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BACK TO SCHOOL

CHANGING THE SUBJECT

No longer content with a walk-on role as research subjects, and empowered by access to more information and the necessity of shouldering a bigger share of the healthcare bill, patients are demanding a speaking role on the global healthcare stage. At the same time, regulators and drug industry bodies have concluded that patient input is key to improving clinical trials, defining meaningful treatment outcomes and assessing the amount of risk that is acceptable for a given amount of benefit.

The goal is more than laudable; the patient voice is essential when worldwide healthcare systems are resource constrained, demand for medical treatments and services is expanding in all major markets and "value" is the watchword on the lips of payers, legislators, physicians and patient groups.

The goal is also real. Patient engagement is BIO and PhRMA's top priority for PDUFA reauthorization and was given an entire section of the 21st Century Cures Act (H.R. 6) passed by the U.S. House of Representatives on July 10 (see "Patient Focus 2.0," page 6).

But a large swath of companies, as well as regulators and health technology assessment agencies, are doing little more than paying lip service to "putting the patient at the center of drug development" in websites, presentations, conference agendas and white papers.

In fact, the rhetoric of "putting patients at the center" itself fails to recognize that patients themselves can show the way when it comes time to translate great science into medicines that they really want and society will pay for.

BioCentury's 23rd Back to School essay argues that patients, patient representatives and caregivers should be helping to set translational research agendas. They should be working alongside drug developers and clinical investigators to develop clinical trial protocols. They should be creating clinical trial networks and establishing, running and managing the data from biobanks and registries. And they should be collaborating with regulators to establish approval parameters and with HTA authorities and payers on coverage and reimbursement policies.

Drug companies should be clearing the path for them to do so by advancing the science of preference research and by helping to build the capacity of patient groups to participate in the drug development process.

Companies also should commit to meeting patient needs beyond clinical trials and the delivery of approved drugs by finding ways to grant access to data and experimental therapies.

There are many pitfalls to comprehensive patient engagement — both real and imagined — including difficulty turning anecdotes into data, fear of recriminations for activities perceived to be off-label marketing, and the complexities inherent in providing support without exerting undue influence that undermines the credibility of patient advocates.

Certainly, making patient needs the basis for decision making throughout the product life cycle will be difficult and uncomfortable. It may lead to dropping programs that companies find exciting — and have already invested in — but that don't meet patient needs. It will require changing deeply ingrained behaviors, processes and beliefs.

But drug sponsors cannot afford to cling to established ways of thinking and focus on risk avoidance to the detriment of product opportunity and patient need. They must recognize that patients taking a seat at the table is both inevitable and essential to improving product offerings, shortening development times and achieving product approval and reimbursement.

All of that means ceding some control in order to make room for new points of view that will reshape the drug development enterprise.

THE SITUATION

Drug sponsors traditionally have reached out to patients only late in the product life cycle, usually to recruit participants for a clinical trial or to increase awareness and education about a new drug. When patient views

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were desired, drug sponsors and regulators historically consulted physicians as proxies.

As a result, prescription drugs remain the only high-value products created with little or no input from the individuals who use them.

It's tempting to shrug off the comparison because communication between manufacturers and consumers in other industries is not regulated to the extent imposed on drug companies. But that would be a mistake. There is no phase of drug development that couldn't be improved by a more active, thoughtful approach to patient engagement.

Drug companies have spent billions of dollars creating products that patients don't want and won't use. Pfizer Inc.'s Exubera inhaled insulin is the apocalyptic example, but a multitude of smaller scale mismatches between patient needs and product characteristics play out in wasted investment of money and other resources.

Vertex Pharmaceuticals Inc.'s Incivek telaprevir is but one example. The HCV drug flew off the shelves following its May 2011 launch, posting $74.5 million in 2Q11 sales. But sales in the U.S. and Canada peaked at $456.8 million in 4Q11 and then steadily declined, which Vertex attributed to a glut of HCV clinical trials in the U.S., and to patients deciding to wait for an interferon-free regimen that was still a year away from the market.

Doctors contacted by BioCentury agreed those were contributing factors, but they added another reason: a difficult time managing some of the drug's side effects, which was time-consuming for physicians and hard on patients.

By March 2014, doctors reported to BioCentury that less than 10% of HCV patients had chosen to take either Incivek or Victrelis boceprevir from Merck & Co. Inc. because of side effects such as anemia, and complicated regimens requiring several doses a day.

Side effects and dosing regimens made compliance difficult — a negative consequence of failing to account for patient needs.

Vertex discontinued Incivek in the U.S. in August 2014.

The scale of the adherence problem has been well documented. According to a 2005 paper published in the *New England Journal of Medicine,* about half of patients with chronic conditions such as high cholesterol or depression stop taking their medications not long after starting therapy. Side effects and complicated dosing are among the reasons, along with poor communication with patients about the benefits and side effects that should be expected, not to mention the high costs of drugs.

Non-adherence hits drug companies right on the top line, as illustrated by Juxtapid lomitapide from Aegerion Pharmaceuticals Inc. Because the discontinuation rate of 14% seen in clinical trials grew to over 30% in long-term real-world use, last October the biotech reduced its FY14 sales guidance to $150-$160 million from prior guidance at the lower end of $180-$200 million.

Aegerion also told investors it was working with nurses and dietitians to help patients understand the drug's GI side effects and keep them on treatment longer.

Industrywide, the costs of non-adherence are staggering, according to a 2012 study by Capgemini Consulting.

"The US pharmaceutical industry alone loses an estimated $188 billion annually due to medication non-adherence. This represents 59% of the $320 billion in total US pharmaceutical revenue in 2011," the consultants wrote.

Moreover, according to Capgemini, the lost revenue amounted to 37% of $508 billion potential total revenue that would have accrued had patients stayed on therapy.

"Extrapolated to the global pharmaceutical market, revenue loss is estimated to be $564 billion, or 59% of the $956 billion in total global pharmaceutical revenue in 2011 and 37% of the $1,520 billion annual *potential* total revenue," the authors wrote.

In addition, because the needs and aspirations of patients are not understood and prioritized, clinical trials — the most expensive part of drug development — take too long to enroll, suffer from high dropout rates and often have endpoints that do not reflect the burden of disease that patients and caregivers experience.

A 2014 study from the Icahn School of Medicine at Mount Sinai found that 25% of 7,776 cancer trials registered on ClinicalTrials.gov between September 2005 and November 2011 were stopped prematurely. One in 10 were terminated because they failed to accrue enough patients, and industry-funded studies were more likely to be stopped prematurely.

Narrow inclusion criteria, limited sites or onerous follow-up requirements can lead to failed trials simply because companies can't accrue patients.

For example, it has become difficult to enroll patients with acute myelogenous leukemia into trials comparing new agents with chemotherapy, because up to 80% of AML patients either are unfit for chemotherapy or refuse it. AML patients with a short life expectancy are reluctant to enter a trial that could make them feel worse or that would require travel to an infusion center or otherwise interfere with the quality of their remaining time.

In addition, standard approaches to study blinding can compromise the ability of participants to seek follow-up care if their disease does not respond or recurs during a trial.

Failing to engage patients when target product profiles are crafted also causes drug developers to miss opportunities to differentiate products based on their impact on quality of life, and to create new products that improve QOL.

Several of these opportunities have surfaced at FDA's patient-focused drug development meetings, where patients have testified that marketed products and most clinical programs aren't addressing the symptoms and side effects that are their most pressing concerns (see "Unmet Need, Indeed").

Even when a company does develop a product that meets patient criteria, the lack of robust engagement from patients, their advocates and caregivers has made the regulation and reimbursement of drugs more difficult, contentious and conservative than necessary.

This is in large part because regulators, physicians and patients assess risk very differently. Side effect profiles that physicians, regulators and payers consider trivial or minor, such as nausea, edema or cosmetic rash, can be very important to patients who have to live with a treatment for years.

Conversely, in exchange for relief of their suffering, some patient populations have shown themselves willing to tolerate risks that have been unacceptable to regulators or physicians.

For example, by conducting a patient preference survey, Johnson & Johnson found that migraine patients would tolerate a much larger risk of heart attack than regulators would condone.

"We studied 200 adult migraine patients and asked them a variety of questions showing them alternative treatments with various benefits and harms, and they would say which one they prefer. They would do this over and over again, and it went into a model," said Bennett Levitan, senior director for benefit-risk assessment in J&J's Janssen Research & Development LLC unit.

"It turns out, in exchange for completely removing their functional limitations — in exchange for taking a patient from being stuck in bed and allowing them to run around and take care of their family or go to school — they would be willing to accept on the order of a two out of 1,000 chance of a heart attack per year," he told BioCentury. "Regulators would almost never approve something like that for such high-functioning patients, but these migrainers are saying they regard that risk as worth the benefit."

Similarly, FDA's patient-focused drug development meetings, which patient advocates negotiated as part of the agency's PDUFA V commitments, have demonstrated that regulator assumptions about what patients want are frequently incorrect.

"Regulators, reviewers, academics and providers thought they understood the patient perspective, and in each one of the meetings they've walked away saying that what they thought was most important to patients was wrong," Marc Boutin, CEO of the National Health Council, told BioCentury.

The NHC is a non-profit advocate for patients with chronic diseases. Its members include more than 100 healthcare organizations and companies.

Perhaps the biggest gap — and the biggest opportunity — is embedding patient perspectives into determination of the value of medical products and subsequently into coverage and reimbursement decisions.

UNMET NEED, INDEED

Patient comments from a sampling of **FDA**'s patient-focused drug development meetings have highlighted symptoms that are not adequately addressed by marketed drugs or most programs in the clinic. Many of their requests relate to quality of life issues and symptoms that are difficult to measure in clinical trials. At other meetings, patients' biggest concerns centered more on specific endpoints and clinical trial designs. *Sources: BioCentury, FDA*

Disease	Patient requests
Chronic fatigue syndrome (CFS)	New therapies that address cognitive dysfunction and fatigue crashes
Narcolepsy	New therapies that have a better awake/sleep balance and resolve excessive daytime sleepiness
Sickle cell disease	Therapies that treat chronic symptoms, including pain, fatigue and difficulty concentrating
Pulmonary arterial hypertension (PAH)	New therapies to treat dyspnea and fatigue

PAIN POINTS

A sample of **FDA's** patient-focused drug development meetings reveals cases where patients want different endpoints, data or trial designs than companies and regulators use. *Sources: BioCentury, FDA*

Disease	Patient requests	Standard practices
Gastrointestinal dysfunction	Patient-reported outcomes that assess both the nuances of pain, nausea and vomiting, and the effects of those symptoms on functioning	Numeric pain rating scale; index of nausea, vomiting and retching; functional living index-emesis (FLIE)
Breast cancer	Use genomics and report detailed subgroup data to predict whether patients will be exceptional responders, non-responders or will experience severe side effects	Report medians
Inborn errors of metabolism	Real-world, patient- and caregiver-reported outcomes	A variety of behavioral and functional scores, depending upon indication
HIV	Trial designs that do not require stopping or interrupting current therapy	Require cessation of current therapy

According to a survey conducted between the end of 2010 and the fall of 2011 by the European Patients' Forum, "Very few HTA agencies currently involve and integrate patients' perspectives in their reports and conduct formal evaluation of the impact of patient involvement in HTA. Apart from financial resource constraints the main challenges are perceived to be the lack of capacity, time and good methodologies to involve patients."

