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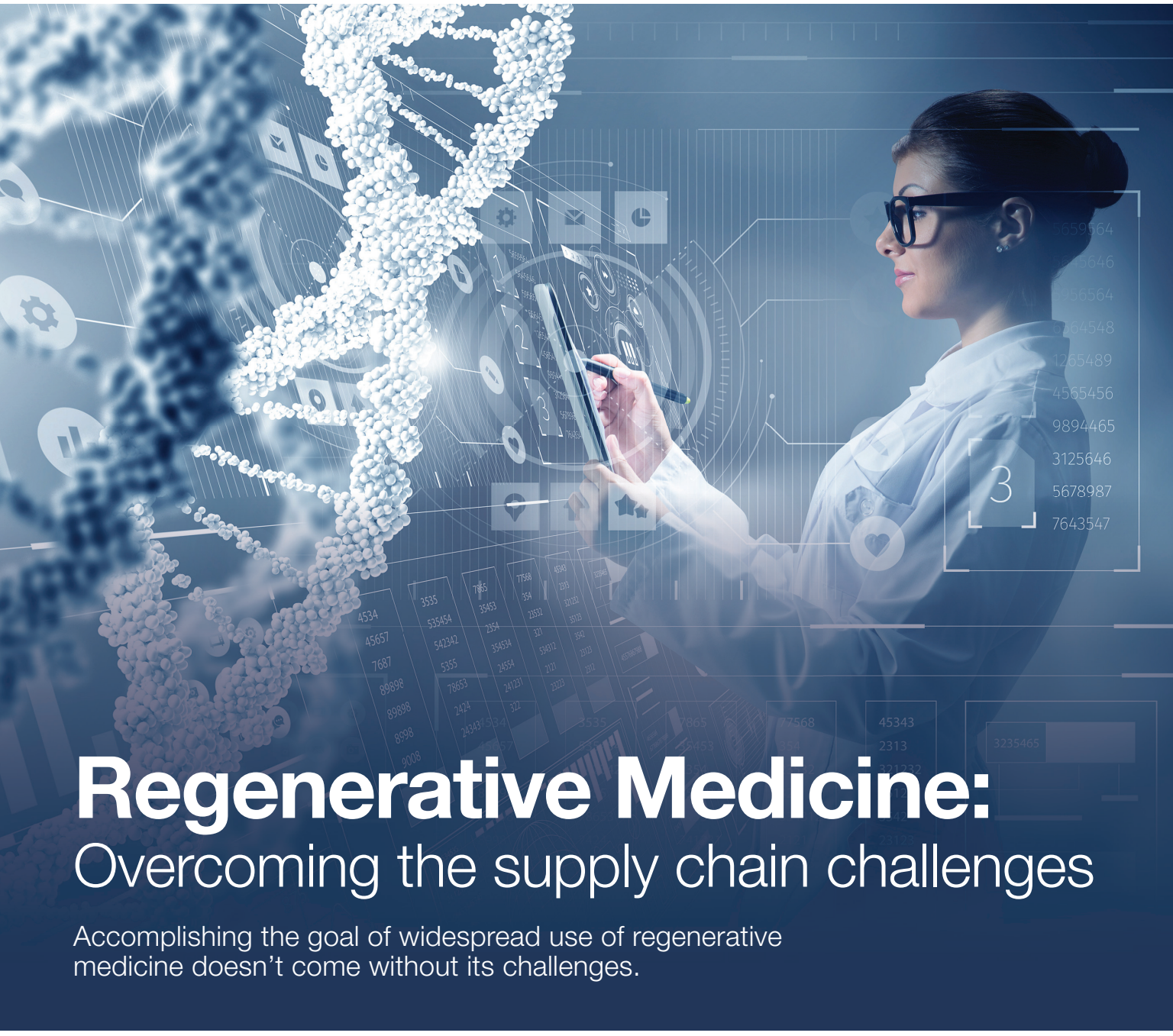


Regenerative Medicine:
Overcoming the supply chain challenges

Accomplishing the goal of widespread use of regenerative medicine doesn't come without its challenges.

Regenerative medicine is one of modern science's most exciting developments. Defined by the Medical Research Council, "regenerative medicine is an interdisciplinary field that seeks to develop the science and tools that can help repair or replace damaged or diseased human cells or tissues to restore normal function".

In the human body, the liver is the only organ capable of regenerating itself spontaneously—even after serious injury—but in the future, any part of the human body may be capable of doing so. Our own cells will also be able to treat and cure diseases and conditions of the blood and immune system, as well as restore the blood system after treatments for specific cancers.

Once only imaginable in science fiction, the latest applications include engineered skin tissue to treat burn victims, custom-grown bones for implants and joint replacements, personalized dietary treatments using gut bacteria and just recently, the world's first 3D vascularized engineered heart was created using a patient's own cells and biological materials.

As scientists' understanding and the tools at their disposal become more advanced, the closer to the widespread commercialization of regenerative medicine the pharmaceutical industry finds itself.

However, offering regenerative medicine therapies at scale requires one of the biggest shake-ups to the global pharmaceu-

tical supply chain ever seen. Without it, the world risks missing out on the curative promises of this next-generation medical technology.

UNDERSTANDING THE POTENTIAL OF REGENERATIVE MEDICINE

Regenerative medicine is one of, if not the most, exciting advancements in modern science which has far-reaching benefits for big pharma, healthcare systems and patient outcomes.

Regenerative medicine is a "growth" industry in more than one sense of the word; as a sector, it's growing from strength to strength. In fact, last year the global regenerative medicine market was worth $28 billion and it's expected to grow to $81 billion by 2023.

As a more efficient and less invasive alternative to transplanting cells or organs to replace damaged or lost tissue, established pharma companies alongside small biotech start-ups are racing to discover and bring to market medicine-based approaches that stimulate the body's natural ability to repair itself.

The cutting-edge innovations of regenerative medicine generally fall into three distinct categories:

- Replenish
- Replace
- Rejuvenate

Stem cells can generate vital growth factors to naturally reduce inflammation, increase muscle mass, repair joints, grow hair and boost the immune system, replenishing the body. Organ regeneration and 3D printing are replacing the reliance on the failing donor system and overcoming the issue of organ rejection. The root causes of aging are being better understood and delayed by using stem cells to rejuvenate the body.

Marking a new era in healthcare and one which has the promise of addressing the needs of an aging population challenged by escalating chronic diseases, regenerative medicine is certainly a game-changer. