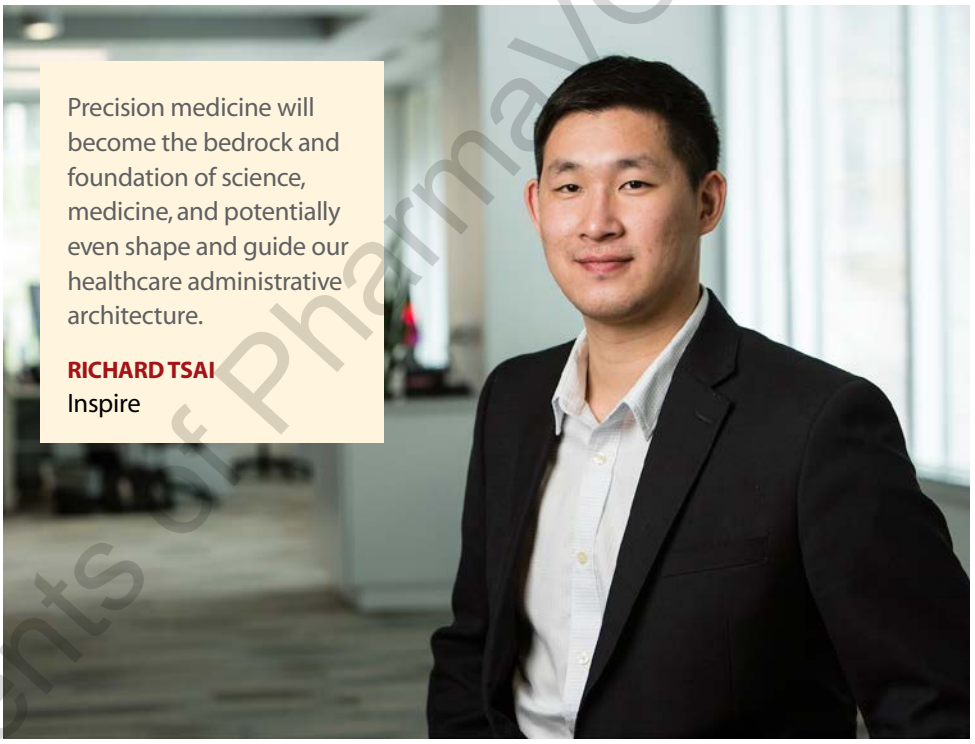
Trending 2017: Precision Medicine

Increasing demand for personalized medicine and advancements in new healthcare technologies will drive the development of precision medicines.

Precision medicine holds great promise for improving patient health outcomes. By identifying genetic causes of diseases, doctors can focus on disease prevention, earlier diagnosis when treatments may be more effective, and avoid giving treatments to patients that may cause adverse reactions or that will fail to work.

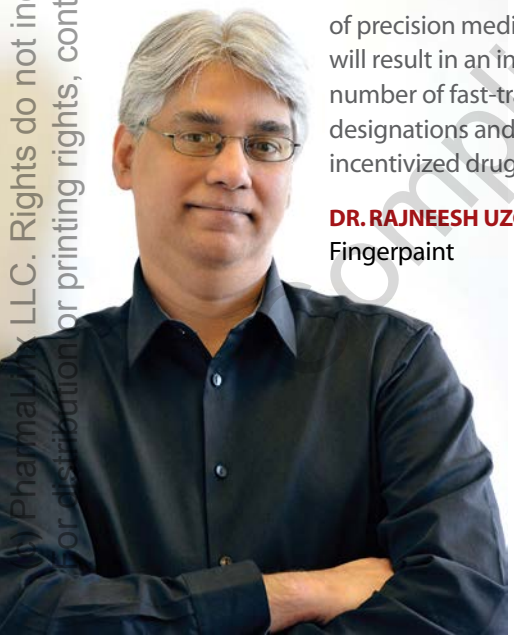
We are just at the beginning of the precision medicine era, but industry leaders say precision medicine will have a major impact on how doctors and patients think about disease and how patients are treated.

While the personalization and digitization in the consumer world is already a thing of history and moving toward predictive interactions, the healthcare industry is very much behind. However, through technological advances like next-generation sequencing, data commoditization, and maturation of our understanding of genomics and other 'omics modalities, the pieces are coming together, says Richard Tsai, VP of marketing, Inspire.



Precision medicine will become the bedrock and foundation of science, medicine, and potentially even shape and guide our healthcare administrative architecture.

RICHARD TSAI
Inspire



The continued adoption of precision medicine will result in an increased number of fast-track designations and incentivized drug pricing.

DR. RAJNEESH UZGARE
Fingerpaint

There are numerous consortiums and programs that are focused on collecting the genomic data, and many organizations from pharma to government are building national biobanks to store biospecimens of various diseases in the hope to extract meaningful biological data and translate them into biomarkers.

But this, Mr. Tsai says, is just the beginning.

"What's even more exciting is that we are also seeing the rise of citizen scientists, who are also patients and helping other patients to better understand what precision medicine is all about and how it can bring hope to them in the very near future," he says. "Precision medicine will become the bedrock and foundation of science, medicine, and potentially even shape and guide our healthcare administrative architecture."

Precision medicine is the future of all healthcare, says Kathy Giusti, founder, Multiple Myeloma Research Foundation & Consortium.

"As a cancer patient, I can tell you that it is the benefits of precision medicine that have helped push me, and many others, into remission," she says. "In a progressively individualized world, precision medicine sits at the confluence of science, technology, and consumerism and requires both patients and the global research community to collectively share and aggregate data."

Precision medicine holds the promise to help physicians and patients answer the question "will this work for me," says Michael Pencina, Ph.D., faculty associate director, director of biostatistics, and professor of biostatistics and bioinformatics, the DCRI Center for Predictive Medicine.

"Precision medicine has the potential to transform chronic disease population manage-

ment by leveraging predictive analytics for forecasting medication adherence," he says. "This can result in more personalized and effective patient adherence programs."

Precision medicine is also expected to drive real improvements in outcomes, especially in the areas where a detailed understanding of each person's phenotype and disease profile is important. For precision medicine to be successful, all stakeholders will have to be more actively engaged in R&D of new cures, says Kate Torchilin, Ph.D., CEO of Novaseek Research.

But, Dr. Torchilin says, for precision medicine to have a strong positive impact on the industry and patients' health, it is important to apply it in a pragmatic way, focusing on areas of biggest impact first, such as oncology.

