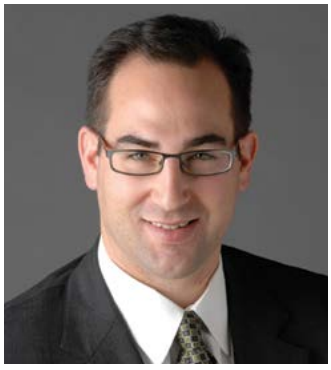
DIAGNOSTIC COMPANIONS

Marketing a diagnostic and drug in tandem requires a new business model. Collaborators Abbott and Pfizer have found success by coordinating marketplace efforts and promoting their wares as a package deal. Theirs is a playbook others may emulate as companion diagnostics become more entrenched. **Joe Dysart** reports

When Pfizer rolled out lung cancer drug Xalkori in 2011, it was faced with an unusual challenge: ensure that marketing for the new drug was directly linked to the diagnostic test that prequalifies a patient to take it.



Schmeltz: Promotion must take a markedly different course

Pharma companies like Pfizer that are developing drugs that require a test before prescription, known as companion diagnostics (CDx), are learning they need to work very closely with the manufacturer of the corresponding test to ensure the drug-test duo is understood—and successfully sold—to doctors and patients.

"The business model for a typical drug is very different than the business model for a companion diagnostic," says Andy Schmeltz, US president, Pfizer Oncology.

Xalkori (crizotinib) is prescribed to a subset of patients with non-small cell lung cancer (NSCLC) who test positive for a genetic marker that makes them more likely to respond well to the treatment—a defect in a gene called ALK (anaplastic lymphoma kinase).

So promotion for the drug, which logged $282 million in sales for 2013, needs to take a markedly different course, explains Schmeltz. Instead of marketing to doctors only, for example, Pfizer has expanded its commercial activity to include messaging to clinicians at hospitals who also spend a lot of time testing for cancer: pathologists, pulmonologists, interventional radiologists, nurse navigators and others.

"Ideally, you find a champion at the facility who is up-to-speed about the importance of such testing," Schmeltz says. "Then our salesperson works with that champion to set up a seminar that educates all these stakeholders at once."

Pfizer has also spent big on print advertising. It invested $722,000 on Xalkori ads in medical journals in 2013, down 25% from 2012, according to Kantar Media. Its "ALK faces" panel has also featured as one of several convention panels in the Pfizer booth at various oncology congresses.

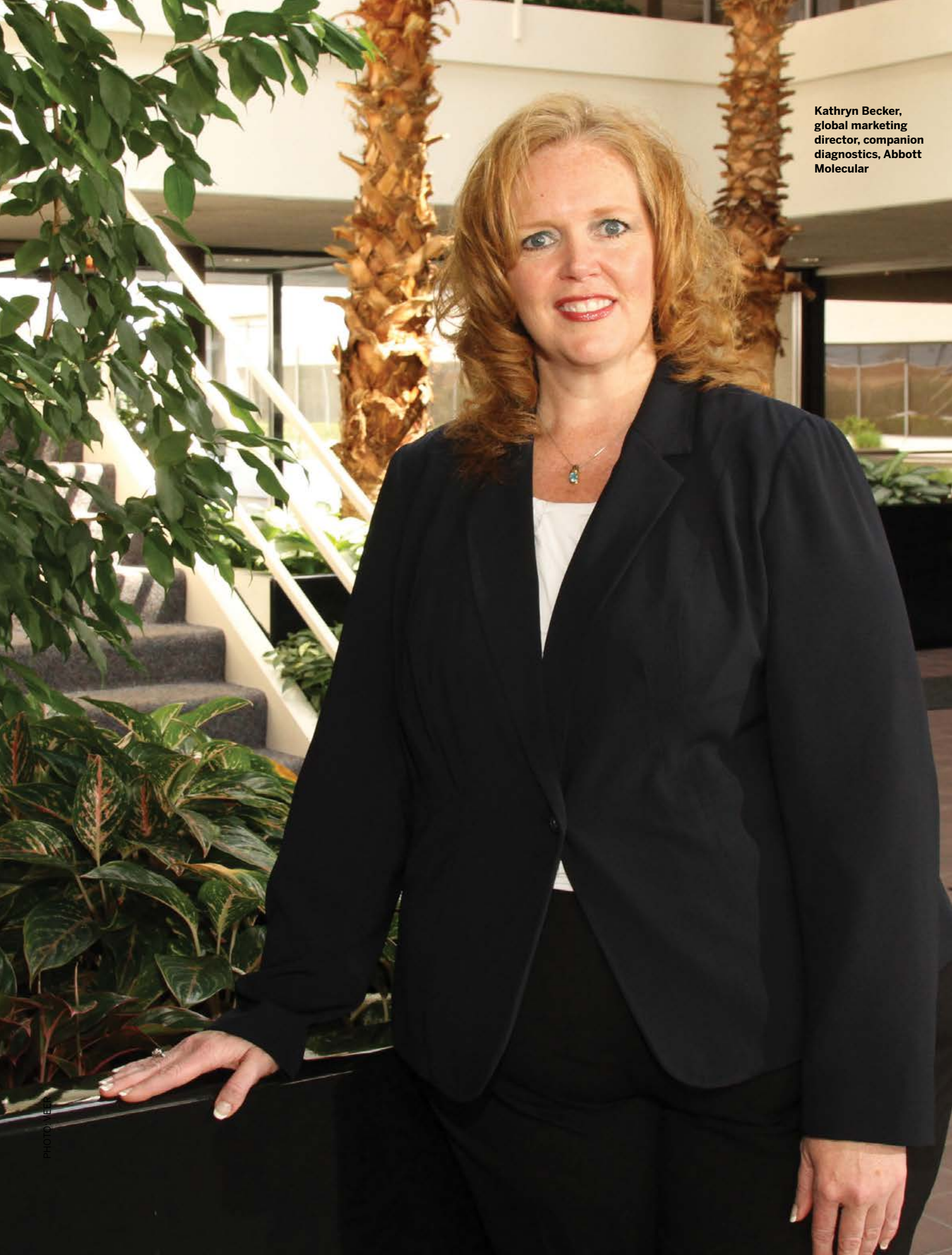
The drugmaker also spends a great deal of time marketing the concept of companion diagnostics to the biggest stakeholder of all in the process—the cancer patient—and is incredibly motivated to ensure he/she gets the best possible treatment.

