

The Personalized Medicine Coalition, representing scientists, patients, providers and payers, promotes the understanding and adoption of personalized medicine concepts, services and products to benefit patients and the health system.

Summer | 2012

Levin Keynote Highlights Personalized Medicine's Progress

Outlines Need for Continued Collaborations Among Academe, Industry, Policymakers and Venture

Speaking at the Personalized Medicine Coalition's (PMC) Eighth Annual State of Personalized Medicine Luncheon in May at the National Press Club, Mark Levin, **Third Rock Ventures** co-founder and partner, put personalized medicine in the context of the history of medicine and described the imperative for cooperation and collaboration across sectors and industries to continue progress in offering patients effective and safe treatments targeted to the molecular bases for disease.

Addressing attendees of the annual luncheon including PMC members from industry, academe and clinical care, as well as representatives from

government and media, Mr. Levin underscored the progress made since mapping of the human genome was completed in 2003.

"Breakthroughs are starting to come," he said, acknowledging that discovering and commercializing personalized medicine treatments and diagnostics has taken longer than many in the industry thought it would. "But," he added, "you haven't seen anything yet."

For progress to accelerate, he said, the health care community and all of the various industries that touch personalized medicine need to come together to make this vision a reality.



ELIE VAN HOUTTE PHOTOGRAPHY

Mark Levin addresses attendees at PMC's annual luncheon

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FROM THE PRESIDENT



Policy Alignment Needed to Accelerate Progress in Personalized Cancer Medicine

BY EDWARD ABRAHAMS

"Personalized medicine," the Personalized Medicine Coalition's strategic plan proclaims, "must overcome numerous hurdles," particularly in the areas of regulation, reimbursement and education in order to accomplish the Coalition's twin objectives: improve care for patients and make the health care system more efficient. But "decades-long patterns of intertwined

and/or misaligned regulations, guidelines, investment, incentives and perceptions, must be changed."

How can we do this?

Our attention this year is focused on two opportunities: to articulate the case for continued progress in cancer research

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POLICY UPDATE

National Bioeconomy Blueprint Showcases Personalized Medicine as Model for Strengthening U.S. Bioeconomy

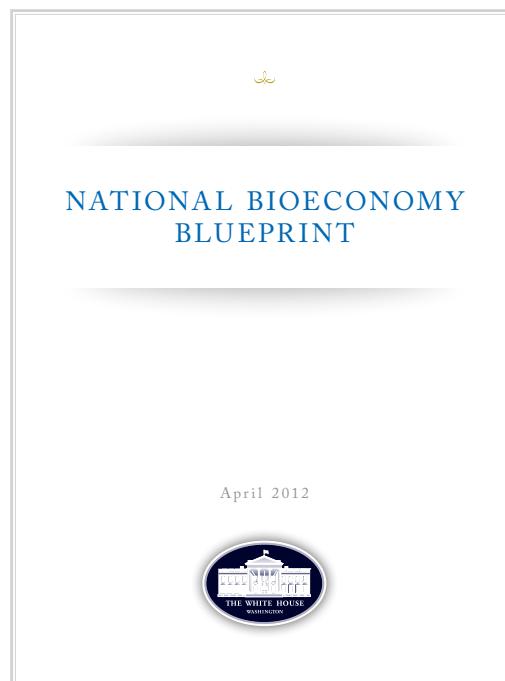
The White House released its *National Bioeconomy Blueprint* that lays out strategic objectives designed to help realize the full potential of the U.S. bioscience sector to create jobs and address societal needs. As an example of how the government's efforts can facilitate the development of a more robust bioeconomy, the report discusses the impact of the Human Genome Project and the development of personalized medicine. It cites PMC's *The Case for Personalized Medicine, 3rd Edition* noting that "advances in recent technologies have increased the momentum of personalized medicine—customized health care based on specific genetic or other information of an individual patient." To move the U.S. bioeconomy forward, the White House report states, policy should aim to:

- Support R&D investments that will provide the foundation for the future U.S. bioeconomy.
- Facilitate the transition of bioinventions from research lab to market, including an increased focus on translational and regulatory sciences.
- Develop and reform regulations to reduce barriers, increase the speed and predictability of regulatory processes, and reduce costs while protecting human and environmental health.
- Update training programs and align academic institution incentives with student training for national workforce needs.
- Identify and support opportunities for the development of public-private partnerships and precompetitive collaborations—where competitors pool resources, knowledge, and expertise to learn from successes and failures.

Legal Questions Remain Despite Supreme Court Rulings in *Prometheus* and *Myriad* Cases

The Supreme Court on March 21 ruled unanimously in the *Mayo v. Prometheus* case that Prometheus' method claims were not patent eligible because they effectively claimed a law of nature. At issue in the case was the patent eligibility of biological methods involving measuring metabolites after administering a drug to a patient to assist in determining appropriate dosage.

Subsequently, the Supreme Court on March 26 asked the Federal Circuit court to reconsider its decision in the *Association for Molecular Pathology v. Myriad Genetics* case. In *Myriad*, the major claims in question regard isolating the BRCA gene, presence of which increases the likelihood that a patient will develop breast or ovarian cancers. Because the case was sent back to the Federal Circuit, it will likely be several months before a ruling on the patent-eligibility of isolated DNA is reached.



