



**RARE DRUG**  
**DEVELOPMENT SYMPOSIUM**



#RDDS



# RARE Drug Development Symposium 2022

**Collaborate to Accelerate**

# A Letter from the CEO



There are more than 10,000 rare diseases, and less than 5 percent have an FDA approved treatment. The discovery of new rare conditions continues to outpace the approval of treatments for known rare conditions. Many are ultra-rare or even N-of-1 conditions, which makes the odds of an academic researcher or industry pursuing drug development in these disease areas extremely low.

The burden to generate interest, funding, and progress toward treatments therefore often falls on caregivers, patients and communities, who simply can't wait for others to get around to it. These innovative and resourceful leaders have moved themselves to the center of drug development efforts and, in some cases, have become drug developers themselves.

Global Genes, in partnership with the Orphan Disease Center of the University of Pennsylvania, held the seventh annual RARE Drug Development Symposium 2022 in Philadelphia in June. The event brought together rare disease advocacy leaders, industry representatives, researchers, and other stakeholders to share their insights, learn how to collaborate better, and discuss ways to accelerate the development of much needed therapies for people with rare conditions.

The event was specifically designed to focus on exploring and identifying solutions via a multi-stakeholder, workshop-based process. We view the gathering of insights from experts in collaborative forums as an essential component of what Global Genes and partners like the Orphan Disease Center can and should do to help enable and equip patient-led drug development efforts.

Our goal is to ensure advocates and early-stage entrepreneurs have the tools, knowledge, and guidance they need to increase their chances for success and accelerate the time it takes to move from envisioning a therapy to treating patients.

A handwritten signature in black ink, appearing to read "D. Craig Martin". The signature is fluid and cursive.

D. Craig Martin  
CEO  
Global Genes

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## Finding a Common Cause

**One of the unique dynamics about rare disease is that oftentimes it's an individual caregiver, parent, or advocate, who out of necessity, takes up drug discovery and development. In many instances, those individuals or patient groups come to the task without existing expertise, but that doesn't dissuade them.**

Global Genes, in partnership with the Orphan Drug Center of the University of Pennsylvania, organizes the RARE Drug Development Symposium to give patient advocates and organizations an opportunity to learn about the drug discovery and development process, how they can cost-effectively advance research, attract partners, and learn from others who have gone before them to increase their odds of success. The event brings together rare disease advocacy leaders, industry representatives, researchers, and other stakeholders.

After the COVID-19 pandemic necessitated a virtual conference in 2021, this year's event returned to being held as an in-person meeting in Philadelphia in June. It featured a pair of panels and a series of speakers but broke from the format of past years by centering on a series of four workshops through which participants rotated during the

two-day symposium. These workshops focused on disruptive innovations in clinical trials, the use of AI to transform drug discovery and development, emerging models for partnerships, and how to accelerate progress through successful collaborations between stakeholders. Subject matter experts framed the workshop for participants, but these were interactive sessions that required a high level of participation and interaction from all attendees as they sought to consider opportunities and challenges, as well as share learnings from their own experiences and seek guidance on how they might address issues they face.

High costs and extended timeframes have long characterized drug development, but therapeutic development for rare diseases has faced additional obstacles including small patient populations that reduce the economic incentives for drug developers, limited understandings of the natural history of these diseases, and the potential difficulty of enrolling adequate numbers of participants in a clinical trial from a small and geographically dispersed population.

Progress in rare disease drug development has often depended on patient advocates laying the groundwork necessary to identify



patients, establish registries, engage researchers, collect data and biosamples, fund discovery efforts, and take other steps that de-risk the development of a therapy to entice a pharmaceutical company to pursue it. As patients have grown more sophisticated about the drug development process, tools for scientific discovery have become more accessible, and the ability to unravel the molecular mechanism underlying diseases has advanced. As a result, advocates have been able to act on the urgency they feel to catalyze research, drive it forward, and take a more hands-on approach when others are unwilling to do so.

The goal of the symposium was to identify steps advocates can take to accelerate drug development in rare disease by understanding the needs of researchers, industry, and regulators and how they can remove barriers to engage needed collaborators. It was also an opportunity to share expertise, knowledge, and ideas as to how to improve upon the



drug development process to get more treatments to patients, collaborate around common needs, and learn from each other's experiences.

Given the critical role collaborations play in the process of rare disease drug development, much of the discussion centered on the human dimension of engaging potential partners, thinking in terms of the incentives that drive stakeholders in drug development, and the importance for advocacy organizations focused on the same rare diseases to set aside differences they may have and work together to advance their common cause. ■





## Accelerating Rare Disease Research

**There have been centers around the world that treated patients with Castleman disease and gathered medical data and biosamples, but there was no process for physicians and researchers to share what they collected about the rare, auto-immune condition.**

David Fajgenbaum, assistant professor at the University of Pennsylvania's Perelman School of Medicine and co-founder and president of the Castleman Disease Collaborative Network, spent several years struggling to find ways to get academic institutions to share their data and samples to advance treatments for the condition.