Specifically, Schmeltz says Pfizer is a supporter of the website LungCancerProfiles.com, which educates patients about the importance of molecular testing in lung cancer, and is also helping push the website's latest awareness initiative, "United We Test Quest."

Slickly designed, the site offers an informative view on the benefits of pre-testing, relying on engaging text and graphics on why it's so important, personal stories of people who've beaten or are fighting cancer via companion diagnostic testing and educational videos.

There's also an interactive tool on the site which patients can use

PHOTO: RON GOULD



Kathryn Becker, global marketing director, companion diagnostics, Abbott Molecular

PHOTO: EEI

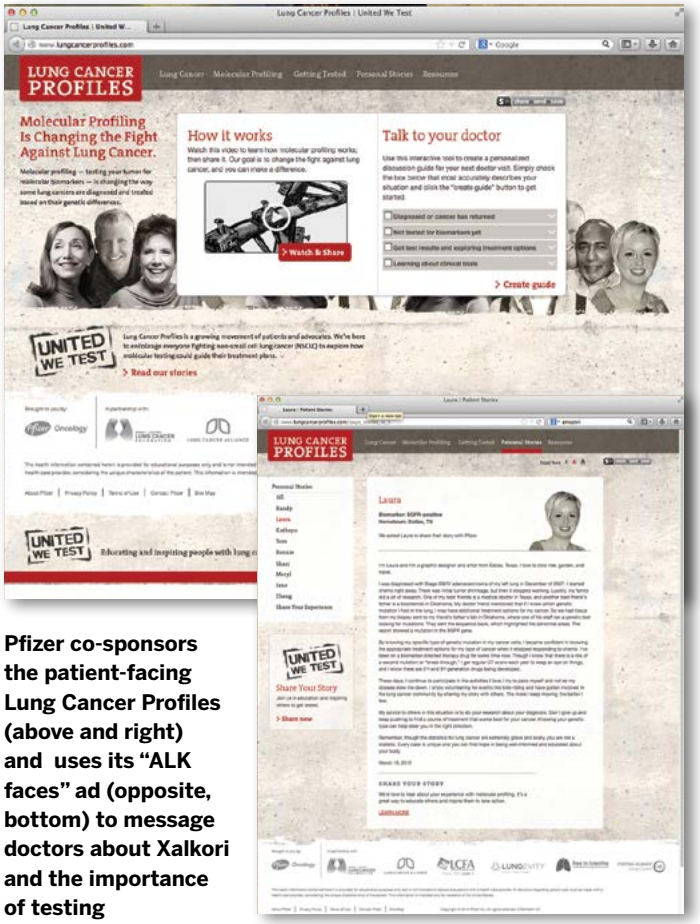
to put together a list of informed questions they can ask their doctor once they've been diagnosed.

