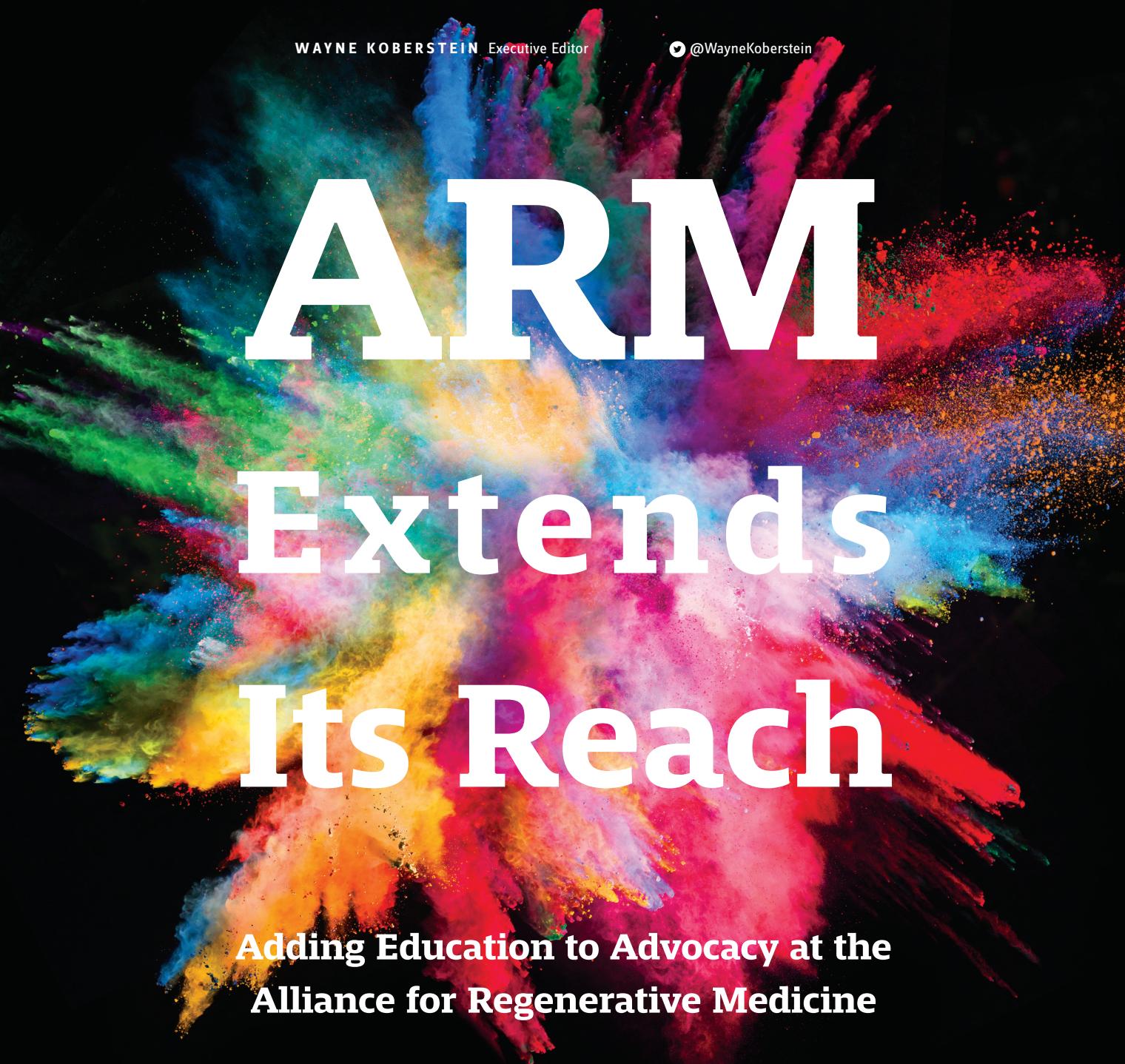


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ARM Extends Its Reach

Adding Education to Advocacy at the Alliance for Regenerative Medicine



In the beginning of the new millennium, a new therapeutic approach also dawned — actually a number of new approaches gathered collectively under the umbrella term “regenerative medicine (RM).” The most notable case in the first years of the 2000s concerned Christopher Reeve, the first A-movie Superman. Reeve injured his spinal cord so severely he could only move his eyes and mouth, and his very survival seemed to hang in the balance minute to minute. He became a strong public advocate for experimental therapies based on stem-cell technology. At the time, political opposition to the technology flared up because it would use stem cells from human embryos discarded by fertility clinics. Industry and business mainly shied away from the sector, and it seemed most of the energy in “tissue engineering” flowed into a search for alternatives to embryonic stem cells, the so-called pluripotent cells in skin and other tissues of full-grown humans. But progress on several fronts continued, and now almost two decades later, nearly 900 companies worldwide are developing RM therapies, and the field has a strong advocate of its own: The Alliance for Regenerative Medicine (ARM).

ARM has mainly focused on advocacy and funding since its inception in 2009, but last June, it announced the launch of its new educational initiative, The ARM Foundation for Cell and Gene Medicine. The move has more than symbolic meaning. It marks a new stage in development of the RM space as it moves from an early era or “promise” to one of fulfillment. Many RM therapies have reached a late stage of development: According to ARM, more than a half-dozen have gained marketing approvals during the past two years, and many others have entered a current total of 93 Phase 3 trials, 560 Phase 2 trials, and 324 Phase 1 trials. Morrie Ruffin, the Foundation’s executive director and ARM’s co-founder and senior advisor, says the RM sector has grown to a point that it demands an international campaign to educate all of the stakeholders in its universe — teaching people how RM technologies work, how they affect patients and healthcare systems, and how their value balances against their costs.

“A large number of the companies are making major investments in this sector, and each of them has its own educational program,” says Ruffin. “We saw the need for a single, unified education outreach, an organized effort by the sector, and that was part of the impetus behind creating the ARM Foundation.” The Foundation has already initiated its first module: the Gene Medicine Education Program, to marshal information, discussion, conventional and social media, and spokespersons covering all aspects of the gene-medicine field. It has announced two others: one on the economic impact of RM therapies, the other, a comprehensive look at

gene- and cell-therapy industrialization. The list of experts contributing to the programs, from every corner of the globe, reflects the organization’s deep-and-wide approach to all subjects.

