



## Background: What's Different About Personalized Medicine

The near-term goal of adopting personalized medicine (note: the authors do not differentiate in this paper between “personalized medicine” and “precision medicine”) is to diagnose and treat disease with the greatest possible accuracy by using novel tools that provide individual-specific molecular insights about the disease, help identify the most appropriate treatments, and deliver improved clinical outcomes. Longer-term, the goal is far more ambitious – nothing less than a shift to a new healthcare paradigm that leverages knowledge of an individual patient’s genetic, environmental, and lifestyle characteristics to sustain health and wellness and prevent or at least slow the trajectory of disease, thereby obviating the clinical and economic burdens that society now faces.

But unlike myriad new technologies that have affected healthcare in recent decades – such as minimally invasive robotic surgery, MRI and CT scans, laser surgery, digitally driven prosthetics, and telemedicine, to name just a

few – the portfolio of molecular technologies that enable personalized medicine cannot be provided with just one-time add-ons within one department or discipline at a provider institution. Rather, the implementation of personalized medicine permeates all healthcare delivery processes, requiring far more extensive investment and infrastructure changes.

Hence, adoption of personalized medicine is different from anything that has come before it, and perhaps belongs not with the examples of biomedical innovation listed above but with encompassing societal shifts provoked by technology. Personalized medicine adoption is difficult not only due to the host of issues internally at each provider organization, but also due to the need for systemic transformation externally (i.e., regulation, reimbursement, patient understanding, ethical concerns, health information management, etc.) that may not progress as rapidly as the science and technology, and that is certainly outside the control of any one provider or group of providers. The interplay of these internal and external factors –

dynamic and interrelated – makes the challenge particularly complex and daunting.

## Case Study Approach

The PMC/FKH team made site visits to eight U.S. provider organizations adopting personalized medicine, chosen to reflect a mix of urban vs rural; northeast, southeast and central regions; specialty centers vs. general healthcare missions; academic vs. community; non-profit vs. for-profit; diverse patient demographics; and varying stages of personalized medicine adoption. The team conducted in-person interviews of 70+ professionals at those institutions, including CEOs, other C-suite executives, physicians, administrators, researchers, geneticists, laboratory managers, scientists, genetic counselors, patient navigators, and information technologists. The interviews focused on challenges, emerging models, and the strategies, processes, programs, policies, and people that are required for – or that facilitate – rapid and effective adoption.



Table 1: Case Study Project Sites

**Geisinger** is one of the nation's largest physician-led integrated health service organizations, serving as the major provider for a low-turnover population of more than three million residents through 45 counties in central, south-central and northeast Pennsylvania and southern New Jersey. With 12 hospital campuses, 1,600 employed physicians, and 30,000 employees, Geisinger prides itself on excellence of care and commitment to medical education, implementation research, and community service. It is both a provider and a payer, through its more than 500,000-member health plan.

**Inova** is a non-profit healthcare system based in northern Virginia that serves more than two million people each year throughout the Washington, DC, metro area and beyond. It is comprised of a comprehensive network of hospitals, outpatient services and facilities, primary and specialty care physician practices, and health and wellness initiatives. With 16,000 employees, Inova serves primarily an educated, suburban demographic. It is known for neonatal care, with 20,000 babies delivered annually.

**Mayo Clinic**, ranked by U.S. News & World Report as #1 in the nation overall, functions as a major academic health center with three major locations in Minnesota, Florida, and Arizona. It has more than 60,000 employees, and provides services to more than 1.3 million patients each year system-wide. Mayo disseminates medical knowledge through news network, radio feed, social media, conferences, and print materials for both consumer and professional audiences.

**Mission Health System** is a non-profit, independent community health system serving western North Carolina. It is comprised of six hospitals, almost 11,000 employees, and more than 1,000 staff members and affiliated physicians. Its 18-county catchment area is older, poorer, sicker, and less likely to be insured than state and national averages. Mission Health has been named a Top 15 Health System by Truven/IBM Watson in five of the past six years.

**Moffitt Cancer Center** is a National Cancer Institute-designated comprehensive cancer center based in Tampa, Florida, with over 5,200 employees. The center has more than 9,000 new admissions each year, and its 23,000 patient visits annually make it the third largest academic cancer center in the country.

