By Robin Robinson

Patients and Patient Organizations POWER RARE DISEASE THERAPIES

Advocacy groups are influencing research and development, regulations, and commercialization.

For most of the pharmaceutical industry, the focus on patient centricity is a relatively new phenomenon, and the industry continues to shift its focus to include patients as stakeholders when planning its marketing strategies, clinical trials, and R&D strategies. However, for the rare disease sector, the patient has always been front and center, championing for new therapies, looking for treatments, and demanding that the industry pay attention to their unmet needs.

In fact, if it weren't for the actions of empowered patients, some rare disease treatments might not even exist. Our experts say patient networks and advocacy groups greatly influence rare disease research and development, clinical trials, regulations, and marketing efforts.

"One of the single most important factors impacting rare diseases and orphan brands is the powerful influence of the patient or caregiver," says Laurie Bartolomeo, executive VP, creative director, Dudnyk. "Patient networks and advocacy groups for rare diseases tend to be more vocal, passionate, and involved than other patient groups."

By definition, rare diseases affect fewer than 200,000 people in the United States. Ultra orphan diseases affect fewer than 10,000 people.

"These conditions often bring together patients looking for answers, connections, and a forum for sharing their experiences," Ms. Bartolomeo says.

Patients are so proactive in searching for a treatment that the biopharma company Pulmatrix actually receives emails from individual patients asking when a drug will be on the market, according to Bob Clarke, Ph.D., CEO, Pulmatrix.

"Patients are among their own best advocates," Dr. Clarke says. "They aggressively pursue what is in development. They devote their own time to understanding what's coming down the pipeline for themselves or their relative in need."

At Pfizer, working closely with the rare disease groups is central to being able to meet the needs of these communities.

"In rare disease, patients are often more integrated into the treatment development and approval process," says Brenda Cooperstone, M.D., VP, medicines development group, Pfizer. "We have found that patient advocacy is a distinguishing characteristic of the rare disease space, and because of the complexity and smaller affected populations, it often falls to patients to be involved in everything from clinical trial recruitment to access and reimbursement."

Yuval Cohen, CEO of Corbus Pharmaceu-

One of the single most important factors impacting rare diseases and orphan brands is the powerful influence of the patient or caregiver.

LAURIE BARTOLOMEO
Dudnyk

FDA Approves 21 Orphan Drugs for Rare Diseases in 2015

Sets Record for Second Consecutive Year

The FDA approved 21 new orphan drugs to treat rare diseases in 2015, nearly half (47%) of all novel new drugs approved for the year. This is the second consecutive year in which the FDA approved more orphan drugs for rare diseases than any previous year in FDA history, according to the Office of New Drugs, Center for Drug Evaluation and Research at FDA.

ticals, says rare disease patients are more motivated to interact with the FDA and pharmaceutical companies than patients living with less acute or less serious conditions.

"In rare diseases, the stakes could not be higher for patients," he says. "We are focused on three orphan diseases; all three involve extreme morbidity and are life threatening."

Joe Kuchta, CEO, Sandbox, notes that patient groups overall are on the rise, but those groups that address rare diseases definitely have more at stake.

"The power and influence of patient groups has grown considerably throughout healthcare, but I believe it is heightened in the rare disease space because of the intensity and impact these conditions and diseases have on people's lives," he says.

Since the initiation of the Orphan Drug Act in 1983, patient advocacy groups have influenced almost every aspect of therapeutic research, development, and commercialization in orphan conditions. Over the past three decades, patient groups have grown with the help of organizations such as the National Organization for Rare Disorders in the United States and RareConnect in Europe that provide disease-specific online communities that enable people living with rare diseases to meet and learn from each other.

"The relationships with the patient advocacy groups are critical for companies working in the rare disease space," Dr. Cohen says. "Companies developing cystic fibrosis products in the United States work with the Cystic Fibrosis Foundation, for example."

Dr. Cohen notes that there has been a tremendous change in how patients are involved in all of the treatment development steps.

"The drugs that have contributed to an extension in life expectancy have benefited from the foundation's work," Dr. Cohen says. "Without the foundation, we would not have the CF therapies that we have today."

And patients are driving these efforts, becoming experts in their disease and taking part in every phase of drug development.

