BY DENISE MYSHKO

PERSONALIZED MEDICINE

The Right Dose at the RIGHT TIME

OBSTACLES AND CHALLENGES STILL REMAIN to make the vision of personalized medicine a reality.

Despite some early successes, the development of targeted medicines and pharmacogenomics-based testing has been slower than anticipated. The shift to developing personalized medicines is going to mean fundamental changes — and challenges — for the bio/pharmaceutical industry and the healthcare industry as a whole.

Ernst & Young analysts say personalized medicine is one of the drivers that will fuel a fundamental reinvention of the business models of biotech and pharma companies. Personalized medicine, they say, has the potential to produce new generations of fundamentally different products, and in doing so, alter the nature of competition in the industry. To stay competitive, drug companies will have to focus on developing products that are truly innovative and deliver real improvements in healthcare outcomes.

"Personalized medicine will require a significant departure from many traditional processes that support healthcare delivery today," says Kris Joshi, Ph.D., senior director, health sciences global business unit at Oracle Corp. "For example, payers have still not developed and implemented changes to their traditional reimbursement model to properly compensate for the additional genetic testing that is tightly coupled with personalized treatments. At the same time, limited physician education and awareness around genetics and personalized treatments limit adoption. The fundamental scientific challenges in developing personalized drugs also remain significant. Although we increasingly understand the genes and clinical pathways associated with major diseases, our ability to apply that understanding to develop new therapies is still rudimentary."

Dr. Joshi says pharmaceutical R&D is not yet geared for the efficient development of targeted drugs, which by definition are meant for a smaller audience, compared with the current "one-size-fits-all" model.

"Part of the problem lies in assimilating and leveraging the vast amounts of data available electronically from healthcare providers, pathology labs, genetic diagnostic labs, and research institutions," he says. "The challenge now is to organize the data and to make sense of it to guide research. Valuable insights typically emerge when phenotypic clinical data can be combined with pathology and genetic data in the context of a specific disease or category of diseases. Hence, personalized medicine will rely heavily on clinical informatics to identify and exploit such insights into the genetic variability of diseases."

Analysts from Deloitte expect the traditional line between biotech and pharma companies will become irrelevant. Pharma companies are increasingly investing in and collaborating with all types of biotech players. The explosion of genetic knowledge and the implications for disease treatments means that this collaboration will only intensify.

Lewis Bender, CEO of Interleukin Genetics Inc., says the biggest challenge for personalized medicine will be for the drug developers in the pharmaceutical industry to abandon what is proving to be an obsolete business model, one that is predicated on the idea that complex diseases are the same for everyone.

"For complex diseases such as diabetes, Alzheimer's, and osteoarthritis, drug failures will continue until pharmaceutical companies begin to subtype disease; for example, adopt personalized medicine," Mr. Bender says.

William Bertrand, J.D., executive VP, legal affairs, general counsel, and corporate compliance officer, at MedImmune, says moving the large pharmaceutical companies away from the blockbuster mentality will be the biggest challenge.

"Not every product of the future needs to be or should be a blockbuster," Mr. Bertrand says. "This is an advantage that the arrangements between large cap pharma and biotech can bring. Biotechs have been living in this new world for the last few years and see the value of

R&D MODELS TO CONSIDER

- R&D strategies that support the assembly of treatment portfolios for the entire disease life cycle
- Virtual, disease-specific R&D networks
- Virtual R&D processes with significant outsourcing to maximize flexibility and manage development risk
- Focused R&D programs based on genotyped patients/subjects and biomarkers
- Partnering and collaborative ventures to access disease knowledge communities

Source: Deloitte, New York.
For more information, visit deloitte.com.

EXPERTS

LEE BABISS, PH.D. Global Head of Pharma Research, Roche, Basel, Switzerland; Roche is one of the world's leading research-oriented healthcare groups with core businesses in pharmaceuticals and diagnostics. For more information, visit roche.com.

LEWIS BENDER. CEO, Interleukin Genetics Inc., Waltham, Mass.; Interleukin Genetics is a genetics-focused personalized health company that develops preventive consumer products and genetic tests for sale to the emerging personalized health market. For more information, visit ilgenetics.com.

William Bertrand *MedImmune*

Not every product of the future needs to be or should be a blockbuster.

truly bringing medicines to market for smaller patient populations, especially if the scientific approach to personalized medicines means the probability of regulatory success is higher and the development costs lower."

