Appendix 1

The Health eHeart Alliance

Our current team is led by researchers from the University of California, San Francisco who have recently launched an internet-based cardiovascular cohort study called the Health eHeart Study (HeH). HeH, with help from the American Heart Association (AHA), Practice Fusion, and three patient-advocacy groups, will form the core of a transformative new patient-powered research network (PPRN). Our team can already claim:

1. A large group of patients who have provided informed consent to participate in research and provided extensive self-reported cardiovascular health information
2. Established vehicles for additional recruitment via commitments from AHA, Practice Fusion, StopAfib.org, Mended Hearts, and the Sudden Arrhythmia Death Syndrome (SADS) Foundation
3. All data collection features of an ideal PPRN, including online surveys (many standard instruments), remote monitoring devices (sensors), mobile/online apps, electronic health records (EHR), and a state-of- the-art data system ready to scale up for collection and analysis of "big data"
4. Partnership with an innovative EHR provider (Practice Fusion) that can provide communication channels to providers as well as patients and a direct means of delivering interventions for comparative effectiveness research trials, quality improvement programs, and dissemination of research findings
5. An infrastructure for conducting very inexpensive trials and observations studies within HeH that can be used by investigators anywhere

Phase I funding: An ideal PPRN focused on cardiovascular health
Funding from PCORI will support creation of a new PPRN – The Health eHeart Alliance. The Health eHeart Alliance will work hand-in-hand with the Health eHeart Study to generate and test new patient-designed interventions for improving cardiovascular health. With the help of our partners, we have engaged a set of highly motivated patient-leaders, named and described in this application, who will form an Interim Steering Committee for the Alliance. We have committed a large portion of Phase I funding to resource this committee and support a deliberate "design process", with the goal of delivering:

- A conference designed to galvanize enthusiasm for crowd-sourcing cardiovascular research ideas
- A new PPRN organization with a mission statement, defined governance structure, and key policies
- Five specific crowd-sourced and PPRN-prioritized trial protocols ready for implementation within HeH Our funding will support the following additional aims designed to accomplish transition to an ideal PPRN:
- Recruitment of 100,000 patient-participants representing diverse demography and heart-related condition
- Capacity for "Blue Button" EHR data consumption, an IRB-approved online HIPAA authorization system, and a pilot natural language processing algorithm that adjudicates hospitalization events
- Demonstration of DNA collection capability and willingness of participants to contribute specimens
- Integration with a CDRN and 2 other PPRNs and collaboration with the NCRN Coordinating Center

Our vision for contributing to the National Clinical Research Network (NCRN): The Health eHeart Alliance will be the hub for cardiovascular health research in the NCRN. Patients with cardiovascular conditions of any type will be welcomed and find a vibrant community and opportunities to contribute by participating in research studies, by joining research idea brainstorming sessions with other patients, and by getting involved in PPRN leadership. As a fully functioning research-grade IRB-approved cohort study that is highly engaging to patients, HeH will provide other PPRNs and CDRNs with a mechanism to collect rich and varied types of

data including core cardiovascular measurements on their own patients through co-enrollment and data sharing. And as an inexpensive platform for testing interventions that will be available for use by outside investigator/collaborators, the Alliance will be a powerful engine for producing, testing and disseminating innovative patient-centered interventions that improve cardiovascular health.

ImproveCareNow (ICN) Network

The ImproveCareNow (ICN) Network is poised to become a reusable, scalable, and sustainable peer production Learning Health System (LHS) in which patients and clinicians collaborate to learn from every interaction, conduct patient-centered outcomes research, and implement the findings. ICN has developed and piloted programs to fully engage patients, clinicians, and researchers as equal partners, but these programs are not yet at scale. ICN has extensive, standardized clinical data, but has not yet collected patient-reported outcomes (PROs) from the vast majority of patients. To complete ICN's transformation, we propose to: 1) implement a full-scale peer-production system that engages patients, families, clinicians, and researchers working together to conduct research and improve health and healthcare, and 2) develop the infrastructure to assemble a comprehensive set of longitudinal patient-centered data.

ICN's mission is to transform the health, care, and costs for children and adolescents with Crohn's disease and ulcerative colitis -- inflammatory bowel disease (IBD). As a network that engages patients, families, and clinicians in research and improving outcomes, ICN has achieved remarkable success. Since 2007, the proportion of patients in remission (with inactive disease) has increased from 55% to 77% and 95% of patients approached have consented for research. ICN has grown to 56 sites that provide care for 17,000 patients in 30 states; about 1/3 of all children with IBD in the US.

With support from an NIH Transformative Research grant (R01 DK085719), ICN has partnered with the C3N Project to develop and test interventions to transform itself into a peer-production system to improve health and healthcare. In a peer production model, the production of new knowledge and know-how is distributed among all participants. Wikipedia, the best-known example of peer production, stands in contrast to the firm-produced (and defunct) Microsoft Encarta. Applying peer production to the LHS model means that patients, parents, clinicians, and researchers collaborate as peers to produce information (e.g., clinical data, patient reported outcomes), knowledge (informal insights and formal research), and know-how (about how to change care) to improve healthcare and health outcomes. With PCORI funding, we propose to implement the peer production model at scale, dramatically expanding and enhancing patient and family participation in governance, research, and dissemination and implementation activities.

With support from an Agency of Healthcare Quality and Research (AHRQ) Enhanced Registries grant (R01 HS20024), we built on open-source software to enhance the ICN registry to enable clinicians to collect data once using the electronic health record (EHR), and to re-use the data to automate chronic care processes, quality improvement (QI), and comparative effectiveness (CE) research. Through continuation funding (AHRQ R01 HS22974), we are extending this infrastructure to capture laboratory and pharmacy data. With PCORI funding, we propose to broaden the range of data collected to include PROs and claims data, and work with other PPRNs and CDRNs to implement data standards for interoperability and exchange of data.

ICN has benefited from substantial federal investment; with PCORI funding, we propose to complete the transformation to a full-scale peer production LHS. As an exemplar PPRN, we are fully committed to accelerating other PPRN's transformation and in participating in the national patient-centered clinical research infrastructure in collaboration with the Coordinating Center. As well, this proposal is one of a federation of 2 pediatric PPRNs (ICN and the National Pediatric Cardiology Quality Improvement Collaborative) and a pediatric CDRN (PEDSNet) that proposes to create a national pediatric LHS.

Crohn's and Colitis Foundation of America (CCFA)

Crohn's disease (CD) and ulcerative colitis (UC) are chronic Inflammatory Bowel Diseases (IBDs) that affect approximately 1.2 million individuals in the United States, cost over $6 billion annually, and cause substantial patient morbidity, missed work and school, and diminished quality of life. We have entered an era of rapid discovery of the genetic and microbiome-related factors involved in disease pathogenesis, and are now at the forefront of "personalized medicine" that delivers mechanistically determined specific treatment for individual patients. To translate these advances in basic science research into improved patient-centered care and outcomes, emerging genomic and microbiome data must be coupled with comparative effectiveness (and safety) research. Ultimately, this will enable patients and physicians to make collaborative choices about when, in whom, and how to use current and future therapeutic options (i.e. medications, surgery, diet, fecal transplant, etc). For this reason, comparative effectiveness research in IBD is recognized by the Institute of Medicine as a top national priority.

Yet, the infrastructure required to conduct high quality, multidisciplinary, patient-centered outcomes research in IBD has, to date, been lacking. This is largely because the fields of IBD genetics, microbiome research, clinical research, and outcomes research have evolved in a parallel, rather than in an integrated fashion, hindering the much needed cross- cutting research. Fortunately, a number of technological advances and changes in health policy have recently converged, enabling the collection and seamless integration of disparate, yet complementary, sources of data (i.e. patient reported data, biometric data, health records, genetic data, and other biomarkers) in a way that has never before been possible—by putting patients in control.

