RARE Drug Development
2020 Report

THE POWER OF PARTNERSHIP
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Daniel S. Levine

August 2020
A Letter from the CEO

This year began with hope for the future and advancements in rare disease and the drug development process. But as the year has progressed and the global pandemic has grown, we have seen adverse impacts to our research and drug development efforts. While this has been disheartening, we are also finding this is an opportunity unlike any we have seen in recent memory to change the drug development process to benefit the rare disease community.

In June 2020 we held our annual RARE Drug Development Symposium in partnership with the Orphan Disease Center at the Perelman School of Medicine at the University of Pennsylvania. In this report we take a look at some of the key takeaways from our guest speakers. What has changed for the rare disease community? What opportunities do we have in this new drug development landscape? How can we be more inclusive in our research efforts and resulting clinical trials? Where are rare disease researchers and advocates finding hope?

The purpose of compiling this report is to provide you with insights for consideration as you move forward with your plans to pick up your research after the pandemic. We can all agree that the only way to make forward progress in rare disease is together. So whether you are an advocate, researcher, or member of industry, we urge you to seek each other out. Listen to one another about your needs, concerns, and ideas. And work together to push for lasting changes to the drug development process that will benefit people in all disease communities for decades to come.

Always in hope,

Kimberly Haugstad, MBA
CEO
Global Genes
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It has been a challenging year for rare disease research as the COVID-19 pandemic has halted or slowed projects and stalled clinical trials. The pandemic was top of mind as gene therapy pioneer James Wilson, director of the Orphan Disease Center at Penn Medicine welcomed participants in this year’s Rare Drug Development Symposium. “Scientists are hungry,” he said, speaking of the delays to studies imposed on researchers as a result of the virus. “There’s nothing worse than telling a scientist you can’t do science.”

In fact, the event was restructured because of the COVID-19 pandemic. Global Genes and the Orphan Disease Center at Penn Medicine decided that it would not be appropriate to conduct the annual RARE Drug Development Symposium in a live venue because of concerns it might expose attendees to infection. Since the event plays an important role in educating rare disease community members, fostering connections, and helping participants understand the role they can play in advancing the rare disease drug development process, the organizations didn’t want to cancel it. Instead, this year's symposium was held as an interactive, two-day event online June 11 and 12. This report provides an overview of the key sessions held during the two days.

The decision to proceed with the event reflected the critical role patient advocates play in advancing therapies for rare diseases. It’s a role that Wilson acknowledged as he discussed how rare disease organizations can drive preclinical research needed to reduce risk for pharmaceutical companies and attract investment needed to develop therapies for rare diseases.

“We need you. We need families. We need foundations committed to individual rare diseases.”
—James Wilson, Penn Medicine
“We need you. We need families. We need foundations committed to individual rare diseases, and you need to take the lead in moving the research bar forward,” he said. “The fact is that business models for developing rare disease treatments aren’t particularly strong, especially if the chance of success is low and the number of patients is not many. As communities, you need to be smart in what you invest in and establish the foundation of science that allows companies to proceed with investments with less risk.”

Susan Brisendine, vice president of engagement programs for Global Genes, told participants that the symposium is intended to help patient advocates explore their role in rare disease drug development and think about it in new and innovative ways. “Our focus continues to be shortening the diagnostic odyssey for families, increasing the number of diseases that have research in the pipeline, and improving patient outcomes. And how do we do that?” she said. “Well, first we need to understand challenges and barriers and access. We need to strengthen care coordination. We need to equip families and foundations with tools and resources, and we need to build data centric communities and organizations. We have to do that hard work.”

To do that, she said, patient groups, drug developers, and academic institutions are all collaborating. Collaboration, in fact, was a central theme at the conference, whether it was how to form collaborations, how to make them robust, or how to become better at it.

“We’re all collaborating to make an impact,” she said.
Chris Austin says he’s witnessed a transformation of fundamental science during his professional career, noting developments ranging from the Human Genome Project to the advent of induced pluripotent stem cells, which scientists can use as an unlimited source of any type of specialized cells in the human body.