Front cover of the *National Bioeconomy Blueprint*

FDA User Fee Legislation Working Through Congress

Congress must reauthorize legislation every five years to provide FDA with the authority to collect user fees from drug and device manufacturers. These fees enable the agency to carry out its mission by providing resources necessary to review the safety and effectiveness of new products in a timely manner. Congress has until September 30, 2012 to pass this legislation without interrupting FDA's funding stream by letting the existing law expire.

In addition to the user fee-focused provisions, both the House of Representatives and Senate versions of the bill include several sections that could improve regulatory processes for personalized medicine products. They include an expedited approval process for drugs that are both developed using biomarkers and used to treat serious or life-threatening ailments and a process that would enhance FDA's ability to evaluate the safety and effectiveness of personalized medicine products by allowing the agency to consult with external experts on the genetic targeting of treatments and innovative trial designs.

The legislation has passed the House of Representatives and Senate. Differences between the two versions must be reconciled before final passage and the president's signature.



National Bioeconomy Blueprint Suggests Incentives and Clearer Regulatory Environment Can Facilitate Innovation; Will Congress and FDA Make the President's Vision a Reality?

BY AMY MILLER | VICE PRESIDENT, PUBLIC POLICY

The White House Office of Science and Technology Policy released the *National Bioeconomy Blueprint* in late April. Two of the five strategic imperatives highlighted in the blueprint mirror PMC's policy agenda. Specifically:

- Support R&D investments that will provide the foundation for the future bioeconomy; and
- Develop and reform regulations to reduce barriers, increase the speed and predictability of regulatory processes, and reduce costs while protecting human and environmental health.

PMC has long held that policymakers should encourage investment in personalized medicine R&D. Such incentives are necessary because personalized medicine business relationships are complex and often fraught with uncertainty given the difficult nature of the science.

PMC has also advocated for regulatory reforms to streamline the currently bifurcated regulatory system and provide additional clarity to diagnostic companies to encourage the development of new personalized medicine tests.

But what the administration says publicly in an election year and what Congress and the Food and Drug Administration (FDA) do to craft and enforce policy based upon the President's goals remains to be seen.

Given the contentious nature of personalized medicine regulation at FDA and the need for Congress to pass legislation reauthorizing drug and device

user fee agreements by September 30, 2012 (or risk a scenario where FDA cannot collect the fees it charges product developers), PMC does not expect Congress or FDA to take any action on personalized medicine until after the user fee legislation is passed by both houses of Congress and signed into law by President Obama.

PMC and others in the personalized medicine community had hoped that the user fee acts would be a vehicle for Congress to enact incentives for personalized medicine. While we were disappointed that it appears Congress will focus only on long-discussed, non-controversial additions to the basic

Even if all regulatory uncertainty is resolved, evidence and payment issues will continue to challenge developers of personalized medicine products.

industry-negotiated user fee agreements, we were pleased that a section of the bill designed to speed drug approval and increase patient access to new medicines contains language that urges the fast-tracking of new drugs developed based on biomarker information.

But once these laws are enacted, we believe that FDA will release draft guidance proposals that will offer some additional clarity to the personalized medicine community, along the lines outlined in the *National Bioeconomy Blueprint*.

While PMC supports the administration's effort to create R&D incentives and streamline regulation, we are also considering proposals for the regulation of the diagnostics industry and working to build consensus among diagnostics stakeholders on what such a regulatory framework could look like.

Laboratory service companies, diagnostic kit manufacturers and specialized diagnostics companies presented their ideas about the regulatory framework to the PMC Public Policy Committee in February. While the clinical laboratory community favors policies that clearly remove FDA from the regulation of laboratory-developed tests (LDTs), diagnostic kit manufacturers maintain that FDA should regulate all diagnostics, including tests preformed as laboratory services. Perhaps the diagnostics sectors and the rest of the personalized medicine community can work together to develop a proposal that brings these two perspectives to the middle as a realistic and holistic solution that permanently removes the regulatory uncertainty. At this point, it seems that many stakeholders agree that there is a place for FDA regulation of LDTs, but that FDA should only regulate the highest-risk tests (though stakeholders differ on ways to define risk).

Even if all regulatory uncertainty is resolved, evidence and payment issues will continue to challenge developers of personalized medicine products. Building on earlier efforts, PMC is working with the **Biotechnology Industry Organization (BIO)** to examine solutions to these challenges.

Cross-Industry Collaboration Needed to Speed Progress

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"We need to get beyond ourselves," he said. "We need to address the challenges that innovators face, starting with the number one challenge for personalized medicine today: reimbursement." Mr. Levin called for collective action to realize personalized medicine's full potential to transform patient care and deliver efficiencies to the health care system.

"We need to put aside our focus on our individual needs, and work together to envision a regulatory and reimbursement system that can inspire continued innovation," he said, adding that pharmaceutical companies, diagnostics companies, payers, regulators, hospitals and the venture community all have a role to play.

Stafford O'Kelly, President of **Abbott Molecular** and chairman of PMC's Board of Directors, emphasized when introducing Mr. Levin the importance of cross-industry partnerships to overcome the scientific, business and policy barriers to personalized medicine, noting that Mr. Levin, as CEO of **Millennium Pharmaceuticals**, had provided the initial funding for PMC and helped define its purpose.