"It was hard to get agreements between academic institutions. We couldn't persuade a lot of researchers to share their samples in part because those samples served as assets for writing grants and for being the leading experts in the field," he said. "We still try to facilitate that but at a certain point we realized maybe we should just go directly to patients. That's where we created a registry and a biobank where patients consent directly to our organization."

By working directly with patients, the Castleman Disease Collaborative Network eliminated the medical system researchers from that process of gathering samples while making the samples it gathers freely available to scientists. What's more, by giving those samples and data to researchers, Fajgenbaum said it has made the community more collaborative as

it has made others holding samples and data a bit more willing to share since the organization is sharing with them.

Fajgenbaum's comments came during an opening panel at the RARE Drug Development Symposium 2022. Global Genes held the event in partnership with the Orphan Drug Center at the University of Pennsylvania. Paul Howard, senior director of Public Policy for Amicus Therapeutics, and Carla Rodriguez-Watson, director of Research and Innovation in Medical Evidence Development and Surveillance Program at the Reagan Udall Foundation for the FDA, joined Fajgenbaum for the discussion. Rodney Samaco, assistant professor at Baylor College of Medicine and board chair of the RARE Drug Development Symposium Advisory Council, moderated the panel.

Fajgenbaum nearly died five times in a six-month period because of his Castleman's disease. In fact, a priest administered him his last rites at one point as he was not expected to survive the night. As such, like many rare disease advocates, Fajgenbaum understands the urgency rare disease patients and their families feel in pursuing needed therapies. The panel discussion focused on keys to accelerating rare disease research and ways advocates might be able to shorten the historically long path to move from discovery to treatment of patients.

Amicus Therapeutics' Howard said patients are being encouraged to take control of their own data

but said they should also demand that others who hold their data be more transparent about how it is being used.

“We have an obligation to tell patients what we’re doing with the data, report out routinely on the data uses and data quality, and be more transparent about that. Hold the rest of us accountable and ask us, ‘What are you doing with my data? How are you sharing my data?’” said Howard. “As we’re asking more and more questions and want to do more and more things with the patient data and specimens we collect, we have more and more of an obligation to be transparent and ethical in how we use that data.”



**“We need to think of better business models. We need to align the incentives that encourage data sharing and high-quality data generation.”**

— Paul Howard

Howard said one of the more difficult conversations at Amicus centered on a promising program for the rare connective tissue disorder epidermolysis bullosa that failed in a late-stage clinical trial.

“We thought we had something, and it turned out that we didn’t. Our response to that was to convey as much information as we could about what we did and what we learned in the hopes that regulators, other companies, and the patient community could learn from the trial,” he said. “There’s no such thing as a failed trial. You learned something. You collected some data. You now have a better understanding of the natural history of the disease.”

Amicus published a peer review paper, presented posters, met with patient partners to explain what it learned and why it was ending the program, and shared the data with other companies working to develop therapies to treat epidermolysis bullosa.

“Part of our culture is to be as patient-centric as possible,” said Howard, who noted Amicus founder and CEO John Crowley has two children with the rare lysosomal storage disorder Pompe disease

and knows the pain families go through. But a lot of the silos that exist, he said, are the result of a lack of incentives and clarity about the “why.” The “why,” he said, “is that we can advance science faster if we do it in common and hold less information [for ourselves].”

“We need to think of better business models. We need to align the incentives that encourage data sharing and high-quality data generation,” said Howard, who noted physician sites often don’t have the funding to gather retrospective data and curate it. “What kind of tools can we create? What kind of new business models can we create so we can make it easier for everyone to access and curate

highly tractable, valuable data to potentially allow a lot more clinical trial sites to enroll patients.”

Fajgenbaum offered how his organization was able to capitalize on a storehouse of

data and biosamples when an employee at Janssen Pharmaceuticals, the producer of siltuximab, the only U.S. Food and Drug Administration approved therapy for Castleman’s disease, let him know that the company had collected a large number of blood and lymph node samples from patients with the condition as part of its clinical studies and the samples were in a freezer.

“This colleague at Janssen didn’t have to tell me about this. He knows who I am, and he knows that if you tell me that, I’m going to break down the walls of Janssen to get my hands in those samples,” he said. “He could have not shared that, but he did. And once I learned that there were these samples it started what ended up being about a two-year process.”

The Castleman Disease Collaborative Network, along with the University of Pennsylvania and seven other academic institutions, put together a study to leverage the samples. Patients had already consented for their use. The study measured 1,300 proteins in the blood of all of these patients and that led to the discovery of a biomarker that can predict who’s

likely to fall into that one third of patients who benefit from siltuximab and who's not likely to respond. It also helped identify a novel therapeutic target for patients who don't respond to siltuximab and showed they could benefit from a JAK inhibitor. A couple of weeks after researchers completed the study it led to the successful treatment of a severely ill Castleman's disease patient and that work is continuing to save lives today.

"A number of patients who were part of that trial are no longer alive. The final remaining opportunity that those patients with this disease had to make a difference for future patients were sitting in those freezers and those samples from those patients who are no longer here are helping patients who are alive today," said Fajgenbaum. "That is a concept that I think is important. Whether you're in the pharmaceutical industry, academia, or advocacy, we should work to unlock those samples."

