Context

In the past decade, regenerative medicine has provided breakthroughs in treatments and technology that the public, policymakers and even scientists struggle to comprehend. Yet few years have begun with as much momentum as well as uncertainty as 2017: a new president, a new session in Congress, new leadership in key health care oversight agencies and the implementation of the 21st Century Cures Act, passed just weeks before the end of 2016.

The $6.3 billion, 1000-page piece of legislation took more than three years to move through Congress, which describes the bill as a force of modernization and innovation. Regenerative medicine has played a key role in both of those currents. Congress recognized this by adding funding and by using the Cures Act to accelerate approval of regenerative medicine products, helping to get therapies for otherwise incurable conditions to the market more quickly without sacrificing patient safety.

The act also defines regenerative medicine, providing a consistent categorization for the first time. According to the legislation, regenerative medicine involves "cell therapy, therapeutic tissue engineering products, human cell and tissue products, and combination products using any such therapies or products," except for those regulated under a separate regulation.

Robert Preti, Chairman of the Alliance for Regenerative Medicine advocacy group, called 2017 an "inflection point." Indeed, the industry is at a turning point, poised to enter the next phase of maturity in which more clinical trials will begin while others begin to yield important data that will help push regenerative medicine further into the health care system. Trends that began several years ago will continue to unfold within a context of political transition, private funding, a push to advance new technologies and therapies and the commercialization of existing ones.

Oncology is likely to remain dominant among clinical trials in all phases. But in 2017, trial designs will become more adaptive, participant-focused and include an influx of late-stage studies that, if successful, could set the stage for ground-breaking science in the years ahead and more clinical trials in the near future. More CROs will begin to focus on developing the specialized expertise they need to run regenerative medicine clinical trials.
The following are trends in regenerative medicine clinical trials on the horizon in 2017. Of course, any predictions depend on the incoming president, the 115th Congress and new leadership in key agencies. How their decisions affect the future of regenerative medicine remains to be seen.

**Therapeutics will have to navigate in new political waters**

In addition to the Cures Act, the year 2017 will start out with a new president, Donald Trump, and beginning of the 115th Congress. Their support for regenerative medicine will do much to determine progress in the industry. Already Trump has nominated U.S. Rep. Tom Price to lead the Department of Health and Human Services, which directly oversees the National Institutes of Health. Originally an orthopedic surgeon, Price serves as chairman of the Committee on the Budget in the House of Representatives and sits on the House Ways and Means Committee – including the Subcommittee on Health. He is a staunch opponent of embryonic stem cell research, which could mean a rollback of policies on the use of fetal tissue and embryonic stem cell research loosened under the administration of Barack Obama. Notable too is the requirement under the Cures Act that the FDA work with the National Institute of Standards and Technology and other stakeholders to create standards and definitions for RM products.

**The industry must prepare for new leadership at the NIH**

A tightening of policies around embryonic stem cell use could also come from the National Institutes of Health if Trump successfully appoints U.S. Rep. Andy Harris to lead the agency, a pivotal partner in advancing regenerative medicine. Harris is an anesthesiologist who has served three years in Congress. He helped write the 21st Century Cures Act and is staunchly opposed to research with human embryonic stem cells and expectations are that his appointment could prompt dissent among NIH leaders and drive them away from the agency. The current director, Francis Collins, has steered the agency since 2009. Collins announced he will stay on if selected by Trump. In talks and statements Collins has shown his enthusiasm for advancing regenerative medicine research and technologies. He endorsed the recommendation of the Institutes of Medicine to limit in-depth review by the NIH Recombinant DNA Research Advisory Committee (RAC) to exceptional cases in which novel therapies or important scientific and ethical issues arise and has signed on to other efforts to centralize and streamline regulatory processes.

**The FDA will see pressure to become more market-oriented**

The U.S. Food and Drug Administration may also see new leadership in 2017. Candidates for the FDA post include businessman Jim O’Neill, who last served in government as principal associate deputy secretary at the Department of Health and Human Services under the administration of George W. Bush. Otherwise, his experience is in the business world. He is currently managing director at Mithril Capital Management owned by Silicon Valley venture capitalist Peter Thiel, who has been a key advisor to Trump. In the past, O’Neill has said he supported reforming FDA approval rules so that drugs could reach the market before they have been proven to be effective if trials show they are safe. The FDA approval process mandates that drugs must be proved safe and effective before they can be sold. The new accelerated approval process authorized by the Cures Act allows regenerative medicine products aimed at serious, otherwise incurable diseases.
Public funding of regenerative medicine will remain steady in 2017

The Cures Act marked $30 million to expand clinical research for regenerative medicine using adult stem cells. However, the Cures Act left out the category of regenerative medicine belonging to gene therapies, an omission the industry intends to correct in 2017. The industry will have a second chance with this year’s reauthorization of the Food and Drug Administration Safety and Innovation Act, or FDASIA.

The extent of therapies and technology included in the legislation is uncertain but organizations such as ARM are already engaged in conversations with Congress.

Outside private financing remains a significant source of funding

A recovering economy and growing interest in biomed research has been opening the doors to an increase in investors interested in the regenerative medicine sector, supplying a source of non-governmental funding. The high point reached $11 billion in 2015. The next year was less promising: total financing in 2016 fell by more than half, to $5.3 billion. VC funding, while weaker than the year before, finished at nearly $1.2 billion. Collectively, the initial public offering market for regenerative medicine was worth $557 million in 2016. The figure was just under $1.7 billion for IPOs the previous year. Companies that did go public in 2016 also held their value in the post-IPO market and continued to trade above their IPO prices. Large pharmaceutical companies continued to enter the sector. As such, merger and acquisitions led the financings with a total of just under $1.1 billion. They will continue along the same path of acquisitions and partnerships in 2017 out of an eagerness to edge out potential competition. However, the numbers are likely to remain flat until the data can show that regenerative medicine products are viable and outperform alternatives already on the market. In 2017, investors will also react to the availability of more data from clinical trials, providing details about the efficacy of products.

