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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

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COMMENTARY & OPINION by...

R. Lewis Dark
Founder & Publisher

Tapping Molecular Pathology's New Gold Mine

IN ONE SENSE, WE CAN SAY THAT THE DECADE OF 2001 THROUGH 2010 was bookended by two one-half billion dollar anatomic pathology acquisitions. Each transaction was a powerful signal to Wall Street investors. Unfortunately, most pathologists are not tuned into that signal and so continue to miss the message.

It was back in 2002 when **Laboratory Corporation of America** stepped up and purchased **Dianon Systems, Inc.**, for the sum of $578 million. At that time, Dianon had annual revenue of around $190 million. LabCorp thus paid a bit more than three times annual revenue to acquire Dianon.

The willingness of Labcorp to spend almost two-thirds of a billion dollars to buy an anatomic pathology company that tested biopsies referred by office-based physicians became a milestone event for the pathology profession. It captured the attention of Wall Street investors and caused lots of investment dollars to flow into the anatomic pathology marketplace throughout the past decade.

Now, in 2010, we have the other bookend. **General Electric** (GE) has agreed to pay $587 million to purchase **Clarient, Inc.**, a company which just barely produced $100 million in revenue for 2009 and posted a $10 million loss that same year. Already, investors are asking, "what does GE know about anatomic pathology, molecular diagnostics, and genetic testing that we don't?"

This old curmudgeon has lived through any number of bull and bear stock markets. So take that into consideration when I say that GE's acquisition of Clarient is likely to be an even more optimistic portent about the rosy future of anatomic pathology than was LabCorp's purchase of Dianon Systems back in 2002. It will pay every pathologist to understand which propietary strategies GE intends to pursue—and how the Clarient acquisition enables those strategies.

It is not often that the world's major healthcare corporations make billion-dollar bets on the wrong thing. Labcorp's bet on Dianon in 2002 turned out well for it. Now GE has placed its own bet on Clarient. Thus, independent pathology group practices should stay alert to these unfolding events and use them to craft effective clinical and business strategies. With the rapid advances in molecular diagnostics and genetic testing, anatomic pathology is likely to become the new gold mine in medicine. Pathologists should be first to tap that gold mine for clinical and financial success. TDR

Sonic Makes Big Play In AP With CBL Path Buy

Sonic Healthcare, Ltd, will pay $123.5 million to acquire CBL Path and its AP testing capabilities

CEO SUMMARY: With the announcement that it will purchase CBL Path, Inc., Sonic Healthcare, Ltd., becomes the latest public laboratory company to buy a sizeable presence in the national anatomic pathology (AP) marketplace. For CBL Path, founded in 2003 by ex-Dianon executives and sales professionals, it is the exit strategy for which they have long planned. CBL Path's sustained growth during the past seven years demonstrates why investors are eager to buy into the anatomic pathology marketplace.

LAST WEEK, IT WAS ANNOUNCED THAT **Sonic Healthcare Ltd.**, of Sydney, Australia, would pay US$123.5 million to acquire **CBL Path, Inc.**, the anatomic pathology (AP) company based in Ocala, Florida.

The sale is expected to close by year end. When it does, it will end the short, seven-year business life of CBL Path. It was 2003 when CBL Path launched business operations. It was formed by a group of executives and sales professionals who had previously worked at **Dianon Systems, Inc.**, prior to its acquisition by **Laboratory Corporation of America** in January, 2003. *(See TDRs, November 18, 2002, and February 10, 2003.)*

Currently, CBL Path is 40% owned by **Galen Partners**, a private equity firm based in Stamford, Connecticut. The balance of CBL Path's ownership is held by management, staff, and other private investors.

CBL Path's timing coincided with the strong expansion in anatomic pathology testing that took place during the past decade. It maintained a steady rate of growth in specimen volume and revenue during the past seven years. Sonic Healthcare disclosed that CBL Path has annual revenues of approximately $80 million. That represents an average rate of growth for CBL Path of about $11.5 million per year between 2003 and 2010.

For Sonic Healthcare, the deal is significant because it immediately propels Sonic into the first rank of national anatomic pathology companies in the United States. It also moves Sonic a big step forward toward the goal of attaining $1 billion in revenue from its laboratory operations in the United States.

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SUBSCRIPTION TO THE DARK REPORT INTELLIGENCE SERVICE, which includes THE DARK REPORT plus timely briefings and private teleconferences, is $14.10 per week in the US, $14.90 per week in Canada, $16.05 per week elsewhere (billed semi-annually).

At the end of its fiscal year of June 30, 2010, Sonic stated that it had revenue from U.S. operations totaling US$766 million. Adding CBL Path's annual revenue to that figure would bring Sonic's total U.S. revenue to $846 million per year.

Another closely-watched aspect of this acquisition will be the price Sonic has agreed to pay for CBL Path. Sonic Healthcare is known to be a careful buyer of clinical laboratories and pathology groups. For, example, during the past two years, it has been outbid for several prime laboratory businesses that were offered for sale.

In studying these transactions, THE DARK REPORT believes that Sonic Healthcare is typically outbid by other buyers when the motive of the seller is primarily to maximize the sales price of the laboratory to be sold. However, when the seller has other considerations, such as protecting the jobs of long-serving lab employees and continuing the name of the laboratory to be sold, Sonic Healthcare is often selected to be the buyer.

In these situations, Sonic's federation business model works to its advantage. Sonic generally continues to operate the newly-acquired laboratory under its same name and will retain both the management team and laboratory staff without major changes. For some sellers, these are important considerations.