Beyond that, though, Fajgenbaum notes the incentives in the current academic system discourage the sharing of data and hamper potential to accelerate research around rare diseases. One of the challenges is that academic research centers give tenure based on the number of first and last author publications. If 10 researchers combine their data together, there might be great insight generated by that collaboration around different data sets, but there can only be two first and two last authors. Six of those contributors are going to be middle authors, and not get the recognition with their academic research system that they need to gain job security and advance in their careers. That's a problem, he said, that needs to be fixed.

Reagan Udall Foundation's Rodriguez-Watson said because patient populations for rare diseases are small, one way to accelerate research is to look across conditions for common phenotypic features. For instance, she said, there are many autoimmune diseases. Ramping up a trial for just one would be challenging, but a different study design approach, such as a basket trial, could increase the sample size and allow researchers to explore what

common surrogate markers exist among them to provide a faster path to determining the safety of experimental drugs.

She encouraged symposium participants to look for cousin diseases with greater prevalence to identify diverse stakeholders within industry, patient organizations, researchers, data aggregators, and health-care delivery systems to provide different kinds of data sources.

"Get together and understand what are those? What's the precompetitive space? What are the biomarkers you need to understand? Do you need to better describe the disease? Better identify important outcomes that are traditionally collected," said Rodriguez-Watson. "Get to work, develop those outcomes, and work on the precompetitive stuff so that a rising tide lifts all boats."

**"Get to work, develop those outcomes, and work on the precompetitive stuff so that a rising tide lifts all boats."**

**— Carla Rodriguez-Watson**



Fajgenbaum noted that Castleman disease shares commonalities with both cancers and autoimmune conditions. He said for every rare disease, there's typically a cousin disease that's more common, but related in some way.

When the Castleman Disease Collaborative Network did its proteomics study from the Janssen samples, it also pooled together a group of samples from groups of patients with Hodgkin lymphoma, rheumatoid arthritis, and HIV. Castleman disease is heterogenous. What the researchers found was that patients who had proteomic profiles most similar to the Hodgkin lymphoma patients responded best to an interleukin-6 blocker. Patients who had a protein profile most similar to rheumatoid arthritis patients were most likely to benefit from a JAK inhibitor.

Howard noted that "Mother nature is lazy," saying that once she finds a pathway that works, she tends

to keep using it. He said in rare conditions, such as CNS diseases, there may be common symptoms that affect core clinical features of the disease, such as gait, sleep, speech, tremors, and seizures. He said there are a set of tools, such as wearable sensors, that can help us understand the phenotype back to

the genotype and recognize those shared symptoms and develop a better understanding of the natural history of the disease.

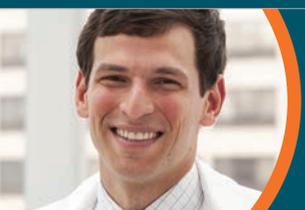
“That,” he said, “can help us tease out those profiles and look for commonalities.” ■

## The Fastest Way to a Therapy Can Be an Old One

When David Fajgenbaum was a medical student, he became severely ill, and physicians diagnosed him with the rare autoimmune condition Castleman disease. On several occasions during an extended stay in the hospital, he nearly died.

prevent organ rejection in people who received kidney transplants, targets mTOR. Though the drug had been available for about 50 years, no one had ever thought to try it for Castleman disease. Fajgenbaum became the first Castleman disease patient to use it and it put him into remission.

extremely limited, repurposing drugs can provide a faster and cheaper route to a treatment that is safe and effective since there is extensive understanding of the safety of a drug and its mechanism of action. It's a strategy with the potential to discover treatments for the disease for which there are no U.S. FDA approved therapies.



**“An existing drug at my neighborhood pharmacy was there for years while I was in an ICU. It is saving my life.”**

— David Fajgenbaum

“I knew that the only way I could survive is if I could figure out what was going wrong in my immune system and then see if there was a drug that was already FDA approved or something else that we could try against my disease,” he said.

Fajgenbaum, who is now an assistant professor at the Perelman School of Medicine at the University of Pennsylvania and co-founder and president of the Castleman Disease Collaborative Network, became his own research subject. After much work and a number of failures, he found that a part of his immune system known as the mTOR pathway seemed highly activated. The drug Sirolimus, which had long been approved to

“I am alive today because of a repurposed drug. I recognized and learned pretty quickly that I didn't realize the potential for drug repurposing, and I realized a lot of other people didn't either,” he said. “An existing drug at my neighborhood pharmacy was there for years while I was in an ICU. It is saving my life.”

Repurposing, the use of a drug approved for one condition and finding another one in which it works, is not a new idea. In fact, some widely used drugs from aspirin to Viagra are used to treat conditions for which they were not originally developed. In the case of rare diseases, where time and money to develop much needed therapies can be

Fajgenbaum said the key to drug repurposing is to gather as much data as possible to understand what common mechanisms might be shared across diseases and then to think about ways to test whether a given drug developed for one condition could be used in another. If a repurposed drug is used in a patient, Fajgenbaum said it is essential to collect data about how it worked to learn from it.

Despite the promise of repurposing drugs, he noted there are obstacles that prevent the full potential of the strategy. Because of systemic barriers, drug companies often choose not to pursue repurposing. With about 90 percent of all approved drugs already generic, drugmakers have little incentive to conduct expensive clinical trials to establish proof of a new use for a drug if they will not be able to recoup that investment and profit from their work. ■



### Strategic Initiative - Alliance Organisational Structure

Organisational structure will be updated per each workflow, however, the goal is to have all five voices present during the pre-Consortium.



## A Framework to Move from Idea to Patient

**Maryna Kolochavina has had unusual visibility into the rare disease drug development process. She's been involved in lifecycle management for more than 220 rare and orphan medicinal products and advanced therapies in 44 therapeutic classes with more than 440 orphan drug designations. She said even though the companies, diseases, and drugs on which she has worked were all different, the problems remained the same.**

Kolochavina set out to deconstruct the rare disease drug continuum by studying 600 rare disease medicines approved prior to July 2021 and took a comprehensive look at what happened to the products starting from preclinical development through the approval process and pricing and reimbursement. She identified 1035 processes and broke them down into 12 workflows.

Those 12 workflows have laid the groundwork for a collaboration led by Kolochavina and the Critical Path Institute to create a framework to standardize and accelerate the development, approval, and access to rare disease therapies. The 5-Voices Pre-Consortium brings together more than 200 stakeholders from across the ecosystem. Those five voices—patients, industry, funders, regulators,

and payors—represent the people who are making decisions about the strategy and development of how a drug goes from idea to the patient.

“Unless we solve the problem, unless we find a way to make the process more predictable in these 12 workflows, we will keep solving it again and again and again,” she said during a presentation at the RARE Drug Development Symposium 2022.

Kolochavina said every drug company has a stakeholder map that it uses to determine when and how to approach each stakeholder during its progress

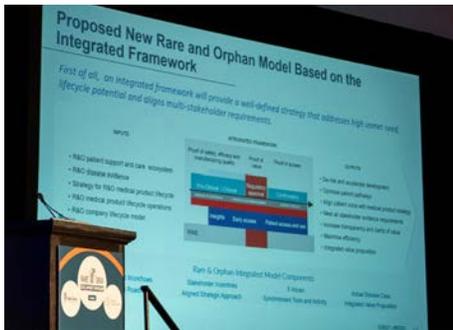
**“Any attempt to bring the patient to the center will fail because the current framework doesn't allow it.”**

— **Maryna Kolochavina**



with a medical product. When she studied 220 stakeholder maps, she said she came to understand that the patient is not in the center of the process.

“Any attempt to bring the patient to the center will fail because the current framework doesn't allow it,” she said. “Then I started to think about how to change it.”



Kolochovina surveyed 100 people in her network from regulatory, medical communities, small and medium biotechs, funders, and payers and they all said they had the goal of getting treatments to patients. What surprised her was that while they all shared a common goal, each had a different way of doing that.

**“Unless we solve the problem, unless we find a way to make the process more predictable in these 12 workflows, we will keep solving it again and again and again.”**

— **Maryna Kolochovina**

Her ambition is to create a flowchart that captures the roles and responsibilities for each stakeholder for every step across the rare disease drug development continuum. For instance, a patient organization may be able to begin by looking at an evidence card when it sets out to create a patient registry and

understand its responsibilities and the process for collecting the data. This would include how to maximize the value of the evidence it collects and when to meet with regulators. It would also highlight pain points for various stakeholders around this step of the process, the experiences various stakeholders

have had with this step, and the opportunities for improvement. The 5-Voices would do that for each stakeholder and each step along the entire lifecycle of a drug.

“What I understood is that if I find a way to harmonize this process between stakeholders, I will make this process more predictable,” she said. “What is the process for regulators? What is the process for payers? How do they work? How do they use the patient voice in their decision-making? If I find a way to do this, by default, I’m putting the patient at the center.” ■



## To Innovate Clinical Trials, Focus on Human Behavior

**Clinical trials for rare disease drug development face several well-known challenges that grow out of the reality that these studies involve small patient populations. Disease natural histories may not be well understood, patients may be difficult to find and geographically dispersed, and notions of statistical significance may be difficult to apply.**

Though most people think of disruptive innovation as being driven by new technologies, trial structures, or endpoints—the participants in a workshop on disruptive innovations in clinical trials during the RARE Disease Drug Symposium 2022 focused on the impact small changes in human behavior can have on improving the process.

The subject matter experts who informed the discussion during the workshop included Research and Data Governance Lead for RARE-X Vanessa Vogel-Farley, Senior Project Manager for Simons Searchlight Jennifer Tjernagel, Founder of Clinical Innovation Partners Craig Lipset, and Research Director of AllStripes Caitlin Nichols.

One change that the participants discussed was the need for improved communications between

stakeholders in clinical trials. Trial sponsors, they said, need to be more thoughtful about how they get patient groups' feedback on clinical trials and how to take that feedback and share it with others in their organization, the patient community, and with regulators.

