BY CYNTHIA BORDA

DNA-based DIAGNOSTICS

Testing for Personalized Medicines

THE SUCCESS OF PERSONALIZED MEDICINE DEPENDS UPON THE DEVELOPMENT OF COMPANION DIAGNOSTICS TO DIAGNOSE PATIENTS AND PREDICT THEIR RESPONSES TO SPECIFIC DRUGS.

THERE WILL COME A TIME WHEN GENETIC TESTING WILL BE AS COMMON IN THE PHYSICIAN'S OFFICE AS A BLOOD PRESSURE READING OR THE USE OF AN MRI.

The pharmaceutical industry is making headway in the personalized medicine arena, and diagnostic companies are actively developing tests to verify the presence of genetic markers — all of which will contribute to a steadily growing market over the next five years.

Although still in its early stages of commercial development, theranostics, the fusion of a drug therapy and a companion diagnostic, will increasingly gain acceptance. Whether these are assays to be run in commercial laboratories or tools for hospitals and physicians, diagnostics are moving pharmacogenomics into mainstream use. In fact, some experts say in 10 years it will be rare if a drug does not have a diagnostic test associated with it.

Analysts at Visiongain predict that all aspects of theranostics will exhibit strong growth in revenue from 2007 to 2012, with significant investments being made by companies in the pharmaceutical, diagnostics, and biotechnological sectors. Visiongain researchers say the market is primarily driven by the need to increase the efficiency of drug discovery and development efforts.

To date, the most prominent theranostic applications and related developments are with anticancer and antiviral therapies

Since the sequencing of the human genome in 2001, much progress has been made in understanding the molecular basis of disease. Going forward, the technologies, as well as the application of

PETER KEELING

Diaceutics

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genomics, are expected to advance at a rapid pace. Sophisticated diagnostics tap into this new understanding.

"The FDA has been at the forefront in pushing genomics and encouraging diagnostic testing and subsequent therapy," says Carol Reed, M.D., senior VP and chief medical officer at Clinical Data Inc. "While the regulatory call has been there, funding has been an issue. From a drug development standpoint, the area of theranostics is a bit murky. Herceptin was a clear commercial success in this arena and has been a positive impetus for further theranostic development, but in other areas there is some fear of market segmentation."

As diagnostic tools become increasingly available to differentiate products within a class for use in certain populations or for those with certain genetic markers, this may change the practice of medicine.

In 2006, molecular diagnostics accounted for 18% of the world *in vitro* diagnostics market, according to Visiongain. By 2012, molecular diagnostics will account for 63% of the market.

DR. CAROL REED

Clinical Data

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The theranostics market is primarily driven by the pharmaceutical companies' need to increase the efficiency of their drug-discovery and development efforts. A parallel driver is the need for better-targeted treatments by all stakeholders in healthcare. This is especially true for serious, difficult-to-treat conditions such as cancer.

"Our view is that about 25% of new drug launches by 2020 will be targeted or personalized," says Peter Keeling, president and CEO of Diaceutics. "The bottom line is that there is likely to be an expansion in the market for theranostics between $1 billion and $2 billion."

According to Visiongain, there are several factors that will no doubt shape the market. First, the complex and diverse range of technological solutions could limit their acceptance by users and decision-makers in the pharmaceutical sector. Second, there is a large dependence on existing systems and paradigms in pharmaceutical R&D, therefore theranostic solutions will likely face competition for resources. Finally, because the diagnostic and pharmaceutical industries have developed separately, there will need to be greater integration of industries, especially more technology transfer and consolidation.

Recent MOVES

Clinical Data is one diagnostic company developing theranostic tests, and in January, the company launched several new tests. One was PGxPredict: Rituximab. Developed by Clinical Data's PGxHealth division, this is a pharmacogenetic test that helps physicians predict the likelihood of a given patient responding to rituximab monotherapy in the treatment of follicular non-Hodgkin's lymphoma (NHL). This test allows oncologists to identify whether a patient is among the 20% of people who will demonstrate a stronger likelihood of responding to rituximab.

Rituximab is marketed as Rituxan by Genentech and Biogen Idec and is an IgG1 immunotherapeutic.

