Report on the California Initiative to Advance Precision Medicine to the California Legislature

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California Initiative to Advance Precision Medicine
Report to the State of California Legislature 2016

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Table of Contents

I. Executive Summary

California is the first US state to launch a precision medicine initiative. Precision medicine is a data driven approach to research and medicine with potential wide-ranging benefits on human health and the State's economy. The State launched the California Initiative to Advance Precision Medicine (CIAPM) in April 2015 and established it in statute in 2016.

The vision for CIAPM is to maximize the use of the State's enormous resources and accelerate progress in precision medicine, improve human health in California, and position California as a leader in this new approach to research, health and health care.

Since it was launched in April 2015, CIAPM has hosted two peer-reviewed, competitive selection processes with internationally and nationally renowned precision medicine leaders assisting California in choosing precision medicine demonstration projects. The selected demonstration projects offer a number of opportunities for California to advance precision medicine, including but not limited to the following areas: 1) Application of precision medicine to specific disease; 2) Challenges of system interoperability; 3) Approaches to economic analysis; 4) Standards for sharing data or protocols across institutions; 5) Navigation of Federal and State regulatory environment; 6) Acceleration of research discoveries to clinical environment; 7) Challenges relating to data, tools, and infrastructure; 8) Protection of privacy and personal health information; 9) Potential for reducing health disparities; and 10) Methods and protocols for participant/patient engagement.

This report describes the strategy for allocating funding for competitively selected demonstration projects, provides an overview of the programmatic highlights including an update of the projects from 2015 as well as the newly selected demonstration projects in 2016. Additionally, the report provides an overview of the CIAPM hosted convenings and policy discussions to advance precision medicine.

Precision medicine is a global endeavor with exciting prospects for better healthcare for all, and California is poised to take a leading role in advancing this new era of big data enabled medicine. Since CIAPM was announced in April of 2015, it has created new opportunities for California to engage and provide leadership with federal partners and beyond. For precision medicine to be successful it will require cross-disciplinary experts coming together from various fields and sectors to collaborate and share knowledge and data in order to maximize benefits and address system level challenges that no one sector alone can address; CIAPM is facilitating and accelerating this process.

II. About the California Initiative to Advance Precision Medicine

Scientific and clinical discoveries have had an enormous impact on human health over the last several decades, yet much progress is still needed to combat persistent health problems of the population as a whole and to overcome differences in health outcomes amongst different groups of people. Health is impacted by several different factors including but not limited to biology, genetics, behavior, exposures, and environment. Although there is a rapid growth of understanding around different factors and the data has grown exponentially, it has been challenging to turn the data into knowledge.

> ***Precision medicine aims to use advanced computing tools to aggregate, integrate, and analyze vast amounts of data from research, clinical, personal, environmental, and population health settings to better understand diseases and develop and deliver more precise diagnostics, therapeutics, and prevention measures.***[1]

California's strength in high-tech and life-science entrepreneurship makes it an ideal place to drive innovation in precision medicine. Equally important, California's world-class public and private universities and research institutes represent an invaluable asset for data-driven medicine. The 10-campus UC system alone comprises expansive scientific, clinical and computational expertise and 5 medical centers that collectively hold over 14 million electronic health records, representing one of the nation's largest and most diverse patient populations. This rich resource is further augmented by other health care providers in California, which also contribute a socioeconomically diverse patient base. The confluence of high tech innovation with scientific and clinical capability places California in a unique position to lead the nation in precision medicine. By advancing big data approaches, catalyzing innovative partnerships, accelerating research discoveries, and driving the best technologies into the clinic, California has the potential to improve medical outcomes and preventative care.

The vision for CIAPM is to leverage the State's many resources to accelerate progress in precision medicine, improving human health in California and establishing California as a leader in this new approach to research, health and health care, while also anticipating and addressing the legal, social, and regulatory challenges necessary to achieve precision medicine. The global precision medicine market is expected to grow over the coming decade with some estimates reaching $88 billion by 2022.[2] Already a leader in tech[3], biotech and life science[4], California is well positioned to both enable

[1] CIAPM definition of precision medicine informed from the National Academy of Sciences "Toward Precision Medicine: Building a Knowledge Network for Biomedical Research and a New Taxonomy of Disease".

[2] https://empowerednews.net/precision-medicine-market-industry-sales-supply-and-consumption-2016-analysis-and-forecasts-to-2022/18440335/

[3] http://sfced.org/why-san-francisco/sectors/information-technology/sector-data/

and reap economic benefit as these innovation sectors come together to drive growth in precision medicine. Gov. Edmund G. Brown Jr. launched CIAPM in April 2015 with an appropriation of $3 million FY 2014/15 and an additional $10 million in FY 2016/17. UC Health with UC San Francisco as the lead hosts CIAPM with oversight by the Governor's Office of Planning and Research. This partnership between the State, the University of California, and other public and private entities, is building a knowledge base to advance precision medicine-oriented data, tools and applications in California. The initiative supports patient-focused demonstration projects intended to have positive health outcomes in the near-term, assembling an inventory of California's precision medicine assets, and hosting topical policy discussions bringing together diverse precision medicine leaders from private sector, entrepreneurs, academics, patient groups and beyond.

III. CIAPM Strategy for Allocating Funds

The pursuit of precision medicine is an inherently collaborative effort, requiring access to large data sets and to diverse technologies and expertise. One of the major goals of CIAPM is to foster such partnerships by supporting demonstration projects that leverage the State's expansive and diverse scientific, technical, and clinical expertise and other resources from public and private partners to illustrate the application of precision medicine. To accomplish this, the projects are patient-centered with the potential for positive impact for patients within a few years. Equally importantly, these projects are expected to identify opportunities and help address challenges of this new approach and inform future infrastructure investment, research priorities, and policy decisions that will help bring precision medicine into clinical reality. CIAPM is also funding an asset inventory to identify strengths and growth opportunities in California, and CIAPM is bringing together precision medicine thought leaders across sectors to catalyze opportunities and overcome barriers.

An update on the competitive, peer-review process to select the 2015 demonstration projects has already been submitted to the legislature.[5] This section provides an update on the Request for Proposals (RFP) and Selection Committee in 2016. The allocation in FY 2016/17 allowed CIAPM to expand the request for proposals, which was limited to the UC system in 2015, to research institutions throughout California. In 2016, public and private academic and non-profit institutions were eligible to submit proposals as principal investigators. Since the funding round was larger than in 2015, a larger selection committee was recruited to review a larger pool of applicants.

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[4] In Q4 2015, for the Bay Area alone, the "Life Sciences & Biotech sector generated $95 billion of economic activity, nearly $30 billion in income, and added 300,073 jobs." http://sfced.org/why-san-francisco/sectors/life-sciences-biotech/sector-data/

[5] The 2016-17 Governor's Budget proposes a $10 million augmentation to the Governor's Office of Planning and Research (OPR) for continued administration and grant making under the California Initiative to Advance Precision Medicine (CIAPM).

Selection committee members were recruited from outside of California to help avoid conflict of interest since the RFP was expanded to institutions statewide.

III.A. Request for Proposals

To achieve the goals of the initiative, CIAPM developed a rigorous proposal solicitation process to select demonstration projects. A highly qualified selection committee was recruited to conduct a peer-review process to identify innovative, collaborative precision medicine projects with potential for tangible benefit to patients within a short timeframe. The CIAPM 2016 RFP was posted on the CIAPM website and included an explanation of the process, eligibility criteria, proposal instructions, and review criteria based on statute and public comment.[6] Pursuant to statute, prior to posting the RFP, CIAPM solicited public input on criteria to be considered for inclusion in the RFP, in addition to those listed in statute. The final RFP incorporated the comments from public comment (Appendix A).

The review process involved two stages. First, applicants submitted short concept proposals; these were evaluated by the selection committee based on the statutory criteria and finalists were selected to advance. Second, the selected finalists were asked to provide full proposals. The selection committee evaluated the full proposals based on the statutory criteria and recommended six demonstration projects for funding.

III.B. Selection Committee

In 2016, pursuant to statute, the office was charged with recruiting a precision medicine expert selection committee to represent various precision medicine-related skills, such as bioinformatics, statistics, health economics, patient engagement, and genomics. The Legislature was offered the opportunity to make nominations for the selection committee to the office for consideration, and CIAPM solicited public nominations during a public comment period. CIAPM received responses from five individuals, and three of the experts suggested by them accepted the invitation to serve on the committee. Thirteen selection committee members in total were recruited, after determining that they were not interested in any contract, including any award of funds by the committee, pursuant to statute, and the Legislature was notified of the selection of the committee members. The 2016 selection committee members are listed, and their brief bios provided in Appendix B.

The selection committee established its procedures for reviewing the proposals and making award recommendations. CIAPM posted the review process it suggested to

[6] AB 1602, Chapter 24, Statutes of 2016, which establishes Article 6. *California Initiative to Advance Precision Medicine* under Chapter 1.5 of Division 1 of Title 7 of the Government Code

the selection committee, Frequently Asked Questions, which provided clarifications of the suggested review process, and the full proposal details on its website (Appendices C, D & E). The CIAPM-recommended peer review process was modeled on the NIH peer review process, and was designed to ensure that applications to the RFP were evaluated in a manner that was fair, equitable, timely and free of bias. Everyone who had access to proposals or who attended the review meetings was required to maintain confidentiality and NIH conflict screening rules applied.

Since there were many evaluation criteria, CIAPM recommended that the selection committee follow NIH scoring guidelines such that projects were rated on 1) Significance; 2) Investigators; 3) Innovation; 4) Approach; and 5) Environment, therefore all of the listed criteria were able to be considered to help determine which individual applications were the strongest.

IV. Program Highlights

CIAPM supports patient-focused demonstration projects intended to have positive health outcomes in the near-term, is developing an asset inventory to identify strengths and growth opportunities in California, and brings together precision medicine thought leaders across sectors to catalyze opportunities and overcome barriers

CIAPM's portfolio of eight demonstration projects comprises broad collaborations across institutions and sectors (Appendices F & G). Together, the eight projects have established fifty-seven partnerships, with universities & research hospitals, companies, patient advocacy groups and government institutions. Overall, forty-eight different institutions, public and private, are involved in the CIAPM demonstration projects.

The projects address diverse disease areas, aim to enable more precise, individually targeted prevention, diagnosis, and treatment of disease, and to illustrate that precision medicine is making a difference now. The eight CIAPM demonstration projects are funded at $1.2 million each; state funds are leveraged by waiving indirect costs and, specific to each project, also include some institutional funds, foundation funds, patient advocate support, and staff in kind services.

IV.A. Projects 2015

Since fall 2015, CIAPM has been funding two demonstration projects: 1) California Kids Cancer Comparison (CKCC); and 2) Precision Diagnosis of Acute Infectious Disease (PDAID). Currently, both projects have completed their 5th quarter reporting, and both are meeting their project milestones. CIAPM funding for these projects will end in 2017, and a final evaluation of each project will be reported to the legislature.

California Kids Cancer Comparison (CKCC)
Principal Investigator: David Haussler, UC Santa Cruz
Partner institutions: UCSF, Stanford University, Children's Hospital Orange County, Children's Hospital of Philadelphia, British Columbia Cancer Agency, University of Michigan, University of Southern California, UC Davis, NuMedii, CISCO, DNAnexus, Translational Genomics Research Institute, CARIS Life Sciences, Unravel Pediatric Cancer, Jacob's Heart, Kids v Cancer, Alex's Lemonade Stand Foundation, Team G Foundation

Synopsis of project:
Each year 500 California children with cancer either do not respond to standard treatments or have no standard therapies available to treat their form of cancer. Many clinical trials are now underway that employ genomic analyses to identify new therapeutic options for patients with these currently incurable tumors. This genomic approach is possible because many modern cancer drugs are developed to target specific molecular alterations, often present in specific tumor types (e.g., lung cancer), which interfere with that type of cancer's ability to grow or survive. Sometimes, a specific molecular alteration may occur in a different tumor type than expected. For instance, an alteration typically found in lung cancer, may be found in a brain cancer, and since the drug is targeted to interfere with that molecular change, it may help fight the brain cancer, even though it was developed for lung cancer. So far genomic analyses yield new treatment possibilities for less than 10% of patients. The California Kids Cancer Comparison (CKCC) project aims to improve this outcome using the power of large-scale computation; by comparing the genomics of a patient's specific tumor with those alterations that have been found in thousands of other tumors, new treatment options may be revealed that were not found with genomic analyses of the individual tumor alone.

The CKCC team is collaborating with ongoing genomic clinical trials for children with cancer who have not benefited from conventional treatments. CKCC obtains each tumor's genomic data, and analyzes it computationally in several novel ways to increase the number of genomics-informed treatment options for these cancer patients. To help rapidly bring state-of-the-art analyses to its clinical collaborators, the team includes researchers and physicians at multiple universities and hospitals in partnership with biotech and computer companies. Through the CKCC project, the aim is to at least double the number of participating children who benefit from a targeted cancer treatment. The project also includes the development of an online tool to facilitate communication between researchers and clinicians, and the CKCC team is engaging patients through the development of a resource that allows them to share their data with researchers worldwide.

