PMC PERSONALIZED MEDICINE COALITION

PERSONALIZED MEDICINE IN BRIEF

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Developments in Brief

PRESIDENT'S BRIEF

The Road to Progress

by Edward Abrahams, Ph.D., PMC President

Marie Curie famously observed that "progress is neither swift nor easy." While she might have added that progress is also not inevitable, she did go on to demonstrate that persistence pays off.

Four months into 2018, the same can be said about personalized medicine, as this newsletter documents.

The pace of scientific progress is steady. In fact, PMC's *Personalized Medicine at FDA: 2017 Progress Report*, released in January, shows that the U.S. Food and Drug Administration (FDA) set six regulatory precedents for the field and approved a record number of 19 new personalized treatments last year, including three gene therapies that offer unprecedented clinical benefits for selected patients.

FDA carried that momentum into 2018 by clearing on March 6 an at-home personalized test marketed by 23andMe that provides information about a patient's personal risk of developing breast and ovarian cancer based on the presence or absence of mutations in the BRCA gene. In so doing, the agency bolstered the trend toward direct-to-consumer genetic testing, despite ongoing objections from some clinicians who believe that accurate interpretation of genetic test results requires a "learned intermediary."

Even on the reimbursement front, which has posed major challenges for personalized medicine for as long as the field has existed, advocates have broken through to the U.S. Centers for Medicare and Medicaid Services (CMS). The agency has agreed to cover next-generation sequencing (NGS) tests nationwide for patients with advanced cancer.

But these developments, though meaningful, do not tell the whole story. Indeed, as Curie faced a relentless army of challenges in her quest for major scientific breakthroughs, we are still encountering many obstacles in our efforts to reconceive the prevailing one-size-fits-all medical paradigm.

As Bruce Quinn writes elsewhere in these pages, the Protecting Access to Medicare Act (PAMA), for example, is disrupting the operations of some of the clinical laboratories upon which personalized medicine depends. The American Clinical Laboratory Association (ACLA) remains concerned that the policy, if unchecked, could put some laboratories out of business entirely by establishing artificially low payment rates for key personalized medicine tests, thereby discouraging future investment.

And although CMS' decision on NGS testing clarified the pathway for commercializing personalized medicine diagnostics for a small subset of scenarios, an uncertain future for regulatory oversight of personalized diagnostics and an immature evidence base to support their use continue to stifle innovation in that area.

Bolstered by the support of a record number of new members since the last edition of this newsletter was published, PMC is expanding its portfolio of initiatives to meet the field's challenges. As outlined on the adjacent page, the Coalition now has a total of four committees to help advance various issues in personalized medicine. Those committees include the newly formed Patient Advocacy Organization Working Group. PMC members can also help advance the field by submitting guest blogs to PMC's *Education & Advocacy* platform or guest articles to this bi-annual progress report.

In addition to organizing the *14th Annual Personalized Medicine Conference at Harvard Medical School*, the Coalition plans in 2018 to establish a Congressional Personalized Medicine Caucus, release a nationally representative survey of Americans that updates our knowledge about public support for personalized medicine, and publish original research that helps establish the clinical and economic value of genetic sequencing.

For more information on PMC's 2018 *Strategic Plan*, I encourage you to read an abridged version of my recent interview with Theral Timpson of *Mendelspod* on pp. 4–5 of this newsletter.

Suffice it to say, your support of the Coalition matters now more than ever.

"Indeed, as [Marie Curie] faced a relentless army of challenges in her quest for major scientific breakthroughs, we are still encountering many obstacles in our efforts to reconceive the prevailing one-size-fits-all medical paradigm."

PAVING THE WAY: PMC's Member Working Groups Tackle Outstanding Challenges Facing Personalized Medicine

With over 225 members spanning the health care spectrum, the Coalition's strength rests in its diversity. To capitalize on this diversity, the organization has multiple forums to engage and build collaborations within and across different stakeholder groups, notably providers, industry and patients.

HEALTH CARE WORKING GROUP

PMC's Health Care Working Group provides a forum for providers interested in integrating personalized medicine into medical practice. The group identifies common challenges, discusses solutions and develops best practices. Last year, it developed a "road map" enumerating best practices for bringing personalized medicine into the clinic.

Chair: Daryl Pritchard, Ph.D., PMC
Senior Vice President, Science Policy

PATIENT ADVOCACY ORGANIZATION WORKING GROUP

In order to integrate the patient's point of view into PMC's efforts to further personalized medicine, the Coalition has recently launched a Patient Advocacy Organization Working Group, which will inform PMC's policy strategy as well as develop shared messages and tools to empower individual patients to advocate for policies that bring personalized medicine closer to the patient.

Chair: Cynthia A. Bens, PMC
Senior Vice President, Public Policy

PHARMA AND DIAGNOSTICS WORKING GROUP

The Pharma and Diagnostics Working Group informs PMC's policy strategy and advocacy activities related to research and development, regulatory oversight, reimbursement, and health care quality. The group collaborates to align policy priorities among PMC members and leverage relationships with policymakers to advance legislation and regulations that promote investment in and adoption of personalized medicine.

Chair: Cynthia A. Bens, PMC
Senior Vice President, Public Policy

POLICY COMMITTEE

Gathering stakeholders from across PMC's membership, the Policy Committee meets at least once per quarter to debate and establish the Coalition's policy priorities and positions. These discussions frequently include government officials as guest speakers, including representatives from the U.S. Food and Drug Administration (FDA), the Centers for Medicare and Medicaid Services (CMS), and the U.S. Congress.

PARTICIPATION

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NEWS BRIEF

Charting a Course for Personalized Medicine

Excerpted from a *Mendelspod* interview by Theral Timpson with PMC President Edward Abrahams

by Theral Timpson, *Mendelspod* Host and Producer

EDITORIAL NOTE — *Following the release of PMC's* Strategic Plan *for 2018, which outlines 10 initiatives the Coalition will spearhead to advance the field, Theral Timpson of* Mendelspod *interviewed PMC President Edward Abrahams about the Coalition's role in promoting personalized medicine and its priorities this year. The following content was excerpted with permission from that interview, which was originally published on* Mendelspod*'s website as a podcast on March 14. The content has been edited for clarity.*

Theral Timpson: The Personalized Medicine Coalition represents so many groups. Tell us the groups you represent.

Edward Abrahams: We represent all of the stakeholders with an interest in developing personalized medicine, and they include pharmaceutical companies, diagnostic companies, venture capitalists, patient groups, academic health centers, community hospitals and really anybody with an interest in improving health care by targeting treatments to those patients for whom it will work.

TT: With such a broad constituency, what I've always wondered is how you guys can do anything for so many people?

EA: We were launched in 2004 based on the assumption that the development of science and technology alone was not going to lead to a new paradigm in medicine, and that the space between the science and the patient was large enough to require what we are and became — an organization with an emphasis on education and advocacy that is positioned to promote personalized medicine so that the government, industry and other stakeholders understand how decisions they make are going to shape this new future. It's really an advantage to represent so many stakeholders because our voice is much larger and amplified than it otherwise would be.

TT: What you're saying is when someone makes a move, you put out a lot of literature about the ripples that that can cause?

EA: But more than that, we tell them what moves they should make.

TT: In advance?