Led By A Pathologist As CEO

Another element should not be overlooked as to why Sonic prevails in some laboratory bidding situations. Sonic consistently points out that it is a laboratory company led by a CEO who is a pathologist. That fact makes it unique among public laboratory companies operating in the United States. Sonic Healthcare also discusses how its corporate culture respects the clinical mission behind laboratory testing and that can be an influencing factor for some sellers.

These observations will help pathologists and pathology practice administrators better understand some factors which may have contributed to CBL Path's decision to sell to Sonic Healthcare over other interested bidders.

The purchase price is $123.5 million. As outlined by Sonic Healthcare, this represents a multiple of approximately eight times EBIDTA (earnings before interest, depreciation, taxes, and amortization). That implies an EBITDA of $15.5 million, based on CBL Path's annual revenues of about $80 million.

1.5 Times Annual Revenue

The $123.5 purchase is also about 1.5 times annual revenue. Both of these figures point to a sales price in line with a number of laboratory acquisitions during the past 36 months.

It is reasonable to speculate that several strategic factors helped tip the scales in Sonic's favor as the eventual buyer. First, it would intend to operate CBL Path under its existing name, existing management team, and existing network of laboratory facilities. That is consistent with its federation model. For a management team interested in continuing with CBL Path post-acquisition, this would be highly attractive.

Second, both buyer and seller have commented on the expected synergies that would come from combining the two operations. Sonic identified these synergies in its press release, writing that "Sonic currently has clinical laboratory operations in eight of the 10 States from which the majority of CBL Path's revenue is sourced."

At a minimum, the Sonic/CBL Path transaction sets up two changes in today's lab testing marketplace. First, it immediately gives Sonic Health a substantial volume of AP specimens and revenue. Second, it removes one more independent laboratory company from the competitive marketplace. TDR

Gauging the Prospects For Anatomic Pathology

During 2010, investors paid aggressive prices for those laboratory companies focused on pathology

CEO SUMMARY: More buyers are crowding into the lab testing industry and looking to acquire anatomic pathology testing companies. These buyers are willing to pay strong prices to acquire AP labs and companies which they determine to be a strategic fit. All of this acquisition activity is happening even as the Baby Boomer generation of pathologists is poised to begin retiring in significant numbers. In coming months, that factor may trigger more intense AP merger/acquisition activity.

IN RECENT WEEKS, both **General Electric** (GE) and **Sonic Healthcare, Ltd.**, announced that each would acquire one of the nation's larger national anatomic pathology (AP) companies.

For GE, the acquisition target was **Clarient, Inc.**, of Irvine, California. GE will pay $587 million to purchase Clarient and the deal is expected to close either before the end of 2010 or early in 2011.

For Sonic Healthcare, the acquisition target was **CBL Path, Inc.**, of Ocala, Florida. It will pay $123 million to buy CPL Path. This sale should be completed by the end of December, 2010.

These two announcements were preceded just nine weeks earlier by the news that **Roche Holdings** would purchase **BioImagene, Inc.**, the digital pathology company based in Sunnyvale, California. Roche will operate BioImagene from within its **Ventana Medical Systems** business division.

If there is a common theme to these three acquisitions, it is the strong—even aggressive—price buyers paid for at least two of the three acquisitions. In the case of Clarient, GE is paying $578 million for a public AP company that, at the end of 2009, reported $100 million of revenue and a loss of $10 million.

The price paid for CBL Path was more in line with the sales prices of anatomic pathology laboratories during the past 24 months. Sonic will pay $123 million for CBL Path, which is about 1.5 times the company's annual revenue of around $80 million during the past year. *(See pages 3-4.)*

Roche To Buy BioImagene

The $100 million price paid for BioImagene surprised many observers. That's because BioImagine is a new company and has just several hundred customers for its digital scanners and digital pathology systems.

This purchase price represents the strategic value BioImagene is expected to bring to Roche. But for pathologists and pathology practice administrators, the fact that Roche is willing to pay such a high price for the potential that BioImagene offers in digital pathology is certainly a sign. It reflects the confidence by one of the world's largest corporations involved in the lab testing market that

anatomic pathology testing will be a high-growth sector of laboratory medicine in coming years.

One could make that same interpretation about GE's acquisition of Clarient. GE will pay almost one half billion dollars to acquire a pathology testing company that has struggled to earn a profit and has revenues of around $100 million per year.

GE And Digital Pathology

But wait! Maybe there is more to the GE story. Don't overlook the fact that **Omnyx, LLC**—GE's digital pathology joint venture with **UPMC**—just announced that its digital pathology system will enter clinical use at four prominent academic center laboratories. They are: UPMC, **Montefiore Medical Center**, **Stanford University Medical Center**, and **University Health Network**.

One speculation is that GE has identified a strategic advantage it can seize in the anatomic pathology marketplace if it can marry Clarient's strengths in advanced molecular diagnostics and genetic testing with the capabilities of the Omnyx digital pathology system. Then, once the Omnyx digital pathology system obtains market clearance from the FDA, GE can offer an integrated diagnostic solution that incorporates technologies and capabilities drawn from both Clarient and Omnyx.

Integrating In Vivo & In Vitro

Some sharp-thinking clients and readers of THE DARK REPORT may also recognize that it is feasible that GE—a dominant global player in radiology and imaging—might also be ready to integrate radiology diagnostics with pathology diagnostics in some innovative and unexpected manner.

THE DARK REPORT thinks such a scenario is unlikely at this time. But it cannot be summarily dismissed, since technology advances in both molecular imaging and molecular diagnostics are moving quite swiftly.