Progress:
The genomic information from each tumor represents a large data set that needs to be transferred from the organization that generates the data for a clinical trial to the CKCC team for their analysis. This poses both technical challenges due to the size of

the data, as well as data security and patient privacy issues. To effectively collaborate with multiple ongoing clinical trials, the team developed data agreements with each of their clinical partners, (*i.e.,* UCSF, Stanford University, Children's Hospital Orange County, Children's Hospital of Philadelphia, British Columbia Cancer Agency, and University of Michigan), and created the infrastructure needed for secure and effective genomic and clinical data transfer, including the de-identification of data to maintain patient privacy, and the handling of the inherently identifiable genomic data in a secure manner. The CKCC team receives both archived tumor data, which it uses to continually test, optimize, and augment its analytical approaches, and tumor data from children actively participating in clinical trials that it analyzes to discover new treatment options, which are communicated to the treating physicians.

Given the unique nature of the CKCC analyses, the team is continually refining its strategy for effectively communicating the results of its analyses and the suggested new treatment options so that the clinicians understand the underlying rationale and make informed treatment decisions. An important aspect of the CKCC project is participation in the molecular tumor board meetings, where clinical specialists and researchers discuss how to interpret and use the results from genomic analysis to favorably influence patient outcomes.

As of the writing of this report, the CKCC team has obtained genomic data from the tumors of 63 children actively enrolled in clinical trials, and has presented 33 cases to treating clinicians in 11 tumor board presentations. In all 33 presented cases, the cancer comparisons revealed molecular alterations that are known to be involved in cancer, but had not been identified through the genomic analyses of the clinical trials; the potential drug targets were not apparent when analyzing an individual patient's data in isolation. However, identifying a possible molecular target does not mean that a targeted treatment is available, since a drug may not yet have been developed against that specific target. In 94% of cases, CKCC was able to identify a novel molecular target that is potentially actionable because the target either had a matching therapy that was already FDA approved for another indication, or a matching therapy was available as part of a clinical trial. During molecular tumor board meetings, several clinicians have reported that they have taken treatment action based on CKCC results, illustrating CKCC's success not only in identifying novel treatment options but also in effectively communicating with treating physicians. In order to further improve and streamline the communication of these novel types of findings to clinicians, the CKCC project includes the development of an online application that uploads, analyzes, and communicates genomic information and associated data to clinicians and researchers, while handling identifiable clinical and genomic data in a manner that protects patient privacy.

The CKCC team also has the goal of engaging with patients and their families to better support their needs and preferences. Toward that end, the team is working to enable patient data sharing, fulfilling families' desires to donate their child's genetic data to research. This is especially important, since pediatric cancer data are tightly controlled

and access is limited. The principal investigator of the CKCC project, David Haussler, is a co-founder of the Global Alliance for Genomics and Health (GA4GH), an international organization dedicated to establishing a framework of approaches to enable effective and responsible sharing of genomic and clinical data. GA4GH promotes the highest standards for ethics and helps ensure that participants have the choice to responsibly and securely share their genomic and clinical data to advance human health. GA4GH is establishing an open source networked archive of adult cancer data, and CKCC is now creating such an archive for pediatric cancer genomic data within GA4GH. Since pediatric cancers are rare and differ significantly in their molecular mechanisms from adult tumors, such a resource will be critical to stimulate research toward better cures for kids' cancers; families have stated that they derive some solace knowing their child's data can contribute in that way.

In conclusion, based on its previously developed computational tools that use genomic data from tens of thousands of patients' tumors, and leveraging existing clinical trials and other resources, the CKCC team is enhancing and implementing innovative computational approaches to identify therapeutic options and improve the treatment of individual patients. The project has made great progress, having established an effective and secure pipeline of data procurement, data analysis and dissemination of the resulting discoveries to inform the individualized treatment of each participating patient. During the remainder of the project, the CKCC team will continue to analyze children's tumor data to provide new treatment options for them, and then analyze their findings in aggregate to determine the overall success rate of its large-scale computational approach. The team will also finalize its online communication tool for researchers and clinicians to facilitate future use of their approach and they will expand the open source networked archive of pediatric cancer genomic data within GA4GH.

Precision Diagnosis of Acute Infectious Diseases (PDAID)
Principal Investigator: Charles Chiu, UC San Francisco
Partner institutions: UCLA, UC Davis, Zuckerberg San Francisco General Hospital and Trauma Center, Children's Hospital Los Angeles (CHLA), Children's National Medical Center (CNMC), Children's Hospital Colorado (CHCO), St. Jude's Children Research Hospital, UC Berkeley, Syapse, DNAnexus, Google Inc., Quest Diagnostics Inc., California Department of Public Health, Illumina Inc.

Synopsis of project:
Current tests in the microbiology laboratory fail to diagnose many life-threatening infections in a timely fashion, resulting in increased health care costs and likelihood of death as many therapeutics may be tried without success. The Chiu team has pioneered the use of state-of-the-art DNA analysis to detect almost all known infectious agents in a single test, quickly revealing the cause of infections that routinely elude physicians. This data-driven precision medicine test, called metagenomic next generation sequencing (mNGS), works by analyzing all DNA in the

infected tissue, such as the fluid surrounding the brain or the blood, and using computational approaches to identify the DNA signature of the infectious agent amongst all DNA. This test can provide diagnostic results very rapidly, within 1-2 days, and proof of principle that this approach works to save lives has already been published in the medical literature. In order to broaden its use and to develop a clinically reimbursable, self-sustaining test, this project is working to i) confirm the sensitivity and accuracy of the test in a licensed clinical laboratory, ii) conduct a clinical study in which both conventional and mNGS-based diagnoses are obtained on hundreds of critically ill patients with neurological infections, and iii) use this data to critically evaluate the impact of this test on overall costs and clinical outcomes compared with the conventional diagnosis approach. Ultimately, the goal is to leverage nonprofit and industry partners to make this test widely accessible to patients in California and beyond.

Progress:

In order to move beyond the research laboratory and offer the mNGS test as a clinical diagnostic test available to most patients, standard operating procedures for all steps of the test need to be developed and the sensitivity and accuracy of the test need to be confirmed in a licensed clinical laboratory. Toward this end, the team optimized the computational software that is required for the complex DNA analysis, established the standard operating procedures for sample handling and shipping and running the assay at UCSF, developed the needed capacity to store samples and perform tests for the clinical study, and completed the clinical confirmation of the test using fluid that surrounds the brain. This confirmation represents an important achievement, as it was required by federal regulatory standards (Clinical Laboratory Improvement Amendments, CLIA) before launching the clinical study of critically ill hospitalized patients with neurological infections. Currently, UCSF, UCLA, UC Davis, Zuckerberg San Francisco General Hospital and Trauma Center, Children's Hospital Los Angeles (CHLA), Children's National Medical Center (CNMC) in Washington DC, and Children's Hospital Colorado (CHCO) are actively collaborating on this project. Each participating patient is enrolled and their consent is obtained using a standardized approved clinical protocol, and a sample of the fluid surrounding the patient's brain is shipped from the participating medical centers to UCSF for processing and analysis. Each center also performs conventional infectious disease testing for each participating patient.

Given the innovation of the mNGS test for the diagnosis of infectious diseases, the team established a multidisciplinary PDAID consult board, which is modeled after tumor boards for cancer and consists of a group of researchers and clinicians who are experts in interpreting mNGS test results. The consult board holds weekly Webex meetings with the treating physicians at the participating medical centers to discuss individual patient cases, provide expert input on the interpretation of the mNGS test results, and aid in developing the best course of treatment for the patient.

As of December 2016, 97 patients have been enrolled in the project. The mNGS assay was positive for an infectious agent in 27 of these cases (27.8%). Notably, in 14 of 97

cases (14.4%), the mNGS test yielded a diagnosis when conventional testing failed, and it confirmed the results of conventional testing in an additional 11 cases (11.3%). These results are very promising, but a formal outcomes analysis for the clinical study, including an analysis of the cases not resolved by this approach, and a cost-benefit analysis by a health economist, is pending. In order to aid in the evaluation of the clinical utility of the test, Dr. Chiu's team has developed surveys for clinicians to provide feedback on their experience with the mNGS test during this study.

The Chiu team is taking several steps to enable the wider use of the mNGS test in the future, expanding beyond neurological infections and for use beyond UCSF. Bloodstream infections, otherwise known as sepsis, are the primary cause of deaths from infection and affect more than 1.6 million people in the U.S. each year. To expand mNGS testing to sepsis, the team is working to validate the test using plasma samples with collaborators at St. Jude's Children Research Hospital in Memphis, TN. They are also migrating the software that is needed for the state-of-the-art DNA analysis to a secure cloud platform that maintains patient confidentiality, so that infectious disease teams in other locations will be able to use this test in the future. Dr. Chiu is also communicating with the FDA to work toward obtaining regulatory approval for this novel type of infectious disease diagnostic test, which would enable implementation of the entire mNGS test pipeline in other hospitals in the country. In anticipation of high demand for the mNGS test for indications ranging from neurological infections to sepsis to pneumonia, the team has started to work on automating parts of their assay using a robotics platform. If automation is successfully achieved, this test will have the potential for wider impact on a large number of hospitalized patients with infectious disease.

Overall, the team has made great progress, having clinically implemented a novel precision medicine approach for infectious disease diagnosis, launched a clinical study to determine the utility of the test and collected preliminary data. At the same time, the team is working to enable broad implementation of mNGS-based infectious disease diagnosis in almost all types of infections and dissemination of the mNGS test to other locations. The mNGS test, through the support by CIAPM, has the potential to transform clinical diagnosis for infectious disease, and save the lives of patients around the world who would otherwise die from treatable infections that go undiagnosed by conventional means.

IV.B. Projects 2016

In November of 2016, following the competitive, peer-review process, CIAPM announced the funding of six demonstration projects that use mobile technology, cutting edge sequencing technology, integration of diverse data, advanced image analysis and patient / physician support tools to advance precision medicine. As of the writing of this report, CIAPM and the six teams are in the process of finalizing the subcontracts, and the projects will begin work in early 2017.

Brief description of each project

Personal Mobile and Contextual Precision Health
Principal Investigator: Nicholas Anderson, UC Davis
Partner institutions: UCSF, UC Berkeley, Overlap Health

Synopsis of project:
Patients are increasingly gathering diverse and ubiquitous personal data through the mobile phones and devices they use in their daily lives. This data is potentially of unique importance to help both patients and their doctors improve the management of chronic diseases, but engaging patients to provide secure and personalized data, and integrating this data in the context of their clinical health remains a major challenge. In this project, the team will develop and provide easy to use tools and processes to track and contribute activity, blood pressure and behavioral health data from mobile phones, and will engage patients to help design and evaluate a patient-centered mobile health system that will allow patients and their doctors to use this data for new approaches to managing chronic conditions such as hypertension and depression.

Early Prostate Cancer: Predicting Treatment Response
Principal Investigator: Sheldon Greenfield, UC Irvine
Partner institutions: UCLA, Veterans Affairs Long Beach Healthcare, Veterans Affairs Los Angeles, Cedars-Sinai Medical Center

Synopsis of project:
Prostate cancer is the most common cancer in men, with over 200,000 new cases diagnosed each year in the US. It is the second leading cause of cancer death in men, and affects roughly 1 in 7 men over their lifetime. An important goal toward achieving better outcomes is to be able to predict, prior to treatment, which therapy will work best for each patient. This proposal focuses on improving these predictions for patients with early stage prostate cancer, based on diverse information, including (i) detailed patient characteristics and patient reported outcomes such as socio-demographic information, health status and disease management burden, (ii) traditional prostate cancer severity indicators and (iii) an already established genomic test that measures the probability of cancer spread after surgery. An important goal of this project is to understand the validity of these predictive measures in an ethnically diverse patient population. The final combined prediction model will aid doctors and patients in personalizing prostate cancer treatment decisions to maximize effectiveness, and choose the treatment optimal for individual patients.

Full Genome Analysis to Guide Precision Medicine
Principal Investigator: David Martin, Children's Hospital Oakland Research Institute

Partner institutions: UCSF, UCSF Benioff Children's Hospital Oakland, UC Berkeley, Illumina

Synopsis of project:

Most inherited diseases become apparent in childhood and many result in symptoms without a specific diagnosis. This is a difficult situation for parents and clinicians, and often subjects the child to a diagnostic odyssey. This project will advance precision medicine by developing methods that improve our ability to identify mutations that cause inherited diseases and to find the cause of previously difficult to diagnose genetic conditions. This will be accomplished by a comprehensive genome analysis that provides a more complete picture of abnormalities in an individual's DNA than is currently achieved. Interpretation of genome data remains a challenge, though, and the team plans to leverage the findings from this project for even greater understanding of these often devastating childhood conditions, by partnering with other international teams with the long-term goal of creating a catalogue of all DNA variants that can cause human disease. This project will also actively seek to include racially and ethnically diverse patient groups, which have traditionally been under-recruited for genetic analysis, thus adding novel and important information to improve diagnosis and care for the population at large.