EA: Yes. We guide them to the kinds of decisions that are going to facilitate investment in personalized medicine and the clinical adoption thereof. That requires a broad-based organization such as ours. A lot of people confuse PMC with a trade association. A trade association is made up of members who share a particular business model. We incorporate multiple business models, and while that sometimes interferes with our developing a consensus when we don't have only winners, it also enables us to play a very important role in this space.

TT: Let's take an example like laboratory-developed tests. What do you think is the best way forward on that topic?

EA: Our overriding position is that the field needs clarity in how laboratory-developed tests are regulated, and without that clarity, investment is going to be much less than it otherwise would be. We also argue that we need a strong diagnostic industry, because unless therapy is linked to diagnostics, we're not going to have personalized medicine.

PMC has developed some principles that we are using to inform the Congressional effort to tackle the problem of laboratory-developed tests. Those principles involve maintaining an environment in which innovation is encouraged as well as patients are protected. Those principles suggest that we should protect health labs, allow flexibility and efficiency when managing modifications, mitigate the regulatory burdens for government and industry, grandfather in the tests that have already been developed, ensure that the regulatory burdens reflect testing volumes, and accept — and this is important — accept valid scientific evidence for regulatory purposes, even if that evidence does not involve data from controlled, randomized clinical trials.

"There's a lot more that Congress will have to do to facilitate personalized medicine."

We want a system that is flexible enough, that has low barriers to entry, but is still regulated so that investors, patients and payers can have confidence in the system.

TT: I think during the holiday on Black Friday, direct-to-consumer tests like 23andMe and Ancestry were up there with Instant Pot as top sellers. We have not seen this level of direct-to-consumer tests being bought before.

EA: Let's be careful and differentiate what we're talking about. We're talking about an explosion of interest in direct-to-consumer ancestry testing. They're not buying predictive tests about health outcomes.

TT: You're right, you're right.

EA: That's what FDA was originally concerned about, but their clearance of 10 tests from 23andMe suggests that they've opened the door for that kind of testing.

TT: Is that enhancing personalized medicine or detracting?

EA: It's bringing it to the public mind quicker than it otherwise would.

TT: We've seen a huge boom in immunotherapy treatments.

EA: Absolutely.

TT: There's two big questions there. Is it really getting to a lot of patients? I saw a report late last year that, still, when it comes down to it, it only helps about eight percent of people. We think of it helping these masses of people. I'm curious what your pushback on that is. And then the drug pricing issue. Do you get into that?

EA: Yes. Those are two different questions, and let me take the first one first. The personalized, targeted therapies are designed to help subsets of the population, so we shouldn't be surprised that immunotherapy works for some patients and not for others.

TT: That's a good thing?

EA: That's how it's supposed to work, and the more definition you get from the diagnosis, the more likely you are to have a positive outcome.

Regarding price, we're moving from an era — and everyone acknowledges this, including the payers — to recognize the benefit of focusing on value, not volume. We really need to have a discussion not just about the price of these therapies, but also about how they're helping people. And then make a decision about what the right price is. That will also encourage investment in even newer and more effective therapies that may be for even smaller subsets of the population.

TT: What's the single most important thing that you personally could do in 2018 for personalized medicine?

EA: To organize a Congressional personalized medicine caucus.

TT: Were you happy with the *21st Century Cures Act*? And did you feel the personalized medicine story did get told to Congress in a nuanced way?

EA: We were extremely happy with the new act that went through Congress at the end of the last session. It has a lot of good ideas in it, not least of which is the consideration of real-world evidence when making decisions about therapies and what to reimburse. But it's a beginning, not a destination. There's a lot more that Congress will have to do to facilitate personalized medicine, some of which we've talked about — establishing an oversight framework for laboratory-developed tests, deciding on value in pharmaceutical pricing, encouraging clinical adoption — all of these things are on the horizon. That's the reason PMC wants to create a personalized medicine caucus that will present information for the House and the Senate as they move forward.

TT: There is no caucus today?

EA: There is no caucus. There's a lot of disease caucuses, but no caucus that crosses multiple indications and considers personalized medicine, which has become a thing in and of itself.

TT: OK, well we wish you the best with that, and we want to follow up with you. Thanks, Ed.

EA: Thank you.

NEWS BRIEF

Systems Grapple with Unprecedented Value Propositions for One-Time Personalized Treatments

by Christopher Wells, M.P.A., PMC Vice President, Public Affairs

Doctors were stunned when they examined Emily Whitehead's immune cells for the first time since she was treated with chimeric antigen receptor (CAR-T) therapy.

After receiving treatment, Emily, who was fighting to keep acute lymphoblastic leukemia (ALL) from ending her seven-year old life when she received it, still had an immuno-army of genetically modified "T-cells" circulating in her bloodstream, relentlessly seeking the CD-19 protein signature that characterizes many ALL cells. Teeing off on CD-19, the T-cells will immediately attack and destroy any such cells that have survived or emerged since the T-cells began their initial onslaught on Emily's disease. CAR-T treatment, it seems, has caused long-term changes to Emily's immune system, ending a struggle that repeated rounds of increasingly intense chemotherapy had been powerless to impact.

This is the power of treatments that use genetic alterations to combat disease.

Since Emily's experimental treatment, the pharmaceutical industry has brought to market two U.S. Food and Drug Administration (FDA)-approved CAR-T therapies — Novartis AG's Kymriah (tisagenlecleucel) and Gilead's Yescarta (axicabtagene ciloleucel) — as well as a different gene-altering treatment called Luxturna (voretigene neparvovec-rzyl). Luxturna, which was developed by Spark Therapeutics, can restore eyesight to people born with a genetic condition that usually causes complete or partial blindness.

Brian Rini, M.D., a hematologist and oncologist at the Cleveland Clinic, characterizes the benefits of gene alteration in oncology as "paradigm-changing," and Katelyn Corey, a patient treated with Luxturna, notes that the treatment has "created a life of independence" for her.

But some say there's a catch.

The clinical benefits of the treatments are not at issue. Instead, the debate over CAR-T therapies like Kymriah and gene therapies like Luxturna, which the American Society of Gene & Cell Therapy estimates are being tested in at least 560 clinical trials, reflects a struggle to determine the economic value of this incoming wave of personalized, one-time treatments that offer unprecedented clinical benefits.

Critics believe these companies have conferred an inflated economic value upon the treatments, in the form of list prices. Novartis set the list price for Kymriah at $475,000, while Gilead charges $373,000 for Yescarta. Luxturna, meanwhile, carries a price tag of $850,000 for treatment of both eyes.

David Mitchell, a cancer patient and President of Patients for Affordable Drugs, a nonprofit organization, recently published an analysis in *Health Affairs* arguing that Kymriah should cost only $160,000. Mitchell says Novartis, which settled on a price that was 36 percent lower than the prevailing estimates from Wall Street analysts, "should not get credit for bringing a $475,000 drug to market and claiming they could have charged people more."

And although Steven D. Pearson, M.D., M.Sc., President of the Institute for Clinical and Economic Review, which conducts influential value assessments that payers and providers may use to inform treatment decisions, said his Institute found that both Kymriah and Yescarta are "priced in line with the value they deliver to patients," the Institute's analysis of Luxturna indicates that the treatment is not cost-effective at a price above $573,000.

Pearson said health insurers worry that prices for gene therapies "could kind of get away from folks and lead to even more problems with affordability."