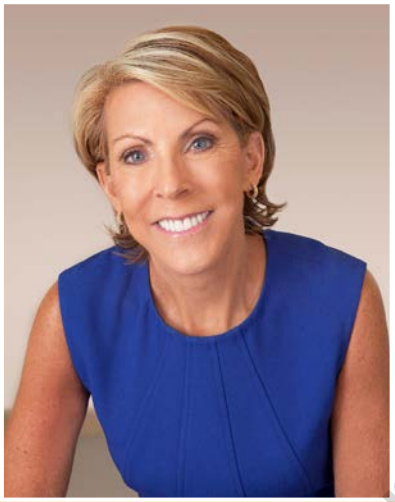
Oncology applications were, in fact, more than 30% of the precision medicine market share in 2015, according to Global Market Insights. Increasing demand for personalized medicine specifically in cancer treatments and advancements in new healthcare technologies will drive the precision global medicine market, which by 2023, is expected to reach $87.79 billion.

Precision medicine affords an exciting approach to cancer treatment, says Panteli Theocharous, Ph.D., VP, global product development, hematology/oncology at PPD.

"By evaluating a patient's genetic makeup or looking for specific genetic changes within a tumor, the hope is to be able to find prevention and treatment strategies that are individualized and ultimately more effective," he says.

Impact on Industry

In January 2015, President Obama announced the Precision Medicine Initiative (PMI). The initiative was supported by an



In a progressively individualized world, precision medicine sits at the confluence of science, technology, and consumerism and requires both patients and the global research community to collectively share and aggregate data.

KATHY GIUSTI
MMRF

Precision medicine is all about data. If we as an industry can tackle the data management challenges, we will identify a lot more targets and be able to put things in the pipeline that are more efficacious.

DR. LISA BOYETTE
Curable

Precision medicine will influence changes throughout the entire life-sciences industry, but is likely to make the greatest impact on two areas: commercialization and quality/manufacturing.

ROBERT GROEBEL
Veeva Systems

While the clinical and commercial challenges appear significant, the potential of precision medicine is likely to attract at least a few manufacturers willing to test their mettle over the next few years.

MATTHEW MAJEWSKI
Charles River Associates

Precision Medicine Insights…

GLEN DE VRIES
President, Medidata

Precisely identifying the patients who will maximally benefit from a particular therapy, and then being able to objectively measure the outcome of that intervention, will change the way drugs are developed, priced, and marketed. Simply put: There will be better outcomes, and in some cases, less confusion with regard to the best possible course of treatment.

LISA GILES
CEO, Giles & Associates Consultancy

The Precision Medicine Initiative has advanced the assignment of patients to clinical trial arms based on therapeutic inhibition of driver genetic alterations. The scope of precision medicine broadens as we understand more about cancer pathobiology. As we gain greater insights into the evolution of driver genetic alterations, and can better predict their impact on patient and therapy selection.

SHARON KARLSBERG
Principal, ZS

There will be an improved value proposition for payers and patients alike. Payers will know that only the subset of patients who express predictive biomarkers will receive treatment, raising the likelihood of positive outcomes for patients.

WILLIAM KING
Founder and Executive Chairman, Zephyr Health

A new commercial model is emerging with the advent of precision medicine, changing the way biopharma companies connect with customers and market products. Engagement strategies today must be insights-driven and as personalized as the product being marketed to be effective.

ALEXANDER MORIN
Manager, Manatt, Phelps & Phillips

The ability to prevent disease altogether using the principles and approaches of precision medicine could not only save lives and extend the overall quality of life for patients predisposed to certain diseases, but also prevent the need for lengthy, costly treatment regimens that in some cases create additional healthcare challenges through various short-term and long-term side effects.

initial $215 million investment, which included several components with efforts from across the federal government. The precision medicine model calls for the customization of healthcare, with medical decisions, practices, and/or products being tailored to the patient.

The Precision Medicine Initiative, says Olivier Lesueur, managing director, Bionest Partners, is bringing together input and data from -omics data, to clinical data on patient responses to treatment, and the development of next-generation technology that can find meaning in the mountains of information and translate it to better, more personalized care.

"The impact of precision medicine on drug development currently depends on whether there is a clear biology-driven target — a particular mutation or other biomarker — that can drive R&D from the start," he says. "However, science is increasingly recognizing that cancer is a complex and changing process that requires placing a new emphasis on understanding the biology of the disease over time."

Precision medicine will mean wholesale change for regulators, industry, and doctors, says Hugo Stephenson, M.D., executive chairman of DrugDev.

"Precision medicine will require a totally different mindset from the traditional blockbuster approach," he says. "This means a change in evaluation and regulatory processes since we will be evaluating a production methodology versus a product. It will mean a change to how developers negotiate reimbursement and market their products, which may become more kit-like for doctors to use. It will also transform the way diseases get treated, since many of these therapies are likely to be curative over short courses instead of chronic treatments."

As we gain further understanding of the biology of particular diseases and develop more relevant tools, data, and diagnostics, we envision precision medicine as enabling the constant monitoring of patient health status in real time.

OLIVIER LESUEUR
Bionest Partners

Trialists will need a plan for appropriate data collection to facilitate construction of predictive models, and these are the essential link between clinical trials and precision medicine.

DR. MICHAEL PENCINA
DCRI Center for Predictive Medicine

Precision medicine will require a totally different mindset from the traditional blockbuster approach. This means a change in evaluation and regulatory process since we will be evaluating a production methodology versus a product.

DR. HUGO STEPHENSON
DrugDev

Precision medicine creates portals for players in medical innovation, from drug development to liquid biopsy and companion diagnostics, says Joy Yucaitis, senior director, oncology strategy, Novella Clinical.

"As we more effectively understand the specific biology of a patient's cancer, we require more options tailored to each mutation," she says. "Almost as quickly as new targets are identified, new treatments enter clinical development. This product development dynamic introduces challenges as well, with securing funding to support development, competition for increasingly rare patients, and the evolution of clinical endpoints to make informed decisions along the clinical development pathway."

Impact on R&D

Precision medicine will change the paradigm for drug development, says Brian Kelly, M.D., president, payer and provider solutions, QuintilesIMS.

"As our knowledge of the biology of diseases advances through our increasing understanding of gene and protein expression, we are able to better identify subpopulations of patients that express specific targets for drug intervention," he says. "It is now very clear that specific types of cancer, for example breast, prostate, and lung, are not single diseases, but a combination of many different pathway abnormalities that although they may share common clinical features, are biologically very different diseases."