"Laura," a patient afflicted with lung cancer who is profiled on LungCancerProfiles.com, for example, is one of the many personal stories on the site touting the benefits of CDx. When her chemotherapy stopped working, she was able get a replacement drug that worked after getting a CDx test, according to the site.

Currently, she's on a biomarker-directed therapy drug and thriving.

And Kathryn Joosten, an actress diagnosed with cancer, found a clinical trial for her ailment thanks to CDx testing.

Meanwhile, Abbott Molecular, manufacturer of the diagnostic that prequalifies a patient for a Xalkori prescription—the Vysis ALK Break Apart FISH Probe Test—has adapted its marketing to ensure the drug and test are perceived by the medical community as a single package, according to Kathryn Becker, director, companion diagnostics and global marketing at the company.



Pfizer co-sponsors the patient-facing Lung Cancer Profiles (above and right) and uses its "ALK faces" ad (opposite, bottom) to message doctors about Xalkori and the importance of testing

During Xalkori's launch, that often translated into joint sales conferences attended by sales reps from Pfizer and Abbott Molecular. Those conferences focused on one goal: educating sales reps on marketing the drug and test in tandem.

Moreover, in some sales regions, sales reps for Pfizer and Abbott were sent on sales calls together to "double-team" doctors and other personnel simultaneously, virtually guaranteeing that the institutions received the message that the drug and test should be perceived as a single solution. "Our figures show that in regions where both reps visited the hospital at the same time, we saw the fastest uptake," Becker tells *MM&M*.

By all measures, Becker says, the close marketing coordination between the two companies has been a homerun. "The ALK test is now being sold in 70 countries worldwide."

Back in 2011, companion diagnostics marketing was still considered novel. But many analysts believe CDx will become a much more common strategy to market drugs, as many drugmakers focus on formulations known to work well on patients with specific biomarkers.

Visiongain, a London-based market research firm, expects greater demand for companion diagnostics over the course of the next decade, due to the way they improve the safety-efficacy profile of drugs and help reduce healthcare costs.

Alberto Gutierrez, PhD, a director at the FDA's Center for Devices and Radiological Health, agrees. He has said that companion diagnostics "play an important role in determining which therapies are the safest and most effective for a particular patient."

Indeed, the FDA has been pushing pharma to pair each new drug it releases with a corresponding diagnostic test since 2011, when it released its draft guidance on the initiative.

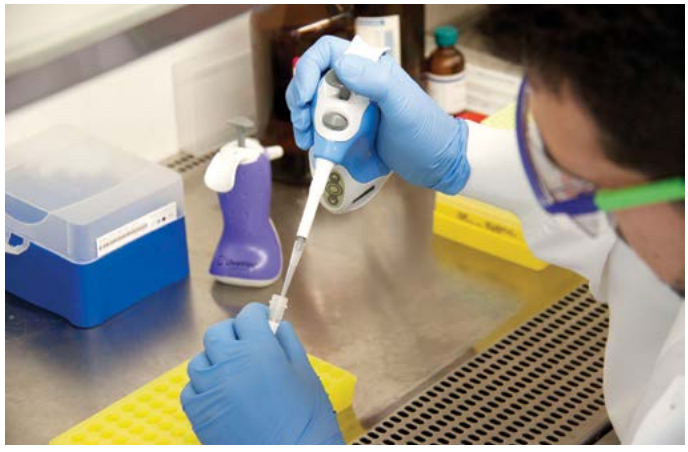
Major drug companies other than Pfizer have also been listening. "Our research approach is driven by an understanding of cancers on a genomic level and developing therapies directed at those targets," Alessandro Riva, president, Novartis Oncology, said in a statement.

And at Roche, two-thirds of all late stage compounds in the company's R&D pipeline are being developed with a companion diagnostic, according to comments made by Severin Schwan, Roche's CEO.

Alexander Hardy, VP, sales and marketing for Genentech's HER2 franchise, told *MM&M* in 2012 that, "Since we developed Herceptin, the first personalized medicine for cancer, we have continued to better understand the underlying biology of a tumor and tailor our medicines to target that tumor's unique behavior."