Deloitte analysts predict large pharma will be vulnerable to new entrants in the industry that will expand and manage disease-specific networks focused on genotyped patient populations and disease life cycles. These new entrants will likely need a different R&D approach incorporating multiple factors. (See box on page 72 for more information).

For big pharma companies, Deloitte analysts say, the major problem will be managing the transition to an organization of many smaller companies. As any company is unlikely to develop all the treatments to cover all genotype segments across the disease life cycle, deal-making, alliances, and collaborations for product acquisition will be of even more importance than they are today.

REGULATORY ISSUES

Industry experts say regulatory issues remain a big challenge. The President's Council of Advisors on Science and Technology (PCAST) says the federal government will have to play a bigger role in funding and coordinating research while also eliminating regulatory and reimbursement hurdles. (See box on page 74 for more on the council's recommendations.)

"Actually, the regulatory agencies are very open and willing to work with us to drive personalized healthcare," says Lee Babiss, Ph.D., global head of pharma research at Roche. "Our challenge is that if we do not pursue the science with commitment and vigor, we run the risk of being told what to do by the regulators. The better scenario is for us to be proactive and help the regulators understand the importance of personalized healthcare for patients by generating high-quality data."

Dr. Joshi points out that concerns related to privacy and security of medical and genetic information will continue to weigh on the minds of patients and, consequently, on the minds of regulators.

"Although the U.S. government recently enacted the Genetic Information Nondiscrimination Act, which protects patients against health insurance and employment discrimination, people could still be concerned about other forms of discrimination, for example, while purchasing life insurance," he says. "Such concerns could make it even more difficult to recruit patients for clinical trials that require genetic information to be collected for personalized therapies. Hence, life-sciences and healthcare organizations must take proactive steps to ensure compliance and prevent security breaches by adopting a comprehensive approach to security and privacy that addresses the issue from a procedural, physical, and IT perspective. Research organizations can further alleviate concerns by using de-identification capabilities that are now commonly available in clinical IT applications and middleware products to strip personally identifiable information from clinical data before sharing with external entities."

LEADING TECHNOLOGIES

Mr. Bender says key technologies will be the development of molecular diagnostic tests that combine both static — for example genetic — and dynamic biomarkers along with improved imaging technologies for complex diseases.

"Such test panels will provide patients with precise personalized information that can guide therapy choices," he says.

Genomic biomarkers are the foundation of personalized medicine. Experts say when biomarkers for diagnosing and treating patients more accurately are more widely available, the industry will be able to stratify patients with different but related conditions and test new medicines only in patients who suffer from a specific disease subtype. (See related story on page 72.)

Biomarkers can be used to detect the predisposition for disease in a population, screen for its presence, confirm its diagnosis, assess its severity, predict its response to available therapies, and measure its clinical course. Biomarkers can be used as targets to discover new drugs, providing improved systems for screening a library of compounds for promising candidates.

The growth trend for biomarkers for drug R&D would be just more than $4 billion in 2008 and having a double-digit growth rate (CAGR) in the high teens, according to business consulting company Takeda Pacific.

The FDA, through its Critical Path Initiative, has encouraged and supported biomarker research and has set up a biomarker qualification pilot process at CDER to take an exploratory biomarker through a series of scientific review processes.

Additionally, Dr. Joshi says rapid and cost-effective gene sequencing and genetic testing technologies will play a central role in the development of personalized medicine, as they provide the primary means for matching patients with personalized drugs and therapies.

"But alongside the clinical and laboratory technologies, information technology will also play a central role," he says. "Accomplishing the integration of applications and data required to support informatics for personalized medicine is a significant challenge for most life-sciences companies today. New Web 2.0 tools promise to simplify the integration and sharing of semantic information in an enterprise. Ontolo-

WILLIAM C. BERTRAND, J.D. Executive VP, Legal Affairs, General Counsel, and Corporate Compliance Officer, MedImmune, Gaithersburg, Md.; MedImmune, an AstraZeneca company, is a biotechnology company focused on infection, oncology, respiratory disease and inflammation, cardiovascular/gastrointestinal disease, and neuroscience. For more information, visit medimmune.com.

KRIS JOSHI, PH.D. Senior Director, Health Sciences Global Business Unit, Oracle Corp., Redwood Shores, Calif.; Oracle is an enterprise software company. For more information, visit oracle.com.

THE FEDERAL GOVERNMENT'S ROLE IN PERSONALIZED MEDICINE

A presidential advisory council released a report in September 2008 that says personalized medicine treatment based on an understanding of each patient's unique physical makeup, including genetic structure, could significantly improve healthcare.