Survey data showed less than half of HTA agencies involved patients in assessments, and less than half of patient organizations had ever participated in an HTA.

Moreover, a quarter of the reimbursement authorities said they had no intention of involving patients (see "Lack of Participation").

In 2014, Back to School proposed that price should be based on the patient- and payer-defined value of the outcomes a drug is expected to deliver, requiring industry to work with patients and payers to develop a consensus on value for money.

That argument still holds in 2015. And while industry and payers are beginning to experiment with new pricing models aimed at tying price to value, the patient voice remains underrepresented.

On the private payer side, interactions with patient groups are sporadic.

Anthem Inc. has started to reach out to patients, but only after developing its new policy for coverage of cancer drugs without any patient input at all.

The insurer launched a reimbursement model that provides a financial incentive for oncologists who follow a specific treatment pathway. It was selected based on feedback from external clinical experts, Anthem's own P&T committee and treatment guidelines from the National Comprehensive Cancer Network (NCCN).

The model does not directly reimburse for physician services that are important to patients, such as counseling to help patients understand their treatment options, and time physicians must take to address treatment side effects.

Anthem began to seek patient feedback after the pathways were developed, but before they were launched in June 2014 and is using the feedback to update them. For example, in response to patient concerns, Anthem updated its breast and colorectal pathways so that patients whose genomic testing results indicate they would not benefit from the preferred treatment pathway can be given other treatment.

THE PATH FORWARD

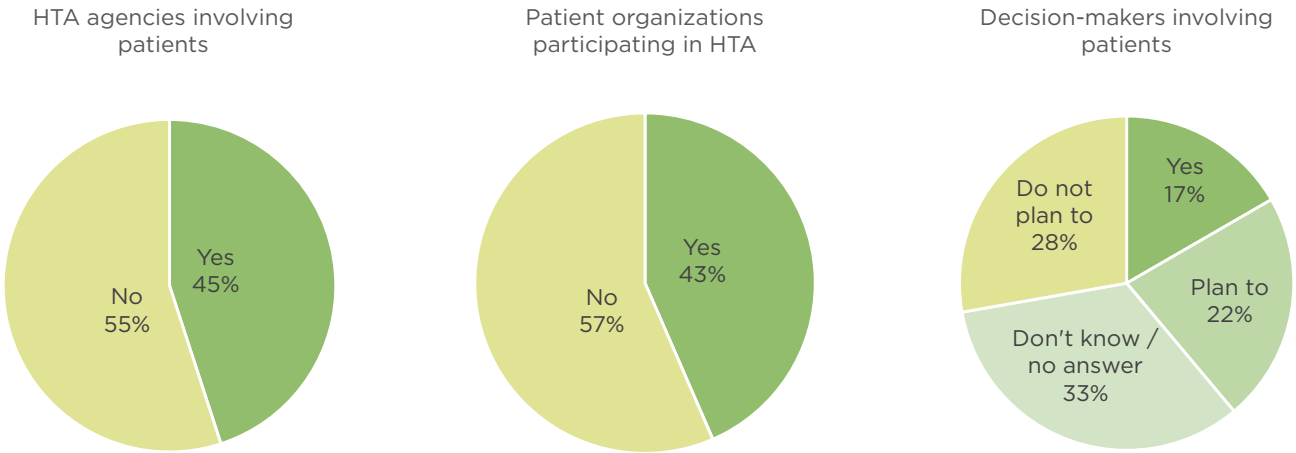
Patients, industry, regulators and, at least outside the U.S., some payers have taken steps to increase the role of patients and caregivers in developing new medical products — sometimes to stunning effect.

The benchmark for patient-driven drug development is the breakthrough therapy pathway, which was conceived by Friends of Cancer Research and included in the FDA Safety and Innovation Act in 2012.

Another case is the patient advocacy group Parent Project Muscular Dystrophy (PPMD). It enlisted the support of patients, caregivers, academia and industry to author a document that FDA then issued as a draft guidance, with fairly minor revisions, on Duchenne muscular dystrophy (see "Patient Power in Duchenne," page 5).

LACK OF PARTICIPATION

According to a survey conducted between the end of 2010 and the fall of 2011 by the **European Patients' Forum**, just under half of the 40 HTA agencies that responded were involving patients in technology assessments. Less than half of the 23 patient organizations that responded to the survey said they had been involved in health technology assessments. Five of the 18 decision-makers, or reimbursement authorities, said they had no intention of involving patients, while six did not know or did not answer the question. *Source: European Patients' Forum*



There also have been a few remarkable examples of patient groups funding and guiding R&D. The Cystic Fibrosis Foundation (CFF) drove the molecule that became Vertex's Kalydeco ivacaftor from a scientific hypothesis into a life-enhancing product, financing the high throughput screening that led to the discovery of the compound and funding its early development.

The foundation also prepared the way for Kalydeco and other therapies by collecting data for decades in patient registries to elucidate the natural history of CF, and creating a clinical trial network to efficiently test investigational agents.

These are exceptions, however; very little has been done to comprehensively focus medical product development on the needs and preferences of the individuals who are supposed to benefit.

In the value-based world, patients and caregivers are demanding an end to paternalistic doctor-knows-best medicine — and are voting with their voices and their wallets as they shoulder an increasing proportion of the costs of healthcare through insurance premiums, deductibles and co-pays.

The reality, as Back to School has been pointing out since 2013, is that meeting today's reimbursement test will require retooling pipelines and R&D programs to focus on patient- and payer-defined needs, and that understanding those needs requires an intensely collaborative effort.

Back to School sees at least four areas where industry should take bold action to accelerate comprehensive partnering with patients.

First, managements should reorient medical product development so that patients are partners in defining what products are needed and in determining both how to develop them, and how to ensure access.

Back to School does not argue that patient priorities should replace or trump scientific inquiry. Industry's ability to bring scientific inventiveness to bear on problems of biology and translation will remain the foundation for medical product innovation.

That said, translational and clinical research should go forward only when there is a clear and compelling need for the results, and a pathway for parlaying them into patient benefit.

Inviting patients to help set translational research agendas will uncover hidden opportunities to create medicines that better meet patient needs.

Further downstream, incorporating patient advice into clinical trial design will enhance recruitment, shorten timelines and improve the information that trials generate, which in turn will support regulatory and reimbursement decisions that facilitate access.

PATIENT POWER IN DUCHENNE

Parent Project Muscular Dystrophy provided a powerful demonstration of how a well-informed and sophisticated patient advocacy group can transform drug development in June, when FDA adopted the group's proposed draft guidance for new treatments, without substantive changes.

In the *Orphanet Journal of Rare Diseases*, PPMD described how it developed its draft with the aid of scientists, patients and caregivers.

PPMD had been working for more than 10 years to educate regulators about the effects of Duchenne muscular dystrophy (DMD) on patients and their families. When EMA issued a draft guidance in 2013 that did not meet the patient community's needs, PPMD assembled an advisory committee to develop recommendations on how to evaluate new treatments.

The group met with FDA several times to discuss developing a guidance for DMD. Lacking the time and resources to develop a guidance itself, the agency invited PPMD to submit a draft.

PPMD began by convening a policy forum to discuss the challenges of designing and running DMD trials, and the need to accelerate approval of new therapies while meeting safety and efficacy standards. There were 200 attendees from the patient, parent, industry, academic and clinical communities, and more than 20 FDA staffers.

At the forum, PPMD committed to completing a draft guidance, with participation from all key scientists and stakeholders, within six months. The group enlisted a regulatory consultant and a project management consultant to ensure the document would be structured and worded appropriately, and delivered on time.

Patients, parents and patient representatives were included in the steering committee and every working group, and on a community advisory board. One working group focused exclusively on strengthening the patient voice throughout the document.

The group deliberately emphasized benefit-risk and patient/caregiver preferences to a much greater extent than other guidances. PPMD partnered with John Bridges, an associate professor at the Johns Hopkins Bloomberg School of Public Health, to conduct a study of how DMD patients and caregivers perceive benefits and risks. Results were published in 2014 in *Clinical Therapeutics*.

Meanwhile, companies and research institutions were gathering natural history data to help interpret endpoints that may not be consistently sensitive across different stages of the disease.

After almost 50 revisions, PPMD submitted "Duchenne Muscular Dystrophy Developing Drugs for Treatment over the Spectrum of Disease" to FDA.

The document became the backbone of the agency's draft guidance, which lists several suitable clinical endpoints according to the stage of disease where they are most likely to show meaningful benefit: the North Star Ambulatory Assessment and timed function tests in ambulatory children ages 4-7; myometry in children 5 years or older; and the six-minute walk test (6MWT) in ambulatory children.

Meanwhile, EMA's final guidance is expected by year end.

Patient partners can also help define the value of medical interventions for payers, and for other patients, in ways that are far more convincing than anything drug developers can say.

To engage with patients as partners, industry will need to advocate for the regulatory clarity that is necessary to enable the free-flowing discussion enjoyed by other stakeholders in the healthcare system — government, payers, regulators and healthcare providers.

Nevertheless, waiting for regulatory safe harbors should not stop drug developers from engaging with patient advocacy groups on topics related to diseases rather than the design of new products. And there are ways to engage in information-gathering about desirable product characteristics without discussing existing or pipeline products in a way that could be construed as promotional — or indeed without discussing them at all.

Second, the drug industry should invest in validating patient-preference research methods via public-private partnerships and third-party research.

Patients are demanding that their judgments about the trade-offs of benefits and risks be given precedence over those of doctors and regulators. But applying patient judgments in development and regulatory decisions requires moving beyond current approaches, which rely too much on anecdotes and personal testimony. What's needed are validated research methods that produce reliable, scientifically rigorous data.

The tools exist, but they need to be validated for use in drug development and medicine. The pharma industry has both the resources and the scientific acumen to move patient preference research toward quantifiable metrics and peer-reviewed social science methods.