The debate is not tangential to the future of personalized medicine. PhRMA argues, for example, that the

"The debate over [gene-altering therapies] reflects a struggle to determine the economic value of this incoming wave of personalized, one-time treatments that offer unprecedented clinical benefits."

downward pressure on list prices for new medicines may stifle investment in innovation. Following Novartis' decision to price Kymriah below analysts' estimates, Spark set an $850,000 price tag for Luxturna that reflects a 15 percent reduction from the $1 million analysts had widely cited as an appropriate number. PhRMA President and CEO Stephen J. Ubl suggests that reduced list prices eat away at the resources available for continued research and development. He also notes that the pharmaceutical industry is aggressively pursuing so-called "outcomes-based" contracts, in which the companies offer rebates when treatments do not work as intended.

"I think our companies are willing to put their money where their mouth is," Ubl said.

Critics counter that these agreements, which Novartis and Spark both touted as major components of their plans to make Kymriah and Luxturna accessible to patients, offer rebates on an already inflated value proposition.

"I think the question is: Are we where we want to be as a society?" said Ameet Sarpatwari, J.D., Ph.D., Instructor, Harvard Medical School.

PMC will examine emerging strategies to develop and facilitate access to personalized therapies during a panel discussion titled "Considering Costs: Evaluating the Viability of Pharmaceutical and Insurance Industry Business Models in Personalized Medicine" at the *14th Annual Personalized Medicine Conference at Harvard Medical School* in November.

PUBLIC PERSPECTIVES ON PERSONALIZED MEDICINE

A Survey Launch Event

MAY 23, 2018 • WASHINGTON, DC

At the Personalized Medicine Coalition's 14th Annual State of Personalized Medicine Luncheon, PMC will unveil the results of a representative survey of 1,001 Americans that explored awareness of and opinions about personalized medicine. The survey was jointly funded by PMC and *GenomeWeb*.

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Featured Speakers

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Deputy Director
All of Us Research Program

SUSAN MCCLURE
Founder, Publisher
Genome magazine

LINCOLN NADAULD, M.D., PH.D.
Executive Director, Precision Medicine and Precision Genomics
Intermountain Healthcare

PUBLIC POLICY BRIEF

CMS Enhances Access to Personalized Diagnostics

by Cynthia A. Bens, PMC Senior Vice President, Public Policy

On November 30, 2017, the U.S. Food and Drug Administration (FDA) and the Centers for Medicare & Medicaid Services (CMS) announced the approval and preliminary coverage of Foundation Medicine's FoundationOne CDx. As part of its announcement, CMS released a draft proposed decision memo for the FoundationOne CDx and similar next-generation sequencing (NGS) tests for use in the diagnosis of advanced cancer.

Under the leadership of Administrator Seema Verma, the U.S. Centers for Medicare and Medicaid Services (CMS) has announced that Medicare will now cover next-generation sequencing (NGS) in vitro companion diagnostic tests for advanced cancer that are approved or cleared by the U.S. Food and Drug Administration (FDA). Many advocates believe NGS tests will play a major role in personalized medicine going forward by allowing doctors to use a single test to determine which of several treatment options are most appropriate for a patient.

The draft coverage proposal was scrutinized by numerous stakeholders during an extended public comment period that resulted in CMS receiving nearly 400 pages of feedback. Many interest groups, including PMC, requested clarification from CMS on different aspects of the proposed decision memo. PMC's comments highlighted the need to extend coverage for NGS testing to earlier stages of cancer and make allowances for retesting during the course of a patient's life. In addition, PMC called on CMS to expand full coverage beyond FDA-approved NGS tests and consult with stakeholders to define a rigorous but less burdensome pathway to coverage with evidence development (CED) for NGS tests that do not meet CMS' proposed criteria for full coverage.

Fortunately, CMS addressed many of the community's concerns in the resulting national coverage determination (NCD) that was released on March 16, 2018. The following is a summary of what PMC views as major changes from the draft NCD:

- **Coverage granted for FDA-approved and FDA-cleared NGS-based in vitro companion diagnostic tests.** FDA-cleared NGS tests for advanced cancer would have fallen under a CED program in the original draft. The final NCD expands the scope of coverage to NGS tests that are cleared as in vitro companion diagnostics through FDA pathways, such as 510(K), in addition to tests that are FDA-approved as in vitro companion diagnostics. Because the final determination does not specify sample type, FDA-cleared or -approved NGS liquid biopsy tests that are in vitro companion diagnostics will be covered as they become available, provided that all of the required patient and test indications are met.
- **NGS tests indicated for use outside of advanced cancer not at risk of immediate non-coverage as previously thought.** Under the proposed NCD, Medicare coverage was uncertain for tests that did not meet the narrow categories of FDA-approved or -cleared tests, and even these

tests would have been subject to CED. Coverage decisions for both NGS-based in vitro diagnostics and laboratory-developed tests (LDTs) in areas such as hereditary testing, screening, and other non-cancer conditions will remain with local Medicare Administrative Contractors (MACs). Under the final NCD, coverage for NGS-based tests in patients with cancer without FDA-approved or -cleared companion diagnostic indications may be handled through the local coverage determination process, subject to the restrictions set forth in the final NCD.

- **CED dropped.** CED was an important but problematic feature of CMS' draft. In the proposed coverage decision, CED programs would have been required for all other NGS-based cancer tests that were not FDA-approved NGS-based in vitro companion diagnostic tests for advanced cancer. Further, CED for LDTs was limited only to those participating in a National Institutes of Health-National Cancer Institute Clinical Trial Network. CED was not included in the final CMS determination, and instead, non-FDA-approved NGS tests will be evaluated by the MACs to determine coverage status.
- **Additional cancer indications included for coverage and one-time testing limitation removed.** The proposed decision memo only provided pathways to coverage for NGS testing for Medicare beneficiaries with recurrent, metastatic and stage IV cancer. In addition to coverage for these patients, the final NCD also covers NGS testing for patients with either relapsed, refractory or stage III cancer when the NGS test meets the diagnostic assay requirements for coverage. The final NCD precludes coverage for patients with stage II or earlier cancer. In the final NCD, CMS also expanded the frequency of testing allowed, from using the same diagnostic laboratory test once to using the same diagnostic laboratory test once for each new primary diagnosis of cancer. Repeat testing for the purpose of treatment monitoring is not included in the final NCD.

The NCD is a net positive for NGS testing, as it now guarantees Medicare coverage at a national level for FDA-approved or -cleared NGS-based companion in vitro diagnostic tests for advanced cancer. PMC has applauded CMS for recognizing that NGS testing is a breakthrough technology that is critical to advancing personalized medicine.

NEWS BRIEF

FDA Continues to Bolster Trend Toward At-Home Genetic Testing with Clearance of Personalized Cancer Risk Test

by Christopher Wells, M.P.A., PMC Vice President, Public Affairs

In an op-ed titled "Personalized Medicine is Here" published in April of last year by *The Wall Street Journal*, Paul Howard, Ph.D., and Peter Huber, J.D., Ph.D., of the Manhattan Institute applauded the U.S. Food and Drug Administration (FDA) for clearing for the first time a group of at-home genetic tests that provide information about patients' risks for developing diseases later in life.

Under the leadership of Commissioner Scott Gottlieb, M.D., the U.S. Food and Drug Administration last year cleared the first 10 at-home genetic risk tests for diseases like Alzheimer's and Parkinson's. The agency has continued to advance the paradigm since then, and cleared on March 6 the first genetic cancer risk test for mutations in the BRCA gene.

