2012 WAS A LANDMARK YEAR FOR GREATER INVOLVEMENT of patients in research, development, and delivery of medical products and care. The U.S. Food and Drug Administration (FDA) Safety and Innovation Act was signed into law on July 9, 2012, with a requirement to foster patient-focused drug development through a series of 20 meetings. The Patient-Centered Outcomes Research Institute (PCORI), created two years earlier under the Affordable Care Act, dedicated 2012 to engaging hundreds of patients and caregivers in setting a national research agenda. And in 2012, digital strategist Leonard Kish declared, “If patient engagement were a drug, it would be the blockbuster drug of the century and malpractice not to use it,” a line seized by patient advocates and media alike to mark a new dawn in the patient-centricity movement.

Five years later, this handful of organized activities to foster patient engagement has precipitated a veritable “gold rush” of endeavors to construct a science of patient input. FasterCures has mapped nearly 100 multi-stakeholder initiatives producing frameworks, methods, toolkits, draft regulatory guidances, training programs, and case studies. These resources are evolving from broad outlines of the “possible,” to more detailed descriptions of what’s practical as experience is gained in a variety of clinical areas and contexts.

The way in which patients are engaged has evolved, too. Early on, patients most often were invited to pinpoint problems with clinical trial recruitment or retention. Now, a wider array of activities are informed by patient perspectives, including setting priorities for early-stage research, selecting outcome measures, making benefit-risk and value assessments, and developing care guidelines. Patient organizations urge even earlier and more frequent opportunities to shape research plans, development programs, regulatory approaches, and care delivery practices.

As real-world evidence rises in value, patient perspective data collected from patient registries, smartphone apps, wearable devices, online communities, and social media provide new windows into the patient experience. Patient preference studies and patient journey maps help illustrate a more complete picture of the impact of disease and burden of therapies. This evidence can be used to align unmet medical need with targets, as well as identify barriers to participation in research and access to care.

While progress is swift by some measures, it has not been even. Leadership from FDA and PCORI has defined new expectations for parts of the system they affect, but much more work is needed to integrate patient perspectives at earlier stages of research and into decisions by payer organizations and health-care systems. Patient organizations representing certain rare diseases and cancers have pioneered much of the emerging practice at the grassroots level, with challenges still ahead to better engage individuals with highly prevalent conditions and those who have been underrepresented in traditional research and care settings.

Patients are the greatest force propelling the change seen over the past five years; incentives created through federal policy measures have accelerated adoption and shifted culture toward more patient-centered decision-making. As the vignettes presented in the next three pages illustrate, we are seeing early benefits as this practice takes hold. Over the next five years we hope to see the leap from application to actualization of the promise patient-centricity holds.
Key Milestones in Patient-Centricity

2012
- Passage of Prescription Drug User Fee Act V requirements for FDA’s Patient-Focused Drug Development initiative
- PCORI begins funding research that engages patients as partners
- External assessment of the National Institutes of Health’s (NIH) large Clinical and Translational Science Award program asserts need for stronger community engagement

2013
- *Health Affairs* dedicates its February issue to patient engagement
- The Clinical Trials Transformation Initiative establishes project to develop models for better engaging patients as partners in clinical trials
- FDA hosts first of 24 Patient-Focused Drug Development meetings and launches the Patient Preference Initiative

2014
- PCORI invests $250 million in creation of PCORnet, composed of Patient-Powered Research Networks and Clinical Data Research Networks
- National Health Council issues tools to help patient organizations collect information that may be helpful to FDA
- Parent Project Muscular Dystrophy submits draft regulatory guidance to FDA— the first-ever by a patient advocacy organization

2015
- President Obama outlines new Precision Medicine Initiative to “empower patients, researchers, and providers to work together toward development of individualized care”
- Medical Device Innovation Consortium issues a framework for integrating patient perspectives in the total product life cycle of medical devices
- FDA issues guidelines for externally led Patient-Focused Drug Development meetings to expand impact
- FDA approves the Maestro Rechargeable System for treatment of obesity, notable because the clinical study did not fully meet its primary endpoints but the device performed in line with patients’ stated preferences for benefit-risk tradeoffs