"We need to get beyond ourselves"



ELIE VAN HOUTTE PHOTOGRAPHY

PMC Board Chairman Stafford O'Kelly looks on while Mark Levin discusses the need for collaboration across personalized medicine sectors at the National Press Club.

"The Personalized Medicine Coalition is a forum for all of the industries and institutions with an interest in the future of health care to come together and work with policymakers to put in place a common agenda that will accelerate the pace of personalized medicine's development," Mr. O'Kelly said.

It appears that policymakers are slowly heading in that direction. PMC's Luncheon was held just days after the White House Office of Science and Technology Policy released its *National Bioeconomy Blueprint*, which called out personalized medicine as a technology with tremendous potential to "transform medicine." The White House cited PMC's *Case for Personalized Medicine, 3rd Edition*, to make the distinction between common treatments whose effectiveness is based on studies of groups of people, and personalized treatments that are designed according to an individual's specific medical needs.

Mr. Levin also addressed those in the venture community who have limited their investments in personalized medicine companies, citing concerns that the regulatory and reimbursement systems are not yet evolved enough to generate the returns that investors seek.

"Third Rock Ventures needs partners to build the cutting edge personalized medicine companies that will deliver the treatments of tomorrow," he said, noting that his firm will invest more than a billion dollars in personalized medicine companies over the next decade, much of it in early-stage projects.

Among Third Rock's current investments is **Foundation Medicine**, an oncology company with a pioneering approach to identifying the right treatment for cancer patients by sequencing cancer tumors and providing physicians with suggestions for combination therapies that attack the mutations in the tumor sample.

Personalizing CER: All Eyes on PCORI

During the U.S. health care reform debate, some legislators looked to the United Kingdom's National Institute for Health and Clinical Excellence (NICE) as a model for evaluating health care value and curbing rising health care costs. Many Americans, however, feared that this British model for comparative effectiveness research (CER) would lock the U.S. health care system into a one-size-fits-all paradigm and restrict patient access to new treatments. Ultimately, Congress chose a hybrid approach to CER; it created the Patient Centered Outcomes Research Institute (PCORI) to fund research into what treatments work best while requiring the institute to align CER with personalized medicine.

Still a young organization, PCORI has chosen Joe Selby, M.D., M.P.H. as its executive director, seated both its board of governors and its methodology committee, hired a few key staff, and asked the public for feedback on its definition of patient-centered outcomes research, draft translation framework components, and draft national priorities for research and research agenda.

PMC does not believe that the institute has developed the internal structure necessary to carry out its mission at this time.

On April 25, PCORI announced the finalization of its research agenda during an open conference call. During the call, the institute announced that on May 10, a methodology report would be sent to the Board of Governors and released for public comment and on May 21, PCORI would issue an announcement specifying the kinds of projects that would be eligible for funding and also announce a pilot project grant program. (Visit the PCORI website www.pcori.org for detailed information.)

Earlier that day, Dr. Selby addressed the PMC Public Policy Committee and discussed the institute's formation and upcoming activities. PMC members impressed upon Dr. Selby the importance of aligning personalized medicine with CER and expressed surprise that the research agenda and national priorities for research would be so quickly finalized in light of numerous public criticisms of the lack of specificity in them.

In public comments, PMC and other organizations discussed concerns that PCORI's broad and vague research priorities leave the personalized medicine community uncertain about whether PCORI-funded research will support the continued

development of personalized medicine as intended by statute. Selby countered that the agenda and priorities were intentionally vague so as to solicit a broad range of research proposals in the future.

"I doubt that PCORI will ever say 'here are the top ten conditions' we will study," he said, emphasizing his hope that PCORI-funded CER studies will answer questions about rare diseases as well as common conditions.

Members also questioned Dr. Selby about the development of PCORI's infrastructure, asking whether the institute has the expertise to align CER with personalized medicine. Although Congress required procedures to assure alignment, PMC does not believe that the institute has developed the internal structure necessary to carry out its mission at this time. Dr. Selby told the policy committee that PCORI would welcome feedback about how to assure that CER-studies align with personalized medicine through its open meetings, public comments and advisory committees.

In a letter to PCORI, PMC offered five recommendations about how the institute could better define its research agenda and build the infrastructure needed to execute its mission as Congress intended. They are:

1. *Public engagement process:* Outline an open, transparent process for obtaining input from stakeholders and detail how stakeholder input will be used.
2. *Personalized medicine expert advisory panel:* Create an expert advisory panel devoted to personalized medicine to assist the institute in aligning CER with personalized medicine.
3. *CER science focus:* Improve the quality of CER by incorporating new information and technological innovations into its studies by reviewing and updating studies as necessary, and by outlining what future research will be needed to address perceived information gaps.
4. *Specific research priorities:* Develop research priorities along the lines envisioned by statute that are both broad—encompassing all aspects of the health care system that relate to high-quality, effective patient care—and specific, calling for a transparent process to identify and prioritize research topics based on explicit criteria and public input.
5. *In-house capacity to engage broad scientific and clinical expertise:* Hire a highly-qualified set of individuals to develop calls for research proposals, evaluate them, make awards, follow the progress of the research, and engage the public in the process.