These and other direct-to-consumer (DTC) tests, the authors contend, "empower patients to become co-directors of their own medical destinies."

Their view contrasts sharply with those of clinicians such as Susan M. Domchek, M.D., of the University of Pennsylvania, who contends in an op-ed recently published by *STAT News* that genetic testing should always come with "appropriate professional support to help individuals live and plan," which, in her estimation, is "something a mail-order kit just can't do."

But the dissenting opinions from Domchek and others have done little to persuade an FDA that, under the direction of Commissioner Scott Gottlieb, M.D., appears wholeheartedly committed to advancing the DTC testing paradigm.

The agency continued its efforts to advance the field with the clearance on March 6 of a test marketed by 23andMe that assesses a patient's personal risk of breast and ovarian cancer based on the presence or absence of mutations in the BRCA gene. That decision is at least the third landmark the agency has set down in this space under Gottlieb's tenure, following the clearance of the 10 genetic risk tests that Howard and Huber welcomed and an 873-word statement from Gottlieb in November, in which he asserted that "[genetic risk testing] can prompt consumers to be more engaged in pursuing the benefits of healthy lifestyle choices and more aware of their health risks." Gottlieb confirmed in the statement that manufacturers of genetic risk tests — including DTC tests — are only required to submit tests for FDA approval one time. After that submission, the manufacturers may market new tests without further review.

23andMe is the only company so far to have secured FDA clearance to market a DTC genetic risk test, having received clearance for the 10 tests last year and the BRCA test in March.

"[Dissenting opinions] have done little to persuade an FDA that, under the direction of Commissioner Scott Gottlieb, M.D., appears wholeheartedly committed to advancing the DTC testing paradigm."

The clearance of the BRCA test, in particular, suggests that FDA will go to great lengths to ensure access to DTC tests. The test can detect only three of the more than 1,000 known BRCA mutations that may increase the risk of developing cancer, raising concerns that a negative result will lull consumers into a false sense of security. In FDA's statement on the clearance, Donald St. Pierre, Acting Director, Office of In Vitro Diagnostics and Radiological Health, noted that the decision "is a step forward in the availability of DTC genetic tests" but that it has "a lot of caveats." Consumers, he warned, should not use the test as a substitute for regular cancer screenings conducted by a physician — a notion seconded by 23andMe.

"It's important to understand that the majority of cancer is not hereditary, our test does not account for all genetic variants that can cause a higher risk of cancer, and [that] people should continue with their recommended cancer screenings," said Anne Wojcicki, CEO, 23andMe.

23andMe is working with PMC on the Coalition's multi-stakeholder effort to update its *Introduction to Informational Genetic Testing* guide this year. Wojcicki's company believes when it comes to personalized medicine, information is power.

"While doctors and genetic counselors play an important role in delivering health care and information, I am an advocate for consumers having more direct access to personalized information so they can take charge of their health," Wojcicki wrote in an op-ed for *STAT News*. "Making genetic testing affordable and accessible enables more people to learn important — and potentially lifesaving — information about themselves."

NEWS BRIEF

US Government's 'Market-Based' Pricing Strategy May Disrupt Business Models for Personalized Diagnostic Developers

by Bruce Quinn, M.D., Ph.D., M.B.A., Principal, Bruce Quinn Associates

EDITORIAL NOTE — *In 2014, the U.S. Congress passed the Protecting Access to Medicare Act (PAMA), which was designed to align the prices that Medicare and Medicaid pay for diagnostic tests — including those upon which personalized medicine depends — with the market-based rates established in the private sector. In so doing, lawmakers hoped to establish fair prices for diagnostic products and services, thereby promoting an innovative and profitable diagnostic industry.*

Industry representatives from organizations including the American Clinical Laboratory Association (ACLA), however, began to raise concerns about the Centers for Medicare and Medicaid Services (CMS)' approach to implementing PAMA soon after CMS outlined that approach in 2015. Among other concerns, advocates argued that CMS' decision to mandate reporting of payment rates from only a subsection of "applicable laboratories" could result in artificially low payment rates that may put small laboratories out of business, reduce patients' access to personalized medicine tests and other important diagnostic tools, and eventually stifle innovation in the sector.

Despite the industry's ongoing objections, CMS began using PAMA to price diagnostics on January 1, 2018.

Bruce Quinn, M.D., Ph.D., M.B.A., Principal, Bruce Quinn Associates, who served four years as the Medical Director for California's Medicare program, provides an update below on the impact PAMA is having on personalized medicine.

What is "PAMA?"

PAMA had 37 sections, but if you are part of the laboratory industry or track U.S. personalized medicine issues, PAMA means one thing. That's PAMA Section 216, which overturned the decades-old way Medicare paid for laboratory tests and replaced it with a completely different pricing method. With some September 2017 announcements, CMS has nearly completed its work on the new fee schedule, which became active for all Medicare Part B laboratory payments on January 1, 2018.

Understanding this change in Medicare's fee schedule for laboratory tests is important for everyone with an interest in personalized medicine in the U.S. These payments support the laboratory industry and the critical laboratory test innovation we must have for progress in personalized medicine.

What Has PAMA Done?

Except for small and erratic inflation adjustments, Medicare's fees for laboratory tests changed little since the 1980s. By 2013, government reports asserted that many private payers contracted with laboratories for test prices at fractions (say, 70 percent) of the Medicare rates. Congress soon responded with lawmaking that sets Medicare laboratory prices at the median of reported private payer rates. This pricing exercise will repeat every three years. The fee schedule is still called the "Clinical Laboratory Fee Schedule," or CLFS. Medicare prices are vitally important for the laboratory industry, since the Medicare fee schedule is often a starting point for price negotiations with private payers.

Between 2014 and 2017, agency rulemaking allowed CMS to fill in many of the details necessary to implement the Congressional plan. Early in 2017, CMS received about 4.9 million lines of data from 1,942 reporting laboratories. The data spanned about 1,200 laboratory test codes, but just 25 laboratory test codes garnered 63 percent of CMS payments. (Conversely, some 100 test codes had little or no utilization.) Reporting laboratories were defined by National Provider Identification numbers (NPIs). The NPI had to (1) be associated with a Clinical Laboratory Improvement Amendments (CLIA) certificate, (2) have gotten more than $12,500 in payments for CLFS tests in 2016, and (3) have gotten more than 50 percent of its Medicare revenue through the CLFS

or physician fee schedules (as opposed to, e.g., hospital fee schedules). Because of these rules, few physician office laboratories or hospital-based laboratories reported data to CMS. CMS took reports from only 21 hospital-based laboratories nationwide.

Where are CMS Prices Going Now?

CMS released millions of lines of pricing data on September 22, 2017, along with several smaller Excel spreadsheets and explanatory documents. Seventy-five percent of all laboratory test codes are being assigned a lower price based on the surveys, and 58 percent of all codes will receive a "phased-in" reduction of 10 percent per year in 2018, 2019 and 2030.