“We are taking the lead in building on the body of knowledge and understanding of the macroeconomic impact this technology will have, because if these treatments are going to cost as much money as some people say they will, how do we know they will benefit the healthcare system, even in the long run? We believe they will, but we have to show that we can model the economics, address issues of value, and measure them in a way that’s meaningful to payers,” Ruffin says.

The industrialization project will deal with challenges in scale-up, manufacturing, and distribution unique to the RM technologies and continuously arising. “This is not the same as developing small molecule drugs and delivering the medicine in a vial or bottle,” he adds. “It is very difficult, especially in the autologous setting. With all of the different stakeholders and people playing important roles along the supply chain, and the investment, we need to address the infrastructure because it’s not very well understood.”

The RM supply chain also has brought in new players, beyond the old fold of pharma and biopharma. Major medical centers are now recognizing they will play a central role in regenerative medicine, unlike those they have in any other case before, except perhaps in bone-marrow transplantation.

ARM ORIGINS

Ruffin was an eyewitness to the growth of the RM sector in the relatively quiet years between 2006 and 2010, and as a business consultant, he developed a large portfolio of projects and clients in the cell-therapy space. During that period, attention shifted from regulating embryonic stem cells to developing therapeutic applications with mesenchymal stem/stromal cell (MSC) platforms. Companies were also addressing technical challenges in delivery of their new therapies, and the AAV [adeno-associated virus] vector eventually became this new wave of gene-therapy companies. A group representing those interests approached Ruffin, saying they would like to consider putting together a national organization to represent the regenerative medicine sector of cell and gene therapy. That led to the creation of ARM in 2009 with 17 charter members, now up to more than 300 members.

“ARM is really the organization at the forefront of advocacy for cell and gene medicine,” he says. “But we recognized fairly early on one of the major challenges in this space would be education, because people just really didn’t understand what these technologies were, what they were capable of, and the benefits

they could bring to patients. They needed to hear how some of the early concerns around safety had been addressed and gain confidence that we can use these therapeutics in a number of different indications. We also talked about efficacy and the data, because obviously it's not worth all the expenditure if you can't show that these things actually work in a living cell. All of this progress was being made but very little that was being translated for laypeople in a way that they could fully understand and appreciate it."