This, he says, creates an opportunity for the industry to develop therapies that while only targeted to certain subpopulations, are highly effective in those groups. If done well, this will not only lead to better clinical outcomes, but can inform which therapy will not work in certain subpopulations allowing us to spare the patient unnecessary morbidity and delay in moving to other more effective therapies and overall increase the safety profile of drugs.

"The need for increased R&D productivity, political pressure on pricing, and advances in understanding key targets have transformed precision medicine from a novel concept to essential strategy," says Ryan Million, partner, Trinity Partners. "Many drug discovery companies are wrestling with the challenge of launching a new product and new companion diagnostic in parallel, essentially creating two markets at once. The trend to do broader biomarker panel tests and next generation sequencing is where leading academic institutions are paving the way to broader implementation in the healthcare system. Companies

that contribute to both spaces, development of innovative medicines associated with individual biomarkers, and an environment to test patients broadly to identify the best therapy plan, will be the leaders in shaping precision medicine's future."

Binh Nguyen, M.D., Ph.D., VP, global product development, hematology/oncology at PPD, believes precision medicine will impact the industry in all functional areas.

"Discovery will need to focus more on specific targets and molecular pathways, clinical development will need to focus more on subgroups of patients with specific tumor markers, and commercialization will have a smaller market size for a specific drug, but at the same time will need to keep the drug price affordable for patients and the healthcare community as a whole," he says.

Dr. Chitra Lele, chief scientific officer at Sciformix, says precision medicine will solve the problem of generalization of results from clinical trials despite the inherent heterogeneity in the population and will enable development of interventions for individuals based on their specific genes, rather than the symptoms they exhibit.

Therefore, she adds, an individual patient is more likely to be prescribed a medicine that will work for him/her, and will not have to unduly bear with adverse effects of treatments that may not work. This is contingent on the effectiveness of the diagnostic tests to differentiate patients who will benefit from a particular drug to those who will not. It also depends on providers proactively identifying patients who will not benefit from, or will be harmed by specific treatments, which requires drug developers to share and mine clinical data.

To be successful, Lisa Boyette, M.D., Ph.D., CEO of Curable, says precision medicine is going to require up-front investment in a new brand of discovery technology and analytic capabilities.

"We do not have a choice," she says. "We have to gear up for the new line of therapies we need to produce in the 21st century, and we know they're going to be — if not personalized — more personalized. Therapies will be aimed at treating patients, not treating diseases. On the one hand, that sounds intimidating; we will have to put a lot of work into tailoring each patient's therapy to their needs, but that's accompanied by the opportunity to treat so many more patients than we're able to treat — and treat effectively — right now. So the work is changing and our approaches to discovery, translation, validation, and regulation will have to change to accommodate the new problems we have to solve."

The potential of precision medicine to deliver improved outcomes with limited side-effects is unfortunately matched by the hurdles to develop and commercialize these medications in today's healthcare environment, says Matthew Majewski, a consultant at Charles River Associates.

"Almost by definition, the limited patient population any one product can satisfy implies a higher product cost than mass-market alternatives," he says. "The biomarker testing required to identify this limited patient population is an additional healthcare expenditure. In a managed care environment where payers are looking to treat more patients with fewer dollars, precision medicine fundamentally conflicts with the practicalities of payer, employer, and patient budgets."

As we learn more about the composition of various types of disease the development model may change.

ANNETTE LESLIE
Carson Leslie Foundation

Using the treatment matched to the patient sooner offers the best chance for remission or cures.

JOY YUCAITIS
Novella Clinical

For precision medicine to have a strong positive impact on the healthcare industry and patients' health, it is important to apply it in a pragmatic way, focusing on areas of biggest impact first.

DR. KATE TORCHILIN
Novaseek Research

Impact on Commercial

On the commercial side, the Precision Medicine Initiative is already having an influence on the industry, or more specifically, patient adherence and support programs, says Kevin Connolly, VP, account management, at C3i Healthcare Connections.

He expects this influence will continue to be placed in the forefront in 2017.

"The growth of individualized patient adherence and support programs has coincided with the trend toward patient-centered care, as well as the sudden and massive growth of the specialty drug market," he says.

The reasons are two-fold: the specialty treatments themselves — and the patients who receive them — require individualized support, and the substantial investment that companies make in these treatments allows for the development of extensive, personalized patient engagement and adherence programs.

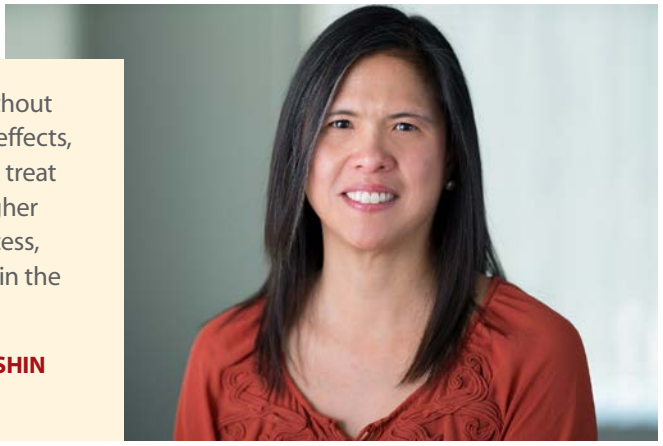
Marketers need to micro-target the right therapies to the right patients, using new tools including smart data, predictive analytics, and technology along with the increase in highly targeted addressable forms of media, says Maryann Kuzel, senior VP, head of healthcare strategy, North America, RAPP.

"The personalization must continue throughout the patient journey, as patients will only let you into their lives if you provide information that's relevant in the moments that matter most," she says. "Each patient experiences his or her disease in a unique way, shaped by an evolving clinical profile, health beliefs and behaviors, preferences, and life situations. Engaging with patient communities is very important as they are highly influential and provide a valuable resource for patient insights as well as co-creation of resources."

This expansion of precision medicine further drives the importance of innovative marketing solutions, where the convergence of data and technology allows marketers to create customized experiences, says Keri Hettel, VP, group director of analytics, Razorfish Health.

"Enabling precisely marketed messages will be even more relevant as treatment solutions become more targeted and specific to the individual, continuing to further move us away from the old-school mass marketing communications," he says.