Genetic tests, including tumor tissue tests, are the most important for the personalized medicine industry. Many single-gene cancer tests did not change much or even rose under the new CLFS. For example, common mutations in the EGFR gene, assessed in lung cancer, were paid $231 under the 2017 fee schedule, an amount that will rise to $325 in 2018 due to PAMA. Another upward-bound code is BRCA1/BRCA2 full sequencing, which rose from $2,195 to $2,396 under PAMA. The system is not entirely rational, as Congress hoped, because a code for BRCA1/BRCA2 full sequencing and duplication deletion analysis falls from $2,503 to $1,616, and this code is more effort than BRCA sequencing alone.

Most of the codes for cytochrome oxidase (CYP) testing as used in pharmacogenetics were remarkably stable — for example, CYP2C19 moves from $293 to $291.

A few genetic codes, however, fall precipitously. Gene panel testing for Lynch Syndrome in colon cancer, for example, falls from $802 to $38. BRCA1 sequencing alone (without BRCA2) falls from $1,446 to $75. These two-digit prices are not rational clinical market prices and probably reflect quirks in the data.

A few gene panel tests rose markedly in price. For example, the Ashkenazi hereditary disorders panel rose from $602 to $2,449. While price cuts are staged at 10 percent per year, price increases are effective immediately. Some genetic tests that had no prices yet on the CLFS got pricing for the first time. For example, the CPT code for 51+ tumor genes will be priced at $2,920, not too far from the reported average market price of the FoundationOne™ test from Foundation Medicine.

What Happens Next?

Organizations such as ACLA have been justifiably concerned that the data gathering rules were flawed, and that CMS failed to carry out Congress' intent that hospital outreach laboratories — a large part of the U.S. laboratory market — should be fairly sampled, even as inpatient hospital labs were excluded since they are usually paid per admission, not by fee schedules. According to ACLA's website, it has raised its concerns to CMS and the Hill, and has asked that PAMA implementation be halted until these issues are resolved.

Assuming PAMA is not halted, laboratories will need to carefully review how they contract, how tests are coded and what strategies will be best to ensure fair market-based pricing in the next survey in 2019.

U.S. lawmakers including Sen. Orrin Hatch (R-UT), a prominent advocate for a strong diagnostics industry and the ranking member of the Senate Finance Committee, supported the Protecting Access to Medicare Act (PAMA) of 2014 in hopes that the bill would facilitate fair prices for the diagnostic products and services upon which personalized medicine depends by tying Medicare's prices for diagnostic tests to market rates established in the private sector. Since the bill's passage, however, the American Clinical Laboratory Association (ACLA) has expressed a concern that the Centers for Medicare and Medicaid Services (CMS) have implemented flawed data gathering rules under PAMA that may result in an inconsistent and unpredictable reimbursement landscape for personalized medicine tests.

SCIENCE POLICY BRIEF

Ascertaining the Clinical and Economic Value of Genetic Sequencing

by Daryl Pritchard, Ph.D., PMC Senior Vice President, Science Policy

No matter how much a new technology can improve medical practice, its uptake can be a slow process because, as Machiavelli explained, most people "do not believe in anything new until they have actual experience of it."

Genetic sequencing is no different.

While the rapid decrease in the cost of genetic sequencing presents new opportunities to analyze genetic alterations that could contribute to various health conditions, most providers and payers have had too little experience with the proposed approach to be confident making the decisions needed to provide access to sophisticated sequencing-based molecular diagnostics.

To address that challenge, PMC will deliver evidence that personalized medicine technologies improve health care at the patient and systemic levels. PMC, working with an expert steering committee and a health economic research team at the Fred Hutchinson Cancer Research Center, set out in 2017 to examine the value, both clinical and economic, of solid tumor next-generation sequencing (NGS)-based diagnostic testing to guide targeted therapies in cancer care. That effort will lead to a peer-reviewed publication that provides evidence for developers, payers, and providers that NGS-based diagnostic testing is both clinically useful and economically efficient.

PMC is now coordinating an initiative to evaluate the clinical and economic value of whole exome sequencing (WES) for patients with rare and undiagnosed diseases. For these patients, the adoption of personalized medicine technologies may have a particularly significant benefit. These patients are often children and are frequently referred to as "diagnostic odyssey" cases, as they bounce around various medical centers for years with numerous diagnostic procedures performed, generating increasingly high health care costs while their disease goes undiagnosed. While going through their diagnostic odyssey, these patients' diseases can progress, and they lose time during which they could be receiving effective therapies or enrolling in a clinical trial.

In many cases, examining all potential disease-related genes simultaneously through WES, rather than examining a few genes at a time using multiple tests, can more rapidly detect any underlying genetic alterations that can contribute to disease. Doctors are therefore able to arrive at a definitive diagnosis sooner, ending the diagnostic odyssey and matching patients to treatments.

While some hospitals recognize the potential value of WES for rare disease and undiagnosed patients, it is not standard practice. Providers and payers are often reluctant to order WES or to cover and reimburse costs because they do not have convincing evidence that the testing has clinical utility or economic benefits. Furthermore, since the diagnostic odyssey applies to many rare or hard-to-diagnose diseases rather than a single condition, there is little research on the benefits of WES across disease states.

To address these challenges, PMC will organize a steering committee consisting of clinical, economic, data, and policy experts to help identify data sources and guide study design. The study will utilize real-world clinical evidence and will involve a payer advisory group to help ensure that project results will be useful for coverage and payment decision-making.

In the process, we hope to demonstrate that pooling information related to genetic alterations, treatment and outcomes can accelerate the understanding of diagnosis and treatment options for rare and hard-to-diagnose diseases.

PMC will present results from *Cost-Effectiveness of Multi-Gene Panel Sequencing for Advanced Non-Small Cell Lung Cancer Patients* and *Clinical and Economic Value of Whole Exome Sequencing in Rare and Undiagnosed Diseases* at the *14th Annual Personalized Medicine Conference at Harvard Medical School* from November 14–15.

Congratulations to the winners of the **2017 Genome Genius Awards**!

OVERALL WINNER

Sharon Briggs

"My colleagues and I compete every day to see who can pull off the best score! Each day triggers a conversation about something new in genetics, which questions we did and did not get right, and especially the times we disagree with the answers :)"

WINNER, CONSUMER CATEGORY

Andy Brubaker

"The Genome Genius app is a fun way to test my knowledge and keep me up-to-date with genetic information. It also provides me with new topics to use with my high school biology students, a couple of whom are frequent users of the app themselves!"

WINNER, GENETIC COUNSELOR CATEGORY

Mitch Cunningham

"I like to play Genome Genius because it's a fun way to challenge myself and expand my knowledge of genetics 'fun facts' outside of my normal clinical practice."

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OBITUARIES

In Memoriam: Michael Christman, Ph.D., President, CEO, Coriell Institute

by Gregory Downing, D.O., Ph.D., Founder, Innovation Horizons LLC

The personalized medicine community is saddened by the unexpected loss of Michael Christman, Ph.D., a longstanding PMC supporter and pioneer in the effort to translate the science of genomic medicine into benefits for patients and the public. Michael, who served as President and CEO of the Coriell Institute in Camden, NJ, for 10 years, died on December 25, 2017. He was 58.

Prior to joining Coriell, Michael served as Professor and Founding Chair of the Department of Genetics and Genomics for the Boston University School of Medicine. I met him in 2005 while he was in Boston, and began to appreciate the vision he had for this new science.

Building on his experience working on the first genome-wide association studies for the Framingham Heart Study, Michael had worked out a strategy for using genomic medicine applications to benefit human health. His opportunity at the Coriell Institute opened the door for his creativity and passion.