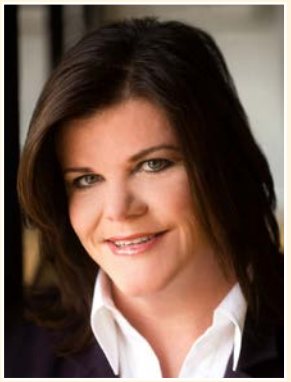
Patient networks and advocacy groups have a tremendous impact on all aspects of drug development — from clinical trials and the creation of patient registries through marketing of treatment and encouraging adherence — because they are hubs for both education and connection.

"Patients are pushing the pace of research and development and demanding a place at the table," says Wendy White, senior VP, rare diseases, Dohmen Life Science Services. "A great example of this is Parent Project Muscular Dystrophy's submission of the results of a patient-centered benefit-risk assessment study to the FDA. Also, patients in ALD and other diseases are funding and collaborating with scientists to speed up the pace of development."

Globally, patient advocacy groups have been active to help establish a focus on rare diseases, which in turn has resulted in regulatory action to expedite research. "These groups have driven international cooperation between regulatory bodies, investigators, researchers, and patients to develop common guidance for study approach, registries building, and other key tools to connect researchers and patients," says Derenda Nichols, director, clinical operations, Medpace. "It's a win-win: patients with rare diseases can find support systems, patient communities, and news about their disease. Researchers can understand the challenges these patients face and adapt programs to drive enrollment and retention."

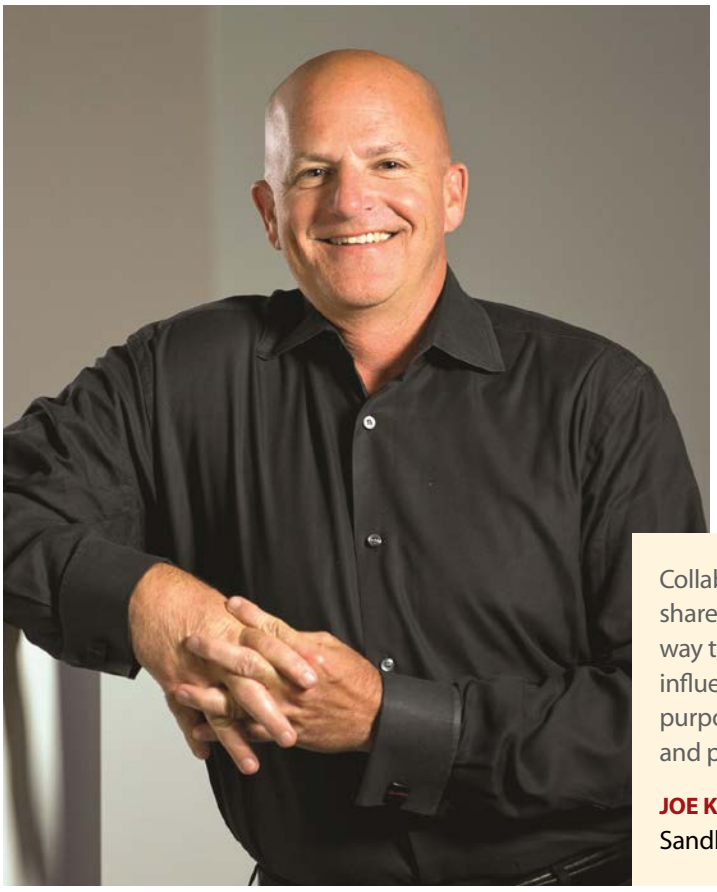
People with rare diseases aggressively pursue treatments that are still in development.

DR. BOB CLARKE
Pulmatrix



Patients are pushing the pace of research and development and demanding a place at the table.

WENDY WHITE
Dohmen Life Sciences



Collaboration, inclusion, and shared goals can go a long way toward helping patient influence be positive and purposeful versus contentious and polarizing.

JOE KUCHTA
Sandbox

Patient Impact on R&D

At Catalyst Pharmaceuticals, interaction

Companies are moving away from the build-it-and-they-will-come mentality and are now actively listening and engaging from the outset.

HEATHER GARTMAN
inVentiv Health

Nowhere has the influence of advocacy groups been more profound than in providing funding for transformational research and development.

MIKE HODGSON
Cambridge BioMarketing

with patients and patient groups has been critical to its research and development efforts, as well as its pre-commercialization activities.