In many cases, industry should not be conducting this research itself lest it be perceived as tainting the outcome. Here, patient groups themselves, public-private consortia and third-party researchers are better placed to produce compelling data that regulators, payers and patients will find trustworthy.

Third, to accomplish the first two objectives, industry must help build the capacity of patient groups to engage with companies and regulators — without compromising the advocates' independence and credibility.

An increasing number of patient advocacy organizations understand the process of drug development and the regulatory system. But they are still the minority, and it has taken the best of these organizations many years to develop their expertise.

Industry should participate with regulators, healthcare providers and other stakeholders to build the skills patients, advocates and caregivers need to fully participate in product development, regulation and reimbursement decisions.

These engagements must include leaders among healthcare providers, researchers, regulators, HTAs and payers, and be based on a consensus on rules of the road, especially when it comes to financing these efforts.

As with preference studies, this may require the creation of precompetitive collaborations dedicated to specific diseases or conditions, funding of third-party organizations, and/or creating and funding an independent body that can award educational grants to patient organizations.

PATIENT FOCUS 2.0

FDA, biopharma companies and patient groups agree PDUFA VI should expand on the patient-focused drug development concept that was introduced in PDUFA V. The goal is to add rigorously collected and analyzed data on patient experience and preferences to the anecdotal information FDA is collecting at its town hall meetings.

"PFDD meetings are affecting how our folks are thinking about things," said Theresa Mullin, director of the Office of Strategic Programs at the Center for Drug Evaluation and Research. "We need to take all these learnings and take the next set of steps."

Although formal PDUFA negotiations will start in September, FDA has already thought about the patient-engagement piece. It will include a commitment from CDER to promulgate guidances, Mullin said.

These guidances will describe how sponsors and patient groups should collect "holistic, comprehensive input from a range of the population that has a disease," and will lead to agreement with FDA on "a set of endpoints that reflect what they care about the most in terms of the impact on the experience of the disease," she said. FDA's goal is "to have that pulled into labeling so it is available to physicians to talk about with patients."

FDA also will request money to increase the agency's capacity to evaluate patient-focused endpoints and to develop guidances in a timely fashion.

"Our capacity to look at this kind of information, even to respond to questions within a disease area, is limited. We have literally a handful of people who can do this kind of work and think through and put together methodologically sound advice," Mullin said. "And if you think downstream about sponsors wanting to bring in this kind of information and consult with FDA during their development program, some additional capacity might be needed."

She concluded: "We aren't staffed to handle a fully operational effort today."

Paul Hastings, chairman and CEO of OncoMed Pharmaceuticals Inc. and chair of BIO's Patient Advocacy Committee, told BioCentury that PFDD 2.0 is a high priority for industry in negotiating PDUFA VI. But while the new user fee agreement can provide valuable resources and structure, he said it would be a mistake for industry or patient groups to wait for Congress to reauthorize PDUFA.

Fourth, companies need to commit to meeting the needs of patients in ways that go well beyond clinical trials and the delivery of approved products.

Patient needs do not end at the conclusion of a clinical trial. And even when studies are optimally designed to meet the new patient-driven sensibilities, some individuals still will not qualify for enrollment. In many cases, this will be learned only after patients have invested their time and endured screening tests or procedures, and many will have no therapeutic options left.

Drug companies have a responsibility to help these patients, and others who cannot wait for new therapies to come to market.

This help could take many forms, including enabling responders to continue to receive therapy at the conclusion of a trial, giving patients access to their individual data to be used in making future treatment decisions, and adopting policies that make compassionate access the rule rather than the exception.

These options can be implemented in ways that do not bankrupt small companies, unblind studies or otherwise jeopardize development and approval of pipeline candidates. If done well, they can provide data that help patients and their physicians make informed treatment choices, and that support reimbursement with real-world evidence.

In combination, Back to School's four prescriptions will result in more efficient development of medical products that improve quality and quantity of life for patients, which will provide greater value for payers.

REASON FOR BEING

Managements should reorient medical product development so that patients are partners in defining what products are needed and in determining both how to develop them, and how to ensure access.

Patients and their caregivers living with illness have the definitive view of disease burden and unmet need. There simply is no substitute for their perspectives on what symptoms are most bothersome, what toxicities they're willing to tolerate, how co-morbidities affect them and what dosing and delivery characteristics are most appropriate.

The most obvious place to engage is in clinical trials, which depend upon patients to volunteer their time and may require them to take personal risk. Smart companies have already started to seek patient counsel in study design, but the work must move beyond piecemeal input. Entire programs can be designed around the way patients experience their disease and its treatment, and the way they live their lives.

The goal should be to get and keep more patients in clinical trials, while producing data that can be put on labels to help patients, physicians and payers choose suitable therapeutic options.

Revisiting endpoints from the patient point of view is job one. Endpoints that do not correlate with symptoms that patients care about provide zero information for choosing the best treatment.

For example, FEV1 is the standard endpoint for COPD, but changes in lung function don't tell patients whether their daily lives will improve in ways that are important to them.

"We end up doing these big clinical studies to measure something that is quite far removed from anything that the patients are bothered about," said James Anderson, head of corporate government affairs at GlaxoSmithKline plc. "The thing they care about most is what are they able to do. Are they able to climb stairs, able to visit their friends? Are they able to participate in sports?"

Some endpoints can exclude patients from enrolling. For instance, the six-minute walk test commonly used in trials for Duchenne

REDUCING BURDENS

Several drug developers are evaluating ways to lower the burden of participating in clinical trials, including reducing the need for site visits and eliminating the risk that a patient will receive either no treatment, or one that patients find unacceptable.

Cyclacel Pharmaceuticals Inc. did both in a Phase III study of sapacitabine in elderly patients with acute myelogenous leukemia (AML). Although an interim futility analysis suggests the study will not meet its survival endpoint, the protocol Cyclacel and FDA agreed to did succeed in enrolling 486 patients by using an active comparator that is not approved for the indication in the U.S., rather than trying to overcome patient reluctance to receive chemotherapy.

The open-label design also reduced visits to the infusion center for patients alternating between oral sapacitabine and the active comparator, instead of a blinded design that would have required all patients to match the weekly schedule of the comparator. Final data are due this half.

Eisai Co. Ltd. was able to enroll 360 Japanese patients with amyotrophic lateral sclerosis into a 7.5-year double-blind Phase III study of mecobalamin by enabling at-home treatments instead of requiring these disabled patients to travel to the hospital twice a week for intramuscular injections.

Rami Suzuki, president and senior group officer in the global business development unit, said Eisai invested in such an ambitious study for an off-patent drug because the need is great. "Given the unmet need in ALS, we felt compelled to do it," she told BioCentury. In June, the company submitted its NDA in Japan.

bluebird bio Inc. worked with leukodystrophy patients and their families to get its ongoing Phase II/III trial of Lenti-D gene therapy enrolled ahead of schedule by providing travel assistance. Leukodystrophy is a rare and debilitating disorder.

"We identified patients around the globe who were candidates, we got them to the trial locations, including transporting them from one country and back to their home country to really make it possible for these patients to participate," said Faraz Ali, VP of global commercial development and external affairs.

Other companies are evaluating mobile technology, which could radically transform clinical trials by reducing site visits while improving the quality of clinical data. For example, Novartis AG is testing wearable technology for at-home monitoring of blood pressure, weight and glucose in clinical trials. The life science division of Google Inc.'s Google X innovation lab also is developing a wristwatch that continuously measures biometric and environmental data, which could be used to measure endpoints in clinical trials.

These technologies have the potential to permit continuous monitoring, giving a health readout that is both more complete than taking episodic measurements, and more reflective of real-world conditions.

muscular dystrophy is sensitive only in patients who have started to lose walking ability but haven't entered the phase of rapid decline. Non-ambulatory patients are frequently excluded from these studies.

In DMD, it was the parent-led advocacy group PPMD that proposed the solution, identifying and helping to validate endpoints that can be used in different stages of disease, which are now included in FDA's draft guidance (see "Patient Power in Duchenne," page 5).

Patient-reported outcomes are the most direct way to measure how patients experience the benefit or harm of a therapy. In some settings — such as pain, fatigue, joint stiffness and many aspects of quality of life — PROs are the only way to measure effects on symptoms that are extremely important to patients.

Quality of life for cardiology patients is another example cited by Bray Patrick-Lake of Duke University, who became a patient advocate after participating in an aborted clinical trial for her heart condition.

"The clinical endpoints tend to be stroke, MI and death. There's a QOL component that is missing," noted Patrick-Lake, who is director of patient engagement, Duke CTSA at the Duke Translational Medicine Institute. The program is funded by a Clinical & Translational Science Award from NIH.

Patrick-Lake is also director of stakeholder engagement at the Clinical Trials Transformation Initiative (CTTI), which FDA and the university co-founded to identify ways to increase the quality and efficiency of clinical trials.

In fact, many PROs used today measure symptoms or benefits that were not selected by patients and are not important to them.

"A PRO conceived by a sponsor without patient input isn't a patient-centered outcome," Patrick-Lake told BioCentury.

Drug sponsors must work with patients to define what new PROs should measure, and then develop and validate PRO instruments in collaboration with regulators and payers to ensure their utility in decisions that affect access. Precompetitive consortia or public-private partnerships would be ideal vehicles for this work.

Even when these and other patient-centric measures cannot supplant existing regulatory endpoints, companies should discuss with regulators how to collect and analyze the data so that they can be included on product labels to help patients and physicians make treatment decisions.

Sponsors also need to engage with patients about how to minimize the burden on those who enroll in trials.

Again, this is happening in some corners of drug development. After listening to patients and their representatives, sponsors have found ways to reduce onerous testing or reporting requirements and the need for frequent office visits that act as barriers to participating in trials.

FOUNDING FRAMERS

Biopharma companies and patient groups have launched the Patient-Focused Medicine Development consortium to develop best practices for patient involvement in drug development. The group plans to expand to include regulators and payers.

PFMD launched in April with an editorial in *Therapeutic Innovation & Regulatory Science* outlining the need to engage patients in drug development. But the idea came from an informal discussion between a group of industry executives after an EMA meeting in 2012.

"We talked about what patient engagement would mean and could look like," said Anton Hoos, VP & head of medical, Europe at Amgen Inc. Hoos was SVP of European Medical for GlaxoSmithKline plc at the time.

The group began to meet to share experiences with patient engagement in drug development, and invited patient groups to join.

"We saw a lot of fragmentation of efforts and gaps and overlaps, and we realized that we're not being the most efficient at moving forward," said Lode Dewulf, chief patient affairs officer at UCB Group.

The international consortium will catalog patient involvement efforts that were under way to understand what works best and develop blueprints for industry and patient groups.