Technology that once seemed to belong to the realm of science fiction today has become routine tools used by first year graduate students. But from a clinical point of view, Austin said there has not been that much change. In fact, he said, going to a doctor today is not that different than it would have been 30 years ago. Despite the ability to understand the biology of some diseases in detail, they still are without treatments.

“I’m a neurologist by training,” said Austin, who is director of the National Center for Advancing Translational Sciences of the National Institutes of Health. “The vast majority of the diseases that I took care of and could not treat 35 years ago, I take care of and cannot treat today, even though we understand them sometimes in exquisite detail.”

Austin, who delivered the keynote address at this year’s Rare Drug Development Symposium, discussed advancing translational research for rare diseases. He said the gap between our understanding of diseases and our ability to treat them is a “translational” problem that needs to be solved. Though he was long taught that if we understood the fundamental basis of human health and disease, treatments would follow, the reality is that has not happened.

While every patient wants a diagnosis—a name to put to their disease—more importantly, they would like a treatment for their condition. For most rare diseases—some 95 percent of them—there is not an approved therapy available today. The numbers are daunting. At the current rate we are going, he said it would take another 2000 years to get approved treatments for all rare diseases.

The problem is evident in the dramatic fall in productivity for the pharmaceutical industry over the past 70 years. The number of new drugs approved by the U.S. Food and Drug Administration per $1 billion invested

“I had this memorable conversation with a mom of a rare disease patient a number of years ago. We were discussing this problem of the research enterprise’s love affair with fundamental discovery alone, without translation. And she said, ‘I love basic discovery. I love papers. I love publications. But the fact is, when my daughter gets sick, I can’t give her a publication.’ And I think of that almost every day because that, to me, crystallizes the problem.”

—Christopher Austin, director of the National Center for Advancing Translational Sciences
in research and development on an inflation-adjusted basis has roughly halved every nine years since 1950. It’s an unsustainable model that drives mergers within the industry and leads to exorbitant prices for drugs.

“We cannot continue doing what we're doing and expect a different result,” he said. The translational process has been one of trial and error. If one in 10,000 compounds will successfully move from discovery to market and improvements are made that double efficiency, he does not believe we will be considerably better off.

“What do you get? One in 5,000? That, my friends, is not something to celebrate,” said Austin. “We need to have one in a hundred. We need to work on order of magnitude improvements. And science is the only way we're going to allow this.”

The answer for Austin lies in transforming the translational process—the process of moving from what's learned through observations and experimentation in the lab to a product that can benefit the health of a patient—from one of trial and error to a predictive science. And that means new ways of doing things—new methods, new technologies, new paradigms for people working together.

Austin said NCATS, which is focused on reengineering translational science, has developed a list of the major causes of translational failure. These problems are specific not to any one disease, but across the therapeutic discovery and development process for any disease. While Austin said we need to understand the translational process better, one essential change that is needed is to move from working on a single disease at a time to working on many diseases at once. “It's looking for commonalities among diseases—either at a genetic level, a cellular level, a symptom level—and working on them together so that you can compare and contrast and get insights very rapidly from one to the other,” he said.

Consider gene therapies, where adeno-associated viruses have become commonly used vectors for carrying corrective genetic payloads into a patient's cells. Gene therapy development is still performed one disease at a time. But unlike small molecule drugs, where companies can patent their formulations, genes can't be patent protected. Instead, companies have competed on the basis of the vectors used for carrying the gene to the cell. “That in our minds is understandable commercially, but silly medically,” said Austin.

Austin said NCATS had sought to figure out what could be done about this, particularly in the case of diseases too rare to garner investment from drug companies necessary to carry a gene therapy through development and to the market.

NCATS launched Platform Vector Gene Therapy, or PaVeGT, a pilot project that seeks to increase the efficiency of a gene therapy trial start up by using a standardized process with the same vector for multiple diseases. The program is developing four therapies using a single vector and plans to make the safety, toxicology, clinical trials, manufacturing, and other data public. The expectation is that this could cut the cost and the regulatory timeline for advancing a gene therapy to clinical studies by, in essence, having a plug-and-play vector that a researcher could use for a gene therapy for a small patient population.