To fill that gap, ARM created what is now the ARM Foundation. "We wanted to set up the Foundation as a separate organization independent of ARM, the advocacy organization, to lead the national effort of education for and about this sector. It is not a membership organization; it's a classic 501(c)(3). We put together a board of 19 individuals who represent all of the major stakeholder groups in the sector with good, strong representation from the patient community as well as the research community, plus veterans of the space such as our chair, Stewart Parker, former CEO of Targeted Ge-

netics and other companies. This technology will continue to move forward, and it will transform medicine. We embraced that challenge early, and that's one reason ARM has been successful — we recognized regenerative medicine wasn't going away, and despite some early setbacks, the technology continues to evolve."

EXPANSIVE SPACE

And boy, has it evolved. A chart in an ARM Foundation "landscape" assessment shows the current RM clinical trials sorted into 18 different therapeutic categories. Oncology leads the pack with 532 trials, or 54 percent of all trials in the space, targeting many cancer types. The next two areas on the list are cardiovascular, with 74 trials or 7.5 percent, and musculoskeletal, with 61 or 6 percent of total trials.

RM has conventionally included gene therapy, cell therapy, and tissue engineering. But the space is becoming more complex as other, sometimes overlapping technologies enter the scene. Those include cell-based immunotherapies, gene-modified cell therapies, and

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MORRIE RUFFIN
Executive Director, Cofounder, Senior Advisor
ARM

genome-editing technologies. We have featured an increasing number of such therapies and their developers in "Companies to Watch," "The Enterprisers," and other *Life Science Leader* articles.

Janet Lambert, ARM's CEO, notes that rare diseases are the top priority for many RM companies. "The new

therapies will touch potentially thousands of different indications over time, so we imagine they will have a very broad impact," she says. "We anticipate that there will be more approaches as time goes on. And now we're not just talking about the promise of this space, but also products in the market and patients being treated."

Lambert believes some of the more recent treatments to achieve market approval have made a "profound difference" in the level of interest by regulators, policy-makers, the public, and investors in the RM space. In turn, the increasing interest is causing expansion in the number of companies and trials as new investors come into the space. As we all see, even sleepy old Big Pharma has awakened to the sector, thanks mainly to Novartis' Kymriah, Gilead/Kite's Yescarta, and additional achievements in oncology by Celgene/Juno and others. There are additionally very notable deals in other RM technology areas, such as the Novartis acquisition of AveXis in neurological gene therapy.

Pure hope has long been a driver of RM dreams, but as the sector passes into the real world of commercial-

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Total Q2 2018 Global Financings



Total Global Financings

\$4.1 Billion raised in Q2 2018

164% increase from Q2 2017

\$7.9 Billion raised YTD 2018

79% increase year-over-year

Gene & Cell-Modified Cell Therapy

\$2.7 Billion raised in Q2 2018

124% increase from Q2 2017

\$5.8 Billion raised YTD 2018

133% increase year-over-year

Cell Therapy

\$2.2 Billion raised in Q2 2018

416% increase from Q2 2017

\$4.2 Billion raised YTD 2018

83% increase year-over-year

Tissue Engineering

\$421 Million raised in Q2 2018

526% increase from Q2 2017

\$784 Million raised YTD 2018

25% increase year-over-year

Total amount raised represents sectorwide figures; please note that some companies utilize technology from more than one technology group. As a result, the total financings amount does not equal the sum of the raises of the individual technology groups.

Figures do not include M&A transaction totals.

ization, its science and the application of science sometimes seem to be progressing faster than the business end. Most of the business challenges, however, appear to emerge from how unique aspects of the technology affect commercial-scale production. Thus, as ARM pushes investment in industrial knowledge, manufacturing, and infrastructure, and as the support systems improve and work through challenges, it also makes sense for the ARM Foundation to deliver related education and training programs for industry.

As Lambert observes, the most outstanding and unique quality of RM is that many of its products are intended to produce an immediate, profound, and lasting benefit. "Therapies in this category are generally anticipated to have a durable or even curative effect, after a limited number of treatments. That presents a whole new set of challenges in the way most public and private insurance is organized to pay for medical treatments.