As a gauge of the state of the laboratory merger/acquisition marketplace, the Clarient and CBL Path sales are evidence that investor interest in anatomic pathology remains quite high, particularly for the most desirable AP lab companies. Also, because many laboratory sales are transacted at the end of the year, it is likely that other significant laboratory acquisitions may be announced during the final six weeks of 2010.

Another factor which could play a major role in increasing merger and acquisition activity in the anatomic pathology sector is the looming retirement of the Baby Boomer generation of pathologists.

Baby Boomer Pathologists

A quick analysis shows why this will be true. Currently there are approximately 3,300 pathology groups in the United States and two-thirds of these groups have four or fewer pathologists.

Since about 30% of all pathologists are members of the Baby Boomer generation (and between 46 and 65 years old), it means that many of these pathology groups are beginning to plan for the retirement of at least one of their partner pathologists. This suggests that they will be motivated to look for sources of cash to buy out their retiring partners.

Collectively, the actions these independent pathology groups must take to accommodate the retirement plans of their Baby Boomer pathologists could trigger a large number of mergers and acquisitions during the next 12 to 36 months. In turn, this could be a factor in reshaping the anatomic pathology profession.

In that sense, the high prices paid for these recent acquisitions of anatomic pathology companies might be an early sign that the pathology profession is be poised to undergo major consolidation. TDR

GE Pulls Plug on Its LIS, No Support after July 2013

Centricity Ultra Laboratory LIS Product will no longer be sold or serviced by GE Healthcare

CEO SUMMARY: Not in recent memory has a laboratory information system (LIS) product been pulled from the market. That is why the announcement by GE Healthcare that it would no longer service or support its Centricity Ultra Laboratory product after July 23, 2013, has caused a stir within the healthcare informatics industry. In the United States, Centricity Ultra LIS laboratory customers are now hustling to select a replacement LIS product and have it installed and operational within the next 36 months.

IT IS A RARE EVENT when an established laboratory information system (LIS) product exits the marketplace. Yet that is what will soon happen to the LIS sold by **General Electric Healthcare** under the name "Centricity Ultra Laboratory."

This summer, GE Healthcare sent written notices to its LIS customers announcing that, as of July 23, 2013, it would cease total support for Centricity Ultra Laboratory. Clinical laboratories around the world currently using this LIS must scramble to replace—in just 36 months—their Centricity Ultra Laboratory LIS with another LIS product.

GE Healthcare has not publicly discussed its reasons for discontinuing sales and support of its Centricity Ultra Laboratory LIS. As of press time, GE Healthcare had not responded to THE DARK REPORT'S requests to interview Marcel Huel, General Manager, Centricity Pharmacy and Laboratory Information Systems.

GE Healthcare's Centricity Ultra Laboratory was originally developed by **Triple G Systems Group** of Toronto, Ontario, under the leadership of CEO F. Lee Green. GE Healthcare paid $54.8 million to acquire Triple G in August 2003. Triple G sold its LIS as "Ultra." *(See TDR, July 7, 2010.)*

In the United States, it is believed that less than 20 customers, representing 100 hospital and other sites, will be affected by GE Healthcare's LIS product termination notice. However, for those labs, it will be a significant challenge to purchase a replacement LIS and have it fully implemented by the summer of 2013.

Implementing A New LIS

"The need to transition to a new LIS in only 36 months will be a disruptive event for these Centricity Ultra Laboratory customers," observed Larry Wimberly, who is Managing Director of **Wimberly Consulting Services, LLC**, in Houston, Texas. Wimberly provides consulting services in LIS and informatics to laboratories and other organizations. He is also a former employee of both GE Healthcare and Triple G.

"Many of the Centricity Ultra Laboratory customers are sizeable laboratory organizations," explained Wimberly. "Examples are **Montefiore Medical**

Center in the Bronx [with 1,188 beds], **Vanderbilt University Medical Center** [833 beds] in Nashville, and **Grady Health System** [953 beds] in Atlanta.

"These are all quite large laboratory organizations and they perform laboratory testing across multiple hospitals and clinics," he stated. "It will be a tight squeeze for labs of this size to conduct a procurement process for a new LIS and have it fully installed and operational in just 36 months."

GE Bought Triple-G

Back in 2003, when GE Healthcare acquired Triple G Systems Group, knowledgeable observers believed that GE wanted to have a suite of health informatics products that would allow it to offer a single integrated informatics solution to hospitals and other healthcare providers.

"Seven years ago, when GE purchased this LIS, it was a competitive product," stated Dennis Winsten, President of **Dennis Winsten & Associates, Inc.**, a Tucson, Arizona-based healthcare systems consulting firm that specializes in clinical information systems. "At that time, GE Healthcare was buying a number of different systems. Although these products did not have the same architecture nor were well integrated, GE included them in the Centricity family.

Questions About Strategy

"It's tough to understand the GE strategy," Winsten said. "Why drop the Ultra LIS when laboratory test data is such a key component to all of clinical care?"

Wimberly made a similar point, noting that GE is terminating an LIS product that is used in some of the largest, most prestigious healthcare institutions in this country. "Clearly, GE sees value in the pathology side of the lab business," he stated. "They are heavily invested in **Omnyx, LLC**, the digital pathology joint venture with the **University of Pittsburgh Medical Center** (UPMC).

"It seems that GE Healthcare leaves a big hole in its health informatics product line-up by not having a competitive LIS product to sell," added Wimberly. "It will be interesting to see what GE Healthcare might do in the future in regards to laboratory information systems." TDR

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Allina Plans to Replace Ultra LIS with Epic LIS

NEEDING SEVERAL IMPORTANT ENHANCEMENTS to the capabilities of its laboratory information (LIS), lab administrators at **Allina Hospitals and Clinics** in Minneapolis, Minnesota, began to look at other options besides the GE Healthcare Centricity Ultra Laboratory LIS it was using.