To advance personalized medicine, CER must explain not only what works best, but also for whom. Answering that critical question—upon which the future of medicine depends—cannot be done without careful construction and consideration.

IT Firms Pioneer Technologies to Propel Personalized Medicine and Manage Big Data Difficulties

Growth in the use of whole genome sequencing, the expansion of proteomics and molecular diagnostics, and the increasing incorporation of electronic systems to record patient encounters and organize records have one thing in common: they all generate volumes of health care data that can be used to identify new trends in health care outcomes and inform clinical decision-making. Confronting personalized medicine is the “big data challenge,” namely, how to store, analyze, and make all of that data clinically useful.

Collaborations Speeding Translation of Data

“There are numerous secondary uses for genomic and clinical outcomes data,” said Neil de Crescenzo, senior vice president and general manager, **Oracle Health Sciences**. “Ultimately it is these secondary uses of data that will help answer the hard and transformational questions in health care—what works, for whom, why, and in what context.”

One such application is making clinical trials faster and cheaper. Using Oracle’s platform, researchers at the **Moffitt Cancer Center** have been able to combine data from their bio-bank with patient-reported information to automate clinical trial candidate identification and advance personalized treatment approaches.

“The analytical capabilities are absolutely critical to the success of Moffitt’s Total Cancer Care™ model,” said Mark Hulse, Moffitt’s chief information officer, referring to the center’s effort to implement personalized medicine by biobanking patient tissue samples, storing patient data, and working with patients over time to suggest cancer treatment strategies based on newly-discovered information about cancer biology.

“With the rapidly dropping cost of whole genome sequencing, the challenge for personalized medicine is moving from generation of the data to analysis,” noted Brian Druker, M.D., director of the **Knight Cancer Institute at Oregon Health and Sciences University**, which, through a development partnership with Oracle for its Translational Research Center solution, a platform that brings together data from electronic medical records and cross-platform “omics” data, is deciphering the molecular underpinnings of disease and tracking changes over time.

Partnerships and collaborations are a common approach in this emerging field. Dell recently announced that it had committed funding and resources to aid the Translational Genomics Research Institute (TGen) by developing a cloud-computing technology to run the first FDA-approved personalized medicine trial for pediatric cancer.

“We hope TGen’s new cloud will help pediatric oncologists develop new ways to eliminate the trial and error in the treatment for pediatric cancer patients,” said Paul Bell, president of Dell Public and Large Enterprise and chairman of Dell’s Strategic Giving Council.

Using the Dell cloud, investigators at TGen have expanded their capacity for processing patient tumors by 1,200 percent, and improved their ability to predict the best drugs for a specific patient.

“Translational medicine based on genetic and molecular data has come into its own,” said Alpana Verma-Alag,

M.D., head of clinical development for **NextBio**, a company that uses big data solutions to improve molecular data interpretation for clinical applications, and identify patients most likely to benefit from personalized treatments.

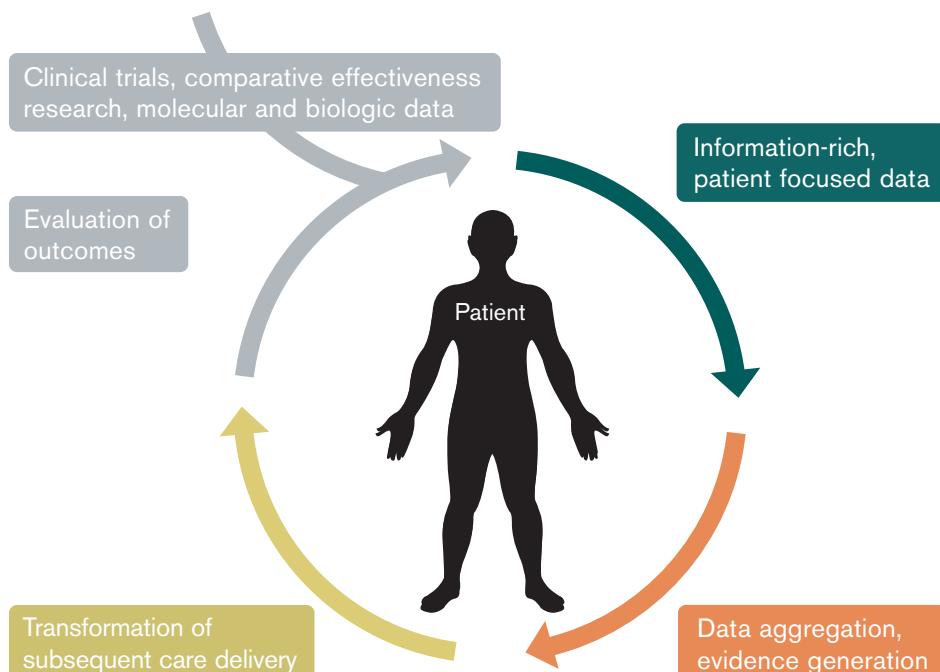
They aim to link de-identified genomic data with translational research findings to identify biomarkers for both drug discovery and clinical personalized medicine applications. “We have formed partnerships with several research hospitals to integrate our solution into their clinical decision-support workflows,” she added.