Founding members include Amgen, UCB, GSK, Pfizer Inc., Merck Sharp & Dohme Corp. (MSD), the National Health Council, the Parkinson's Disease Foundation, the European Patients' Academy on Therapeutic Innovation (EUPATI), the European Patients' Forum, the Society for Participatory Medicine, the Cancer101 Foundation, and the Clinical Trials Transformation Initiative (CTTI). MSD is a subsidiary of Merck & Co. Inc.

The consortium will have a 12-member board, with at least 30% representation from patients, and no more than 50% from industry, "to guarantee that industry does not become overrepresented and ensure substantial patient participation," said Nicholas Brooke, secretariat of PFMD and executive director of The Synergist, a not-for-profit that brings together stakeholders to work on social and health issues.

PFMD will meet on Oct. 14-15 to elect the board and decide on a formal name. The group also will start to outline its priorities and work plan.

Brooke said the consortium plans to disseminate much of its work, including white papers, via an online portal where companies and patient groups will be able to submit their own best practices.

Industry participation requires a financial commitment, while patients and patient groups can participate for free. PFMD expects to offer membership to regulators and payers, but wants first "to understand the bigger picture, the landscape and what's the way forward. Then we will engage," Brooke said.

Dewulf said he envisions that PFMD could become an international body that standardizes patient engagement best practices much like the International Conference on Harmonization does for non-clinical testing requirements.

In other cases, based on patient concerns, sponsors have worked with regulators to design protocols that minimize the chance patients will receive no treatment, or an undesirable one (see "Reducing Burdens," page 8).

"No matter how sophisticated you are, you can learn from patients about trial design," said Patrick-Lake.

Industry also should expand clinical trial inclusion criteria to increase participation and better reflect the patient population that will be taking the drug.

Drug companies automatically may reject this notion, not the least because trial enrichment is the accepted strategy for increasing the odds of a positive statistical outcome. But this long-held thinking will not hold up in the world of value-based reimbursement.

Moreover, FDA leadership supports the idea. In a commentary published in *Clinical Trials* in December 2014, Robert Califf wrote, "Reducing unnecessary exclusion criteria is a critical element of improving the clinical trials enterprise." At the time Califf was vice chancellor of clinical and translational research at Duke University School of Medicine. Today he is FDA deputy commissioner for medical products and tobacco.

While it may be more difficult to detect and interpret efficacy or safety signals in a heterogeneous population, protocols that include prespecified analyses in prespecified subgroups show it can be done.

For example, studies in multiple myeloma patients who have received multiple prior therapies frequently include subgroup analyses based on the specific type of prior treatment as a co-primary or secondary endpoint.

The master protocol approach being piloted in cancer and Alzheimer's disease could be adapted to expand enrollment criteria. Those studies assign patients to treatment arms based on biomarkers, but other approaches could enroll all comers who would be assigned to cohorts based on risk factors, co-morbidities or disease severity.

"Companies could start with a patient registry and open the trial to all of the patients," said Patrick-Lake. While one of the subgroups could be a very narrow, low-risk population, other arms with high-risk patients or co-morbidities could be used to collect additional efficacy and safety data.

"It could also be good for identifying new indications," she added.

EMA's adaptive licensing pathway could provide another approach. The pathway allows for a drug to be approved quickly in a very narrow indication based on promising but early data, with the requirement that the sponsor continue to study the drug in a wider range of patients to receive full approval.

"You do the trial in a very small, controlled population and then you broaden it. I think this could work very well to address patients' concerns," said Anton Hoos, VP & head of medical, Europe at Amgen Inc.

Hoos is an architect of the Patient-Focused Medicine Development (PFMD) initiative, a collaboration of biopharma companies and patient groups.

LEGAL-EASE

While FDA has endorsed patient engagement in both word and deed through its patient-focused drug development meetings, many drug companies say they do not feel safe engaging with patients about a specific product or clinical program. They fear they may be accused of promoting an unapproved product or off-label use of an approved drug.

"In the past, FDA has cast the net so broadly in terms of what it considered to be promotional that any discussion with a patient around a product runs the risk of preapproval promotion of that product or off-label promotion," said Daniel Kracov, partner at Arnold & Porter LLP.

"There are a lot of hoops a company has to jump through from a compliance perspective," he said, noting patients often must be put under consulting agreements. "It's just a very restrictive environment for trying to have a real discussion with patients about their needs."

Engaging with patients on disease-related issues may carry less risk, Kracov said, but "if FDA thinks that the way the messaging is framed is trying to suggest something about your product, it will take it as promotional."

Public-private partnerships could help to avoid some of these issues, but according to Kracov it gets more complicated the closer the conversation gets to a specific product. "There will be times where you want to talk about proprietary information, and forums like this wouldn't be appropriate because then you are dealing with IP issues and contracts around that," he said.

He recommends that before engaging with patients on any topic, companies "should subject the plan to careful compliance and internal review" by its legal team.

UCB Group said its legal group is helping it navigate the waters.

"The number one obstacle that is cited is legal compliance. But that is done without having anyone from those functions in the room," said Lode Dewulf, chief patient affairs officer. "If you work with your legal team from the beginning, they can be a great helper."

Deborah Dunsire, president and CEO of neurology company Forum Pharmaceuticals Inc. and a member of BIO's executive committee, told BioCentury that companies need formal guidance from FDA to know where the "electric fence" is that they cannot cross.

FDA says industry overstates the compliance risk, but acknowledges that better guidance for engaging with patients and patient groups is in order.

"I think there's a perception of a barrier to companies engaging early," said Theresa Mullin, director of the Office of Strategic Programs at the Center for Drug Evaluation and Research. "I think it is a misperception. There probably are some narrow circumstances or activities we could clarify that would be construed as promotion of an unmarketed product. A guidance to clarify that would be helpful, we've heard."

Yet another option is to conduct two trials in parallel: one in a narrow population and another with more relaxed enrollment criteria, which would better reflect real-world experience.

"If they only look at narrow populations preapproval, it may not reflect the real world and they will have to do a lot of work postmarket. It is in the best interest of patients and industry to do this in combination and not wait," Hoos said.

Payers may also find the data more convincing.

"If companies make the enrollment criteria more relaxed to increase enrollment and try to make it broader to capture the real patient experience and reflect a real-world setting, that could be beneficial," said Mark Cziraky, co-founder and VP of research at HealthCore Inc., a subsidiary of Anthem (see "Convincing Payers," page 11).

Embedding patient advice into endpoint selection and study design is the low-hanging fruit in the quest for products and data that better meet patient needs. The transformative step would be using patient input to help drive target product profiles and candidate selection.

"Early researchers are the ones who should have the greatest knowledge in terms of a candidate's profile, its side effects, its safety, how it's dosed and used. They are the most influential of what a drug will eventually look like when it comes to market, and yet they are often the least connected to patients," said Walter Capone, president and CEO of the Multiple Myeloma Research Foundation.

MMRF is a patient-founded organization that funds and conducts its own research and advocates for patient-centered policies.

With a biological and scientific rationale already in hand, discovery or preclinical researchers could translate information from patients into new models or assays to identify drug candidates that avoid specific side effects that limit the use of medicines, or that ameliorate symptoms that are unresolved by existing treatments.

UCB Group has a patient representative on its SAB, which advises the company on research and pipeline decisions.

"They provide an additional valuable perspective beyond the purely scientific, which should help to guide us to where we should and should not go," said Lode Dewulf, chief patient affairs officer. "It can be a real shark tank if you expose your project to patients who might ask, 'Why is this relevant to me other than being a new receptor?' But that is what needs to happen."

Incorporating patient perspectives would uncloak the kinds of misguided assumptions that drive companies to pour billions of dollars of investment into the next Exubera or Incivek. Moreover, patients can help uncover product opportunities that are not obvious — or even that fly in the face of conventional wisdom.

That was the case with Receptos Inc.'s ozanimod. By the time the oral modulator of sphingosine 1-phosphate receptor 1 had entered the clinic, it was years behind the marketed S1P1 agonist Gilenya fingolimod from Novartis AG. Moreover, physicians told BioCentury they had become comfortable managing Gilenya's cardiovascular side effects.

Multiple sclerosis patient message boards told a different story.

Online posts during 2011-12 revealed that many MS patients declined to take Gilenya because they would have to remain in the doctor's office for six hours of heart rate monitoring after the first dose. Others were put off by physician warnings of potential liver toxicity, which had led to a 15% discontinuation rate in trials.

Listening only to physicians would have led to the conclusion there was no need for another S1P1 agonist. But patients made it clear Gilenya was not meeting their needs.

Ozanimod is now in Phase III, and Receptos was acquired by Celgene Corp. for $7.2 billion.

Naysayers will cite many reasons for not engaging with patients in product discovery and development, especially fear of ending up on

CONVINCING PAYERS

Anthem Inc.'s HealthCore Inc. subsidiary has been working directly with patients for more than eight years to get feedback on endpoints that are important to them and to understand how drugs affect quality of life. It then connects that information to its claims data.

The insurer uses the data from HealthCore's patient preference surveys to help make formulary decisions.

Mark Cziraky, who co-founded HealthCore and is its VP of research, said that as drug sponsors begin to do similar work with patients, they can make the data more relevant for payers by using the same instruments for gathering patient-reported outcomes both before and after approval.

"Surveys and PROs are being used in randomized controlled trials, and when it comes to postapproval they use completely different ones," he said. If companies used the same tool in both settings, "it would give us more of a continuum around the patient and how the drug affects them."

Cziraky also suggested clinical studies should be designed to better reflect the intended real-world use of a drug, for example by broadening enrollment criteria or by employing pragmatic designs in which treatment arms are randomized, "but then you step back and let standard care take place."

If premarket studies better reflected the real world, he said, it would be easier for payers to assess the value of a new drug when it comes to market, rather than the company having to conduct additional studies.

Cziraky also said studies linking tolerability with adherence and outcomes would be persuasive.

"There is a lot of value in less AEs if it leads to better adherence. We need better adherence by the patient and then need to show that better adherence leads to better outcomes," he said.

the wrong side of regulatory compliance. But industry trailblazers and FDA say that's no reason to sit on the sidelines.

"In my experience, this is actually a myth that often serves as an excuse for a lot of people not to move forward," said Dewulf. "If you work with your legal counsel from the beginning, they will and should help you find ways to work with patients in a way that is legally compliant," he said (see "Legal-ease," page 10).

Theresa Mullin, director of the Office of Strategic Programs at the Center for Drug Evaluation and Research, told BioCentury that the agency may issue guidance to clarify the "misperception" that FDA regulations concerning off-label or unapproved marketing are a barrier to patient engagement.