"With respect to our lead program, Firdapse, for the treatment of a rare neuromuscular condition called Lambert-Eaton myasthenic syndrome, a disease for which there is no FDA approved treatment, meetings with patients and caregivers helped us to understand precisely what the medical needs were," says Patrick McEnany, CEO, Catalyst Pharmaceuticals.

"What we discovered from these interactions with patients was that what patients wanted most was access to an effective and FDA-approved therapy," Mr. McEnany says. "We found that many patients were initially misdiagnosed and then had trouble finding effective treatment without traveling to a few specialized academic centers."

Advocacy groups have become more than voices; they are an essential source of transformational therapeutic advances, says Mike Hodgson, chief creative officer, Cambridge BioMarketing. Perhaps nowhere has the influence of advocacy groups been more profound than in providing funding for transformational research and development efforts.

For example, the CFF provides not only funding, but has a nonprofit drug discovery and development affiliate called Cystic Fibrosis Foundation Therapeutics, which also supports the foundation's extensive clinical trial network and operates its own research laboratory.

"The CF Foundation is not alone," Mr. Hodgson says. "Across multiple, life-threatening conditions, advocacy groups are playing increasingly active roles in drug development and commercialization, from MS to Duchene muscular dystrophy, securing funding, driving urgency, and helping inspire innovative new approaches to life-threatening conditions."

Patient Impact on Clinical Trials

In an inVentiv Health survey of almost 50 patient advocacy organizations, patient advocates shared that their No. 1 request was to be involved in the development process earlier and more often. From working with patients in clinical trial design to ensure acceptable protocols, to tapping patient networks to help raise awareness of ongoing clinical trials, or mounting viral disease awareness efforts that help to condition the markets, today's increasingly empowered and savvy patients are a powerful voice, and with the rise of social sharing online traditional boundaries have evaporated.

"We've been counseling and helping our pharmaceutical and biotech clients engage with patients to inform the clinical development process," says Heather Gartman, regional managing director (DC), inVentiv Health PR Group. "Companies are moving away from the build-it-and-they-will-come mentality and now are actively listening and engaging from the outset and we give them the regulatory guidance to do so compliantly, which is often a major barrier for some."

People with rare diseases and/or their caregivers are usually well-educated about their conditions, often more so than the healthcare professionals they go to for help, Ms. Bartolomeo says. As a result, they are often the drivers of research and development and can be heavily involved in clinical trial participation and design.

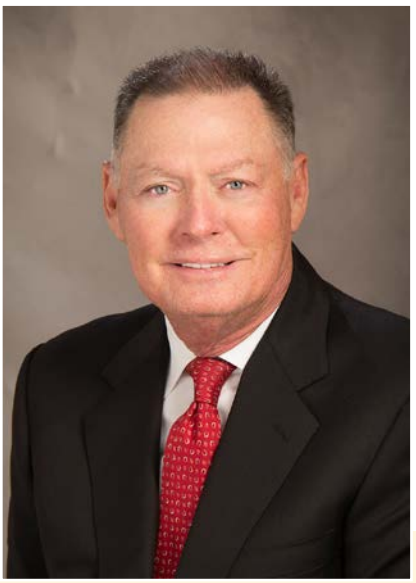
According to Steven Roberds, Ph.D., chief scientific officer, Tuberous Sclerosis Alliance, patient advocacy groups are impacting clinical trials in many ways, including raising awareness among the patient community of what it means to participate in clinical research in general, and what types of questions to ask about clinical studies. Patient networks are also contributing early to clinical trial design by representing the patient voice to sponsors and identifying what patients will see as barriers to participation, for example, frequent travel, or overly restrictive inclusion criteria.

By publicizing clinical trials to the patient community, potential participants become aware of the opportunity through their trusted network as other patients help spread the word via social media and at community gatherings.

Amir Lewkowicz, VP of strategic partnerships at Inspire, and a company co-founder, says the health community company works with its pharmaceutical clients to help them interact with the patients and caregivers.

"Industry is increasingly monitoring social networks to learn from Inspire patients and caregivers, particularly around clinical trial design and the efforts to identify treatments," Mr. Lewkowicz says. "They are also increasingly looking at rare disease social networks as a source for medical safety information as well."

Catalyst discovered that no formal patient group existed to advocate for patients with LEMS. Consequently, its pre-commercialization activities for the treatment Firdapse includes working with NORD to help LEMS pa-



Interaction with patients and patient groups has been critical to our research and development efforts, as well as pre-commercialization activities.

PAT MCENANY
Catalyst Pharmaceuticals

Rare Disease Requires a Rare CRO.

Conducting studies for Rare Disease and Orphan Drugs is challenging. The need is real and time is of the essence. That's why it's important to have a team that possesses the expertise to navigate regulatory requirements, patient recruitment and study feasibility.

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History of Rare Disease Day

RAREDISEASEDAY.ORG

Rare Disease Day was first observed in Europe in 2008. It was established by EURORDIS, the European Rare Disease Organization. In 2009, EURORDIS asked the National Organization of Rare Diseases (NORD) to be its partner in this initiative and to sponsor Rare Disease Day in the United States. The concept has continued to expand beyond the United States and Europe. In 2014, more than 80 countries participated.

Each year, Rare Disease Day is observed on the last day of February (Feb. 29 in leap years and Feb. 28 in other years).

To learn more about the global initiatives supported through rare disease day, please visit rarediseaseday.org.

tients launch a group aimed at providing them with information, education, and support.

"We are helping to create a group where none existed," Mr. McEnany says. "Disease awareness and patient education initiatives led by patient groups will help reduce the misdiagnosis rate and guide patients to the most appropriate treatments."

Patient Impact on Regulations

It is not uncommon for rare disease patients to attend FDA regulatory meetings to share their stories and advocate for the approval of new therapies, Ms. Bartolomeo says.

"Patients with rare diseases have more input into approval of treatments," she says. "Both patients and advocacy groups may be involved in the development of practice guidelines, new research, and even product approvals. "

It is interesting to see the depth of influence some patient groups actually have, Mr. Kuchta says.

"In the past, most people would have assumed that influence would be strongest at post-approval and/or market availability, but that's no longer the case," he says.

For example, at a recent public FDA Advisory Panel hearing considering treatments for Duchenne muscular dystrophy, patients and patient groups actively participated and had the opportunity to be heard along with physicians and company representatives.

Rare disease patients are very well informed and are motivated to participate in new treaments; they don't need convincing to do so.

DR. YUVAL COHEN
Corbus Pharmaceuticals

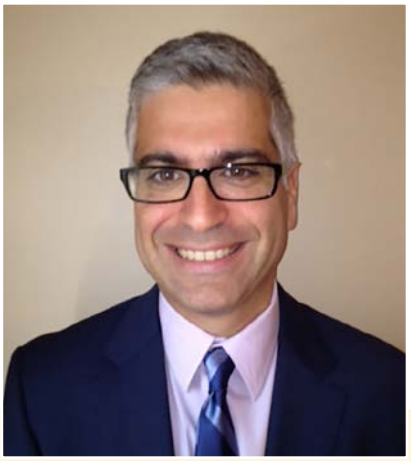
"This is not unusual in today's world, but that level of patient involvement would have been surprising just a decade or so ago," Mr. Kuchta says.

Many rare disease patient advocacy groups are having dialogues directly with the FDA. In turn, the FDA is giving patients the opportunity to be heard, Dr. Cohen adds. For example, the advisory committee hearing for the latest CF drug from Vertex involved participation from patients who testified both to the impact of the disease and of the drug on their daily lives.

"This interaction had a very positive and significant effect on getting the drug approved," he says. "We saw a recent example of this with the treatment for Duchenne. We will continue to see more patients interacting with the FDA through advocacy groups. The FDA has stated that no one is better qualified to discuss a disease than someone who has that disease and deals with it intimately on a daily basis."

Patient Impact on Marketing

With orphan conditions, strong relationships with patient networks and advocacy groups are critical for launch success.



Industry is increasingly looking to social networks to learn from patients and caregivers, particularly around clinical trial design and identifying treatments.

AMIR LEWKOWICZ
Inspire

FAST FACT

ONE IN 10 AMERICANS WHO HAS OR WILL DEVELOP A RARE DISEASE WILL ENCOUNTER A 95% LIKELIHOOD OF ZERO TREATMENT.

Source: NORD

"What's more, using the principles of health literacy — organizationally, visually, and verbally — to communicate has never been more important," Mr. Hodgson says. "The strength and influence of patient networks and advocacy will only continue to grow as personal health information — once exclusively the domain of healthcare professionals and hospital networks — becomes increasingly accessible to all of us."

The biggest marketing challenge in rare disease is the need for companies to be collaborative and engage in a dialogue.

