Siren Interactive White Paper

RARE DISEASE AS AN EFFECTIVE MODEL FOR MULTI-STAKEHOLDER COLLABORATION

SPEEDING ORPHAN DRUG DEVELOPMENT, COMMERCIALIZATION AND ACCESS

This white paper summarizes insights on multi-stakeholder collaboration shared at Siren Interactive's workshop, *Critical Issues in Patient Advocacy Engagement & Collaboration: How Do We Find Common Ground?* at the World Orphan Drug Congress in April 2014. Participants included representatives from industry, rare disease patient advocacy group (PAG) leaders and patient opinion leaders (POLs). Special thanks are due to our moderator Wendy White, founder and CEO of Siren Interactive, and panelists:

- **Barbara Wuebbels**, vice president of patient advocacy and medical affairs at Audentes Therapeutics
- **Pat Furlong**, founding president and CEO of Parent Project Muscular Dystrophy
- **Ben Lenail**, co-founder and business strategy officer of ALD Connect
- **Julie Raskin**, executive director of Congenital Hyperinsulinism International
- **Carrie Burke**, director of alliance development at Shire Pharmaceuticals
- **Nicole Boice**, founder and president of Global Genes/Rare Project

EXECUTIVE SUMMARY

Rare disease communities are models of what can be accomplished by joining together to achieve common goals. Healthcare reform, the growing power of patients and caregivers, and opportunities in global markets are creating seismic shifts in the world of orphan drugs and rare diseases. Rare disease patients tend to be highly motivated, highly social and hyper-connected. While they may feel alone in the early stages of their journeys, patients and caregivers gain strength from sharing their experiences and knowledge. Because of these strengths, rare disease communities are now becoming models of how to build effective multi-stakeholder partnerships. New and innovative partnerships are developing between industry, national and global patient organizations, academic and clinical centers and governmental bodies all with the common goal to speed development of treatments, improve clinical trial design and expand access to care. In this white paper, we look at how these partnerships have enabled all those involved to master the new dynamics of healthcare and identify the keys to successful collaboration.

"I am thinking of this as a four-legged stool; you need patients, you need pharmaceutical companies, you need government and you need academia." – Barbara Wuebbels

WHAT CAN COLLABORATION ACCOMPLISH?

Effective collaborations can mean the difference between success and failure for rare disease drug development. "The biggest danger of not aligning is that you won't have any patients for your trial and you won't have any patients to sell your drugs to," explains Barbara Wuebbels, vice president of patient advocacy and medical affairs at Audentes Therapeutics. "Not knowing who the key treaters are is another obstacle, as well as not having any numbers to build a marketing plan around. It's also possible that news won't be delivered clearly. Say your clinical trial is going to be delayed six months and you've got to get that out to the patient community or they'll think your company is folding or your drug doesn't work. If you don't have a relationship, you can't tell them."

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SUCCESS IN GLOBAL MARKETS

Pharmaceutical companies and biotechs that operate on a global scale confront challenges created by varied regulations on interactions between industry and patients, language barriers and cultural differences. Collaborating with local advocacy groups can help develop a global strategy for access and awareness that is fueled by each foundation's physician network and patient supporters

"Working with foundations is the best bet for companies," says Pat Furlong. "Through social networking foundations get up to speed quickly on what is happening in the space. Foundations are a trusted resource for patients. They know diagnostics. They know standard of care if it exists. They know where to reach the patient population. They know nuances of that population. They might know outcome measures and discuss with you what does or doesn't make sense. They will direct and connect you. If they trust you, they will introduce you to the patient population."

Of the more than 7,000 rare diseases, only 15% have dedicated patient organizations. What if there are countries that don't have a patient group? According to Furlong, "Organizations like PPMD that I represent are very willing to help smaller organizations get on their feet and tell them about things we did well or less well and big mistakes we made along the way. Even if they operate in the U.S., they may know international patients through social media. I have seen amazing things happen in a rare disease where a patient really gathers the patient population within a few years in a registry on a Facebook site."