In any case, companies can partner with patient groups to gather information on disease burdens with little worry of running afoul of regulatory authorities. Companies also can work precompetitively to establish frameworks on how to engage patients during early R&D.

For instance, the PFMD consortium was established this year as a public-private partnership for companies and patient groups to develop some of these blueprints and best practices (see "Founding Framers," page 9).

Companies also can fund third-party research on patients, and can work via patient advocacy organizations to avoid potentially improper communications with individuals.

"We can help to run interference," said Veronica Todaro, VP of national programs at the Parkinson's Disease Foundation.

She said the foundation can help survey patients about their disease burden and needs that are unmet by available therapies, and also coordinate groups to meet with companies to provide input on clinical trial design.

Another concern is that partnering with patients — just like partnering with anyone — means ceding some control. But investing in products that patients actually want to use will lower the more expensive risks of commercial failure.

Dewulf acknowledged the challenge but said industry needs "to form new partnerships with patients where you give up some control. Yes, sometimes you will fall, but it's the only way forward."

An essential step in transforming product development with patients is one where industry has the least control: working with regulators, HTAs and payers so they recognize when a product meets patient needs, and make approval, appraisal and coverage decisions that ensure access (see "Paying Attention").

In fact, Back to School's prescriptions do not excuse regulators and HTAs in particular from their obligations to embed patient perspectives into the core of their evaluations of medical products — and both have a long way to go. But industry can facilitate interactions between patients and these other stakeholders.

Here, as Back to School recommended in 2013, drug companies need to gather stakeholders to arrive at a shared consensus of value. If these discussions focus on solutions rather than new products, there is less risk that the message will be clouded with concerns about bias or conflict of interest, and a greater chance that regulators and reimbursement authorities will recognize the benefits of new therapies when they become available.

To align all these stakeholders, the drug industry also can be instrumental in developing robust patient preference data that all these stakeholders will need to support approval and reimbursement of new products.

WHAT'S YOUR PREFERENCE?

Industry should invest in validating patient-preference research methods via public-private partnerships and third-party research.

For decades, drug companies, researchers and regulators have assumed — incorrectly — that they knew what patients and caregivers wanted, or at least what was good for them. On the basis of these flawed presumptions, regulators and sponsors have then argued over the relative importance of benefits and risks in the approval process.

Formal patient preference studies can replace the guesswork with hard data that identify the specific benefits, risks and harms that patients care about, and quantify both the relative importance of these factors, and the willingness of patients to make trade-offs among them.

"Statistics will tell you how many events you've prevented and how many events you've caused, but it doesn't tell you how important those are compared to one another. That's where preferences come in," said Janssen's Levitan.

Preference studies also can identify and characterize subpopulations that might benefit from a product — and populations for whom no amount of benefit would outweigh the risks.

"While we may understand the average preferences of patients, even more important is understanding the heterogeneity or diversity of viewpoints," Levitan said.

"We've spent years and years studying the middle, but to satisfy the market, you have to study and satisfy the extremes as well," said UCB's Dewulf.

Not every development program will need or benefit from formal preference research. It is most useful when a patient has many treatment options, when none is clearly superior on all important parameters, when the evidence is uncertain, or when views about the most important benefits and acceptable risks of a product vary within the patient population.

In these instances, data on preferences can help innovators understand the clinical need, and the product characteristics and data benchmarks necessary for success.

Understanding preferences in this way also can improve recruitment and retention in clinical trials.

Finally, rigorous preference data can be put on labels and communicated to physicians and patients.

While FDA has opened the door to this essential step in patient-driven regulation, so far there is only one instance of patient preference data making it onto the label of an agency-approved product, and there is little evidence such studies have influenced reimbursement policies or prescribing practices (see "CDRH: Preferences in Action").

The problem is not a lack of methods; it is a lack of standards.

Indeed, while marketers have been studying consumer preferences for products ranging from coffee to cars since the 1950s, applying such research to benefit-risk assessments of medical products is a nascent field. To move patient preference data from the pages of academic journals onto medical product labels, industry should work to define best practices and criteria for assessing preference studies.

Draft guidance issued in May by FDA's Center for Devices and Radiological Health provides a partial blueprint, although work needs to be done to extend the principles to biopharmaceuticals.

CDRH notes preference studies could be useful throughout the product life cycle, from initial device design to the market and beyond. The longitudinal approach is important because preferences change over time as the benefit-risk profiles of products become clearer in the postmarket setting and as new treatment options become available.

Drug companies therefore need to work with patient groups and regulators from early days to determine how to build a body of knowledge about patient preferences throughout the course of product development, just as a program of preclinical and clinical studies contributes to the body of knowledge about efficacy and safety (see "Applying Preference Research," page 14).

"If you just do one patient preference study, it's a snapshot in time. You really need to involve them throughout the life cycle of a drug, during the design of study protocols, the discussion of results and then at these certain points in time you can also talk to them about patient preferences," said Amgen's Hoos.

CDRH already has recognized several methods that can be used. The majority involve stated-preference approaches, in which patients are offered a series of hypothetical choices to elucidate and quantify their trade-offs (see "Preference Methods," page 15).

The publicly funded Patient-Centered Outcomes Research Institute (PCORI) also is funding research on patient preferences and on preference research methodologies, but a broader and more systematic approach is needed.

Industry needs to assert a role in validating preference research techniques that have been used for decades in other industries.

For instance, the Medical Device Innovation Consortium has noted very little has been done to compare the outputs of preference studies using different methods to answer the same question.

MDIC is a public-private partnership that includes FDA, medical device manufacturers, patient advocates and academic researchers.

Industry should support the creation of a registry of patient preference studies that would aid sponsors and patient groups in designing and implementing new studies and enable comparison of different methods of collecting and analyzing the results. The registry could include published patient preference studies conducted by sponsors, FDA, academics, patient groups and others.

As a model, MDIC suggested the Cost-Effectiveness Analysis Registry run by the Center for the Evaluation of Value and Risk in Health at Tufts University. The CEA Registry is a searchable online database containing 4,339 cost-utility analyses for a range of diseases and treatments.

The registry could be run by a public entity such as FDA or PCORI, or by a public-private partnership like the Critical Path Institute or a consortium modeled on Project Data Sphere LLC.

The CEO Roundtable on Cancer launched Data Sphere in 2014 as a platform for researchers to access de-identified, patient-level, comparator arm data from Phase III trials sponsored by industry and academics.

PAYING ATTENTION

The Canadian Agency for Drugs and Technologies in Health formally includes patient advocacy groups in health technology assessments and has begun incorporating their input into scientific advice given to drug sponsors.

CADTH is an independent HTA agency that makes recommendations to federal, provincial and territorial governments about funding medical products on public insurance plans.

The agency directly solicits input via emails to patient advocacy groups and on its website 20 days before a new drug is expected to be submitted for coverage. Patient groups have 35 business days to respond. The Canadian Drug Expert Committee (CDEC), which includes two lay people representing the general public, weighs the comments and evidence submitted by patients and the drug sponsor and makes recommendations to CADTH on coverage. The lay members cannot represent a specific interest, group or organization.

CADTH's pan-Canadian Oncology Drug Review (pCODR) uses a similar approach to gather patient comments, and includes three patients on its review committee.

Patient advocacy groups are again asked for feedback when CADTH or pCODR post their initial recommendation. In the final coverage decision, both bodies include a written description of how the patient comments were used and/or the impact patient input had on the recommendation.

CADTH also incorporates patients into a new scientific advice program launched in January. The consultation provides sponsors advice on early development plans, with a focus on the type of evidence needed to support reimbursement. As part of the program, CADTH interviews at least one patient to discuss current therapies and unmet needs, which is taken into consideration as CADTH develops its scientific advice. CADTH can share the patient information with the drug sponsor.

MDIC also called for research into how to best select a population sample, because differences in patient preferences may not correlate with demographic or other observable characteristics.

It also may be difficult to avoid sample bias that could lead to results that are not representative of the intended population for a treatment.

"One of the biggest challenges in finding the right sample for a patient preference study is avoiding bias that could be introduced through self-selection," MDIC noted. "It may be that those who choose to participate may have preferences that differ systematically from those who choose not to participate."

According to the device consortium, research into sample selection could be accomplished by conducting the same study in different samples with different characteristics in order to determine the sensitivity of the research method to the choice of sample.

There also is no standard set of tests to ensure the validity of patient preference studies. In this case, the MDIC authors proposed that benchmarks might be derived from the standards now used to assess the validity of PRO studies.

It is important to note that the level of validation, and the appropriate research method, will depend upon how the information is to be used. For instance, a study of benefit-risk preferences intended to support approval would need to meet a higher standard than an earlier stage preference study intended solely to inform trial design.

According to CDRH's draft guidance, qualitative information may be used to determine what outcomes, endpoints or product attributes are most important to patients, and what factors affect their tolerance for risk or perspectives on benefit.

Quantitative information, the agency wrote, can provide an estimate of how much those outcomes or product characteristics matter to patients, and the trade-offs patients are willing to make among them.

If patient preference research shows that "a significant number of reasonable and well-informed patients would accept the probable benefits despite the probable risks, this may help support a favorable benefit-risk profile," according to the guidance.

Industry, patient groups and regulators also will need to collaborate to develop best practices for communicating preference data to patients and healthcare providers, including product labeling and communications between physicians and patients.

"We've got to make these tools usable, not just for patients, but for doctors," said NHC's Boutin. "It's not just about safety and efficacy, but about how this might be valuable to the patient. So we need to engage with patients about how we communicate this and develop labels."

In some settings patient groups themselves may be better placed to do preference studies.

"If the collection of patient preference data is left in the hands of drug companies, FDA will erect high regulatory hurdles to overcome skepticism about the objectivity of the data. This would make it harder and more expensive to collect data," said Boutin.

He argued that research related to disease burden can be done in the precompetitive space via international efforts. "I believe there is a

CDRH: PREFERENCES IN ACTION

FDA's Center for Devices and Radiological Health established an important precedent when it used patient preference data to approve the Maestro Rechargeable System from EnteroMedics Inc. to treat obesity.

The device missed the primary endpoint of a 10% improvement in weight loss compared to a control group. But a preference study conducted by CDRH revealed that a group of patients would accept the risks associated with the device for the amount of weight loss it was expected to provide.

It was the first time FDA explicitly cited quantitative evidence of patient risk-tolerance in an approval decision.

FDA said its decision was based in part on a stated-choice survey of 540 obese adults. Participants were randomized to take one of 15 versions of a survey containing eight choice questions. In each choice question, participants were shown a comparison of eight characteristics of two virtual weight-loss devices and were asked, "Which weight-loss device do you think is better for people like you?"