Artificial Intelligence for Imaging of Brain Emergencies

Principal Investigator: Pratik Mukherjee, UC San Francisco

Partner institutions: Zuckerberg San Francisco General Hospital and Trauma Center, UC Berkeley, Stanford University, Brain Trauma Foundation, Community Regional Medical Center in Fresno

Synopsis of project:

Every 28 seconds, an American suffers a catastrophic neurologic emergency, most commonly stroke or traumatic brain injury (TBI). Neurologic emergencies affect 15 million U.S. adults and children annually at a cost of $115 billion, which is 7% of total U.S. healthcare spending per year. Since the brain is susceptible to irreversible injury within minutes, immediate diagnosis and treatment are essential. Computed tomography (CT) scanning is currently the only type of imaging used worldwide to diagnose neurologic emergencies. Immediate diagnosis aided by rapid automated evaluation of head CT could greatly improve care in situations where minutes count.

This project will apply state-of-the-art artificial intelligence (AI) technology to automatically recognize life-threatening findings on emergency head CT scans in patients suspected of having TBI, stroke or bleeding due to ruptured brain aneurysms and aims to assist physicians to make a quicker diagnosis. Another important advance enabled by this technology is the ability to catalogue clinically significant "digital markers" that are recognizable across scans, which will facilitate future precision medicine research by combining data from quantitative image analyses with other types of data. Importantly, the team will implement this AI system in the "cloud" so

that its use does not remain limited to advanced hospital settings, and CT scans can be uploaded for analysis from anywhere in the world.

Remote Monitoring to Predict Heart Failure
Principal Investigator: Brennan Spiegel, Cedars-Sinai Medical Center
Partner institutions: UCLA, HealthLoop, Neoteryx, Beckman Coulter, SCIEX, Thermo Fisher Scientific

Synopsis of project:
Cardiovascular disease is the leading cause of death for both men and women in California. Tragically, many people develop a heart attack, stroke or other complication of cardiovascular disease because they were under-treated, not taking their medicines, or not receiving the care they needed in the first place; this is especially common among younger women and racial/ethnic minorities. One reason for this is that early signs of disease can be easily missed, and also because people spend most of their life far away from a doctor or hospital where it is challenging to monitor disease progression. In this study, researchers will look for the earliest signs of impending disease by monitoring patients remotely, outside the four walls of the hospital or doctor's office. Patients will wear a specialized watch that measures activity, sleep, heart rate, and stress levels. They will also report their levels of anxiety, depression, and quality of life using a smartphone or computer. Finally, they will periodically send a small finger prick blood sample by mail, allowing doctors to measure over 500 different blood chemicals. By combining these different types of data, the researchers will seek a "signal in the noise" that predicts who may be about to have a heart attack or stroke. If successful, patients could greatly benefit from more effective prevention and treatment as a result of earlier disease detection, but in order to broadly implement innovative new technologies, it is also important to understand their potential cost impact on the medical system. The team will therefore perform an economic analysis to estimate the cost effectiveness of this remote monitoring approach.

Precision Medicine for Multiple Sclerosis: Making It Work
Principal Investigator: Walter Stewart, Sutter Health
Partner institutions: UCSF, Jordan Research and Education Institute, National MS Society (NMSS)

Synopsis of project:
Multiple sclerosis (MS) is a nervous system disease that affects the brain and spinal cord when the body's immune system mistakenly attacks healthy cells. MS usually starts between 20 to 40 years of age. Patients may face decades of physical disability and uncertainty around how the disease will progress. While precision medicine holds the promise of being able to predict and slow the course of MS, these advances in MS care have not yet made it to every doctor's office. Sutter Health and UCSF are

partnering with patients and the National Multiple Sclerosis Society to develop an interactive app that builds on technology created and tested at UCSF and shown to improve outcomes. For example, patients were significantly less likely to need a cane (10% versus 50%) when treated by neurologists using this technology. In this project, Sutter Health's Research & Development team will develop the interactive app, called MS-SHARE, which will instantly combine the latest precision medicine data with real-time data from the patient's electronic health record, and with information that patients report about their symptoms between medical appointments. Doctors and patients will be able to view the app together during appointments to see how a patient's unique characteristics compare to other patients like them. Knowing how MS may develop over time for a patient can help the doctor and patient select the treatments most likely to slow disease progression and meet patient needs. The team will implement MS-SHARE in multiple Sutter general neurology practices and measure use and patient experience as first steps toward getting precision medicine into everyday care. This partnership holds the promise of bringing precision medicine – precise treatment decisions to address needs of individual patients– directly to the diverse populations living with MS in Northern California.

IV.C. Inventory

An important goal of CIAPM is to develop an inventory of public and private precision medicine assets in the state and to identify strategic areas for future development across California. California's enormous capacity in the biotech and high-tech industry, combined with its first-rate universities and research institutes, forms the basis for significant innovative potential, and CIAPM aims to facilitate the coordination of these resources and identify strategic opportunities by creating an inventory of precision medicine projects (basic, pre-clinical, clinical, health outcomes, social / behavioral, ethics and technology research, etc.), databases, cohorts and computational infrastructure, as well as expertise held by faculty and technology professionals, diverse and engaged patient groups, and legal, ethical, and social science experts.

<u>Progress to date</u>

In order to identify assets across California, CIAPM team members reached out to and met with stakeholders at UC campuses, other California universities, research organizations and companies to learn about their projects and products. In addition, assets were collected through internet searches, social media, attending conferences, and through information provided by stakeholders.

The assets were entered into a database, and each asset was tagged to enable searches for asset characteristics that will be of interest to inventory users. CIAPM has developed a controlled vocabulary (Appendix H) for asset tagging that will allow identification of asset subsets. The construction of the inventory is still in progress.

The inventory will help connect different resources, facilitate economic value analysis of precision medicine, and identify different opportunities for growth in California.

IV.D. Convenings and Policy Discussions

California is a large, diverse state with several complementary efforts going on within private sector, biotechnology, technology, academia, patient groups, and entrepreneurial endeavors. Although there are several convening opportunities within individual professional groups, there is a lack of coordinated opportunities for such cross-disciplinary partners to come together to discuss cross-sector needs to advance precision medicine. CIAPM has hosted three convenings to bring different partners together. In 2015, two of the convenings were organized and hosted at UCSF and each was attended by about 50 individuals, and in 2016, UCLA co-hosted an event in Southern California, attended by over 150 individuals. CIAPM staff conducted outreach to stakeholders prior to the events to inform the event content, and attendees represented academia, non-profit organizations, industry and governmental institutions.

The convenings have provided:

- Context on what is happening with national and international initiatives
- Opportunities for demonstration projects applicants to present ideas, network, and connect with new partners
- Focused panel discussions on:
    - Challenges and opportunities in NGS-based molecular diagnostics and in big data
    - Promoting wellness and disease prevention in precision medicine
    - Ways to reduce health care cost through use of precision medicine approaches
    - Overcoming the diverse barriers to data sharing
    - Ways to effectively engage with patients as partners in precision medicine projects

In 2017, CIAPM will convene domain experts from across the state and demonstration project leads to host more in-depth policy discussions on a range of issues that have emerged, including but not limited to: data privacy and security, the changing regulatory environment, ethical implications of precision medicine, and clinical implementation of precision medicine. The goal is for the State of California, with its prominent role in driving technology and healthcare innovation, to be prepared to implement precision medicine in a responsible way that benefits all Californians.

V. Impact Beyond CIAPM

CIAPM has created a path for California to have a role in the national and international dialogue in precision medicine. The engagement and visibility of the State of California in precision medicine via CIAPM serves as a model for, provides motivation to, and enables partnership with other states, organizations, nations and federal agencies, and ensures that California continues as a global leader in technological innovation, health care, and economic growth.

V.A. Relationship between Federal and State Funding for Precision Medicine

State representatives and CIAPM team members have been working collaboratively with members from the White House Office of Science, Policy, and Technology, the FDA, and the NIH to ensure coordinated and synergistic efforts.

A few months before CIAPM was launched, the White House Precision Medicine Initiative (PMI) was announced by President Obama in his State of the Union address in January 2015, with $215 million allocated towards federal work. The federal PMI has several major goals, with $70 million directed to the NCI for Precision Oncology efforts, and $130 million of the funds dedicated to an NIH led effort to build a voluntary national research cohort of a million or more volunteers, called "All of Us".[7] This cohort will be a resource for investigating human variation in health and disease. This year, Californian institutions were selected to contribute to PMI recruitment efforts. This group is called the California Precision Medicine Consortium, a broad coalition led by UCSD with sub-awards to Cedars-Sinai Medical Center, San Diego Blood Bank, UC Davis, UC Health, UCI, UCSF and UCLA. PMI is also funding Scripps Research Institute to enroll participants into the federal initiative.

Importantly, the federal PMI also provides funds for the Food and Drug Administration (FDA) to acquire additional expertise to support the regulatory structure needed to advance innovation in precision medicine and protect public health. This is critical for precision medicine advances, such as those in California, to eventually be broadly implemented into clinical practice, removing hurdles that would otherwise impede success of investments in therapeutic development, technologies, and clinical trials for precision medicine. CIAPM demonstration projects are already working with FDA to help shape approaches and address regulatory challenges for precision medicine efforts. And finally, PMI also supports the Office of the National Coordinator (ONC) to develop interoperability standards and requirements that address privacy and enable secure exchange of data across systems; these crucial issues are also addressed by

[7] https://www.whitehouse.gov/the-press-office/2015/01/30/fact-sheet-president-obama-s-precision-medicine-initiative

CIAPM projects to help ensure safe and fair data exchange needed for effective precision medicine practices.

Additionally, the White House, Gates Foundation, and UCSF hosted a Precision Public Health Summit in 2016. CIAPM team members were able to play a foundational role in informing the content for this convening.

CIAPM's approach to promoting precision medicine is distinct but complementary to the federal PMI. By funding proof of concept projects with the potential to improve health outcomes in a short time frame, California is identifying and tackling critical hurdles and implementing new advances into clinical practice in broad and diverse populations. CIAPM's demonstration projects, and its effort to create an inventory of the State's precision medicine assets, position California to better utilize its own and national resources, making the State and its institutions more competitive in obtaining grants, philanthropic support and other investments, and helping create the infrastructure needed for California to maintain its leadership role in the global precision medicine endeavor.

V.B. National and International Precision Medicine Efforts

Many companies and international initiatives are developing in the emerging precision medicine space and CIAPM is actively engaged in these discussions. Discussions and interest with aligning programs have occurred with:

- California Institute for Regenerative Medicine (CIRM), California's stem cell agency
- British Consulate, Science and Innovation, and Innovate UK, the UK's innovation agency
- Dutch Techcentre for Life Science, non-profit network organization (FAIR - Findable, Accessible, Interoperable and Reusable) and Personal Health Train initiatives
- Australian Genomics Health Alliance, Murdoch Children's Research Institute
- Government of Israel Economic Mission
- Genome British Colombia and Genome Canada
- GlaxoSmithKline (GSK), Emerging Platforms, Platform Technology and Science
- Thermo Fisher Scientific, Precision Medicine
- German State of Schleswig-Holstein, German Consulate in San Francisco

In order to raise awareness about the State's involvement in precision medicine in stakeholder communities, CIAPM has been represented at several meetings:

- Personalized Medicine World Conference 2016
- Precision Medicine Summit, Bay Area Council & Oracle 2016
- Informed Health Summit at UCSF 2016
- Precision Medicine Leaders Summit 2016

- BIO, California Life Sciences Association (CLSA) 2016
- World Alliance Forum 2016
- Connected Health Conference 2016
- American Medical Informatics Association (AMIA) 2016 Joint Summits on Translational Science, Panel "Precision Medicine: Leveraging Genomics in Diverse Indications"
- Demystifying Big Data for Healthcare: Insights, Opportunities, and Challenges, CIAPM is a featured case study in the book, publication in 2017
- Association of Academic Health Centers (AAHC) Research Meeting 2016, Precision Medicine: Promises and Challenges, talk in session on Precision Medicine: Institutional Initiatives to Facilitate Collaboration

VI. Conclusion

Since its launch in April 2015, CIAPM has stimulated state-wide collaborations, discussions, and innovation to advance precision medicine. CIAPM has selected and is supporting eight patient-focused demonstration projects anticipated to yield positive health outcomes in the near-term, is developing an asset inventory to identify strengths and growth opportunities in California, and continues to convene precision medicine thought leaders across sectors to catalyze opportunities, overcome barriers, and coordinate with federal agencies. During this time, other governments, as well as corporations, academic institutions and innovators worldwide have continued to recognize the economic and transformative potential of precision medicine, and have been forming initiatives, consortia and large collaborative efforts to enable progress toward more precise prevention, diagnoses and treatments for patients.