Michael led the Coriell Personalized Medicine Collaborative Research Study (CPMC), one of the first U.S.-based efforts to combine genomic information with data about patients' family histories, lifestyles and environments to enable predictions about risk for disease and response to therapy. CPMC now involves more than 10,000 participants in 48 states, multiple hospital partners and numerous research collaborators. The study has earned more than $15 million in federal grants and has been recognized by *MIT Technology Review* as one of the top personalized medicine research projects in the world.

Michael also spearheaded Coriell's launch of a for-profit spin-off company — Coriell Life Sciences — that provides a comprehensive medication management tool for clinical use. Coriell Life Sciences was named "Global Entrepreneur of the Year" during an IBM-sponsored Silicon Valley competition featuring 1,200 start-ups in 2014. Over the years, Michael always greeted me with a beaming smile, and he took great pride in introducing me to the team and announcing their latest achievements and milestones. He became a trusted source of insights, and I grew to admire the leadership he had established throughout the Delaware Valley in leading the Institute.

Michael Christman, Ph.D., a longstanding PMC supporter and pioneer in the effort to translate the science of genomic medicine into benefits for patients and the public, died unexpectedly on December 25, 2017. He was 58.

I also recognized his ability to understand the importance of the public policy changes that would be necessary to advance personalized medicine. He committed his time, energy and the imprimatur of Coriell to helping me, PMC and others in that cause.

On behalf of myself and PMC, I express our collective sorrow to his family, friends and colleagues at the Coriell Institute. His vision, passion and lifetime achievements are a beacon to those who follow him in our endeavor.

OBITUARIES

In Memoriam: U.S. Rep. Dorothy Louise McIntosh Slaughter (D-NY)

by Daryl Pritchard, Ph.D., PMC Senior Vice President, Science Policy

In this era of rapidly increasing knowledge about the role of genetics in human health and the evolution of health care from traditional one-size-fits-all treatment to more personalized care, the U.S. Congress needs champions to help ensure that the laws and policies that govern our health care system are built appropriately.

Louise M. Slaughter, United States Representative for New York's 25th Congressional District and author of the Genetics Information Nondiscrimination Act (GINA), was one of these champions. She passed away on March 16, 2018.

Slaughter was the first woman to chair the powerful House Committee on Rules, and was serving as its ranking member. Her signature achievements in personalized medicine include key legislation on diversity in research and genetics nondiscrimination.

Diversity in Research

Prior to 1993, all clinical trials at the U.S. National Institutes of Health (NIH) were being conducted only on white men. Congresswoman Slaughter led the charge to fix this discrepancy, culminating in the NIH Revitalization Act of 1993, which mandated that the NIH include women and minorities in all human subject research and established the Office of Research on Women's Health (ORWH) at the NIH. These achievements were prelude to her work on GINA, as she recognized that incorporating diversity leads to good biomedical research.

Genetics Nondiscrimination

Congresswoman Slaughter was a strong supporter of the Human Genome Project and was excited about the future of genetics upon initiation of the project in 1994. She recognized, however, that patients might be deterred from getting genetic tests because of fears that perceived negative results could lead to employment and health insurance discrimination. She also recognized that the fear of genetic discrimination could prevent patients from participating in research, which would stifle scientific advances in genomic medicine. She authored and sponsored GINA, which became law in 2008 after a 14-year Congressional battle. The late U.S. Senator Ted Kennedy called GINA "the first civil rights bill of the new century."

U.S. Rep. Dorothy Louise McIntosh Slaughter (D-NY), who passed away on March 16, 2018, helped pave the way for personalized medicine by authoring the Genetic Information Nondiscrimination Act (GINA), which prohibits the use of genetic data for certain discriminatory purposes.

GINA prohibits health insurers and employers from using genetic information to discriminate against an individual. In so doing, the law helps deter discrimination and diminish the chilling effect that a lack of information privacy protections would have on research.

Harvard Business School — Accelerating Innovation in Precision Medicine

by Richard Hamermesh, D.B.A., Faculty co-Chair, Accelerating Innovation in Precision Medicine, Harvard Business School

Dear Colleague:

For the past 12 years, I have had the good fortune to teach a Harvard Business School (HBS) case at PMC's *Annual Personalized Medicine Conference*. And for the past two-and-a-half years, I have been the Faculty co-Chair of the HBS Kraft Precision Medicine Accelerator (KPMA), along with Kathy Giusti, Founder of the Multiple Myeloma Research Foundation and the Multiple Myeloma Research Consortium.

At the conference and through my ongoing work with KPMA I have learned — and continue to learn — of many innovative approaches to speeding the pace of innovation in precision medicine. I believe that if we can share these best practices across the broader ecosystem, progress in precision medicine will happen more quickly.

I am pleased to invite you to a brand new executive course at HBS that attempts to do just that — share successful ideas that can be adopted and put into practice to get new precision medicine therapies to market faster.

This immersive course, Accelerating Innovation in Precision Medicine, will be offered at HBS from September 5 – 7, 2018. It has three main objectives: to share new business models that will accelerate progress; to develop organization-specific business plans; and to get participants to work with other members of the precision medicine ecosystem.

During the program, we'll work through several brand new cases focused on how to remove the roadblocks to innovation. It will include topics such as reaching cancer patients through direct-to-patient work; bringing together competing data sets from institutions working on the same disease; adaptive trials and impact investing. To complement the cases, we will have numerous guest speakers and, most importantly, you will engage in application exercises.

The exercises will be customized for you, focus on the issues you are facing, and give you the opportunity to apply the learnings from the cases directly to your organization. For example, after the data and analytics cases, we will conduct exercises to explore questions such as: Who's holding the genomic data and clinical information on patients with your disease? Assuming you had all the data, what would be the two or three most important questions you'd like to answer?

As someone who is involved with PMC and a key leader in precision medicine, I encourage you to attend this program. Participants in other health care programs tell us it's even better if you can attend as a team. Working in teams provides a real opportunity to bring the right people together in a unique environment, uninterrupted by day-to-day work, to focus intensely on problem solving. Teams could include a CEO, a Chief Medical Officer, a marketing person and a pharma partner. Or a team could be comprised of a Chief Scientific Officer, a researcher and a leading philanthropist. I envision that the class will have a healthy mix of roles, opinions and perspectives.

I know there are many conferences on precision medicine and they are terrific. But this is something different. This is a unique, action-oriented, immersive two-day course taught by faculty from HBS. You will draw upon real-world experiences and critically apply the learnings to bring them back to your organization. In this course, you are the case protagonist answering the questions: What should you do? What should your organization do? What is your plan?

I invite you to learn more about this new program at **www.exed.hbs.edu/programs/aipm** and I hope you will consider attending so we can continue to build a stronger, faster and more collaborative precision medicine ecosystem together.

Yours sincerely,

Richard Hamermesh, D.B.A.
Faculty co-Chair, Kraft Precision Medicine Accelerator
Faculty co-Chair, Accelerating Innovation in Precision Medicine
Harvard Business School

ACCELERATING INNOVATION IN PRECISION MEDICINE

JOIN FORCES WITH LEADERS DEDICATED TO FIGHTING DISEASE

Precision medicine holds great promise for treating genetic diseases—such as certain types of cancers—but bottlenecks in the system are slowing its progress. To break down these barriers, Harvard Business School Executive Education in partnership with the Kraft Precision Medicine Accelerator has created **Accelerating Innovation in Precision Medicine**, a new program focused on developing business solutions for this emerging area. As a participant, you will join top leaders from business, science, medicine, and technology to explore strategies for bringing new therapies to patients faster.