The Health Information Technology for Economic and Clinical Health (HITECH) Act and the resulting Meaningful Use Stage 2 Final Rule have empowered patients to View, Download, and Transmit (VDT) their own health records. The proliferation of mobile health (mHealth) apps and devices now allows patients to record and track their health related activities (fitness, sleep, diet, etc.) and physiological/biometric responses—as often as they choose. The internet provides a means to efficiently conduct patient surveys, making the recruitment and long-term follow up of patient cohorts relatively cost effective. Social media now provides easy access for patients to create disease-oriented communities in which they can learn about their disease, share insights with others, and contribute to research. Widespread and low-cost genetic sequencing has turned this and other previously labor-intensive resources into a commodity. Finally, novel bioinformatics approaches have paved the way for the seamless integration of these data.

The Crohn's and Colitis Foundation of America Partners (CCFA Partners) study is a novel and highly successful internet cohort of over 13,000 patients with IBD (~1% of US IBD population), focusing on patient-reported exposures, health behaviors, and outcomes. In this application, we propose to radically transform CCFA Partners into a full-scale Patient Powered Research Network (PPRN). We have developed a partnership with Crohnology, the leading social network for patients with this condition, and have identified best-in-class vendors to assist us in integrating data from mHealth apps and devices and electronic health records. Together, we will accomplish the following specific objectives: 1) Enhance network growth, diversity, and retention; 2) Build a robust network community, including patient governance structures that allow greater involvement of patients in research 3) Expand the network database to include electronic health records, data from mHealth apps and devices, and biological samples, 4) Develop a customized, yet scalable and adaptable, distributed data network (i.e. virtual database) by repurposing NASA-built technology, 5) Develop and test patient and provider-focused tools that utilize individual patient data to improve health behaviors, healthcare decisions, and, ultimately, outcomes, 6) Further engage the scientific community through open collaboration and data sharing, and 7) Rapidly disseminate new knowledge to patients, enabling them to improve their health.

Our team is uniquely positioned to develop this IBD-focused PPRN. The sponsor of this proposal, the CCFA, is the leading, non-profit IBD patient organization, founded in 1967 to "cure CD and UC and improve the quality of life of those affected". We have activated a highly engaged Patient Governance Committee and assembled an internationally recognized, multidisciplinary scientific team, representing disciplines of IBD basic science, epidemiology, computational mathematics, qualitative methods, patient-reported outcomes, health behavior design, computer programming, and bioinformatics. Finally, as IBD is model for other complex, chronic illnesses,

we look forward to working collaboratively with other PPRN and CDRN awardees, through the Steering Committee, to assist in the development of a national patient-centered clinical research infrastructure.

Arthritis Patient Partnership With comparative Effectiveness Researchers (ARPoWER)

Rheumatoid arthritis (RA) is a chronic, systemic, often disabling, autoimmune disease affecting 1% of adults and 2-3% of older individuals (1-4). A companion inflammatory arthritis, spondyloarthritis (SpA) has a similar prevalence and includes subtypes such as psoriatic arthritis, inflammatory bowel-related arthritis, and ankylosing spondylitis. These debilitating types of arthritis typically strike younger people (median age 30s and 40s), in the prime of work and family productivity, and are usually lifelong. There are genetic and environmental factors associated with their onset, but there is no known cure. According to the Center for Disease Control, arthritis is the leading cause of disability in the U.S. (5). New biologic medications that target specific components of the immune system have proved effective for most patients, with major improvements in quality of life (6). However, their high cost (~$3,000 per month) and requirement for ongoing use, along with many unresolved safety questions, makes inflammatory arthritis a key disease focus for comparative effectiveness research. Indeed, the Institute of Medicine put the need to conduct new comparative effectiveness studies of these medications for RA and SpA in the highest tier (first quartile) of importance (7).

In recognition of the importance of filling evidence gaps in inflammatory arthritis-related research, our established Creakyjoints (CJ) arthritis patient network, part of the Global Healthy Living Foundation (GHLF) (http://www.ghlf.org), proposes the Arthritis Patient Partnership With comparative Effectiveness Researchers (ARPoWER) PPRN. CJ was established in 1999 as a 501(c) (3) non-profit organization based in New York, with the mission to improve the quality of life for people with arthritis. CJ, as part of the GHLF, accomplishes this by advocating nationally for improved access to care and by educating the community about the importance of diagnosis, early and innovative medical intervention, long-term lifestyle improvement, and therapeutic compliance with arthritis treatments. Co-founded in 1999 by arthritis patient and patient advocate Seth Ginsberg, CJ is a network of approximately 55,000 arthritis patients and caregivers in all 50 U.S. states. The CJ focus is on the most dominant disease in our network, RA, with an additional large patient base of SpA. Other diseases represented by the GHLF include osteoporosis (CreakyBones.org, ~5,000 patients) and psoriasis (RedPatch.org, ~5,000 patients) and systemic lupus erythematosus. For more than 10 years, CJ has provided in-person education, advocacy, and grassroots patient mobilization that occurs through live community programs and partnerships with provider networks, other patient organizations, and professional societies. We also include vibrant online communities with an active presence on Facebook, Twitter, YouTube, and other social media tools. Annually, we have more than 20,000 one-on-one interactions with patients through community-based education and advocacy events; partner with more than 100 other patient groups in the U.S.; have an Internet presence with 19 million unique website hits; 100 million “impressions” from traditional media; >250,000 YouTube views; and relationships with numerous U.S. Congress and State legislatures for patient advocacy. The CreakyJoints Facebook page (www.facebook.com/creakyjoints) is the most popular arthritis page in the world, with between 10,000 and 30,000 “conversations” per week.

The AR-PoWER PPRN is vital to translating our high-impact patient advocacy and education-focused organization into an equally high-impact patient-centered network able to conduct research. This PCORI proposal builds on an established track record of collaboration between CJ and comparative effectiveness researchers and informatics experts who are part of the Agency for Healthcare Research & Quality (AHRQ)-funded UAB Center for Education and Research and Therapeutics (CERTs) of Musculoskeletal Diseases. Our relationship with UAB is well established, with multiple projects ongoing or under review (8, 9). Our other partners include a CDRN (DISCVER), the American College of Rheumatology (ACR), CORRONA [a doctor-led arthritis research network], and IMS Health, a healthcare network representing 23 million patients, 88 health plans, and 40,000 physicians.

We will satisfy and exceed all PPRN milestones and: 1) develop sophisticated information technology tools to securely capture our patients’ data; 2) collect informed consent from our

membership; 3) map our data to a common data model, and exchange encrypted information with other CDRNs and PPRNs, as well as 3 additional external data sources; 4) establish an expanded governance structure to ensure patient privacy and transparency about research activities, involving data security, privacy and Institutional Review Board experts. Our novel and timely PPRN will augment our already appreciable education and advocacy efforts with a greatly expanded research capacity to conduct comparative effectiveness studies in a key area deemed of major public health importance by the IOM. Additionally, CJ has a well-establish mechanism to allow CER results to be disseminated directly from their source to our expansive patient base, as well as through more traditional sources like the peer-reviewed scientific literature. Our patient network, led by arthritis patients and supported with substantial expertise from our federally-funded research experienced collaborators, and effectively leveraging an existing ARHQ-funded infrastructure, allows us to have tremendous effectiveness to support PCORI's mission to provide timely information on risks and benefits of treatments directly to arthritis patients in making real-world decisions.