To achieve the vision of precision medicine, many issues beyond the technical and scientific challenges must be addressed, transforming the research, health and healthcare enterprise and ensuring that all people will benefit in a safe and fair way. Through the execution of the focused demonstration projects, and also targeted policy and bioethics discussions, CIAPM will continue to facilitate and advance precision medicine.

Appendices

A. CIAPM RFP 2016
B. Selection Committee 2016
C. Recommended Review Process 2016
D. Frequently Asked Questions about the Recommended Review Process 2016
E. Full Proposal Details 2016
F. List of Eight Demonstration Projects
G. List of Demonstration Project Partnerships
H. Inventory Controlled Vocabulary

California Initiative to Advance Precision Medicine

CIAPM Request for Proposals 2016

Request for Proposals Announced	July 7, 2016
Concept Proposals Deadline	**August 8, 2016**
CIAPM Convening - Proposal Presentations	August 26, 2016
Notification of Finalists	August 31, 2016
Full Proposal Deadline	**September 30, 2016**
Awardees Announced	First week of November, 2016
Projects Commence	December 2016
Duration of Projects	18 months
Funding	Approximately 6 projects, likely up to $1.2M total per project; no indirect costs

I. Precision Medicine

Precision medicine holds promise to profoundly transform health, healthcare and biomedical research. As envisioned in the 2011 National Academy of Sciences' (NAS) report, "Toward Precision Medicine: Building a Knowledge Network for Biomedical Research and a New Taxonomy of Disease," precision medicine aims to use advanced computing tools to aggregate, integrate and analyze vast amounts of data from research, clinical, personal, environmental and population health settings, to better understand diseases and develop and deliver more precise diagnostics, therapeutics, and prevention measures.

II. California Initiative to Advance Precision Medicine

The California Initiative to Advance Precision Medicine (CIAPM) was established by the State of California to help coordinate public, private, and non-profit partners to advance precision medicine approaches and foster the creation of new technologies and therapies that can improve the health of diverse populations. The initiative brings together state precision medicine leaders as well as supports projects aimed at demonstrating the power and application of precision medicine to the people of California.

III. Precision Medicine Demonstration Projects

The NAS report emphasizes the need for strong partnerships and collaboration to achieve the vision of precision medicine and recommends that pilot projects be undertaken at various levels to identify barriers, define effective practices and achieve some early, albeit modest scale, successes. Therefore, one of CIAPM 's main approaches is to support collaborative demonstration projects that leverage the state's expansive and diverse patient data, research expertise, and technological capabilities to advance precision medicine.

For this RFP, $7.2 million is provided by the state for approximately 6 proof-of-principle demonstration projects. Projects will be hosted by a lead public, private academic or non-profit institution in California and rely on integral partnerships with and contributions from other non-profit or for-profit partners. Projects will be selected through a two-stage process involving (1) concept proposal submission and optional presentation at an August 26, 2016 CIAPM convening and (2) development of selected concept proposals into full proposals from which the final selection of awards will be made. It is highly recommended that applicants attend the August 26 convening. After the selection committee makes their recommendations on awards CIAPM will work with awardees to

develop concrete metrics and goals to track the progress of the demonstration projects over the 18-month project period. The selection committee and its processes are described below.

Depending on the availability of funds, CIAPM may offer an opportunity for a competitive renewal to all awarded CIAPM demonstration projects. This would occur within 12-24 months of release of this RFP.

IV. Applications

A. Application process

Stage 1: Concept proposals

Applicants will be asked to submit short concept proposals and will have the opportunity to pitch and discuss their proposal at the CIAPM convening on August 26, 2016 in Los Angeles. This convening will provide an opportunity to help strengthen and build partnerships, and to present to the members of the selection committee. There will be an opportunity to provide a video instead of participating at the event.

Stage 2: Full proposals

The selection committee may select approximately 10-15 concept proposals to move onto the full proposal stage. Recommendations for submission of full proposal materials will be made available on the CIAPM website for the finalists advancing to the next stage after the convening on August 26, 2016.

The committee will recommend a number of final projects based on appropriated funds that may include up to six projects for funding to the Governor's Office of Planning and Research (OPR), which will approve and announce the final funding decision.

B. Eligibility - *Eligibility criteria are set forth in Sections 65057 and 65058 of the California Government Code. Those criteria include:*

1. Public and private academic and non-profit institutions are invited to submit proposals as principal investigators.
2. Demonstration project proposals should advance greater understanding in one or more focus areas, including:
    - The application of precision medicine to specific disease areas.
    - The challenges of system interoperability.
    - Economic analysis.
    - Standards for sharing data or protocols across institutions.
    - The federal and state regulatory environment.
    - The clinical environment.
    - Challenges relating to data, tools, and infrastructure.
    - The protection of privacy and personal health information.
    - The potential for reducing health disparities.
    - Methods and protocols for patient engagement.
3. The demonstration project should be located in California.

In addition to the eligibility requirements described above, the statute also allows the selection committee, and the Office of Planning and Research, to consider additional factors in weighing the proposals for recommended awards including the completeness of the application proposal, described below in Sections C and D. Additionally, at least one award should be made in both northern and southern California. To enable the selection committee to make fully informed award recommendations, applicants are strongly encouraged to include the information described below in Sections C and D in their written proposals.

C. Logistical Considerations

Each submitting institution, please provide answers for Section C1, C2 & C3, in a maximum one-page Institutional Cover Letter; minimum Arial 11 font; 0.5 inch margins; no appendices. For questions, please contact ciapm@ucsf.edu.

1. Host institutions: Identify the institution that is submitting one or more proposal(s) and will administer grant(s) if awarded.
2. Lead investigator(s): For each proposal submitted from your institution, identify a lead investigator who will serve as principal investigator (PI), and describe their capacity to serve the PI function. Capacity includes past success with previous and/or current scientific funding such as National Institute of Health and National Science Foundation funding.
3. Institutional focus: Describe your institution's commitment to each of the demonstration projects submitted from your institution. For example, limiting submissions to no more than two proposals per institution may be evidence of commitment. If more than two proposals are submitted, submitting a rank order of applications by the institution may be evidence of the relative level of commitment.
4. Authorized submission: The institutional letter (C1-C3) and the proposals (section D) should be submitted electronically by the vice chancellor for research or other equivalent or designated authorized institutional official.
5. Convening: Applicants, or their designees, are highly encouraged to participate in a convening on August 26, 2016, in Los Angeles. Due to limited availability of administrative funds, CIAPM will not be able offer travel support to applicants or their designees.

D. Concept proposals

Each applicant, please provide answers for Section D in a maximum of two-page Concept Proposal; minimum Arial 11 font; 0.5 inch margins; no appendices. For questions, please contact ciapm@ucsf.edu.

1. Impact on precision medicine: Describe how the proposed project will address a knowledge gap or need in a specific disease area(s), health issue, technology or fundamental biological process and, in doing so, demonstrate the promise of precision medicine. Provide rationale for the project by outlining existing strengths, resources and opportunities available (e.g., ability to obtain molecular measurements, remotely collect behavioral or other data, subtype the disease, link genomic data to EHR; access to existing biobanks; databases, medical records; an engaged participant community, established mechanisms for responsible data sharing, etc.).
2. Focus area: Describe which relevant focus areas(s) the project will address (see section IV,B, 2 above). Provide rationale for the selected focus area(s) by outlining the current associated challenges to and opportunities for the advancement of precision medicine.
3. Project plan: Describe the components of your proposed project (specific aims and research strategy).
4. Patient data: Each proposal should demonstrate its commitment to the use of robust data. For example, your proposal could make use of patient data from at least two data sources, such as eligible institutions, health care providers, or other sources of health-related data. Use of additional data sets is encouraged. Briefly describe the data set(s) you propose to use and the rationale for their choice.

5. Precision medicine capabilities: Describe the precision medicine capabilities that will be developed as a result of this project (i.e., infrastructure and tools that will be built as a result of this project including physical capacity, new consortia, collaborations, personnel competencies, databases, software or computational development, startup company opportunities, intellectual property, patient cohorts, participant communities and networks, models for responsible data sharing, etc.).
6. Participant engagement: Describe strategies to engage patients (e.g. opportunities to build trust, approaches to ensuring consent, approaches to data sharing, privacy, security, etc.).
7. Impact for patients: To the extent it is applicable to the project, describe opportunities to improve patient outcomes within the 18-month project timeframe—and beyond.
8. Economic impact / value analysis: As appropriate for your project, describe the anticipated clinical utility and the economic impact (impact on healthcare spending) of your proposed intervention or platform, if implemented into clinical practice (see e.g., http://meetinglibrary.asco.org/content/152750-156 and Lamond et al., Expert Rev Pharmacoecon Outcomes Res. 2013, 243-50).
9. Health disparities: Describe the impact the project will have on reducing health disparities.
10. Anticipated challenges and proposed solutions: Describe potential barriers to the project's success, especially those that could delay the launch, progress or completion (e.g., human subjects), and describe potential solutions to these challenges.
11. Project Team: Provide a brief description of the PI, team, and key collaborators. Partnership is highly valued. Describe collaborations with at least two additional California non-profit or for-profit organizations as part of your proposal. Additional partners are highly encouraged. Describe the nature and strength of any existing collaborations.
12. Budget overview: Briefly outline how CIAPM funds (approximately up to $1.2M) will be used and how other resources will be leveraged. Comment on why CIAPM funds are needed as opposed to other funding sources such as federal or philanthropic grants. Examples of other resources that may be leveraged include: experts' time; molecular characterization, including DNA, RNA and genomic sequencing; computational platforms, including genome analysis, data visualization, innovative databases, data sharing, data privacy and security, or high-performance computing; mobile platforms to reach patients between medical encounters, to track their health and outcomes, etc. Please see existing CIAPM demonstration projects for examples.

    Note: CIAPM funds are intended to be used exclusively in California. If the project necessitates the use of CIAPM funds outside of California, provide a brief justification and estimate of the funding that will leave the state. The amount of funds that can leave the state will be subject to the final award agreement.

E. Submission – Concept proposals must be submitted electronically as a single PDF to ciapm@ucsf.edu by 5:00pm PT on Monday, August 8, 2016.

V. Selection

A. Selection Committee

A committee will be established that includes subject matter experts representing the breadth of stakeholders involved in the overall initiative. Selection committee members may include nominees of the legislature, public solicitation, or academic referral. Selection committee members shall not be deemed to be interested in any contract including any award of CIAPM funds and will be screened for conflict of interest consistent with NIH procedures. The names of selection committee members will be provided on the CIAPM website. The selection committee will establish its procedures for reviewing the proposals and making award recommendations. CIAPM will strongly recommend a process consistent with NIH practices to ensure proposals are evaluated in a manner that is fair, equitable, timely and free of bias.

B. Selection criteria - *Section 65057 of the Government Code sets forth the following selection criteria:*

- The potential for tangible benefit to patients within two to five years, including the likelihood that the study will have an immediate impact on patients.
- The depth and breadth of data available in the disease focus areas across institutions.
- The prospects for efficient and effective data integration and analysis.
- The expertise of potential team members.
- The resources available for the project outside of the initiative, including the potential for leveraging non-state funding.
- The clinical and commercial potential of the project.
- The potential to reduce health disparities.
- The potential to scale and leverage multiple electronic health records systems.
- The potential to develop the use of tools, measurements, and data, including publicly generated and available data.

The selection committee may also choose to consider additional factors in reviewing the proposals such as:

- The potential for positive economic impact of the proposed intervention or platform, if implemented into clinical practice.
- The innovative concepts, approaches or methodologies, instrumentation, or interventions to advance precision medicine.
- The feasibility of the project (can the project plan be achieved within the proposed timeline).
- The quality and extent of patient engagement.
- Where the project is located in California to balance geographic equity of awards.
- Overall impact to advance precision medicine.

C. Results

The selection committee will report on the justification for selecting the demonstration projects that are awarded funding and will provide a list of the demonstration projects that were not selected on the CIAPM website. Therefore, do not include in the title of a project any proprietary or confidential information or information that could identify the PI and applicant institution, unless you do not object to being identified.

VI. Applicants of those proposals that are selected will be asked to enter into an agreement with CIAPM through the University of California, San Francisco. The agreement will address project implementation, including the following:

A. Indirect Costs: Due to statutory limits of funding, no indirect costs will be provided with CIAPM funds. Awardees are asked to waive indirect expenses.

B. Intellectual Property Agreement: Agree to terms of previously established patent agreement for existing CIAPM projects.

C. Start Date: Initiate work, if funded, within 30 days of receiving the award notification.

D. Reporting: Submit quarterly progress reports, work with CIAPM staff throughout their project, if funded, on milestone and budget development and adjustments, and participate in conference calls and convening activities. If awarded, precise post-award expectations will be specified in award agreements.

