BY DENISE MYSHKO

Creating VALUE through ▶ PERSONALIZED MEDICINE

THE USE OF PHARMACOGENOMICS TO DEVELOP PERSONALIZED MEDICINE WILL LEAD TO A CULTURE CHANGE FOR THE PHARMACEUTICAL INDUSTRY. WHILE INITIALLY DISRUPTIVE, PERSONALIZED MEDICINE WILL LEAD TO LONGER-TERM SUCCESS FOR PHARMACEUTICAL COMPANIES.

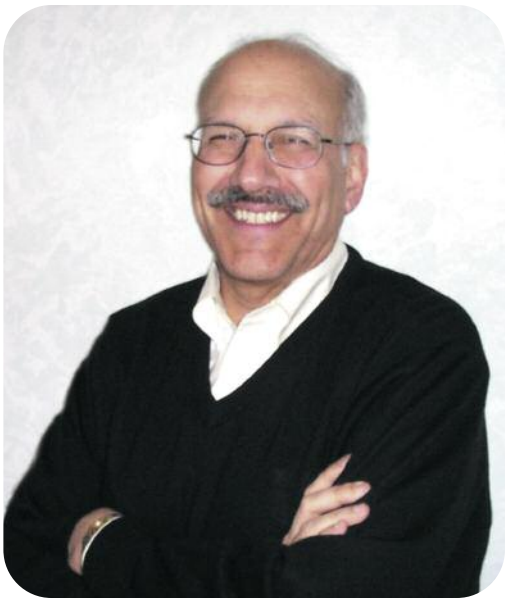
▶ DR. GARY KURTZMAN
Safeguard Scientifics
There will be a greater impetus on pharmaceutical companies to demonstrate that their products are an improvement over the existing standard of care and to identify which patients will have unwanted side effects.

The era of traditional blockbuster pharmaceutical products, experts agree, is probably gone. Companies will have to develop a new model for success, one that focuses on targeted therapies for those patients most likely to respond. This will require all stakeholders — bio/pharmaceutical companies, device manufacturers, regulators, policymakers, physicians, consumers, payers, and partners — to work together in a way previously not seen and share information about biomarkers, genomic data, predictive toxicology, and serious adverse events.

Those bio/pharmaceutical companies that are willing to take the risk to adopt a personalized medicine strategy will be the ones that succeed in the future. While the risk that personalized medicine will stratify patients and markets is very real, so too is the value such products will provide to pharmaceutical companies and their shareholders.

The value will come in several ways, including more efficient R&D processes; greater efficacy of products; the ability to identify patients who could have adverse events; the ability to stratify patients in trials, which would then require fewer patients; the ability to differentiate products in the marketplace; and better data to support product reimbursement.

"There is growing recognition — and not just in the pharmaceutical community but in other parts of healthcare as well — that the era of trial-and-error, one-size-fits-all medicine is coming to an end," says Vijay Aggarwal, Ph.D., CEO of Aureon Laboratories. "In five years or 10 years, it will be inconceivable to prescribe a medical device or a pharmaceutical for most diseases without understanding the particular biochemistry of that individual patient. We are entering an era in which the tools that enable this approach will accelerate."



▶ DR. VIJAY AGGARWAL
Aureon Laboratories
In five years or 10 years, it will be inconceivable to prescribe a medical device or a pharmaceutical for most diseases without understanding the particular biochemistry of that individual patient.

IDENTIFYING AN ROI

A report released in January 2009 by the

▶ DR. LINGSING CHEN
QPS

Gone are the days of just buying data; people want to buy knowledge.

▶ DR. VANCE VANIER
Navigenics

If we were in an era of business as usual and the public and the FDA had fewer safety concerns, then it would be harder to inspire innovation proving the value of biomarkers because they segment patients.

Deloitte Center for Health Solutions found significant opportunities for the adoption of personalized medicine to produce a positive return on investment across key stakeholders in the U.S. healthcare system. Deloitte researchers found that personalized medicine will change the product paradigm from blockbuster treatments to more therapies and smaller markets. Early adopters could receive significant ROI as highly effective targeted therapies displace traditional therapies.

THE MARKET FOR COMPANION DIAGNOSTICS IS ESTIMATED TO BE AT $27 MILLION AND IS LIKELY TO GROW TO $130 MILLION BY 2018.
KALORAMA INFORMATION

Husseini Manji, M.D., VP of CNS and pain at Johnson & Johnson Pharmaceutical Research and Development, says companies recognize the need for a different model.

