Precision medicine took a big step into broader awareness and utility in 2015-2016, building on the success of the Human Genome Project, the rapid decrease in sequencing costs, and the global effort to sequence and annotate genomes worldwide. Among other uses, the potential for sequence data to be used to stratify populations for response to drugs in development began to be introduced into clinical practice through the efforts of leading diagnostics and biopharmaceutical companies. Consequently, an increasing menu of diagnostics have been developed to identify patients who are candidates for specific drugs for certain diseases, greatly expanding the scope of companion diagnostics (CDx). In the time since, the number of approved CDx in the U.S. has increased significantly.

Physicians use these CDx assay results to prescribe a precise medicine indicated for targeted patients. Currently, CDx are used to identify a genetic or proteomic change, such as a single gene mutation or alteration in the structure or expression of a protein – e.g., assaying PD-L1 levels for a patient’s response to an immunotherapy. Ongoing research and development promise to expand the types of mutations and biomarkers that CDx can assess, helping to bring patients powerful new treatments for oncology and potentially other diseases.

LabCorp took a leadership role in the precision medicine space under the tenure of David P. King. Until his retirement on October 31, Dave served as the President and CEO of LabCorp, a leading global life sciences company, since January 2007, and as Chairman of LabCorp’s Board of Directors since May 2009. Prior to that, he was Executive Vice President and Chief Operating Officer of LabCorp from 2005 to 2006; before that he had served as Executive Vice President, Strategic Planning and Corporate Development, and Senior Vice President, General Counsel, and Chief Compliance Officer.

Although Dave is stepping away from his day to day leadership of LabCorp, he will stay deeply involved in his new role as Executive Chairman, supporting Adam Schechter’s transition into the role of LabCorp’s President and CEO. We are fortunate that Dave has kindly agreed to address questions currently pressing the diagnostics industry, as well as questions about the future strategic direction of the industry.
Dave, thank you for doing this Q&A with us. We have several questions on recent actions by FDA in pharmacogenomics, but we also would like to hear your thoughts on the business direction of the diagnostics industry over the next few years.

Diagnostics companies have traditionally had a role as a service provider – “sample in, data out.” With the advent of precision medicine, pharma and diagnostic companies learned they had to partner with each other. Drivers for partnering include, for example, ensuring that the respective data sets are validated and filed in parallel so that the drug and diagnostic offerings hit the market at the same time. What are LabCorp’s plans to build strategic partnerships to move deeper into the precision medicine space?

First, thank you for giving me the opportunity to talk with you about these vitally important topics. Obviously, I feel very strongly about the critical importance of combining diagnostics and therapeutics to improve patient care, and in particular the ways that diagnostic and biopharmaceutical companies must work together.

“...We have greatly increased our engagement with consumers over the past few years as we work to inform all stakeholders about the value of diagnostics generally, and CDx and precision medicine specifically.”

LabCorp has long been a leader in the development of companion diagnostics, beginning with our role in the development of the Her-2 assay to assess the appropriateness of Herceptin therapy for breast cancer in 1998. Over the years our Clinical Trials business had a strong track record in development of companion diagnostics, strengthened by our acquisition of Esoterix in 2005. We took companion diagnostics to a new level, though, with our 2015 acquisition of Covance, the world’s most comprehensive CRO. Covance brought us deep drug development expertise and partnerships with global biopharmaceutical companies, from small and emerging biopharma all the way to the largest global drug companies. One of the top three priorities that we announced after the Covance acquisition closed was to solidify our industry leadership in companion diagnostics, and I am proud to say that we have accomplished that goal. We’ve now supported more than 60% of all CDx on the market today and we will continue to invest in growing our capabilities and building even stronger relationships with our biopharma partners because of the powerful impact that CDx have on patient care and outcomes.

LabCorp, like many of its peers, places a premium on demonstrating the scientific basis of a specific test as well as its clinical relevance, reliability, and reproducibility to the question asked by clinicians. How has LabCorp changed its approach in this regard as partnering with pharma becomes critical for precision medicine and companion or complementary diagnostics?

What we do to validate tests begins with our people. We have an exceptional scientific team and, in my opinion, we do not get enough credit for the terrific science we do at LabCorp and Covance. We’ve had to learn different methodologies, such as next-gen sequencing, and extend into new therapeutic areas, such as gene therapy, as we have grown and matured as a business. But our approach has not changed: we are guided by a deep commitment to outstanding science and an engrained culture of rigorous process to assure the clinical relevance, accuracy, and reproducibility of results.

As diagnostic companies gear up to partner with pharma companies, precision medicine also requires bringing all parties in an ecosystem up to speed – e.g., clinical labs, consumers, providers, payers, thought leaders, and others. What steps or initiatives is LabCorp taking to close the educational gaps with these parties?

We spend a lot of time with regulators and payers explaining how companion diagnostics work and how they benefit patients. We spend a similar amount of time with physicians explaining how diagnostics generally, and companion diagnostics in particular, can and should be used. This educational process ranges from engaging with medical thought leaders to interacting with community-based and primary care physicians, many of whom are managing complex patients with significant clinical needs. And consumers are becoming an increasingly important part of this conversation, as they have access to more information (some good, some bad), and take greater responsibility...
for their healthcare choices and costs. So we have greatly increased our engagement with consumers over the past few years as we work to inform all stakeholders about the value of diagnostics generally, and CDx and precision medicine specifically.