Precision medicine will influence changes throughout the entire life-sciences industry but are likely to make the greatest impact on two areas — commercialization and quality/



No medicine is without potential adverse effects, but if we're able to treat patients with a higher probability of success, we stack the deck in the patients' favor.

DR. JUDITH NG-CASHIN
INC Research

The growth of individualized patient adherence and support programs has coincided with the trend toward patient-centered care, as well as the sudden and massive growth of the specialty drug market.

KEVIN CONNOLLY
C3i Healthcare Connections

manufacturing, says Robert Groebel, VP of global medical strategy at Veeva Systems.

"In terms of product launch and commercialization, the role of medical affairs will naturally expand significantly as this group is asked to lead an increasing number of scientific engagements with a growing network of healthcare professionals and influencers," he says. "As such, medical teams will need to embrace enterprise systems to gain visibility and develop a broader, organizational understanding of their impact on commercial strategy and vice versa. Similarly, medical affairs will need to deepen their grasp of disease landscapes and consider how they can improve impact on healthcare decision makers, shape scientific engagement, and ensure HCPs appropriately use precision products."

Impact on Patients

The ultimate goal of precision medicine is to increase treatment effectiveness, says Judith Ng-Cashin, M.D., chief scientific officer at INC Research.

"By more accurately matching the right patient with a specific disease to the right therapy, we will improve the benefit-to-risk ratio of new treatments," she says. "No medicine is without potential adverse effects, but if we're able to treat patients with a higher probability of success, we stack the deck in the patients' favor. This has implications for better physician confidence in prescribing, more favorable likelihood for payer reimbursement, and, therefore, improved patient access to new medicines."

Industry leaders say precision medicine will benefit patients by delivering safer, more effective medications. The obvious benefit for patients is the hope that more precise, individualized treatment will lead to better, more meaningful responses and lasting outcomes.

Precision medicine is "patient-centric" medicine, says Rajneesh Uzgare, Ph.D., medical strategy, Fingerpaint.

"It acknowledges the multifaceted nature and varied manifestation of the disease in each patient and proposes to use robust, validated treatment regimens designed specifically for that patient's disease," he says. "Improving outcomes through more holistic approaches to diagnosis and treatment is a key goal of the Precision Medicine Initiative, and as such the potential benefits to patients are significant."

Lee Fraser Ph.D., senior VP, group director science and medicine, at Digitas Health LifeBrands, says currently the success of any therapy is measured in terms of patient outcomes.

"We should expect precision medicine to be no different," he says. "By identifying the underlying nature of the disease and targeting therapies accordingly, we should expect better activity and efficacy, less off-target toxicity, more predictable performance and shorter cycles of waiting to see if ineffective medicines work before moving on to other options. Moreover, the ability to predict outcomes includes not just patients who will benefit from a given therapy, but also may identify people with genotypes that may predict given toxicities and other adverse events."

Patients are ready to be the industry's partners and usher in a new era of precision medicine and are pushing for additional guidelines and the framework to do so.

HEATHER GARTMAN
inVentiv Health

"Precision therapies hold particular promise for children," says Annette Leslie, cofounder, Carson Leslie Foundation. "Through genetic profiling, we are increasingly able to better understand a child's specific cancer tumors and direct therapies in a much more targeted way as opposed to traditional treatments that tried to treat all cases of medulloblastoma, for example, in the same way."

Precision medicine also holds great promise for patients with rare and hard-to-treat diseases but we still have progress to make to truly get there, says Heather Gartman, managing director, inVentiv Health PR Group DC, and global CTR lead, inVentiv Health.

"The issue we face is that to have true precision medicine we must involve the patients from the beginning of the development of compounds into treatments," she says. "We know that many biopharma companies are just at the beginning of figuring out to how to truly partner with patients in the clinical stage as the internal frameworks are not set up yet. In addition, both regulatory bodies and payers must accept and welcome patient-reported outcomes and real-world data when making their decisions and decide that quality of life is important in all diseases. From what we see and hear, patients are ready to be industry's partners and usher in a new era of precision medicine and are pushing for additional guidelines and the framework to do so." PV

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A Selection of Biopharma Approaches to Precision Medicine

BLUEPRINT MEDICINES

KATE HAVILAND
Chief Business Officer
BLUEPRINT MEDICINES

Precision medicine has the opportunity to greatly enhance how we research, develop, and practice medicine. Although advances have been made in precision medicine, this vision has a long way to go before it becomes a reality for many patients.

At Blueprint Medicines, we are pursuing precision medicine through our efforts to redefine cancer by targeting a primary genetic driver across a variety of tumor types. We believe this targeted approach may enable a more efficient path to discovering, developing, and commercializing potentially transformative new therapies.

Blueprint Medicines is developing a new generation of highly selective and potent kinase therapies for patients with genomically defined diseases. Since starting operations in 2011, the company has advanced two lead drug candidates, BLU-285 and BLU-554, into three Phase I clinical trials.

ALI FATTAEY, PH.D.
President and CEO
CURIS

Precision medicine, by definition, implies that the use of a particular medicine is based on a known specific feature of the patient or their condition, and therefore the patient should have a higher likelihood of benefiting from treatment with such a medicine.

The value of a given medicine is the sum of two things: the level of clinical benefit it provides, and the degree of predictability that it may provide that level of benefit upon treatment. For our industry, based on this equation, the more precise or predictable a medicine is, the greater its value.

Curis is focusing on the development of drug candidates in the fields of immunocology and precision oncology. The company has two candidates in development.

CUDC-907 is a small molecule inhibitor of HDAC and PI3K enzymes being investigated in a Phase II trial in patients with MYC-altered diffuse large B-cell lymphoma and in a Phase I trial in patients with MYC-altered solid tumors. CA-170 is a small molecule antagonist of PD-L1 and VISTA immune checkpoints in a Phase I clinical trial in patients with advanced solid tumors or lymphomas.

HUGH O'DOWD
CEO
NEON THERAPEUTICS

Neon Therapeutics is an immuno-oncology start up, formed in October 2015, which is developing neoantigen-based therapeutic vaccines and T-cell therapies to treat cancer. The vast majority of neoantigens are patient-specific, thus the approach of our lead program, NEO-PV-01, is to interrogate the tumor for its mutations via DNA and RNA sequencing, process these mutations with highly sophisticated algorithms to determine the best immune targets, then generate fully customized vaccines that are individualized for every patient, essentially the most intimate form of personalized medicine. Our first clinical trial is under way combining NEO-PV-01 with an anti-PD-1 checkpoint inhibitor.