"We wanted to add functionality to support bedside bar coding for patient identification, along with improved connectivity features for our lab outreach clients," stated Rick Panning, Vice President, Laboratory Services, at Allina. "At that time, the managers at GE Health were upfront with us, stating that 'these software enhancements were not in their future roadmap'.

"That was the moment when we began to suspect that GE was not going to support the Centricity Ultra LIS product going forward," explained Panning. "The product termination letter in July simply confirmed those suspicions and we were already one year into planning for an LIS change."

Panning says that Allina has selected Beaker, the Epic LIS product, to be its new LIS. "Our lab staff is excited about this change," stated Panning. "The health system already uses the Epic electronic medical record (EMR) in all 10 hospitals and 70 clinics. So it will be a big advantage for our LIS to be more tightly integrated with the EMR, since the two systems constantly talk to each other."

IVD Market Update

Several Laboratory Companies On Road to Public Stock Offering

ONE OF THE FEW PUBLIC STOCK OFFERINGS involving a lab testing company was completed last Wednesday. **Exact Sciences, Inc.**, of Madison, Wisconsin sold $69 million worth of new shares to the public.

Exact Sciences has proprietary diagnostic technology that it describes as "for non-invasive, molecular screening technology for the detection of colorectal cancer." During 2009, Exact Sciences had revenue of $4.7 million and a net loss of $9.1 million.

Over the course of 2010, four companies involved in the laboratory testing industry have disclosed or updated plans to conduct public offerings of their stock.

However, as of press time for this issue of THE DARK REPORT, only Exact Sciences had successfully tapped the public stock market as a way to raise capital.

Largest of the lab testing companies expressing an interest in a stock offering is **Aurora Diagnostics, Inc.**, of Palm Beach Gardens, Florida. Aurora has been acquiring dermatopathology practices and anatomic pathology practices since it was formed in 2005. On October 25, 2010, Aurora Diagnostics updated its S-1 stock registration with the Securities and Exchange Commission (SEC).

IPO For Aurora Diagnostics

This document had originally been filed earlier in the year. At the time, Aurora Diagnostics stated it wanted to raise $150 million with its IPO. Aurora Diagnostics reported revenue of $171 for 2009.

The other two companies involved in laboratory testing which declared an interest in offering stock during 2010 are **Med BioGene, Inc.** (Vancouver, British Columbia) and **Rules-Based Medicine, Inc.** (Austin, Texas).

Med BioGene, Inc., has spent most of 2010 working to complete an IPO. It wanted to sell its shares on the The NASDAQ Capital Market and the Toronto Stock Exchange. It has wanted to offer approximately 2.8 million shares for as much as $10.00 per share, which would raise as much as $27.8 million.

Med BioGene's Flagship Test

Based in Vancouver, British Columbia, Med BioGene describes itself as "a life science company focused on the development and commercialization of genomic-based clinical laboratory diagnostic tests for cancer." Its flagship molecular assay is the LungExpress Dx, designed for stratifying post-surgical risk for patients with early-stage non-small-cell lung cancer, or NSCLC, who, following surgical removal of their tumor, are at a higher and lower risk of mortality."

The fourth company which has announced its plans to conduct an IPO is Rules-Based Medicine. In December, 2009, it filed financial documents with the SEC for an IPO and told investors that it hoped to raise $90 million. Last month, Rules-Based Imaging launched VeriPsych, its proprietary multi-marker assay that is "the first and only blood-based diagnostic test to aid in confirming the diagnosis of recent onset schizophrenia."

During the 1990s, a number of lab companies successfully placed IPOs. However, since passage of the Sarbanes–Oxley Act in 2002, it has been much more difficult for companies to sell stock to the public. TDR

CEO Summary: Pathologists at Beth Israel Deaconess Medical Center in Boston, Massachusetts, in a collaboration with GenomeQuest, Inc., will produce whole human genome sequences of patient tumors and other specimens. These whole genome sequences will be studied to learn what diagnostic, therapeutic, and prognostic information they contain. GenomeQuest CEO Richard Resnick discusses what is required to sequence a tumor specimen and how the resulting data will be used.

Rapid sequencing can create primary care opportunities for pathologists

Whole Genome Sequencing: Is It Ready for Prime Time?

PATHOLOGY AND LABORATORY MEDICINE are poised to make a full entry into genetic medicine. That's because the cost and accuracy of producing a whole human genome sequence is falling at startling rates.

This is a trend that has disruptive potential for both clinical laboratories and anatomic pathology groups. Once it becomes possible for clinical labs to cheaply and accurately sequence—and evaluate—hundreds and thousands of genes for a single patient, the resulting diagnostic, prognostic, and therapeutic knowledge will be immense.

One landmark event in the effort to bring rapid genome sequencing into clinical diagnostics is the collaboration announced last month involving the Department of Pathology at **Beth Israel Deaconess Medical Center** (BIDMC) in Boston and **GenomeQuest, Inc.**, of Westborough, Massachusetts.

In exclusive interviews with THE DARK REPORT, Jeffrey Saffitz, M.D., Ph.D., Chairman of the Department of Pathology, and Mark Boguski, M.D., Ph.D, Associate Professor of Pathology at BIDMC, discussed the goals of this partnership. They introduced the concept of the "primary-care pathologist."

"Our company has been involved with the latest generation of sequencing machines since the earliest days of this technology," stated Resnick. "Until recently, customers of this technology were largely pharma and academia. However, we've always suspected that the end game in this field would ultimately be pathology.

