Denise Myshko

Partnering for DIAGNOSTICS

Companion diagnostic codevelopment has the potential to significantly alter the drug development process.

Molecular diagnostics, one of the fastest growing segments in the diagnostics market, are key enablers in delivering personalized medicine. According to industry consultants, molecular diagnostics are set to become the dominant platform in clinical medicine. But currently only about 10% of labels for FDA-approved drugs contain pharmacogenomic information.

One of the challenges, experts say, is the current regulatory environment; diagnostics are evaluated by the FDA as devices. But this could change shortly. Last year, the FDA made a commitment to developing new scientific standards to establish what genetic information companies must show to prove their devices and drugs are effective. The agency's goal is to develop an efficient review process that produces diagnostic-therapeutic approaches through which companies can make specific, FDA-backed claims about benefits.

A recent study by Tufts Center for the Study of Drug Development found that while most companies believe companion diagnostics are needed for therapies to be truly personalized, those diagnostics should not necessarily be included on the label because therapies that work for a large share of a population may not benefit from a diagnostic test.

Biopharma companies are employing different approaches to develop companion diagnostics. Some have established internal divisions working across therapeutic areas to focus on biomarkers and personalized medicine. Other companies are teaming up with external partners to advance the development of companion diagnostics.

FACT

THE MOLECULAR DIAGNOSTICS MARKET IS EXPECTED TO GROW ABOUT 11% ANNUALLY THROUGH 2015.

Source: Kalorama

There is a paradigm shift in the way the industry develops drugs, says Cecilia Schott, Pharm.D., business development director of the personalized healthcare and biomarkers function at AstraZeneca.

"The development of a companion diagnostic in conjunction with a drug represents a shift from the way drugs are traditionally developed," she says.

Hans Johansson, VP of Phadia and head of Phadia development business, says because drug companies are not used to developing diagnostics, there has to be a close relationship between the pharma company and the diagnostic company to go from a test to a clinical outcome. "The process must be a very integrated one," he says.

The Business Model

Pharmaceutical and diagnostic companies are working together to develop diagnostic tests for use with drug therapies. And they are approaching this in various ways. For example, this year AstraZeneca launched a new function within the company specifically geared toward personalized healthcare and biomarkers. Within this function, the company is bringing in external experts around the diagnostic space to address the company's personalized medicine and biomarker strategy.

AstraZeneca executives say they are looking to provide targeted therapies across all therapeutic areas. Each of the drug projects that has a personalized healthcare strategy has a multidisciplinary diagnostics subteam that works with external diagnostic partners.

"Within AZ, each drug project with a personalized healthcare approach has a diagnostic team," Dr. Schott says. "Within the diagnostic team, there is multidisciplinary representation, including regulatory, technical and scientific, commercial and clinical development."

Dr. Schott emphasizes that the company's core business is pharmaceuticals.

"We are not in the diagnostics business," she says. "When we partner with a diagnostic company, we easily gain the benefit of their knowledge and work toward a common goal. We have a very flexible model. We can interact with any diagnostic company and leverage its expertise, technologies, and scientific knowledge. The diagnostic space is very seg-

mented by technology so not every company has the same expertise."

AstraZeneca has a collaboration with Dako to develop companion diagnostic tests for the company's oncology projects, including biologics and small molecules, in various stages of discovery and development. Under the umbrella of AstraZeneca's Personalized Healthcare strategy, this collaboration enables the company to develop novel, reimbursable products.

Another company pursuing personalized medicine and companion diagnostics is Merck.

"We are addressing companion diagnostic needs through a partnering strategy," says Cynthia Gawron-Burke, Ph.D., director, scientific liaison external scientific affairs for oncology licensing at Merck. "A personalized medicine approach is key to our oncology franchise product development efforts," she says. "Through our partnering relationships, we can access novel assays that can be used to predict responses to a particular oncology therapeutic, which allows us to deliver the right drug to the right patient."