"If we care about your clinical endpoints, we will demand access." – Pat Furlong

COLLABORATION IN ACTION

When patients and industry walk hand in hand through the whole drug development and commercialization process and continue those relationships after the drug is launched, everyone benefits. Advocacy groups can help industry find patients and key opinion leaders (KOLs), initiate natural history studies that will increase understanding of the burden of disease and help patients fight for access to treatment after it's available. Pharmaceutical companies can use their power and resources to increase the patient advocacy group's effectiveness and reach. Regardless of your role in the life cycle of drug development and marketing, encouraging collaborative relationships each step of the way will pay benefits.

CASE STUDY 1: SPEEDING TREATMENT DEVELOPMENT, INNOVATION AND APPROVAL

On the day that Pat Furlong discovered that her two sons both had Duchenne Muscular Dystrophy (DMD), she borrowed $100,000 and decided that she was going to fix the disease. Posing as a post-doctoral candidate, she scoured medical libraries, only to find that there was no data about the disease whatsoever.

Her fight to conquer DMD continued long after she lost both of her sons to the disease. In addition to supporting patients and families, the organization she founded, Parent Project Muscular Dystrophy (PPMD), maintains a patient registry, meets regularly with key government organizations and raises funds for research.

PPMD also works to speed development of treatment for this devastating disease by collaborating with pharmaceutical companies. One strategy PPMD has used is to propose new indications for existing drugs. "Children with Duchenne have very cold extremities," Furlong notes, "which led us to wonder if these boys were vasoconstricted."

To find out if the boys would benefit from more blood supply to muscles, PPMD funded a pilot comparing VIAGRA® and CIALIS®, which eventually led to a conversation with Eli Lilly and Company, maker of CIALIS®. "They were very interested in the new indication because their patent was expiring. They were also interested to know about cardiac problems that these children have so they could create a protocol that avoided cardiac risk. Our knowledge of the population helped reduce some of the barriers for them."

According to Furlong, there are now more than two dozen companies asking PPMD to help them identify key opinion leaders, understand the patient experience, design clinical trials, choose outcome measures, and recruit participants.

"When we first went to the National Institute of Neurological Disorders and Stroke (NINDS) we said, 'We are here to get your help.' And they said, 'No, you don't understand. You are here to help us. We've got 600 neurological conditions. We can't know any of them as well as you know yours, so please help us communicate with your scientists and your patient families.' So it's not can or should you meet with them. You must meet with them."

Recently PPMD has been breaking new ground by organizing a group of 80 stakeholders, including patients, researchers and pharma, to provide input to the FDA on clinical trials. One of the issues raised by the DMD community was that they objected to the use of placebo. "First of all the port is a risk and then an IV infusion of a placebo doesn't make any sense in a progressive debilitating disease in which every single day muscle cells are lost.," Furlong says. "So the FDA has agreed that these studies will be open label, that in fact the boys will receive drug. Not only that, but they will accept children younger than the typical age of seven and non-ambulatory patients."

In June 2014, PPMD provided the FDA with the first-ever patient-initiated guidance to help accelerate development and review of potential therapies for Duchenne Muscular Dystrophy. This guidance includes recommendations for benefit/risk assessments, clinical trial design and outcome measures. By working with all stakeholders, PPMD has demonstrated to their pharma partners that collaboration can improve their prospects for a successful clinical trial and a smoother path to approval.

"Patients have the ability to raise their voices about inclusion criteria, about protocol development and flexibility in labeling, so I think this encourages all of us to work together in the most appropriate and most urgent way." – Pat Furlong

CASE STUDY 2: UNIFYING PATIENT DATA TO ACCELERATE DIAGNOSIS AND RESEARCH

After experiencing gait problems in his early 40s, it took Ben Lenail another two years to receive a diagnosis of Adrenoleukodystrophy (ALD). This was not the end of his search, but the beginning. "The neurologist who diagnosed me at USCF was very honest. He said, 'I don't know this disease. Nobody on the West Coast knows about this disease. It's on you as a patient to research this disease. I'm sure there's a specialist somewhere in the U.S. that you should make contact with, but I don't know who that is.' The medical community was siloed, with some gaping holes."