2016
- European Union Patient Academy for Therapeutic Innovation (EUPATI) releases an online “Toolbox on Medicines R&D” in seven languages
- FDA issues guidance on how patient preference information may be considered in assessment of the benefit-risk profile of medical devices
- 21st Century Cures Act is signed into law on Dec. 13, 2016, expanding opportunities for patient input to be factored into regulatory decisions

2017
- FDA commitment letters for reauthorization of user fee acts for drugs and medical devices reflect dedication to advance the science of patient input
- FDA proposes a central Office of Patient Affairs to be housed within the Office of the Commissioner
- NIH launches beta phase of Precision Medicine Initiative’s “All of Us” cohort
Illustrations of Impact

**BY THE NUMBERS:**

**SCALING FOR IMPACT**

**80**
80 resources annotated in FasterCures’ Patient Engagement Resource Library

**115**
115 patient organizations’ research assets searchable through FasterCures’ online Patients Count Network directory

**179**
179 patient-centered initiatives mapped by the Patient Focused Medicines Development consortium

**110,000**
110,000 visitors to EUPATI’s online “Toolbox on Medicines R&D” training materials, available in seven languages, in its first year

**500,000**
500,000+ patients with more than 2,700 conditions participating in PatientsLikeMe’s online community to share their health data to track their progress, help others, and influence medical product development

**100 MILLION**
100 million covered lives represented in PCORI’s PCORnet, comprised of 13 Clinical Data Research Networks and 20 Patient-Powered Research Networks. The network has been leveraged in 20 studies and is featured in 70 peer-reviewed journal articles

**PROGRESSIVE PATIENT ORGANIZATIONS** are at the forefront of integrating patient perspectives in the development and delivery of medical products and access to care.

**DIABETES | COALITION OF DIABETES GROUPS AND PATIENTS INCLUDING DIATRIBE AND JDRF**

In preparation for a 2014 FDA webcast meeting on unmet medical need in diabetes, diaTRIBE gathered more than 7,500 responses to a patient survey. Survey results and the meeting heightened FDA’s understanding about the many outcomes important to patients besides the “gold standard” hemoglobin (Hb) A1C level. In 2016, FDA convened the “Diabetes Outcome Measures: Beyond HbA1C” workshop to gain greater appreciation of the extent to which the current regulatory paradigm for antidiabetic drug therapies addresses the needs of patients with diabetes and to identify additional outcomes, beyond HbA1C, that are of direct relevance and importance to patients living with the disease. JDRF and the Leona M. and Harry B. Helmsley Charitable Trust are currently sponsoring a patient preference study to better document patient preferences for treatment benefits and priority outcomes of therapies.

**ACUTE MYELOID LEUKEMIA (AML) | LEUKEMIA & LYMPHOMA SOCIETY (LLS)**

In 2009, inspired by a retired physician with AML who had seen no new therapies for AML in his entire medical career, LLS launched its “Beat AML” initiative and partnered with Celator Pharmaceuticals to study an innovative formulation of existing therapies. By 2015, LLS’s annual investment in AML research had grown to $17.6 million, supporting study of four compounds and 66 academic research programs. In 2016, it launched a precision-medicine-based multi-arm trial, the first of its kind for blood cancers. LLS also hosted a patient-focused drug development meeting with FDA’s oncology division, bringing 14 patient-survivors to meet with division head Richard Pazdur and 20 reviewers. While fear of death was the top worry among patients, the second biggest worry—long-term side effects—drove home the need for newer and better treatments. LLS is currently conducting a study to understand AML patient experiences and expectations, and preferences for the tradeoffs between benefits and risks of treatment. Results will be used to help ensure that both the FDA and drug manufacturers consider patients’ and caregivers’ perspectives in the drug development process.

**DUCHENNE MUSCULAR DYSTROPHY (DMD) | PARENT PROJECT MUSCULAR DYSTROPHY (PPMD)**

Extensive interaction with FDA over several years led PPMD to pioneer publications about DMD patient and caregiver priorities for drug development, benefit-risk tradeoffs, and preferences. PPMD was among the first patient organizations to conduct a patient preference study, establishing that the DMD “gold standard”
outcome measure of improvement in the six-minute walk test was not aligned with patient/caregiver priorities for maintaining upper body strength and limiting disease progression. PPMD also led a 2013 policy forum with 17 members of FDA's review staff and drafted guidance through a multi-stakeholder process that resulted in FDA-issued guidance in 2015 to foster patient-centered drug development for DMD.