The product pipeline will continue to grow and diversify, adding more trials

The year begins with more than 759 regenerative medicine companies in operation worldwide, more than half in the United States. New companies are expected to expand that number and add to the trials, which rose in 21 percent. More importantly, a small but growing number of the trials are in the pivotal stage, promising to produce data in the near future. As the year ended, Phase I trials had grown by 41 percent, from 192 to 271 over the past year. The number of Phase II trials also rose from 375 to 465, an increase of 25 percent. Phase III trials also increased slightly, by 5 percent, from 63 trials to 66. Today there are an estimated 2,500 regenerative medicine clinical trials underway, involving tens of thousands of patients. The majority -- 45 percent -- are in oncology, a trend that increased over the past year although the stage is set for more programs in neurodegenerative and rare metabolic diseases.
Pressure to reshape trial designs will intensify

The Cures Act recognized that one-size-fits-all, large randomized clinical trials no longer match 21st century demands, which increasingly revolve around active participation of patients and innovative, efficient designs. The legislation reflects this recognition by calling for adaptive design methods in clinical trials that allow the trial or its statistical procedures to be modified after the study has begun. Regenerative medicine trials create yet more incentive for innovative designs because, unlike traditional models of medical treatments which involve ongoing treatments, regenerative medicine can alter the fundamental mechanisms of disease. Its curative nature, focused on rare diseases, incentivizes nimble, tailored designs. In addition, the NIH announced at the end of 2016 that NIH-funded, multi-site clinical research studies conducted in the United States using the same protocol should expect to employ a single IRB to complete the ethics review of proposed research. The bottom line is that, overall, the trend will be toward small, niche trials that help contain costs.

The regenerative medicine toolbox will expand dramatically

In late 2016 a team of scientists in China tested the groundbreaking gene-editing technique CRISPR for the first time in a human trial. In October, the team at Sichuan University in Chengdu inserted the cells modified (or, "edited") using the CRISPR-Cas9 enzyme into a patient with aggressive lung cancer as part of a clinical trial. The first human study employing CRISPR in the United States will certainly launch in 2017. Trials will also be underway using other similar techniques such as zinc-finger nucleases and TALEN although they have not created the excitement generated by CRISPR, an excitement tempered by the technique’s lack of precision. However, the search for more adept versions have already begun and will flourish in 2017. That is likely to bring to the forefront regulatory concerns over the capacity of gene-editing techniques to make permanent DNA changes.

CROs must be conversant in new models to be competitive

The distance between promise and proof is still long for regenerative medicine. But given the legislative victories and financing available, CROs must be prepared to see regenerative medicine as more than a niche market and master the expertise needed to conduct clinical trials in the sector. PRC Clinical has been focusing on regenerative medicine for many years. It is challenging because it requires thinking about disease and data differently. The design of early-phase clinical trials often differs from the design for traditional pharmaceutical products because they involve cellular, tissue, and gene therapies. The FDA advised that the design of early-phase clinical trials of these products often involves consideration of clinical safety issues, preclinical issues, and chemistry, manufacturing, and control issues rarely encountered otherwise. Just establishing dose and modes of delivery are more challenging. CROs will need to understand the market, the regulatory challenges and the nature of regenerative medicine in order to participate.

Next Steps

The discovery-to-trial pathway has developed considerably in the past decade. In 2017 the attention will be on developing new technologies, data and the viability of regenerative medicine approaches needed to unlock further political support and fundraising. On a parallel track, the regulatory and commercialization of the industry needs work. Gene editing techniques will force further discussions with authorities that the industry welcomes as an opportunity to negotiate
wider issues related to the regulatory process that is still evolving in regard to regenerative medicine. This will be necessary to move forward with large-scale production that is necessary to continue to grow the industry and should complement the Cures Act requirement for oversight agencies and stakeholders to develop definitions and standards. Look for legislation in 2017 to establish a body that would coordinate standards in regenerative medicine and advanced therapies. Another priority this year includes raising awareness and acceptance among clinicians to regenerative medicine treatments, a role that CROs are in a position to fulfill during clinical trials. That said, wider adoption among clinicians will entail ironing out insurance reimbursement policies, which are ill-equipped for the curative nature of regenerative medicine as opposed to the traditional healthcare model. Ultimately, although these factors seem distant from CROs, they, like the other issues covered here, will influence the growth of regenerative medicine clinical trials.

PRC Clinical is the CRO of choice for many pharmaceutical, biotech and regenerative medicine developers worldwide, offering a next-level clinical trial management experience.

Our innovative approach to executing studies merges our high-touch human element with high-tech tools, extensive experience and deep knowledge – far exceeding the level of service offered by large CROs. PRC Clinical offers full Clinical Trial Management services including Clinical Project Management, Site Monitoring, Quality Assurance, Drug Safety, Payment Services, Biostatistics, Data Management, Regulatory Strategies, and Site Selection.

PRC Clinical has significant CRO experience in a wide range of therapeutic areas: Regenerative Medicine / Stem Cells / Gene Therapy, Ophthalmology, CNS, Oncology, Neurology, ALS, Parkinson’s, Pain, GI, Device, Anti-infective, Cardiovascular, and Pulmonary.

PRC Clinical is collaborating with the California Institute for Regenerative Medicine (CIRM) and a member of the Alliance for Regenerative Medicine (ARM), joining more than 200 organizations working in research, development, investment, and commercialization of regenerative medicine treatments worldwide.

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