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*From the Desk of R. Lewis Dark...*

# THE DARK REPORT

**RELIABLE BUSINESS INTELLIGENCE, EXCLUSIVELY FOR MEDICAL LAB CEOs / COOs / CFOs / PATHOLOGISTs**



Restricted information, see page 3

# COMMENTARY & OPINION by...

R. Lewis Dark
Founder & Publisher

## Powerful Forces Are Reshaping Lab, Pathology

THERE IS NO BETTER WAY TO UNDERSTAND HOW THINGS ARE CHANGING within the house of laboratory medicine than to survey current news. Understanding why and how breaking news stories are indicators of deeply-rooted and forceful trends is essential for lab administrators and pathologists who want to keep their labs positioned to offer sophisticated and financially-sustainable lab testing services.

One case in point is the exclusive analysis we are publishing on pages 10-16 of this issue. In this article, we describe a new and powerful dynamic in the field of genetic testing and next-gen sequencing: the interest of big pharma and equity investors in purchasing control of patents and the intellectual property behind the latest diagnostic and gene sequencing technologies.

Why is there such keen interest in controlling laboratory test diagnostics? Interest is high because of the growing importance of companion diagnostics. Pharma companies see that a laboratory test costing $200 to $5,000 can determine whether a patient needs a $50,000 to $500,000 cancer drug, for example. Thus, there is a sound business strategy behind the idea to control companion diagnostic tests used to qualify a specific patient for a specific therapeutic medication.

Another important lab industry trend in the news this month and that we cover in this issue of THE DARK REPORT on pages 7-9 are comments made by **FDA** Commissioner Scott Gottlieb, MD. At a lab industry conference, he explained that the lab industry's unhappiness with the FDA's earlier plans to regulate laboratory-developed tests caused the administration to reconsider how it should handle that issue.

Of course, another story in this issue will be welcome news to many lab executives and pathologists. Our lead story on pages 3-5 about Theranos and the charges filed against it by the **Securities and Exchange Commission** demonstrate that the egregious behavior of this lab testing company and its management is leading to serious consequences.

For readers interested in gaining a more comprehensive understanding of the forces of change in the clinical lab industry and the anatomic pathology profession, our upcoming 23rd annual *Executive War College* in New Orleans on May 1-2 will feature 60 sessions and 100 speakers on these and other topics. TDR

# SEC Charges Theranos with 'Massive Fraud'

## CEO Elizabeth Holmes settles with SEC, COO Sunny Balwani chooses to fight charges

***CEO SUMMARY: In an action against Theranos and two of its executives, the SEC said in a federal court filing this month that the company, CEO Elizabeth Holmes, and former COO Ramesh "Sunny" Balwani deceived investors into believing that the company's portable blood analyzer could conduct comprehensive blood tests from drops of blood collected via a fingerstick. Theranos and Holmes agreed to a settlement while Balwani will fight the charges.***

EARLIER THIS MONTH, officials at the **Securities and Exchange Commission (SEC)** announced what it called a massive fraud settlement involving **Theranos** and its top executive.

The SEC said Theranos, its CEO and its former COO raised more than $700 million from investors through an elaborate, years-long scheme that involved exaggerating or making false statements about the company's technology, business, and financial performance. The two executives are the company's founder, Chairman, and CEO Elizabeth Holmes and former COO Ramesh "Sunny" Balwani, who left the company in 2016.

Theranos and Holmes, age 34, settled with the SEC while not admitting nor denying the charges. Balwani, age 52, will contest the charges.

In documents filed March 14 in U.S. District Court for the Northern District of California, the SEC said Theranos, Holmes, and Balwani deceived investors into believing that the company's portable blood analyzer could do comprehensive laboratory blood tests from drops of blood collected via a fingerstick.

In truth, Theranos' proprietary analyzer could complete only a small number of tests, and the company conducted the vast majority of patient tests on modified, industry-standard commercial analyzers, the SEC said.

To settle the charges, Holmes agreed to pay a $500,000 fine and give up almost 19 million shares of Theranos stock, the SEC said. Also, she will lose voting control of the company and be barred from running a public company for 10 years.

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Given that the SEC regulates public companies, Holmes could still run a private company. Either way, the fraud charges reflect a substantial drop in the company's value and in the stake Holmes held in the company.

After dropping out of Stanford University at age 19, Holmes founded Theranos in 2003. By the end of 2014, the company was valued at $9 billion and *Forbes* listed Holmes as one of America's richest people with an estimated net worth of $4.5 billion, based on her 50% stake in Theranos stock.

## No Jail Time for SEC Charges

The SEC charges are civil and so would not involve jail time. But the **Department of Justice** could bring criminal charges and, if successful, Holmes could face a prison sentence, reported Ellie Kincaid and Michela Tindera for *Forbes*. Of Holmes, one lawyer said, "She is subject to criminal charges because she outright lied," they reported. In a criminal case, prosecutors would need to prove that Holmes acted recklessly or that she had intent to deceive investors, Kincaid and Tindera added.

In its court filing, the SEC also charged that Theranos, Holmes, and Balwani claimed that the **Department of Defense** (DOD) used the company's products on the battlefield in Afghanistan and on medevac helicopters and that, as a result of its work with the DOD, the company would generate more than $100 million in revenue in 2014.

"In truth, Theranos' technology was never deployed by the U.S. Department of Defense and generated a little more than $100,000 in revenue from operations in 2014," the SEC said.

In coverage of the case, *Forbes'* Matthew Herper reported that the fraud "appears to be even worse than previously thought." As an example, he cited how the SEC filing identified a company it called Pharmacy A.

The SEC said in its court filing that Theranos had spent at least five years trying to develop its proprietary analyzer, the Theranos Sample Processing Unit (TSPU) to analyze blood taken from a fingerstick. "The earlier-generation TSPU was designed to perform only one method of testing—immunochemistries—and could process only one sample at a time," the SEC said. In 2009, Holmes and Balwani wanted to develop a new version of the TSPU, which they called the miniLab, and that could run a wider range of tests.