In 2016, the agency’s review of a new drug application from Sarepta for Exondys-51 activated the patient community to secure approval for the drug that had been tested only in a small open-label study. An FDA advisory committee hearing attracted nearly 1,000 participants including top FDA leadership. Advisory committee members were not persuaded by the company's evidence of efficacy, but were moved by reports from patients in the trial who experienced delayed progression and other signs of benefit, even though scores on the six-minute walk test did not significantly improve. However, the committee voted against approval. On Sept. 16, 2016, following much internal debate, the agency approved Exondys-51 for patients with a particular genetic mutation and required Sarepta to conduct additional studies. The decision to approve the drug was made based on the “totality of evidence,” including data presented by PPMD and testimonials of patients and caregivers.

**SPINAL MUSCULAR ATROPHY (SMA) | CURE SMA**

In the early 2000s, Cure SMA provided seed grants to Ionis Pharmaceuticals in support of a novel therapeutic approach to this rare but fatal genetic disease. After a decade of research, phase III trials of Spinraza began in 2014 (now with co-development by Biogen), and Cure SMA signaled its support of placebo-controlled trials as the most efficient and effective means to pursue approval and access for the largest group of patients possible. This stance received mixed response from the patient/parent community, with some favoring open label trials. Cure SMA provided input on clinical trial protocols and assisted with clinical trial recruitment, keeping the community regularly informed about progress. In 2015, Cure SMA launched the FDA Engagement Initiative. Staff and patients met regularly with FDA, and Cure SMA produced the “Voices of SMA” booklet to describe patients’ drug development priorities, the impact of SMA on patients and their families’ daily lives, and preferences and expectations for therapy.

On Oct. 28, 2016, Biogen announced that FDA had accepted its new drug application for Spinraza, and on Dec. 23, 2016, FDA approved Spinraza for all patients diagnosed with SMA without restrictions, four months ahead of the scheduled decision date. Cure SMA is now working to rapidly expand the number of treatment centers so that patients and families can receive care closer to their homes. It is also assisting patients in obtaining coverage of and reimbursement for this medicine. Mindful that Spinraza is not a cure, the organization held a Patient-Focused Drug Development meeting with FDA in April 2017 to communicate the expectations and priorities for current and future treatments, highlighting several areas of remaining unmet medical need.

**PARKINSON’S DISEASE (PD) | MICHAEL J. FOX FOUNDATION FOR PARKINSON’S RESEARCH (MJFF)**

In 2014, MJFF established a new priority to strengthen relationships with payers as a complement to the foundation’s research agenda. Timing coincided with the anticipation of new innovations coming through the pipeline. MJFF contracted with an external firm to interview national and regional payers about their understanding of PD and found they were not educated on the science of PD and had no understanding of endpoints being used in therapy development. It convened a roundtable of 20 payers, physician researchers, and policy experts to discuss the current state of PD and challenges to the patient population. This meeting highlighted the need to collect data to close the gap between regulator and payer, including building registries of large patient populations; collecting patient
perspective data to explain unmet needs, burden of disease, and evidence of meaningful improvements; and amassing evidence of real-world effectiveness.

Following the market research and payer workshop, MJFF collected data on patient perspectives on the burden of disease, starting with “off-time”—when PD medication wears off before the next scheduled dose and symptoms return or worsen. It quickly received more than 3,000 responses to a nine-item survey about time spent in “off” state and its impact on daily activities, well-being, and disability. In early 2015, MJFF-grantee Impax Pharmaceuticals received FDA approval for Rytary, a new extended-release formulation of levodopa that showed benefit in clinical trials of reducing off-time by 1.5 hours per day. On March 21, 2017, Newron received FDA approval for Xadago, shown in clinical trials to reduce off-time. MJFF continues working with payers to ensure fair patient access to these and other therapies.