Not surprisingly, smaller drug companies are following the lead of the titans. Clovis Oncology, for example, is developing its cancer drug rucaparib for FDA approval in tandem with the genetic test for its efficacy—which is being developed by Foundation Medicine.

"We are pleased to advance our collaboration with Foundation Medicine—and utilize their unique genomic profiling platform and expertise—to identify patients most likely to benefit from rucaparib,"



In Myriad's re-analysis of olaparib, patients with BRCA mutations had double the PFS of placebo, illustrating CDx's impact

Patrick Mahaffy, president and CEO of Clovis, said in April.

And Myriad Genetics was able to use its BRAC*Analysis* test to resurrect AstraZeneca's PARP-inhibitor olaparib—a cancer drug once discarded as ineffectual. With careful testing, Myriad proved that olaparib works on a subset of the population, and the drug is undergoing FDA priority review for treating ovarian cancer patients who have a BRCA mutation, as identified through a CDx. The agency is scheduled to decide in October whether to approve the drug.

"To date, we have 25 ongoing collaborations in various stages in companion diagnostics," Mark Capone, president, Myriad, tells *MM&M*.

Meanwhile, pharma companies are also using the diagnostic tests to find patients for clinical trials. A patient whose cancer has no known treatment, for example, can at least participate in a clinical trial once their genetic mutation has been identified.

"Companion diagnostics will help to fulfill the promise of personalized medicine," Chris Tobias, PhD, EVP, chief scientific officer at communications firm Dudnyk told *MM&M* in December. "In the next five to 10 years, I expect that all new therapies in difficult diseases like oncology will have a companion diagnostic to determine whether or not the person is a candidate for the medication, or if the person will metabolize the drug faster or slower."

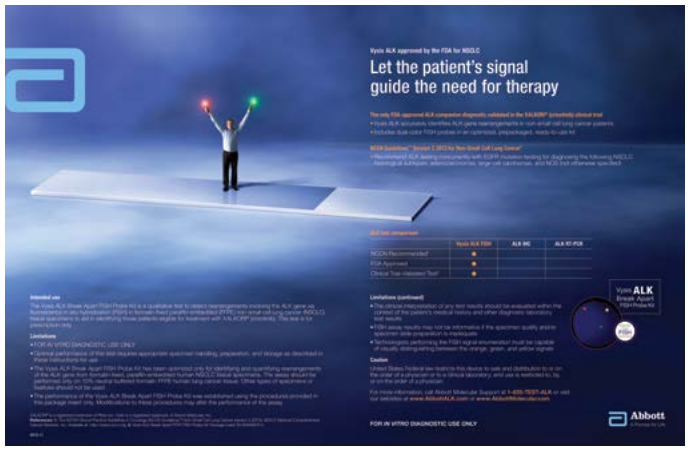
All told, McKinsey & Co. sees companion diagnostics "poised for rapid growth," according to the consultancy's 2013 report on personalized medicine. Fueling that growth are overall advances in the field, coupled with the emergence of increasingly sophisticated testing technology.

McKinsey foresees a 200% to 300% spike over the next four years in drugs receiving FDA approval that will be linked-at-the-hip with a diagnostic test.

So far, the primary market for companion diagnostics has been in cancer drugs, which are often designed to target patients with specific biomarkers, according to a Frost & Sullivan 2014 report on the global CDx market.

Driving the market are cancers caused by mutations, such as late-NSCLC and melanoma, according to the Frost & Sullivan report. By 2013, at least 387 oncology drugs, either on the market or in the pipeline, had already been paired with a CDx test, the consultancy noted.

Another factor driving the market is the success researchers have had distinguishing between the forms of cancers that occur in patients. In lung cancer, for example, researchers now know there are more than 10 genetic mutations that can cause lung cancer, according to LungCancerProfiles.com, the cancer patient advocacy site funded in part by Pfizer.