At Novartis, executives have approached personalized medicine and companion diagnostics through strong internal expertise. In 2008, the company launched Novartis Molecular Diagnostics.

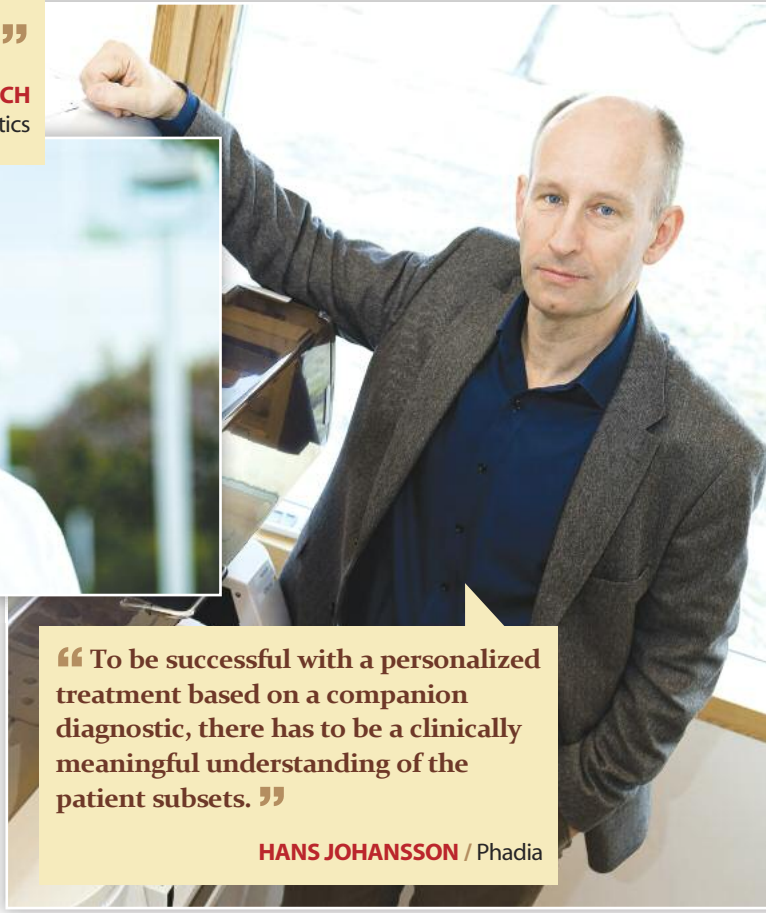
"We built this unit from scratch to realize our vision of personalized medicine and companion diagnostics," says Michael Nohaile, Ph.D., head of molecular diagnostics at Novartis Molecular Diagnostics. "We realized that the pharmaceutical industry is moving toward targeted therapies with an increasing need for high-quality diagnostics. This unit supports that vision. It was founded as a fully integrated unit within Novartis Pharmaceuticals, although we operate independently."

Mr. Nohaile says Novartis doesn't manufacture tests — the company relies on partners for this capability. Rather, the company's goal is to develop strong internal experience in the diagnostic realm.

"Very few established diagnostic companies have the regulatory experience we have," he says. "We're not just interested in the analytical validity, which has traditionally been the focus within the diagnostic industry; we're also interested in the clinical validity of these tests. We needed the internal capabilities to ensure that we could manage a significant amount of clinical data and validate the analytics at the same time."

To further strengthen its internal capabilities, in March Novartis acquired Genoptix, a specialized laboratory providing personalized diagnostic services to hematologists and oncologists. The acquisition is a strategic fit with Novartis' skills and expertise, as well the current portfolio of companion diagnostic programs within Novartis Molecular Diagnostics.