"The founding concept of ALD Connect was that the current system is broken, so let's create an umbrella organization that's going to unify all the patient groups and the medical community into this new hybrid concept which is the Patient-Powered Research Network or PPRN."

Lenail's 25 years of technology and start-up experience served him well in his efforts to shed light on the disease. ALD Connect received a PCORI grant to create a unified registry with a set of natural history studies, case report forms and biomarkers. "We don't have that today; we're building it. We have to federate siloed registries into a new registry, and one idea that we had was to integrate the private social network with the registry."

"The idea was to create a new private social network where people would be asked to give informed consent and report some of their clinical information and measurements, and we would do a data extract from that every day or every week into the registry."

Lenail is still working through some obstacles. "Mostly people have privacy concerns. Yet when you tell them that it's the way to get profiled for clinical trial enrollment they are willing to do it. But they would prefer that it be done manually."

The issue of registries is complex and many questions remain to be answered. What is clear is the value of reducing fragmentation and bringing the data into one centralized registry and—if appropriate—conducting newborn screening. "Every year we have boys who go into Addisonian shock and die whose parents had no idea that their child had adrenoleukodystrophy," says Lenail "So newborn screening is absolutely essential to get the visibility, the planning, and to also get more data, frankly speaking, into the registry and see how those kids evolve and what kind of interventions can be done on them."

Industry has been key to ALD's achievements on many different levels. For example, bluebird bio has been a valuable partner for ALD Connect since inception. They have a strong interest in the patient community being better informed, more organized, and more connected to clinicians and researchers. Lenail says, "Tara O'Meara and Faraz Ali are two exemplary bluebird staffers who have wholeheartedly invested themselves into ALD Connect's teamwork. bluebird bio funding helped get ALD Connect off the ground before the federal funding arrived. bluebird bio has contributed to some of our key campaigns, such as the inclusion of ALD in states' newborn screening panel; and better physician awareness of the disease to speed up diagnosis and understand all the options."

"In the U.S. especially, the patient voice is key to developing or changing policy in a way that may help create greater awareness, diagnosis and access to necessary medical specialists and treatments." – Carrie Burke

CASE STUDY 3: COLLABORATING ON HEALTHCARE ACCESS POLICY AND CONNECTING PHARMA TO THE COMMUNITY

As U.S. healthcare reform transfers more decision-making power from the federal to the state level, pharma and patient organizations are discovering the value of policy initiatives that operate on a local scale. New Jersey Rare is an example of a successful coalition.

Julie Raskin, executive director of Congenital Hyperinsulinism International (CHI) and the mother of a child with this rare disorder, was one of the organizers of this coalition that was formed in 2012 with assistance from the National Organization for Rare Disorders (NORD). The original goal was to stage an educational and awareness briefing at the New Jersey State House. This initiative was so impactful that the group decided to continue meeting in order to tackle other issues on behalf of the 900,000 rare disease patients in New Jersey.

"We are patients, patient advocates, rare disease patient organizations, biotech representatives, trade organization representatives, researchers and clinicians, government and national and global umbrella groups," Raskin explains. "We put together an outline for rare disease community engagement at the state level and tested it out with the Healthcare Institute of New Jersey (HINJ), a trade organization for New Jersey life sciences. They helped us put together a program for government, health and human services, and the insurance industry, and we saw that we could have an influence on what's going on with the Affordable Care Act, the exchanges, reimbursements and patient advocacy within biotech companies." Speakers at events have included John Crowley, chairman and CEO of Amicus Therapeutics, a biopharmaceutical company focused on rare genetic diseases and Francois Nader, CEO of NPS Pharma.