ALAN SHULDINER, M.D.
VP and Co-Head, Regeneron Genetics Center
REGENERON PHARMACEUTICALS

We know that precision medicine will be a huge part of the future of drug discovery and development, and the establishment of our Regeneron Genetics Center nearly three years ago reflects this belief. It's always been true that effective medicines must be based on a deep understanding of biology, and new technologies enabling access to the genome have allowed us to go even deeper.

Regeneron discovers, invents, develops, manufactures, and commercializes medicines for the treatment of serious medical conditions. The Regeneron Genetics Center has built one of the world's most comprehensive genetics databases, pairing the sequenced exomes and de-identified EHRs of more than 100,000 people so far. The RGC conducts gene sequencing projects, functional biology, disease modeling and the translation of genetics findings into Regeneron's preclinical and clinical pipeline.

The company is using this database to identify new drug targets and therapeutic indications, to validate our existing programs and to build better-informed clinical trials.

RAMI LEVIN
President, North America
SOBI

While precision medicine is impacting multiple functional areas of the industry, we believe its greatest impact is in the "D" portion of R&D. Massive clinical trials of all comers will no longer be commonplace. Moving forward, companies will design trials more precisely, selecting patients that are most likely to benefit from treatments, with the ultimate goal of driving greater response rates.

Precision medicine is about transforming how we look at communities. It's about bringing the humanity back and valuing all lives.

Sobi is an integrated biopharmaceutical company whose product portfolio is primarily focused on hemophilia, inflammation, and genetic diseases. Sobi was recently granted orphan designation by the European Commission for SOBI003, a chemically modified human recombinant sulfamidase for the treatment of mucopolysaccharidosis type IIIA (Sanfilippo A syndrome).

THE IMPACT OF Precision Medicine

Industry leaders provide their perspective on how precision medicine will impact the future of the life sciences.

In June, The Senate Labor, Health and Human Services, and Education Appropriations Subcommittee passed an appropriations bill that would provide the National Institutes of Health with $34 billion in 2017 in part to advance precision medicine research as part of the Precision Medicine Initiative.

The Precision Medicine Initiative has both short-term and long-term goals. The short-term goals involve expanding precision medicine in the area of cancer research. Researchers at the NCI hope to use this approach to find new, more effective treatments for various kinds of cancer based on increased knowledge of the genetics and biology of the disease. The long-term goals focus on bringing precision medicine to all areas of health and healthcare on a large scale. To this end, the NIH plans to launch a study involving a group of at least 1 million volunteers from around the United States. Participants will provide genetic data, biological samples, and other information about their health. These data will be used by researchers to study a large range of diseases, with the goals of better predicting disease.

Precision medicine's original premise was to match an individual's tumor DNA to a specific therapy, says David Cooper, M.D., Ph.D., scientific officer, Giles & Associates Consultancy. It is transitioning to benefit patients in three major areas.

First he says, where validated effective therapy options are not available, new hope of efficacious therapy in development is possible through expansion into first-in-man and Phase I clinical trials. Precision medicine enables clinical studies, sufficient in size, for clinical trial advancement due to establishment of patient cohorts, built across multiple cooperative institutions and based on innovative drugs matched to tumor genotype/phenotype. With the advent of basket studies, patients gain broader access to the most promising treatment in clinical development.

The second area of transition, according to Dr. Cooper, is the growing field of immunotherapy, which shows extraordinary promise in assisting or replacing standard chemotherapy. The early success of checkpoint inhibitors has brought greater attention and investment to other areas as well, including: advances beyond checkpoint inhibitors; activation of T-cell receptors by various approaches (e.g. bi-specific antibodies) to overcome the suppression of the cytotoxic T-cell response allowing tumor proliferation; targeting of inducible T-cell co-stimulator (ICOS) to promote T-cell function and antitumor response; and control of the immune response against cancer by the tumor microenvironment.

Finally, Dr. Cooper says newly diagnosed patients will be treated by a combination of drugs designed for both a specific driver mutation and to generate significant and specific immune responses. Patients will further benefit from the increased understanding of mechanisms associated with resistance, subclonal proliferation and/or morbidity associated with current multiple drug combination therapy. These developments reflect a second generation in precision, beyond first generation precision medicine driver mutation/drug matching.

"Big data and cognitive machine learning will play a crucial role, as we improve our understanding and integration of data fields associated with patients and their medical history, treatment and outcomes," Dr. Cooper adds. "For example, next-generation precision medicine will use combined data from multiple technologies (i.e. NGS, proteomics, metabolomics) and biomarker classes to stratify patients more appropriately."

Olivier Lesueur, managing director, Bionest Partners, says the future view of precision medicine is likely to be broad.

"As we gain further understanding of the biology of particular diseases and develop more relevant tools, data, and diagnostics, we envision precision medicine as enabling the constant monitoring of patient health status in real time," he says. "This vision for precision medicine goes beyond biomarkers or individualized treatment for disease, to the ability to catch and intervene in potential health problems at their earliest, most treatable stages, as well as in real time throughout the disease journey. In addition, precision medicine could raise the quality of life for many by better maintaining their health and prioritizing treatments matching patients' medical, financial, and societal needs."

The hope is to be able to engage patients more fully to directly participate in research, regardless of where they live, and contribute to the effort to improve outcomes for all subjects, particularly with advanced cancers, says Panteli Theocharous, Ph.D., VP, global product development, hematology/oncology at PPD.

"This approach highlights the possibilities that arise for advancing research when patients and researchers are able to collaborate," he says. "By working together, the hope is that researchers will be able to gather more information about diseases such as metastatic breast cancer, which appears to be a strategic area of focus for the NIH initiative, that can lead to new treatments for patients across differing disease entities."

Kate Haviland, chief business officer, Blueprint Medicines, says focusing on the drivers of disease and the subsets of patients believed to be most likely to respond to a given treatment may make the path to clinical development more efficient, and potentially increases the likelihood of improved patient outcomes.

"Precision medicine has the opportunity to greatly enhance how we research, develop, and practice medicine," Ms. Haviland says, "The ultimate goal of medicine is to provide the right patient, with the right treatment, at the right time. Although advances have been made in precision medicine, this vision has a long way to go before it becomes a reality for many patients. This ultimately provides the industry with a multitude of new challenges and opportunities."