In 2010, its miniLab analyzer was not ready for commercial use but Theranos wanted to offer it in retail settings with chain drug and grocery store companies, which the SEC identified as Pharmacy A and Grocery A. Pharmacy A is believed to be **Walgreens**, Herper wrote.

In September 2013, Walgreens and Theranos announced an agreement in which Theranos would provide lab testing services in Walgreens' pharmacies. Theranos also had a partnership with **Safeway** supermarkets, according to John Carreyrou who reported for *The Wall Street Journal* that the Theranos-Safeway partnership began at least in 2011 but unraveled in 2015.

## Analyzer in Grocery Stores

"Safeway Inc. spent about $350 million to build clinics in more than 800 of its supermarkets to offer blood tests by startup Theranos Inc.," wrote Carreyrou. When the tests never started, the companies ended the partnership, he said.

"In connection with discussions about a potential partnership with Pharmacy A, Holmes approved and provided presentations and other written materials to Pharmacy A executives representing that Theranos had the ability to conduct a broad range of tests on its proprietary analyzer, including general chemistry tests, wellness tests, and some predictive and diagnostic health tests (which involved methods beyond immuno-

chemistries)," the SEC said. "These materials stated that Theranos would be ready to begin blood testing on its proprietary analyzer at Pharmacy A stores by the fourth quarter of 2010."

## Hundreds of Tests

In addition, Holmes also told the executives of Pharmacy A that Theranos could do hundreds of blood tests via a fingerstick, that its testing could be done in less than an hour, and that the testing would cost less than what competitors charge, SEC documents show. Holmes also told Pharmacy A that its analyzer was already deployed on military helicopters.

By 2013, however, the miniLab was unable to do what Theranos promised it could do. Instead, Holmes and Balwani asked Theranos' engineers to modify analyzers from commercial manufacturers so they could analyze fingerstick samples. "Holmes and Theranos never told Pharmacy A and Grocery A about Theranos' technological challenges," the SEC said.

"At all times, however, Holmes, Balwani, and Theranos were aware that, in its clinical laboratory, Theranos' proprietary analyzer performed only approximately 12 tests of the over 200 tests on Theranos' published patient testing menu, and Theranos used third-party commercially-available analyzers, some of which Theranos had modified to analyze fingerstick samples, to process the remainder of its patient tests," the SEC said.

## Criminal Investigation

News reports say that the **Department of Justice** continues to investigate Theranos and its executives. It is possible that federal prosecutors may bring criminal charges against Theranos, its executives, as well as consultants and advisors who provided advice to the company and acted on its behalf.

It is ironic that the same news outlets that trumpeted the innovations of Theranos and the genius of its founder and CEO, Elizabeth Holmes without much skepticism now devote extensive news coverage to the SEC charges and Theranos' ongoing struggles to survive. TDR

*—Joseph Burns*

## Theranos Is Subject of Book, Movie, and Documentary

**FOR YEARS,** clinical laboratory professionals and pathologists questioned the legitimacy of claims Theranos made about its secretive diagnostic technology, its lab analyzers, and its ability to use fingerstick blood specimens for hundreds of medical laboratory tests.

That skepticism was well-founded. In the past two years, federal agencies have disclosed failures to comply with federal regulations. First was the federal **Centers for Medicare and Medicaid Services**, which inspected the clinical laboratories operated by Theranos and issued letters to the company describing CLIA deficiencies and failures in its laboratories.

Second was the SEC's court filing earlier this month that describes the allegations of fraud in how Theranos and its executives misled investors and the public.

This spring, new details will emerge about Theranos. Publisher **Alfred A. Knopf** will release a book on May 21, "Bad Blood: Secrets and Lies in a Silicon Valley Startup." For this book, author John Carreyrou interviewed more than 150 people, including dozens of former Theranos employees, the *New York Times* reported.

Carreyrou's book will be the basis for a movie. The working title is "Bad Blood," and news accounts say that Jennifer Lawrence will star as Elizabeth Holmes. Adam McKay is slated to be writer-director. He is known for his film "The Big Short."

Also in production is a documentary about Theranos and Holmes by documentarian Alex Gibney. There have been no announcements of public release dates for the movie or the documentary.

Market Update

# Facing Lawsuit Filed by Humana, Ameritox Closes Lab, Sells Assets

*Urine drug testing and drug-monitoring company puts assets up for sale, sets closing of two facilities*

In May, the long-struggling **Ameritox, LLC**, is scheduled to close its laboratory in Greensboro, N.C., according to reporting in the *Triad Business Journal*. Early this month, the drug-monitoring and urine-analysis company filed a notice with the North Carolina Department of Commerce that it would close the lab and lay off 113 workers.

Also, the company will close its headquarters in Columbia, Md., and lay off 99 employees there, according to *The Baltimore Business Journal*.

In the notice to North Carolina officials, Ameritox CEO Todd Gardner wrote, "The reason for the closure is an asset sale of tangible assets and closure of all company operations and facilities."

In addition to the operations in Maryland and North Carolina, Ameritox has a facility in Midland, Texas, where the company was founded in 1996, the TBJ reported and it was unclear if the Texas facility would close.

TBJ speculated that the closures could be one result from a lawsuit that **Humana** filed against Ameritox in which the health insurer alleged that Ameritox filed millions of dollars worth of false claims. A jury is scheduled to hear the case next year in U.S. District Court for the Middle District of North Carolina.

One lab executive familiar with Ameritox said that the venture capital funding companies that had backed Ameritox sought to sell the company last fall in a bid to keep the company open. The lab executive did not wish to be named. "The word is that the funding companies were unable to come to terms with any of the bidders for a sale," the lab executive said.

## Funders Split Assets

Unable to sell the company, the funders are believed to have purchased a portion of the book of business and hired the company's sales staff that was associated with that portion of the business. The website **Crunchbase** lists two venture capital funding companies for Ameritox, **Bain Capital Ventures** and **Sequoia Capital**.