> "We have to get better at informing payers about the value of diagnostics."
>
> **DR. WALTER KOCH**
> Roche Molecular Diagnostics



> "To be successful with a personalized treatment based on a companion diagnostic, there has to be a clinically meaningful understanding of the patient subsets."
>
> **HANS JOHANSSON** / Phadia

Novartis also has a collaboration with Cepheid, an in vitro diagnostics technology company, to develop and commerialize an FDA-cleared, standardized, and more sensitive test that monitors the BCR-ABL gene transcript in peripheral blood specimens from patients diagnosed with Philadelphia chromosome-positive chronic myelogenous leukemia (Ph+ CML).

Partnering Best Practices

Experts agree it's important for biopharmaceutical companies to engage a diagnostic partner early in the development of a new product.

"If a company wants to optimize a treatment with a new drug based on the right companion diagnostic, it needs to create that understanding no later than Phase II trials, which means it has to start development of the test in Phase I trials," Mr. Johansson says.

Stephen Little, Ph.D., VP of personalized healthcare at Qiagen, says sometimes there is a misconception that because the approval of a diagnostic is straightforward, it should be simple to get approval.

"Actually, this can be a long and complex process," he says. "Understanding the guidelines and requirements of both sides is key to a good partnership. For example, the same Phase III trial that is used to demonstrate that a drug works could also be used to demonstrate that the companion diagnostic works."

The challenge, Dr. Little says, is timing.

"We don't want the development of the diagnostic to slow down the development of the drug," he says. "And we do not want regulatory approval of the diagnostic to slow up regulatory approval of the drug. If the drug requires a diagnostic, it's important that the two are approved at the same time.

> "If pharmaceutical company executives think it's too early to engage with a diagnostic partner, it's too late."
>
> **DR. CECILIA SCHOTT** / AstraZeneca

"Finally, we don't want the availability of the diagnostic to limit the availability of the drug," he continues. "This means we have to have a good sales and distribution network in place for the diagnostic to make sure it is broadly available when the drug is launched."

> **"There is a misconception that because the approval of a diagnostic is straightforward, it should be simple to get a companion diagnostic approved."**
>
> **DR. STEPHEN LITTLE** / Qiagen

Walter Koch, Ph.D., VP, head of global research at Roche Molecular Diagnostics, says ideally the time to bring a diagnostic company into a project is well before biomarker analyses are used in clinical trials.

"This way, the diagnostic company can have a prototype assay run on the same system with the same software and, ultimately, the same algorithms to interpret the data," he says. "It saves a tremendous amount of time to have the test in place for the pivotal trials."

Dr. Koch says a partnership at this level requires mutual trust.

"The best experiences we've had is when the diagnostic team is at the same table with the drug development team," he says.

Dr. Gawron-Burke says full transparency and timely communications are important to make collaborations with diagnostic companies work.

"We need to know about the performance of the assay as it develops and how it will be deployed geographically as we commercialize our drug," she says. "At the earliest stages of the codevelopment program, there should be comprehensive project plans. It's important to engage senior management in the partnership to make sure there is alignment between the partners. Other factors in a successful partnership include flexibility and contingency planning."

The Market

About 350 companies are actively involved in molecular diagnostics today, according to Kalorama. Although growth in the market for molecular assays has been very strong, it hasn't been quite as robust as anticipated in 2007. Kalorama forecasts growth of about 11% annually through 2015.

The primary growth drivers are the continued discovery of genetic markers with proven clinical utility, the increasing adoption of genetic-based diagnostic tests, and the expansion of reimbursement programs. Kalorama experts say the most attractive growth areas are molecular tests for women's health, infectious diseases, organ transplant testing, and oncology.

But companion diagnostics face some barriers, including reimbursement programs that still lag behind the speed of innovation, competition from test services in some segments, complexity, and limited quality control products and programs, according to Kalorama.

In fact, there are significant limitations in the current reimbursement system for novel diagnostics, which leads to inconsistent coverage decisions, according to a January report by the Biotechnology Industry Organization.