Precision medicine, by definition, implies that the use of a particular medicine is based on a known specific feature of the patient or their condition, and therefore the patient should have a higher likelihood of benefiting from treatment with such a medicine, says Ali Fattaey, Ph.D., president and CEO of Curis.

Matthew Majewski, a consultant at Charles River Associates, says for this area of medicine to become more mainstream, foundational changes need to occur within the clinical development and commercial functions of biotech and pharmaceutical manufacturers.

On the clinical side, Mr. Majewski says most clinical development programs focus on biomarker identification later in the asset

development cycle, creating challenges in pairing precision metrics with clinical trials. Biomarker identification will need to move earlier in the product lifecycle to gain necessary clinical support.

"While the clinical and commercial challenges appear significant, the potential of precision medicine is likely to attract at least a few manufacturers willing to test their mettle over the next few years," he says.

Binh Nguyen, M.D., Ph.D., VP, global product development, hematology/oncology at PPD, says this means clinical researchers will need to screen many more patients to find only those with a specific tumor marker that are eligible for a clinical trial, for example fewer than 10% of lung cancer patients have ALK-positive tumor expression. This would potentially add to the timeline as well as the cost of the overall clinical development plan of these targeted agents."

The future of precision medicine is not about finding off-the-shelf drugs for the right patients, but instead tailoring bespoke medicines for each and every patient, says Hugh O'Dowd, CEO of Neon Therapeutics.

In December 2015, the company announced a collaboration with Bristol-Myers Squibb. The collaboration will evaluate the combination of Neon Therapeutics' proprietary personalized neoantigen vaccine, NEO-PV-01, and Opdivo (nivolumab), which is approved to treat several cancers, include non-small lung cancer, metastatic melanoma, renal cell carcinoma, and classical Hodgkin lymphoma.

Neon's lead program is a personalized neoantigen vaccine that builds upon initial clinical trials developed collaboratively by the Broad Institute and Dana-Farber Cancer Institute. Dana-Farber is conducting two investigator-initiated trials studying the personalized neoantigen vaccine in melanoma and glioblastoma.

Rami Levin, president, North America, SOBI, also believes precision medicine opens new avenues of research never before deemed viable and is transforming the business models of some industry players.

Sobi is in the late stages of preclinical development of SOBI003. Preclinical studies to date with repeated systemic infusions have demonstrated efficacy in reducing substrate levels in the brain and signs of disease modifying effects. Sobi is preparing for clinical studies, which it plans to start in 2018.

Olivier Lesueur, managing director, Bionest Partners, believes there is a need to integrate more longitudinal biomarker monitoring before, during, and after treatment for an increased variety of treatment regimens. The resulting boom in data influx, initially mostly retrospective, will require companies to become increasingly agile and rapid in making decisions related to development strategy and to act upon this new knowledge coming down their way, in order to seize new opportunities."

Rajneesh Uzgare, Ph.D., medical strategy, Fingerpaint, says treatment with personalized medicines may lead to a higher percentage of patients responding to treatment and/or a better outcome for patients. He points to a recent study of more than 13,000 cancer patients who reported that six times more patients responded to personalized treatments compared with nonpersonalized treatment and remained cancer-free for a longer period of time. Personalized treatment can also mean fewer side effects, either due to the targeted nature of the therapy or by avoiding the need

Precision Medicine's Impact on R&D

As our understanding of the biology of disease progresses through genomics, proteomics and the other 'omics, researchers and the life-sciences industry should increasingly be able to target therapies to select populations affecting all aspects of the R&D lifecycle.

- Trial sizes are decreasing, primarily because drugs are now better targeted to patients with defects specifically addressed by the new therapy. As a result, the drug is not given to patients who did not have the pathway abnormality and therefore clinical efficacy can be shown with a smaller sample size.
- Recruitment for clinical trials is becoming more difficult and dependent on access to real-world data. For clinical trials in precision medicine, researchers need to find patients with very specific clinical and often lab (biomarker and other genetic) features. Finding these patients quickly and efficiently requires access to data and networks of investigators and clinicians that are driving new partnerships and paradigms in drug development. Access to rich data assets in clinical research is enabling smarter, more efficient clinical development.
- Increased requirements for post authorization safety studies (PASS) and postmarketing registries is another impact of precision medicine. Better targeting of patients can show efficacy with much smaller studies. However, these studies have a higher chance of missing rare but potentially serious side effects. As a result, regulators are likely to require postmarketing studies and registries for these new medicines.
- Precision medicine should result in an increased demand for postmarket data, to inform safety and effectiveness of drugs in different types of patients in the real world. Real-world evidence studies increasingly will need to compare different populations and be used by regulators, payers, and health-technology assessment bodies to evaluate price, reimbursement, and guide how products are used and commercialized.

Source: Brian Kelly, M.D., President, Payer & Provider Solutions, QuintilesIMS

THE REALITIES OF Precision Medicine

Industry experts discuss the potential of precision medicine and the impact this will have on R&D and commercial operations.

LISA BOYETTE, M.D., PH.D.
CEO of Curable

We're learning that just about every cancer is a unique cancer. We know there are huge gaps in meeting the needs of rare disease patients, who constitute 10% of the population collectively. We all want to live in a world where we can take the minimum required therapy for our disease and get well, and the goal of precision medicine is to use data at the individual patient level to make that happen. That means more refined therapies for patients who currently have access to treatment, and it means getting access to medical therapy for patients who currently have nothing available to them.

It also opens up more avenues for therapeutic approaches like cell-based therapies. Ultimately, precision medicine also means having real understanding of what is going on in our own bodies, which is something we all would like to have when something goes wrong

KATHY GIUSTI
Founder, Multiple Myeloma Research Foundation & Consortium

Going forward, we need to continue to create precision medicine models because we know they work in both cancers and other disease areas. The MMRF was one of the first organizations to be founded on this principal; our research model pairs big data with powerful analytics to uncover new drug targets and inform clinical trials, tripling patient lifespans. Patients immediately reap the benefits of medicines that are tailored specifically to them. With the amount of research needed to understand and create these new treatments, healthcare companies also stand to benefit. Additionally, improved treatments will help keep patients out of hospitals, saving money for our healthcare system. In order to progress precision medicine, we need to focus on both sharing data and having transparent conversations with different industries to expedite therapies and prolong patient lives.