"As our mindsets continue to change, there will be a segmentation and biomarker approach brought to bear very early in the discovery process," he says. "Today, companies take this approach for a specific disease after it becomes apparent that a product has a positive effect on a specific subset of a given disease. There is the hope that in the future we can make medication development more streamlined. It's also quite possible that many of the compounds that fail in clinical trials today do so because they are being developed too broadly."

Thomas Metcalfe, head of the personalized healthcare portfolio at Roche, says even though some sources believe personalized medicine will reduce the target market, it is important to note that patients will realize an improved safety/benefit ratio.

"We believe this approach puts the medicine in a stronger competitive position, and there are likely to be other benefits that will accrue," Mr. Metcalfe says. "It's likely patients will be more compliant and stay on the medicine longer; companies are likely to achieve a better market share; and there may even be better pricing."

Mr. Metcalfe says Roche looks at personalized medicine more holistically.

"By applying these approaches during the development of a medicine, there is the ability to find out which patients are likely to derive the most benefit," he says. "This allows the company to put a package together for healthcare authorities and payers. Researchers can also learn more about the medicine during development and they can expand the use of the medicine into other indications if they are able to find molecular markers that determine which patients are going to benefit from that medicine the most."

The Deloitte study seems to confirm that the potential for more indications could yield greater market share and that companies that are slower to adopt a personalized medicine strategy risk losing market share.

Stan Bernard, M.D., president of Bernard

BENEFITS OF PERSONALIZED MEDICINE

- The detection of disease at an earlier stage, when more effective treatment can be delivered, such as in the case of cancer.
- The selection of optimal therapy, thereby reducing or eliminating trial-and-error prescribing.
- The reduction of adverse drug reactions.
- An increase in patient compliance with therapy.
- Improved selection of targets for drug discovery.
- Reduction in cost, time, and failure rates in clinical trials.
- Revival of drugs that failed earlier clinical trials or were withdrawn from the market.
- A shift in the emphasis in medicine from reaction to prevention.
- A reduction in the overall cost of healthcare.

Source: Kalorama Information.
For more information, visit kaloramainformation.com.

RELATED EVENTS

CHI'S BIOMARKER WORLD CONGRESS
May 27 - 29, 2009
For more information, visit biomarkerworldcongress.com.

THE BURRILL PERSONALIZED MEDICINE MEETING
Nov. 9 - 10, 2009
For more information, visit burrilland-co.com/personalized_medicine_2009/

▶ DR. STAN BERNARD
Bernard Associates
Personalized medicine is not an option for the pharmaceutical industry; it is an imperative. The personalized medicine marathon is not going to be a spectator sport.

Associates, agrees that pharmacogenomics has the potential to increase sales and market share in a number of ways.

"Personalized medicine can enhance compliance because there is the potential for better therapeutic response; there also is an opportunity to steal market share from nonresponders of competitive treatments," he says. "With confirmed safety and efficacy, there is the potential for higher reimbursement. Personalized medicines might have greater applicability for earlier preventive use. The key for marketers is to analyze each product to determine whether a pharmacogenomic approach can increase or decrease market share and sales."

Gary Kurtzman, M.D., managing director in the life-sciences group at Safeguard Scientifics, says there will be greater impetus on pharmaceutical and biotech companies to demonstrate that their products are an improvement over the existing standard of care and to identify which patients will benefit and which patients will have potentially unwanted side effects.

"One way to make this determination is to stratify patients," he says. "Currently this is accomplished using a population-based view or through an evidence-based approach. Increasingly this will become more personalized or individualized through diagnostic testing."

The potential return on investment for companies adopting a personalized medicine approach could be significant; Deloitte analysts say legislators may provide special incentives for biotech, pharmaceutical, and diagnostic companies, just as the Orphan Drug Act (ODA) of 1983 provided support for diseases that affect less than 200,000 people. Deloitte outlines several potential incentives, including tax benefits for companies that produce or research personalized therapeutics; protections beyond typical patents to prolong product exclusivity; subsidized funding of clinical research; funded research collaborations that help researchers take advantage of larger patient populations for their clinical trials to decrease the time and costs of patient recruitment; funded technologies, such as grid services and health information exchanges; innovative payment options for patent holders and inventors; and public-private entities that can manufacture products, particularly diagnostic tests, that might not initially have large markets.

BIOMARKERS AND DIAGNOSTICS

Personalized medicine is still in its early days, and its application could take many forms, including using biomarkers to identify targets to select patients to enroll in clinical trials and for Phase IV surveillance.