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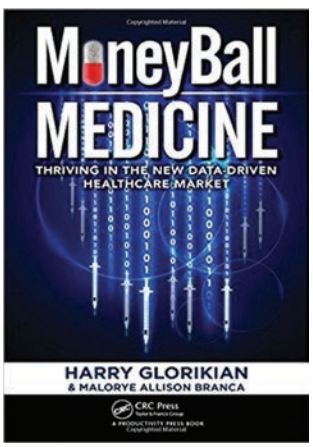
It's the Data, Stupid

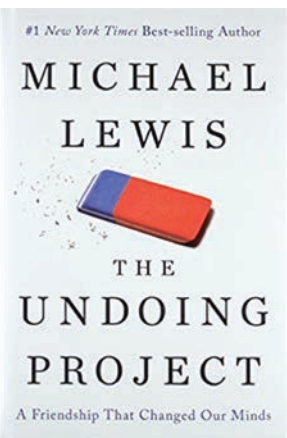
by Edward Abrahams, Ph.D., PMC President

When PMC was launched in 2004, it assumed, then as now, that advances in science and technology, notably a rapidly developing ability to harness the significance and power of aggregated data, could provide new insights that would inform biomedical research and clinical care. Those insights, in turn, PMC contended, would lead to a new era in health care. In contrast to one-size-fits-all, trial-and-error medicine, we called this data-driven, evidence-based health care "personalized medicine."

A few years later, some biomedical researchers began to fear, albeit without any evidence that such was the case, that the term "personalized" would be misunderstood. They sought therefore to rebrand the idea that the health care system could become more efficient if we targeted particular interventions only at those subpopulations that would benefit as "precision medicine," a bit more clunky a term and eschewed by patients, but one adopted by President Obama's science advisors when they rolled out his Precision Medicine Initiative. Then and now, the two terms are used more or less interchangeably, although personalized medicine tends to put the patient at the center more than precision medicine.

In a new and comprehensive book, *MoneyBall Medicine: Thriving in the New Data-Driven Healthcare Market*, which surveys how data is transforming health care today, Harry Glorikian, General Partner, New Ventures Funds, and Malorye Allison Branca have come up with a new name for the field. While patients are unlikely to clamor for "moneyball medicine" any time soon, Glorikian, one of the leading consultants in the field, and Branca, a science writer, both of whom I know and respect, correctly argue that data, as it has for other fields, open new opportunities for biomedical research and value-based medicine, if political obstacles can be overcome and they can be shared and integrated into planning and analysis by companies, providers, payers and the health system generally. As they write, "the new healthcare business paradigm is to measure → optimize → transform."





The alternative, they contend, is to "remain on the sidelines" and become "increasingly irrelevant."

The term "moneyball," students of baseball know, comes from Michael Lewis' *Moneyball: The Art of Winning an Unfair Game*, an analysis of the Oakland A's successful 2002 season, which was grounded on following the wisdom of data instead of time-honored baseball instinct. If massive amounts of data could help a team win a pennant with no-name players at a fraction of the cost, Glorikian and Branca write, surely its lessons apply even more dramatically to health care, which has its own time-honored inefficiencies built into it.

They also contend that before Lewis published *Moneyball* in 2003 the idea that "analyzing massive amounts of data could help pick a better baseball team than the wisdom of experts seemed laughable." Actually, that is not correct.

As Lewis explains in a subsequent best-selling study he published last year titled, *The Undoing Project: A Friendship That Changed Our Minds*, the roots of the logic that explain why it is so important to follow the data, especially in medicine where the stakes are high, can be found in the academic papers of two Israeli psychologists, Daniel Kahneman,

> "Today the smart money in almost every field not only trusts algorithms more than intuition but is also placing an increasingly large bet on the assumption that artificial intelligence will reshape the world we live in."

Ph.D., and Amos Tversky, Ph.D., published decades earlier. Kahneman, who went on to win a Nobel prize in economics, and Tversky, who unfortunately died before the significance of their work was recognized, demonstrated how built-in biases in human thinking undermine smart decision-making. More than anyone, Kahneman and Tversky have led us to the present moment, where today the smart money in almost every field not only trusts algorithms more than intuition but is also placing an increasingly large bet on the assumption that artificial intelligence will reshape the world we live in.

While less so in medicine because there are so many unknown variables — not to mention inefficiencies that do not respond to market pressure — the handwriting is also on the wall for health care. According to its proponents, the logic of artificial intelligence can take the doctor out of the equation just as easily as it proposes to take drivers out of cars.

Although I am not sure that the American Medical Association will be mollified by his assertion, Eric Schmidt, for example, the former Alphabet CEO and one of the leading architects of using new technologies to make medicine more efficient, would like to keep a "human in the loop." Still, Schmidt envisions a world in which biomedical research and delivery of health care become more personalized and precise — as well as more profitable for those who embrace, in Glorikian and Branca's words, "the new data-driven healthcare market."

MEDIA BRIEF

From the PMC News Desk

CMS Makes Personalized Medicine Testing More Accessible to Cancer Patients Nationwide with Coverage Decision on NGS Tests

The U.S. Centers for Medicare and Medicaid Services (CMS) made personalized medicine testing more accessible to cancer patients nationwide in March with a decision to cover next-generation sequencing (NGS) tests that are approved or cleared by the U.S. Food and Drug Administration (FDA) for use with a specific therapeutic product. In its final decision on the topic, CMS reversed course on an unpopular draft memo that would have inadvertently usurped coverage from a larger set of NGS-based laboratory tests now covered by local Medicare contractors by requiring that those tests, too, receive FDA approval or clearance in order to secure only limited "coverage with evidence development."

PMC had submitted a comment letter to voice concerns about the impact of those sections of the draft memo.

"We applaud CMS for recognizing that NGS testing can improve care for cancer patients and for seeking to facilitate patient access to FDA-approved platforms and assays," PMC President Edward Abrahams told *STAT News* as part of a story on the original decision memo that was also published in *The Boston Globe*. "To ensure that NGS testing is available to all the patients who might benefit from it, we strongly urge CMS to engage with all stakeholders to revise its decision memo as it pertains to evidence required for coverage and coverage with evidence development."

Wired (March 2018)
The Boston Globe (February 2018)

Analysis of 2017 Approvals Suggests Encouraging Future for Personalized Treatments at FDA, Agency Commitment to Improving Challenging Regulatory Landscape for Personalized Tests

PMC's latest analysis of the U.S. Food and Drug Administration (FDA)'s work in personalized medicine, released in January, suggests an encouraging future for personalized treatments at the agency and a commitment from its leadership to improve a challenged regulatory landscape for personalized tests.

The report, titled *Personalized Medicine at FDA: 2017 Progress Report*, shows that FDA approved a record number of 19 personalized treatments — 16 new molecular entities (NMEs) and three gene therapies — in 2017. The 16 personalized NMEs accounted for 34 percent of all NME approvals last year, making 2017 the first year that personalized medicines accounted for more than 30 percent of all NME approvals.