ROBERT GROEBEL
VP of Global Medical Strategy, Veeva Systems

Manufacturing is the other big area to be impacted by precision medicines. While highly personalized drugs can produce better outcomes for patients, they also make manufacturing processes more complex as these products typically have greater product variants and smaller batch sizes. Their unique physical requirements will also impact how they move through the supply chain. Simply put, precision products are finicky and need to be handled with extra care. Traditional manufacturing and quality functions will struggle to keep pace unless there is a fundamental change to the way manufacturers produce and how they collaborate with external partners. Transparency will be key to maintaining quality and compliance. This is where modern cloud technologies can be instrumental because they enable full visibility in real time.

BRIAN KELLY, M.D.
President, Payer and Provider Solutions, QuintilesIMS

Understanding how patients metabolize a variety of drugs through pharmacogenomic testing should allow significant improvements in our ability to properly dose patients, leading to better clinical outcomes and fewer adverse side effects.

Cancer patients and patients with rare diseases will likely be among the earliest beneficiaries of precision medicine. Within oncology, knowing whether a specific drug will help a patient before it's administered spares that patient the side effects associated with that agent. Furthermore, it allows the oncologist to move immediately to another therapy with a better chance of helping the patient thereby treating the cancer sooner.

In rare diseases, precision medicine often allows us to know if a drug will work in an individual patient based on our understanding of the disease. As all drugs have potential side effects and many of these new therapies are very expensive, it allows us to give these therapies selectively to patients who'll benefit. As our understanding of altered biological pathways expands through precision medicine, combining different drugs addressing those variances furthers our ability to fight cancer and find cures in rare diseases.

ANNETTE LESLIE
Co-founder, Carson Leslie Foundation

Applying precision medicine to reveal the biological basis of many cancers has transformed how we think about treatments, and potential cures. We now better understand its many subtypes and the mechanisms, pathways, and alterations shared among different cancer types.

Precision medicine focused on genetic changes has enabled numerous indication approvals for molecularly targeted treatments. It has also helped advance the checkpoint inhibitors, unleashing the best disease-fighting machine ever invented — the human immune system — to overcome cancer. These therapeutic approaches hold tremendous potential for patients but only if all cancer patients, adults and children — with all cancer types — have treatments advanced against their diseases.

OLIVIER LESUEUR
Managing Director
Bionest Partners

Precision medicine may provide increased value to both industry and customers, positively impacting drug development efficiency, development risks, clinical trials cost and duration, and eventual clinical outcomes.

Precision medicine provides a great opportunity for three industries, until now somewhat distinct, to draw bridges and add value together. Drug, diagnostic, and data industries will indeed increasingly need to work together across the whole value chain from research to commercialization to realize the full potential of precision medicine.

Cancer is an area where we have already seen some clear successes; where biomarkers have been used to both support research efforts toward more targeted therapies and to enrich patient populations to improve overall clinical outcome. At the same time, critics point out that this trend could be pushed to the point that cancer — or indeed any indication — becomes a collection of ultra-orphan indications addressed with treatments priced at ultra-orphan price levels. Such a scenario might not be economically sustainable in the long run.

MICHAEL PENCINA, PH.D.
Faculty Associate Director, Director of Biostatistics and Professor of Biostatistics and Bioinformatics, DCRI Center for Predictive Medicine

Precision medicine is likely to have a profound impact on development of new therapies. We are already witnessing a shift from one-size-fits-all to more personalized approaches in the conduct and analysis of clinical trials. That means trialists will need a plan for appropriate data collection to facilitate construction of predictive models. Why? Because predictive models are the essential link between clinical trials and precision medicine. Data from large trials that historically summarize overall average treatment effects are being used for a more deliberate investigation of which patients actually benefit.

We are seeing this shift in cardiovascular disease prevention with the emergence of novel cholesterol-lowering medicines such as PCSK9 inhibitors. These expensive drugs need to demonstrate their value over and above what can be accomplished with highly effective statins. This creates the need for a personalized assessment of individuals who might benefit most, including those who are statin-intolerant or do not fully respond to statins. Such assessment can be augmented with the help of advanced analytic techniques, including machine learning methods, which can incorporate both phenotypic and genetic data to construct predictive modeling trajectories that recognize patient diversity in responses to therapy.

HUGO STEPHENSON, M.D.
Executive Chairman, DrugDev

Anything that improves patient outcomes is good for the industry, and precision medicine has the power to disruptively improve outcomes at scale. But this approach requires turning the process of drug development on its head. Instead of developing and testing small molecules in many thousands of patients, this model requires developers to evaluate a process that will produce a very tailored therapy — usually an antibody or immunomodulator — that will only work in the patient it was created for. We will be evaluating the effectiveness of a production process to produce custom products versus evaluating an end product.

PANTELI THEOCHAROUS, PH.D.,
VP, Global Product Development, Hematology/Oncology, PPD

With genomic testing of tumors becoming increasingly available, studies will help more patients benefit from precision medicine approaches. Although it is still too early to draw conclusions, recent drug development findings in the breast cancer setting suggest

to take nonspecific drugs that may have greater side effects.

"Increased efficacy and fewer side effects are value propositions that the insurance industry is likely to embrace more easily, and they may reduce patient burden for treatment costs," Dr. Uzgare says.

Richard Tsai, VP of marketing, Inspire, says the industry needs to look beyond precision medicine, and leverage other patient data such as digital, behavioral, emotional, and other sources of information. Combined with genomic data and other structured/unstructured data over time, we will be able to better understand health outcomes and personalized treatment regimens.

"From smaller, well-defined patient groups to large populations with chronic disease, the opportunity and challenge is to put massive data sets and genetic information to work to better inform treatment choices — achieving better relief, faster time to relief, and reduced likelihood of adverse events," says Michael Pencina, Ph.D., faculty associate director, director of biostatistics, and professor of biostatistics and bioinformatics, the DCRI Center for Predictive Medicine.

Brian Kelly, M.D., president, payer and provider solutions, QuintilesIMS, says to harness the opportunity of precision medicine, the industry will require new skill sets and more agile, data-driven approaches.

"For example, access to extensive real-world data to quickly locate and enroll patients for clinical trials, as well as new partnership models with healthcare providers, are needed across all phases of the drug development cycle," he says. "A deep understanding of genomic lab data and the ability to integrate it with clinical and cost data in real-world evidence hubs and then apply advanced analytics and machine learning will be required."

Lisa Boyette, M.D., Ph.D., CEO of Curable, says precision medicine is all about the data.