Dr. Bernard says personalized medicine's broad reach is ultimately going to impact the vast majority of pharmaceutical companies and products.

"This doesn't mean there will be pharmacogenomic tests in every category," he says. "But there will be information in the marketplace that will potentially influence the use, the adoption, the pricing, and the perception of products. For example, the perception and sales of the anti-clotting agent Plavix have already been hampered by genetic information showing that Plavix may not work in nearly 30% of patients, despite the fact that there is no commercially viable pharmacogenetic test for the drug."

▶ THOMAS METCALFE
Roche
There needs to be further clarity on the regulation of companion diagnostics, particularly diagnostics that are used in therapeutic decision making.

Dr. Bernard says the biggest change that personalized medicine brings to drug development is the addition of a third dimension to clinical research.

"Historically, the research and practice of medicine has been two-dimensional, at the organ macro level and at the cellular micro level," he says. "Personalized medicine provides a third dimension, the molecular level. For example, instead of researching small cell lung cancer, we now focus on a more granular level, such EGFR2 small cell lung cancer."

Dr. Aggarwal says about 10% of the trials conducted today are done in conjunction with some diagnostic test that would identify a responder.

In fact, a search of clinicaltrials.gov, a service of the U.S. National Institutes of Health,

ALAN MINSK
Arnall Golden Gregory

One way to incentivize companies to evaluate personalized medicines might be to look to the orphan drug laws. The statutory provisions for orphan drugs, as well as FDA's guidances, provide clear rules, parameters, and benefits for companies to develop certain types of therapeutic products that might otherwise have limited commercial appeal or value.

found 292 studies with a pharmacogenomic or pharmacogenetic approach.

"As a society, it makes great theoretical sense to identify patients who respond to a drug and those who won't; unfortunately, the actual penetration of this approach is fairly small at the current time," Dr. Aggarwal says. "Five or 10 years ago most pharmaceutical companies were not focused on companion diagnostics or understanding the use of biomarkers in clinical trials. The picture has changed, and virtually every pharmaceutical company that is conducting preclinical research is looking at biomarkers and the mechanisms of action and ways to predict responders and nonresponders. This approach has not yet translated to Phase II and III clinical trials."

THE REGULATORY CHALLENGES OF A PERSONALIZED APPROACH

The potential disruption in the marketplace should have companies rethinking the blockbuster model, particularly because of the FDA's increasing focus on safety, says Vance Vanier, M.D., chief medical officer at Navigenics.

"The FDA is now even more safety-oriented and more conservative," Dr. Vanier says. "In this new climate, segmenting markets by efficacy and adverse-event response becomes more important than ever before. If it were still business-as-usual and the public and the FDA had fewer safety concerns, then it would be harder to inspire innovation proving the value of biomarkers."

Experts interviewed by PharmaVOICE agree that there is need for more clarity around personalized medicine from a regulatory perspective.

LingSing Chen, Ph.D., VP of translational medicine research at QPS, says gaps exist at the FDA level.

"The FDA is pushing for the submission of genomic data, but this information is not required," she says.

Alan Minsk, partner and leader of the food and drug practice at Arnall Golden Gregory, says some companies are likely to employ a wait-and-see approach until there is clearer regulatory guidance and/or some incentives to create value for the company.

"If the FDA can issue guidance that provides more clarity to the regulatory pathway, this would eliminate trial and error from the process," he says.

He suggests personalized therapeutics could be treated by regulators in a manner similar to orphan drugs where there are rules and incentives for development of products

THE MARKET FOR BIOMARKERS

THE CURRENT MARKET FOR COMPANION DIAGNOSTICS IS ESTIMATED TO BE $27 MILLION. CONSERVATIVE ESTIMATES PREDICT GROWTH TO $130 MILLION BY 2018. SOME OF THE FACTORS TAKEN INTO CONSIDERATION FOR THIS FORECAST:

- No one is quite certain as to how companion diagnostics development will coordinate with therapeutics at this time.
- There is significant risk for companion diagnostics based on the success of the therapeutics both in clinical trials and in the marketplace.
- Regulatory authorities currently appear to support the use of companion diagnostics, but it is unlikely that the agencies have a complete appreciation of the concept.
- While some significant biomarkers have been identified, there is no forward-looking guarantee as to the continued discovery of significant markers.
- Current companion diagnostics are focused toward cancer applications, with a small number of exceptions (e.g., warfarin sensitivity). Projecting expansion of the market becomes riskier as time goes on; however, limitation to cancer applications with minimal contributions in other areas is expected.