“The market is responding. The problem is that the need is going up exponentially. If we're doubling capacity every three or four years, and we're doubling the number of trials every year, we are never going to catch up,” he said. “We can't build our way out of this problem. We have to increase efficiency.”
With the pandemic as a backdrop for this year’s Rare Drug Development Symposium, the response to COVID-19 provided a source for inspiration for discussions on the way biomedical researchers have embraced collaboration to find treatments for the virus. Though urgency and collaboration have been hallmarks of rare disease research, discovery, and development, the unprecedented efforts around COVID-19 had symposium participants wondering how to capture that same type of energy and willingness to remove barriers to cooperation as seen in response to the pandemic.

Chris Austin, director of the National Center for Advancing Translational Sciences at the National Institutes of Health, said he has long argued for the need for greater collaboration to tackle shared problems of drug development, but often has heard excuses from one group or another why this or that couldn’t be done.

“Almost overnight, the entire research ecosystem started working together as a single team. And what you’ve seen is incredible progress to the degree that the public is worried about the safety of these drugs, which I understand is because this is being developed so much faster and they think that shortcuts must have been taken,” said Austin. “I can tell you shortcuts are not being taken. It’s just all the stupid duplicative secrecy and tribalism and siloism that has gone away. And that has to be celebrated. It shows you how much more efficiency we can get if we just act the right way and we could do it tomorrow.”

For Austin, excuses will no longer work because drug developers and government agencies have demonstrated that the level of collaboration that we’ve seen around COVID-19 is possible. If they are not doing the same for rare diseases, he said the rare disease community should challenge them.

“Let me get this straight,” he said. “You are willing to do this for COVID, but you’re not willing to do it for this child with a rare disease? Are you kidding me?”
David Fajgenbaum, associate director of patient impact at Penn Medicine’s Orphan Disease Center, said the silver lining from the pandemic has been unprecedented data sharing and collaboration in response to the COVID-19, whether it is making every published paper on COVID-19 freely available to anyone and everyone, or researchers like him depositing data on resources available to others prior to submitting them for publication.

“There is sharing like I’ve never seen before. And what I hope we as a rare disease community can do is to say, ‘Wait a minute. If we can do this for a pandemic, I’ve got a child with a rare disease,’ or ‘I have a rare disease,’ or “There’s an entire community that has a similar sense of urgency,” he said. “We can push forward to make sure that this same sort of data sharing that we’ve done for COVID-19 occurs in the rare disease space.”

One learning from the experience is the shared sense of urgency people feel around COVID-19 that has helped to drive collaborations. Though rare disease advocates know that feeling of urgency, others outside the rare disease community don’t. One reason Austin said this has happened for COVID-19 in a way that it hasn’t for rare diseases in general is that the urgency that rare disease advocates feel is not one the public shares with regard to rare diseases.

The reason they don’t feel that is that they haven’t had a rare disease yet. They haven’t had a child born with a rare disease or had a diagnosis themselves. When that happens, people become transformed and become evangelists. He said we need to capture that sense of urgency people have felt around COVID-19 and get that same drive directed to rare diseases, many of which have greater morbidity and mortality than COVID-19.

“The community has learned that they can do this, and the world will not come to an end. They’ve learned that productivity really does skyrocket, and that’s a good thing,” Fajgenbaum said. “You need to play a big role in this and prevent us from going back to our old ways.”

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**Unprecedented Data Sharing**
Researchers, government agencies, and publishers are sharing data and collaborating in unprecedented ways.
- All published papers are open-access (LitCOVID)
- Preliminary findings are being shared on pre-publication websites (MedRxiv)
- Raw data being deposited for public use (GEO)

Let’s fight for similar data sharing for rare diseases!

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**A Sense of Urgency and Coordination**
Several public-private partnerships have been established to coordinate/delegate and prioritize research.
- Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV)
- Operation Warp Speed
- Institutional COVID-19 clinical trial review committees

Let’s facilitate similar urgency and coordination for rare diseases!

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**Focus on Drug Repurposing**
Given the urgency to identify treatments for COVID-19, many drugs are being repurposed against COVID-19.
- High-throughput drug screens, translational approaches, and AI-driven repurposing efforts
- CORONA project has identified >150 drugs in the first 20,000 published COVID-19 patients: CDCN.org/CORONA

Need to evaluate existing drugs hiding in plain sight!