Sleep Apnea-Patient Centered Outcomes Network (SA-PCON)

Breathing and sleep are both essential to life. Unfortunately, millions of adults and children suffer from sleep apnea, which causes nightly, recurrent interruptions of breathing during sleep due to collapse of the tissues in the throat.1 Sleep apnea deprives individuals of oxygen during sleep, and results in sympathetic nervous system over-activity, profound blood pressure surges, and sleep disruption. The immediate sequelae of Sleep Apnea and hypoxemia cascade into life threatening health problems with major public health impact. The consequences range from sleepiness, depression and impaired quality of life to hypertension, myocardial infarction, stroke, diabetes and early mortality.2-9 Sleep apnea affects 17% of adults and 1-4% of children,10 with rates increasing in association with the obesity epidemic.11 Sleep apnea aggregates in families;12 affects all age groups; and disproportionately affects minorities13 and those from poor neighborhoods.14

Though much has been learned about the epidemiology and pathophysiology of sleep apnea, management of the disease is disjointed and often suboptimal. Minority and disadvantaged groups are at increased risk for sleep apnea,13 yet are less likely to receive effective treatment.15 Use of diagnostic tests (home or lab-based sleep studies) is more often influenced by the patient's insurance than by clinical factors. Treatments include positive airway pressure (PAP), mandibular advancement devices, various surgeries, and behavioral interventions. However, there are little data to inform which treatments, or combinations of treatments, work best in given patients.16 Treatment strategies often reflect which specialist (e.g., pulmonologist, ENT, etc.) the patient sees rather than his or her clinical presentation or preferences. Traditionally, treatment has focused on improving a number- the Apnea Hypopnea Index- rather than improving patient-centered outcomes such as quality of life. Achieving optimal adherence to treatments such as PAP is a challenge.17 Efforts heretofore to develop strategies for improving adherence have not involved the patient; furthermore, minimizing treatment burden is not routinely considered. Behavioral approaches including modifying diet, physical exercise, and sleep position are not often systematically addressed. The sleep apnea patient is left to his or her own devices to find relief, which is particularly troubling for poor and minority patients with fewer resources. Thus, the Sleep Apnea-Patient Centered Outcomes Network (SAPCON) proposes to address the dual need to conduct critically important comparative effectiveness research while actively engaging patients and other key stakeholders in every aspect of research and implementation by participating as a PCORI Patient Powered Research Network (PPRN). Patients (including children via caregivers), particularly minorities and the medically underserved, will be given a voice in directing Sleep Apnea research that focuses on outcomes that matter to them.

The SAPCON represents an exciting collaboration of the American Sleep Apnea Association (ASAA), the nation's sole sleep apnea patient-centric organization, which serves as an information clearinghouse and support network for people who suffer with sleep apnea and their loved ones, with major research and clinical partners that include Harvard's Brigham and Women's Hospital and Informatics for Integrating Biology & the Bedside (i2b2) / Shared Health Research Informatics Network (SHRINE) and the Centers for Translational Science Award (CTSA) Sleep Research Network (SRN). Already, novel collaborations have been initiated with other PPRN and CDRN applicants, with plans for co-development of informatics tools and

infrastructure and for co-enrollment. The team has the talent and resources needed to efficiently build a PPRN of actively engaged patients and to collect and share health information needed to support critically needed research. Over an 18 month period, 50,000 patients will be recruited from a pool of over 10 million patients, using a broad strategy including social media and targeted clinic-based recruitment. A patient friendly web- portal will be built using open-source and robust tools that will provide each patient a "dashboard" for contributing health information, coupled with powerful visualization and aggregation tools for viewing and monitoring data. "Blue button" technology under development by our partners (national leaders in health exchange information) will be leveraged to rapidly deploy a standardized, interoperable and scalable network model using the same standards of clinical data exchange already required by Federal regulation to support patients in gaining access to and controlling flows of their health information.

The COPD Patient Powered Research Network

The Chronic Obstructive Pulmonary Disease (COPD) Foundation, in collaboration with the CONCERT and COPDgene research networks proposes to develop and host the COPD Foundation Patient Powered Research Network (PPRN). The collaboration brings together a patient developed and governed patient education, advocacy and support group with the research expertise of two federally funded research networks to establish the COPD Foundation PPRN. The COPD Foundation PPRN will enroll 100,000 people with COPD, approximately 0.5% of the U.S. COPD population, into a registry with scalable data hub for the sole purpose of supporting patient-driven, patient centered outcomes research (PCOR). Enrolled patients will represent the spectrum of COPD disease severity—most with multiple morbidities, across diverse geographic regions, broad age and socio-economic ranges, both gender, and all racial and ethnic groups.

Chronic obstructive pulmonary disease (COPD) is a critical part of U.S. health care affecting 12–24 million individuals in the nation, is responsible for 800,000 hospitalizations per year, and recently became America's 3rd leading cause of death.1-7 COPD related health expenditures are estimated to be as high as $50 billion per year, driven primarily by costs of hospitalization and a 25% hospital 30 day readmission rate.8-12 Healthcare expenditures for re-hospitalizations in patients with COPD exacerbations rank as the third highest among Medicare beneficiaries; provisions in the 2010 Affordable Care Act specifically list re-hospitalizations within 30 days after COPD exacerbations as a target for potential financial penalties by the Centers for Medicare & Medicaid Services (CMS).13,14 In recognition of the substantial and increasing impact of COPD on the health of the U.S. population, the U.S. Centers for Disease Control, the National Heart, Lung, and Blood Institute (NHLBI), and others have recently collaborated in the development of public and health professionals awareness campaigns to increase disease understanding, reduce stigma, and foster the use of evidence-based treatment and prevention approaches for COPD. The continuing lag between clinical practice and treatment options described by efficacy studies to improve the quality of life, functional status, and survival in patients with COPD, make COPD ripe for patient-centered outcomes research.1-9,15-24

The COPD Foundation is a national not-for-profit organization established by patients in 2004 solely dedicated to representing individuals with chronic obstructive pulmonary disease in the United States. The mission of the COPD Foundation is to improve the quality of life for those affected by COPD. The Foundation's activities span research, education, and public health/policy related programs and services to patients, caregivers and healthcare providers. The collaboration with the two large, federally funded research networks (CONCERT and COPDGene) will both expand services and capacities of the Foundation as a PPRN and enhance the ability of CONCERT, COPDGene, and others within the PCORI infrastructure to conduct PCOR empowered by patients with COPD. The COPD Foundation will lead an effort to expand its current network with registrants to its PPRN willing to share clinical information, patient-reported outcomes (PRO), and participate in PCOR. Active outreach for enrollment will include the 228,701 patients with linked administrative and clinical data of the CONCERT network as well as another 10,300 with patient reported outcomes and genetic data of the COPDgene network. COPD patients currently enrolled in the existing research studies will have the benefit of outreach and participation in the other Foundation's activities including Peer Health coaching and extensive educational material maintained by the COPD Foundation. Amongst the participants in the CONCERT data hub, outreach can take advantage of existing demographic data across its diverse health care delivery

sites and regions to target under-represented groups including those defined in terms of race/ethnicity, socioeconomic status, geographic location, clinical severity, and multi-morbidity. From this large pool of patients with currently available data and the members across the COPD Foundation and affiliates networks, we are confident we can enroll at least 100,000 patients who will provide PRO and demographic information and sign comprehensive consent and data sharing agreements to allow common shared data use for the COPD Foundation PPRN and across PCORI networks.

Multiple Sclerosis Patient-Powered Research Network

Accelerated Cure Project for Multiple Sclerosis (ACP) is a patient-founded, patient advocacy organization, highly successful in engaging patients to create resources that catalyze innovative collaborative research. In 2006, ACP launched a patient network centered on an open-access biosample and data repository for use in investigating causes and mechanisms of multiple sclerosis (MS). Today, our network has an enthusiastic base of 3,200 participants (patients and control subjects), clinician-researchers at MS specialty clinics located across the USA, strong relationships with over 60 research teams in academia and industry, and an invaluable collection of tens of thousands of biological samples (DNA, RNA, serum, plasma, and white blood cells) linked with extensive medical data and patient-reported information that, to date, has supported 77 research studies worldwide.

In partnership with the Computational Sciences & Informatics of Complex Adaptive Systems at Arizona State University and Feinstein Kean Healthcare, ACP proposes to expand the repository network to an MS Patient-Powered Research Network (MS-PPRN), so that a large number of MS patients across the USA can participate in ACP's mission and in the National Patient-Centered Clinical Research Network (NPCCRN). The MS-PPRN will be supported by an integrated IT and communications platform featuring a patient-driven and controlled portal (iConquerMS) that can be accessed regardless of geographical location and healthcare provider. This portal will give patients the opportunity to provide health-related, demographic, and electronic health record (EHR) information that can be shared in a de-identified fashion with researchers who are investigating topics that are important to patients, such as comparative effectiveness of therapeutic agents. Patients will also have the option of contributing biosamples through home-based collection or local laboratories to support biomarker research in MS. To catalyze research using MS-PPRN biosamples and data, ACP will mobilize the scientists who have already used ACP Repository resources and will also leverage its MS Discovery Forum website to reach a wider audience of investigators.

ACP's 18-month goal for enrollment in the MS-PPRN is 20,000 people with MS (5% of the estimated population of MS in the USA), beginning with the 3,200 participants in the current ACP Repository network. Outreach will be made through ACP's existing participant and supporter base, its network of top-tier MS clinics, other MS clinics and community neurologists, MS advocacy organizations who have agreed to bring our invitation to their members, and social media and other communications channels. In addition to increasing the size of the network, an equally important goal is to enroll participants that reflect the full diversity of the population of Americans with MS. Programs will be put in place to ensure that people in underrepresented groups learn about the opportunity to join the network, perceive the benefits of the network for themselves and for the MS community in general, and feel welcomed and valued as participants.

ACP's top-level direction is set by people with MS and family members, and ACP includes patients and other stakeholders in research decisions and operations. For the MS-PPRN, a patient-centered governance structure will be established that includes a Governing Board, and Research, Membership, and Communications Committees, all chaired by MS patients. Network participants will be invited to fill open governance positions and continually encouraged to participate in research topic generation, priority setting and decision-making by providing input via the portal. Educational content about the nature and practice of research, information about the participant cohort and studies supported by the MS-PPRN, and direct communications with researchers will be provided via the portal to give participants an enhanced level of knowledge about MS research and greater motivation to not only learn more but also contribute their own opinions and ideas.

The iConquerMS portal will be constructed in a modular fashion, composed of well-vetted, open-source components. Portal technology and data collection instruments will be standards-based

whenever possible to enable seamless integration with other NPCCRN components and streamlined research across networks to facilitate investigations spanning multiple organizations and disease areas. The MS-PPRN team will be eager and active participants in the data standards and policies development activities of the NPCCRN.

American BRCA Outcomes and Utilization of Testing Patient-Powered Research Network (ABOUT)

The ABOUT Network is a national patient-powered research network (American BRCA Outcomes and Utilization of Testing Patient-Powered Research Network) focused on hereditary breast and ovarian cancer (HBOC) that will be expanded in significant ways through the proposed funding and is well positioned to participate in and contribute to the planned U.S. patient-centered network for comparative effectiveness research. Most HBOC is due to inherited mutations in two genes, BRCA1 and BRCA2 (BRCA) that put women and men at very high risk for breast, ovarian, and other cancers and are associated with aggressive and earlier onset cancers and multiple primary cancers in the same individual and family members, including men.

The ABOUT Network is the product of a nine-year collaboration between the leading national nonprofit advocacy organization for individuals and families impacted by HBOC: Facing Our Risk of Cancer Empowered, Inc. (FORCE) and a team of HBOC researchers based at the University of South Florida (USF). Both partners—led by patient advocates— have combined their strengths in advocacy, research, and engaging community participation to pursue better information, services and outcomes for the patient community to which they belong and conduct collaborative research that extends beyond academia to research powered by patients being cared for in communities across the country. Patient governance is fundamental to the ABOUT Network. The leaders of both partner organizations (Co-PIs in this application) are premenopausal breast cancer survivors (a clinical red flag for HBOC) and most of the other members of the ABOUT Network team have been personally impacted by HBOC.

The proposed efforts build on extensive, scalable research infrastructure, including a secure web-based data system and electronic interfaces developed by an experienced USF team that currently supports 1) enrollment and longitudinal follow-up, 2) patient-reported data collection, 3) real-time data sharing across the network, and 4) automated data transfer, including with health plans (for participant medical claims data) and genetic testing labs (for participant genetic test results). The work builds on a novel strategy for broad recruitment of individuals with HBOC in partnership with health plans, and a successful proof-of-concept project with, Aetna that successfully enrolled 4000 individuals with HBOC over a single year, including consent for: longitudinal engagement and recontact, use of the data in future research, obtaining participant medical claims data, genetic test results and leftover DNA samples; which has expanded to recruit an additional 5000 newly diagnosed breast cancer patients over the next three years.

The proposed funding will be used to expand recruitment beyond current targeted efforts to all individuals with HBOC in the U.S., increase community engagement in research by operationalizing patient governance of the network and incorporating community input to direct research priorities, promote HBOC research opportunities, and optimize enrollment into HBOC-specific studies, as well as report back new research findings to the community. This will be accomplished by 1) enhancing the ABOUT data system to enable anyone with HBOC to easily establish a secure account that automatically generates an individualized dashboard for longitudinal interactive engagement and VDT capabilities, 2) partnering with related advocacy organizations across the country to expand HBOC patient engagement, governance and representativeness in ABOUT, to set a patient-powered framework for research collaborations 3) partnering with the MI Department of Community Health Cancer Genomics Program in a method and model to engage and coordinate efforts between all relevant stakeholders (i.e., patients, providers, health plans, Medicaid, Medicare, military, public health officials and other policy makers), 4) expanding data collection in multiple ways (i.e., incorporate EHR data, integrate participant data of all types, implement questionnaires for additional relevant patient subgroups (i.e., beyond current high- risk women without cancer, women with breast cancer and men, to include ovarian cancer patients, women with metastatic disease, linked family members) and 5) implementing a biospecimen banking and automated tracking system. The ABOUT Network is committed to growing our capabilities, sharing our experience, best practices, and resources and

fully participating in the national patient-centered network for comparative effectiveness research.

Mood Patient-Powered Research Network

Mood Patient-Powered Research Network The mood disorders, Major Depressive Disorder (MDD) and Bipolar Disorder (BP), are highly prevalent and are among the top 10 causes of disability worldwide1. The lifetime risk for MDD is about 17% with 12% for men and 25% for women; BP is about 2-4% for men and women2-4. With yearly costs of about $100 billion and $151 respectively5,6, MDD and BP are associated with decreased earnings7, increased health care utilization for medical conditions and premature death with up to 25 years of lost life8,9. After multiple, sequential interventions, about 50% of MDD patients10 and 30% of BP patients11 achieve remission. Nevertheless, 90% can experience relapses within 6 months and recurrences thereafter12-14. Inter-episodic subsyndromal symptoms including cognitive dysfunction also persist and render many patients incapable of functioning, or holding a job15. Furthermore, while neuroscience has determined that mood disorders result from dysregulated brain circuits16, people with mood disorders continue to experience stigma even from physicians who provide their primary medical care17. Therefore, many patients with mood disorders feel disenfranchised and would welcome the opportunity to become more active and engaged in research collaborations to improve their lives. PCORI's funding of a PPRN that focuses around patients with psychiatric disorders will empower a patient group that often feels marginalized and unheard.

Mood disorders are complex conditions3, 4, and effective treatments can make substantial differences on the trajectory of these illnesses but we are currently unable to match patients to treatments . Therefore, we propose to establish a Mood PPRN that will not only provide opportunities for patients to participate in comparative effectiveness research, but will engage them in all stages of research – from setting priority questions, to governance and oversight of studies, to dissemination of results with the ultimate goal of enhancing their sense of empowerment and agency through unprecedented collaboration with the research community. This Mood PPRN proposal centers on patients as collaborators to form a new patient-researcher-clinician community.

The ultimate goal of the Mood PPRN is to improve the lives of patients with mood disorders through prospective comparative effectiveness trials embedded within routine care18 and through patient reported outcomes as well as outcome data from electronic medical records (EMR)19. Clinicians who care for people with mood disorders frequently encounter uncertainty when making treatment decisions. Currently, no clinical or biological data can robustly guide clinicians to match patients with treatments. Instead, when faced with competing treatments, patients and clinicians must decide what course to take in the absence of adequate comparative effectiveness data. Even under optimal conditions when shared decision making occurs, those decisions are made under conditions of uncertainty. Thus, the Mood PPRN can be used to determine the best interventions for mood disorders that lead to the best patient-defined relevant outcomes.

The main aim of the Mood PPRN is to bring together at least 50,000 patients with mood disorders who will be willing and able to participate in prospective comparative effectiveness studies and provide longitudinal data through their EMR19 and patient recorded outcomes. Our main strategy to achieve this extraordinary aim within 18 months will be to collaborate with multiple mood disorder advocacy groups with their broad reach through their membership and websites to provide opportunities for patients to volunteer. From the very start, patients will be true partners in this initiative and will be instrumental in determining priorities. Key members of the team include the Medical Director of the National Alliance on Mental Illness (NAMI), the President of the Depression Bipolar Support Alliance (DBSA), the President of the International Bipolar Foundation, and most important, the members of these patient advocacy groups as well as patients who receive care from a wide network of clinicians. In collaboration with the Partners Healthcare System, we will also have the expertise to aggregate data from multiple EMRs20-22

and integrate patient reported outcome data into a comprehensive database as well as setting up the infrastructure to obtain and process biosamples that will form a foundation to advance our understanding of the biology of mood disorders for personalized care.

Patients, Advocates and Rheumatology Teams Network for Research and Service (PARTNERS) Consortium

The CARRA Registry and PR-COIN have enrolled almost 9,000 patients with pediatric rheumatic disease – a significant proportion of children in the U.S. with this uncommon condition – into next- generation registries at 62 pediatric centers. We use this achievement as a starting point to invert the current model to a patient-centric, patient-powered network. PCORI offers us the extraordinary opportunity to make patients and their families full collaborators in research and governance of a PPRN—the Patients, Advocates and Rheumatology Teams Network for Research and Service (PARTNERS) Consortium—bringing together children with the most prevalent pediatric rheumatic diseases, Juvenile Idiopathic Arthritis (JIA) and childhood-onset Systemic Lupus Erythematosus (cSLE), which share overlapping biological, clinical, therapeutic, and psychosocial features. PARTNERS formally links patients, family members, and other stakeholders including healthcare providers, 3 advocacy groups (Arthritis Foundation [AF]; Friends of CARRA [FoC]; Lupus Foundation of America [LFA]), a clinical research network (Childhood Arthritis & Rheumatology Research Alliance [CARRA]) and a quality improvement learning network (Pediatric Rheumatology Care & Outcomes Improvement Network [PR-COIN]).
PARTNERS will drive forward research based on patient-centered scientific priorities and integrate patient input into all aspects of research, from study design to analyses, creating a patient-centered learning health system. Complementary perspectives, infrastructure and expertise empower patients, clinicians, and researchers to learn together from every patient interaction by conducting patient-centered outcomes research, and implementing the findings in a virtuous cycle (see Fig 1). Patient engagement is the core—patients connect, participate in the governance structure, and contribute to comparative effectiveness research through data collected at clinical visits and on electronic devices. We will leverage existing outreach and technology capabilities of PARTNERS community building organizations, the AF, FoC and LFA, to reach out to patients affected with JIA and cSLE and optimize capture of diverse patient perspectives, focusing on engagement of underserved populations. These organizations will anchor PARTNERS in the JIA/cSLE community, raising awareness around the importance and opportunities of patient engagement for research purposes. LFA will extend its online patient registry to enhance cSLE enrollment and electronically link to the CARRA Registry. AF and FoC will partner with PR-COIN to expand current JIA patient engagement to reach a wider community. This approach will increase patient enrollment to support health care innovations. Registry (CARRA 6170 JIA patients, 921 SLE, 62 sites) (PR-COIN 1100 JIA patients, 11 sites) informatics infrastructure will connect physicians and researchers to patients.
PARTNERS governance structure links both strategic approaches. Patient groups learn from community building initiatives and build bridges with physicians developing technology driven health care innovations. Patients in the Project and Community Teams, will test innovations, provide feedback, and use AF, FoC and LFA patient networks to encourage other patients to adopt the technology and submit their own data. During the award period, we focus on: 1) establishment of a shared governance model, in which patients and advocates fully partner with clinician-scientists in network leadership; 2) implementation of consortium-wide strategies and metrics for enhanced patient engagement and adoption of patient-directed research priorities; and, 3) coordination and standardization of data collection and sharing across the consortium, extending existing online platforms for patient reported outcomes (PROs) and direct data transfer from electronic health record (EHR) to PARTNERS databases. These innovations eliminate duplicate collection of data and vastly increase the feasibility of widespread participation and promote integration of QI and research in a learning health system. PARTNERS will share open source tools and technical innovations (including i2b2) with other PPRNs and CDRNs, thus expanding the reach and scope of our accomplishments.

ALD Connect

The ALD Connect consortium empowers patients, caregivers and their affinity groups to move beyond conventional research participation, advocacy, and fundraising efforts to improve care for and ultimately eradicate the debilitating single-gene disorder, X-linked Adrenoleukodystrophy (ALD). Through direct participation in decisions on research and drug development, patients will influence research priorities and directions. The ALD Connect collaborative network will introduce a novel all-inclusive model to improve care and drug discovery for well-defined single-gene disorders. Towards this end, we will accomplish two goals within the 18-month period:

1) Conduct an inventory of existing resources, design common data elements and collect information from resources around the world (patient registries, advocacy groups, electronic health records, academic databases, brain and tissue banks). Data will be captured, harmonized and aggregated in the NeuroBANKTM platform through a partnership of the ALD/AMN Global Alliance, the largest patient advocacy group for ALD, and the Neurological Clinical Research Institute at Massachusetts General Hospital.

2) Create a social network platform that allows for dynamic engagement of the patient community through two- way communication between patients and researchers. Examples include ALD Knowledge Portal, where patients vote on research projects, track their disease progression, and report outcomes, as well as ALD Patient Learning Academies, where patients learn about clinical research and therapy development and become ambassadors for ALD clinical research and champions of the latest methods, treatments and recommendations in clinical care.

An enormous advantage of utilizing the NeuroBANK™ platform and Global Unique Patient ID (GUID) technology is that patient-reported information will be aggregated along with the clinicians' and researchers' captured data. This approach alone will validate and enhance patient-reported outcomes within the overall repository.

Unique to our efforts is the transformative collaboration between patients, patients advocacy groups and academic centers that will allow for data comparison and validation, patient feedback on research directions, and more rapid trial development because of an educated and engaged patient community. Social network maps and analytics will assess the level of activity in our network and directly measure and improve its success.

Phelan-McDermid Syndrome Data Network (PMS_DN)

Objective: To collect all available patient data from Phelan-McDermid Syndrome (PMS) patients to make meaningful, well-annotated clinical data available to researchers and to share insights with members of the PCORI network.

PMS is an orphan genetic condition caused by deletions of 22q13 or mutations of the SHANK3 gene. The syndrome presents with an array of characteristics, but the manifestations are profound, and parents and caregivers must advocate for PMS patients throughout the life's course. The PMS Foundation (PMSF) is a parent-driven non-profit 501(c)3 organization, founded in 2002 by families of children diagnosed with PMS. The mission of PMSF is to provide family support and to accelerate research for individuals with PMS. PMSF parents recognized a need to compile health records in a meaningful fashion to further research, and together with researchers and advisors, they launched an international patient registry, the PMSIR, that is directed, governed and implemented by patient families. IRB approval was obtained in 2011 there are currently 546 active participants, 49.6% of the world's known patients.