Source: Kalorama Information. For more information, visit kaloramainformation.com.

KEY TERMS

- PERSONALIZED MEDICINE: the use of molecular analysis of genes, gene expression, proteins, and metabolites to achieve optimum health outcomes in a person's disease or disease predisposition.
- TARGETED THERAPIES: therapies designed to target molecular mechanisms of disease, based on knowledge of relevant variations between individuals with that disease, and by relevant molecular variations in the expression of that disease.
- PERSONALIZED MEDICINE INTERVENTION: a diagnostic test or targeted therapy based on molecular analysis of genes.
- GENOMICS: study of the entire DNA contained in an organism or a cell; the entire genome of an organism.
- PHENOTYPE: those traits that are observable in an organism such as hair color, skin color, height, or the presence or absence of a disease.
- PHARMACOGENOMICS: study of the genetic basis for individual variation in drug response.

Source: Deloitte Center for Health Solutions. For more information, visit deloitte.com/centerforhealthsolutions.

DR. ANTHONY EVERHART
Chiltern

As academic centers, universities, and small biotech companies have identified genes that are potential targets for personalized medicine, they've patented their discoveries. In these early days, we could run into a lot of problems with intellectual property claims.

that otherwise have limited commercial appeal.

THE NEED FOR COLLABORATION

Dr. Manji says personalized medicine cannot be achieved by any single company or entity.

"Companies, universities, and the government will need to work together to bring about personalized medicine, and they will have to do a great deal of work to understand diseases better," he says. "In many cases, databases will need to be integrated to yield large enough patient sets. One example of a current collaboration is the Foundation for NIH Biomarkers Consortium. J&J is working with other companies, the government, and

STAKEHOLDER IMPLICATIONS

CONSUMERS

- **Personalized medicine** will likely require an up-front cost for consumers/patients, as these therapies may be more expensive than conventional treatments. Long-term benefits of personalized medicine create an incentive to adopt these care modalities.
- **Education** regarding personalized medicine diagnostics and therapeutics will be required for consumers to make more informed treatment decisions with their healthcare providers.
- **Consumers** and their employers may exert pressure on health plans to promote the use of personalized medicine. Awareness and educational campaigns will be needed to clarify risks and benefits, including potential for improved health outcomes, available through access to personalized medicine.

PROVIDERS

- **Personalized medicine** will offer new tools to improve patient care, which providers will need to understand and use with patients and with payers. They will need to provide evidence of treatment efficacy as demonstrated value to payers for reimbursement.
- **As providers** move to EHR/EMRs, new decision-support tools will facilitate rapid identification and dissemination of disease-specific standards of practice; improve provider management with real-time outcomes data; prioritize therapies based on potential drug interactions and patient clinical profiles; and identify at-risk patients for earlier intervention.

PAYERS

- **As the employer-provided** group health insurance model moves toward a retail (individual) health insurance model, the issue of employee turnover should mitigate the hesitancy of insurers to adopt personalized medicine due to the lack of a near-term ROI.
- **Employers**, as a financer of healthcare, may benefit from early adoption of personalized medicine. This new care paradigm has the capacity to slow the advancement of conditions and diseases that, left untreated, result in more expensive acute interventions and institutionalized care.
- **The evolution** of the commercial insurance market to a retail market will also prompt the design of customized products and services, which provides opportunity for inclusion of personalized medicine products.
- **When personalized medicine** is used for specific patients, it may be a trigger for enrollment into other health plan quality initiatives, including early detection initiatives, wellness programs, genetic counseling, disease management, etc.
- **Payers** will need to rationalize formulary and benefit design to leverage personal medicine appropriately. Members will need education to understand why a treatment is or is not required based upon diagnostic test results.
- **New actuarial models** will be needed to account for smaller risk classes. Health plans will need to balance the risk of adverse selection against the benefit of more patients receiving personalized medicine's positive impacts. Health plans will need to expand analytics to incorporate clinical biomarker data to refine patient risk segmentation.
- **Payers** may desire government subsidies, premium tax reductions and abatements to make coverage of personalized medicine more profitable.

POLICYMAKERS

- **The Centers for Medicare and Medicaid Services (CMS)**, as one of the

RAAJ TRIVEDI
Clarient

Pharma companies are going to have to find a way to partner with the diagnostic companies to help deliver their messages to the marketplace.

academic sites to understand the complexities of the diseases we're all grappling with."