E. Use of Data: Investigators and demonstration teams are expected to share data and research findings consistent with academic standards.

F. Protection of Privacy and Health Information: Investigators and demonstration project teams are expected to follow state and federal law to protect privacy and personal health information, and rights of human subjects.

Appendix B. CIAPM Selection Committee

California Initiative to Advance Precision Medicine

CIAPM Request for Proposals 2016

Selection Committee

Overview by Expertise

Selection Committee Member	Institution	Expertise
Nancy Cox - Chair	Vanderbilt University	Genomics / Statistics
Elaine Mardis	Washington University	Genomics / Cancer
Marylyn Ritchie	Geisinger Health System	Genomics / Bioinformatics
Isaac Kohane	Harvard University	Statistics / Computation
Eric Hekler	Arizona State University	Digital Health
Stanley Shaw	Harvard University	Digital Health
Shawneequa Callier	George Washington University	Health Disparities / Ethics
Akinlolu Ojo	University of Arizona	Health Disparities / Global Health
Rachel Ceballos	Fred Hutchinson Cancer Research Center	Health Disparities / Behavioral Health
Jeffrey Kahn	Johns Hopkins University	Ethics
Ya Chen Tina Shih	MD Anderson Cancer Center	Health Economics
Timothy Coetzee	National Multiple Sclerosis Society	Patient Engagement
Margaret Anderson	Faster Cures	Patient Engagement

Listed in alphabetical order

Margaret Anderson
Executive Director
Faster Cures, Milken Institute

Margaret Anderson is the executive director of FasterCures, a Milken Institute center that works to speed up the process of getting new medicines from discovery to patients. She is a founding board member and past-president of the Alliance for a Stronger FDA, a member of the NIH National Center for Advancing Translational Sciences Advisory Council and Cures Acceleration Network Review Board, the National Health Council Board of Directors, United for Medical Research Steering Committee, and the Institute of Medicine's Forum on Drug Discovery, Development and Translation. Previously, Anderson was the deputy director and team leader of the Center on AIDS & Community Health at the Academy for Educational Development; program director at the Society for Women's Health Research; health science analyst at the American Public Health Association; and analyst and project director at the Congressional Office of Technology Assessment in the Biological Applications Program. Anderson holds a bachelor's degree from the University of Maryland and a master's degree in science, technology, and public policy from George Washington University.

Shawneequa L. Callier, JD, MA
Assistant Professor
Department of Clinical Research and Leadership
School of Medicine and Health Sciences
The George Washington University

Ms. Shawneequa Callier has over a decade of experience analyzing the ethical, legal and social issues raised by genetic research. Her current scholarship focuses on topics related to precision medicine, race and genetics, pharmacogenomics, and the use of personalized genomic testing as an educational tool. Ms. Callier is a Special Volunteer at the National Human Genome Research Institutes' Center for Research on Genomics and Global Health. In addition, she is a full time assistant professor of Bioethics and Health Care Law and Regulation in the School of Medicine and Health Sciences at George Washington University (GW), and a Part-Time Professorial Lecturer of Genetics and the Law at the GW School of Law.

Prior to joining the GW faculty, Ms. Callier completed a post-doctoral fellowship at the Center for Genetic Research Ethics and Law, an interdisciplinary center for excellence funded by the National Human Genome Research Institute and located in the Bioethics Department of Case Western Reserve University's School of Medicine. From 2006 to 2009, Ms. Callier practiced health care law in Washington, D.C. Earlier in her career, she also interned at the World Health Organization and the Nuffield Council on Bioethics where she examined international healthcare ethics policies and human genetics laws and guidelines.

Rachel Ceballos, PhD
Assistant Member, Public Health Sciences Division
Fred Hutchinson Cancer Research Center
Affiliate Assistant Professor, School of Public Health
University of Washington in Seattle

Dr. Ceballos is currently an Assistant Member in the Division of Public Health Sciences at the Fred Hutchinson Cancer Research Center and Affiliate Assistant Professor in the School of Public Health at the University of Washington in Seattle, WA. Her research focuses on the development of culturally appropriate interventions to improve emotional well-being and health education opportunities for Latino and African-American cancer survivors. This includes examination of underserved Latinos' interests, beliefs, and preferences for biomedical research participation. Her research methods emphasize community based participatory research practice, which engages in reciprocal learning and community collaboration at all levels of the research process. She is the recipient of a career development award funded by the National Cancer Institute. Dr. Ceballos received her doctoral degree from the Department of Biobehavioral Health at Penn State University. She is trained as an interdisciplinary scientist with both laboratory and community-level research experience. Dr. Ceballos is a Steering Committee Member for the National Latino Cancer Summit, an Advisory Board member for the Susan G. Komen Puget Sound LGBTQ Initiative, and is a Board Member for Cancer Lifeline (a Seattle-based community cancer support center).

Tim Coetzee, PhD
Chief Advocacy, Services, and Research Officer
National Multiple Sclerosis Society

Timothy Coetzee, Ph.D., is the Chief Advocacy, Services and Research officer at the National Multiple Sclerosis Society (NMSS) in New York. Dr. Coetzee has been engaged in multiple sclerosis research and advocacy work throughout his career. He leads the Society's federal and state activism programs, manages its investment in basic, clinical and commercial research, and oversees the delivery of nationwide educational programs and services for people living with MS. He has also helped launch and served as president of Fast Forward, an initiative of the NMSS to speed the commercial development of new treatments for multiple sclerosis. He earned his Ph.D. at Albany Medical College in New York, pursued postdoctoral training at the University of North Carolina at Chapel Hill. Prior to joining the Society, he was a faculty member of the Departments of Microbiology and Neuroscience at the University of Connecticut Health Center.

Nancy J. Cox, PhD
Director, Vanderbilt Genetics Institute
Director, Division of Genetic Medicine
Mary Phillips Edmonds Gray Professor of Genetics
Vanderbilt University

Nancy J. Cox, PhD is a quantitative human geneticist with a long-standing research program focused on identifying and characterizing the genetic component to common human diseases. Dr. Cox earned a BS in Biology from the University of Notre Dame in 1978, a PhD in Human Genetics at Yale in 1982 and did post-doctoral research at Washington University and the University of Pennsylvania before joining the University of Chicago in 1987. She spent 28 years at the University of Chicago rising to Professor and Chief of the Division of Genetic Medicine before moving to Vanderbilt University in 2015 to become the Mary Phillips Edmonds Gray Professor of Genetics and inaugural Director of the Vanderbilt Genetics Institute, and Director of the Division of Genetic Medicine. Dr. Cox is the President-elect of the American Society of Human Genetics (2016-18), a Fellow of the AAAS, was part of a team winning the Landon Award in 2008 from the American Association for Cancer Research, and achieved the Leadership Award in 2010 from the International Genetic Epidemiology Society. Dr. Cox's current research is now focused largely on integrating data on genome variation and genome function with electronic health records to push the next round of translation of genome discovery into healthcare. Currently funded research projects on which Dr. Cox is PI or co-PI include using these data integration approaches to analyze whole genome sequence data generated by the Centers for Common Disease Genomics, and developing the new Center of Excellence in Health Disparities for Personalized Medicine and Population Health at Vanderbilt.

Eric Hekler, PhD
Assistant Professor, School of Nutrition and Health Promotion
Director, Designing Health Lab
Arizona State University

Dr. Eric Hekler, PhD, is an Assistant Professor in the School of Nutrition and Health Promotion at Arizona State University and directs the Designing Health Lab @ASU. His research focuses on facilitating individualized and "precise" behavior change for fostering

long-term health and well-being via digital health/mHealth technologies. For example, his NSF-funded work is focused on developing mathematical models for guiding an intervention that determines an individualized "ambitious but doable" daily step goal to strive for each day. The long-term goal is to develop a comprehensive intervention that provides the right type of support for physical activity only when it is needed. Dr. Hekler's Robert Wood Johnson Foundation grant is focused on developing a methodology for the more rapid collective development of technology-delivered behavior change strategies, a process he has labeled Agile Science. His Google-funded work is focused on teaching individuals fundamentals of behavior change and self-experimentation and giving them tools (e.g., home sensors and feedback) to allow them to self-experiment with behavior change techniques to optimize their health. Prior to ASU, Dr. Hekler completed his postdoctoral training at Stanford University and received his Ph.D. in Clinical Health Psychology from Rutgers University.

Jeffrey Kahn, PhD, MPH
Andreas C. Dracopoulos Director of the Johns Hopkins Berman Institute of Bioethics
Robert Henry Levi and Ryda Hecht Levi Professor of Bioethics and Public Policy
Professor, Department of Health Policy and Management
Johns Hopkins University Bloomberg School of Public Health

Dr. Jeffrey Kahn is the Andreas C. Dracopoulos Director of the Johns Hopkins Berman Institute of Bioethics. He is also Robert Henry Levi and Ryda Hecht Levi Professor of Bioethics and Public Policy, and Professor in the Department of Health Policy and Management in the Johns Hopkins University Bloomberg School of Public Health. His research interests include the ethics of research, ethics and public health, and ethics and emerging biomedical technologies. He speaks widely both in the U.S. and abroad, and has published four books and over 125 articles in the bioethics and medical literature. He is an elected Fellow of the Hastings Center, and has chaired or served on committees and panels for the National Institutes of Health, the Centers for Disease Control, and the Institute of Medicine/National Academy of Medicine, where he is currently chair of the Board on Health Sciences Policy. His education includes a BA in microbiology (UCLA, 1983), MPH (Johns Hopkins, 1988), and PhD in philosophy (Georgetown, 1989).

Isaac Kohane, MD, PhD
Marion V. Nelson Professor of Biomedical Informatics
Chair, Department of Biomedical Informatics
Harvard Medical School

Isaac Kohane, MD, PhD is the inaugural Chair of the Department of Biomedical Informatics and the Marion V. Nelson Professor of Biomedical Informatics at Harvard Medical School. He develops and applies computational techniques to address disease at multiple scales: from whole healthcare systems as "living laboratories" to the functional genomics of neurodevelopment with a focus on autism. Over the last 30 years, Kohane's research agenda has been driven by the vision of what biomedical researchers could do to find new cures, provide new diagnoses and deliver the best care available if data could be converted more rapidly to knowledge and knowledge to practice. In so doing, Kohane has designed and led multiple internationally adopted efforts to "instrument" the healthcare enterprise for discovery and to enable innovative decision-making tools to be applied to the point of care. At the same time, the new insights afforded by 'omic-scale molecular analyses have inspired

him and his collaborators to work on re-characterizing and reclassifying diseases such as autism, rheumatoid arthritis and cancers. Kohane's i2b2 project is currently deployed internationally to over 120 major academic health centers to drive discovery research in disease and pharmacovigilance (including providing evidence on drugs which ultimately contributed to "black box"ing by the FDA). Dr. Kohane has published several hundred papers in the medical literature and authored a widely-used book on Microarrays for an Integrative Genomics. He is a member of the Institute of Medicine and the American Society for Clinical Investigation.

Elaine R. Mardis, PhD
Robert E. and Louise F. Dunn Distinguished Professor of Medicine
Professor of Genetics and Molecular Microbiology
Co-director, McDonnell Genome Institute
Washington University School of Medicine

Elaine Mardis graduated Phi Beta Kappa from the University of Oklahoma with a B.S. degree in zoology. She then completed her Ph.D. in Chemistry and Biochemistry in 1989, also at Oklahoma. Following graduation, Dr. Mardis was a senior research scientist for four years at BioRad Laboratories in Hercules, CA. In 1993, Dr. Mardis joined the faculty at Washington University School of Medicine. Recruited for her expertise in DNA sequencing and automation technology, she served as Director of Technology Development at the (then) Washington University Genome Sequencing Center, helping create methods and automation pipelines for sequencing the Human Genome. She has served as Co-director of the McDonnell Genome Institute since 2002. In 2014, Dr. Mardis was named the Robert E. and Louise F. Dunn Distinguished Professor of Medicine. Dr. Mardis has research interests in the application of next-generation sequencing to characterize cancer genomes and transcriptomes, and using these data to support therapeutic decision-making. She co-led the teams that first used next-generation sequencing to characterize the whole genome of an AML patient (Nature 2008), first sequenced and compared a primary tumor to its metastasis and xenograft, and first reported whole genome sequencing of samples from a breast cancer clinical trial. Beyond cancer genomics discoveries, Dr. Mardis is leading efforts to facilitate the translation of basic science discoveries about human genetic diseases into the clinical setting, especially focused on the use of next-generation sequencing. Her translational research efforts aim to devise NGS-based diagnostics, decision-support tools and databases, and the use of genomics to design personalized cancer vaccines. Dr. Mardis was elected to the AACR Board of Directors in 2015. She serves as an associate editor of Molecular Cancer Research, Disease Models and Mechanisms and Annals of Oncology, and acts as a reviewer for Nature, the New England Journal, Cell and Science. She is the Editor-in-Chief of Molecular Case Studies. She serves on the scientific advisory boards of Qiagen Ingenuity, DNA Nexus, and ZS Genetics, and is a member of the Supervisory Board of Qiagen N.V. Dr. Mardis received the 2010 Scripps Translational Research award for her work on cancer genomics, and was named a Distinguished Alumni of the University of Oklahoma College of Arts and Sciences in 2011. Discover Magazine featured her work in cancer genomics as one of their top 100 science stories of 2013. In 2014 and 2015, she was one of the most highly cited researchers in the world, according to Thompson-Reuters. She will receive the Morton K. Schwartz award from the American Association of Clinical Chemistry for Significant Contributions in Cancer Research Diagnostics in 2016.