Such collaborative projects are not just happening in the U.S. Working with two of the largest research hospitals in London, Kings Health Partners in breast cancer and Imperial College Hospital in pulmonary hypertension, **IDBS** has developed a translational medicine platform that consolidates de-identified patient information from multiple clinical sites, and integrates biobank, imaging, pathology and omics data into one system.

These cross-hospital projects are an extension of IDBS’ previous experience with clinical cohort selection and omics analysis, but taken to the enterprise level, based on hosted solutions. “With the trend towards personalization of treatment, our platform is supporting a large variety of translational research scenarios and is now being drawn into supporting clinical decisions,” said Simon Beaulah, IDBS marketing director, translational medicine.

“With the rapidly dropping cost of whole genome sequencing, the challenge for personalized medicine is moving from generation of the data to analysis.”

—Brian Druker, M.D., Director of the Knight Cancer



Rapid learning health care model, by Amy Abernethy, M.D.

Scaling Data Solutions Continues to Elude Innovators

To date, most of the systems developed have focused on integrating data within specific niches and developing translational capacities for only a select group of patients or providers although some companies are trying to implement tools more broadly.

GenomeQuest, for example, has developed an informatics platform to store, manage, and analyze sequencing data so that molecular laboratories can produce actionable diagnostic reports based on next generation sequencing runs.

"The fact that next generation sequencing technology is becoming faster and cheaper is irrelevant to the

clinic if molecular labs cannot quickly analyze millions of variants to make specific, repeatable diagnoses. Manually identifying key genetic variation that has specific, well-characterized clinical relevance takes days for even the most sophisticated laboratories—too slow for clinical decision making," said GenomeQuest CEO Richard Resnick.

Still, it remains to be seen how big data solutions will interface with electronic medical records and practice-management tools on a larger scale and what clinical decision-support systems that seamlessly bring all of the pieces together will look like.

"The real win is going to be combining genotype and phenotype data into a common and robust

analytical system," said Donald Rucker, M.D., chief medical officer for **Siemens**. He noted that imaging tools are now able to produce thousands of image slices—more than an individual physician is capable of comprehending—and while Siemens has developed visualization tools to aid in clinical analysis, challenges to systematize the data remain. "Everything we know about a patient must converge," Rucker added.

Public Policy Challenges

Solving the big data challenge is critical for the future success of personalized medicine because clinicians depend on data-informed diagnoses to effectively select the best treatment for each patient. But despite protections offered by the Genetic Information Nondiscrimination Act, Health Insurance Portability and Accountability Act, Americans with Disabilities Act and the Common Rule, concerns over privacy complicate the secondary use of health care information.

Policymakers have noticed the big data challenge, but have yet to enact policies to fill the analytical gap left where the U.S. government's \$44 billion investment in electronic medical records systems left off. As the *Presidential Bioeconomy Blueprint*, issued in April 2012, noted, "new information technologies to enable scientists to handle so-called 'big data' will help stimulate the next transformative step toward realizing the potential of biological research across sectors." But it remains to be seen what incentives policymakers will put in place to facilitate that research as well as its translation into clinically-useful analytical tools.

FROM THE PRESIDENT

Conference to Highlight Policies Needed to Spur Cancer Progress

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and care to develop consensus among the Coalition's multiple constituencies regarding regulation, coding, payment and evidence requirements that govern adoption of personalized medicine concepts and products.

PMC, along with co-hosts the **American Association for Cancer Research** and **Feinstein Kean Healthcare**, will convene a national conference, *Turning the Tide Against Cancer Through Sustained Medical Innovation*, on June 12 at the Grand Hyatt in Washington, DC. Speakers and participants will consider how to sustain the notable progress made during recent years in fighting cancer, progress documented in AACR's *Cancer Progress Report 2011*.

But in an era of rising and unsustainable health care spending and increasing efforts to limit the introduction of and access to new technologies, progress in fighting cancer could be threatened unless we commit ourselves to policies that ensure that innovation, upon which patients' lives depend, is not stifled.

Given the growing role of personalized medicine in prevention, detection and treatment, the conference will focus on:

1. Understanding the evolving cancer care ecosystem;
2. Clarifying the dynamics of rapid change in the standard of care from multiple points of view, especially that of payers; and
3. Most importantly, accurately defining and measuring the value of tests, treatments, and technologies.

Indeed, the overall theme of the conference is that unless we can learn to appreciate *value*, we will put at risk the progress achieved—and the progress yet-to-be achieved—in both preventing



Keynote speakers Mark McClellan, M.D., Ph.D.; Siddhartha Mukherjee, M.D., DPhil.; and John Mendelsohn, M.D.

cancer and prolonging the lives of those inflicted by the dreaded disease.

Keynote speakers include:

- Mark McClellan, M.D., Ph.D., Director, Engelberg Center for Health Care Reform, Brookings Institution;
- Siddhartha Mukherjee, M.D., DPhil., Assistant Professor, Columbia University, and author of *The Emperor of All Maladies: A Biography of Cancer*; and
- John Mendelsohn, M.D., Professor, Department of Experimental Therapeutics, Division of Cancer Medicine and Co-Director, Institute for Personalized Cancer Therapy, The University of Texas MD Anderson Cancer Center.

The conference will also explore policies that support personalized medicine, upon which the health system depends.