"When it comes to clinical applications of whole human genome sequencing, we think pathology will lead the charge and take us forward," observed Resnik. "Pathologists at BIDMC recognize this opportunity.

"In order to produce clinically-actionable knowledge from a genetic sample, four steps must happen," noted Resnick. "Three of these steps involve processing the specimen and collecting the data. The fourth step is where the pathologist evaluates this data and identifies information that is useful to the patient.

GenomeQuest will sequence the genes of tumors and other patient specimens provided by BIDMC. GenomeQuest will then warehouse and manage the resulting data produced by whole genome sequencing. Pathologists and informaticists at BIDMC will analyze the whole human genome data to identify useful diagnostic markers and clinical information. *(See TDR, November 15, 2010.)*

Having explained how pathologists at Beth Israel Deaconess Medical Center will use whole human genome data, THE DARK REPORT now turns to GenomeQuest to provide lab administrators and pathologists with a more detailed understanding of advances in the field of rapid genome sequencing. Richard Resnick, CEO, spoke on behalf of GenomeQuest.

Analysis Requires Four Steps

"In our collaboration with the pathology department at BIDMC, GenomeQuest will perform the first three steps," he explained. "Pathologists at BIDMC will then handle the fourth step.

"In the first step, the specimen is sequenced and mapped," continued Resnick. "Sequencing technology produces strings of DNA sequences. Think of each as a little puzzle piece. We then assemble the puzzle pieces back together using the Human Genome Project as a reference dataset. The assembly of these DNA sequences is called 'mapping.'

"In the second step, we compare the individual's genome sequence to the canonical human genome," stated Resnick. "This step allows us to identify regions where there is variation from the canonical human genome, if you will.

"During this step, a variety of algorithms are used to determine all the regions where the sample varies or differs from the canonical human genome.

'Variant calling' is the term used to describe this process," he said.

"The third step is called 'variant annotation.' We annotate each location on the specimen's genome where there is a variation," stated Resnick. "The annotation carries with it an explanation.

Annotating Gene Sequence

"For example, we might say, 'this particular variation is inside of this gene, and if this actually were to happen, it would truncate the protein that is encoded by this gene. In turn, that would have the following effect downstream on these biological pathways'," he explained.

"Our annotation goes further," noted Resnick. "As a component of the annotation step, we identify whether each variant has already been identified by earlier research. Our annotation will include references to the papers which have been published about that particular genetic sequence to explain what the medical community already knows about that genetic variation. We then gather the full annotation for this genome into a report, which is an interactive database on this organism's genome.

Searching For Variations

"That resulting database of the specimen is where the real magic begins to happen," said Resnick. "Researchers can now query this database. They can ask questions like 'Show me all of the variations that are on chromosome 2 inside of genes or on the 500 base pairs on either side of the target genes that affect the protein and are variations that have not been previously identified in the public domain.'

"The ability to investigate the specimen's genome using these types of queries is rapidly advancing our knowledge of the human genome," he declared. "Our existing customers—pharma and academic researchers—thrive because of this feature. It allows them to conduct basic research in the biology of disease and better build new drugs.

"This brings us to the fourth step," observed Resnick. "The fourth step asks the question 'which of these variants are clinically actionable, based on the patient's presentation?"

"Here is where the pathologist will have a key role," he noted. "Our collaboration with the pathologists at Beth Israel Deaconess Medical Center is aimed squarely at providing pathologists with the annotated database of the whole genomes of patients.

"Working together, our goal is to identify which key information sets must be developed to support accurate diagnosis," said Resnick. "We want to identify and validate the data that are clinically relevant, and that form the basis of our collaboration.

Clinical Applications

"GenomeQuest and Beth Israel Deaconess plan to jointly share computational capability and analytical capability for the purpose of advancing the clinical methodology," he commented. "Eventually we want to provide and generate diagnostic reports which are usable by a pathologist.

"What is exciting about this work is its potential to expand the value that the pathology profession contributes to clinical care," stated Resnick. "Pathologists should want to 'own' the interpretation of genomic data for an important reason. This data will not only have diagnostic value, but it will also have prognostic value.

"This is a key insight," he noted. "Once you sequence the genome of a healthy individual, or of a patient who presents with some kind of a disease, that [whole human genome] data is permanently available.

"That means any future care for the patient may be simply a query on that individual's genome data set," Resnick observed. "Whole human genome sequencing is disruptive because of this potential. It gives the pathologist the

Large Volume of Raw Data Produced By Whole Human Genome Sequencing

HOW BIG IS THE INFORMATION PRODUCED by a whole human genome sequence? How much storage is required to hold the entire genome? Can it be put on a single hard drive? Richard Resnick, CEO at GenomeQuest, Inc., in Westborough, Massachusetts, outlined what is required to store databases full of genomic information.

"A whole human genome is about 3 billion base pairs," noted Resnick. "Each base pair is about a byte of information, so approximately three gigabytes of data must be stored. However, that is the finished whole human genome sequence.

More Than One Copy

"In the first phases of sequencing, as the machines produce strings of genetic sequences, for each position, more than one copy of the same base pair will be produced," he noted. "Thus, the raw data produced may be 30 to 40 times the data in the finished whole human genome sequence. That is why, during the sequencing step, as much as 100 gigabytes of raw sequence data is produced per whole human genome.

"Next comes the analysis of the raw data," continued Resnick. "Sequence strings are mapped, variants are identified, and annotation is performed. Only at this point in the entire process do you end up with a reasonably small data set.