Akinlolu O. Ojo, MD, MPH, PhD, MBA
Associate Vice President for Clinical Research and Global Health Initiatives
Professor of Medicine & Health Promotion Sciences
University of Arizona Health Sciences

In January 2016, Dr. Akinlolu ("Lolu") Ojo was appointed as the Associate Vice President for Clinical Research and Global Health Initiatives at the University of Arizona Health Sciences in the Office of the Senior Vice President for Health Sciences. Dr. Ojo came from the University of Michigan, Ann Arbor where he served as Professor of Medicine and the Inaugural Florence E. Bingham Research Professor in Nephrology. Dr. Ojo is an internationally recognized physician scientist with expertise in chronic kidney disease, kidney and kidney-pancreas transplantation and Global Health Research. At the University of Michigan, Dr Ojo was the PI of research studies totaling >$70 million and he played leadership roles on major NIH-funded clinical trials and cohort studies including the African American Study of Hypertension and Kidney Disease (AASK), the Folic Acid Vascular Outcome Reduction in Transplantation (FAVORIT), the Chronic Renal Insufficiency Cohort Study (CRIC), the Adult-to-Adult Living Donor Liver Transplantation Study (A2ALL) and the Nephrotic Syndrome Study Network (NEPTUNE). Dr. Ojo directed the Department of Medicine Global Health Research Program and the joint University of Michigan-International Society of Nephrology (UM-ISN) fellowship program to train nephrologists for low resource settings. Dr. Ojo is currently the PI of the Human Heredity and Health in Africa (H3Africa) Kidney Disease Research Network – a research and training program that is conducting genetic studies on kidney disease in 8,000 participants through 10 academic medical centers in five countries in sub-Saharan Africa. The H3Africa Kidney Disease Research Network is also engaged in the development of clinical and translational research infrastructure and research workforce capacity in Africa as part of a larger $76 million NIH-Wellcome Trust funded initiative to advance genomics research and develop clinical and translational research capacity in sub-Saharan Africa. Dr. Ojo has served as the Chair of the Steering Committee of the H3Africa Consortium which is comprised of 24 research projects and >350 investigators from 37 African countries. Dr. Ojo received his medical education from the University of Lagos, Nigeria and residency training in internal medicine at the University of Kentucky, Lexington. He earned a Master of Public Health (MPH) degree in Global Health from the University of Alabama in Birmingham and completed nephrology fellowship, PhD in Epidemiology and the Master of Business Administration (MBA) at the University of Michigan. Dr. Ojo has over 170 peer-reviewed publications and serves on editorial boards and on NIH study sections. Dr. Ojo maintains active clinical research collaboration with investigators in Latin America, the Caribbean, West Europe and East Asia. Dr. Ojo has mentored >20 research scientists and physician scientists and has been elected into several honorific societies including the American Clinical and Climatological Association (ACCA), American Society of Clinical Investigation (ASCI), and the Association of American Physicians (AAP).

Marylyn D. Ritchie, PhD
Director, Biomedical and Translational Informatics
Chief Research Informatics Officer
Geisinger Health System

Dr. Marylyn Ritchie, PhD is a Professor in the Department of Biomedical and Translational Informatics at Geisinger Health System. Dr. Ritchie is a statistical and computational geneticist with a focus on understanding genetic architecture of complex human disease.

She has expertise in developing novel bioinformatics tools for complex analysis of big data in genetics, genomics, and clinical databases, in particular in the area of Pharmacogenomics. Dr. Ritchie has received several awards and honors including selection as a Genome Technology, Rising Young Investigator in 2006, an Alfred P. Sloan Research Fellow in 2010, a KAVLI Frontiers of Science fellow by the National Academy of Science for each of the past four consecutive years (2011-2014), and she was named one of the most highly cited researchers in her field by Thomas Reuters in 2014. Dr. Ritchie has extensive experience in all aspects of genetic epidemiology and translational bioinformatics as it relates to human genomics. She also has extensive expertise in dealing with big data and complex analysis including GWAS, next-generation sequencing, CNVs, data integration of meta-dimensional omics data, Phenome-wide Association Studies (PheWAS), and development of data visualization approaches.

Stanley Shaw, MD, PhD
Assistant Professor of Medicine, Harvard Medical School
Associate Member of the Broad Institute of Harvard and MIT
Co-Director, Center for Assessment Technology and Continuous Health

Stanley Shaw, MD PhD is the co-founder and co-director of the Center for Assessment Technology and Continuous Health (CATCH) at Massachusetts General Hospital (MGH), Associate Dean for Executive Education at Harvard Medical School, an Associate Member of the Broad Institute of Harvard and MIT, and a founding Principal Investigator in the MGH Center for Systems Biology.

His research seeks to better assess human wellness and disease through new phenotypes (measurable traits), including patient-derived cells, Electronic Medical Records (EMR), the gut microbiome in human disease, and digital health. Dr. Shaw recently led the development of GlucoSuccess, an iOS ResearchKit app for type 2 diabetes patients, in partnership with Apple.

Dr. Shaw received his AB in Chemistry & Physics from Harvard College, and his MD and PhD (Biophysics) from Harvard. He is a practicing cardiologist in the Corrigan Minehan Heart Center at Massachusetts General Hospital.

Ya-Chen Tina Shih, PhD
Professor of Health Economics
Chief, Section of Cancer Economics and Policy
Department of Health Services Research
University of Texas MD Anderson Cancer Center

Ya-Chen Tina Shih, Ph.D., is Professor of Health Economics and Chief of the Section of Cancer Economics and Policy at the Department of Health Services Research, University of Texas MD Anderson Cancer Center. Dr. Shih received her Ph.D. in Economics from Stanford University, with a concentration on labor/health economics and econometrics. She has served as Principal Investigators on research grants related to various economic aspects of cancer funded by the National Cancer Institute, National Human Genome Research Institute, Agency for Healthcare and Quality, American Cancer Society, and Lance Armstrong Foundation. Dr. Shih has close to 20 years of experience with economic evaluation, health

services, and comparative effectiveness research, using both modeling approach and econometric techniques applied to observational as well as trial data. Her research concentrates on the application of quantitative methods to examine the economic aspect of cancer care. Major themes in her work include studying the diffusion of new medical technologies among various patient and provider subgroups and/or geographic areas; examining the impact of new technologies on the outcomes and costs of cancer care; estimating disease burden of cancer and cancer-related complications; and exploring the effect, especially the unintended consequences, of technology diffusion, health policies and regulations on cancer patients. Other research interests are assessing the cost-effectiveness of medical as well as behavioral interventions. Dr. Shih has over 120 publications, serves as a co-editor for Value in Health, and is on the editorial board of PharmacoEconomics. She is a member of the National Cancer Policy Forum at the National Academies of Sciences, Engineering, and Medicine (formerly Institute of Medicine) and also serves on the American Cancer Society Guidelines Development Workgroup.

California Initiative to Advance Precision Medicine

CIAPM Recommendation to Selection Committee: Peer Review Process for CIAPM RFP 2016

Overview

CIAPM Request for Proposals (RFP) 2 is posted at ciapm.org. The CIAPM peer review process is modeled on the NIH peer review process, and is designed to ensure that applications to this RFP are evaluated in a manner that is fair, equitable, timely and free of bias.

The application process consists of two stages. (1) Applicants will submit a short concept proposal, and (2) selected applicants (finalists) will be invited to submit a detailed full proposal. A Selection Committee will evaluate the concept proposals and full proposals and will select finalists (stage 1) and make recommendations for final awards (stage 2) to the Governor's Office of Planning and Research (OPR). The Selection Committee is composed of experts who have expertise in disciplines relevant to this RFP and the proposals. The list of Selection Committee members, once established, can be viewed at ciapm.org.

The peer review meetings are announced at http://www.ciapm.org/news-events. Following a public comment session, the scientific review meetings are closed to the public during the deliberative process as it relates to reviewing and ranking proposals and making final decisions. Everyone who will have access to proposals or who will attend the review meetings will be required to maintain confidentiality and NIH conflict screening rules will apply.

Triage Process

Depending on the volume of responses, the Selection Committee may limit the number of concept proposals from each institution that will be accepted into the review process. The Selection Committee will consider the information provided in the Institutional Cover Letter (e.g. institutional commitment and ranking) when deciding which applications will be reviewed from each institution. Institutions are highly recommended to include no more than two proposals. If a high volume of proposals are submitted, and, if a ranking is provided by an institution submitting more than two concept proposals, at least the two highest ranked proposals will be reviewed.

Review of Proposals (concept and full proposals)

CIAPM Request for Proposals 2016 specifies the review criteria and other considerations that will be used in the evaluation and selection of proposals.

A. Peer Review Roles

The Selection Committee process is overseen by a Scientific Review Officer (SRO). The SRO is responsible for ensuring that each application receives an objective and fair peer review, and that the process described herein is followed.

Scientific Review Officer:

- Analyzes the content of each application, and checks for completeness.
- Documents and manages conflicts of interest.
- Assigns applications to reviewers for critique preparation and assignment of individual criterion scores.

- Attends and oversees administrative aspects of peer review meetings.
- Keeps detailed minutes of all the meetings
- Works with the Selection Committee to report on the justification for selecting the demonstration projects that are awarded funding and provide a list of the demonstration projects that were not selected. This report shall be posted on the CIAPM website.

Selection Committee Members

Chair:

- Serves as moderator of the discussion of merit of the applications under review.
- Is also a peer reviewer for the meeting.

Reviewers:

- Declare Conflicts of Interest with specific applications according to NIH conflict screening rules.
- Receive access to the grant applications prior to the peer review meeting.
- Prepare a brief written critique for each application assigned, based on review criteria and judgment of merit.
- Assign a numerical score to each scored review criterion.
- Make recommendations concerning the scientific and technical merit and the potential impact on advancing precision medicine, in the form of final numerical scores.
- Work with the CIAPM SRO to report on the justification for selecting the demonstration projects that are awarded funding.
- Make recommendations concerning appropriateness of budget requests.

Other CIAPM affiliated individuals:

- CIAPM affiliated individuals are permitted to attend closed review meetings.
- These individuals may provide administrative and programmatic input during the review meeting.

B. Peer Review Meeting Procedures

- Applications are reviewed based on established review criteria (see CIAPM RFP 2016).
- Assigned reviewers summarize their prepared brief written critiques for the group.
- A discussion with Selection Committee members follows.
- Final scoring of overall impact scores is conducted by private ballot.

C. Peer Review Criteria

Review Criteria

Concept proposals and full proposals are submitted to CIAPM and are evaluated for their scientific and technical merit and their potential impact on advancing precision medicine.

Scored Review Criteria. Reviewers will be asked to consider the selection criteria listed in CIAPM RFP 2016 in the determination of merit. To facilitate consideration of the proposals, the criteria have been grouped into the five categories described below. Reviewers will be asked to give a separate score for each of the five main review criteria categories under which they are listed.

1. **Significance.** Does the project address an important problem or a critical barrier to progress in precision medicine? Is there a strong rationale for the project? If the aims of the project are achieved, how will precision medicine be advanced?
    - Potential for tangible benefit to patients within two to five years, including the likelihood that the study will have an immediate impact on patients;
    - Potential to reduce health disparities;
    - The potential for positive economic impact of the proposed intervention or platform, if implemented into clinical practice.

- Potential to scale and leverage multiple electronic health records systems;
- Potential to develop the use of tools, measurements, and data, including publically generated and available data;
- Clinical and commercial potential of the project.