In a complaint filed July 28, 2016, Humana said it was seeking to recover millions of dollars it allegedly overpaid Ameritox for services that weren't covered under its health plans, *Bloomberg Law* reported. "Ameritox LLC fraudulently sought and received substantial payments from Humana by submitting 'false and fraudulent claims' for urine testing services Ameritox knew or should have known weren't covered," according to an article by Carmen Castro-Pagan.

Allegations of fraud and abusive business practices have dogged this drug testing company for years. In 2010, Ameritox settled one federal whistleblower lawsuit and agreed to pay $16.3 million, while not admitting nor denying the charges. TDR

*—Joseph Burns*

# FDA's Gottlieb Favors Flexibility with LDTs, NGS

## In remarks to labs, FDA chief says third parties could assist in LDT and NGS test review, approvals

***CEO SUMMARY: FDA Commissioner Scott Gottlieb said the FDA wants to reduce the regulatory burden on developers of next-generation sequencing (NGS) and laboratory-developed tests (LTDs). He also wants to give the FDA more flexibility in how it conducts clinical analysis and validation. To do so, the agency would work with third parties, such as the New York State Department of Health, to speed test review and approval. It also wants to use third-party databases to cut the time needed for review of clinical validity.***

EARLIER THIS MONTH, Scott Gotlieb, MD, Commissioner of the **Food and Drug Administration**, outlined how the federal agency is reforming the premarket review process for diagnostic and laboratory-developed tests (LDTs).

Premarket review is a high-profile issue for clinical laboratories because in 2012, the FDA said it intended to change how it regulated LDTs. At the time, lab executives and pathologists directed harsh criticism at the agency's draft LDT rules. *(See TDRs, Nov. 3, 2014; Dec. 28, 2015.)*

### Rethinking Earlier Proposals

Since the Trump administration took office last year, the FDA has shown a willingness to rethink its earlier proposals for regulating clinical laboratory tests, including LDTs.

In a presentation at the annual meeting of the **American Clinical Laboratory Association** (ACLA) in Washington, D.C., on March 6, Gottlieb discussed two possible reforms intended to reduce the regulatory burden on developers of next-generation sequencing (NGS) technologies and the potential for giving the FDA more flexibility in how it conducts clinical analysis and validation of new lab tests.

First, he mentioned that it may be possible to qualify third-party reviewers, such as the **New York State Department of Health**, to help with reviews and approvals for clinical laboratory tests, including LDTs.

Second, Gottlieb stated that it might be feasible to exempt from premarket review many individual tests that meet pre-specified standards in cases where the FDA has confidence in the lab's underlying standards.

"We must continue to ask ourselves, How do we adapt payment schemes, regulations, and enforcement policies that were designed for the technologies and market of the 1970s for today's innovations?" he said.

"The FDA is clearly trying hard to be innovative," commented Bruce Quinn, MD, PhD, Principal, at life science con-

sultant **Bruce Quinn Associates LLC**. "That said, meeting any of these FDA standards would still be very costly for a hospital or regional lab. A lab's customers are its doctors, patients, and payers. Until it's clear that these FDA accreditations matter to them, it would be a doubtful investment for the lab."

From his remarks, Gottlieb appears to understand the challenges labs face. As test developers innovate, the FDA needs to ensure that regulations keep pace, he commented.

Two of the most significant innovations Gottlieb discussed involve the FDA's review and approval of LDTs. "The first is qualification of the New York State Department of Health as a third-party reviewer," the commissioner said. "The second is the agency's flexible, modern approach to how it reviews next-generation sequencing or NGS.

## One Application; Two Okays

"The New York State accreditation means that labs whose tests have been approved by the New York Health Department—including laboratories with advanced NGS-based tumor profiling tests—do not need to submit separate applications to FDA," he explained. "Instead, they can choose to request that their New York State application, and the state's review memorandum and recommendation, be shared with FDA for possible 510(k) clearance.

"The third-party accreditation program is designed to reduce the burden on test developers and streamline the regulatory assessment of eligible innovative products," Gottlieb added. "Going forward, we hope that additional accredited, third-party reviewers will become eligible to conduct reviews, make recommendations to FDA, and provide even more options to test developers."

The second innovation involves writing policies to improve the development and review of advanced NGS tests, he said. "To take one example, we recently provided public information describing the three-tiered approach that FDA is taking to our review of NGS onco-panel tests in order to minimize the burden on developers," he added.

## Reduced Burden on Labs

"Under this approach, we're communicating with developers about the flexibility they have in developing analytical and clinical evidence to support marketing authorization, depending on the type of claim being made," Gottlieb explained.

Soon, the FDA will provide final guidance to developers on a broader and more flexible regulatory approach to NGS tests, he said. "We're developing policies that will permit more clinical lab tests to be exempt from the burdens of premarket review," he commented. "For some tests, we may be able to establish initial controls that provide a reasonable assurance of analytical and clinical validity."

All of these changes are among the FDA's new approaches to reviewing diagnostic tests. "These new policies recognize that we have unique opportunities to reform and innovate as we consider the right role for FDA with respect to laboratory-developed tests," he added. The best way to do so is with legislation, he commented, but, in the meantime, the FDA recognizes the need for increased efficiency in how it reviews LDTs.

## Changes to PMA Review

Therefore, the agency's device center has proposed changes to the premarket review of diagnostics by developing what Gottlieb called a pre-cert pilot. Pre-certification is commonly used for digital health products but was first used to review direct-to-consumer (DTC) genetic health risk tests.

"In the setting of these DTC tests, we realized that if we had enough confidence in the quality of a lab's underlying system, we could exempt from premarket review many individual tests that met pre-speci-

# FDA Seeks to Speed Lab Test Okays Through Parallel Review With CMS

**IN REMARKS to the** American Clinical Laboratory Association, FDA Commissioner Scott Gottlieb, MD, touted the work the agency did last year with the Medicare program to review and approve an NGS-based *in vitro* diagnostic test for **Foundation Medicine**.