Among other things, the health care system needs:

1. A regulatory system that is flexible enough to accommodate our rapidly evolving understanding of individual variation;

2. More responsive coverage, coding, and payment policies based on reasonable evidence requirements for personalized medicine products as well as a payment system that rewards innovation; and
3. Tax and other incentives that encourage the integration of different business models to create new products.

Progress in fighting cancer could be threatened unless we commit ourselves to policies that ensure innovation

As PMC Vice President for Public Policy Amy Miller explains in her column on public policy, progress on these fronts is real, albeit slower than we would like. As she writes, our focus will be to organize thinking regarding the regulation of diagnostics, in particular, complex genetic testing and exploring levels of evidence necessary for reimbursement and clinical adoption.

California Reception Highlights an Exciting Time for Personalized Medicine

The remarks below were excerpted from a speech by Sue Siegel, General Partner, Mohr Davidow Ventures, at PMC's California reception on February 22, 2012. Ms. Siegel recently announced that she will become CEO of GE's Healthymagination unit.



Sue Siegel

This is our opportunity to celebrate our collective successes in driving medicine toward personalized care and to reinforce where we need to continue in our efforts.

There are so many examples of progress in personalized medicine technology and policy. Today sequencing genomes is much more affordable (and faster); the Food and Drug Administration (FDA) is engaged and working more collaboratively with innovators; Medicare reimbursement seems to be improving with Palmetto's new guidelines; new drugs being approved and dispensed in isolation are becoming more of the exception than the norm; sequencing-based diagnostics are coming to the clinic fast and furious.

These changes have been hard-earned, but they are happening and they are making a real difference in patients' lives. It's incredibly rewarding to witness.

While we celebrate our accomplishments, we must also take advantage of the momentum we've created to further accelerate progress.

We must show Medicare's regional contractors what Palmetto is doing in our region and continue encouraging them and private payers to reimburse for complex diagnostic tests.

We can continue to encourage investment in innovation. Personalized medicine provides important products for patients and returns to investors. With many of the personalized medicine start-ups now in full commercialization, lots of the early risks have been reduced.

For those of us who have been involved in personalized medicine for a long time, it has, on occasion, felt like progress has been as slow as molasses. But if we tally the advancement in its entirety, we can begin to see just how much progress has been made and, furthermore, how it is accelerating.

We need to ensure the creation and publication of good health economic data quantifying the value that personalized medicine products can provide to the health care system. We also need to develop and share standard processes that people can work with to provide their health economics dossiers to payers.

We must also continue our dialogue with legislators and get behind the efforts of important organizations like the PMC, which unites the health care ecosystem behind a common agenda to advance the interests of the entire personalized medicine community. Specifically:

- Continue to communicate with the FDA regarding appropriate premarket oversight of In Vitro Diagnostic Multivariate Index Assays (IVDMIA) and continue our dialogue on the balanced oversight of other laboratory-developed tests (LDTs); and
- Work with the Centers for Medicare and Medicaid Services (CMS) and Congress on the implementation of the "Date of Service" modification legislation to ensure that these changes to the Medicare laboratory billing rules will improve patient access to advanced diagnostics and support innovation.

I should also call out that we are moving from a "patient" to a "consumer" mindset around health. More than ever before, new technologies (e.g. mobile technologies, social media, ubiquitous wireless sensors, etc.) are engaging consumers, and more importantly, are giving people the tools to take a more active role in managing their own health.

As consumers are fully activated, we will see an incredible multiplying effect in the demand for and participation in personalized medicine-related products and services. It is with the **E² consumer** (*E² = empowered and engaged*) that we will really see personalized medicine evolve to be as much about "well-care" as it is currently about "sick-care."

Changing the practice of medicine is a Herculean effort. The personal and collective efforts of many, many people are creating the multiplier effect needed for long-term, positive change. I feel proud of where we are and inspired for the future.

I look forward to working with you as we continue our mission to improve patient care and bring affordable personalized medicine to large populations, making it routine and the new standard of care.

The views expressed in this article are those of Sue Siegel and do not necessarily represent the opinions of the Personalized Medicine Coalition.

Personalized Medicine is Complex: We Must Make Our Message Accessible

BY AMY ABERNETHY, M.D.

Personalized cancer care holds much promise. It gives us confidence that targeted treatments will eliminate cancers and spare us the one-size-fits-all cancer treatments of our past. For the sake of simplicity, we want to think of personalized cancer care as a lock and key: each tumor has a specific puzzle interface, and when the puzzle piece is identified, the cancer melts. This simple message of "lock and key" suggests that we can achieve a new reality where we assess a tumor and choose a treatment in a very simple way, based on a tumor's genetic makeup.



Amy Abernethy, M.D.

We have many exciting new targeted cancer treatments in our toolbox—consider, crizotinib (Xalkori[®]) for non-small cell lung cancer and vemurafenib (Zelboraf[®]) for BRAF mutation-positive metastatic melanoma. These therapies have been effective in patients with specific gene mutations, but, after time, the cancers still return. As the science advances, research continues to reveal the underlying complexities of cancer and the diversity of tumors. To effectively target more cancer mutations,

we need to create thoughtful treatment cocktails to address multiple mutations simultaneously.