"Patient networks and advocacy groups expect a shared sense of urgency, transparency, and openness around pricing, compassionate use, and clinical trial design and real collaboration in the tactics that are developed," Ms. White says. "Because these are small communities, the brand experience isn't limited to the treatment. It includes all of the manufacturer's

interactions with the community, patients, and healthcare professionals."

Success in orphan drug marketing requires credibility with each of the rare-disease stakeholder constituencies: patients, families, and caregivers; advocacy groups; primary care providers; specialty providers; specialized rare disease centers; and specialty pharmacies, says Mark Stevens, senior VP, strategy and commercial effectiveness, Publicis Touchpoint Solutions.

Advocacy groups can be tremendous allies, but they can also be fierce opponents if patients do not feel connected.

MARK STEVENS
Publicis Touchpoint Solutions

"Keeping an open line of communication with advocacy groups is critical," he says. "They can be tremendous allies, but fierce opponents if they do not feel connected and experience challenges."

Many rare disease communities wield tremendous influence; through their own interconnectedness — particularly via social media — they can augment or subvert the work done by a company's field-based clinical and sales teams. Some advocacy groups focus on helping patients/families locate physicians with expertise treating those with extremely rare conditions.

Patient advocacy groups are impacting clinical trials in many ways, including raising awareness among the patient community.

DR. STEVEN ROBERDS
Tuberous Sclerosis Alliance

"Having worked directly with both the companies that develop and commercialize therapies and the patient groups that stand to benefit, I have seen some relationships work well and others struggle," Mr. Kuchta says. "The best experiences involve open, honest dialogue between the two groups, with a mutual respect and understanding of what both hope to achieve. Things tend to break down when either side disregards the role of the other and either ignores their needs or places unreasonable demands or expectations on the situation."

However, Mr. Kuchta has witnessed great things from these relationships when they go well.

"When company representatives and key patient advocates or spokespeople successfully work together to understand what each can do to help the people affected by a specific disease collaborate and share goals, that goes a long way toward helping patient influence be positive and purposeful versus contentious and polarizing," he says.

According to Dr. Roberds, patient advocacy groups will not market or advocate for any specific product; for example, the TS Alliance has a corporate relations policy to guide interactions with manufacturers. However, there are ways for marketing groups and advocacy groups to work together.

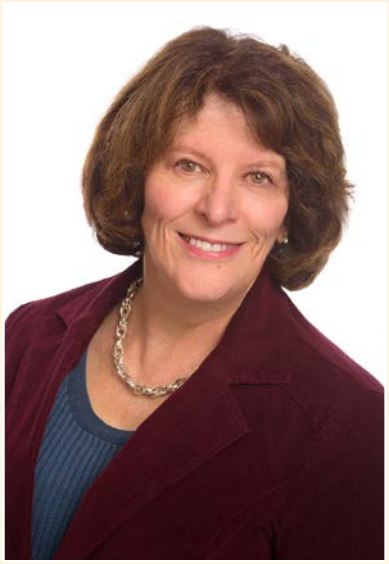
Providing patient access to commercial organizations through sponsorship of educational meetings, community events, or fundraising activities that help patient advocacy groups support their rare disorder community is critical.

A commercial organization that is developing materials for a rare disease population will benefit from having a patient advocacy group review materials to ensure the message will resonate with patients and the terminology is consistent with what patients have heard from the advocacy group or other sources.

Additionally, orphan drug marketing plans have smaller salesforce footprints, as physicians are eager to treat those with rare diseases, but more focus may need to be put on support and clinical teams.

"Over time, manufacturers can build long-lasting alliances with patients and advocacy groups," Mr. Stevens says. "Such alliances play a crucial role in a host of commercialization activities, from sourcing clinical-trial patients to promoting the availability of new treatments."

This area is an opportunity for companies to deliver value that really matters to patients and to influence their lives beyond therapy, Mr. Kuchta says.



Advocacy groups have driven international cooperation between regulatory bodies, investigators, researchers, and patients.

DERENDA NICHOLS
Medpace

"Since marketing is really quite a different animal when it comes to therapies for rare diseases, I believe patients have much more influence on what companies do to support those patients on therapy and help them navigate their daily living and the expectations that come with treatment," he says.

In particular, Dr. Cohen has seen a dramatic change in CF awareness among the audiences he addresses.