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“We can push forward to make sure that this same sort of data sharing that we’ve done for COVID-19 occurs in the rare disease space.”
—David Fajgenbaum, Penn Medicine’s Orphan Disease Center
Onno Faber is a native of the Netherlands, a country where 60 percent of the population lives at least five meters below sea level. To prevent flooding, people construct water barriers around their homes. He noted for a single home, it would require four barriers with one on each side. A cluster of four homes arranged two by two would require eight barriers or two per home. Finally, a cluster of 16 homes arranged four by four would require 16 barriers, or one per home.

Founder and chairman of RDMD, a research platform for rare disease communities, Faber used the example as an analogy for the benefits of collaboration within the rare disease community, where he said he sees a lot of competition where collaboration would be the better option.

“Under the right circumstances, competition can make things better for everyone. This is how we shaped our society and our economy. The idea of competition is the best solution wins, but it’s predicated on each of the competitors having enough resources to generate a viable solution,” he said. “If nobody has enough resources to generate a viable solution to compete, we all end up with nothing. We have to be very mindful about what things we want to compete against each other and where we don’t want to compete.”

Faber spoke during the Rare Drug Development Symposium as part of a panel discussion on how to be a great research partner, along with Nan Doyle, R&D patient engagement lead for rare diseases at the pharmaceutical company Takeda; and L. Adam Sherman, research development and partnerships director for the International FOP Association.
Doyle said being a great research partner requires “seeing the world through the patient lens.” She said it’s important for pharmaceutical companies to make the effort to listen to patients and make medicines that are of true value to patients.

One way she said Takeda has done this is by not just thinking of patient engagement as something to do around clinical trials and approved products, but to push early into the discovery and development process to engage with patients.

“The gap that the company identified long before I joined was that in R&D we could do more to understand the patient perspective earlier than the time that something is in late-stage clinical trials and getting ready to be marketed,” said Doyle. “We can understand more about the patient experience. What’s it like to live with a particular condition, either as a patient or a care partner, especially if it’s a condition that Takeda doesn’t know much about and we’re not as active in it.”

She said what Takeda has learned from its various patient engagement activities is to set clear expectations for patients so they know what to expect during clinical trials, reduce the clinical trial burden on them, and take steps to share results from trials with patients and patient partners.

IFOPA’s Sherman said patient organizations and their representatives should appreciate that they are bringing a lot to the table in collaborations with drug companies. “This is really a give and take. And you give as a patient organization. You bring those patient points. You represent the patient community,” he said. “The more you can organize your community, and the more you can bring that forward, the more value you’re bringing to these researchers and drug developers.”

During the panel, the topic of natural history studies and the importance of patient control of them came up again as it had at other points in the symposium. Sherman urged the patient community to start thinking about treatment data from studies as community data and not sponsored data, especially in ultra-rare diseases where it’s difficult to run these studies, especially once there are treatments ongoing. That’s because it’s almost impossible to get people to participate in a long natural history study, which means the advantage goes to that first company that conducts that natural history study.

“If we, as a community treat this as the community’s data and not the sponsor’s data, I think it will [create] a little bit more pressure,” he said. “It’s in the best interest of the community to share this data. And if we want the best treatment for our patients, that’s the approach I think we have to take.”
The Power of Artificial Intelligence to Improve Drug Discovery and Development

It takes an estimated ten years and $2.6 billion to take a single drug through discovery and development to the market, but the use of artificial intelligence has the potential to dramatically improve the efficiency of drug development.

A panel of AI experts addressed the Rare Drug Development Symposium on how artificial intelligence and machine learning is reshaping the drug development process from discovery through development.

Annastasiah Mhaka, co-founder of the Alliance for Artificial Intelligence in Healthcare, said more than 200 companies are applying AI to the research and development process to make it faster and cheaper while delivering more new medicines. Mhaka said AI can yield population-level insights by drawing from electronic health records, lab tests, and a range of real-world data. It can also pull from medical, scientific, and business intelligence to generate hypotheses to improve drug discovery by drawing from multi-omic datasets, phenotypic screening, and data on the interaction of drugs on multiple targets. In addition to helping discover new therapies, AI is also being used for clinical development, identifying patients for enrollment in drug trials, measuring results, and monitoring patients.