The Biomarkers Consortium, launched in late 2006, is a public-private biomedical research partnership managed by the Foundation for the National Institutes of Health that aims to develop, validate, and qualify biomarkers to speed the development of medicines and therapies for detection, prevention, diagnosis, and treatment of disease and to improve patient care.

Roche and Johnson & Johnson have made significant commitments to the advancement of personalized medicine.

Dr. Manji says J&J is moving away from the notion of therapeutics as solely a pill and is evaluating a number of different modalities, including biotech and marrying drugs and devices.

J&J researchers use genomics, biomarkers, molecular and cell-based diagnostics, and bioinformatics routinely as part of their R&D efforts to develop personalized approaches to medicine. A pharmacogenetic approach is used for almost every compound J&J develops now.

For Roche, personalized medicine is a core element of the company's strategy, Mr. Metcalfe says.

"A personalized healthcare approach is instrumental to the creation of clinically differentiated medicines and therefore to the innovation process," he says. "Roche is in a fairly unique position in terms of diagnostic collaborations because we have our own diagnostics division within the company and therefore access to technologies to develop

nation's largest insurers, can play a pivotal role in the adoption of personalized medicine and its marketplace acceptance. Medicare and Medicaid have already begun the transition to an individualized retail market and thus may provide leadership to commercial health plans who need assistance to understand the value of personalized therapies for individual health insurance.

- **Policymakers** (and federal payers) will need to provide incentives for commercial health plans to adopt personalized medicine by leading by example — e.g., reimbursing these technologies. Many health plans make coverage decisions based upon CMS practices.
- **Policymakers** may need to rationalize and leverage the linkage or opportunity of personalized medicine with the Orphan Drug Act.
- **Policymakers** should consider supporting R&D tax credits (or other strategies) to the biotech/pharma industry to encourage their personalized medicine development efforts. This could reduce R&D costs and thus price points, making the personalized therapy more affordable for patients and payers. Policymakers should consider subsidizing and funding clinical research in personalized medicine to advance the field and develop the evidence base to support clinical effectiveness.
- **Policymakers** could grant competitive product windows before generics enter the market. They could time the exclusivity period to be coterminous with the ROI timing of the therapy. Policy makers could offer to take on more of the risk of personalized medicine from R&D to market release so that payers would be closer to breaking even. Government could offer prize funds, facilitate industry collaboration on R&D, and/or centralize knowledge on safety to "nationalize" the expense of personalized medicine against the overwhelmingly positive society benefit.

BIOTECH/PHARMACEUTICAL AND DIAGNOSTIC COMPANIES

Biotech/pharmaceutical companies may need to consider more virtual R&D to address smaller markets with more targeted therapies. This could reduce R&D expenditures.

- **Biotech/pharmaceutical companies** may view personalized diagnostic companies as prime investment or acquisition targets. Life-sciences companies with limited capital may seek partnerships with more established and capitalized partners for investment, sales, and distribution support.
- **Biotech/pharmaceutical companies** producing targeted therapies should start to consider strategies to integrate marketing, sales, and distribution with companion diagnostics to improve the cost-effectiveness of these activities.
- **Biotech/pharmaceutical companies** may focus on developing compounds whose improved profits and shorter development cycles could offset lower revenues from smaller, non-population-based therapies.
- **Biotech/pharmaceutical companies** may demand protection from generics to help fund product development.
- **Biotech/pharmaceutical companies** will need to generate an evidence base to demonstrate the efficacy of personalized medicine to garner public policy and payer support.
- **Biotech/pharmaceutical companies** may begin to develop research and information collaborations with affiliates, academic medical centers, and research organizations to support patient recruitment and multicenter trials required for targeted study populations. This could also reduce R&D expenditures and lower price points for broader adoption.

companion diagnostics. As an industry, there has been a sharpened focus on personalized medicine over the last five years. And while it's an extremely long path and significant challenges remain, we believe there is a great deal of untapped opportunity."

Anthony Everhart, M.D., director, medical monitoring, Americas, at Chiltern, says there are likely to be more collaborations in the area of personalized medicine since most large pharma companies may not have specific expertise in diagnostics.

"Large pharma companies are no doubt going to have to work more with smaller diagnostic companies," he says. "There also will probably be a surge in acquisitions, where larger companies are going to acquire the more aggressive smaller biotech companies that already have a head start in personalized medicine."

Dr. Everhart says in these early days of personalized medicine, there will be problems with intellectual property claims and patent infringement issues.