Last fall, the FDA worked with the federal **Centers for Medicare and Medicaid Services** under a new FDA-and-CMS initiative called the Parallel Review Program. This program helps Medicare patients gain access to innovative medical technologies and helps labs secure payment approval, he said.

In November, the FDA approved the FoundationOne CDx (F1CDx), which was the first breakthrough-designated, NGS-based IVD test that can detect genetic mutations in 324 genes and two genomic signatures in any solid tumor type, the agency said. At the same time, CMS proposed coverage of the F1CDx. The test is the second IVD to be approved and covered under the program's overlapping procedure.

The first use of the FDA-CMS parallel approval program involving an IVD test came in August 2014, when the FDA approved Cologuard, from **Exact Sciences**.

By leveraging the FDA's Breakthrough Device Program and Parallel Review with CMS, Foundation Medicine secured FDA approval and an immediate proposed Medicare coverage determination, within six months of the FDA receiving the application, Gottlieb explained.

To do so, the FDA helped Foundation Medicine use the agency's Breakthrough Devices Program to speed review of tests that help doctors diagnose life-threatening or debilitating diseases and for which there are no approved or cleared alternatives, or for which the test offers significant advantages over alternative tests, he added.

For diagnostic tests submitted under this program, FDA and CMS concurrently review for marketing authorization and coverage and work with sponsors during test development to provide guidance on the evidence laboratories will need to support the two agencies' decisions. These efforts reduce the decision-making time for the two agencies, Gottlieb added.

fied standards," he said. "And we could better leverage post-market data to make our processes more efficient."

## Meeting Scientific Standards

Another way the FDA seeks to improve efficiency is by developing innovative approaches for labs to demonstrate analytical and clinical validity, Gottlieb said. "For example, a developer may be able to demonstrate analytical validity by showing that its test conforms to FDA-recognized standards—perhaps including standards established by the scientific community or standards-development organizations."

To implement this approach, the FDA plans to qualify third-party databases that the FDA could use to help establish clinical validity, he added. "For next-generation sequencing, in particular, this could include our adoption of ClinGen as a reference database," he said.

ClinGen is a database the **National Institutes of Health** maintains that aggregates information about genomic variations and their effects on health. "Under this approach, a new NGS test can rely on a reference database, such as ClinGen, to help demonstrate clinical validity," commented Quinn. "We are closely following all the work in this space and want to leave the door open to other databases, in addition to ClinGen, to qualify." TDR

*—Joseph Burns*

➤➤ ***CEO SUMMARY: A disruptive force that involves precision medicine, pharmaceutical companies, and venture capital investors is poised to reshape the clinical laboratory industry. Genetic knowledge makes it possible to match cancer drugs to specific mutations. Pharma companies and professional investors recognize that control of diagnostic technologies and companion diagnostic tests enable them to gain better access to information on patients who would benefit from cancer drugs. For these reasons, pharma companies and others are investing heavily in clinical laboratories and diagnostic technologies.***

## It's not about the lab test ... but the expensive drug indicated by the test

# Why Pharma, Private Equity Want to Reshape Lab Industry

WHILE LABORATORY LEADERS ARE FOCUSED on the urgent need to cope with deep cuts in clinical laboratory test prices and more restrictive managed care networks, a greater disruptive threat to the clinical lab industry is gathering momentum.

This threat is the control that pharmaceutical companies and venture capital investors are gaining over diagnostic technologies, patents, and intellectual property. The basis of this threat is companion diagnostic tests. It is a threat which could upend the historical control that the pathology profession and *in vitro* diagnostics manufacturers have on clinical laboratory testing and diagnostic technologies.

This disruption will not happen quickly. But market evidence is accumulating and several business transactions involving lab testing companies support this development.

The influence of pharmaceutical companies and venture capital in the clinical laboratory market was discussed in a presentation made at this year's *Frontiers in Laboratory Medicine* (FiLM) conference in Birmingham, England, in January. THE DARK REPORT and the United Kingdom's **Association for Clinical Biochemistry** co-produce the FiLM conference.

The speaker was William G. Morice II, MD, PhD, Chair of the **Mayo Clinic** Department of Laboratory Medicine and Pathology, and President of **Mayo Medical Laboratories**. He discussed how new developments in science, technology, and finance will influence laboratory medicine.

Since his appointment to this position in 2015, Morice has taken on new responsibilities, one of which is helping the leadership of Mayo Clinic understand the speed and direction of changes in clinical laboratory testing, gene sequencing, and precision medicine.

"I've spent the past three years working with the institutional leadership of Mayo Clinic, helping them to understand what we do in the laboratory," he explained. "The reason for that—as most of us know—is that many of our physician colleagues and our administrative partners don't understand the scope of the work we do and the importance we bring to healthcare.

"My role is to support the practice, which means that, in a place like Mayo Clinic, we cannot be about only the current state of medicine," Morice said. "We have to create the future state."

Doing so is particularly challenging today, given that the clinical lab industry is in transition, influenced by new disruptive factors it has not faced previously.

About these trends, Morice discussed three specific ones that Mayo Medical Laboratories considers to be disruptive. "First is massive parallel multi-analyte analysis," he stated. "This is particularly true in the fields of next-generation sequencing and mass spectrometry.

"The second is high-speed, high-complexity computing," said Morice. "This technology supports advances in machine learning and self-improving algorithms.

"Disruptive trend number three is the miniaturization of many technologies used in clinical diagnostics, as well as nanotechnologies," he stated. "One example involves organic, light-emitting diodes which can deliver much lower limits of detection, compared to existing clinical laboratory instrumentation."

### ➤ Finance Is Disruptive Field

Finance is another field that will disrupt the clinical laboratory marketplace. In addition, Morice pointed out that both government and private payers will continue to influence how labs are paid and the stability of lab finances.