“While I am a huge advocate for AI, I see it as a tool, and research and patient advocates should also view it as such,” said Mhaka. “Ask the question first, and then find the right tools for it. AI is just one piece of the longer story, and sometimes there are tools that are better suited.”

Swagatam Mukhopadhyay, chief scientific officer of Creyon Bio, said AI can help understand complex biological systems by approaching drug discovery as an engineering problem. Creyon is seeking to make precision medicine on demand by using AI to help design oligonucleotide therapies targeted to a patient’s genetic condition.
Mukhopadhyay said while there has been a significant increase in understanding genetic drivers of disease—there are some 4,000 genes that have strong associations with rare diseases. Nevertheless, the number of new drugs approved each year is around 60.

While oligonucleotides are promising because of their ability to regulate gene activity, there are challenges in engineering them so they are not toxic and can be delivered to their desired target and optimized.

“We have a unique vision. We want to engineer, eventually, new personalized medicine immediately following diagnosis. That's our goal. That's our vision.”

On the clinical side, AI is being used to improve the time and cost of clinical studies. Harsha Rajasimha, founder and CEO of Jeeva Informatics, said what he heard from rare disease stakeholders was that every time a clinical study is undertaken, it feels like the first trial undertaken by mankind. They face recruitment problems, in part due to the burden on patients who participate, particularly because of difficulty traveling and the number of site visits needed.

Jeeva is using digital health technologies to minimize the need for clinical trial participants to make site visits. Instead, Jeeva relies on smartphones and other mobile devices that can be used to connect the patient to the investigator and collect data.

He said while there is a lot of hype around AI and machine learning, there is a limited amount of data today that combines genomic sequencing and behavioral data and social determinants of health and the environmental factors that are gathered in a way that they can be queried and made use of using AI models. He said what is needed is good quality data.

“AI is not going to replace drug developers, but drug developers who use AI will soon replace drug developers who don’t.”
—Harsha Rajasimha, Jeeva Informatics

Rajasimha said the traditional way of having patients visit brick-and-mortar trial sites is changing, but regulatory barriers around telehealth and other barriers, from the way participants are pre-screened for eligibility to patient reported data, are slowing the transformation.

The other thing that is needed are validated tools that can address different types of clinical trials. What works for a small molecule will not necessarily be appropriate for a cell or gene therapy trial. Jeeva is developing technology that can aggregate and track data from past clinical trials to provide continuous learning to improve the efficiency of the next trial.

“AI is not going to replace drug developers,” he said, “but drug developers who use AI will soon replace drug developers who don’t.”
When Nasha Fitter’s daughter Amara was seven months old, she began having seizures. Soon after that, she was diagnosed with FOXG1 syndrome, a rare, genetic neurodevelopmental disorder. Fitter, co-founder, CEO, and head of research for the FOXG1 Research Foundation, set out to do what she could to help find treatments for her daughter’s condition.

During the Rare Drug Development Symposium, she joined David Rich, vice president of global development of rare diseases for Ipsen Biopharmaceuticals, for a fireside chat to discuss what patient communities can do to drive better understandings of their diseases and help speed the translation of research into new therapies. For both Fitter and Rich, natural history studies are a starting point. These studies provide a critical way of understanding how a disease emerges and progresses over time in a population.

“We need to, ourselves, understand our disease better so we can, as we’re waiting for therapies, make better day-to-day decisions for our children. What medications should we give? What are we going to experience? Giving the control to us to really understand our disease.” said Fitter. “I had a great mentor, a CEO of a biotech company, who told me early on that if you do nothing else, just get a natural history study done. That will attract biopharma to your disease.”

Fitter said that it’s important for patient advocacy groups to make sure that they have full control over natural history studies. While biopharma companies may offer to pay for a natural history study, it won’t serve patients’ needs in the long run. By maintaining control of the studies, patient groups can allow multiple biopharmaceutical companies to access that data.