PMSF has pioneered the concept of the patient-driven registry within a population of patients with a rare condition, through the perseverance of devoted parents. PMSIR provides a solid foundation upon which to build a network that can create new information in the form of meaningful data for researchers. Founded by parents, PMSIR is driven by parents, governed by parents, and will be transformed by parents who are stakeholders in the success of a standardized research data network. This network empowers both researchers and parents to address issues fundamental to the quality of a PMS patient's life. PMS parents have proven they are willing and able to collaborate with the medical community, researchers, clinicians, and consultants to bring a concept to fruition, evidenced by the current capacity of PMSIR and collaborations with researchers noted in this proposal. Because PMSIR is well established and parent constituents are committed to the mission, PMSF is uniquely positioned to expand the

existing parent network through building transformative infrastructure to become a model Patient-Powered network as defined by the PCORI vision. The proposed PMS Data Network (PMS_DN) will continue to encourage active participation and leadership of PMS families, and enhance organizational structure and capacity to further develop PMSIR into a comprehensive data network An existing Parent Advisory Committee (PAC) is charged with ensuring PMSIR meets the needs of families and is in alignment with the community's goals. Outreach to PMS families is an important strategy for increasing participation.
The real value in biomedical research lies not in the scale of any single source of data, but in the ability to integrate and interrogate multiple, complementary datasets simultaneously. Combining data across different scales and resolutions such that reliable results can be generated to address important questions is non-trivial. Thus the principal challenge is not a lack of data, but how best to make sense of it. This project will build a dedicated PMS_DN to enable scientists to have access to all available knowledge from PMS patients. Multiple data feeds will be established to extract and link data from well-characterized patient and population cohorts into the backbone informatics architecture provided by the open source, i2b2 based, tranSMART platform. Such datasets must meet the needs of researchers (including support for diverse scientific collaborations with CDRNs or outside PCORI) while simultaneously preserving security and maintaining appropriate privacy and ethical safeguards.
PMSF is excited to participate in the PCORI program-wide steering committee to share insights with the constituency of the PCORI network. PMSF is willing to share insights with other PPRNs who are just starting to build a patient network. PMSF believes that not only should patients be at the center of research, those that are doing it well have a commitment to the greater community to share best practices.

PI Patient Research Connection: PI-CONNECT

Primary Immunodeficiency (PI) represents a group of more than 185 related, rare genetic diseases with a diagnosed population prevalence of about 1:1200, although the prevalence for each specific diagnosis varies from 1:1000 to less than 1:1,000,000.1,2 The challenges for the study of these rare diseases are the geographic spread of patients making single center studies impossible except for the most common diseases, a lack of integrated effort by clinicians with research experience and the patients who are invested in specific answerable questions, and the infrastructure challenges of broad- based recruitment of patients for studies. This proposal describes a unique fusion of efforts to address those challenges, leveraging new technologies to answer important questions regarding the care of patients with PI.
Currently, a curated, data-validated, longitudinal registry of patient data exists, however, patient recruitment depends on physician entry and the cohort is strongly skewed towards academic centers. A second data set, produced to give patients a unified home for their medical information, has been developed. Our goal is to meld these two data sets to maximize the breadth of data and to promote improvements in patient care. Importantly, the melding of the data sets will also bring together the major groups invested in improving patient care: researcher/physicians and patients. Once the investment in technology infrastructure has been completed and the collaborations with like-minded groups established, we view this effort as self- sustaining.
Founded in 1980, the Immune Deficiency Foundation (IDF), the national nonprofit patient organization dedicated to improving the diagnosis, treatment and quality of life of persons with PI, believes that advances in the medical care of patients with PI will require partnerships between patients and researchers. IDF developed the eHealthRecord, an electronic personal health record (ePHR) designed specifically for the PI community. This simplifies tracking healthcare information and activities by PI patients and caregivers. A backend database allows de-identified aggregate data to be analyzed for educational and research purposes. IDF also administers the United States Immunodeficiency Network (USIDNET), overseen by a steering committee of the leading clinical immunologists in the United States. USIDNET developed and maintains a patient-consented registry of U.S. and Canadian patients with the goals of providing a comprehensive clinical picture of each disorder and to serve as a resource for clinical and laboratory research.
In order to blend the personal patient information with clinical data, IDF is proposing to build a PPRN that would combine the eHealthRecord patient-entered data with the USIDNET patient-

consented registry with the working title of the PI Patient Research Connection, or PI CONNECT. PI CONNECT will create a venue for researchers and patients to communicate about proposed research involving the network data, giving patients a voice in research, as well as giving researchers better access to the PI community.
IDF has built a strong bond with the PI community, including patients, clinicians and researchers, based on trust, reliability and understanding. Last year, nearly 13,000 patients and healthcare professionals attended more than 160 IDF educational presentations in 123 cities in 37 states. IDF answers patient inquiries and features educational materials and publications from a website that generates 33,000 visits per month. Electronic and mailed newsletters are read by tens of thousands of people. Promotion using existing IDF channels will grow participation in the PPRN while new modes of engaging the population, like the launch of a mobile application, will ensure continued value and use of the network. To expand the clinical information, the eHealthRecord will use Blue Button technology to integrate users' existing medical records into the network.
USIDNET and IDF bring strong records of success. With the development of PI CONNECT, we will be able to revolutionize acquisition of data and patient-powered research agendas. PI CONNECT will bring together the strengths of USIDNET (a robust database of longitudinal patient information and a tradition of clinical research) and the IDF patient organization (outstanding patient buy-in and a strong tradition in addressing patient concerns and the IDF ePHR). This integration will also complement each group's traditional limitations (USIDNET: recruitment skewed towards academic centers and limited patient-reported data; IDF: de-identified aggregate cross-sectional approaches), crystallizing into a productive force. By integrating efforts, PI CONNECT will enable superior outcomes research, quality of life research and identify potential markers for risk stratification. Importantly, the direct involvement of patients will focus those studies using the lens of their own experiences and unanswered questions.

Vasculitis Patient-Powered Research Network (V-PPRN)

The Vasculitis Patient-Powered Research Network (V-PPRN) is the product of a more than 10-year productive collaboration among patients, patient advocacy organizations, academic clinical investigators, expert clinicians, biomedical informaticians, qualitative and quantitative methodologists, and funding organizations all dedicated to conducting high-quality clinical research in vasculitis aimed at addressing key scientific and clinical issues considered of high-priority to both patients and physicians. We propose to expand the role of patients such that they are fully involved and direct network governance, demonstrate that we will have patient-reported data collected for at least 80% of the cohort, build upon our extensive experience and expertise in incorporating data standards suitable for sharing, leverage our established infrastructure, resources, and positive and productive relationships among stakeholders, and evolve and transform the V-PPRN into a model PPRN within the overall National Patient-Centered Clinical Research Network (NCRN).
The V-PPRN is comprised of the Vasculitis Foundation (VF), the umbrella vasculitis patient advocacy group in the United States (US), the Vasculitis Clinical Research Consortium (VCRC) which includes every major center for clinical investigation in vasculitis in the US and Canada (and a significant international community of investigators), an established on-line group of patients with vasculitis dedicated to conducting meaningful research, the clinical community caring for patients with vasculitis, and experts in applying data standards in federated databases including the electronic health record (EHR), disease-specific health data, and patient-reported outcomes. These linked stakeholder groups have worked together for more than a decade with a common mission of improving the lives of those affected with vasculitis Vasculitis is a set of rare organand life-threatening diseases of vascular inflammation linked by similar pathophysiologies. Despite improvement in the overall prognosis of vasculitis since the introduction of regimens based on combination immunosuppressive therapy, the cumulative morbidities and mortality from both disease and treatment for most patients, the social impact, and the costs remain enormous. Given the many challenges of conducting research in rare diseases, we bring a remarkable set of skills, successful experiences, and resources to this initiative.
Utilizing resources provided by a PCORI award and the NCRN, the V-PPRN is poised to increase our membership and patient representation, expand data access and availability, and address

disease-specific outcomes. The V-PPRN will be a vibrant, flexible, sustainable patient community ready and committed to participate in clinical research through sharing of electronic medical records to address important issues facing patients and other stakeholders.
This application outlines the existing infrastructure of the V-PPRN, the outstanding scope of our Network from both the patient and investigator perspectives, our capabilities including capture and merger of electronic health records from patients with vasculitis with patient-provided outcomes, plans for feasible growth and change to fulfill the requirements and great potential of a PCORI PPRN, and evidence of our leadership structure in which all stakeholders have a substantive voice in decisions and prioritization of the research agenda.