Morice added, however, that another source of change will have outsized influence on reshaping the services laboratories offer and how labs are organized to provide those services. "Compared to the past sev-

eral decades, we are about to see pharmaceutical companies and venture capital investors become major drivers in clinical laboratory testing and anatomic pathology services," predicted Morice.

## Disruptive Financial Inputs

"We already have these entities putting disruptive financial inputs into the system," Morice commented. "These disruptions are happening not just in the United States, but worldwide. We see, for example, a growing interest among pharmaceutical corporations and venture capital companies to invest in the laboratory industry."

One early example of the financial influence pharmaceutical companies can have on the clinical laboratory marketplace was **Novartis'** acquisition of **Genoptix** in 2011. In 2016, the Swiss-based pharmaceutical company had annual revenue of $48 billion.

"In 2001, Novartis introduced Gleevec, the first FDA-approved targeted therapy for cancer," said Morice. "In 2011, that single drug accounted for $1.5 billion of revenue for Novartis out of $32 billion of its total pharma revenue.

## Novartis Buys Genoptix

"In that same year, Novartis announced the purchase of Genoptix for $470 million," he explained. "Genoptix started in San Diego as a private laboratory doing bone-marrow analysis. They'd go into the physician's office, leave a test kit, and the physician would send the bone marrow to Genoptix for a full workup.

"At the time, academics and pathologists were confused about why Novartis would buy Genoptix. But in the financial industry, it was clear," he said. "The annual revenue of Genoptix was $190 million. It was a shrewd move for this $48 billion pharma company to pay $470 million to then own a lab testing company that expanded its access to a yearly $1.5 billion cancer drug opportunity.

"The financial markets loved it because the deal made sense for two reasons," Morice explained. "First, Novartis could grow the Genoptix revenue from the actual lab-test activity.

"The second reason, however, was perhaps the more important one: Having these bone-marrow specimens gave Novartis improved access to a $1.5 billion market for a single cancer drug," he noted. "This deal was the first big notice that pharma was interested in the clinical laboratory industry.

"Since then, the numbers have gotten bigger," he continued. "In 2015, sales of therapeutic drugs staged by a companion diagnostic test totaled more than $25 billion. To be prescribed, these drugs require a laboratory diagnostic test."

## A Parallel Trend

The explosion in knowledge about how genetic mutations are involved in cancer is a parallel trend that fuels growth in the number of drugs that require a companion diagnostic test.

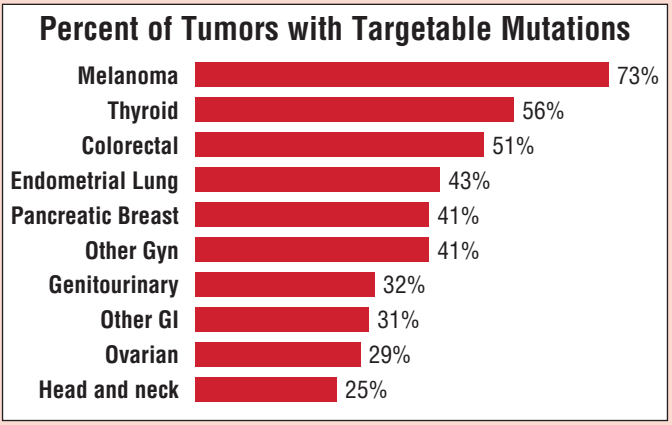
"The number of cancers known to have mutations that can be targeted with a specific therapy is growing rapidly," Morice stated. "With melanoma, for example, 73% of cases have targetable tumors." *(See page 13, "Percent of Tumors with Targetable Mutations.")*

"In that $25 billion market, 90% of the sales are from oncology drugs, which fits right into the targeted therapy approach," he added. "And 80% of those drugs are from three companies: Novartis, **Bristol-Myers Squibb**, and **Roche**. These facts demonstrate how a huge amount of revenue for these giant companies increasingly depends on the availability of a clinical laboratory to do the diagnostic test.

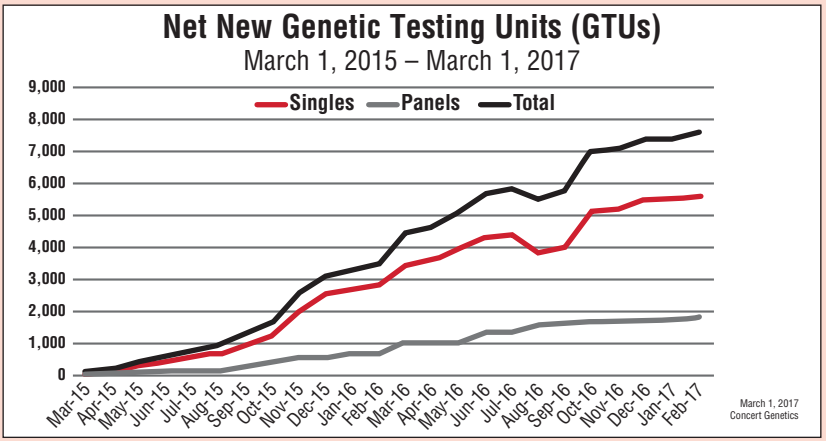
"It explains why pharma companies are interested in having greater control over the diagnostic technologies used in companion diagnostic tests for cancer, as well as the clinical laboratories that perform these tests," Morice said. "Oncologists need these

# Big Pharma, Venture Capital Investors Seek Control of Companion Diagnostic Tests

**WHAT IS FUELING A NEW DISRUPTIVE TREND IN THE CLINICAL LABORATORY INDUSTRY** is the growth in genetic medicine, particularly in the field of oncology. Research is uncovering genetic mutations in tumors that will respond to specific cancer drugs. Companion diagnostic tests are used to identify those gene mutations and help oncologists select appropriate therapies. William G. Morice II, MD, PhD, of Mayo Clinic and Mayo Medical Laboratories, used the table below to show which types of tumors have targetable mutations.