**NorthShore University Health System** is a large system in the Chicago metropolitan area, comprised of four hospitals and a network of 80 primary care office locations, with approximately 1,000 employed doctors and hundreds of physician affiliates. The patient demographic leans towards affluent and educated.

**Partners HealthCare Personalized Medicine** is a division of Partners HealthCare, an integrated healthcare system founded by Brigham and Women's and Massachusetts General Hospital, both Harvard-affiliated teaching hospitals, and the largest independent hospital recipient of National Institutes of Health (NIH) research funding in the United States.

**West Cancer Center**, a for-profit provider located in the greater Memphis area of Tennessee and parts of Mississippi, was formed through a partnership among the West Clinic, University of Tennessee, and Methodist Healthcare. Unlike solely academic or community cancer centers, West is a multi-disciplinary hybrid that conducts research and offers comprehensive adult cancer care for more than 7,000 new cancer patients per year at 17 locations. West's patient demographics range from well-educated urban professionals to rural areas where disadvantaged and/or uninsured patients often experience healthcare disparities.

## Challenges and Concerns

While the case study sites differ considerably in their characteristics, they are very consistent in describing the challenges faced by any provider that seeks to integrate personalized medicine into care at this early stage.

The commitment to adoption appears to require leadership from a “visionary” — each of the sites credited an individual and his originating concept. Such visionaries and the teams that implement their vision must grapple with the core challenge of developing a viable business model in the absence of routine reimbursement. While certain molecular diagnostic tests and targeted drugs are routinely reimbursed by payers — especially in cancer — reimbursement for molecular technologies overall is still inconsistent and usually obtained on a case-by-case basis with great difficulty, if at all.

The conundrum is that providing patients access to personalized medicine relies on reimbursement; reimbursement relies on evidence of clinical utility and cost-effectiveness; and getting the necessary evidence depends on outcomes from large-scale usage, which is difficult to deploy without being able to provide consistent access. A frustrating circle. The amounts and types of evidence required for reimbursement are still unclear, and may vary from payer to payer. Regardless of how high the evidence hurdle at any one payer, development of evidence is a costly undertaking, and tracking patient outcomes to demonstrate clinical effectiveness can take months or years. In addition to the direct costs of testing, the requisite infrastructure investment for personalized medicine is high. Hence, no systemic, sustainable business model has yet emerged for providers that adopt personalized medicine, other than “confidence” that over time reimbursement norms will change in a fundamentally positive way.

Information technology infrastructure — electronic health records (EHRs) in particular — also remains a widespread challenge. The Office of the National Coordinator for Health IT (ONC) reports that nearly 96% of U.S. non-federal acute care hospitals possess a certified EHR technology. But most EHR systems were developed for administrative purposes, and are therefore not suited for integrating genomic profiling data or patient-reported outcomes data — or for providing clinical decision support in real-time much less to dynamically update knowledge of biomarkers and their significance. Such capabilities are needed to offer personalized medicine at scale, and require significant financial investment.

Change in medical practice relies on collective wisdom and amassing compelling evidence. Outside cancer and pharmacogenomics, however, most professional societies have not yet defined genomics-based guidelines; in the absence of such guidelines, some medical disciplines appear to have a “wait and see” attitude regarding personalized medicine approaches.

The cultural change associated with moving from traditional fee-for-service, or volume-based care, to value-based care also remains a pervasive issue. In addition, individual clinicians vary in their willingness to shift away from traditional clinical practices. Broad consensus has not yet emerged on the most appropriate incentives to encourage clinicians to practice new personalized medicine techniques. A lack of physician and patient education slows adoption as well. Due to the rapid expansion of genomics discoveries but the paucity of genetics curricula in medical schools, most physicians do not feel well prepared to practice personalized medicine approaches. Patients are also lacking information about personalized medicine, and may rely solely on web-

based searches to stay informed in the absence of a trusted educational resource. Moreover, there is a dearth of personnel — such as genetic counselors, pharmacists and other clinicians — with relevant expertise in interpretation of results and counseling patients. No national workforce initiative to facilitate personalized medicine has yet emerged.

Overall, as David Ledbetter, Ph.D., Chief Scientific Officer of Geisinger, puts it: “There’s a widening gap between the engine of basic science generating massive amounts of new molecular data and the demanding realities of day-to-day clinical practice.”