The DuchenneConnect Patient-Report Registry Infrastructure Project

DuchenneConnect is an established patient-report registry for Duchenne and Becker muscular dystrophies, and it is a model for rare-disease registries. The registry platform and functionalities, created through collaboration between DuchenneConnect and PatientCrossroads, have been extended to support registries for more than 250 disorders. DuchenneConnect has over six years of experience and has collected a robust, longitudinal patient-report dataset that has been utilized by industry, clinicians, and academic researchers for uses that may lead to advances in Duchenne/Becker muscular dystrophy (DBMD). Parent Project Muscular Dystrophy, a parent-led foundation, founded and supports DuchenneConnect.
DuchenneConnect's years of experience have provided important lessons learned, as well as a clear understanding of registry needs. We must balance obtaining sufficient and robust information with the monitoring burden and providing participation benefits back to registrants. We must explore novel data collection approaches. This includes EHR integration to reduce registrant burden, allowing evaluation of the accuracy of specific patient-report outcomes, and improving our capacity to answer questions about natural history and care. We must improve the standardization of registry items while continuing to be responsive to data required to answer emerging research questions. We must build on our history of successful data sharing with the TREAT-NMD neuromuscular registry network and academic and industry collaborators with improvements to coding and standardized information exchange. Though the registry is currently guided by a multidisciplinary advisory committee that includes parents and individuals with DBMD, we must more systematically engage advisors, registrants, and the broader DBMD community in posing questions of interest. We must develop a multifaceted outreach approach to reach a more demographically representative and larger proportion of DBMD patients. Finally, we must continue to seek out opportunities such as PCORI's Network to engage in innovative efforts that have the possibility to improve patient empowerment, care recommendations, and/or our understanding of DBMD natural history.
In 2011, DuchenneConnect began a successful first step toward comparative outcomes research through collaboration with the Department of Human Genetics at UCLA. This collaboration provided clinically relevant results that are of importance to the patient community. The experience invigorated DuchenneConnect to begin our next phase of growth—exploring information needs of our community, and working to address those needs through collaborative research that is efficient and cost-effective. We are extremely enthusiastic about the possibility of maturing the registry with input and support from the PCORI Network, while concurrently sharing our experiences (and ultimately data sets) with the Network partners. Many of DuchenneConnect's achievements through this program would become available to other disease registries under the PatientCrossroads model, thereby extending the reach of PCORI-led PPRN recommendations and improvements to a broader range of patient networks.
DuchenneConnect has always employed a collaborative growth model. The proposed project team brings impressive professional expertise and organizational resources that allow us to tackle challenging problems. Collaborators from PatientCrossroads and Geisinger Health System are prepared to identify and solve problems related to electronic health information integration. Geisinger will provide bioethics consultation and IRB access. UCLA collaborators will work with DuchenneConnect and PatientCrossroads to improve data standardization and export, and explore novel approaches to reach a more representative registrant population using large data sources. PatientCrossroads will implement advisor- recommended improvements to the data collection interface, as well as new capabilities for registry access and data input.

DuchenneConnect welcomes the opportunity to engage with other PPRNs and CDRNs to explore the challenging and important issues that emerge from PCORI's Network goals—an effort of particular appeal to rare disease communities, where traditional research approaches may be especially difficult to implement.

NephCure Kidney Network for Patients with Nephrotic Syndrome

Focal Segmental Glomerulosclerosis (FSGS), Minimal Change Disease (MCD), and Membranous Nephropathy (MN) – collectively referred to as primary Nephrotic Syndrome (NS) – are rare but serious kidney diseases that pose a substantial physical, psychological, and financial burden for those affected and often lead to kidney failure requiring dialysis or other major medical complications.1-6 Diagnostic, prognostic, and therapeutic advances in the field have been stunted by the rarity of the condition, resulting in a patient experience marked by significant lag times to receive a proper diagnosis, limited effective treatment options, and numerous barriers to efficient coordination of care. Clinical data are frequently housed in the local institutions of care providers and are thus siloed across the United States. We propose a collaborative effort to develop the NephCure Kidney Network (NKN) as a Patient-Powered Research Network (PPRN) to serve as a resource for future comparative effectiveness research (CER) of relevance to patients with this disease. This new PPRN will allow important clinical and patient-reported data to be contributed, under patient control, to a centralized repository, facilitating rapid development and execution of research studies.

The proposing team is composed of experts from Arbor Research Collaborative for Health (Arbor Research), the NephCure Foundation (NCF), and the University of Michigan (U-M), specializing in adult and pediatric clinical nephrology, clinical research in NS, epidemiology, patient advocacy, and data management. We will build on NCF's recent development of the NKN as part of the pilot project of the National Institutes of Health (NIH) Office of Rare Diseases Research (ORDR) to establish the Global Rare Diseases Patient Registry and Data Repository (GRDR), scheduled to launch in fall 2013. Under this award, the proposing team seeks to transform the NKN from a static repository of limited cross-sectional data to a rich clinical and patient-reported outcomes (PRO) database, with patients as active participants to facilitate efficient and accurate CER. We propose the following aims for the 18-month award period:

1) Establish a network governance structure that includes substantial patient representation to ensure patient involvement in policy development and key decision-making.
2) Successfully recruit a minimum of 1,250 patients with distributions of demographic and clinical characteristics sufficient to support CER across a range of populations.
3) Establish strategies for network member engagement to maintain willingness and readiness to participate in CER.
4) Develop a set of standardized data elements designed for interoperability across research networks.
5) Develop the capacity and conduct proof of concept testing for data collection via mobile applications.
6) Develop the capacity and conduct proof of concept testing for electronic health record (EHR) data collection.
7) Assess patient willingness to contribute biosamples and develop the capacity for collecting, storing, and tracking biosamples in the future.

Interoperability with currently existing and future disease networks is one of the hallmarks of the NKN. When launched, the NKN will be implemented using the Patient Crossroads (PXR) CONNECT platform, designed specifically for use of common data elements (CDEs) and standardized terminology to facilitate mapping across all participating networks in the GRDR pilot program. Additionally, the NKN has plans to extend beyond the GRDR, with collaborative agreements in place to share data with the National Registry of Rare Kidney Diseases (RaDaR) in the United Kingdom (UK). With firm dedication to data interoperability, an open and proactive approach to sharing and collaboration, and a strong record and commitment to protection of human subjects, the NKN is a promising resource for future CER related to NS and other chronic kidney diseases (CKD).

The establishment of a research network with readily available clinical and patient-reported data, an organizational structure that includes patients in the governance process, and direct

partnership with patients who are seeking opportunities to be a part of the solution to better health will facilitate much-needed advances for patients with this rare and devastating condition. Success of this network will undoubtedly have broader applications to conditions with clinical overlap (such as obesity and CKD) as well as to other rare diseases sharing similar barriers to research progress.