The table below shows the rapid and ongoing increase in the number of genetic tests available for physicians to order and use in patient care. The data is from Concert Genetics, which states that it can currently identify 69,104 genetic tests offered for clinical use. Of this number, 8,535 are next-generation sequencing tests. Concert Genetics predicts genetic testing will be a $10 billion market by 2024.




companion diagnostic tests to diagnose the patient and identify if a patient's tumor has a genetic mutation that will respond to a specific cancer drug.

"These are the reasons why that first development in 2011—the Genoptix acquisition by Novartis—triggered a huge influx of capital into healthcare compa-

nies involved in clinical diagnostics and clinical laboratory testing," he noted.

"Another milestone event in this trend is the story of **Foundation Medicine**," he explained. "In 2009, Foundation Medicine was founded as a molecular information company, not a laboratory testing company.

"In 2012, Foundation Medicine launched its FoundationOne test in the U.S. market," Morice stated. "This test is basically a cancer panel for targetable mutations. Three years later, in 2015, Roche purchased Foundation Medicine for $1 billion. For me, this was a real eye-opening moment."

During conversations with biopharmaceutical industry leaders, Morice has gained insight into the drive of these companies to enter or expand their activities into genomic clinical laboratory testing.

## Drive Revenue From Drugs

"Roche has long-standing businesses in both laboratory diagnostics and pharmaceuticals. If you look at its purchase of Foundation Medicine, though, it was about more than just generating lab revenue," Morice explained. "Roche recognized that the results of the FoundationOne test could drive revenue from the drugs that would be prescribed to cancer patients based on the results of this test.

"In 2015, Roche's pharma revenue was $39 billion, and it had four or five key products," continued Morice. "Today, it has a growing number of oncology drugs generating billions of dollars that depend on companion diagnostic testing.

"Foundation Medicine's revenue was miniscule compared to that of a $50 billion pharma company," he added. "But this lab company continues to grow, in small part because of clinical testing and in large part because of companion diagnostics."

At this point, Morice encouraged pathologists and laboratory managers to understand the fundamental shift happening within the profession of clinical laboratory medicine. "These investments by pharma companies are twisting the existing paradigm within which most clinical labs operate," he said. "Clinical laboratory professionals are trained to think about how to create knowledge that's of value to the patient.

## Value Proposition for Pharma

"But in today's clinical testing marketplace, we see some lab companies creating knowledge that has a totally different value proposition for biopharma—distinct from the patient and the physician. And, as we know, biopharma companies are multibillion-dollar enterprises working to shape the future of healthcare.

"Biopharma companies are not alone in this arena," Morice explained. "Venture capital companies are making similar forays.

"Within the investor community, there is now a growing school of thought that says the future is big data, and the greatest source of big data is in medicine," he noted. "Venture capital companies recognize the value of big data and are looking for ways to invest in healthcare, particularly in laboratory medicine."

One form of big data may come from the development of liquid biopsy tests. "New companies will use next-generation sequencing-based blood tests to look for circulating, cell-free DNA that is cancer-related," Morice explained.

## Global Cancer Screen Market

"Currently, the market for this screening test is small, but it's estimated to be a $1.3 billion market within four years," noted Morice. "There are already estimates of a potential $425 billion global market for a screening blood test for cancer. That's huge!

"If the future is to invest in big data, then liquid biopsies may be the perfect complement to drive healthcare through laboratory medicine," he said. "To con-

# Concern Rising Among Health Insurers About Swift Increases in Genetic Test Costs

**HEALTH INSURERS HAVE BECOME INCREASINGLY CONCERNED** about the rising number and cost of genetic tests in the past few years, said William G. Morice II, MD, PhD, Chair of the Mayo Clinic Department of Laboratory Medicine and Pathology and President of Mayo Medical Laboratories.

"In the United States, there are almost 70,000 genetic tests available, including more than 8,000 next-generation sequencing panels," he said. "Genetic testing is predicted to be a $10 billion market by 2024. *(See chart on page 13, "Net New Genetic Testing Units.")*

"This level of spending is getting payers' attention," he added. "Traditionally, the cost of clinical lab testing is a low proportion of the overall healthcare budget, but insurers are concerned."

Morice has met with executives of **UnitedHealthcare**, one of the nation's largest health insurers, to discuss spending for genetic tests. "They're perplexed because genetic-test spending is rising dramatically, and they've heard how 20% to 40% of lab testing is unnecessary.

"What's more, their data show that this testing isn't being used properly, and they don't know why because the coding system for genetic-testing reimbursement is antiquated," he added. "As a result, they don't have good data that tells them what they're spending money on.

"If a payer's business model depends on knowing what it is spending its money on, and the payer can't do that, it is extremely frustrating," he explained. "That's why UnitedHealthcare and **Anthem** have started onerous, pre-authorization mechanisms for molecular and genetic tests to screen out inappropriate testing.

"Health insurers also know that companion diagnostics are driving targeted therapies," Morice added. "Currently, these specialty pharmaceutical drugs make up 2% of the formulary. However, because of their high cost, they represent a disproportionate amount of total pharmacy expenditures.

"Health insurers recognize two things," emphasized Morice. "First, what they spend on molecular and genetic testing is steadily increasing. Second, health insurers understand that companion diagnostic tests are driving up their costs for prescription drugs and they don't have a good way to control that spending."

nect the dots, another venture capital deal will illustrate this point.

"In 2016, **Illumina** founded **Grail**," Morice said. "Grail aims to develop a blood-based cancer-detection tool and has $100 million in capital. Its goal is to support lab testing for cell-free DNA."

When Grail was founded, Jeff Huber, formerly of **Google**, was named Grail's CEO. "So, the company's first CEO was not a 'lab guy.' He was a 'data guy' from Google," Morice commented. "Currently, Huber is vice chairman of the board at Grail. Previously, he worked at a company called **Google X** that described itself as being at the intersection of life science and computer science. Before that, Huber led the development of Google ads, apps, and maps."