Even when the issue turned to often articulated challenges, such as data silos, the groups saw this as being a problem of human behavior and attributed it to mistrust between organizations and motivations like greed or ambition. With regards to the use of validated measures that might kill promising drugs because of the lack of measures

**Emotions and attachments that individuals have to their group and their mission, rather than looking at which other groups may be more mission aligned, was blamed for friction between groups working in the same disease area.**

for what might be new endpoints in rare disease studies, participants blamed a legacy mindset. And emotions and attachments that individuals have to their group and their mission, rather than looking at which other groups may be more mission-aligned, was blamed for friction between groups working in the same disease area.



In that vein, there was discussion about the need to have a better understanding of the challenges various stakeholders face—patients, researchers, industry, regulators, and investors—to enable people to be more collaborative and craft incentives that would encourage cooperation.

When the topic turned to how to best capitalize on existing data to accelerate drug development, concerns turned to silos that prevent researchers from accessing data that could be used to advance the understanding of a disease. Participants expressed interest in learning how to ensure data quality in disparate sources of data, how to curate these, and how to use data in ways that may be different than the original purpose for which it was collected. As such, the conversation turned to consent agreements and the need to involve lawyers in discussions about how to put incentives in place to get people to share the data they have.

While human behavior may underlie many of the structural impediments to making faster advance-

ments in rare diseases, industry representatives in the room bemoaned the fact that no one from their own legal departments was present. They said the legal teams need to understand the problems, and why it's important to think beyond the parochial interests on which they may be focused on protecting to the detriment of the long-term goals of the broader set of stakeholders.

Clinical Innovation Partners' Lipset shared an anecdote that speaks to the need for a change in mindset with regards to industry's approach to partnering with patient organizations. He recounted an exchange one patient advocate had with a pharmaceutical company that said it was making a seat at the table for patients. The advocate responded, "It's great that you are making a seat at the table for patients, but who said this was your table in the first place?"

Lipset said people may get excited when companies make a seat at the table for patients but wondered whether these same companies appreciate that their own mindsets may not really be collaborative. ■



## Turning a World of Data into Actionable Information

**As the ability to capture and generate both biologic and real-world data increases, the drug discovery and development process is increasingly dependent on the ability to acquire and analyze large sets of data. The integration of artificial intelligence into this process not only represents a powerful tool to accelerate the advancement of new therapies, but a necessary one to make sense of what is becoming a Big Data problem.**

The potential for AI has generated much excitement because it not only promises to make drug development better, cheaper, and faster, but is enabling insights in ways that were previously not possible by finding new correlations between genotype and phenotype, discovering biomarkers, and through image analysis recognizing significant changes at the cellular level that may have been undetectable by traditional human analysis.

A workshop during the RARE Drug Development Symposium 2022 had attendees exploring the promise of AI and barriers to realizing its potential in advancing therapies for rare diseases. While many attendees saw significant potential for the technology, the discussion focused on fundamental questions about the technology, what its advent meant for rare disease organizations seeking to advance drug development, and how they can access the technology.

Senior Vice President of Scientific Operations for the New York Stem Cell Foundation Rick Monsma, Vice President of Computational Biology for Rarebase Amina Qutub, Lead Clinician and Clinical Trials Advisor for INADcure Foundation Darius Adams, and CEO of Creyon Bio Chris Hart served as subject matter experts for the workshop.

The workshop attendees discussed the potential for AI to look across diseases to find commonalities between one rare disease and another, as well as between a rare disease and a more common condition, which could identify candidates to repurpose or new avenues of research to leverage funding.

One idea that captured the imagination of workshop attendees was the potential to create so-called digital twins—using AI to create a virtual match of a patient based on the analysis of extensive data to predict how a disease would biologically progress. Doing so could provide an alternative to a placebo-arm in a clinical study by using a digital twin as a control to limit the number of patients needed for a trial and ensure that all participants in a clinical trial received the actual therapy being studied.

It's not hard to imagine the integration of AI into all aspects of drug development, as well as the diagnosis of patients and the delivery of clinical care, but

given the state of the technology, the availability of datasets with which to work, and regulatory and financial barriers, early-stage drug discovery at the cellular and molecular level is where the technology is likely to have its biggest impact in the near term.

In part, that's a reflection of what data can be gathered and generated. The full promise of AI would involve taking multiple modes of both structured and unstructured data and leveraging them to provide predictive models, find novel targets, identify patients for clinical studies, and improve diagnoses and treatment.

Participants were interested in what it would take to get adequate amounts of data to enable the use of AI, how an AI approach would be validated, and how

regulators look at the incorporation of AI into the drug development process and whether they would accept synthetic controls, such as the use of digital twins.

Some of the participants felt they lacked a basic understanding of AI and said that education of the lay public is needed to understand how the technology works, how it is being used, and why it matters for patient advocates, particularly if groups are going to encourage patients to share their medical data to advance research.

Others wondered about opportunities for patient advocacy groups to start with AI, how to get access to the tools, and what they could do to leverage the technology to advance the development of treatments. ■





## Different Diseases, Common Challenges

**While each rare disease may be unique, common barriers to advancing therapies can open opportunities for stakeholders to work together.**

“No two rare diseases are identical,” said Daniel Lavery, chief scientific officer of the CDLK5 Deficiency Disorder-focused Loulou Foundation, “but the challenges are.”