## Findings

In the absence of a national “manual” for adopting personalized medicine and guided by the oft-stated belief that “each institution is unique,” most of these sites say they are developing their own customized institutional approach to the challenges described above. Those approaches, nonetheless, have several core areas in common (Vision/Strategy, Operating Models, Workflow/IT, Education, and Evidence Generation).

## Vision and Strategy

At Moffitt Cancer Center, William Dalton, Ph.D., M.D., who served as President and CEO from 2002 to 2012, was the original driving force for personalized medicine. Describing the Moffitt commitment, he says: “The most essential element of leadership is the ability to describe a vision of the future so compelling that others will gladly join you in making the vision a reality.” The philosophy of the Moffitt team is that personalized cancer medicine cuts across both individual cancer patient management and population analysis. The organization sees clinical care and research as inextricably linked, since, in a rapid learning system, research provides insights that directly affect care (and vice versa).

Knox Singleton, CEO of Inova in northern Virginia, sees personalized medicine as the next frontier, and believes that by predicting risk with genomics and then managing lifestyle accordingly, it will be possible to get paid by insurers to prevent disease and thereby reduce healthcare costs. The Inova vision encompasses personalized medicine and beyond: to move from being a hospital system that offers fee-for-service treatment of disease to a community health center where knowledge of every individual's genomic characteristics guides personal health and wellness decisions through a continuing relationship between patients and the health center. Inova is investing \$150 million of its own resources over five years to address and integrate every aspect of technology, clinical care, infrastructure, operations, and the patient journey.

"After the move to germ theory that revolutionized healthcare in the 20th century," Mr. Singleton says, "the next big inflection point is to prevent chronic diseases in an aging population."

Ronald A. Paulus, M.D., joined Mission Health as President and CEO in 2010 to help shape the future of healthcare delivery in western North Carolina. As part of that effort, his team is integrating personalized medicine into routine practice in an effort to be "best in class" for cutting-edge technology in a community hospital system and to serve as a role model for other systems. Mission is currently constructing the Mission Hospital for Advanced Medicine, envisioning genomic knowledge embedded into clinical processes for all therapeutic areas and a system in which emerging technologies — genomic, digital, robotic, artificial intelligence — can come together to transform prediction and prevention to generate superior clinical outcomes. "When you know that a movement in medicine will be transformative, it is not an option to sit back and just see what happens. Our system must be engaged, both for ourselves and as a model for others," notes Dr. Paulus.

Janardan Khandekar, M.D., a medical oncologist and Director of Innovation and Education at the NorthShore Center for Personalized Medicine, was the visionary for NorthShore University HealthSystem. Speaking of his original plan, he notes: "You need a team. To accelerate adoption, there must be a willingness to work together, to think differently about the patients and not ourselves as physicians, and even to change our language from 'my patient' to 'our partnership with patients.'"

At Partners HealthCare Personalized Medicine, founder Raju Kucherlapati, Ph.D., has become one of the most recognizable faces of personalized medicine globally. His vision for genomic medicine was among the earliest in the nation, emphasizing discovery and translational research to accelerate the move from bench to bedside. Scott T. Weiss, M.D., now Scientific Director, states that the strategy is to enable Partners' 2,200 NIH-funded investigators to access the services and information technology they need to be leaders in the field and in the national dialogue.

At Mayo Clinic, the business strategy for personalized medicine involves a significant financial investment of its own resources, with the belief that over time the economic value to payers and the healthcare system will be realized. Gianrico Farrugia, M.D., and Keith Stewart, M.B., CH.B., the former and current Directors of the Mayo Center for Individualized Medicine, respectively, and Scott Beck, administrator for the Center, believe that the paradigm shift to personalized medicine is inevitable. They are implementing a comprehensive strategic plan based on a carefully engineered, evidence-based change management process that works top-down and bottom-up and across all disciplines. The intent is to move tens of thousands of Mayo employees in the new direction. "Our definition of success?" asks Mr. Beck. "When every healthcare provider uses genomic medicine to improve care."

At Geisinger, eminent physician/scientist Glenn Steele, M.D., Ph.D., was CEO from 2001 to 2015. He saw the opportunity for Geisinger to use its greatest assets — its stable, homogeneous population with families of three or more generations within the Geisinger system and its integrated payer/provider system — to create a "laboratory" for personalized medicine. "Geisinger is as close to Iceland as you'll find in the United States," he once noted. The Geisinger strategy is top-down: plan research; sequence biosamples and track how the genomic data affect outcomes; analyze clinical and cost effectiveness; and, if justified through a scientific advisory committee, implement via practice guidelines and system-wide reimbursement.