A journal ad promoting Abbott Molecular's ALK test. The company has adapted its marketing to ensure that the test and Pfizer's lung-cancer drug Xalkori are seen as a single package

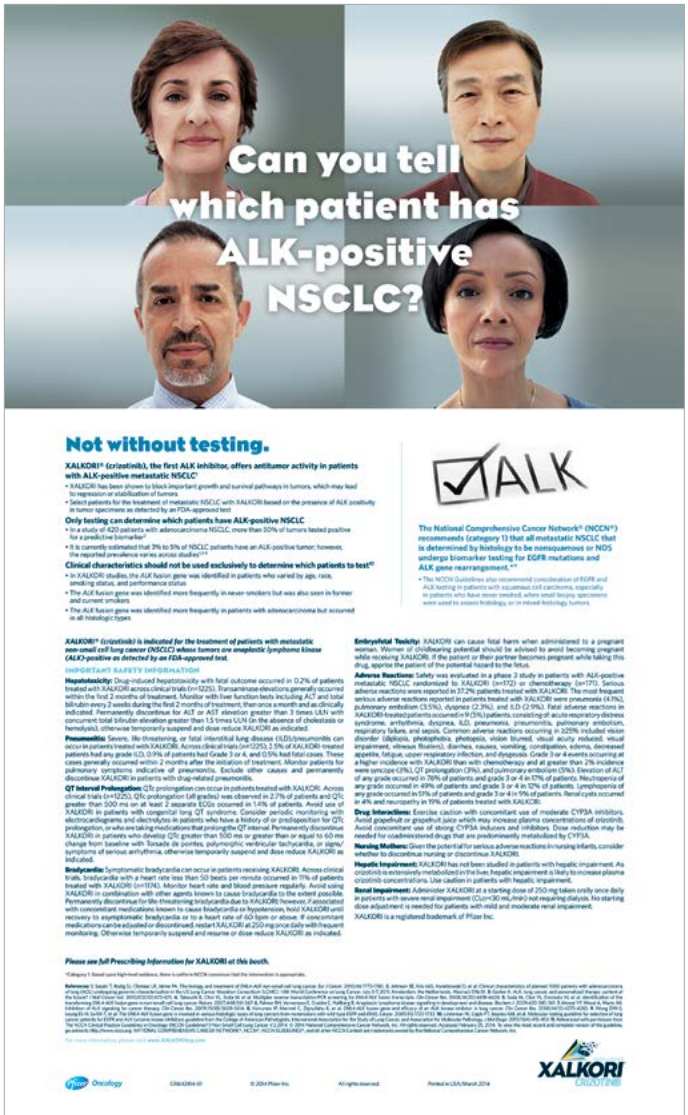
That research, in part, prompted Roche to roll out a new test approved for use outside the US last year, which helps caregivers distinguish between the two main types of lung cancer—small cell and non-small cell. The test represents a major advancement for patients afflicted with small-cell cancer, given that previously, their cancer was usually diagnosed only when the disease "reached an advanced stage, when the chances of a cure are very low," stated Roland Diggelmann, COO at Roche's diagnostics division.

In fact, cancer drugs have so far dominated companion diagnostics, given that so many only work for a subset of the population with specific genetic markers.

But in coming years, Frost & Sullivan says such drugs will also emerge in other markets, including treatments for neurological, cardiovascular, gatrointestinal and muscular diseases, according to its report.

And Myriad's Capone sees companion diagnostics also popping up in the treatment of diabetes and rheumatoid arthritis in coming years.

Another emerging market for CDx is a new drug class, known as antibody drug conjugates (ADC), which are being developed by Roche, ImmunoGen and Seattle Genetics, according to Frost & Sullivan's report.



For med-tech compliance, several challenges are looming

Device firms should brace for more regulatory scrutiny, says one life sciences consultant.

Manufacturers that haven't faced regulatory issues—and by extension don't have very robust compliance programs in place—may not be able to stay out of the spotlight.

Threatening to raise their profile is the release of physician payment data reported by med-tech and biopharma firms as required by the Physician Payments Sunshine Act, starting in September and covering August to December 2013.

"To me, what's frightening to the med-tech sector is [they] have a lot of high-dollar transfers of value to physicians," says Marc Eigner (pictured), partner and co-founder at Polaris, a consulting company focused on compliance in life sciences.

The med-tech sector is one of the highest in terms of HCP spend, says Eigner. Whereas drugs typically originate in company labs, many devices stem from inventions by clinicians, who often maintain a monetary share in their real-world performance. Companies then frequently rely on KOLs to promote their products and train other doctors to use them.

In one case, a 2014 CBS News investigation found that spinal implant makers like NuVasive and Medtronic paid some spine surgeons hundreds of thousands of dollars for royalties, consulting and speaking on device systems.

Some of these doctors were among those who performed the most spinal fusions on four or more vertebrae on Medicare patients between 2011 and 2012, creating the appearance of a conflict of interest. (Medtronic told CBS the surgeons are not paid royalties for devices they implant during their own surgeries.)