Raaj Trivedi, VP of marketing at Clarient, agrees, says it is very unlikely that a single company can own all of the drugs that turn the pathways on and off.

"Companies will have to work together to direct these key pathways, as well as set up the

PERSONALIZED MEDICINE IN ACTION

INDUSTRY EXPERTS INTERVIEWED BY PHARMAVOICE STRESSED THE IMPORTANCE OF HAVING A BUSINESS AS WELL AS AN R&D STRATEGY THAT INCORPORATES PHARMACOGENOMICS AND PERSONALIZED MEDICINE.

"Each and every product in a company's portfolio needs to have a personalized medicine strategy," says Stan Bernard, M.D., president of Bernard Associates. "Companies need to think through how personalized data and tests can be used both as a competitive advantage and as a competitive threat. Instead of rejecting the technology, companies need to embrace personalized medicine and leverage it to discover and develop products, promote products, and to benefit patients, providers, and other important stakeholders."

While experts often mention Genentech's Herceptin for the treatment of HER2-positive breast cancer and Novartis' Gleevec for the treatment of chronic myeloid leukemia, there are more recent examples of the application of biomarkers.

A common development approach is to genotype for cytochrome P450, says LingSing Chen, Ph.D., VP of translational medicine research at QPS.

The CYP450 family of metabolizing enzymes is responsible for breaking down more than 30 different classes of drugs. DNA variations in genes that code for these enzymes can influence their ability to metabolize certain drugs.

"Genetic polymorphism is pretty common; and an individual's ethnic makeup can influence drug metabolism," she says. "Drug developers are using this information to predict and assess the pharmacokinetic profiles because drugs are metabolized differently and this can affect dosing and side effects."

An example is the use of CYP2C9 and VKORC1 genotyping for the administration of warfarin, an anticoagulant. In 2007, the FDA worked with the manufacturers of warfarin (marketed as Coumadin) to modify the product label to recommend genetic testing and to guide the warfarin dosing regimen.

Researchers know that two genes, CYP2C9 and VKORC1, which vary slightly among individuals, can influence warfarin's effectiveness. Researchers from more than 20 teams in nine countries on four continents joined to form the International Warfarin Pharmacogenetics Consortium (IWPC). The consortium was spearheaded by scientists involved in the NIH Pharmacogenetics Research Network and PharmGKB, an online pharmacogenomics resource where data from the study are freely available to scientists. The results of a 5,700-patient study released in February 2009 revealed that when genetic information was included, dosages were more accurate, especially for patients at the low or high ends of the dosing range.

Virco's HIV Program

Another example is the work that Virco, a Johnson & Johnson company, is doing in the area of HIV genotyping to measure drug resistance.

Husseini Manji, M.D., VP of CNS and pain at Johnson & Johnson Pharmaceutical Research and Development, says Virco provides an alternative way to measure viral susceptibility or resistance. VircoTYPE HIV-1 combines genotypic and phenotypic information to give both a qualitative and a quantitative assessment of viral susceptibility or resistance. Virus from the patient is sequenced and software then searches Virco's database, which has 37,000 matching genotype/phenotype pairs covering more than 5,000 different patterns of resistance, for previous samples with the same patterns of resistance mutations.

This is important because patients whose treatment was guided by drug-resistance testing had a greater reduction in viral load. Using HIV drug resistance information can also save money by reducing the use of ineffective drugs.

"Being able to sequence the whole HIV genome and identify mutations that the virus may create to resist drugs and to show the resistance in laboratory tests allows researchers to come up with an algorithm that identifies treatments that specific HIV statins may respond to," Dr. Manji says.

Roche's Cancer and Hepatitis C Programs

At Roche, the company is approaching personalized healthcare by using new molecular insights and molecular diagnostic tests to better tailor medicines and better manage diseases.

In 2007, Roche acquired 454 Life Sciences, which develops and commercializes the innovative 454 sequencing system for ultra-high-throughput DNA sequencing, and NimbleGen, a manufacturer and supplier of a proprietary suite of DNA microarrays, consumables, instruments, and services.

One Roche program is BRAF in malignant melanoma and other cancers. R7204/PLX4032 is

right trials to make sure the drug is applied at the right part of the pathway," he says.

IMPLICATIONS FOR MARKETING

Dr. Manji says personalized medicine is also going to change the way marketing is done.

"There will have to be a new mindset; marketing can't be based on the premise that one drug is better than another drug," he says. "The case will be that Drug A is a more appropriate treatment for one subgroup of people, whereas Drug B may be the better choice for another subset of people. Marketers will have to provide healthcare providers and patients with new information rather than competing for supremacy."