Small patient populations, limited resources, and other barriers to conducting basic research on a rare condition and advancing therapies make collaboration essential for accelerating the development of needed treatments.

A workshop on emerging models for collaboration at the RARE Drug Development Symposium 2022 featured a group of subject matter experts who have been involved in using novel models for advancing research and development of therapies. This included people involved in a global partnership for resource-sharing, a foundation’s coordination of a pre-competitive observational study involving seven industry partners, an NIH-sponsored research collaborative, a non-profit foundation developing customized therapies for populations of 30 or fewer, as well as a collaborative research, funding, and

advocacy model that supports a group of related metabolic diseases.

While there were different models represented within the workshop, there were commonalities in terms of the issues any of these models faced that centered on how to communicate with partners, how to align interests of the different groups involved, and how to incentivize partners.

The subject matter experts for the workshop included Loulou Foundation Chief Scientific Officer Daniel Lavery, n-LoRem Senior Director of Communications and Donor Relations Amy Williford, PriZm Therapeutics Scientific Co-Founder Khemraj Hirani, and National MPS Society Chief Scientific Officer Matthew Ellinwood.

Participants discussed the need for improved communication between biopharmaceutical companies and patient organizations around clinical trials design and execution. Patient community representatives said patients do not feel supported while participating in a clinical trial. They expressed concerns about drug developers bringing patients into the discussion about clinical trial designs too late in the process and said they should be consulted from the start.



Representatives of small patient foundations said they find it difficult to get pharmaceutical companies to include them in planning discussions and that patients often feel that they are not being heard.

They argued that it is critical to educate clinicians and industry on the importance of listening to what matters to patients when designing clinical trials. For instance, travel to clinical trial sites can limit the ability or willingness of patients to participate in a study for both financial and logistical reasons.

are funding research should consider incentivizing collaboration by funding people with a proven track record of collaboration or requiring researchers to share data.

Patient groups should also look for ways to piggy-back with organizations that have similar interests to leverage limited resources. Younger and smaller organizations shouldn't be afraid to reach out to other organizations that have forged successful collaboration and embrace them as mentors.

**Participants placed an emphasis on the need for patient groups, researchers, and pharmaceutical companies to share data as an important way to accelerate advances.**

In the end, this has a significant cost for pharmaceutical companies because when patients view clinical trials as poorly run, word can spread fast through a small patient community, and it limits the willingness of others to participate. That adds to a fundamental enrollment challenge inherent in rare disease studies because of the small population of patients.

There was agreement about the importance for stakeholders to work collaboratively to drive research forward. To do that, organizations need to find ways to identify potential partners who have common interests and similar values. Groups that

It is also important to learn from drug development success stories in both larger and smaller indications. Groups that have been successful at advancing drug development should share their stories of success so others can replicate their model.

Participants placed an emphasis on the need for patient groups, researchers, and pharmaceutical companies to share data as an important way to accelerate advances. People recognized that each of the various stakeholders may have incentives to hold, rather than share, data. Because of that, new incentives are needed, such as tying funding to a data sharing requirement, or academic institutions rewarding faculty for how widely data sets they create are used, much like the way publications help advance their careers. ■



## Fostering Successful Connections

**A sense of urgency often drives rare disease patient organizations as they seek to advance research into their conditions and work to drive development of potential therapies. While collaborations are essential to achieving this, one of the takeaways from a workshop on fostering successful collaborations was that it may be best to go slow.**

The subject matter experts participating in the workshop at the RARE Drug Development Symposium 2022 included representatives from the Rare Epilepsy Network, a partnership between epilepsy organizations and academia; the Epilepsy Research Roundtable, which brings regulators and industry together to collectively address roadblocks; the Epilepsy Learning Healthcare System, which layers research on clinical practice to generate real-world evidence and real-world data; and the NIH-funded Rare Diseases Clinical Research Network, a collaboration between 20 teams of scientists, clinicians, patients, families, and patient advocates.

Epilepsy Foundation's Chief Outcomes Officer Brandy Fureman, Rare Epilepsy Network Director Ilene Miller, and Co-Founder, Director of Research for Ring14 and Coordinating Committee Chair of the Rare Epilepsy Network Yssa DeWoody participated in the workshop as subject matter experts.

Before jumping into partnerships, workshop participants were encouraged to take time to do their

research, learn what efforts are already underway, and what they could do to fill unmet needs to get treatments and support to families rather than duplicating existing efforts.

It can be difficult for patient advocates to realize what they don't know. For that reason, they should use their own network of contacts, reach out to people who can serve as mentors, and seek help from friends. This can help them find other patient groups, researchers, and companies with whom they can collaborate. Having a direct introduction to potential collaborators can also help direct a request to the right person and avoid wasted time trying to navigate a large corporation or university in search of the right person to contact.