The relationships that Raskin has built with industry partners have been powerful in many different ways. XOMA is investigating XMetD, a potential novel treatment for congenital hyperinsulinism (HI). Raskin initially contacted XOMA in 2012 and invited them to the annual conference attended by patients, families and clinicians. "At our 2012 conference we set up a meeting between XOMA and leading researchers and clinicians who were attending our conference," Raskin says. "We invited a few CHI board members and patients to attend this meeting so that they too could learn about these new interesting concepts XOMA was exploring. After that meeting, XOMA continued to connect with our research partners, some of whom became active participants and KOLs on the project. When in Berkeley, California for a CHI family meeting, I had an opportunity to visit the XOMA headquarters and present to a whole cadre of XOMA scientists the patient experience of living with HI. I could sense it was very motivating to the scientists to understand the patient perspective in order to grasp just how devastating the condition can be and how much unmet need there is."

Raskin also helped forge connections for Xeris Pharmaceuticals, a company engaged in developing a continuous basal infusion delivered with an OmniPod patch pump for treatment of severe, persistent hypoglycemia related to congenital hypoglycemia. "We invited Xeris and the scientific advisor to speak at one of our patient family conferences. Through CHI, they have now formed a consortium of clinical experts, which are all CHI scientific advisors in the U.S., E.U., U.K. and Israel in advance of conducting a Phase 2 clinical trial in early 2015."

By continuing to attend CHI events, Xeris has made more contacts with researchers who have become KOLs on their project. Equally important, Xeris has developed a deep understanding of the patient experience. "At the same time," Raskin adds, "patient engagement in the work is high because Xeris presents status updates at our patient meetings and conferences."

SIREN RECOMMENDED ACTIONS

Industry, patient groups, government and researchers all want the same thing: to get better treatments to market as quickly as possible. But effective relationships take time to develop. They require trust and mutual understanding. Take the initiative and begin networking. The earlier you start, the better the outcome will be.

1. **Begin an internal conversation.** How can your company or organization benefit from collaboration? What are your goals? Who can help you achieve them? What is the task for your collaborators? When is it appropriate? What are the rules of engagement?
2. **Devote time to relationship building.** Multiple interactions and discussions are needed to combat the distrust that sometimes exists between healthcare segments. Build understanding of what each stakeholder can contribute and think long-term.
3. **Develop and share best practices on policy advocacy.** Make sure your partners and alliances are all well-informed on the issues, understand the rules of engagement, and know how to be strong advocates from a policy perspective.
4. **Work to unite the global community.** Although many companies rely on country managers to help them navigate the global market, foundations can also be helpful with global alliance development, since they are usually acquainted with other organizations and may have an international presence on social media.

CONCLUSION

Bringing everyone to the table can provide benefits for all stakeholders. Collaborations can uncover new indications for industry, allow patients and caregivers to weigh in on preferred outcomes and help researchers design productive trials. Building trusting and collaborative partnerships where all stakeholders can work towards common goals is a key piece of orphan drug development that cannot be overlooked or undervalued. The investment of time and attention from all stakeholders can lead to positive outcomes along all stages of the drug development cycle.

CONTACT

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ABOUT SIREN INTERACTIVE

Siren Interactive is a rare disease marketing agency with unmatched expertise in addressing the challenges and unmet needs of patients, caregivers and physicians dealing with the over 7,000 rare diseases affecting over 300 million people worldwide. For more than 15 years, across more than 30 different disease states, we've had 1 focus: finding rare disease patients and connecting them to our clients' brands. As trailblazers in recognizing that patient-driven decision making is central to successful orphan drug commercialization, we are constantly innovating to meet patients and caregivers where they live. To learn more about our proprietary approaches to building trust relationships with rare disease stakeholders visit sireninteractive.com. Siren Interactive is a subsidiary of Dohmen Life Science Services. More information can be found at DLSS.com.

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