**NON-SMALL-CELL LUNG CANCER (NSCLC) | LUNGevity**
The rapid emergence of new treatment options for NSCLC, including FDA approval of seven new drugs in 2015-2016 alone, is followed by increased complexity of treatment decisions for patients who must balance not only improvements in overall survival and progression-free survival—the “gold standards” of cancer efficacy—but also side effects, quality of life, and other factors. With this in mind, LUNGevity launched Project Transform in partnership with Johns Hopkins School of Public Health to quantify patient preferences for the expected benefits and tolerable risks of various treatments. Results of these studies will be shared with patients, researchers, industry, regulators, and clinicians for use in advancing lung cancer research, care, and policy that align with patients’ needs and preferences.

**PSORIASIS | NATIONAL PSORIASIS FOUNDATION (NPF)**
When the Institute for Clinical and Economic Review (ICER) announced its intention in 2015 to evaluate eight treatments for moderate to severe plaque psoriasis, NPF geared up for a year-long engagement to ensure that patient perspectives were reflected in the assessment that would likely affect payers’ coverage of these therapies. It highlighted the complexity of psoriasis, challenges in disease management, and pervasive impacts of the disease as ICER gathered its evidence and at an in-person meeting where experts deliberated and voted on the value each therapy presented to the system. NPF’s participation in the process yielded substantive changes from the draft report released in September 2016 to the final recommendations issued in December 2016. ICER’s final assessment, that all eight of the treatments offer a good value and that payers should limit or abolish “step therapy” in covering these medications, were responsive to patients’ perspectives.

**SETTING THE TERMS OF ENGAGEMENT**
This new era of patient-centricity relies on trust and transparency among partners, especially in situations where interests may differ. Several organizations, including FasterCures, are working to identify common issues that can bog down or derail potentially valuable collaborations, with the objective of advancing general principles to guide expectations as parties seek to work together. The Arthritis Foundation is setting the pace, developing standard memoranda of understanding (MOUs) that it will use when engaging with industry partners. The goal of each MOU is to help ensure that all participants—whether it’s an individual patient, an industry partner, or the foundation itself—understand the goals, expectations, and unique considerations that come into play with each relationship.

Another trendsetter is LLS, which has recently clarified its position on the rising costs of cancer care, recognizing the strain on individual patients and the health care system as a whole. In addition to pledging transparency about the sources of its funding and being vigilant about board members’ financial interests, LLS has committed to “advancing only those policy solutions that: offer meaningful improvements for patients; increase access to benefits and services for which there is an evidence base; allow utilization management to serve an appropriate role in cost containment; and are data-driven and feasible to implement, both administratively and financially.” LLS set out a comprehensive set of policy recommendations that it urges all stakeholders to adopt as a step toward reducing the financial distress facing blood cancer patients.
Through its Patients Count program, FasterCures aims to improve health by driving adoption of methods by which patients’ perspectives shape processes for discovering, developing, and delivering medical products and services. The resources featured below and 75 others collected from partnering organizations in the U.S. and abroad can be found in our online Patient Engagement Resource Library at http://www.fastercures.org/programs/patients-count/patient-engagement-library/.

**Patient-Perspective Value Framework**

*Version 1.0*

*MAY 2017*

The framework offers a methodology to assess the patient perspective on value and change the value conversation in health care.

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**Expanding the Science of Patient Input: The Power of Language**

*NOVEMBER 2016*

This guide shares key findings and recommendations to build towards a shared patient engagement taxonomy.

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**Expanding the Science of Patient Input: Pain Points and Potential**

*APRIL 2016*

This workshop report highlights the growing pains associated with patient-centricity as well as emerging good practices.

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**Science Translational Medicine**

*APRIL 2016*

Momentum is building to incorporate patient preferences into R&D. This article tracks more than 70 initiatives in the science of patient input.

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**Expanding the Science of Patient Input: Building Smarter Patient Registries**

*FEBRUARY 2016*

This guide is a starting point for learning more about best practices for building and maintaining patient registries.

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**From Anecdotal to Actionable: The Case for Patient Perspective Data**

*NOVEMBER 2015*

As stakeholders work to define and scale patient engagement, this paper outlines concepts for the collection and use of patient perspective data.

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**ABOUT FASTERCURES**

FasterCures, a DC-based center of the Milken Institute, is driven by a singular goal: to save lives by speeding up and improving the medical research system. We work across sectors and diseases to accelerate the process by which great advances in science and technology are turned into meaningful medical solutions for patients.

**WWW.FASTERCURES.ORG**