"In the groups I speak to, most people, if not all, have heard of cystic fibrosis," he says. "There are only about 30,000 patients in the United States affected by CF. It's remarkable how the foundation has so successfully increased awareness."

Dr. Cohen's company, Corbus Pharmaceuticals, is also working on a treatment for dermatomyositis, a life-threatening, rare inflammatory disease that has the same number of patients as CF, but is almost unheard of outside of the world of rheumatologists.

"You see the difference that patients standing together empowering a foundation can make. Given the success of the CFF, I believe it is a model that more patients and patient foundations can emulate," he says. PV

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The Importance of Partnerships in Rare Diseases

Alone We Are Rare; Together We Are Strong

This slogan used by NORD for its Rare Disease Day initiative encapsulates the overall feeling that the rare disease space is more dependent on partnerships than broader therapies. Only through collaborations with all stakeholders will innovative and effective breakthroughs be made. Our experts explain their views on why working together is so important for success — for patients and for drug companies.

BRENDA COOPERSTONE, M.D.

VP, Medicines Development Group, Pfizer

As one of the world's largest biopharmaceutical companies, Pfizer has worked alongside the rare disease community for decades. We have found that innovative collaborations and partnerships — sometimes between unexpected organizations — can help ensure the patient voice is heard and accelerate the delivery of life-changing therapies.

These types of partnerships will hopefully drive more focus on addressing the needs of the rare disease community in new and innovative ways, bringing together organizations with varying expertise to best help patients. New models of collaboration can open doors to scientific innovation and technology platforms that otherwise would be inaccessible.

When seeking a treatment for rare diseases, a greater focus on collaboration is necessary at all levels. For example, we were recently able to hear the moving testimony of a familial amyloidosis patient at a forum where the Amyloidosis Research Consortium (ARC) and the FDA brought together patients to hear their perspectives on how amyloidosis impacts their lives. Working in rare diseases, we get to be uniquely close to the patient, understand their journey, and their perspective.

Additionally, since 2012, Pfizer and Cystic Fibrosis Foundation Therapeutics have collaborated to help speed the discovery and development of potential therapies that target the most common underlying defect leading to cystic fibrosis. The program's goal is to potentially advance one or more drug candidates into the clinic by the end of the six-year research collaboration. We believe that there remains a significant unmet need in this patient population and by working in partnership with CFFT. As a partner in these communities, we value efforts to include stakeholder and patient insights in the process.

HEATHER GARTMAN

Regional Managing Director, inVentiv Health PR Group

The continuing efforts from EURORDIS, NORD, and Global Genes Project to bring Rare Disease Day global may be a prominent example, but we see parents, patients, companies, and researchers working together to get creative to find solutions. Parents are working with researchers and regulators to fundraise and start clinical trials or get access to medications. And advocacy groups are changing the game too. For instance, the Multiple Myeloma Research Foundation's COMPASS Study maps the genetic profile of multiple myeloma patients, and that effort is supported by 17 academic centers, five pharmaceutical companies and the U.S. Department of Veterans Affairs. In the past that level of collaboration and progress would have been unheard of. All these collaborations and partnerships are bringing renewed hope to rare disease patients.

AMIR LEWKOWICZ

VP of Strategic Partnerships, Inspire

We see much more direct interest in the rare disease space from industry, pharma as well as genetic testing companies, and the interest to collaborate with our nonprofit partner organizations for purposes of research, patient education, and patient registries. We also we see nonprofit organizations collaborating and sharing with each other, particularly around strategies for developing patient registries. And we see more patients and caregivers — especially parents of young children affected by rare diseases — using social networks to create partnerships at a grassroots level.