At West Cancer Center, Executive Director Lee Schwartzberg, M.D., has spearheaded early adoption of all aspects of "personalization" of care. He and his colleagues began to use molecular approaches systematically several years ago, bolstered by an expanding research portfolio. In addition, they have been early leaders in the application of technology and services to respond to the "whole patient" and his/her values, including physical, emotional, psychosocial, and financial needs.

### Operating Models

The most common model among both the academic health centers and community systems studied here is the establishment of a center for personalized medicine to serve as the "front door" for patients and clinicians, and as a hub for personalized medicine education and services. Such centers vary from a small suite of offices to a dedicated building, to a virtual center with personnel dispersed among different disciplines where only the executive leaders have dedicated personalized medicine roles. They usually encompass a laboratory and/or capability for managing external specialty laboratories; genomics and genetics expertise; patient educational programs and materials; services to guide usage of molecular diagnostic tests; staff to consult

with both physicians and patients; processes to track clinical outcomes; and responsibility for development of plans for immediate and longer-term implementation of personalized medicine approaches at that institution.

Often, the center for personalized medicine is designed as a research program to discover/validate biomarkers, develop proprietary diagnostic tests, and examine strategies to integrate them into the clinical setting to sustain cutting-edge care. Such centers are intentionally separate from traditional medical departments, so that they can operate across medical disciplines. At some sites, the center is intentionally “virtual” to obviate competition among traditional medical specialty silos. At some bricks-and-mortar sites, leaders acknowledge that while their center is a focal point to advance personalized medicine, the absence of being integrated into the medical disciplines of the hospital is a drawback they hope to overcome as personalized medicine evolves from implementation research to standard medical practice. In contrast to the research-focused centers, other centers do not conduct research per se, but develop programs in response to specific clinical needs identified by the institution’s medical specialties.

Moffitt’s DeBartolo Family Personalized Medicine Institute is a virtual center and “matrix” that functions across disciplines. “We’re in the tie-breaker business, since there is often more than one therapeutic option for a patient, and determining the best one requires maximizing insight,” describes Howard McLeod, Pharm.D., the Institute’s Medical Director. Moffitt has developed more than 50 disease-specific clinical pathways so far to help embed genomics into the day-to-day work flow. Dr. McLeod’s team is also piloting a one-button “power order” capability in the pathways for breast and ovarian cancers and lymphoma that fires off not just a single test order but a cascade of actions, including gene panels and sequencing. The DeBartolo Institute

also oversees Total Cancer Care®, Moffitt’s signature research partnership established in 2006 among patients, doctors, and researchers, along with pharmaceutical members — intended to improve all aspects of cancer prevention and care. More than 120,000 patients had joined the project by late 2016. As partners in Total Cancer Care®, Moffitt patients participate over their lifetime, starting with next-generation sequencing and donation of their genomic and clinical data and biosamples. Patients can track the Total Cancer Care® study’s progress via a dedicated patient portal. Researchers can analyze the huge database to identify molecular diagnostic tests that could be incorporated into the Moffitt in-house laboratory. Clinicians can access the database to match patients to clinical trials and seek recommendations from the DeBartolo Family Personalized Medicine Institute on specific issues in patient care. Pharmaceutical partners can access anonymized data and use it in the development of new targeted treatments.

In addition, the Moffitt team includes business strategists gathering evidence to demonstrate the value proposition from a healthcare economic viewpoint. First, they build models based on the medical literature (i.e., “If we reduced chemotoxicity in patients, what are the savings?” or “If we conduct pharmacogenomics testing on certain patients, what is the financial impact?”). They then work with Moffitt Collaborative Data Services to run the models with Moffitt’s own clinical data.

Comparable hubs exist at many of the case study sites: the Mayo Center for Individualized Medicine has translational and infrastructure programs; the Inova Translational Medicine Institute ties genomics research to disease conditions to improve clinical care; Geisinger has both the Weiss Center for Health Research for basic science and the Geisinger Institute for Genomic Medicine for implementation

research; and Partners HealthCare Personalized Medicine has a “one-stop shop” with a Laboratory for Molecular Medicine, a Translational Genomics Core, and a biobank.