In the midst of the discussion about big data, Morice offered a warning and provided an example. "Not every foray into this area is successful," he cautioned. "A case in point: **OPKO**, a pharmaceutical company that purchased **BioReference Laboratories Inc.** (BRLI) for about $1.47 billion in 2015.

"BRLI is a reference lab that's about the same size as Mayo Medical Laboratories," commented Morice. "The

reality of the OPKO-BRLI deal is that OPKO did not have the straight connection between its business model and the capabilities of BRLI.

"After spending almost $1.5 billion for BRLI, the stock prices have fallen precipitously, and the president that OPKO installed to oversee BRLI operations, Gregory Henderson, MD, recently resigned," he stated. "Opko is now searching for a new BRLI president. So, this strategy of having a large pharma company buying a clinical lab does not always work as designed."

Morice outlined other ways that big data will be used in healthcare. He offered as one example the announcement in October 2016 that **IBM Watson Health** would work with **Quest Diagnostics** to launch **IBM Watson Genomics**. In an effort to combine computing power with genomic-tumor sequencing, the **Memorial Sloan Kettering Cancer Center** in New York will supplement Watson's scientific data with OncoKB, a precision oncology knowledge base, to help physicians make treatment choices with cancer patients, as Quest said when it announced the deal.

William Morice, MD

**➤"The message here is that pathologists and clinical laboratory scientists need to stay engaged because many non-traditional forces are investing massive amounts of money in laboratory medicine. If that's the case, how do we keep our clinical labs and pathology groups relevant? Basically, we have to promote our role in healthcare. We have to embrace an uncertain future and stay informed about what is coming."**

Big data also will supplement health insurers' efforts to manage population health, the goal of which is to keep patients out of the hospital.

"The only way to provide adequate healthcare for patients while slowing the growth rate of annual healthcare spending is to keep patients out of the hospital," he said. "The drive to keep patients out of the hospital will drive disruption in laboratory medicine.

"These disruptions will include availability of lab tests in convenience-driven locales, such as pharmacies, and replacement of laboratory tests by wearable monitors," he added. "Overall, these trends are beneficial not only to the economics of healthcare, but for individual patients through earlier disease detection and better disease management. As laboratory and pathology professionals, we must be ready to respond."

## ➤Need to Stay Engaged

In closing, he added another caution. "The message here is that pathologists and clinical lab scientists need to stay engaged because many non-traditional forces are investing massive amounts of money in laboratory medicine. If that's the case, how do we keep our clinical labs and pathology groups relevant?" he asked. "Basically, we have to promote our role in healthcare. We have to embrace an uncertain future and stay informed about what is coming.

"Also, our labs must leverage partnerships and relationships," he added. "Here at Mayo, that means we have to be willing to work with other organizations that are outside of healthcare and with collaborators in other healthcare settings and in other industries. Given that there's an ever-changing platform in big data, who are better positioned to do this work than those of us who work in the laboratory?"

Morice will be a keynote speaker at this year's *Executive War College* in New Orleans on May 1-2. His session is titled, "*How Pharma Money and Private Equity Investors Are Poised to Use the Coming Generation of Genetic Testing and Clinical Diagnostics to Reshape the Lab Test Marketplace.*" TDR

*—Joseph Burns*

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Legal Update

# D.C. Circuit Court Reverses Medical Necessity Ruling

MANY LAB EXECUTIVES were concerned last year after a judge in the District of Columbia Circuit Court ruled that clinical laboratories need to determine that all lab test services physicians order are medically necessary.

The court also ruled that ordering physicians do not need to determine medical necessity, noted the law firm **McDonald Hopkins** in a commentary about the court case.

The judge's ruling was made in June 2017, in the case of *United States ex rel Groat v. Boston Heart Diagnostics Corp.* This ruling was viewed as a challenge to long-standing precedents in how lab tests are ordered. For decades, the general practice has been that the physician ordering the test makes the primary decision as to the medical necessity of the test. Upon receiving a physician's test order, the clinical laboratory is responsible for performing that test.

## Second Ruling in December

Thus, clinical laboratory directors and pathologists will welcome a new development in this case. In December, the judge's ruling was overturned in a clarification, McDonald Hopkins explained. While the December ruling means that lawyers can cite the ruling when arguing issues related to medical necessity, the ruling does not apply to all court decisions going forward and may not apply at all, given that the case is pending in the circuit court, attorneys told THE DARK REPORT.

In the second ruling issued Dec. 11, the court found that a laboratory cannot—and is not required to—determine medical necessity. Instead, labs can rely on ordering physicians' determinations that the laboratory tests they order are medically necessary.

"It is important to note that—while the decision is positive for labs—this decision merely provides that labs are not solely responsible for determining and certifying medical necessity for services submitted as claims to Medicare," McDonald Hopkins wrote in an advisory to clients. "Labs should educate referring physicians that each physician's medical records must support the medical necessity for each service ordered."

In an effort to clarify the issue, THE DARK REPORT interviewed lawyers familiar with the case: Jane Pine Wood, Chief Legal Officer for **BioReference Laboratories Inc.**, and Courtney G. Tito, an Associate with McDonald Hopkins.

"This ruling in December is good, but it's limited because it is specifically applicable only in the District of Columbia," stated Wood. "It was a narrow ruling in a false claim case. The plaintiff argued the fact that the laboratory knew the service in question wasn't medically necessary, so the laboratory claims submitted for the testing were false claims. And the court basically said, 'No, simply the fact that it turns out to be medically unnecessary does not in and of itself make it a false claim.'

## When Is It a False Claim?

"In essence, under the federal False Claims Act, when a lab has a test for a Medicare patient, just the fact that it happens to be medically unnecessary does not by itself mean it's a false claim," added Wood.

Tito identified another reason for caution. "The whistleblower in the case still has to make the case with enough detail for this ruling to get beyond what's called 'the pleading stage' so that it can move forward into more substantive issues," she said. "If the case does not move beyond the pleading stage, the December ruling may be moot."