Another reason for the importance of patient groups maintaining control over natural history studies is the problem of patient burnout. “Once a patient enrolls in one study, there is a slim to none chance of them enrolling in a second one. In our rare communities, that’s a real threat,” said Fitter, who recommends the use of open platforms. “We have so few patients to begin with. It’s important that you choose platforms that are patient-controlled, advocacy group-controlled, and multiple parties can access the data.”

As part of those efforts, Fitter said including patient-reported outcomes are important, but she warned the U.S. Food and Drug Administration will take few
patient-reported outcomes seriously when it comes to drug submissions. Because of that, it’s important to collect medical records and clinician-reported outcomes, which the FDA will validate and use. As such, Fitter recommends platforms that allow for the collection of both.

One other important step is finding a principal investigator for the natural history study, such as a geneticist. “My recommendation is to find someone who’s young and hungry,” she said. “You don’t have to get a famous geneticist that everyone is trying to get a call with. You just need to get someone who’s good, who wants to make a name for themselves, and who is going to invest in your disease.”

Ipsen’s Rich said when his company began working on the rare bone disease fibrodysplasia ossificans progressive, the first thing the company did was start a natural history study. In addition to the importance of the data gathered in the study, he said it allowed the company to start building a network of patient advocacy groups and clinical centers with which to work.

“We have to be able to then prove that it’s a clinical benefit to the patient,” Rich said. “That’s why having patient involvement and advocacy group involvement in designing what endpoints you collect is important. What we need to do is not just report on the endpoints and showing some significant benefits in respect to those, but that it makes a positive difference in terms of a clinical benefit to the patients as well.”

“Without a natural history, you don’t know those types of aspects that are centrally important to these rare and very rare diseases,” said Rich. “Why that’s important is because if you want to start a drug study, you need to know what you’re going to be looking for, what you’re going to be measuring and counting.”

He notes that in some cases, regulatory agencies may allow the use of a natural history study as comparative data in a clinical trial as an alternative to using a placebo control. The studies can also be valuable to drug developers and regulators for identifying endpoints for clinical trials of experimental therapies and help validate their significance to patients.

“Without a natural history, you don’t know those types of aspects that are centrally important to these rare and very rare diseases.”

—David Rich, Ipsen Biopharmaceuticals
Representatives of drug companies advancing innovative therapies to treat rare diseases offered a view into the different ways their therapies work; but regardless of the modality of a therapy, what they shared in common was the role the patient voice played in shaping their programs.

Anita Hill, vice president and lead for global medical affairs in hematology for Alexion Pharmaceuticals; Katherine Beaverson, senior director and patient advocacy lead for the rare disease research unit of Pfizer; and Pushkal Garg, chief medical officer for Alnylam Pharmaceuticals, addressed the Rare Drug Development Symposium and discussed how their companies have embraced the voice of the patient.

Alexion’s Hill discussed the company’s efforts to develop targeted therapies for paroxysmal nocturnal hemoglobinuria (PNH), an ultra-rare condition in which the body’s immune system destroys red blood cells, which in turn can result in progressive anemia, fatigue, dark urine, and shortness of breath. The condition can cause the formation of blood clots, which can damage vital organs and cause premature death.

Alexion has developed therapies to inhibit part of the immune system known as the complement system, which prevents activation of the process that destroys the red blood cells in the condition. While she said the company was able to improve survival, it has continued to work on improving therapeutic options for patients by listening to patients about quality of life issues. It’s been able to extend time between dosing by moving from IV infusion every two weeks to every eight weeks, and improve the concentration of the drug to shorten the time it takes to infuse a patient. It also developed a subcutaneous injection to give patients more independence, and is working on a possible oral tablet.

“We have huge learnings from the registry, and this is an enormous way that patients contribute to future developments.”

—Anita Hill, Alexion Pharmaceuticals
“Patients have a huge role to play in the global PNH registry. We have huge learnings from the registry, and this is an enormous way that patients contribute to future developments,” said Hill. “I hope that it shows that through the partnership among all of us—the industry, the physicians, the scientists, the patients, and organizations for those patients—allows us not to become complacent and always strive to improve the care for patients with rare diseases.”

Pfizer’s Beaverson discussed the company’s efforts to develop a gene therapy for the rare and progressive disorder Duchenne muscular dystrophy and some of the challenges inherent in developing a gene therapy, but she also talked about how the company has worked with the Duchenne patient community.