At some centers, a personalized medicine operations director “shepherds” personalized medicine approaches throughout the system. While the title may vary, this person is usually seen throughout the organization as the advocate for personalized medicine, responsible for all requisite planning and implementation. For example, at Mission, Jonathan Bailey, Chief Program Development Officer, saw personalized medicine as the tip of the spear for “a whole new way to deliver healthcare.” Lynn Dressler, Dr.P.H., was recruited by Mission’s CEO, Dr. Paulus, in 2013 to establish and direct the Mission Health Personalized Medicine Program, whose services now include clinician and community education, development of uniform best practices, quality improvement studies, and clinical consultation for cancer and non-cancer patients. Dr. Dressler’s role involves translating relevant evidence-based research into practice, integrating personalized medicine into each service line using Mission’s “care process models,” and working with Mission’s information technology staff to develop clinical decision support, embedding warnings, triggers, and results into the EHR with minimal impact to inpatient and outpatient work flow. More generally, Dr. Dressler serves as the primary catalyst for shifting care to a personalized medicine paradigm.

### Work Flow and Information Technology

There is broad consensus that information technology paves the road to adoption of personalized medicine at scale. Several providers, such as Mission Health, NorthShore and West, note that with the right software tools, everything can be “made easy” for the clinical team to seamlessly integrate personalized medicine approaches into the work flow. The key issue is scalability: how

to embed data in the IT system of a provider in a way that “grabs” molecular and other information and presents it for rapid, accurate, easy, and patient-centered decision-making. At Partners HealthCare Personalized Medicine, information technology has been central to all activities. Sandy Aronson, A.L.M., M.A., Executive Director of Information Technology, working closely with Heidi Rehm, Ph.D., F.A.C.M.G., Director of the Laboratory for Molecular Medicine, developed a core IT platform called GeneInsight™. GeneInsight™ is a suite of software tools now available commercially that provides not just laboratory infrastructure, but the ability to manage the interpretation of genomic data, draft the reports, keep the database updated, and fire alerts to the physician’s desktop when interpretation of the variants changes over time. They are now working on real-time population-based analytics to be made available via digital apps at the bedside, enabling physicians to project their patient’s disease trajectory based on the historical experiences of large numbers of similar patients. The team believes that use of such apps will overcome the “standards logjam” that has plagued the field, and will help move medicine towards a “plug and play” infrastructure that lowers the cost of adoption. Demonstration of such value underlies much of these informatics efforts: Dr. Weiss notes that “It’s a high bar to deliver better outcomes at lower cost, but that’s what will lead to rapid adoption of personalized medicine.”

Efficient personalized medicine data integration into a health information management structure can also help foster larger networks and potential health system-wide collaboration. For example, Moffitt co-founded – along with the Ohio State Comprehensive Cancer Center – a research partnership called ORIEN (Oncology Research Information Exchange Network). The 12+ cancer centers that have joined ORIEN all apply the Total Cancer Care® protocol to standardize clinical, molecular,

and epidemiological data, thereby tapping into huge clinically annotated cancer tissue repositories and data that expedite evidence generation.

### Education, Culture Change, and Patient Empowerment

Every one of the case study sites stresses the importance of physician and patient education, and bemoans the lack of a national initiative to accomplish it on a large scale. Although there has been an increase in genomics curricula in medical, pharmacy, and nursing schools, the biggest gap in clinician knowledge is not from new graduates but among clinicians in established practices. Thus, there is a need for educational initiatives targeting practicing physicians. Some of the case study sites are investing substantial resources to build branded educational programs of their own.