Another question that labs will want answered is whether the December decision applies only in the District of Columbia. If it applies only in that one district, does that mean labs and their lawyers may not be able to cite the case in a similar lawsuit in another district?

## Second Ruling in December

"Labs and lawyers for labs could still cite the case, but a court in another jurisdiction doesn't have to follow it, even though courts generally will defer to earlier decisions," Wood explained. "While they may give deference, courts also will disagree.

"That said, the December ruling is much better than the initial ruling," she noted. "The initial ruling was particularly troubling for pathologists and clinical labs because labs are not in a position to make that determination, either factually or legally. Labs don't practice medicine.

"While the December ruling is better than the one in June, it would have been ideal if the court said that the ordering physician is the final arbiter of medical necessity for all purposes," Wood explained. "This ruling has only the narrow purpose of determining whether or not a false claim allegation in this court case could be made. It doesn't do anything to touch what is the bane of laboratories, which is: will the lab face recoupment because the physician did not adequately document medical necessity?

"That said, the ruling is useful for clinical labs anywhere, whether they are in D.C. or not," she added. "Lawyers can cite the case and I have done so in letters I've sent to private payers about medical necessity. I've explained that the determination of the physician should prevail.

"So, in that way, this ruling may be useful in cases involving medical necessity or in cases in which a payer is seeking recoupment," she added. "Many times, health insurers will ask labs for patients' medical records to support claims of medical necessity. In those cases, labs need to go back to the ordering physician for those records, and that's quite a burden." TDR

*—Joseph Burns*

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## Court Decision May Have Limited Application for Labs

**LAWYERS FOR CLINICAL LABORATORIES** will follow closely the whistleblower case of *United States ex rel Groat v. Boston Heart Diagnostics Corp.* that generated the medical-necessity decision, said Courtney G. Tito, Associate with the law firm of McDonald Hopkins.

"As this case progresses, this and other decisions may become what's called the law of the case and become part of the substance of the court's determination," she explained. "In that way, the decision could have far-reaching implications. But right now, it's very focused on this particular pleading and whether that determination was necessary to make a dismissal decision or not.

"Some labs will look at this December ruling as one that will be important later," Tito added. "Other labs are relying on it now when they argue over denied claims. While labs can rely on the December ruling that physicians need to make the determination of medical necessity, the ruling does not strip labs of their legal duty to make sure that each lab test claim they submit is medically necessary and that they have the proper documentation."

# INTELLIGENCE

## LATE & LATENT

*Items too late to print, too early to report*

On March 6, one of the lab industry's long-serving executives and consultants, Jack Mattice, PhD, of Vancouver, Wash., died from flu complications. He was 77 years old. Mattice earned a PhD in medical microbiology from **University of Oregon**. Within a few years, he was handling market development for **United Medical Laboratories** (UML), of Portland, Ore. UML reached a then-record volume of 25,000 specimens per day and was acquired before 1980. Mattice, Charlie Dexter, and James Root, MBA, founded **Lancet Labs** in Portland during the 1970s.

### MORE ON: *Mattice*

Lancet Labs was itself acquired just a few years later by **MetPath, Inc.** Following that sale, Jack Mattice, along with partner Charles Dexter, purchased an ownership interest in **Physicians Medical Laboratories** (PML) in Portland, Ore. When PML was sold to **Nichols Institute** in 1989, Mattice left to concentrate on growing his lab and medical consulting business, **J.A. Mattice & Associates**. The website states his consulting company had more than 200 hospitals as clients.

### 40% ERROR RATE IN GENE TESTING?

This month, *Genetics in Medicine*, a *Nature* journal, reported "that researchers at a clinical laboratory re-tested 49 patients' samples and compared them to raw data from their direct-to-customer (DTC) tests. Two in five variants in the DTC information were incorrectly reported." The study shows the complexity associated with genetic testing, given the current state of sequencing technology. The lead researcher, genetics counselor Stephany Leigh Tandy-Connor from **Ambry Genetics**, stated, "Such a high rate of a false positives in this particular study was unexpected. Of all the BRCA1 and 2 variants in the study, for example, 17 were correctly identified, while eight were false positives. Across the study, 94% of the false-positive calls were for cancer-related genes."

### TRANSITIONS

- **TriCore Reference Laboratories** of Albuquerque, N.M., appointed pathologist Michael Crossey, MD, PhD, as its President and CEO. Crossey has been affiliated with TriCore since 1997.



***That's all the insider intelligence for this report. Look for the next briefing on Monday, April 16, 2018.***

**SPECIAL SESSION!**

## Learn and Master Strategies to Add Value to Your Lab's Data!

### Mara Aspinall, MBA
**President and CEO, Health Catalysts**

### Big Changes in Clinical Diagnostics: Why Your Lab is Now in the Information Business, with a Wet Lab on the Side

Every lab professional knows that clinical laboratory testing is becoming more complex. Genetic testing and useful new clinical biomarkers in the proteome, microbiome, and metabolome are generating scads of raw data that must be validated and stored, then analyzed to produce clinically-actionable information for physicians.

Here is an exceptional opportunity to hear one of the industry's leading strategic thinkers explain how and why the daily testing activities of clinical labs and anatomic pathology groups will be generating ever-greater volumes of data. You'll learn which diagnostic technologies will fuel this trend, as well as specific opportunities for your lab to provide these services to your physician-clients.

Aspinall is widely-respected for her insights and accomplishments in the diagnostics industry. Join us for this invaluable session. Guarantee your place by registering today!

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# UPCOMING...

- ***World's Largest Consolidation of Clinical Lab Services Underway in Canada: We Take You Inside the Project.***
- ***Lessons from Prospering Pathology Groups on Delivering Services that Add More Value.***
- ***Amicus Briefs in ACLA vs. HHS lawsuit Describe Flaws in Medicare Lab Price Cuts, Consequences.***