But the President's Council of Advisors on Science and Technology (PCAST) says the federal government will have to play a bigger role in funding and coordinating research while also eliminating regulatory and reimbursement hurdles that currently hinder the creation and adoption of innovative products and medical treatments.

The report, Priorities for Personalized Medicine, is a blueprint for eliminating some of the barriers that prevent widespread adoption of personalized medicine by healthcare providers. Those barriers include: ambiguous and incomplete regulation of genomic-based tools and services; limited coverage of genetic tests and treatments by health insurers, including the federal government; and a lack of translational research.

PCAST recommends that the federal government develop a strategic, long-term plan that coordinates public and private sector efforts to advance research and development relevant to personalized medicine. PCAST recommends that an office should be established within the Department of Health and Human Services to specifically coordinate their activities related to personalized medicine.

PCAST began its study on personalized medicine in January 2007 with the ambitious goal of assessing eight major policy areas, including: technology/tools, regulation, reimbursement, information technology, intellectual property, privacy, physician and patient education, and economics.

Specifically, the advisory council recommends:

- **Technology and tools:** the federal government should develop a strategic, long-term plan that coordinates public and private sector efforts to advance research and development relevant to personalized medicine; and the federal government should make critical investments in the enabling tools and resources essential to moving beyond genomic discoveries to personalized medicine products and services of patient and public benefit.
- **Regulation:** The FDA should implement a more transparent, systematic, and iterative approach to the regulation of genomics-based molecular diagnostics; the FDA Critical Path Initiative should be adequately funded to support its envisioned research efforts that are critical to the progress of personalized medicine; and the biopharmaceutical industry should adopt a proactive and constructive role as the FDA seeks to identify and fulfill its regulatory responsibilities related to personalized medicine.
- **Reimbursement:** Public and private payers should determine coverage policies and payment rates for genomics-based molecular diagnostics in light of their overall impact on patient care, as demonstrated by evidence from clinical trials and other well-designed empirical studies.
- **HHS coordination:** HHS should establish a Personalized Medicine Coordination Office within the Office of the Secretary of HHS to coordinate all activities relevant to personalized medicine.

Source: President's Council of Advisors on Science and Technology (PCAST), Office of Science & Technology Policy, Washington, D.C. For more information, visit ostp.gov.

Lewis Bender *Interleukin Genetics*

The biggest challenge for personalized medicine will be for drug developers to abandon what is proving to be an obsolete business model — one that is predicated on the idea that complex diseases are the same for everyone.

gy-based search engines can help researchers find and correlate relevant scientific insights buried across multiple data sources, taking content management and data mining to a whole new level. While these tools are still in the early stages of development and adoption, they provide hope that the informatics revolution will continue to power the transformation of pharmaceutical R&D and prevent the deluge of data from overwhelming scientists."

Dr. Babiss says non-invasive imaging technologies will play a big role in supporting the preclinical and clinical development of Roche's CNS programs.

"In addition, emerging quantitative imaging technologies will play an increasingly important role in our metabolism, oncology, and inflammation disease areas," he says. "We will continue to see improvements in our ability to interrogate DNA, RNA, and protein to derive biomarkers with our diagnostics colleagues and drive personalized healthcare. Our biggest challenge remains gaining alignment and individual commitments across the pharmaceutical and diagnostic value chains, so that what we say we will do actually gets done."

An increasing number of pharmaceutical companies are exploring the codevelopment of drugs and diagnostic tests (Rx-Dx combinations). The most successful approaches are planned from the beginning at the earliest stages of drug development and involve partnerships with diagnostics companies and interactions with regulators, analysts at Decision Resources say. ✦

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

MORE Options.
MORE Opportunities.
MORE Results.

The Next Generation of Publication Marketing

The PharmaVOICE WebLinx Program

PHARMAVOICE MODERATED • EDUCATION RICH • LIVE • INTERACTIVE • SPONSOR HOSTED

Accelerate your marketing campaign with a program designed to generate qualified leads and measurable results.

- Customize to your target audience — establish your expertise
- Leverage the PharmaVOICE brand to deliver interested participants — generate qualified leads
- Capitalize on pre- and post-seminar pull-through — build sustainable interest
- Use an experienced provider with proven results

For more information about WebLinx Programs, call 609-730-0196 to speak with Lisa Banket, Publisher (lbanket@pharmavoice.com), or contact Marah Walsh, New Business Development 215-321-8656 (mwalsh@pharmavoice.com)

Read. Think. Participate.

www.pharmavoice.com/weblinx