2. **Investigators.** Are the PI, collaborators, and other team members well suited to the project? If investigators are in the early stages of independent careers, do they have appropriate experience and training? If established, have they demonstrated an ongoing record of accomplishments that have advanced their field(s)? Do the collaborators have complementary and integrated expertise; are their leadership approach, governance and organizational structure appropriate for the project?
    - Expertise of potential team members.
3. **Innovation.** Does the application challenge and seek to shift current research, clinical practice or other relevant paradigms? Does the project's innovation apply to one field of research or is it novel in a broad sense? Is it seeking the refinement, improvement, or new application of existing approaches?
    - Innovative concepts, approaches or methodologies, instrumentation, or interventions to advance precision medicine
4. **Approach.** Are the overall strategy, methodology, and analyses well reasoned and appropriate to accomplish the aims of the project? Have the investigators presented strategies to ensure a robust and unbiased approach, as appropriate for the work proposed? Are potential problems and alternative strategies presented? Are the proposed milestones, timeline and success metrics well thought out and achievable? If the project is in the early stages of development, will the strategy establish feasibility and will particularly risky aspects be managed? Have the investigators presented adequate plans to address relevant biological variables, such as sex, for studies in human subjects? If the project involves human subjects and/or clinical research, are the plans to address 1) the protection of human subjects from research risks, and 2) the inclusion (or exclusion) of individuals on the basis of sex/gender, race, and ethnicity, as well as the inclusion (exclusion) of children, justified in terms of the scientific goals and research strategy proposed?
    - Feasibility of the project (can the project plan be achieved within the proposed timeline);
    - Prospects for efficient and effective data integration and analysis;
    - Quality and extent of patient engagement.
5. **Environment.** Will the professional environment in which the work will be done contribute to the probability of success? Are the institutional support, equipment and other resources available to the investigators adequate for the project proposed? Will the project benefit from unique features of the professional environment, subject populations, or collaborative arrangements?
    - Depth and breadth of data available in the disease focus areas across applicant institutions
    - Resources available for the project outside of the initiative, including the potential for leveraging non-state funding.

Overall Impact. Reviewers will provide an overall impact score to reflect their assessment of the likelihood for the project to exert a sustained, powerful influence on advancing precision medicine, in consideration of the above review criteria. A proposal does not need to be strong in all categories to be judged likely to have a major impact.

D. Scoring

Scores will be used to guide the review process, they will not be provided to the applicants. CIAPM will use the NIH scoring system, which utilizes a 9-point rating scale (1 = exceptional; 9 = poor) for overall impact scores. (NOT-OD-09-024). A modified system, using letters (a= exceptional; e=poor), will be used for criterion scores.

- Before the peer review meeting, each reviewer assigned to an application gives a separate score for each of the scored review criteria categories.
- In addition, each reviewer assigned to an application gives a preliminary overall impact score for that application.
- During the first review, to select the concept proposal finalists, the preliminary scores may be used to determine which applications will be discussed in full at the meeting. Reviewers may, however, bring concept proposals designated as "not discussed" up for discussion.
- For each proposal that is discussed at the meeting, a final impact score is given by each eligible reviewer (without conflicts of interest) including the assigned reviewers.
- Each reviewer's score reflects his/her evaluation of the overall impact that the project is likely to have on advancing precision medicine, rather than being a calculation of the reviewer's scores for each criterion.
- The final overall impact score for each discussed application is determined by calculating the mean score from all the eligible reviewers' impact scores, and multiplying the average by 10. Thus, the final overall impact scores range from 10 (high impact) through 90 (low impact).

E. Decision Process

Merit as determined by the final overall impact scores will be the main determinant of concept proposal selection and final award recommendations. However, OPR aims to fund a balanced portfolio that represents diversity in several areas, including but not limited to, approaches, disease areas, focus areas, types of partners, and types of patient populations. Furthermore, statute requires that public institutions in both northern and southern California are included.

Therefore, at the concept proposal stage, where approximately 10-15 proposals deemed meritorious will be advanced to the second stage, CIAPM will ask the Selection Committee to draw a concept proposal selection line based on rank order of final overall impact scores. Subsequently, the Selection Committee may move additional proposals into the "select" category, based on considerations of OPR's goals to achieve a balanced portfolio as described above. Using this process if necessary, they have to ensure that proposals from public institutions in both northern and southern California advance to the full proposal stage.

At the full proposal stage, the Selection Committee will be asked to select up to 6 proposals to recommend for funding, based primarily on rank order while also ensuring that at least one proposal each from a public institution in northern and in southern California is included. The Selection Committee may also choose to adjust the list of recommended proposals to achieve a balanced portfolio as described above.

During the decision making process, Robert's Rules of Order will be used to take actions.

F. Review Results

Scores will be used to guide the review process, they will not be provided to the applicants.

Based on the review discussions for the concept proposals, the PIs who are selected to submit a full proposal will be provided with brief feedback that describes opportunities for improvement, for their consideration when preparing full proposals. The feedback will be provided in the context of one or more of the five main review criteria and the selection criteria listed in section C and in CIAPM RFP 2016. They will not receive written comments for their full proposals. PIs of concept proposals not selected for submission of a full application will not receive written comments.

CIAPM will work with the Selection Committee to prepare a report on the justification for selecting the demonstration projects that are awarded funding and provide a list of the demonstration projects that were not selected. This report shall be posted on the CIAPM website.

California Initiative to Advance Precision Medicine

CIAPM Request for Proposals 2016

Frequently Asked Questions

Funding for this RFP is provided by the State of California, and is appropriated under AB 1602, Chapter 24, Statutes of 2016, which establishes Article 6. *California Initiative to Advance Precision Medicine* under Chapter 1.5 of Division 1 of Title 7 of the Government Code. Eligibility criteria in the RFP are set forth in the statute. Please consult the answers to frequently asked questions for clarifications of the suggested CIAPM RFP 2016 review process.

Does the CIAPM RFP 2016 limit the number of proposals each institution may submit?

This is a new funding opportunity and we therefore do not have knowledge from previous submissions to estimate how many proposals CIAPM will receive. To enable thorough initial review of all proposals, institutions are highly recommended to include no more than two proposals. Focusing on no more than two well-developed proposals will demonstrate institutional commitment, which may factor in the committee's award recommendations. Similar to a “limited submission” process, the goal is to ensure thorough evaluations of proposals while including broad participation of institutions across California. Depending on the volume of responses, the Selection Committee may limit the number of concept proposals from each institution that will be accepted into the review process, while accommodating a given number of proposals from each institution. The purpose of RFP section IV.C.3 is to aid the Selection Committee during the triage process. This section suggests that applicant institutions limit their submissions to no more than two proposals, and if they submit more than two proposals, that they provide a rank order for their applications. If more than two proposals are submitted by an institution, being able to consult the rank order of applications as provided by the institution will ensure that the most competitive proposals from each institution are accepted into the review process. If an institution submits more than two proposals and does not provide a rank order, the Selection Committee may have to implement another process to choose proposals from that institution for consideration for the review process.

How many concept proposals will the Selection Committee review?

Given timing and available resources, and depending on the submissions received, we anticipate the Selection Committee may review approximately 40 concept proposals, or as necessary to accommodate at least two proposals from each institution.

What factors will the Selection Committee consider during the final decision process?

The statute identifies a breadth of possible focus areas for proposals, as listed in the RFP under section IV.B.2. These focus areas are reflective of the diverse fields and goals that comprise precision medicine. In order to maximize the overall impact of the funded portfolio of projects, the Governor’s Office of Planning and Research (OPR) asks that the Selection Committee

consider a balance of project types, including but not limited to, types of approaches, disease areas, research focus areas, partners, and patient populations, during its deliberations. Thus, while selecting highly meritorious proposals based on final overall impact scores of the individual proposals, the Selection Committee will also consider the overall potential impact of the portfolio to advance precision medicine in California, when making funding recommendations to OPR.

Will all applicants have the opportunity to present at the CIAPM workshop in August?

The RFP states that applicants will have the opportunity to pitch and discuss their proposal at the CIAPM convening on August 26, 2016 in Los Angeles. Applicants whose concept proposals are reviewed will be invited to present during the time of the workshop dedicated to RFP applicants. If the Selection Committee limits the number of concept proposals accepted into the review process (see above), the applicants of triaged proposals will not be invited to present, but will likely be invited to attend. Such applicants and other precision medicine stakeholders will be given the opportunity to present an elevator pitch during the reception.

Appendix E. Full Proposal Details

CIAPM RFP 2016 - Full Proposals

Principal investigators (PIs) of concept proposals, selected through a peer review process to advance to the second stage of review, will be invited to submit a full proposal. The recommended CIAPM review process is posted on the CIAPM website.

CIAPM asks applicants to prepare a full proposal as listed below. **Use minimum Arial 11 font; 0.5 inch margins, and submit as a single PDF to ciapm@ucsf.edu by 5:00 pm PT on September 30, 2016**.

1. Cover Page: 1 page maximum
    a. Title of the proposal
    b. Lead PI's name, institution, email address
    c. Vice Chancellor of Research or other Authorized Institutional Official's name and email address
    d. Key team members / collaborators, listed by institution/organization (including external partners)

2. Overview: 1 page maximum
    a. Scientific / technical abstract
    b. Public abstract: In lay language, briefly describe the proposed work and how it will contribute to the advancement of precision medicine. This Public Abstract will become public information and will be available online; therefore, do not include proprietary or confidential information or information that could identify the PI and applicant institution.

3. Cover Letter: 1 page maximum, addressed to the review committee, summarizing your response to their feedback. Brief comments and suggestions from the review committee will be provided to PIs selected to submit full proposals on or before Sep 9, 2016.

4. Project Plan: 5 page maximum; expand on the information provided in the concept proposal (items a-k below), taking into consideration reviewer feedback.
    a. Impact on precision medicine: Describe how the proposed project will address a knowledge gap or need in a specific disease area(s), health issue, technology or fundamental biological process and, in doing so, demonstrate the promise of precision medicine. Provide rationale for the project by outlining existing strengths, resources and opportunities available (e.g., ability to obtain molecular measurements, remotely collect behavioral or other data, subtype the disease, link genomic data to EHR; access to existing biobanks; databases, medical records; an engaged participant community, established mechanisms for responsible data sharing, etc.).
    b. Focus area: Describe which relevant focus areas(s) the project will address (see RFP section IV,B, 2). Provide rationale for the selected focus area(s) by outlining the current associated challenges to and opportunities for the advancement of precision medicine.
    c. Project plan: Describe the components of your proposed project (specific aims

and research strategy).

d. Patient data: Each proposal should demonstrate its commitment to the use of robust data. For example, your proposal could make use of patient data from at least two data sources, such as eligible institutions, health care providers, or other sources of health-related data. Use of additional data sets is encouraged. Briefly describe the data set(s) you propose to use and the rationale for their choice.
e. Precision medicine capabilities: Describe the precision medicine capabilities that will be developed as a result of this project (i.e., infrastructure and tools that will be built as a result of this project including physical capacity, new consortia, collaborations, personnel competencies, databases, software or computational development, startup company opportunities, intellectual property, patient cohorts, participant communities and networks, models for responsible data sharing, etc.).
f. Participant engagement: Describe strategies to engage patients (e.g. opportunities to build trust, approaches to ensuring consent, approaches to data sharing, privacy, security, etc.).
g. Impact for patients: To the extent it is applicable to the project, describe opportunities to improve patient outcomes within the 18-month project timeframe—and beyond.
h. Economic impact / value analysis: As appropriate for your project, describe the anticipated clinical utility and the economic impact (impact on healthcare spending) of your proposed intervention or platform, if implemented into clinical practice (see e.g., http://meetinglibrary.asco.org/content/152750-156 and Lamond et al., Expert Rev Pharmacoecon Outcomes Res. 2013, 243-50).
i. Health disparities: Describe the impact the project will have on reducing health disparities.
j. Anticipated challenges and proposed solutions: Describe potential barriers to the project's success, especially those that could delay the launch, progress or completion (e.g., human subjects), and describe potential solutions to these challenges.
k. Project Team: Provide a brief description of the PI, team, and key collaborators. Partnership is highly valued. Describe collaborations with at least two additional California non-profit or for-profit organizations as part of your proposal. Additional partners are highly encouraged. Describe the nature and strength of any existing collaborations.

5. References: List references cited in the project plan. No page limitation.

6. Milestones: 1 page maximum
In order to track and deliver proposed project outcomes it will be necessary to develop and institute meaningful and agreed upon milestones. Continued funding of awarded

projects is not guaranteed. It is, instead, contingent on meeting agreed upon milestones and demonstrating measurable progress towards these milestones as evidenced through quarterly progress reports and possibly site visits as determined by the CIAPM management team.

Provide draft milestones in the form of a table, listing each deliverable, the metric that indicates its successful achievement, and the anticipated start and end date for associated work. This draft will be part of the assessment by the Selection Committee, and will serve as a basis for negotiation with CIAPM to finalize the milestones for the project, if funded.

7. Protection of human subjects: no page limitations
   Applications must designate if human subject research is proposed. **Please see Appendix A for**
   - **"Protection of human subjects" form (append filled out form after section 7)**
   - **"IRB review tool" (append filled out tool after section 7)**
   - **Details for the narrative for this section 7.**

8. Project Team Biographical Sketches - no limit to number of biosketches; provide NIH format biographical sketches for project team members.