In looking for potential partners, patient organizations should think broadly about commonalities. For instance, a technology company or one focused on accessibility may prove to be a good partner for patient organizations, even though they may not be involved in their specific rare disease. When organizations arrange a meeting with researchers, industry, or others, it's good to go in with a plan and know what they want to ask before they sit down.

At the same time, patient advocacy organization leaders need to put aside their egos and avoid competing against other organizations working in the same space. People discussed the importance of changing such a mindset. While patient organiza-

tions from time to time may seek funding from the same sources, creating a perception that everyone is fighting for resources instead of sharing or creating resources together can be harmful. It's best to recognize common goals and find ways to work together.

Collaborations can be challenging to maintain. At times, conflicts may arise. When collaborating with others, it is good to have someone who can act as a neutral third-party peacemaker and serve as a mediator to help resolve disputes when they arise. It is sometimes easier to hear things about changes you may need to make from a neutral third-party than it is from a partner.

Organizations seeking to connect with researchers should consider inviting them to a conference or event. It's also a good idea to look beyond directors of programs and think about reaching out to junior researchers as they are more likely to respond. Holding a roundtable with researchers, patient advocates, and industry representatives to meet with medical staff and regulators staff is a good way to discuss challenges and opportunities around addressing a specific condition.

Because universities have good meeting spaces, working with them as a partner to hold a roundtable or similar event is an effective way to start small and can lay a foundation on which to build future

collaborations. Similarly, working on a toolkit or paper together, or standing together to support specific legislation, can be a way to start a relationship.

It's likely that someone thinking of pursuing a collaboration will find someone else who has already done something similar to what they are seeking to do. It's good to reach out to other organizations that have done similar types of collaborations to seek advice about what worked and what didn't. One person suggested a mentorship program should be created where bigger, more established advocacy

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**It's good to reach out to other organizations that have done similar types of collaborations to seek advice about what worked and what didn't.**

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organizations can help guide smaller ones, so they learn from the experience of others to help them adopt approaches that have proven to work.

In that same vein, the participants discussed the idea of an advocacy incubator where patient organizations can come together and exchange their ideas to foster more productive collaborations. Meetings like the RARE Drug Development Symposium were recognized as being ways to foster collaborative connections. ■





## Fostering Collaborations

**A decade ago, Nicole Boice found herself serving as an arbitrator between six warring patient organizations that were part of a highly fractured rare disease community. Even though they were all concerned about the same condition, there was great animosity among them that threatened to hamper progress for all. A pharmaceutical company wanted to support the community, but the groups were all asking for funding to do the same thing.**

Boice, founder of Global Genes and founder and executive director of the rare disease patient data platform RARE-X, invited the leaders of the organizations to join Global Genes for a meeting and asked each to bring with them a description of their core values. When they all sat down together, they mapped out what each group did, their various workstreams, and determined which group was best equipped to tackle each of various tasks. While there was some overlap, one group was focused on research, another on family conferences, and a third on social media. By the end of day, each of them not only had defined lanes in which to operate, they no longer hated each other.

“Collaboration is hard. Sometimes it is about compromise. Sometimes it’s about finding lanes. You might not even like each other, but if you can commit and agree on that endgame, then you might be able

to make it happen,” said Boice. “The disease areas are too small to have things become fractured. If you truly are about the patient and the community and that end goal, then you’ve got to get over some of that early ego and work extra hard to figure out how to collaborate.”

Boice spoke during a panel discussion on fostering collaborations between various stakeholders. Clinical Director of the Orphan Disease Center at the Perelman School of Medicine at the University of Pennsylvania Eric Marsh, and E.WE Foundation Founder and CEO Sarita Edwards joined Boice for the discussion, which Assistant Professor at Baylor

**“If you truly are about the patient and the community and that end goal, then you’ve got to get over some of that early ego and work extra hard to figure out how to collaborate.”**

**— Nicole Boice**



College of Medicine and Board Chair of the RARE Drug Development Symposium Advisory Council Rodney Samaco moderated.

Collaborations between patient organizations can be difficult because of individual personalities, competition, and differing visions on how to best achieve their goals, but they may be easier than collaboration with industry, academia, and other stakeholders where

needs, goals, and ways of working can be quite different. Nevertheless, collaborations between different stakeholders are essential to advance understanding and treatments for rare diseases.

“We’re all better off working together than we are apart. Having multiple organizations go at the same thing dilutes the money. It dilutes the talent. It dilutes everything,” said Marsh. “Getting people together to do it, even if there are disagreements,

ship. By understanding each other’s perspectives as well as their strengths and limitations, it would allow collaboration to be more efficient and successful.

At the same time, Marsh said clinician scientists need to be honest about what they can and can’t do with the resources that they are offered. He said researchers shouldn’t ask for half the money they need to do a job because all that will mean is half the money will just go to waste.



**“It starts with relationship building. It’s not about creating opportunities. It’s about building relationships that lead to opportunities.”**

**— Sarita Edwards**

work through those. We’re all trying to go for that same goal and getting there all together is going to be much more likely than getting there separately.”

Marsh said when multiple organizations collaborate, it’s critical that they communicate with each other to ensure they are not stepping on each other’s toes and not fighting for the same pot, or duplicating efforts.