Statistical analysis of the responses revealed the relative importance of the device characteristics, which included the method of implantation, amount and duration of weight loss, recommended dietary restrictions, reductions in the need for medications, duration of side effects and risk of hospitalization or death.

CDRH developed a tool to estimate the minimum weight loss patients would accept from a device with specific characteristics. For instance, the study showed that a risk-tolerant patient would accept a device with 0.001% mortality risk if it produced a 10% weight loss that lasted at least five years.

The device center plans to use the tool to make approval decisions and to help reviewers set minimum clinical effectiveness thresholds for clinical trials of obesity devices.

CDRH statisticians and collaborators wrote in a paper in *Surgical Endoscopy* that the conceptual framework and quantitative methods used in the study are generalizable to a "wide variety of medical treatments and are particularly relevant when patients and regulators face difficult decisions when weighing potential treatment benefits against serious risks."

Notably, the CDRH officials said approval decisions based on risk-tolerance data will seek to accommodate patients who are willing to accept high degrees of risk.

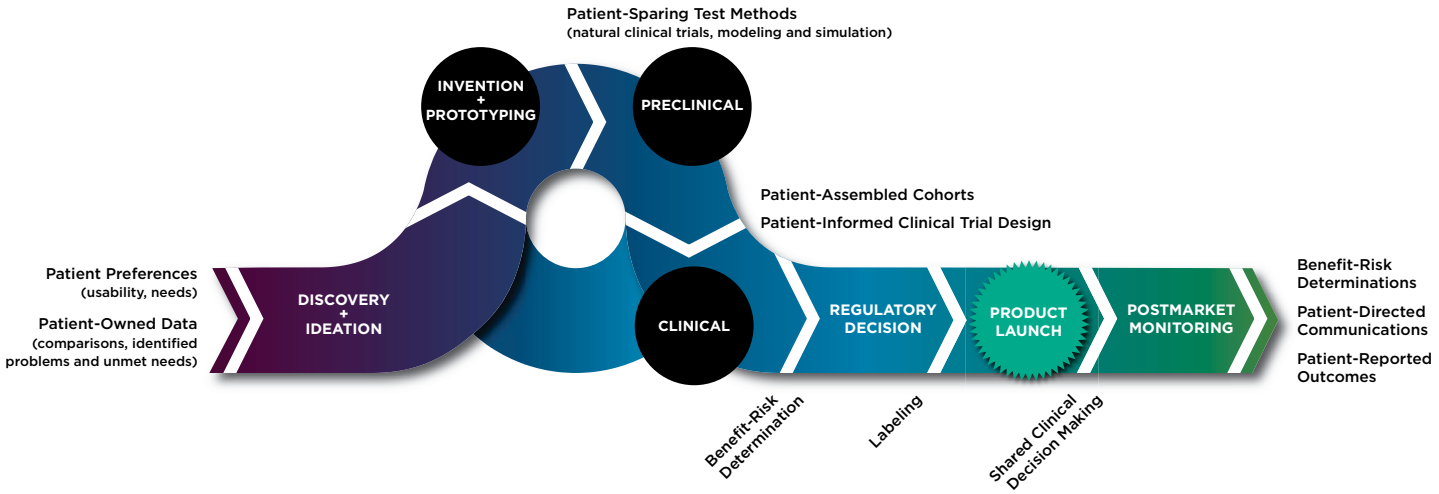
"CDRH will consider approving a medical device that demonstrates meaningful benefits even though its benefit-risk profile would be acceptable only to a subset of patients who are risk-tolerant," the authors wrote.

APPLYING PREFERENCE RESEARCH

According to a draft guidance from **FDA**'s Center for Devices and Radiological Health, patient preference research may be used throughout the product life cycle. During the earliest phases, patient preferences may help inform product design. In the clinical phase, preference information can help identify what endpoints are important to patients, what aspects of study design may affect participation, and how much benefit patients require to accept a certain amount of risk.

The agency suggests that in many cases, each stage of preference research can be used to inform the next. For example, qualitative patient preference information that informs device or clinical trial design may shape quantitative studies that could in turn inform FDA's benefit-risk assessments.

According to the agency, preference data used in an approval decision should appear on the label, where it can be used by patients and healthcare providers in shared decision making about treatment options. In the postmarket setting, preference data may be used to support label expansions and may lead to product improvements or new products. *Source: FDA*



need for a public-private partnership that also includes regulators. It should go beyond the U.S. — North America and Europe could do this together," he said.

Paul Hastings, chairman and CEO of OncoMed Pharmaceuticals Inc. and chair of BIO's Patient Advocacy Committee, said transparency is key to ensuring the results are accepted, no matter who conducts the study.

"If it is sponsored research," Hastings said, "it will become like third-party publications today — people will read it based on how well it is done."

Boutin also argued that preference data could be used to inform more nuanced reimbursement policies.

"None of this will matter if the payer community doesn't participate and embrace the use of preference data," he said. "One way to counter blunt efforts to control prices and access to expensive therapies is to assess individual patients' needs and aspirations, match those to the best therapies, and make those therapies easiest/cheapest to access."

Companies can encourage payers to use these data by sponsoring studies to demonstrate the clinical relevance of patient preferences. For example, a study could be designed to show whether patient preferences for more convenient dosing translate into greater adherence and better outcomes.

"A payer would want to see data," said Robert Epstein, former CMO at Medco Health Solutions Inc., a managed healthcare company that was acquired by PBM Express Scripts Holding Co. "They may push manufacturers to develop evidence that subtle differences actually play out in the real world to provide an advantage."

The work to develop and validate preference studies will require drug sponsors to bring social scientists into the fold, either as third parties or as employees. For some stakeholders, this will require an attitudinal shift.

"We need to get social scientists involved. Medical doctors have very distinct, and often negative opinions on this stuff, and specialists are even worse," said Michael Kauffman, CEO of cancer company Karyopharm Therapeutics Inc.

"There are a lot of people in academia, regulatory agencies and pharma, all of whom are science-based and who still believe that patient input is not scientific, and because it's not scientific, it's not valuable," said Dewulf.

FDA recognizes that it needs more expertise and will ask for funds in PDUFA VI to hire social scientists with experience in designing and evaluating preference studies (see "Patient Focus 2.0," page 6).

PREFERENCE METHODS

The **Medical Device Innovation Consortium** (MDIC) and **FDA**'s Center for Devices and Radiological Health both describe a variety of patient-preference research methods. There is no consensus on what methods are most appropriate for a given product or research question. In a draft guidance on the topic, CDRH noted that a majority of studies that identified and compared methods for measuring patient preferences used methods belonging to the stated-preference class. *Sources: MDIC, FDA*

Class	Description	Methods
Stated preference	Measure quantitative preferences by analyzing how patients respond when offered various hypothetical choices.	Direct-assessment questions
		Threshold technique
		Conjoint analysis and discrete-choice experiments
		Best-worst scaling exercises
Structured weighting	Used to derive weights in multicriteria decision methods. Multicriteria decision methods help people make evidence-based decisions by systematically combining clinical evidence with subjective judgments or weights.	Simple direct weighting
		Ranking exercises
		Swing weighting
		Point allocation
		Analytic hierarchy process
		Outranking methods
Health-state utility	Yield an estimate of preferences for a health state (described as a single attribute or a profile) when compared with death and perfect health.	Time trade-off
		Standard gamble
Revealed preference	Used to analyze patients' choices and behaviors in the real world. Often cannot be used to derive weights for or the relative importance of individual attributes or changes in attribute levels.	Patient-preference trials
		Direct questions in clinical trials

GROWING THE BASE

Industry must help build the capacity of patient groups to engage with companies and regulators — without compromising the advocates' independence and credibility.

Living with a medical condition provides a unique perspective that should be brought to bear throughout the life cycle of a drug; however, it does not convey expertise in science, medicine or the processes by which a drug is developed, approved and paid for.

The extraordinary efforts of patient- and caregiver-led groups such as Friends of Cancer Research, PPMD, the CF Foundation, MMRF and the Michael J. Fox Foundation for Parkinson's Research are transforming research, development, regulation and policy in their respective disease areas. But these groups took many years to develop the expertise and infrastructure they needed to be effective, not to mention the trust and respect of collaborators within industry, regulatory agencies, research institutions and governments.

As a result, these groups are among a handful that are equipped to meaningfully improve drug development and access.

"We need to move people from the walkathon phase. So many people are raising awareness and getting nowhere," said Bray Patrick-Lake of the Clinical Trials Transformation Initiative.

Building the necessary capacity will cost money, and it is appropriate and necessary for industry to provide both funding and education. At the same time, given the disparity in the scale of financial and human resources between pharma companies and even the biggest patient groups, and the hair-trigger sensitivity among politicians, academics and consumer groups to even the suggestion of conflict of interest, it will be necessary to develop rules of engagement to prevent a descent into the kind of distrust and excessive regulation that tarnishes medical product company relationships with physicians.

It will be crucial for the patient community, regulators and medical product developers to agree on principles to govern financial interactions between the stakeholders.

Although it should be obvious, the first principle is that contributions from just one company should never be the primary source of funding for any patient group, and companies should neither fund nor partner with patient groups that do not publicly disclose their funding sources.

Any organization's credibility can vaporize in a flash of attention to real or imagined impropriety. Moreover, if too much of a patient group's funds come from a single biopharma company, the group may feel it can't speak critically about the sponsor's programs or plans, or that it can't partner with other companies working in the same disease area.

"Companies shouldn't be owning a specific patient group or patient. It is about helping these communities," said Michele Rhee, patient advocate at bluebird bio Inc. Rhee is also a rare disease and cancer survivor.

To avoid this, industry should be prepared to fund an entity managed by an independent board to award grants specifically to help patient groups build scientific and regulatory capacity. Government agencies, including HHS's Agency for Healthcare Research and Quality (AHRQ) and NIH, as well as the publicly funded PCORI, also should fund this kind of capacity building.

The European Union already co-funds with industry the European Patients' Academy on Therapeutic Innovation.

EUPATI was started in 2012 as an initiative of the public-private Innovative Medicines Initiative (IMI). EUPATI received €5.25 million in IMI grants and €5.24 million of in-kind contributions from the

European Federation of Pharmaceutical Industries and Associations (EFPIA) to educate and empower patients to "engage more effectively in the development and approval of new treatments and become true partners in pharmaceutical R&D," according to the IMI website.

EUPATI has a formal training course in which it has already educated 50 patient advocates, with 60 more in training (see "Academy for Advocacy").

"It's not about Christmas wish lists, but about educating patients about what science can do while still challenging the process. That is where educated patients come in and say where you need to rethink things," said EUPATI Director Jan Geissler.