Mayo, for example, initiated general education programs about the promise of personalized medicine in the year 2000. Leaders now speak of the “levers” they employ to catalyze change: education of pharmacists was among the first, since pharmacogenomics is one of the most relevant examples which can rapidly influence care. Online training modules and experiential learning programs were developed, through which 600 pharmacists Mayo-wide were introduced to genomic-based medicine and woven into the pharmacogenomics testing processes. Other educational levers include genomics as part of the core curriculum at the Mayo Clinic School of Medicine, a genetics/genomics education portal for patients, exemplary patient vignettes, and a bibliography of additional resources for those who wish to learn more. Geisinger holds a monthly case conference, which is web-cast and attracts several hundred attendees each month, while Partners, in partnership with Harvard Medical School, has one of the oldest and largest genetics training programs in the country, offering residencies and fellowships in clinical genetics, molecular genetic pathology,

pediatric genetics, etc. At Inova, physician education has been built into the MediMap® pilot described below as a requisite for the program’s success. Some sites are addressing cultural change systematically through required adherence to treatment protocols and guidelines; others through softer “invitations” to participate, awareness/education efforts, and high-touch services to support individual physician usage. For example, instead of describing personalized medicine to primary care physicians as a “radical change,” the NorthShore Center for Personalized Medicine simply presents personalized medicine as “new knowledge.” Such knowledge is delivered in the most convenient way – from rapid, “bite-size” Best Practice Alerts in their EHR system to more detailed versions for greater depth of analysis and discussion. Additionally, through NorthShore’s Genetic Health Assessment, patients are now being introduced to genomic medicine in the primary care offices. At Mission Health, pilot feasibility studies have been implemented in primary care practices, where test cost is covered through a state grant and clinician education and training are provided through the personalized medicine program. This approach allows physicians to become familiar with testing in everyday care, and enables Mission to identify other barriers to provision of testing in a busy practice.

### Evidence Generation

Most of the centers for personalized medicine refer to the need for more robust evidence generation to demonstrate the value proposition of personalized medicine. These sites are implementing personalized medicine in the context of a research program, and many studies are designed to validate clinical efficacy and effectiveness. The scale of the pilot programs ranges from a few dozen patients to tens or even hundreds of thousands of patients. Some studies are self-funded. Others are implemented with funding from NIH or philanthropy. Dr. Ledbetter comments

that “There is not enough funding of implementation research. But genomic medicine cannot be practiced just on faith in the technology. We need to demonstrate clinical effectiveness and utility.”

The Geisinger MyCode® Community Health Initiative is a large-scale genomic sequencing research program intended to identify genetic contribution to illness, advance knowledge of genomic medicine, and provide new and improved treatment for disease. All Geisinger members are encouraged to participate, and once consented, their blood samples are collected and stored in the biobank. To date, MyCode® has exceeded expectations: after meeting the original goal of 100,000 enrolled participants in the study by 2016, Geisinger set a new target of 250,000 patients.

Whole exome sequencing of the biosamples is conducted via a research collaboration between Regeneron Pharmaceuticals, Inc. and Geisinger Health System. Regeneron uses the data for discovery research into new treatments, while Geisinger uses it for clinical effectiveness and implementation research. As sequencing data are collected and then combined with each participant’s medical record, the Geisinger team analyzes biomarkers, including the Geisinger-76, an expanded version of the American College of Medical Genetics and Genomics (ACMG)’ guidelines for 59 genes whose variants are considered medically actionable.

With participant input, the Geisinger Genomic Medicine Institute has an explicit process, called Genome FIRST, to return data to the 3 - 4% of participants with variants associated with the presence or increased risk of disease. Doctors and patients review the data and decide on interventions or periodic re-evaluation. Patient-facing genomic interpretive reports are available through Geisinger’s patient portal. Furthermore, a process to capture the outcomes related to

the return of results has been set up. The outcomes have been defined and a system for routine measurement has been implemented.

Geisinger clinicians believe that MyCode® has the potential to improve individual health through appropriate screening and early intervention of those who would not otherwise realize their genetic susceptibility. In addition, they see it affecting population health, since parents and children of those with genomic variants have a high likelihood of being affected as well. Using the initial return of results, they can identify at-risk family members and test them using a “cascade” approach. This approach can magnify the effect of the testing and extend the impact to patients beyond the Geisinger system. Geisinger has also developed the infrastructure (collection, sequencing, analysis, communications, ethics, data management, education) necessary to work at scale and to serve as an exportable model so that others around the country can apply it.

Translational research and health outcomes studies around genomics are requisite for adoption, says Robert C. Green, M.D., M.P.H., Associate Director for Research at Partners HealthCare Personalized Medicine. The healthcare pathway, Dr. Green says, relies on evidence to allow professional societies to make their clinical recommendations, and those guidelines in turn trigger reimbursement. To accelerate progress along that continuum, he directs the G2P (Genomes to People) Research Program, which aims to elucidate the protocols, processes, and procedures needed to build the evidence base.