Q Solid information and data are needed by diagnostics companies to make forecasts and develop models to invest in production, innovation, and new capabilities. How does LabCorp go about gathering data to:

- Assess the value of precision medicine in LabCorp’s future strategies;
- Balance the potential short-term impact vs. long-term savings through improved outcomes; and
- Estimate trade-off in investing in precision medicine vs other healthcare initiatives

A We begin by looking for unmet medical needs. That is the guidepost for deciding whether to invest in test development and commercialization. Then, as you might expect, we assess the potential market, determine how the particular test or investment stacks up against other priorities and consult with our internal experts in the process of reaching a decision. I want to note that I believe that healthcare will increasingly move toward valuing precision medicine and all of the tools that allow us to deliver it more effectively for each patient, so it is an important long-term priority for LabCorp and Covance.

Q Several groups are taking the initiative to expand precision medicine beyond its original remit for oncology and sequencing technologies. LabCorp has an expansive portfolio of assay technologies; in that spirit, how does LabCorp plan to position its portfolio to introduce new offerings in different therapeutic areas for effective treatments for responders, alternative treatment for non-responders, and exploration of new treatments?

A As I noted in the last response, we’re doing that today. We have the industry’s broadest portfolio of therapeutic drug monitoring tests to help physicians assess individual patient response to treatment and adjust treatment modalities accordingly. We’re involved in research to identify biomarkers and therapies for a wide range of conditions beyond oncology, including neurological and cardiovascular disease. The future of precision medicine is really exciting, and we intend to continue leading in this space.

Q Diagnostics companies need to manage risk in several areas—e.g., business risk (investing in the right growth area), risk in the clinic (accuracy, reproducibility), and regulatory risk (FDA review, coverage determinations). One way to manage regulatory risk is to maintain close communication with regulatory agencies. Could you please comment on LabCorp’s approach in this regard? How do you see such approaches evolving as more precision therapeutics and diagnostics are introduced?

A We greatly value and work hard to maintain an open and constructive dialogue with local, state and federal regulators and lawmakers. Again, they are very important constituencies and we spend a lot of time hearing their concerns about healthcare and diagnostics, and educating them about the important contributions that diagnostics make.

I can’t tell you how much time my colleagues and I, and indeed the entire laboratory industry, have spent in Washington, DC, talking with agencies, the administration, and legislators about modernizing the regulation of LDTs and fixing the egregious flaws in the implementation of PAMA. We recognize that legislation and regulation are processes, that they move more slowly than medicine and science, and that in advocating for sounder healthcare policy we have to play the long game.

“We fully support ACLA’s position as set out in its September 18, 2019 letter to FDA, noting significant problems with the way FDA has handled its “quasi-regulation” of PGx. In requiring an undisclosed group of labs to remove drug-gene associations from their reports to physicians, FDA is literally leaving doctors in the dark in interpreting the laboratory reports. I find this mystifying.”

LabCorp’s Center for Esoteric Testing (CET) laboratory in Burlington, NC
In the preliminary call we had about this Q&A, you expressed an interest in FDA’s warning letter to Inova. In the letter, FDA expressed concern about whether data existed to establish the relationship between genotypes assessed by the tests and assertions regarding drug response for multiple drugs.

Inova’s initial response to FDA was essentially that MediMap tests are laboratory developed tests (LDTs) and that “Inova believes it is properly operating within the scope of FDA’s LDT exemption and thus is not subject to FDA’s premarket review or labeling requirements.”

Subsequently, Inova ceased its MediMap offering. Inova’s MediMap page has the following message: “Thank you for visiting our site. If you have questions about MediMap testing, please call 703-776-8200 or email Medimap@inova.org.”

Inova appears to have misunderstood the regulatory risks and failed to communicate with FDA ahead of the letter. What guidance would you provide to the diagnostics industry regarding pharmacogenomics’ role in diagnostics? How is this guidance put in practice at LabCorp?

Can you please comment on this action in light of activity around the VALID Act to establish a new regulatory framework for LDTs and other in vitro clinical tests?

D: I don’t know the full factual context surrounding the Inova warning letter so I cannot comment specifically on that situation. Nonetheless, it is unusual for the recipient of a communication from the FDA to respond in the manner Inova apparently did and, predictably, it did not turn out well.

Nonetheless, the FDA’s approach to its recent initiative to regulate pharmacogenomics is deeply disappointing and concerning. FDA proceeded by sending emails and making phone calls to certain labs asking them to make changes in their claims for PGx testing. FDA’s position is a complete turnaround from its prior regulatory position, yet there has been no new statutory authority, no regulatory activity and no explanation why this new policy is needed or justified under the least restrictive alternative approach. There has been no public disclosure of which labs were targeted, and labs have received conflicting and contradictory information during individual calls with the agency. At a recent meeting, FDA officials expressed concern about “misleading” statements regarding drug-gene association, and “outright fraud” in claims by some labs, but provided no specifics to support their position. We fully support ACLA’s position as set out in its September 18, 2019 letter to FDA, noting significant problems with the way FDA has handled its “quasi-regulation” of PGx. In requiring an undisclosed group of labs to remove drug-gene associations from their reports to physicians, FDA is literally leaving doctors in the dark in interpreting the laboratory reports. I find this mystifying.

Furthermore, we’ve been closely involved in discussions for several years about a legislative solution to modernize regulatory oversight of LDTs. The VALID Act is the latest iteration of multi-party negotiations designed to reach a solution that appropriately balances the need to provide credible scientific evidence of clinical validity, without drafting a cumbersome and time-consuming regulatory process designed for devices on to diagnostics. A critical element of any solution that would be acceptable to the diagnostics community is a provision that recognizes the validity of tests already well-established in the market, but FDA’s recent PGx activities cast serious doubt on their commitment to this critical principle. That’s not what we signed up for, and the industry is not going to be able to accept it.

JPM: Thank you for that reply. Any final words or insights into future direction of the industry?

D: I became involved in this industry more than 20 years ago, and I am amazed at how far we have come over that time. At the same time, I’m convinced that we’ve barely scratched the surface of the role diagnostics can and should play in healthcare.