"Despite myriad challenges, the diagnostic and pharmaceutical industries are deeply invested in making health care more effective and efficient by developing products that guide treatments to only those patients who will benefit from them," PMC President Edward Abrahams said. "As this report shows, FDA is increasingly committed to supporting that effort."

GenomeWeb (January 2018)

FDA Expands Frontiers of Personalized Medicine With Approval of First Gene Therapy for Treatment of Eye Disease, Spark Prices Therapy at $850,000

In a development that expands the frontiers of personalized medicine, the U.S. Food and Drug Administration (FDA) approved in December the first gene therapy for the treatment of eye disease. The treatment, called Luxturna (voretigene neparvovec-rzyl), restores eyesight to patients with a genetic condition that causes partial or total blindness. Spark Therapeutics priced the treatment at $850,000, significantly lower than analysts' expectations of $1 million or more.

Pharmacy benefits managers and health insurance companies, which have in recent years been critical of high prices for personalized treatments, responded favorably to the price for Luxturna.

"To be very frank, they've hit on a responsible price," said Steve Miller, M.D., Chief Medical Officer of Express Scripts, a pharmacy benefits manager. "Is it inexpensive? Absolutely not. But it's responsible."

Forbes (December 2017)

Study Finds Most Value Assessment Frameworks Could Unintentionally Undermine Personalized Medicine

A PMC white paper published in December shows that most of the value assessment frameworks (VAFs) that influence reimbursement decisions could unintentionally undermine personalized medicine. The report, titled *Personalized Medicine and Value Assessment Frameworks: Context, Considerations, and Next Steps*, examines the extent to which popular VAFs incorporate five considerations that frameworks must account for to accurately assess the value of personalized medicines.

"To achieve their articulated goal of calculating rational prices for pharmaceutical products, VAFs must acknowledge human heterogeneity and incorporate the principles of personalized medicine," said PMC President Edward Abrahams. "PMC's report suggests that most VAFs have a long way to go, and could have the unintended consequence of slowing progress in health care."

STAT News (June 2017)

CLINICAL LABORATORY TESTING SERVICES
AlphaGenomix Laboratories
Empire Genomics
Laboratory Corporation of America (LabCorp)
Metabolon, Inc.
Quest Diagnostics
Taliaz Health

DIAGNOSTIC COMPANIES
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Alacris Theranostics GmbH
Almac Diagnostics
AltheaDx
ASURAGEN, Inc.
Biological Dynamics, Inc.
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CareDx, Inc.
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Foundation Medicine, Inc.
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MolecularMD
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Siemens Healthcare Diagnostics, Inc.
SomaLogic, Inc.
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Aravive Biologics
AveXis
Freenome
Ignyta
Loxo Oncology
Neon Therapeutics
Regeneron Genetics Center
Relay Therapeutics
Tango Therapeutics
Syros Pharmaceuticals
Unum Therapeutics
Zinfandel Pharmaceuticals, Inc.

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Harvard Pilgrim Health Care

INDUSTRY/TRADE ASSOCIATIONS
American Clinical Laboratory Association (ACLA)
BIO (Biotechnology Innovation Organization)
Biocom
PhRMA

IT/INFORMATICS COMPANIES
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Concert Genetics
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Bulgarian Association for Personalized Medicine
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Fight Colorectal Cancer Foundation
Food Allergy Research and Education
Friends of Cancer Research
Global Liver Institute
International Cancer Advocacy Network ("ICAN")
LUNGevity Foundation
Multiple Myeloma Research Foundation
National Alliance Against Disparities in Patient Health
National Alliance for Hispanic Health
National Blood Clot Alliance
National Health Council
National Patient Advocate Foundation
Susan Gurney
THRIVORS

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American Medical Association (AMA)
Association for Molecular Pathology (AMP)
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Brigham and Women's Hospital, Genomes2People Research Program
Brown University
Business Finland
Cancer Treatment Centers of America
Center for Medical Technology Policy
The Christ Hospital
College of American Pathologists
Colorado Center for Personalized Medicine
Coriell Institute for Medical Research
CREATE Health Translational Cancer Centre, Lund University
CureOne
Duke Center for Research on Personalized Health Care
Essentia Institute of Rural Health
Geisinger
Genome British Columbia
Genome Canada
Georgetown Lombardi Comprehensive Cancer Center
Harvard Business School
Helmholtz Zentrum München
Hospital Albert Einstein
Inova Health System
Instituto de Salud Carlos III
Intermountain Healthcare
International Society of Personalized Medicine
The Jackson Laboratory
Johns Hopkins Individualized Health
Kaiser Permanente
King Faisal Specialist Hospital and Research Centre
Manchester University School of Pharmacy
Marshfield Clinic
Mayo Clinic
MD Anderson – Institute for Personalized Cancer Therapy
Mission Health, Fullerton Genetics Center
Moffitt Cancer Center
National Pharmaceutical Council
Nicklaus Children's Hospital Research Institute
North Carolina Biotechnology Center
NorthShore University Health System
Ontario Genomics Institute
Partners HealthCare Personalized Medicine
Poliambulatorio Euganea Medica
Precision Health Initiative at Cedars-Sinai
Precision Medicine Alliance LLC
Qatar Biobank
The Quebec Network for Personalized Health Care
Rutgers Cancer Institute of New Jersey
Sanford Imagenetics, Sanford Health
Stanford University School of Medicine
Sylvester Comprehensive Cancer Center – University of Miami
Swedish Cancer Institute
UC Davis Mouse Biology Program
University of Alabama, Birmingham
University of Arizona Health Sciences
University of California, San Francisco (UCSF)
University of Florida
University of Maryland School of Pharmacy
University of Pennsylvania Health System
University of Pittsburgh Medical Center (UPMC)
University of Rochester
University of South Florida Morsani College of Medicine
Vanderbilt University Medical Center
Virginia Commonwealth University Health System
Wake Forest Baptist Medical Center
West Cancer Center

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Bruce Quinn Associates
Cambridge Healthtech Institute
Ceres Health Research
Center for Individual Opportunity
Clarity Research & Consulting
ConText
ConvergeHEALTH by Deloitte
CRD Associates LLC
Credit Suisse
Defined Health
EdgeTech Law LLP
EY Parthenon
Feinstein Kean Healthcare
Foley & Lardner LLP
Foley Hoag LLP
Genome magazine
GlobalData PLC
Goldbug Strategies LLC
Harry Glorikian
Health Advances LLC
Hogan Lovells LLP
Innovation Horizons
Jane Binger, EdD
Jared Schwartz, MD, PhD, LLC
The Journal of Precision Medicine
Kinapse
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Professional Genetic Interactions
Quorum Consulting
Ramon Matawaran, PhD
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Colorado Center for Personalized Medicine
Cota Healthcare
Edico Genome
Emily's Entourage
Fight Colorectal Cancer
Food Allergy Research and Education
Freenome
Genome Medical
Harry Glorikian
Health Advances
Hospital Albert Einstein
International Vitamin Corporation
Loxo Oncology
Medidata Solutions
National Alliance Against Disparities in Patient Health
National Blood Clot Alliance
National Health Council
Nicklaus Children's Hospital Research Institute
Panaceutics
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MISSION: The Personalized Medicine Coalition (PMC), representing innovators, scientists, patients, providers and payers, promotes the understanding and adoption of personalized medicine concepts, services and products to benefit patients and the health system.

PMC
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