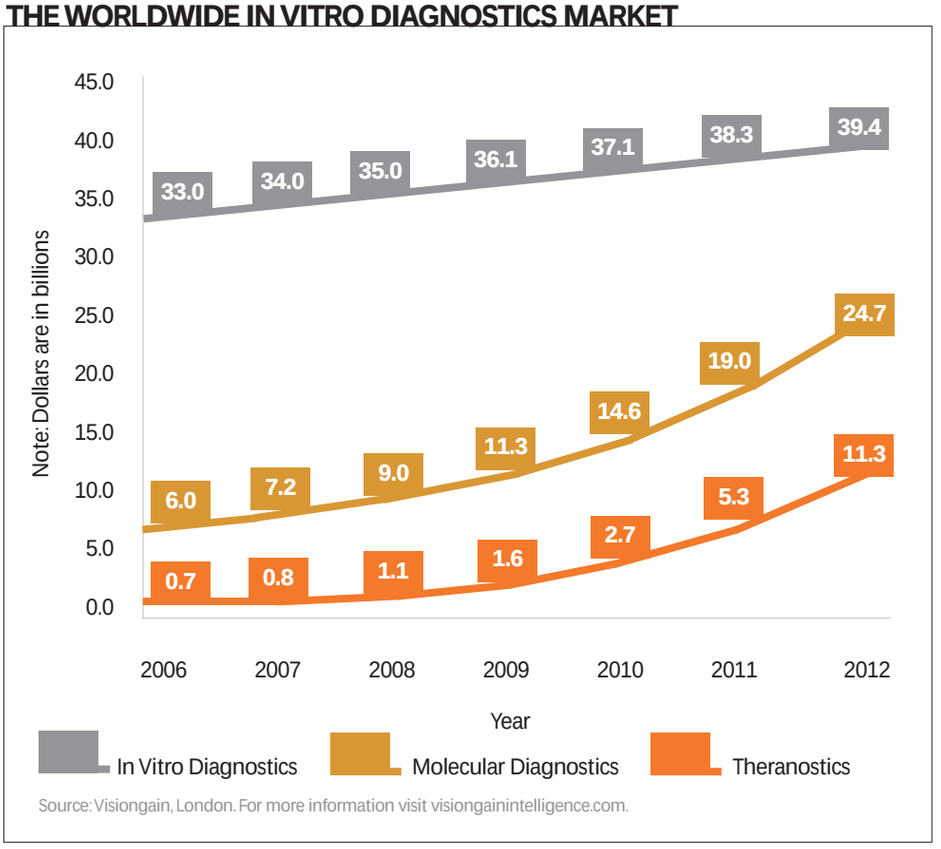
The test identifies a single nucleotide polymorphism, referred to as V158F, in the FCGR3A gene. This gene encodes the Fc gamma IIIa receptor on lymphocytes to which rituximab binds. Based on two independent studies in 49 and 87 patients, respectively, patients with follicular, CD20-positive, B-cell NHL who carried the 158V/V version of the variant in the FCGR3A gene were more likely to respond to rituximab monotherapy than patients with other variants.

Clinical Data also released PGxPredict: Clozapine, a pharmacogenetic test designed to aid physicians prescribing or considering prescribing clozapine, a generic product that is used for treatment-resistant schizophrenia. This test will provide information on whether a patient is at higher or lower risk of developing clozapine-induced agranulocytosis (CIA) compared with the untested population.

Agranulocytosis is a condition in which there is an insufficient number of white blood cells called neutrophils or granulocytes. This can be caused by a failure of the bone marrow to make sufficient neutrophils, or when white blood cells are destroyed faster than they can be produced. Affected people are susceptible to infections.

Through the analysis of a blood sample and the genotyping of two single nucleotide polymorphisms in the gene HLADQB1, the test places patients into one of two categories: higher risk or lower risk. The HLADQB1 gene has been shown by PGxHealth to be associated with CIA in two independent case control cohorts.

THE WORLDWIDE IN VITRO DIAGNOSTICS MARKET



Source: Visiongain, London. For more information visit visiongainintelligence.com.

Clinical Data also provides Familion, a genetic test designed to identify mutations in people with inherited cardiac channelopathies, such as long QT syndrome (LQTS) and Brugada Syndrome; PGxPredict: Warfarin, a pharmacogenetic test that measures variation in two genes related to response to warfarin; and a pharmacogenetic assay that tests for mutations in the thiopurine S-methyl transferase (TPMT) gene.

Other companies that are pursuing theranostics are Celera Genomics Group and Specialty Laboratories.

In October, Specialty Laboratories announced the commercial launch of its hepatitis C virus (HCV) Liver Fibrosis GenotypR test, the first genomic clinical test to predict progression to liver fibrosis and cirrhosis in HCV patients.

This test is based on Celera's cirrhosis marker discoveries, which were licensed to Specialty Laboratories in June 2006.

The HCV Liver Fibrosis GenotypR test is the first of its kind to identify a patient's genomic signature.

This test identifies the patient's genomic signature of seven single nucleotide polymorphisms (SNP), which combined with gender, provides a cirrhosis risk score (CRS) correlating with relative risk of progression to liver fibrosis or cirrhosis.

The test can identify which HCV patients are at reduced risk of progression to fibrosis as well as those with up to a four-fold increased risk compared with the low-risk patients.

The Celera cirrhosis risk score is expected to help thousands of HCV-infected patients and their physicians to identify those who are at high risk and at an early stage of disease, who previously might not have been eligible for pegulated interferon therapy.

Celera, a molecular diagnostics business, also has a strategic alliance with Abbott through which the companies sell and support molecular diagnostic products.

To identify novel diagnostic markers and potential drug targets, Celera is leveraging capabilities in proteomics, genomics, and bioinformatics to better understand the association between common diseases (cardiovascular, autoimmune, and cancer) and patterns of genetic variation and protein expression.

LEGISLATION to Come?

Personalized medicine was a recent focus of a bill proposed on Capital Hill. Senator Barack Obama (D–IL) introduced the Genomics and Personalized Medicine Act of 2006 (S. 3822). The bill proposed to increase funding for research on genomics, expand the genomics workforce, provide a tax credit for the development of diagnostic tests that can improve the safety or effectiveness of drugs, and reaffirm the need to protect genetic privacy. This bill, however, did not pass in 2006.

"Even though this particular piece of legislation will probably not be re-introduced, from a medical and scientific perspective, theranostics will continue to gain momentum," says Bill Sietsema, Ph.D., VP, U.S. regulatory consulting and submissions, at Kendle.

Senator Obama and his staff are working to develop a compromise bill that will be introduced in 2007.

"Overall, legislation for theranostics is a good idea, but having a dialogue around research and pharmaceutical dimensions is a great idea," Mr. Keeling says. "This may halve the 30- to 40-year time requirement for changing the way we do things." ✦

PharmaVOICE welcomes comments about this article. E-mail us at feedback@pharmavoice.com.

Experts on this topic

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