The price for a product will be set, there may be only one treatment, and the patient will be cured, permanently or for a significant amount of time. So RM companies are interested in entering into novel payment

arrangements with public and private payers, such as paying for a little bit of a drug's cost every month over a long period of time. Most people think that sounds fine, but the practical reality of implementing it is quite challenging in both the public and private domain."

Companies also have been open to talking with payers about pay-for-performance plans and other innovative models, according to Lambert. "That also is generally pretty appealing for companies as a way to get in the game, but it runs into a spigot of regulations and rules that weren't really designed to prevent it, but make it difficult for payers to actually enter into such agreements."

One example she cites is the set of Best Price requirements in Medicare and Medicaid, which pharma companies have to be careful to follow. "Those requirements could conflict with a model in which somebody pays nothing for a drug because the drug didn't work for them," she says. "Another potential complication in pay-for-performance is that, even though companies may be willing to refund money, doing so might violate antikickback statutes. All such details need to



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CEO, ARM

be examined to make sure that pay-for-performance agreements are lawful for public payers. On the private side, it's more about standard ways of doing business than about government rules and regulations, but there's a bit of both."

LINE OF EDUCATION

Can it be difficult to distinguish between advocacy and education — to see clear boundaries between the two? Perhaps not always in theory, but in practice, education becomes a singular and primary concern, necessary for advocacy to succeed. Once a new industry sector breaks into the consciousness of "innocent" investors and other potential stakeholders, the educational burden swells overwhelmingly, and an industry association must either take on a new function or hand it over to a separate, dedicated, but allied organization as ARM has done with its educational foundation.

"We heard from our member companies that they were each trying to find various buckets of money in their marketing departments or elsewhere, to put together some educational material to explain to the public, their patient community, and their investors what these therapies were and how they fit into the existing landscape of healthcare," says Lambert. "We thought it would make more sense for everyone to come together in a more comprehensive strategic communications campaign. And as much as we are proud that most of the key stakeholders in regenerative medicine are members of ARM, we know other people also care about advancing this space, who may not be members of ARM, but might support a foundation in this communications effort. So the point of our Foundation was to combine the efforts of multiple parties, including ARM members and non-ARM members."

Lambert is happy with the Foundation's early progress and output thus far, but she sees more refinement

of the organization and its process for analysis and targeting of topic areas and audiences. "We're still working out all of the operating mechanisms, and the team here has done a great job, but the demands of running the organization for its members has limited the portfolio we can develop for educating, say, patients and their caregivers," she says. As the RM sector leaves the sheltered world of discovery and early development for the harder commercial and industrial reality, it enters a game with much higher stakes, and many new players.

"We know more and more people are being brought into the conversation, and we want to make sure they have access to credible and trustworthy information that helps them understand and feel comfortable with these therapies. We want folks to participate in clinical trials, to read more about them, and see what might be appropriate for them."

It may be possible that regenerative medicine in all of its forms will become the new life science universe, or at least more ubiquitous in healthcare, even challenging the now-dominant model of engineered proteins. When ARM surveyed people's understanding of the term "regenerative medicine," it found a variety of perceptions.

"It became evident there's no universally held view of what regenerative medicine is," Lambert says. "We often remind people it's cell therapy, gene therapy, and tissue engineering, but new kinds of companies are coming up, and we wonder, are they within our current definition? I don't believe that regenerative medicine will swallow up all medicines, but I know for sure it will be a large and healthy sector." That prediction is likely to come true, considering how many RM programs now include early stage candidates for treating large-population diseases along with their late-stage programs aimed at orphan indications.

"There are definitely interesting things happening in rare disease, but so much of the activity in this space is focused on oncology, which has had such a broad impact around the country and the world," says Lambert. "There's so much energy, interest, and activity right now in blood cancers, but there is also a lot of work going on in solid tumors, too. There are other diseases with large patient populations being targeted by RM companies as well."

It also seems notable that the RM sector is creating a new beacon of hope for long unserved or even neglected medical needs such as sickle cell. As the science of regeneration uncovers more mechanisms that may disturb or help maintain homeostasis in complex metabolic systems, it is finding keys for unlocking age-old mysteries and maladies. Nowadays, the sector represents not only distant but near-term hopes as well. 