"That dataset for a whole human genome sequence actually may turn out to be far smaller than the expected three gigabytes, for an important reason," he stated. "It is not necessary to store every base pair in an individual human genome. It is only necessary to store the base pairs that contain the differences and variations.

"This means that, early in the sequencing process, the informatics needs are immense in terms of storage and computing resources," commented Resnick. "As the raw sequencing data is processed, the individual whole human genome sequence ends up being a much smaller amount of data that is easier to manage and easier to query.

"This is why the informatics of whole human genome sequencing are immense," said Resnick. "Next year, the industry will sequence about 50,000 individuals. The following year, that number may explode to 500,000 individuals. Very quickly, this becomes a petabyte [one quadrillion bytes, or 1,000 terabytes] problem. Obviously, comparing 100 billion of anything to a reference will be an expensive informatics challenge.

"GenomeQuest currently stores this data on internal servers," noted Resnick. "We consider storage of the whole human genome sequence data to be an added-value service. Our experience to date is that our academic and pharma customers want the benefit of a secure infrastructure where the data is stored, regularly backed up, and always available. GenomeQuest provides that service."

responsibility to assess this data and guide the patient's care team."

Clients and regular readers of THE DARK REPORT know about the race to be first to achieving the goal of the $1,000 whole human genome sequence. Resnick had useful insights about the pace of improvements to rapid gene sequencing technologies.

"In recent years, the capital invested in whole-genome sequencing and analysis is nothing short of astounding," said Resnick. "It has played an essential role in driving down the cost of whole-genome

sequencing and analysis to the point where we can sequence and analyze a whole human genome for about the same price as maybe five or 10 genetic tests.

"Depending on the technology and the specimen, the cost now ranges between $9,000 and $20,000," he stated. "For comparison, recall that, just 10 years ago, the cost to do a single human genome approached $1 billion. That's what was spent on the Human Genome Project. Today we can sequence 100 billion base pairs in a week."

"This cheaper, faster, and more accurate sequencing technology now allows us to scale up and produce full sequences of patient specimens," noted Resnick. "That opens the door for pathologists to step up and begin developing clinical applications using this technology.

According to Resnick, massive throughput in whole human genome sequencing is around the corner. "Each improvement in rapid sequencing technology adds orders of magnitude of efficiency," explained Resnick. "It takes only 12 to 24 months for a new generation of sequencing technology to reach the market.

"This cheaper, faster, and more accurate sequencing technology now allows us to scale up and produce full sequences of patient specimens," noted Resnick. "That opens the door for pathologists to step up and begin developing clinical applications using this technology.

"I believe pathologists will be one of the medical specialties where this new technology enables a whole new series of applications that were previously unavailable to us," he continued.

"The informatics support of a whole human genome sequence now makes it possible for pathologists to understand what's different between this individual and some canonical representation of the human genome," noted Resnick. "Similarly, they can use this data to distinguish the differences between cancer tumors," he said.

Advanced Genetics

"There are already examples of advanced genetics in hospitals across the country," continued Resnick. "**TGen** as an example in Phoenix. These sites are doing whole human genome sequencing to treat advanced forms of cancer, simply by categorizing the cancer against what is already known.

"Now, if you overlay that clinical application with the industry's current overall capacity to sequence, by 2011, we might be able to sequence something like 50,000 of these types of cases in the course of the year," speculated Resnick.

"But that is a conservative prediction," he added. "That number is 10 times more than our industry could have done in 2010 and it is predicted that the sequencing industry will add another 10 times more sequencing capacity by 2012, making it possible to sequence 500,000 individuals per year!"

Public Genome Data Sets

Resnick observes that plenty more needs to be done before pathologists will be able to use whole human genome sequences for diagnostic and therapeutic purposes. "Currently, in the public domain, there are a growing number of genome data sets," he noted. "Many of these genome data sets were financed by the National Institute of Health (NIH).

"Other data sets are for commercial use and—for a particular genetic variation—describe the potential implications of particular variations," said Resnick. "These data sets may also have informa-

tion about the potential clinical actions a physician might consider when a patient presents with those genetic variations.

"The challenge is that, at the moment, these databases exist all over the world," he continued. "They are not homogenized, and exist in many different formats. Thus, it will be important for the scientific community to establish standards for these types of data repositories."

Meanwhile, the collaboration involving GenomeQuest and pathologists at Beth Israel Deaconess Medical Center is already moving forward. GenomeQuest will be sequencing the patient specimens provided to it by BIDMC. It will then annotate these whole human genome sequences and provide data storage and query services to the BIDMC pathologists.

Knowledge About Disease

For their part, pathologists at BIDMC will be interpreting this data and looking for ways that it can be used to support patient care. The initial research emphasis will be on certain types of cancer. However, that is likely to broaden as pathologists better understand how individual genetic variations play a role in other diseases and health conditions.

THE DARK REPORT is first in the laboratory testing industry to provide pathologists and laboratory administrators with an inside understanding of this unique collaboration between the pathology department at Beth Israel Deaconess Medical Center and GenomeQuest. It can be expected that the research conducted by these two parties will confirm that pathology analysis of whole human genome sequences will generate useful clinical information.

Further, because the pace of technology enhancements in this field is so rapid, it may not take long for the knowledge developed by BIDMC and GenomeQuest to find its way into clinical practice. **TDR**

Contact Richard Resnick at 508-599-9803 or resnick@genomequest.com.

Whole Human Genome Sequencing Costs Falling

"GENOME SEQUENCING COSTS are falling at an incrediable pace," stated Richard Resnick, CEO at GenomeQuest, Inc., based in Westborough, Massachusetts.