She said the patient community can have a profound impact on clinical development strategy, protocol designs, and patient recruitment. With regards to Duchenne, Pfizer worked with the patient organization Parent Project Muscular Dystrophy to explore preferences and risk tolerance for emerging gene therapies. It has also worked with the Jett Foundation to study the burden of illness and current treatments and to define treatment goals by assessing what matters most to patients. And, it is working with a multi-stakeholder collaboration led by Duchenne UK called Project Hercules, to help educate payers on the condition and develop a model for determining the value of innovative therapies.

“Those patient voice meetings were incredibly influential. I can't overestimate how critical it was for drug developers and regulators to hear the patient perspective. What are patients going through?” he said. “Many of these diseases that we’re talking about, most physicians, most regulators have never heard about, certainly not seen a patient with these diseases. There’s nothing like seeing and hearing from the voice of a patient, or a caregiver, or an advocate, what the patient has experienced. What is it like? What is the burden of that disease? How does it affect their day-to-day life?”

Pushkal Garg, chief medical officer for Alnylam Pharmaceuticals, discussed the company’s RNA interference, a class of therapies that work by disrupting the process of translating a gene’s coding into the production of a protein involved in a disease state, such as the company’s drug Onpattro, which is used to treat hereditary transthyretin-mediated amyloidosis and rare and progressive liver disease.

He said the patient voice meetings were “incredibly influential” in developing the drug and noted that there's been a sea change in how drug developers think about incorporating the patient voice in their work.
patient advocate participating in this year’s Rare Drug Development Symposium noted the drama, competing factions, and lack of trust that existed within her small patient community and wanted to know what she could do to overcome that.

Christian Rubio, vice president of strategic advancement for Global Genes and moderator of the event’s closing session, noted that it was the type of question we get too often. He said many people in the rare disease community find themselves in the same position and he asked the panel what an individual might do to make a difference and build relationships?

“‘There’s a lot of diversity within some of these disease communities.’”
—Katherine Beaverson, Pfizer

Katherine Beaverson, senior director and patient advocacy lead of the rare disease research unit at Pfizer; Jeremy Levin, chairman and CEO of Ovid Therapeutics; and David Fajgenbaum, associate director of patient impact at Penn Medicine’s Orphan Disease Center shared their thoughts on what patient advocates could do to foster collaboration.

“We look at communities as one, but there’s a lot of diversity within some of these disease communities,” Beaverson said. “While we would love everyone to be speaking with one voice, sometimes that’s not possible, but every voice does matter.”
David Fajgenbaum, who is also co-founder and executive director of the Castleman Disease Collaborative Network, said no one can do this work alone.

“There is not a single scientist or patient or advocate in the world that can do this on their own,” he said. “I don’t think that anyone should feel like they can’t make a difference, but they should realize that they can make a difference if they connect with the right people and if they create a team.”

Fajgenbaum said he would have made a fraction of the progress that’s been achieved in Castleman’s disease, a rare autoimmune condition that nearly robbed him of his life on multiple occasions, had he been working on his own. He discussed the need for patient advocates to align themselves with other patients, researchers, or physicians and find ways to join together to move forward.

He noted that within Castleman’s disease there were two foundations before his organization started. Rather than creating a third organization, he said, the existing organizations came together.

“That’s been really critical for us,” he said. “I encourage all advocates to recognize we can’t do this alone.

We have to do it together and to do it together, we do need to work together as one.”

Levin said with any group of people, there will be diverse views. Even in a small community, individuals will have a different perspective. His advice was instead of looking for big changes, build on incremental ones.

He said throughout his career he has had to work with people he may not like or who did not share his values, but he nevertheless needed to build a relationship with them. The way he did that, he said, was by finding something small he could build on.

“When you’re building a base of individuals who’ve got a similar disorder, a similar suffering, there has to be something there,” he said. “I urge you to find it because they may be scared. They may be angry. They may be frustrated. They may be egotistical—all of the above. But at the end of the day, they have the same issue that anyone in that group has, which is getting to improve their situation. And you can start building on something small, and then take something a little bigger after that. I absolutely believe in building blocks.”
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