These arm's length vehicles would be in a position to sponsor webinars and workshops in which researchers, regulators, payers and other experts educate patient audiences about the basics of preclinical testing; how a clinical trial works; what blinding, randomization and active controls are and how they are important in ensuring the integrity of the trial; and how regulators and reimbursement authorities make decisions about clinical benefit, risk and cost effectiveness.

"We can't really ask patients to contribute to the clinical trial protocol if they've never seen one before," noted Roslyn Schneider, global patient affairs lead at Pfizer.

Invited speakers could include patient advocates who have achieved a level of influence to talk about where and how patients can engage in drug development and regulation.

The Patient-Focused Medicine Development initiative is already providing one forum for patient advocates, as well as industry, to develop and disseminate best practices and how-tos. The precompetitive, international initiative has five biopharma members, including Pfizer and UCB, and seven patient groups, including EUPATI.

What industry should *not* do is attempt to form *de novo* patient groups, even though it is tempting in disease areas where patients are scarce and/or poorly organized. When there are no patient networks in place, industry should find ways to bring patients and KOLs together.

"They shouldn't facilitate the foundation of patient groups. Industry could support leaders to build their own capacity and get together with other leaders, academics, NGOs," said Geissler.

bluebird took this approach in childhood cerebral adrenoleukodystrophy, a disorder that affects about one in 20,000 boys worldwide. Before the gene therapy company even had a candidate in the clinic, it organized a global summit on leukodystrophy, inviting patients, caregivers, researchers and clinicians to discuss the challenges of the disease.

In countries without a patient group, bluebird works on the ground to identify and reach out to patient opinion leaders.

"We would never want to create a group. It doesn't work if there isn't authenticity of the group itself and the company that is interacting with them," said Faraz Ali, VP of global commercial development and external affairs at bluebird.

"Companies have to show the ability to build trust with patients," added Rhee. "In some of these cases, they won't accept money from a pharma or biotech because they don't trust us. But we can ask what is it that the group is looking to do, and help to support that."

Pfizer's Schneider also noted that different patient groups are focused on different segments of the product life cycle.

RULES OF ENGAGEMENT

UCB Group has developed a framework to ensure its employees engage with patients in ways that are both legally compliant and respectful of a patient's condition and privacy.

The framework was developed in collaboration with patients. It outlines criteria for "planned interactions," such as when a patient is invited to a meeting with the company or when employees attend professional events like scientific conferences where they are likely to meet with patients.

It also outlines criteria for "unplanned interactions," which include spontaneous encounters at charity events or in a public place. In these instances, UCB employees are encouraged not to seek personal health information and not to ask specific questions about a patient's identity or condition, unless the individual first engages the employee in those conversations. In those cases, the framework cautions employees should "use their best judgment."

Planned meetings must undergo a legal compliance check to ensure that the patient interactions do not violate regulatory rules in the patient's home country as well as in the country where the meeting is taking place. A formal contract with the patient is required to ensure that an individual's rights are protected in cases where his or her information is used by the company.

If a patient is asked to visit the company's office for a meeting, UCB employees are instructed to provide accommodations that might be necessary such as a place to rest or take medications.

The framework was published in the journal of *Therapeutic Innovation & Regulatory Science*.

"If the group is focused on research, then that's where we should be working with them. It doesn't make any sense to have a group who is focused on market access and a group who is interested in the basic science at the same meeting together because they will not be aligned and it won't be as productive," she said.

Finally, the need for capacity-building also extends to companies themselves, which need to hire or develop qualified patient leaders via internal education programs that teach employees how to engage with patients in a manner that is respectful, helps to build trust and is legally compliant.

UCB developed an instructional framework for its employees on how to engage with patients. The document provides a general overview of the types of approvals the employee must obtain and how the patient should be treated (see "Rules of Engagement," page 16).

WIN-WIN

Companies need to commit to meeting the needs of patients in ways that go well beyond clinical trials and the delivery of approved products.

Partnering with patients means working to meet their needs both within and beyond the clinical trial process. If industry expects patients

who are already taxed by the effects of their illness to contribute to the development of drugs — drugs which may not be approved in some of these patients' lifetimes or before they become irreversibly disabled — then sponsors need to make it worth their while.

There are many ways to ensure that patients benefit from their interactions with industry, and Back to School does not presume to have thought of them all. Here especially, sponsors must discuss with patient groups how best to meet their needs.

That said, public comments and the medical literature offer several thought-starters. These range from expanded access for patients who are not eligible for trials and cannot wait for drugs to be approved, to putting data in the patient's hands that they can use to manage their health.

Even when a sponsor designs its studies with the most liberal enrollment criteria possible and ensures its protocols and drug candidates are optimized to satisfy patient preferences, there still will be individuals who do not qualify for enrollment.

As BioCentury outlined in 2014, compassionate or expanded access should be granted to as many patients who are out of options and could benefit as possible, even if access cannot be provided to all of them. And when there are impediments to compassionate access, *all* the stakeholders have a responsibility to try to lift them.

The key to equitable implementation of expanded access is the creation of an independent third party that can make recommendations and provide a safe harbor for sponsors based on a dispassionate assessment of the facts. Public funding should be used when manufacturers do not have the means to provide treatment. And sponsors and regulators must apply themselves to devising solutions that will mitigate the risk that expanded access would slow or prevent approval.

If structured properly, expanded access can both produce generalizable knowledge and improve drug development. In the case of Josh Hardy, for example, FDA and Chimerix Inc. created a pilot trial of the company's brincidofovir that enabled the medicine to reach the boy and created a path to a registration study in a second indication.

Other approaches can be seen. For instance, expanded access for patients who don't meet enrollment criteria can be written into a study protocol from the start, making IRB review for each individual patient unnecessary.

Expanded access also is a way to care for patients who have no other options — including other clinical trials — when companies have to discontinue or deprioritize programs due to limited resources, rather than lack of safety or efficacy.

"It's simple to say we're doing patient-centric development, but it's harder to do because we are required to make choices of where is the best investment of our capital," said Deborah Dunsire, president and CEO of neurology company Forum Pharmaceuticals Inc. "I think it is incumbent on every member of the system to be caring for patients."

Johnson & Johnson has already started down the path.

In May, the company said New York University School of Medicine would establish the Compassionate-Use Advisory Committee (CompAC), an independent body to help evaluate requests from individuals seeking access to an undisclosed J&J drug candidate. The 10-member advisory committee includes practitioners, bioethicists and patient representatives, and the project could be extended to other unapproved candidates (see "J&J's CompACt," page 18).

ACADEMY FOR ADVOCACY

The European Patients' Academy on Therapeutic Innovation is providing patients with formal training about drug development and regulatory and reimbursement decisions with the aim of producing a cadre of well-informed advocates who are capable of partnering in pharmaceutical R&D.

The EUPATI Patient Expert Training Program consists of a 250-hour e-learning curriculum and 8-10 days of face-to-face training sessions, which takes about 14 months to complete. The curriculum covers six modules: discovery and planning of medicines development; non-clinical testing and pharmaceutical development; exploratory and confirmatory clinical development; clinical trials; regulatory, safety, pharmacovigilance and pharmacoepidemiology; and health technology assessment (HTA).

In the face-to-face sessions, participants receive instruction from academics, patient advocates, regulators and drug developers about how patient involvement can be integrated practically into the drug life cycle.

The program is provided free of charge, but participants have to pay for their travel.

Participants are tested at the end of each module. Once they obtain a pass rating of at least 70% in each module, they receive a certificate. According to EUPATI Director Jan Geissler, certified individuals may participate in patient engagement opportunities posted on EUPATI's website by 33 organizations, including 21 biopharma companies.

"They go back to their home countries and work on the national level to contribute to things like research agendas and how trials should be conducted," said Geissler, who is a cancer survivor.

Applicants must be patients, caregivers, or employees or volunteers of patient advocacy organizations. Criteria for participation also include residency in the European region, an interest in drug R&D, the ability to speak English and a commitment to apply the knowledge to increase patient representation and communication in the drug development process.

For its first session, EUPATI received 300 applications and accepted 50. The group now has its second class of 60 advocates in training.

EUPATI is in its fourth year of a five-year initiative sponsored by the Innovative Medicines Initiative (IMI). Geissler said the group has a plan to continue through 2017, but still needs to secure funding.

Beyond expanded access, sponsors also must meet their continuing obligations to clinical trial subjects in the period between a study's conclusion and the commercial availability of the drug.

For responders, sponsors should endeavor to provide continuing therapy through extension trials or registries that simultaneously allow the collection of longer-term data on safety, efficacy, quality of life and patient preferences.

When trials must include a placebo arm, and when the available data support exposure of additional patients to the investigational therapy, sponsors should seek ways to allow patients to cross over to treatment both as a way to increase participation and retention, and as a way to collect additional data.

For non-responders or progressors, the study protocol should allow timely unblinding of treatment assignment to the patient and his or her physician to inform the choice of follow-up care, including determining whether the patient is eligible for a different trial.

Such protocols are common. For instance, Tesaro Inc. used a mechanism that was included in the protocol for the Phase III NOVA trial of niraparib to unblind the treatment assignment for a patient whose ovarian cancer progressed during the study.

Disclosing the process for providing this information to patients when they enroll, and education about how and why studies are blinded, would help mitigate the risk that individuals might disclose their personal data in a way that risks unblinding the study.

While it is not standard practice to bind clinical subjects to confidentiality agreements, the prospect of assistance in identifying subsequent trials and follow-on care should motivate non-responders to keep their personal data confidential.

This assistance may best be managed via an independent third party funded by industry to provide case management and other services to patients who have participated in clinical trials. Such an organization also could collect data on subsequent treatments and patient preferences that could be fed back into a learning system.

Eisai Co. Ltd. has gone so far as to provide its epilepsy drug Fycompa perampanel to German patients for free while the company haggles with reimbursement authorities over price.

"Because we used placebo in Phase III, we cannot agree on a price," said Rami Suzuki, president and senior group officer in the company's global business development unit. "It is costing us quite a lot, as you can imagine. But we should be able to collect real-world data, and data on comparators."

In addition to unblinding for progressors, companies should return individual data to clinical trial participants. Even the Precision Medicine Initiative announced by the Obama administration in January does not have a comprehensive policy on returning the data to participants. Yet access to these data, even in raw form, would empower patients to participate more in the drug development process and to seek targeted therapies where they are available.

"Clinical data and genomic data ethically should belong to the patients, and pharma should have preferred access," said Suzuki.

"I think we will automatically get a higher level of patient engagement as we democratize that data," said Dunsire.

J&J'S COMPACT

Johnson & Johnson and New York University School of Medicine are testing a model for evaluating compassionate access requests via an independent third party. The medical school has established the Compassionate-Use Advisory Committee (CompAC) to advise the pharma on requests it receives for a single, undisclosed drug candidate.