"One year ago, a $600,000 sequencing machine would require between two and four weeks to cover an entire human genome at a sufficient depth of coverage," he explained. Now, just 12 months later, spend the same $600,000 on a current generation sequencing machine and it will take only half a week to process the same volume of genome sequences. It is expected that sequencing technology will continue advancing at this accelerated pace.

"The economics of whole human genome sequencing are thus changing favorably," added Resnick. "Currently, considering the fully-depreciated cost of the instrument, reagents, and labor, it is now possible to do the entire sequence for between $9,000 and $20,000 at most.

"Expectations are that the cost of whole human genome sequencing, once it falls to $1,000, will continue dropping to as low as several hundred dollars," predicted Resnick. "My expectation is that larger laboratories like **Quest Diagnostics Incorporated** and **Laboratory Corporation of America** will then acquire this technology and, because of their economies of scale, they may then find it possible to sequence the entire human genome for a cost that is much less than the cost of a single genetic test today."

Aetna Sues LabCorp Over Lab Marketing Practices

➤Aetna's lawsuit spotlights business tactics used by out-of-network public lab companies

➤➤CEO SUMMARY: Aetna, Inc., sued Laboratory Corporation of America in federal court, seeking injuctive relief for actions taken once LabCorp became an out-of-network laboratory provider for Aetna in July 2007. LabCorp is also accused of a "malicious scheme to continue to receive revenue" from Aetna. However, as an out-of-network laboratory provider, LabCorp has only been using the same marketing schemes and tactics that are standard industry practices long used by public lab firms in similar managed care contract situations.

BY NOW, MANY IN THE LAB TESTING INDUSTRY know about the lawsuit that **Aetna, Inc.**, filed in August against **Laboratory Corporation of America**.

This lawsuit is a first in the lab industry. It opens a window into the often-strained business relationships that major managed care companies have with each of the two Blood Brothers. At the heart of Aetna's claims against LabCorp are the marketing schemes LabCorp has used to retain access to Aetna patients as an out-of-network provider since July 1, 2007, the date when LabCorp ceased to be an in-network lab.

➤Aetna's Lawsuit

The lawsuit was filed on August 19, 2010, in the United States District Court for the Eastern District of Pennsylvania. Plaintiff Aetna asserts, as described in a LabCorp public document, that LabCorp engaged in "unfair competition, misrepresentation, interference and breach of contract, and violation of trade secret laws. Aetna is seeking unspecified monetary damages and equitable relief."

In the same document, LabCorp stated that it "believes that the allegations are wholly without merit and will vigorously defend the lawsuit." LabCorp officials declined further comment to THE DARK REPORT on this matter.

"Aetna has negotiated discounted rates with network providers," stated an Aetna spokesperson to THE DARK REPORT. "By using an out-of-network provider, [Aetna] members who use LabCorp and have no out-of-network benefit in their health plan would have no coverage at all and be responsible for the entire [lab testing] bill."

"[Aetna] members who used LabCorp and have an out-of-network benefit in their health plan could be responsible for a higher cost-sharing level," continued the spokesperson. "This is based on the potentially higher billed rates from LabCorp, even if LabCorp was to waive co-pays. LabCorp still has the ability to balance bill the member for [lab test] charges that aren't covered. In general, this raises costs for everyone. Higher medical costs contribute to higher premiums."

Court Papers Detail How LabCorp Sought Patient Referrals as a Non-Network Provider

ONE STANDARD TACTIC of the two Blood Brothers when they find themselves excluded from a managed care plan's provider network is to send letters directly to physicians stating that they will waive charges to patients that the payer may require for out-of-network laboratory testing services.

In its lawsuit against Laboratory Corporation of America, Aetna says LabCorp sent these types of letters to physicians participating in Aetna's network. LabCorp wanted to retain the lab business of these physicians, despite the fact that Aetna had an exclusive contract with **Quest Diagnostics Incorporated** as of July 1, 2007.

Aetna's lawsuit described one such letter sent by LabCorp to physicians, which included the following language: "Our commitment to you is that your Aetna patients will not pay more for services performed at LabCorp after July 1, 2007, than they would pay if the services were performed by an in-network laboratory provider."

Aetna's complaint further states "This matter arises out of Defendant LabCorp's malicious scheme to continue to receive revenue from Plaintiffs after LabCorp had lost its bid to renew its contract as Plaintiff's national in-network provider of laboratory services. Recognizing that the loss of Aetna's in-network business would negatively affect its earnings, Defendant LabCorp, … using confidential and proprietary information obtained from Plaintiffs when LabCorp was their in-network provider of laboratory services, purposefully sought to confuse and mislead Plaintiff's members and their doctors into believing that Plaintiff's members would receive the same services at the same in-network rates that had applied when LabCorp was an in-network provider of laboratory testing services."

The Aetna complaint continues, saying, "LabCorp's scheme was designed to mislead and confuse Plaintiff's members and their doctors so that they would refer those patients' laboratory tests to LabCorp, instead of Plaintiffs' in-network provider of such services. As a result of LabCorp's intentional scheme, Plaintiff's members' laboratory tests were sent to LabCorp, and, therefore, Plaintiffs were forced to pay more money for such services than they would have done if such tests had been sent to Plaintiffs' in-network provider and Defendant LabCorp received payments that it would not have received had such tests been properly sent to Plaintiffs' in-network provider of laboratory services."

Essentially, the tactics and schemes employed by LabCorp to continue serving Aetna members after it became an out-of-network laboratory in 2007 are the standard response public lab companies have used in similar situations over the past 20 years. Public lab companies with non-network status do two things that displease the patients' health insurance companies.