In the March 8 issue of *The New England Journal of Medicine* (NEJM), the authors of "Intratumor Heterogeneity and Branched Evolution Revealed by Multiregion Sequencing" provide an exquisite roadmap of how heterogeneous and complex one individual's cancer can be, with many evolving mutations lurking within each tumor mass. The picture presented suggests the need for many keys to many locks, each tailored for a particular tumor at a particular point in time. The simple message of lock-and-key personalized medicine, where simple one-to-one decisions can be achieved, doesn't recognize the complexity of cancer biology.

The media portrayed this study as a signal that the personalized medicine approach has created a false sense of hope. I don't think that it is false hope, but rather a false sense of simplicity.

But the study shed light on the need for continued leadership in educating physicians, policymakers and the media about personalized medicine. How do we illustrate the complexity of the science, but still make the descriptions accessible to a broad audience? How do we demonstrate how new personalized medicine tools will enhance our treatment toolbox, while maintaining a balanced viewpoint that more innovation and science are needed? How do we place scientific studies into context in a way that resonates with a non-scientific audience? And, how do we safely communicate the message that advances in personalized medicine are needed, while not scaring the public with the concept that current health care is not personalized?

The first steps in conveying the complexity of cancer and the biology underpinning other diseases is to create

an accessible language of personalized medicine that underscores the opportunities to improve care through the integration of targeted therapies into clinical practice, to iteratively match patient characteristics to treatments as more details become available, and to use more sophisticated decision-support tools and informatics platforms to help clinicians identify the best treatment for individual patients.

My vision as the new chair of the clinical science committee is to help PMC frame these issues, develop the

If we don't frame the discussion of personalized medicine, we risk hampering public support for the paradigm.

language of personalized medicine, and outline a method for connecting emerging personalized medicine trends with clinical practice.

The need is clear. If we don't frame the discussion of personalized medicine, we risk hampering public support for the paradigm and ultimately limiting our collective opportunity to improve the efficiency of the health care system. If we don't build the systems needed to deal with the deluge of complex information—to sort it, understand it, and ultimately figure out ways to employ it clinically, in real time, we risk locking our health care system in the status quo instead of developing a learning health care system that supports personalized medicine and our collective goal: improving patient outcomes.

Personalized Medicine Coalition Announces New Board Appointments

The Personalized Medicine Coalition has elected three leaders in personalized medicine to its board of directors: Neil de Crescenzo, Senior Vice President and General Manager for Health Sciences at **Oracle**; Lawrence J. Lesko, Ph.D., F.C.P., Professor and Director, Pharmacometrics and Systems Pharmacology, Department of Pharmaceutics, College of Pharmacy at the **University of Florida**; and Aidan Power, MB BCH BAO, MSc, MRCPsych, Vice President and Head of Pharma Therapeutics Precision Medicine at **Pfizer**.

The new board members add diversity of experience to PMC's Board of Directors and bring a wealth of knowledge of health informatics, pharmacology, regulatory policy and drug development.

"PMC's ability to attract a commitment from senior leaders in personalized medicine like de Crescenzo, Lesko and Power helps build the organization so that our message will be more clearly heard," said Stafford O'Kelly, chairman of the PMC Board of Directors and president of **Abbott Molecular**.

Neil de Crescenzo brings to the PMC experience implementing enterprise software solutions that facilitate applications of personalized medicine in clinical research and care and more than 20 years of operational and IT leadership experience with Oracle, IBM, multiple medical centers and a major health insurance company.

Lawrence Lesko, the leader of the University of Florida's Center for Pharmacometrics and Systems Pharmacology, previously worked as director of the Office of Clinical

Pharmacology in the FDA's Center for Drug Evaluation and Research. He started the FDA's Voluntary Genomics Data Submission Program and is a highly regarded, well-known proponent of personalized medicine.

Aidan Power is an international scientific leader in personalized medicine and sponsored Pfizer's founding membership in the Personalized Medicine Coalition. Inside Pfizer, Power led the planning, design, and management of Phase III clinical trials for the SSRI sertraline (Zoloft™) and the atypical antipsychotic ziprasidone (Geodon™). He also helped establish Pfizer's biobank of clinical trial samples. Outside of Pfizer, Power is a founding and current board member of the Serious Adverse Event Consortium (iSAEC) and a member of the Institute of Medicine's Roundtable on Translating Genomics Based Research for Health.



New board member photos: Left, Lawrence Lesko, Ph.D., F.C.P. Right, Neil de Crescenzo; (Aidan Power not pictured.)

New Personalized Medicine Coalition Members 2012

3G Biotech (China) Company
Adriana Jenkins Foundation
for Personalized Medicine
Almac Diagnostics
Australian Institute for
Bioengineering and
Nanotechnology
Baylor Health Care System
Precision Medicine Institute
Cancer Commons
Caprion Proteomics
Clarent, a GE Healthcare
Company
Clark & Elbing LLP

CREATE Health Translational
Cancer Centre, Lund University
Cureline, Inc.
Curetis AG
Cynvenio Biosystems, Inc.
Decatur Memorial Hospital
EdgeTech Law LLP
Essentia Institute of Rural Health
Eurolab
Fairleigh Dickinson University
Medco School of Pharmacy
Genome Canada
Hanson Wade
IDBS