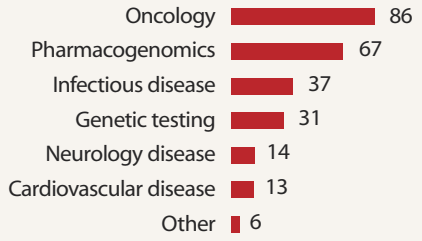
Dr. Koch says unlike therapeutics, which get value-based pricing, diagnostics are typically reimbursed based on procedural codes.

"These codes do not capture the value created by the diagnostic information that is provided," he says. "We have to get better at informing payers about the value of the diagnostics, as well as the increasing efficacy and safety of the therapeutic that we couple these tests with."

The next 10 years will witness significant developments in reagent systems and automation, as well as the introduction of a wide range of new products that will require innovative marketing approaches, according to market research company Venture Planning Group.

Growth Areas in Molecular Diagnostics

The most promising major application areas for molecular diagnostic testing over the next five years



Note: Results based on a 250-person Web survey of individuals involved in molecular diagnostics research, development, and use.

Source: CHI Molecular Diagnostics Survey.
Fore more information, visit insightpharmareports.com.

EXPERTS

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Advertising is dead. Maybe. Fewer than 3% of viewers will read this text. But many more will visit the site above and engage with the ever-changing content you will find there. So maybe advertising isn't dead; it's just evolving.

LLNS

Get Engaged

Tapping Into the *Power* by Getting PERSONAL

Robin Robinson

The industry can no longer conduct business as usual; it must get personal by using social media to build healthy relationships.

More and more patients are using Facebook, YouTube, Twitter, and other social media outlets to discuss their health and treatments with peers and caregivers. Social media tools have become an effective way to expand reach, foster engagement, and increase access to credible, science-based health messages, reports the Centers for Disease Control and Prevention. The interactions must be personal within the social media space if consumers are to trust and become an advocate for a brand. Not unlike the paradigm shift from a product-centric to patient-centric business model, mapping health populations through social media will move the focus away from product messaging and toward building relationships.

Not so long ago, patients and their caregivers had little share of voice in affecting the process of healthcare, but because of the proliferation of patient networking sites, this has changed seemingly overnight. With hundreds of nonpharmaceutical company-supported patient sites that allow for informing, sharing, and educating fellow sufferers and survivors for all types of diseases and conditions, patients are becoming empowered.

Should this power of the patient be seen as a threat to the life-sciences industry? Absolutely not, our experts say. The more patients share their health experiences online, the more informed the industry will become, enabling it to improve its efforts of tracking disease and monitoring health outcomes.

"More sophisticated technology enables different methods to gather, exchange, and analyze information, which will undoubtedly contribute to more sophisticated modeling of patient populations in critical health management areas," says Michael Parks, executive VP, Vox Medica. "Such modeling has the potential to educate the industry on ways to refine product and disease-state awareness efforts, implement compliance and outcomes programs, improve prescription assistance programs, and enhance the dialogue between patients and the other critical touchpoints within a given patient population."

According to a Pew Internet & American Life Project report on peer-to-peer health relationships, one in four Internet users has gone online to talk with other people who are dealing with the same disease, condition, or medications.

This peer-to-peer healthcare movement is gaining ground fast because it is an extremely important part of the communication landscape for patients, especially for people with a chronic disease who need emotional support and help with everyday issues, says Steve Rothman, president and chief creative officer, Cell Division.

"For example, patient sites such as inspire.com, which as had 175,000 people sharing health experiences, and patientslikeme.com, which provides granular analytics about the patient treatment experience," Mr. Rothman says.

Brand-sponsored patient communities that build relationship equity are also on the rise, and both types of sites have a common link.

"Both brand and unbranded sites allow for people with chronic and serious diseases to connect, share, and learn from each other," Mr. Rothman says.

CDC at the Forefront of Patient Communities

The CDC is at the forefront of using social media to educate patients and monitor health trends. Several of the experts interviewed for this article praised the agency's innovative thinking and cited it as a good example of