Mr. Metcalfe agrees marketing will have to be driven by better-supported data.

> THE U.S. HEALTHCARE SYSTEM IS THE WORLD'S LEADER IN PERSONALIZED MEDICINE. IT IS THE EPICENTER FOR PERSONALIZED MEDICINE RESEARCH AND DEVELOPMENT THAT BENEFITS CITIZENS AND GOVERNMENTS OF THE WORLD.
> DELOITTE CENTER FOR HEALTH SOLUTIONS

an investigational targeted cancer therapy that selectively inhibits B-Raf^{V600E}, a mutated form of the BRAF gene. Roche, along with alliance partner Plexxikon, is developing this new small molecule therapy to block the mutated gene product to prevent uncontrolled cell growth and carcinogenesis. The target of the candidate drug is also the predictive biomarker that could potentially be used to identify patients who are most likely to benefit from the treatment.

Roche Diagnostics is developing a test to identify patients with the B-Raf^{V600E} mutation, which may offer a new treatment modality for the estimated 100,000 cancer patients in the United States who carry the B-Raf^{V600E} gene. BRAF has been associated with increased tumor aggressiveness and decreased survival in many types of cancers and is a common cancer-causing gene. The B-Raf^{V600E} gene is found in about 50% to 70% of malignant melanomas, 10% of colorectal cancers, and large number of thyroid tumors. Roche and Plexxikon currently have a Phase I trial open to accrual in metastatic melanoma patients who are positive for the B-raf^{V600E} mutation in the BRAF gene. In the near future, additional patients with colorectal cancer bearing the BRAF mutation will also be evaluated in this trial.

Another Roche program is in hepatitis C. Roche provides Pegasys (pegylated interferon alfa-2a) and Copegus (ribavirin) combination therapy. Coupled with this, Roche provides two diagnostic tests, the COBAS TaqMan HCV Test for measuring hepatitis C viral load by PCR and a test for determining the genotype of the hepatitis C viral infection.

These two tests are used to determine duration of therapy, allowing treatment to be tailored to specific groups of patients. Physicians use these tests to identify the type of infecting virus and the amount of that virus in the patient's blood, enabling treatment duration and dose to be modified to best fit the patient's needs.

Amgen's Colon Cancer Program

In December 2008, Amgen requested a label change for its colon cancer drug Vectibix. In March 2008, a study from an analysis of the first randomized, controlled clinical trial showed that metastatic colorectal cancer patients with mutated KRAS tumors do not respond to Vectibix monotherapy. In addition, patients with wild-type KRAS tumors treated with Vectibix have a better response rate and prolonged progression-free survival.

Amgen executives believe the KRAS gene is a predictive biomarker in patients with metastatic colorectal cancer treated with the anti-epidermal growth factor receptor (EGFr) antibody Vectibix (panitumumab). Worldwide Vectibix sales were $153 million in 2008 versus $170 million in 2007.

Amgen executives say they are still in discussion with the FDA about how best to present these data, as the American Society of Clinical Oncology and the National Comprehensive Cancer Network (NCCN) updated their guidelines to include the recommendation that a determination of the KRAS gene status of either the primary tumor or a site of metastasis should be part of the pretreatment workup for patients diagnosed with metastatic colorectal cancer. The guidelines recommended that EGFr inhibitors, including Vectibix, should only be used in patients with tumors characterized by the wild-type KRAS gene.

Prometheus' IBS Program

Prometheus Laboratories recently launched Prometheus IBS Diagnostic, the first blood test for irritable bowel syndrome (IBS). This test incorporates 10 biomarkers, two of which are proprietary, along with a proprietary algorithm to help physicians clarify or validate other clinical findings. The diagnosis of IBS is typically made through a process of elimination. The symptoms of IBS may seem similar to those of other gastrointestinal disorders, such as inflammatory bowel diseases (ulcerative colitis or colitis and Crohn's disease) and celiac disease.

The company also markets Lotronex, which is indicated for women with severe diarrhea-predominant IBS. In January 2008, Prometheus Laboratories, a specialty pharmaceutical company, acquired the exclusive rights to Lotronex in the United States from GlaxoSmithKline.

This product has had serious adverse events associated with it. Lotronex was approved in February 2000, but in November 2000 Glaxo withdrew the product from the market because of the risk of ischemic colitis.