Invivoscribe Technologies
Knight Cancer Institute— Oregon
Health & Sciences University
Laboratory for Personalized
Molecular Medicine (LabPMM)
Jones Public Affairs
Manning & Napier Advisors, LLC
Miraca Life Sciences
National Patient Advocate
Foundation
NuGEN Technologies
Onyx Pharmaceuticals
Personalized Medicine World
Conference

Rare Genomics Institute
RIKEN GENESIS
Sanford Rose Associates -
San Diego
Silicon Valley Biosystems
TELEMEDICAL.COM
University of Florida
University of Kansas
University of Maryland School
of Medicine
University of South Florida
College of Pharmacy
YourGenomicDoctor.com

PMC IN THE PRESS

Mark Levin's call for collaboration in the health care industry to advance personalized medicine resonated in the media following his speech at PMC's State of Personalized Medicine Luncheon. "Personalized medicine has the potential to revolutionize biotech and pharma, but only if stakeholders work together," noted **Fierce Biotech**, **The Pink Sheet** and **Journal of Commercial Biotechnology**. **The Pink Sheet** and **Journal of Commercial Biotechnology** also covered the challenges Levin highlighted in relationships between the pharmaceutical and diagnostics industries.

The **Vancouver Sun** and **The Province** discussed the opportunity for personalized medicine to inform health care decision-making. The articles quote PMC to define the field, noting that personalized medicine refers to "the use of new methods of molecular analysis to better manage a patient's disease or predisposition to disease."

Following the release of the Patient Centered Outcomes Research Institute (PCORI) draft research priorities for public review and comment, **CQ Healthbeat** and **GenomeWeb** covered PMC recommendations that the institute develop a more specific research agenda and infrastructure that concretely demonstrates how funded comparative effectiveness research (CER) studies will enable personalized medicine as Congress intended.

In a feature for the March issue of **Genome Technology**, PMC President Edward Abrahams joined Scripps Research Institute's Eric Topol and the **Institute for Systems Biology**'s Leroy Hood in discussing the clinical adoption of personalized medicine. Although there has been remarkable progress in bringing new personalized medicine products to the market, the article cited reasons why clinical adoption trails scientific innovation. Abrahams pointed to regulatory, reimbursement and cultural barriers that continue to impede widespread clinical adoption.

Inside Health Policy documented the clash between clinical laboratories and diagnostic kit manufacturers over whether FDA has the authority to regulate laboratory developed tests and the two industries' opposite positions on legislation introduced by Rep. Michael Burgess (R-Texas) that would prohibit FDA from regulating the tests. In an effort to bring the community together to discuss incentives to spur development of new diagnostics, PMC assembled a panel discussion in February that engaged Alan Mertz, president of the **American Clinical Laboratory Association**, Andrew Fish, executive director of **AdvaMedDx** and Paul Radensky, an attorney with **McDermott, Will & Emery**, and counsel to the Coalition for 21st Century Medicine in a lively discussion of each group's vision for diagnostics regulation.

Bloomberg News weighed the legal and regulatory gray areas regarding the growing use of genetic information in health

care and innovation. The report cited data from PMC's *Case for Personalized Medicine, 3rd Edition* and discussed how the regulation of laboratory-developed tests (LDTs) and pending legal questions surrounding patents on genetic material to create uncertainty for companies.

With the announcement in February that **Siemens** had entered the companion diagnostics field and partnered with Viiv Healthcare Ltd. and Tocagen Inc. to develop tests for their therapeutics, **Bloomberg Businessweek** reviewed the growth in cross-industry partnerships to facilitate the development of personalized medicine products. Noted PMC Communications Director Gwen Gordon: "[Companies have] recognized that there is a market for tailored therapies for patients that know that the drug is going to work."



GenomeWeb's Pharmacogenomics Reporter

Reporter covered a talk by Elizabeth Mansfield, Head of the FDA's Office of In Vitro Diagnostic Device Evaluation and Safety at the **Personalized Medicine World Conference** in January. Mansfield said that the FDA has learned from its experiences with the approvals of personalized medicine drug/diagnostic product combinations and is seeking to develop the regulatory clarity that stakeholders, including the Personalized Medicine Coalition, Pharmaceutical Researchers and Manufacturers of America (PhRMA), Biotechnology Industry Organization (BIO) and Advanced Medical Technology Association (AdvaMed) have requested.

Edward Abrahams was quoted in a pair of **NJBIZ** stories discussing how pharmaceutical companies consider numerous factors when setting prices for drugs. "Overall, costs should decline system-wide because efficiencies will be introduced into the system" he said.

The need for supercomputing capabilities to store, process, and mine health care data was highlighted when billionaire scientist Patrick Soon-Shiong's CSS Institute for Advanced Health in California announced that it had built such a computer in Phoenix. In an article that ran in the **Arizona Republic** and **USA Today**, Edward Abrahams noted that increased computing capacity lays the groundwork for personalized medicine.

Genomics is redefining how medicines are developed and dosed, thereby improving drug efficiency. However as Brian Munroe, Chair of PMC's Public Policy Committee told the **Memphis Commercial Appeal**, despite advances in genomics and personalized medicine documented in *The Case for Personalized Medicine, 3rd Edition*, regulatory, reimbursement and educational barriers to the widespread adoption of personalized medicine remain.