Medtronic began disclosing HCP payments in 2009, after scrutiny elicited by two whistleblower lawsuits alleging the company paid surgeons sham consulting and royalty fees for implanting its devices. One of those suits was settled in 2006 for $40 million (the company denied wrongdoing); the other suit was dismissed.

Otherwise, device companies have not had to disclose details of their financial arrangements with doctors. Later this year, all payments greater than $10 will be revealed under the Sunshine Act.

Nobody knows how the public will react to the data, but to the extent they do, Eigner says there will be more surprise from dollar amounts paid in the device world than in pharma. "[You] will start to have a lot of people question what's going on, fair or not."

He recalls how the big orthopedics manufacturers—Zimmer, DePuy Orthopedics, Biomed, Smith & Nephew and Zimmer—were put under deferred prosecution agreements in 2007 to resolve criminal and civil charges of fraud and kickbacks.

The agreements forced the firms to appoint an independent "monitor" who became privy to their consulting arrangements with doctors, and the high transfers of value. Soon, the public will see those high TOVs.

Eigner recommends firms that haven't had deferred prosecution agreements to make sure they have controls in place to make sure they spend the right amount on physicians and track spend. Med-tech, he says, is typically about three to four years behind pharma in that level of compliance.

One thing that's uncertain is whether diagnostics firms are covered under or exempt from the transparency law. Says Eigner, "It's not 100% clear as to whether or not a diagnostic or test even counts toward this." *—Marc Iskowitz*

Simultaneously, some drug companies are also putting their own spin on companion diagnostics marketing by offering treatment packages that feature two pre-qualified drugs that target a specific ailment. Novartis, for example, has a cancer drug in the late-stage development pipeline—LDK 378—which could be used to back up an already existing treatment for the same types of cancers—Xalkori.

And key players in the testing-side sector are looking to solidify their positions by gobbling up smaller testing companies. Roche, for example, further cemented its position in companion diagnostics testing in April with the acquisition of IQuum, a company that specializes in companion diagnostics/molecular diagnostics testing.

"Patients will benefit from on-the-spot and accurate diagnoses, which will allow healthcare professionals to make rapid, informed treatment decisions in flexible settings," Roche Diagnostics' Diggelman said in a statement.

So far, most of the marketing partnerships in companion diagnostics have been in the US and in Europe, according to the Frost & Sullivan report—with Novartis and Roche leading the industry. Other key players include AstraZeneca, GlaxoSmithKline, Pfizer, Sanofi and Bristol-Myers Squibb. But while the sector shows promise, skilled hands like Pfizer's Schmeltz say marketers will need to do their legwork to ensure their drugs are accepted by all stakeholders.

Pathologists, pulmonologists, interventional radiologists, nurse navigators—all these hospital personnel must be convinced that treatment with a companion-diagnostics drug requires a new approach and a new treatment system at the hospital.

These days, too many hospitals rely too heavily on diagnostic and treatment systems designed to accommodate one-size-fits all drugs, Schmeltz says. Such hospitals are not aware that the personnel required to administer such tests must be brought into the process much earlier when it comes to companion-diagnostics drugs.

These same hospitals are also not aware that simple precautions must be taken during the initial testing for cancer to ensure a companion diagnostics test can be done—such as taking more biopsy tissue than normal from a patient to ensure hospital testing staff can do prequalification testing for a drug like Xalkori, Schmeltz adds.

Moreover, getting the message out requires salespeople from the drugmaker and test-maker to know the languages of two cultures—those who treat patients and those in the lab who diagnose via tests.

"If you are in the personalized space, your reps have to master the whole continuum—it is a much more rigorous sales training," Jim Adelizzi, partner at ZS Associates, the sales and marketing consulting firm, told *MM&M* in December. "It is going to be a much more sophisticated, science-based conversation."

Moreover, partnering with a testing company to help market your drug can be a delicate business for a drugmaker, Schmeltz continues. You want a working relationship with a testing company to ensure your drug will be prescribed. But you don't want to be tied too closely to that test maker, given that other diagnostics tests may emerge down the line—made by other testing companies—which can also be used to prequalify patients for your formulation.

But even before the marketing, perhaps most critical to the sector's growth will be the hand-in-glove cooperation needed to ensure that a new drug and its companion-diagnostic test are approved simultaneously by the FDA. The last thing a drug company wants is its targeted drug floundering around in the market without a CDx screen. "Success will really depend on communication and coordination," says Alan Wright, Roche's chief medical officer. ■