundamental problems with the conduct of the study reflect the lack of understanding of the study investigators concerning basic sample collection procedures that are critical for the integrity of their study and its conclusions," the letter said. Neither Schadt nor the Icahn School of Medicine responded to requests seeking comment.

Other observers were less critical. Michael Cherny, an analyst with EverCore ISI, raised concerns in a recent report that Theranos had tried to halt the publication of the study.

"We have refrained from piling on to the negative Theranos narrative too much ... while we have moved past the point of viewing Theranos as a potential near-term risk, we continue to point to studies like this as further evidence of our standing, and we continue to wait on Theranos to release the data it promised in order to try to change the narrative," Cherny wrote. "All-in, this is another crack in the Theranos armor."

In its latest act of damage control, Theranos has appointed an eight member scientific and advisory board. Among them are physicians from New York Presbyterian/Weill-Cornell Hospital, a former director of the Centers for Disease Control and Prevention and a former president of the American Association of Clinical Chemistry.

"It is clear that Theranos has done what people thought was impossible," said David Helfet, M.D., director of the orthopedic trauma service, for New York Presbyterian Hospital, and a cochair of the advisory board along with Chief Executive Officer Elizabeth Holmes, who left Stanford University as a teenager to start the company. "Theranos invited groups of independent experts in the fields of pathology and laboratory medicine and literally took the lid off of the box. Experts were shown Theranos' technology, met with Theranos scientists, and had access to any data."

Takeaway: Although the storms buffeting Theranos continue unabated, the company's determination to succeed so far appears undaunted.

Invitae Greatly Expands Testing Panels, Introduces Pricing for Uninsured, *from page 1*

introducing testing for inherited metabolic conditions and immunodeficiencies that are part of most newborn screening programs," said Invitae CEO Randy Scott. "With this menu expansion, we now have more than 1,000 genes in production a full quarter ahead of our 2016 plan."

> *"The sooner an expanded testing panel is employed in the diagnosis of an acutely ill, undiagnosed child, the greater the value of the test in terms of reducing other diagnostic expenses and speeding beneficial care."*
>
> — Steven Bleyl, M.D.

The company issued a variety of collateral marketing materials to support the test expansion, including video interviews with employees, scientists and executives with non-profits that advocate for taking proactive stances against rare childhood conditions. The predominant message was that early testing was the best way to head off the impact of an unknown disease in a newborn or toddler.

"The hardest process as a parent was really trying to find an answer for why my children were sick, and it is something I really hope this is something that can change for future patients," said Heidi Bjornson-Pennell, a San Francisco attorney who sits on the board of the PCD Foundation. Her two children presumably were diagnosed with primary ciliary dyskinesia, a rare genetic disorder that causes severe respiratory tract issues.

"The sooner an expanded testing panel is employed in the diagnosis of an acutely ill, undiagnosed child, the greater the value of the test in terms of reducing other diagnostic expenses and speeding beneficial care," said Steven Bleyl, M.D., the medical director of the Clinical Genetics Institute at Intermountain Healthcare.

Straightforward pricing for the testing was also released. Invitae said the list price per panel was $1,500, but that most insurers would pay around $950. Uninsured patients would not be charged more than $475 per panel—a significant drop in price for such tests compared to several years ago. However, the expansion of the testing and the relatively low prices invites questions as to whether overutilization could occur. SCID, one of the disorders for which it tests, only occurs in about one in 100,000 births.

In a conference call discussing the expansion of the testing, Robert Nussbaum, M.D., Invitae's chief medical officer, noted that the tests have high sensitivity but relatively low selectivity, meaning only about one in five positives actually means the child has the condition for which they are being tested. Confirmation would have to come in the form of follow-up blood and genetic tests, he said.

"It is the responsibility of the clinician to determine who is best suited for genetic testing. We do look at guidelines that have been set by professional medical societies and often refer clinicians to look to those guidelines," said company spokesperson Katherine Stueland. "We also suggest that clinicians look at a patient's family history to help inform the decision."

Invitae performed 19,000 billable tests in 2015, nearly half of which were delivered during the fourth quarter. It forecasts delivering between 50,000 to 70,000 billable tests in calendar 2016.

Takeaway: Invitae has greatly expanded its test panels, and will be pushing for greater testing for rare genetic diseases.

INDUSTRY BUZZ

Foundation Medicine Releases New Data It Says Validates Its Genomic Cancer Test

Genomic cancer laboratory company Foundation Medicine said it has further validated the accuracy and practicality of its assays in conjunction with Memorial Sloan Kettering Cancer Center.

The company's FoundationOne Heme assay analyzes DNA alterations in 405 cancer-related genes and sequences RNA in 265 genes to capture gene fusions that may be indicative of how a specific cancer should be treated.

"Foundation Medicine has an established track record of developing genomic profiling assays with the highest standards of analytical and clinical validation."

— Vincent Miller, M.D., CMO, Foundation Medicine

The study, which will be published later this year in the journal *Blood*, compared the DNA/RNA testing against FoundationOne's prior DNA test, which the company said had been widely validated. The results concordance between the two on 76 specimens was 99.4 percent. It was also compared against FISH, PCR and a test distributed by Sequenom. It achieved 99 percent concordance.

Additionally, the Heme assay detected 126 somatic alterations that could not be spotted using other assays, including changes in the KRAS, TET2, EZH2, and DNMT3A genes.

The test also detected in more than three-quarters of the specimens at least one alteration linked to a commercially available cancer therapy or one that is under development. And more than 60 percent of the cases harbored at least one alteration with a known prognostic relevance.

"Foundation Medicine has an established track record of developing genomic profiling assays with the highest standards of analytical and clinical validation," said Vincent Miller, M.D., Foundation's chief medical officer, in a statement. "Publication of our validation data in this highly regarded, peer-reviewed journal supports the clinical significance of the FoundationOne Heme assay ... for its ability to identify specific therapeutic targets, to help refine underlying diagnosis, and to improve prognostic and risk stratification of hematologic cancers."

The company's stock, which had been trading at nearly $50 a share in the spring of 2015, is now in the $17 range. Foundation said it would release its first quarter earnings report early next month.

Takeaway: Foundation Medicine has released data strongly suggesting that its genomic profiling could find avenues of care currently unknown for some cancer patients.

References

Aurora Diagnostics 561-626-5512	**Foundation Medicine** 617-418-2200	**Pacific Pathology Associates** 503-561-5350
DiaSorin 651-439-9710	**LabCorp** 336-229-1127	**Quest Diagnostics** 800-222-0446
Evercore ISI 212-857-3100	**Memorial Sloan Kettering** 212-639-2000	**Theranos** 650-838-9292

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