Rare Epilepsy Network (REN)

The Rare Epilepsy Network (REN) PPRN is an initiative created by and for patients with catastrophic rare epilepsies. The REN's goal for this proposal is to build a patient-centered and driven data base designed to provide the patients and their families an opportunity to participate in research that will improve lives and quality of care for people with rare epilepsies. Our PPRN is led by the Epilepsy Foundation (EF), a patient advocacy organization dedicated to the welfare of the almost 3 million people with epilepsy living in the US. EF will lead this grant through our Principal Investigator, Dr. Janice M. Buelow. Dr. Buelow is director for all programs and research at EF and interfaces with all EF affiliates in the US and with each of the patient advocacy organizations that compose the REN. Network organization: Each of 7 partnering organizations is represented by a caregiver who has a loved one with the disorder (Figure 1). They are joined by two co-investigators/epidemiologists, Drs. Hesdorffer (Columbia University) and Kroner (RTI International), and a consultant neurologist Dr. French (NYU). Columbia University will design the clinical database and manage the data and harmonization.
RTI will host the database and serve as the genetics and biospecimen repository. Dr. French, an expert on epilepsy clinical trial design and new strategies for drug approval, and director of the Epilepsy Clinical Trials Consortium, will assign epilepsy seizure type and syndrome. Governance: The key considerations for our patient network governance include policy creation, development of standards, outreach and member engagement to create a robust patient-centered research enterprise for rare epilepsies. The inclusion of the leaders of the partnering organizations as members of the SC ensures that caregivers and individual organization members are involved directly or indirectly in all aspects of REN decision making on data elements, policy formulation, research questions, data sharing, dissemination and social participation, responsiveness of patients, safeguards of privacy, and sustainability. Clinical Database: The REN will use Consilience Software's Maven database and their extensive experience implementing health information interfaces to import clinical information into databases. A major reason that the REN selected the Maven database was Consilience's experience using HL7 to populate databases with the electronic health record (EHR).
Two integration interfaces will be used - an automated HL7 import interface and a user- initiated blue-button generated HL7 data upload. Maven will enable the automated HL7 message portion through secure FTP. Other assets of Maven include the ease of configuring the database fields, and easily created real time data checks within and between tables with queries sent to patients while they are entering data. In addition, creation of customized automated reports is straight forward for documenting our progress to PCORI and the REN patient organizations. All data will reside on secure network servers in two RTI data centers. RTI's networks are fully compliant with FISMA data security standards and are protected by industry-standard firewalls that require data to be encrypted in transit thereby protecting the submitted EHR data. Sample, Recruitment and Retention: We currently have 857 patients in the REN and expect 690 to have data entered by the end of month 6. We expect that the size of the REN will increase 75% to 1500 by month 18. Each REN organization and EF has identified specific recruitment strategies including web-based and face to face recruitment.
Data Collected: Where possible we will use NIH common data elements (CDE) for epilepsy and other data elements for caregiver-reported patient outcomes. At baseline, the epilepsy CDEs will be used for demographics, seizure type and adaptive behavior. Additionally we will collect other data such as assessment of intellectual function and comorbidities. Follow-up information will be collected every 6 months. Sustainability: We will apply for future funding through public and private sources. EF is prepared to sustain this database through their own fund-raising efforts and to make the database available to all rare epilepsy organizations in order to foster research. EF has a strong commitment to supporting the best research possible to both improve care and

to promote cures of epilepsy for patients. We believe that REN data base represents a strong mechanism to support our cause.

The Community-Engaged Network for All (CENA)

The Community-Engaged Network for All (CENA), led by Genetic Alliance, is comprised of 10 disease networks. Genetic Alliance (GA) is an established umbrella organization supporting a network of 1000+ disease advocacy organizations (DAOs), including the 10 DAOs in CENA. Each DAO has a preexisting participant-powered network. Through CENA, online registries for each condition will be launched and/or upgraded, and additional participants will be invited and engaged in participant-centric research. The DAO networks will benefit from an award-winning registries platform and technical assistance for engaging communities to safely share their information online, as well as community building and collaboration between condition communities. CENA will use and improve participant-led governance models that GA has pioneered for more than a decade, bringing leaders and affected individuals from each condition community together to oversee CENA. CENA also includes two leading academic institutions, the Universities of California San Francisco (UCSF) and Davis (UCD). These partners will test the ability to recruit patients from academic medical centers into participant-led models. Through a partnership with another PPRN applicant (Health eHeart) at UCSF we will also assess the utility of CENA for recruiting for a comorbidity (cardiovascular disease). In addition, CENA will pilot new methods of facilitating collaboration between researchers and participants by supporting a broadly accessible online environment where communities and researchers have equal voice in the development of research hypotheses.

The ten DAOs participating in CENA are Alström Syndrome International, Dyskeratosis Congenita Outreach, Inflammatory Breast Cancer Research Foundation, Hepatitis Foundation International, Joubert Syndrome Foundation, KS&A, MLD Foundation, National Gaucher Foundation, National Psoriasis Foundation, and PXE International. The conditions range from rare to common and cover a broad spectrum of demographics. The DAOs were selected based on their readiness to participate in the PCORI PPRN vision. Four were selected as the strongest networks in the existing Genetic Alliance biobank network, and the additional six were selected through a competition among DAOs facilitated by GA in August 2013 in preparation for this proposal. More than a hundred DAOs applied, and the top six were selected based on network readiness, existing resources brought to the table, and engagement with the PPRN vision.

The DAO-led communities will be supported and grown through inter-community collaboration, sharing best practices, and an award-winning platform. The Platform for Engaging Everyone Responsibly (PEER) will allow for extremely cost- effective data capture from participants in a manner that ensures granular privacy permissions management. PEER employs an interface that is gamified to maximize retention and flexible to allow for continual fine-tuning or addition of questions, including changes based on input from DAOs and academic research partners. PEER's potential to radically accelerate participant engagement and the collection of participant-reported outcomes has been recognized with wins in the Sanofi Collaborate | Activate and Ashoka Changemaker Challenges, as well as with a Forbes "Best Business Model" award. CENA proposes to fully leverage PEER through engagement with the 10 diverse communities. In addition to increasing recruitment, retention, and data collection, CENA communities will expand their recruitment through cross- condition activity, their ability to identify potential participants through common data sets (from the Universities, the Oracle Health Sciences Network, and Inspire community), and coordination in identifying underserved communities.

UCSF and UCD will invite researchers and their patients into a participant-driven network. We believe that shifting research culture from one where academic researchers reach out to participants, to one where participants lead, requires a common environment that supports dynamic and meaningful communication between DAOs' and researchers' communities. We will test whether patients at academic medical centers can be engaged through the participant-centric vision, and how best to do so. Especially for rare diseases, academic medical centers serve as specialized centers and focused points of engagement for recruitment into participant-led networks. We will ask how we might serve the research mission by providing an alternate route to recruitment for already successful studies at UCSF and UCD, such as Health eHeart, which primarily focuses on cardiovascular disease. We will assess the effectiveness and utility of drawing on participants' interest in engaging on a comorbidity even if their participation in CENA comes from initial interest in a specific (non-cardiovascular) condition. Finally, using a novel

approach and tool developed at UCSF called Open Proposals, we will engage the 10 DAOs' members in a conversation with UCSF and UCD researchers interested in those conditions. As the DAOs prepared this proposal, great benefit accrued from planning to build a research network in a multi-condition forum. We believe significant benefits will continue to result from refining research hypotheses related to individual conditions in an open, transparent manner between researchers and participants, and between condition communities. CENA is offered by a collaborative (hereafter called the Team) composed of Genetic Alliance, UCSF, UCD, and Private Access; and 10 disease advocacy organizations chosen for this specific project (collectively referred to as the Steering Committee), governed by a patient Governance Board.