When it comes to collaborating across patient organizations, academic research institutes, and industry, communication becomes that much more critical. The panelists talked about the importance of taking the time to understand the different needs of everyone who comes to the table. Patient groups need to understand what’s in it for them, but also what industry needs, what researchers need, and what clinicians need if they are going to build a successful partner-

“Too often we all just say, ‘Yeah, we’ll do it,’ and then we fail because we don’t have what we need to do it,” he said. “Even within the collaboration where everyone says they’re going to

collaborate, they’re going to contribute, and then one part or two parts don’t contribute because they didn’t have what they needed in the first place to get it done. And that becomes hard.”

The E.WE Foundation’s Edwards acknowledged there is a feeling of urgency in the rare disease community, but she cautioned advocates against moving too fast because they may find themselves having to backtrack.

“You have to take those baby steps sometimes to figure out if this person is a good fit for my organization, if they align with our mission and our goals,” she said. “If that conversation aligns with what you’re trying to achieve, then you move to the next conversation. It starts with relationship building. It’s not about creating opportunities. It’s about building relationships that lead to opportunities.” ■



# Ten Takeaways from the RARE Disease Drug Symposium 2022

## 1 Collaboration is Critical

Drug development is costly and complex. Collaborating with others is essential to accelerate the process. Search broadly for potential collaborators. Seek out conferences and other opportunities to interact with potential partners. Also, consider convening a stakeholder roundtable to bring them all together to discuss advancing research in a disease and identifying potential obstacles that need to be addressed.

## 2 Start Slow

A sense of urgency drives many patient advocates. Many rare diseases are progressive and deadly, and it can be frustrating to deal with the slow pace that characterizes the drug development process. Nevertheless, when it comes to collaborations, it may be best to start slow and build on small projects, such as a paper, to get to know partners, how they work, and what is important to them.

## 3 Change your Mindset

Rare disease organizations working on the same disease may feel as if they must compete for funding and patients. This can create chaos and confusion that may lead to other stakeholders not wanting to get involved in research and development of a potential therapy. Understand common goals with other organizations and focus on how to best use each other's strengths to get to your goals faster. If disputes arise, find a neutral mediator to help resolve them.

## 4 Find a Cousin

For most rare diseases, there is a more common disease that shares phenotypic characterizations, biologic pathways, and other aspects. Rare disease groups seeking to advance an understanding of their condition can look to other broader diseases to gain an understanding of their condition, leverage new sources of funding, and attract researchers and industry partners who might not otherwise be interested in pursuing a small disease population.

## 5 Communication is Key to Success

Poor communication between stakeholders can breed distrust and confusion. It is important not only to create channels of communications between stakeholders, but also to create feedback loops so perspectives from one stakeholder can reach others throughout an organization or community to inform future work.



## 6 Understand Stakeholders

Though rare disease stakeholders may share the common goal of seeing a therapy developed to treat a rare disease, their needs may differ. It is important to understand not just what you are trying to accomplish together, but the rules under which a partner operates, the constraints they may face, and what they require to be successful. By doing so, it may be possible to address obstacles that might otherwise derail a project and prevent progress.

## 7 Learn from Others

Rare disease patient advocacy organizations looking to become involved in driving research and drug development for their condition can avoid wasted time and costly mistakes by seeking the counsel of organizations that have gone before them to learn from the success and failure of others. Experienced rare disease advocates have demonstrated a willingness to help newer advocates seeking their guidance. Find a mentor.

## 8 Look to Already Approved Drugs

One way for patient advocates to more quickly identify therapies for their disease is to look to already approved drugs for other conditions that share symptoms, pathways, and other commonalities. Understanding how a rare condition relates to a more common one for which an approved drug may exist could lead to finding drugs that are known to be safe and can bypass the need for extensive pre-clinical and early clinical testing. Though repurposing drugs is a proven approach, there may be little incentive for drugmakers to pursue such strategies, particularly in the case of drugs that are available in a generic form. Nevertheless, the world of approved drugs is finite and there are technologies and methods that are accessible for screening existing compounds to determine if one might provide benefit.

## 9 A Matter of Interpretation

New technologies are enabling the capture of both molecular and real-world data that can provide unparalleled insight into the underlying cause of a disease, how it progresses, and how it can be treated. Artificial intelligence is providing a powerful way to capitalize on the growing amounts of data to capture new insights into diseases with greater speed. The potential to make predictive models is creating the possibility to create synthetic patients and so-called digital twins that may act as controls in a clinical study as an alternative to a placebo-controlled study that requires more patients, some of which will not receive the trial drug under study.

## 10 The Future is about Data

Though many people think of drug discovery and development taking place within a wet lab, it is increasingly becoming a data science. The small patient populations for specific rare diseases make individual patient data within a rare disease community all the more precious. High quality data is essential but needed data and bio-samples that could advance research and drug development for a specific disease may be siloed and remain out of reach for the researchers who need them. It is vital that rare disease communities take control of their data and put themselves at the center of data collection efforts. This can assure researchers who should have access to the data will have it, and also provide leverage for disease communities to get other data holders to share their data. ■



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