In June 2002, the FDA approved a supplemental new drug application with restrictions. The drug's indication has been narrowed to only treat women with severe, diarrhea-predominant IBS who have failed to respond to conventional IBS therapy. Limiting the use of Lotronex to this severely affected population is intended to maximize the benefit to risk ratio.

▶ DR. HUSSEINI MANJI
Johnson & Johnson Pharmaceutical Research & Development

Companies, universities, and the government will need to work together to bring about personalized medicine, and they will all have to do a great deal of work to help everybody understand diseases better.

"There will be richer data packages and marketing approaches will be more scientifically and clinically driven," he says. "This also means that more work will be needed to ensure that the diagnostic testing component is included in our marketing plans."

Mr. Trivedi says marketing efforts will have to be coordinated, with the same message being delivered to the oncologist and to the pathologist.

"Pharmaceutical companies need to develop a parallel educational effort to address both the therapeutic and diagnostic, otherwise there will be a disconnect and adoption rates will not be what they would anticipate," he says.

Dr. Vanier says physicians have an incredibly high interest in genomic testing.

"We get to spend hours with physicians instead of minutes because their interest is so high and their hunger for education is high," he says. "This is a big opportunity for pharma companies as physicians are spending less and less time with sales reps."

Dr. Bernard says patient education also is crucial.

"There is a need to distinguish between genetic disease susceptibility testing and diagnostic testing that identifies patients who are more likely to respond to a particular pharmaceutical product," he says. "Most patients are concerned about the use and possible misuse of disease information, but there is less concern about drug response testing information." ✦

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

Experts on this topic

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9TH ANNUAL PHARMALINX CHARITY GOLF OUTING

Hosted by PharmaVOICE Magazine

TO BENEFIT THE LANKENAU INSTITUTE FOR MEDICAL RESEARCH

CALL NOW
to reserve space or secure a sponsorship

PLACE

Jericho National Golf Club
New Hope, PA

DATE

Monday, September 14, 2009

TIME

Arrival Time — 10:00 am
Tee Time — 11:00 am shotgun start

PLAY

Foursome ... $1,250
Single ... $375

Registration By August 17, 2009
Payment must accompany registration

CORPORATE SPONSORSHIPS AVAILABLE

PLATINUM ... $6,500 – receives 4 player spots and e-sponsor advertising package, including leaderboard sponsorship* (one sponsorship available)

GOLD ... $4,500 – receives 4 player spots and e-sponsor advertising package* (unlimited sponsorships available)

SILVER ... $2,500 – receives 2 player spots and e-sponsor advertising package* (unlimited sponsorships available)

BRONZE ... $1,500 – receives 1 player spot and e-sponsor advertising package* (unlimited sponsorships available)

HOLE SPONSORSHIPS AVAILABLE

The sponsorship fee includes e-sponsor advertising package*

Holes with prizes ... $1,000
Men's longest drive • Men's closest to the pin
Men's straightest drive • Women's longest drive
Women's closest to the pin • Women's straightest drive
Hole with car prize for hole-in-one – Car dealer sponsorship

Holes without prizes ... $750 – All holes excluding prize holes

* E-sponsor advertising package includes: advertising on electronic scorecard, sponsorship of 1 hole, hole signage, listing in program and PharmaVOICE magazine, opportunity to add promotional item to give-away bag

ADDITIONAL SPONSORSHIPS AVAILABLE

Carts ... $2,000 (limited to three sponsors)
The sponsorship fee includes sponsor advertising package+

Lunches ... $1,000 (limited to three sponsors)
The sponsorship fee includes sponsor advertising package+

Putting Competition ... $1,000 (limited to one sponsor)
The sponsorship fee includes sponsor advertising package+

Refreshment Stations ... $1,000 (limited to three sponsors)
The sponsorship fee includes sponsor advertising package+

Chair-Massage Station ... $1,000 (limited to three sponsors)
The sponsorship fee includes sponsor advertising package+

+Sponsor advertising package includes: signage at sponsored area, advertising on event Website, listing in program and PharmaVOICE magazine, opportunity to add promotional item to give-away bag

PROGRAM ADS

This advertising fee includes a black-and-white ad in the event program, and name of sponsor listed in the November/December issue of PharmaVOICE.

Full Page Ad ... $300 (5" x 7 1/2") • **1/3 Page Ad** ... $75 (5" x 2 3/8")

Please contact Marah Walsh at PharmaLinx at 215-321-8656 for additional information or e-mail mwalsh@pharmalinx.com

www.pharmalinx.com/golf