9. Budget Narrative: 1 page maximum
   a. Propose a budget of up to $1.2 million. Note: no indirect costs will be provided with CIAPM funds.
   b. Budget overview: Briefly outline how CIAPM funds will be used and how other resources will be leveraged. Comment on why CIAPM funds are needed as opposed to other funding sources such as federal or philanthropic grants. Examples of other resources that may be leveraged include: experts' time; molecular characterization, including DNA, RNA and genomic sequencing; computational platforms, including genome analysis, data visualization, innovative databases, data sharing, data privacy and security, or high-performance computing; mobile platforms to reach patients between medical encounters, to track their health and outcomes, etc. Please see existing CIAPM demonstration projects for examples of leveraged resources.

   Note: CIAPM funds are intended to be used exclusively in California. If the project necessitates the use of CIAPM funds outside of California, provide a brief justification and estimate of the funding that will leave the state. The amount of funds that can leave the state will be subject to the final award agreement.

10. Budget - 1 page maximum; provide a detailed budget breakdown to support the narrative

11. Letters of Support - no maximum

For questions about the full proposal, please contact ciapm@ucsf.edu

Appendix A

Protection of Human Subjects Form – please fill out and append this form after section 7

Replace boxes "□" with an "X" to choose answers to questions 1-4, as appropriate.

1. Does your proposed work involve Human Subject Research? Yes No

Please use the "IRB Review tool" (next page) to answer this question, and append the tool page after this form.

If you answered "yes" to question 1:

- your project requires IRB review
- please answer questions 2-4

2. Does your work qualify as "exempt"? Yes No

To answer this question, consider the four categories listed at http://irb.ucsf.edu/levels-review#exempt under "Exempt Certification". If the entire scope of your proposed research falls into one or more of the four categories, your research qualifies as "exempt".

2a. If you answered Yes to question 2: your project requires IRB review, but gets *acknowledged* rather than *approved*

- Has IRB acknowledgment been obtained from your institution? Yes No
  - If yes: IRB acknowledgement date:
  - If no: have you submitted an application to your IRB? Yes No

2b. If you answered No to question 2: your project requires IRB review AND approval

- Has IRB approval been obtained from your institution? Yes No
  - If yes: IRB approval date:
  - If no: have you submitted an application to your IRB? Yes No

3. Are you proposing a clinical trial? Yes No

4. Are you proposing a NIH-defined phase III clinical trial? Yes No

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- For definitions of "human subjects" go to http://irb.ucsf.edu/research-needing-irb-review
- For definition of "clinical trial" go to http://grants.nih.gov/grants/glossary.htm
- In addition to IRB requirements at your institution, awards made by CIAPM will require UCSF IRB review or approval if Human Subject Research will be conducted under the award.

Appendix A continued - IRB Review Tool

Please fill out and append this tool after the "Protection of Human Subjects" Form

If you have any questions about this form, please contact Kate Nolan, Regulatory Knowledge and Support, UCSF, at 415 476 3067 (mention CIAPM RFP 2016)

In order to be able to expedite the necessary IRB review at UCSF in case your proposal is awarded CIAPM funding, please use this IRB screening tool to determine whether your proposed research is Human Subjects Research.

"Identifiable" information includes the following:

- Names
- All geographical subdivisions smaller than a State, including street address, city, county, precinct, zip code
- Dates directly related to an individual including birth date, admission date, discharge date
- Phone numbers, fax numbers, email addresses
- Social Security numbers, medical record numbers, account numbers, Certificate/license numbers, vehicle identifiers and serial numbers, license plate numbers
- Device identifiers and serial numbers, Web Universal Resource Locators (URLs), Internet Protocol (IP) address numbers
- Biometric identifiers, finger and voice prints, identifiable photographic images

IRB Pre-Screening

1. Does your project involve the initial collection of identifiable tissue specimens for research purposes?

☐ Yes ☐ No

2. Are you interacting with research subjects? Interaction includes communication (e.g., phone call or email) or interpersonal contact between the researcher and subject.

☐ Yes ☐ No

3. Does the research involve human stem cells?

☐ Yes ☐ No

4. Does the research involve drugs, biologics, or devices regulated by the Food and Drug Administration?

☐ Yes ☐ No

5. Will anyone on the research team have access to any identifiable information about the subjects at any point?

☐ Yes ☐ No

- If the answer to ANY of the above questions is "Yes," your project requires IRB review.
- If the answer to ALL of the above questions is "No," your project does not constitute Human Subjects Research.

Appendix A continued

Instructions for section 7 "Protection of human subjects" in full proposal

Questions 1-4 refer to questions on "Protection of Human Subjects" Form

1. If your work does not involve human subject research, the "Protection of Human Subjects" section is not required. Please enter "N/A" in section 7 of your full proposal.

Please provide the following narratives in section 7 of your full proposal, if questions 2a, 2b, 3, and / or 4 apply to your proposed work

2a. If your work involves human subject research and qualifies as "exempt", indicate which "exempt category" it falls under (see four categories listed at http://irb.ucsf.edu/levels-review#exempt under "Exempt Certification")

2b. If your work involves human subject research and does not fall into one of the four "Exempt categories":

- **Describe risks to subjects**
- **Describe adequacy of protection against risks**
- **Describe potential benefits of research to subjects and others**
- **Describe importance of knowledge to be gained**
- **Describe inclusion of women, minorities and children**

3 & 4. If you are proposing a clinical trial:

- **Include information listed under 2b.**
- **Include a Data Safety and Monitoring Plan**

- For information on Data Safety and Monitoring Plans, go to https://www.nlm.nih.gov/ep/dsm.html and https://humansubjects.nih.gov/data_safety

Appendix F. CIAPM Portfolio of Demonstration Projects

Year of award	Principal Investigator	Lead institution	Project title	Disease focus
2015	David Haussler	UC Santa Cruz	California Kids Cancer Comparison	Childhood Cancer
2015	Charles Chiu	UC San Francisco	Precision Diagnosis of Acute Infectious Diseases	Acute Infectious Disease
2016	Nicholas Anderson	UC Davis	Personal Mobile and Contextual Precision Health	Hypertension, Depression
2016	Sheldon Greenfield	UC Irvine	Early Prostate Cancer: Predicting Treatment Response	Prostate Cancer
2016	David Martin	Children's Hospital Oakland Research Institute	Full Genome Analysis to Guide Precision Medicine	Severe Genetic Disorders in Children
2016	Pratik Mukherjee	UC San Francisco	Artificial Intelligence for Imaging of Brain Emergencies	Traumatic Brain Injury, Aneurysm, Stroke
2016	Brennan Spiegel	Cedars-Sinai Medical Center	Remote Monitoring to Predict Heart Failure	Heart Disease
2016	Walter Stewart	Sutter Health	Precision Medicine for MS: Making It Work	Multiple Sclerosis

Appendix G. Demonstration Project Partners

Principal Investigator	Host Institution	Partner Institutions
David Haussler	UC Santa Cruz	UCSF
		Stanford University
		Children's Hospital Orange County
		Chilren's Hosptial of Philadelphia
		British Columbia Cancer Agency
		University of Michigan
		University of Southern California
		UC Davis
		NuMedii
		CISCO
		DNAnexus
		Translational Genomics Research Institute
		CARIS Life Sciences
		Unravel Pediatric Cancer
		Jacob's Heart
		Kids v Cancer
		Alex's Lemonade Stand Foundation
		Team G Foundation
Charles Chiu	UCSF	UCLA
		UC Davis
		Zuckerberg San Francisco General Hospital and Trauma Center
		Children's Hospital Los Angeles
		Children's National Medical Center
		Children's Hospital Colorado
		St. Jude's Children Research Hospital, Memphis, TN
		UC Berkeley
		Syapse
		DNAnexus
		Google Inc
		Quest Diagnostic Inc
		California Department of Public Health
		Illumina Inc
Nicholas Anderson	UC Davis	UCSF
		UC Berkeley
		Overlap Health
Sheldon Greenfield	UCI	UCLA
		Veterans Affairs Long Beach Healthcare
		Veterans Affairs Los Angeles
		Cedars-Sinai Medical Center
David Martin	Children's Hospital Oakland Research Institute	UCSF
		UCSF Benioff Children's Hospital Oakland
		UC Berkeley
		Illumina
Pratik Mukherjee	UCSF	Zuckerberg San Francisco General Hospital and Trauma Center
		UC Berkeley
		Stanford University
		Brain Trauma Foundation
		Community Regional Medical Center, Fresno CA
Brennan Spiegel	Cedars-Sinai Medical Center	UCLA
		HealthLoop – Mountain View, California
		Neoteryx – Torrance, California
		Beckman Coulter – Brea, California
		SCIEX – Redwood City, California
		Thermo Fisher Scientific – San Jose, California
Walter Stewart	Sutter Health	UCSF
		Jordan Research and Education Institute
		National Muliple Sclerosis Society (NMSS)

Appendix H. Controlled Vocabulary for CIAPM Asset Inventory

This table shows the controlled vocabulary used to tag each asset entered into the database. These represent the keywords that can be used for searching the inventory. The yellow cells indicate column titles, and the white cells show the allowed vocabulary for each column, where applicable. Blue highlights indicate a shared vocabulary across types of assets.

Name of organization			
Location			
Principal investigator / Contact person			
Email address			
Name of initiative / consortium (if applicable)			
Name of asset			
Website link			
Additional information			
Disease area	**Disease area - detail**		
Aging			
Autoimmune	e.g., Multiple Sclerosis		
Blood			
Cancer	Specify type		
Cancer - Hereditary	Specify type		
Cardiovascular disease	e.g., Stroke		
Congenital malformations			
Digestive system			
Ear			
Endocrine, nutritional, metabolic			
Eye			
Genitourinary			
Infectious diseases			
Mental, behavioral, neurodevelopmental			
Muskuloskeletal			
Nervous system			
Pregnancy, childbirth			
Respiratory	e.g., Asthma		
Skin			
Transplantation			
Health			
Pharmacogenetics			
Type of organization	**Type of organziation - detail**		
Government	Pharma		
Industry	Biotech		
Non-profit	Healthcare organization		
	High Tech		
	Payer		
	Health IT		
	Trade organization		
	Business strategy		
	Academia - UC		
	Academia		
	Research		
	Research / Hospital		
	Life sciences policy / Public education		
	Venture capital		
	Philanthropy		
	Patient foundation / advocacy		
Asset category	**Asset Category detail**		
Local Initiative			
Consortium			
Organization			
Laboratory / research group / expert			
Study / project / trial	Experimental validation		
	Clinical trial		
	CLIA validation		
Sharable asset			
Product	Commercial		
	Laboratory-developed		
	Open source		
Education	Life sciences policy		
	Physician education		
	Patient / lay person education		
	Researcher education		
Patient engagement	Patient access to data		
	Participation		
	Consent		
	Ethics		
Funding	Venture capital		
	Philanthropy		
	Academia - industry collaboration		

Stage in precision medicine pipeline	Type of asset	Type of asset - detail 1	Type of asset - detail 2
Data	Database	Size, content (see e.g. data collection)	
	Cohort	Size, characteristics	
	Data handling	Data integration	EHR / genomic
		Data security / privacy	
		Data sharing platform	Amongst researchers
			Physician - patient communication
	Data tools		
	Computational infrastructure		
	Facilities / core capabilities		
	Large scale data collection on humans	Molecular	
		Biological	
		Demographics	
		Genome	NGS
Research/Analysis	Treatment / prevention / drug (target identification, factors affecting human health / disease)		Tumor gene panel
	Diagnostic / prognostic (Biomarker identification)		Germline gene panel
Clinical implementation / translation	Treatment / prevention / drug (development)		WES whole exome sequencing
	Diagnostic / prognostic (development)		WGS whole genome sequencing
Clinical practice	Treatment / prevention / drug (product)		Genetic effects
	Diagnostic / prognostic (product)		Gene - drug interactions
		Transcriptome	Gene expression panel
			Microarray
			RNA-seq
		Epigenome	
		Proteome	
		Metabolome	
		Microbiome	Metagenomic sequencing
		Other 'ome	Specify
		Behavior	
		Gender / age	Specify (gender or age)
		Race / ethnicity	
		Clinical phenotype	
		Pathogen sequencing	Metagenomic sequencing
		Environmental exposures	
		Socio-economic conditions	
		Wearables	
		Image analysis / imaging	
		Companion	
		Liquid biopsy	Cell-free (cf)DNA
			Circulating tumor cells (CTC)
	Drug repositioning		
	Analysis platform / data mining / math modeling		
	Knowledge network across data types		
	Model for experimental validation	Cells	Specify type of cell
		Animal	Specify species
	Biobank	Human tissue	Specify human tissue type
		Human DNA / RNA	
	Regulatory strategy		
	Digital / mobile health	Device development	
		Collecting patient / participant data	
		Influencing patient / participant behavior	
	Physician / patient/ payer support	Specify	
	Reimbursement / payer coverage		
	Economic value assessment / comparative effectiveness		
	Health disparities		
Outcomes in Real World	Population health		
	Health outcomes		
	Economic value assessment / comparative effectiveness		
	Adoption level		
	Reimbursement / payer coverage		
	Patient-centered outcome research		