Among the G2P studies is MedSeq™, the first NIH-funded randomized trial to explore the use of whole genome sequencing in the clinical practice of medicine. The MedSeq™ research protocol – which took a team of over 50 experts to design – employs a new methodology for conducting a trial in this

space, including new ways to recruit doctors, patients, and healthy individuals; track the clinical outcomes and cost; and educate primary care physicians to apply the data. To translate many aspects of the study to clinical practice, however, cultural change is needed, Dr. Green notes, including breaking down barriers to publishing results that may run counter to current dogma in the scientific literature.

Additional trials at Partners include Baby Seq™, an early randomized trial to look at the outcomes of sequencing both healthy newborns and those in intensive care; the REVEAL (Risk Evaluation and Education for Alzheimer’s Disease) series of multi-site, randomized controlled clinical trials to address ethical, social, and translational issues in genetic susceptibility testing for common diseases; and the PeopleSeq (Personal Genome Sequencing Outcomes) Consortium, one of the first large-scale longitudinal studies to examine the experiences, attitudes, and outcomes of ostensibly healthy adults who have chosen to pursue personal genomic sequencing.

At Inova, the MediMap® program was designed to think through everything from IT, finance, legal, marketing, and technical aspects. Through MediMap®, parents of every baby born at the Inova Women’s Hospital are offered, at no charge, a pharmacogenomics test that provides information about how their child may respond to as many as 21 different medications. Currently all testing costs are covered by Inova, so there are no reimbursement challenges.

MediMap® VIP 360 has followed, as part of Inova’s concierge medicine service. The MediMap® pilot includes an educational session featuring pharmacogenomics testing for all Inova physicians, to bring them on board for using genomics in a clinical setting. Inova sees the approach as a low-risk and non-controversial first step that will pave the

## The Personalized Medicine Coalition,

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.

For more information:

[personalizedmedicinecoalition.org](http://personalizedmedicinecoalition.org)

202.589.1770

1710 Rhode Island Ave, NW, Suite 700  
Washington, DC 20036



way towards the concepts of prevention and sustaining health. This approach, in turn, may create provider/patient relationships that can incentivize patients to stay in the system.

Mayo has embedded its genomic approach in rare and undiagnosed disease for its “Diagnostic Odyssey” service, as well as in oncology and pharmacogenomics. In addition, Mayo is conducting dozens of pilots in areas such as neurology, cardiology, gastroenterology, and pediatrics. The emphasis is on genomics-based research to improve patient care. A study such as the Breast Cancer Genome-guided Therapy (BEAUTY) trial, for example, sought to understand why certain women succeed or fail on chemotherapy, and to enable individualized treatment for each breast cancer patient.

Another highlight at Mayo is the 10,000-patient pharmacogenomic sequencing study. This study leverages clinical decision support rules built into the EHR that alert the provider when the patient has a genetic mutation that could impact the way he/she processes medications.

The NorthShore Genomic Health Initiative – both a biorepository and a research study – builds on NorthShore strengths in EHRs and phenotypic diagnostics. As of Spring 2017, over 18,000 NorthShore patients had been consented for the study, and 5,000 have already been molecularly profiled using ACMG’s panel of 59 “actionable” genes and sequenced when applicable. The research objectives include assessment of the impact of genomic information on clinical care (i.e., what decisions were made, and with what outcomes); social aspects (i.e., what results get returned to patients, how the work flow unfolds for physicians, etc.); and economic/operational parameters (i.e., patient throughput and cost/benefit to the NorthShore system).

West Cancer Center does not use the term “pilot,” but is compiling the outcomes of all their patients treated with molecular

approaches to demonstrate that outcomes truly improve. By late 2016, of approximately 1,250 cases, 400 had been reviewed by the Molecular Tumor Board; of those, 120 patients were enrolled in clinical trials and about 30 patients had recommendations for off-label therapies.