First, with their financial clout, the public lab companies are willing to write off substantial amounts of the out-of-network patient co-pays, deductibles, and out-of-pocket payments assessed by health insurers to motivate patients to stay "in network." The public lab companies promise the referring physicians that they will never bill the patients for these charges.

The pay-off for the public lab company is that, when it receives the patient specimens, it can then file a claim with the health insurer and be reimbursed at rates which are typically much higher than the deeply-discounted lab test fees the man-

aged care company pays to its in-network laboratories.

Several experienced managed care contracting experts told THE DARK REPORT that Aetna was not likely to prevail in its lawsuit against LabCorp. The consensus was that LabCorp's defense will be "This is a standard practice in the lab testing industry. All labs do it."

Is UnitedHealth Watching?

However, one contracting expert, who did not want to be identified, said that, were Aetna to prevail in its lawsuit against LabCorp—whether by court judgement or favorable settlement—it is likely that **UnitedHealth Group** would go after **Quest Diagnostics Incorporated** for the same tactics.

It must be pointed out that big dollars can be a factor in Aetna's decision to sue LabCorp. Aetna says that it paid LabCorp $100 million in 2006 as an in-network laboratory provider. Assume that Aetna's in-network discounted fees were at 50% of Medicare rates at that time. Next, assume that LabCorp has been able to keep, say, 80% of its pre-July 2007 Aetna patient test volume.

If LabCorp was continuing to serve that number of Aetna patients, it would mean that, every year since LabCorp became an out-of-network laboratory in July 2007, the money paid by Aetna to LabCorp represents tens of millions of dollars in additional spending.

Aetna's Contract With Quest

Moreover, there is one more dimension to this legal battle between Aetna and LabCorp. "Keep in mind that Aetna and Quest Diagnostics have, during the past year, renewed the contract which makes Quest Diagnostics the sole national laboratory for Aetna," stated one knowledgeable laboratory executive. "Leakage was a big issue during these negotiations.

"I would assume the biggest source of leakage is LabCorp and that Aetna has been disappointed with Quest's ability to reduce leakage," continued this executive. "There is a persistent rumor that, in order to retain its exclusive national network lab status, Quest dropped its price to Aetna as one response to the leakage problem.

"It would be expected that Quest, in exchange for the price discount, would ask Aetna to be more aggressive with LabCorp," he added. "One way that Aetna could become more aggressive with LabCorp is to file a lawsuit."

At a minimum, these opinions and insights provide a useful framework for understanding why Aetna would go to federal district court and file a lawsuit against LabCorp. Although some experts believe Aetna will have a difficult time prevailing in its lawsuit, the potential remains that a favorable settlement or court judgement for Aetna could provide the precedent for other big health insurance corporations to file copy-cat lawsuits.

Paradox Of Their Own Making

THE DARK REPORT observes that the managed care plans are caught in a paradox of their own making. For the past 20 years, the largest health insurers have extracted huge discounts in lab test prices from public lab companies, in exchange for exclusive or near-exclusive network provider status.

Health insurers were the direct beneficiaries of these deeply-discounted in-network lab test fees, particularly when the public lab could move leakage over to contract rates. But, as the gap grew between the rock-bottom network prices and the more generous out-of-network reimbursement the health insurers have always paid out-of-network labs, public lab companies recognized the economic benefits of staying out-of-network and billing payers at those higher prices.

Seen in this context, Aetna's lawsuit against LabCorp may be a first indication that public lab companies are willing to optimize the "out-of-network" strategy because the additional reimbursement is much too attractive to ignore. TDR

INTELLIGENCE

LATE & LATENT

Items too late to print, too early to report

During this last election, a pathologist ran for the U.S. Senate, but his campaign did not draw much attention within the lab testing community. Pathologist Eric Wargotz, M.D., was the Republican nominee for the U.S. Senate in Maryland. His opponent was Democratic Senator Barbara Mikulski, running for her fifth term. On election day, Mikulski outpolled Wargotz by 62% to 36%.

MORE ON: *Wargotz*

Between 1989 and 2007, Wargotz served as Medical Director and Chief of Pathology at 192-bed **Doctors Community Hospital** in Lanham, Maryland. He is affiliated with **E & W Pathology, LLC**. Had Wargotz been elected, he would have been the only pathologist to serve in the upcoming 112th Congress. In the current 111th Congress, only 16 senators and representives are physicians. By comparison, there are 225 senators and representatives who have earned law degrees.

EXONHIT & REDPATH CANCEL PENDING ACQUISITION

It is not often that an acquisition of a laboratory testing company unwinds. However, that is the case for the purchase of **RedPath Integrated Pathology, Inc.**, by **ExonHit Therapeutics S.A.** of Paris, France. The surprise development came after a positive coverage decision by Medicare carrier **Highmark Medicare Services, Inc.**, to cover RedPath's PathFinder TG assay for use in diagnosing pancreatic cancer, cysts, and masses. ExonHit was disappointed that the Highmark decision did not extend coverage to other assays that would be based on the Pathfinder TG technology.

ADD TO: *RedPath*

In response to these events, ExonHit wanted to renegotiate a lower price for RedPath. RedPath declined the offer of a lower purchase price. The two companies then agreed to void the existing purchase agreement.

TRANSITIONS

• **Aperio Technologies, Inc.**, of Vista, California, announced that Steven V. Russell had joined the company as Vice President of Corporate Development. Russell was most recently at **QuadraMed** and has also worked at **Compucare Company** and **Cerner Corporation**.

That's all the insider intelligence for this report. Look for the next briefing on Monday, December 6, 2010.