PAT MCENANY

CEO, Catalyst Pharmaceuticals

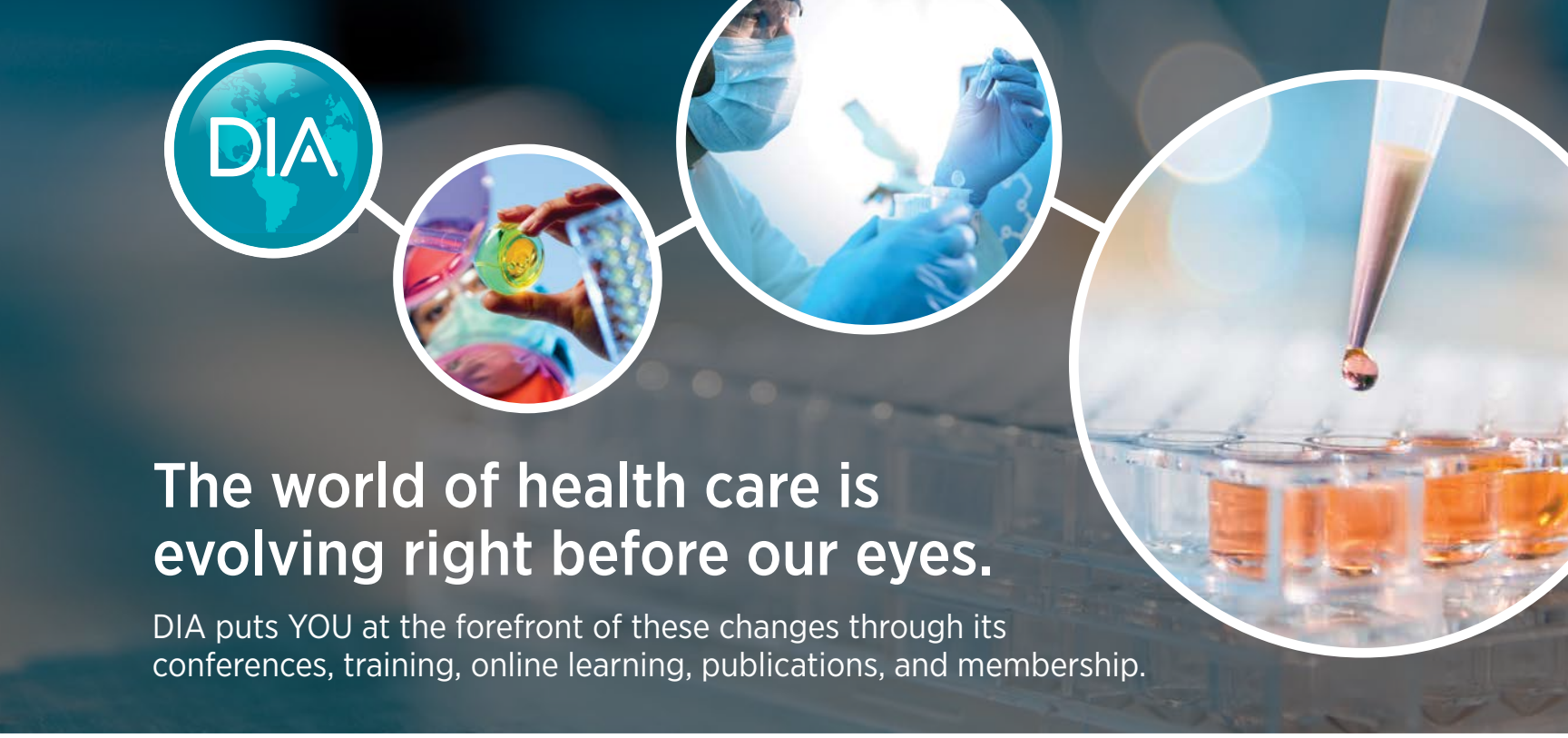
Rare disease research has always required significant cooperation between specialist clinicians, academia, and industry. More than ever, having patients and patient advocates as partners in new drug development is key to bringing effective therapies to patients in need. We currently collaborate closely with advocacy groups such as NORD and the Muscular Dystrophy Association (MDA). As medical science becomes more complex and drug development costs continue to rise, the importance of developing partnerships with patient groups will grow. These groups can help disseminate information about new treatments, provide direction to ongoing clinical trials, and keep patients informed of the progress of those therapies in the regulatory process.

WENDY WHITE

Senior VP, Rare Diseases Dohmen Life Science Services

Partnerships are the future of rare disease. These communities are small, so interconnected support is essential to achieve better outcomes and avoid redundancy and confusion.. Technology-aided solutions are the only way to really address the 7,000 different diseases that no physician can possibly be an expert on. This is especially true when it comes to diagnosis. It's exciting to see initiatives like Find Zebra and the IBM/Boston Children's initiative, which may reduce the average 4.8 years from symptoms to diagnosis that rare disease patients currently experience.

There needs to be collaboration between physicians and KOLs, POLs, networks, and technology all grounded in creating the right patient experience and developed with patients' needs foremost in mind.



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