### Conclusion: A Program of Action to Accelerate Adoption

The innovative providers at these case study sites are investing major financial, technological, and human resources into a future of health-care that they believe will improve patient outcomes and shift the paradigm towards prediction, prevention, personalization, and patient participation. Moreover, the pioneering sites are acutely aware of the need to build the requisite evidence base of clinical utility and cost effectiveness, and while that takes time, they are actively doing so. Although most stress that their institution is unique and must therefore pursue unique strategies for adoption of medicine, they express a willingness to share experiences with other institutions that are implementing personalized medicine. It appears that emerging models have much in common, and that key elements could be replicated in other provider sites that are willing to invest in the shift.

In anticipation of that evidence, however, it appears that much more could be done to “bend” the traditional curve of adoption through efforts made by the overall community of stakeholders acting in concert. Dr. Dalton has summarized what is needed for the paradigm shift: “The transition to personalized medicine from the old model does not occur overnight. But the more we build networks with partners, the faster and more effectively we can see the changes happening,” he says. “To fulfill on the promise of personalized medicine, there needs to be a new ecosystem ... with partnerships of multiple stakeholders who collaborate to find solutions.”

Such a new ecosystem – comprised of academic and community providers, industry, professional societies, government, consumers, and patient advocacy groups – could advance the following initiatives on a national and potentially international scale:

The Personalized Medicine Coalition and Feinstein Kean Healthcare gratefully acknowledge the generous contribution from N-of-One for this case study project.

**Table 2: A Program of Action to Accelerate Adoption: Recommendations**

**A resource for personalized medicine strategic and operational experience.**

While no one model will “fit” every institution, a shared informational clearing house could help with the development and dissemination of information about business models; templated operational processes; best practices; change management systems; genomics curricula; etc. Such a resource could also be used to archive and curate the emerging evidence base on clinical and economic effectiveness. A common core of knowledge, dynamically maintained, with systematic sharing of lessons via seminars, case studies, and online workshops, could help providers customize the most successful strategies of pioneering organizations for use at their institutions.

**A national campaign of awareness and education for the public, policymakers, and patients.**

There is a long and successful tradition of “social marketing” conducted by government and non-profit organizations to inform the public and catalyze healthy behaviors (e.g., smoking cessation, cancer screening, cholesterol monitoring, etc.).” A national campaign of awareness and education could be conducted around genetic and genomic understanding of disease and personalized medicine approaches to prevention and appropriate treatment. Pioneering institutions, including the case study sites, could be partners in such a national effort.

**A common fund to build the requisite workforce.** The Federal and state governments could expand existing educational programs and establish new training and financial assistance programs to address the shortage of geneticists, genetic counselors, and other healthcare professionals with expertise in genetics. The personalized medicine community, with help from state and/or local governments, could identify specific workforce needs and advocate for and support enhanced programs.

**Third party certification.** There is currently no standard as to what constitutes effective “adoption” of personalized medicine. A certification from a third party, analogous to the LEEDS certification from the U.S. Green Building Council, could be established to define the benchmarks of successful integration of personalized medicine.

The field of personalized medicine does not lack for enthusiastic, dedicated pioneers who are moving forward expeditiously to clinical adoption. As the evidence base expands, much more can and should be done to accelerate the process for the benefit of individual patients, the healthcare system, and society overall.

**Daryl Pritchard, Ph.D.** is the Vice President of Science Policy at PMC, where he leads PMC’s efforts to develop and promote optimal science-related policies and to increase awareness and understanding of personalized medicine amongst health care providers, patients, policy decision-makers and other stakeholders. This includes working to identify and address barriers to the adoption of personalized medicine into the health care system, including the development and promotion of appropriate clinical, health care infrastructure, regulatory and payment policies.

**Marcia A. Kean, M.B.A.**, is Chairman, Strategic Initiatives, of Feinstein Kean Healthcare, a leading communications firm dedicated to advancing innovation in the life sciences and healthcare. Marcia focuses on the impact of new waves of technology, and she has partnered with academic, non-profit, commercial and government organizations to drive adoption of personalized medicine.

References

1. Daryl E Pritchard, Franziska Moeckel, Mary Susan Villa, Laura T Housman, Catherine A McCarty & Howard L McLeod; Strategies for integrating personalized medicine into healthcare practice. *Personalized Medicine*, March 2017, Vol.14, No.2, Pages 141-152 (<http://www.futuremedicine.com/doi/full/10.2217/pme-2016-0064>)
2. *ONC Data Brief*, No. 35, May 2016
3. *The Risk Evaluation and Education for Alzheimer’s Disease (REVEAL)*