"If we as an industry can tackle the data management challenges of the rapidly expanding knowledge base we're collecting in trials and in the clinic, and learn to make the most of that knowledge, we will identify a lot more targets and be able to put things in the pipeline that are more efficacious," she says. "Implementing precision medicine will require overhauling our clinical trials system and changing our mentality about what constitutes an effective therapy for the individual patient. It will entail growing pains. But if we do it right, adopting a precision medicine approach will enable us to serve a much bigger slice of the public, and that's a boon for the industry."

Kevin Connolly, VP, account management, at C3i Healthcare Connections, adds as drug treatment becomes more narrow and precise, so too must the patient-support programs.

that, for example, HER2-targeted therapy could be expanded beyond the current indications of HER2-positive breast and gastric cancers.

Recent research also has shown us that a liquid biopsy such as a simple blood draw can be a highly informative, minimally invasive alternative when a tissue biopsy is insufficient for genotyping or cannot be obtained safely. Moreover, this test provides an unparalleled opportunity to monitor changes in the cancer as it evolves over time, which can be critical for patients and physicians.

KATE TORCHILIN, PH.D.
CEO, Novaseek Research

The impact of precision medicine will be that patient-centricity becomes even more critical at all stages of R&D, from discovery through the commercialization of new therapies and procedures. During the discovery and development stage, this means designing studies and trials that more accurately reflect real-world patients. Historically, life-science research has not been run efficiently, and one of the reasons that so many trials fail is because too diverse of a patient cohort, which is not always the right fit for the treatment being investigated, are enrolled into the study.

We need to transform how clinical researchers access and interact with clinical patient data and draw insights to design better, more successful trials that get the right medicines to the right patients sooner. Equipping clinical researchers with real-world clinical data, as well as biospecimens annotated with historical and longitudinal clinical information, is one way we are moving in that direction. Researchers benefit through easy access to data gathered from actual patients that inform complex inclusion/exclusion criteria, as well as access to advanced planning analytics, ultimately decreasing the risk of R&D projects and improving study success.

JOY YUCAITIS
Senior Director, Oncology Strategy Novella Clinical

Multiple technologies are beginning to translate and realize this dream of personalized care — particularly in the cancer field — including gene therapy, targeted sequencing, biomarker research, and oncology diagnostics. Decreasing the cost of next-generation sequencing has enabled its integration into the clinical decision-making process, including within cancer research. It is common practice now to screen cancer patients for specific biomarkers to better evaluate and determine the optimum treatment for them. Until very recently, standard of care treatment cocktails were prescribed to newly diagnosed cancer patients based on the cancer type. Upon the failure of these treatments, alternative treatments were offered to find a combination that works for the patient. Using the treatment matched to the patient sooner offers the best chance for remission or cures. It also reduces the opportunity costs of removing potential patients from the recruitment pool for targeted treatments, delaying the clinical development of promising new treatment options.

Providing patients with the treatment most likely to succeed for them from diagnosis reduces healthcare costs associated with treatments not likely to benefit specific patients and may preserve tumor sensitivity to other treatments, raising the chances for treatment response in the case of recurrence. By understanding tumor type and monitoring mutations as they evolve through cycles of chemotherapy, patients may find improved outcomes and quality of life. However, it will be important to track long-term clinical outcomes of patients whose treatment decisions were influenced by precision medicine to confirm the success of this strategy.

"When developing patient-support programs, precision medicine challenges companies to consider the entire person, not just the patient who is receiving the treatment," he says. "As a result, this means designing programs that are adaptive to the stages of a treatment program and a more detailed consideration to the level and type of support the patient receives. This might mean pairing a patient with a single health coach throughout the entire journey, who then becomes a trusted partner; forgoing a script to encourage patient-driven conversations; and providing nontraditional supplement services, such as social work, insurance navigation, and even transportation. Collectively, these patient-centered factors will only help increase adherence and, in some cases, enhance patient satisfaction with the treatment."

On the commercial side, Mr. Majewski says teams will need to launch and manage more precision medicine products targeted at smaller niches to keep revenues up. Access challenges within managed care may be doubled to accommodate biomarker testing. Furthermore, precision medicine products are likely to have more complex patient treatment pathways due to the related diagnostic testing. The need for more nimble teams with skillsets catered to precision medicine implies that a new commercialization model may be required.

Alan Shuldiner, M.D., VP and co-head, Regeneron Genetics Center, Regeneron Pharmaceuticals says precision medicine is already increasing efficiency in the selection of new drug targets, the design of clinical trials, and even the diagnosis and treatment of certain diseases.

"We know that precision medicine will be a huge part of the future of drug discovery and development, and the establishment of our Regeneron Genetics Center nearly three years ago reflects this belief," Dr. Shuldiner says.

The company's partners at Geisinger Health System and other collaborators are already using genomic data in their clinical care.

"After we sequence de-identified patient DNA, our collaborators are able to screen for certain findings that are known to be potentially causative or diagnostic of disease and then confirm those findings in a CLIA-certified lab," he says. "It's a top priority to ensure that any information being returned to patients is fully confirmed and delivered by qualified clinicians. Indeed, we already know of several instances in which the return of genetic results has impacted patient care in very positive ways. In the long-term, the anticipated benefit is of course the development of new and improved medicines based on the early research findings that we are seeing today." PV

Considerations for Diagnostics

DR. CHITRA LELE
Sciformix

The benefits of precision medicine come at a significant cost. Affordability for the patient, government assistance, the basis for payer's reimbursement decisions are all open questions that will determine the extent to which the potential benefit of precision medicine can be actually realized by the patients.

Reliable genetic testing is a prerequisite for the success of precision medicine. Although regulations have facilitated speedy commercialization of diagnostic tests based on genomic sequencing, the tests are often quite expensive and their reliability is questionable, with high rates of false negatives and false positives. This makes it difficult for insurance companies to decide about paying for these tests.

The following factors merit attention in the context of diagnostic tests:

- Commercialization of the drug has to be tied with the accompanying diagnostic test. The biopharmaceutical company needs to partner with the diagnostic testing company so that the test will receive regulatory clearance at the same time.
- Genomic sequencing is not common, limiting the number of people who can participate in clinical trials for precision medicine products. It also makes robust evaluation of the diagnostic tests difficult. Advances in analytical tools in the HEOR framework and real-world evidence can be used to harness the vast amount of genomic and clinical data and derive insights that will help in the commercialization of precision medicine.

Source: Dr. Chitra Lele, Chief Scientific Officer, Sciformix