CompAC is a 10-member group that includes physicians, bioethicists and patient representatives and is chaired by Arthur Caplan, director of the division of medical ethics at the school.

In a blog post discussing the pilot, J&J CMO Joanne Waldstreicher, and Amrit Ray, CMO of the Janssen Pharmaceutical companies of J&J, said CompAC "brings independent advice to further ensure that individual patient requests are evaluated in the most objective, fair and ethical manner."

CompAC will make recommendations to J&J on whether or not to provide access to the drug candidate, "including available information on the patient, the product and available drug supply."

Janssen's physicians will make the final decision on whether to provide compassionate access.

J&J said it modeled the program on its collaboration with Yale School of Medicine's Open Data Access Project, in which the school independently assesses public requests for access to the pharma's clinical trial data.

The goal is to create a process that is transparent and patient-centric. An important metric will be CompAC's ability to uphold the fair and equitable principles set out by the partners.

"When the pilot project ends, Janssen and the university will evaluate how well CompAC was able to meet these goals," the company said in a statement to BioCentury.

The initial partnership with NYU will run through year end, but if the CompAC pilot is successful, Waldstreicher and Ray said the pharma would expand the program "more broadly" across its clinical pipeline.

Another opportunity is for drug companies to support the development of disease-specific apps and other tools that help patients manage their disease, including helping them choose among different treatments.

Ideally, drug companies in a crowded disease category would join other stakeholders in supporting and funding patient groups to design and build the apps, thereby precluding the inevitable mistrust if just one company made a tool purporting to help patients choose among its own and competitors' drugs.

UCB's Dewulf suggested companies should pool their resources to develop a single solution, "because once you realize it's all about the patient, it makes sense to truly collaborate."

For all of the patient-centric approaches that industry and individual companies will devise, transparency about how companies will engage with patients, and how both companies and patients will measure the success of that engagement is crucial.

For example, UCB and the Parkinson's Disease Foundation are drafting a charter that will outline their shared goals, each party's commitment, and a work plan for a broad collaboration (see "Chartered Territory," page 19).

More broadly, drug companies should expect to track and report their goals for making patient-centered medicine a reality through a patient scorecard or similar vehicle. Increasingly empowered patient groups will be holding companies accountable, making it harder simply to pay lip service to patient-focused drug development.

"Industry needs to develop metrics to measure to what extent they are really involving patients. What percentage of your trials today involve patients in the design, what are your plans to change that, and how big will that percentage be in three years?" said EUPATI's Geissler.

In the age of social media, this kind of transparency will be essential to incenting patients to meet their own obligations in the process. Indeed, Back to School would remind patients that collaborating with drug developers, regulators and healthcare providers will result in faster, fairer solutions than viral campaigns that ultimately result in unequitable access to treatment only for those with the loudest megaphone.

GET TO WORK

Back to School does not suggest that embedding patient engagement in the medical product life cycle will be accomplished easily, or by drug companies acting on their own. It will require both collaborative and parallel efforts by sponsors, patients and their advocates, regulators, HTA bodies, payers and, most likely, entities that have yet to be created.

But it is in the drug industry's self-interest to expand nascent efforts to engage patients, ultimately to arrive at a more comprehensive, systematic and scientific paradigm that can transform everything from drug discovery and development, to approval and reimbursement, through to marketing and patient compliance.

Back to School has described four places where drug companies can amplify the patient voice to develop better drugs faster, while amassing a body of evidence of the benefits these products provide.

First, partnering with patients throughout the product life cycle will identify the unmet needs, generate data that patients will expect payers to support, and enable many more patients to participate in the process.

Second, advancing the science of patient preference research will enable drug developers to identify product characteristics that patients will endorse, increase compliance, and result in more compelling information being added to product labeling.

Third, equipping patient groups with sophisticated know-how about drug discovery, development, regulation and reimbursement will enable them to be more effective partners and equally importantly be effective advocates for the outcomes of patient-driven drug development to other stakeholders.

And fourth, committing to the needs of patients beyond the conduct of clinical trials will complete a virtuous circle of true patient engagement in the development of healthcare innovation and provide industry with the opportunity to create goodwill that it has squandered despite its remarkable innovations.

Adopting these approaches will require changing deeply ingrained industry practices, investing in new capabilities, and a willingness to comply with the rules of engagement to ensure that patients neither become nor are perceived to be mere industry mouthpieces.

It will require similar changes in the behavior of regulators, HTA agencies and payers, none of which have any less obligation to join with patients. Drug companies will need to be ready to sit at this big table, and indeed, advocate for these kinds of assemblies.

All of this will require significant investment. But the payoff will be a trove of information that will be used to improve product characteristics

CHARTERED TERRITORY

UCB Group and the Parkinson's Disease Foundation are developing a charter to align their expectations, goals and work plan for a new company-patient collaboration, which could serve as a template for future partnerships.

Chief Patient Affairs Officer Lode Dewulf said the partnership is broader than a specific trial or development program. "Basically, we will have something like a master partnership in place and then we can specifically engage around topics as they come up," he told BioCentury.

Dewulf said UCB needed clear guidelines on how to partner with patient organizations that addressed more than just the legal requirements. UCB and the foundation are therefore outlining what each party would like to get out of a collaboration to identify where their objectives overlap. They will write a charter around those shared goals, as well as a continuity plan to demonstrate each party's commitment to meeting the goals.

"Historically, patient organizations have had a lot of complaints about working with industry, that it wasn't a true partnership and that there were gaps in what each party thinks it can offer the other," Dewulf said. He added, "People in medical and commercial roles often move to a different job every two or three years, and patient groups can then feel like they have to start all over again to build a relationship with their new contact."

"We want to be really clear about what we want to accomplish, what is needed in our community and how we will deem it a success," said Veronica Todaro, VP of national programs for the foundation.

Once the charter is complete, UCB and the foundation will publish the document as a best practice.

UCB markets the PD drug Neupro rotigotine and has NPT200-11 in preclinical testing. NPT200-11 inhibits oligomerization of alpha synuclein (SNCA), a protein implicated in PD.

and trial designs and to develop evidence that drug companies can use to prove the value their products deliver to society. BC

The 23rd Back to School Commentary is a collaborative work led this year by BioCentury Editor Susan Schaeffer. It was co-written by Senior Editor Erin McCallister and includes contributions from Washington Editor Steve Usdin. The package was edited by Chairman & Editor-in-Chief Karen Bernstein, President & CEO David Flores and Managing Editor Jeff Cranmer.

COMPANIES AND INSTITUTIONS MENTIONED

Aegerion Pharmaceuticals Inc. (NASDAQ:AEGR), Cambridge, Mass.
Agency for Healthcare Research and Quality (AHRQ), Rockville, Md.
Amgen Inc. (NASDAQ:AMGN), Thousand Oaks, Calif.
Anthem Inc. (NYSE:ANTM), Indianapolis, Ind.
Biotechnology Industry Organization (BIO), Washington, D.C.
bluebird bio Inc. (NASDAQ:BLUE), Cambridge, Mass.
Canadian Agency for Drugs and Technologies in Health (CADTH), Ottawa, Ontario
Cancer101 Foundation, New York, N.Y.
Celgene Corp. (NASDAQ:CELG), Summit, N.J.
Chimerix Inc. (NASDAQ:CMRX), Durham, N.C.
Clinical Trials Transformation Initiative (CTTI), Durham, N.C.
Critical Path Institute (C-Path), Tucson, Ariz.
Cyclacel Pharmaceuticals Inc. (NASDAQ:CYCC), Berkeley Heights, N.J.
Cystic Fibrosis Foundation, Bethesda, Md.
Duke University, Durham, N.C.
Eisai Co. Ltd. (Tokyo:4523), Tokyo, Japan
EnteroMedics Inc. (NASDAQ:ETRM), St. Paul, Minn.
European Federation of Pharmaceutical Industries and Associations (EFPIA), Brussels, Belgium
European Medicines Agency (EMA), London, U.K.
European Patients' Academy on Therapeutic Innovation (EUPATI), Brussels, Belgium
European Patients' Forum, Brussels, Belgium
Express Scripts Holding Co. (NASDAQ:ESRX), St. Louis, Mo.
Forum Pharmaceuticals Inc., Waltham, Mass.
Friends of Cancer Research (FOCR), Washington, D.C.
GlaxoSmithKline plc (LSE:GSK; NYSE:GSK), London, U.K.
Google Inc. (NASDAQ:GOOG), Mountain View, Calif.
Icahn School of Medicine at Mount Sinai, New York, N.Y.
Innovative Medicines Initiative (IMI), Brussels, Belgium
Johns Hopkins Bloomberg School of Public Health, Baltimore, Md.
Johnson & Johnson (NYSE:JNJ), New Brunswick, N.J.
Karyopharm Therapeutics Inc. (NASDAQ:KPTI), Natick, Mass.
Medical Device Innovation Consortium (MDIC), St. Louis Park, Minn.
Merck & Co. Inc. (NYSE:MRK), Kenilworth, N.J.
The Michael J. Fox Foundation For Parkinson's Research, New York, N.Y.
Multiple Myeloma Research Foundation (MMRF), Norwalk, Conn.
National Comprehensive Cancer Network (NCCN), Fort Washington, Pa.
National Health Council (NHC), Washington, D.C.
National Institutes of Health (NIH), Bethesda, Md.
New York University School of Medicine, New York, N.Y.
Novartis AG (NYSE:NVS; SWX:NOVN), Basel, Switzerland
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Parent Project Muscular Dystrophy (PPMD), Hackensack, N.J.
Parkinson's Disease Foundation, New York, N.Y.
Patient-Centered Outcomes Research Institute (PCORI), Washington, D.C.
Patient-Focused Medicine Development (PFMD), Brussels, Belgium
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Pharmaceutical Research and Manufacturers of America (PhRMA), Washington, D.C.
Project Data Sphere LLC, Cary, N.C.
Society for Participatory Medicine, Newburyport, Mass.
The Synergist, Brussels, Belgium
Tesaro Inc. (NASDAQ:TSRO), Waltham, Mass.
Tufts University, Medford, Mass.
UCB Group (Euronext:UCB), Brussels, Belgium
U.S. Centers for Medicare & Medicaid Services (CMS), Baltimore, Md.
U.S. Department of Health and Human Services (HHS), Washington, D.C.
U.S. Food and Drug Administration (FDA), Silver Spring, Md.
Vertex Pharmaceuticals Inc. (NASDAQ:VRTX), Boston, Mass.
Yale School of Medicine, New Haven, Conn.

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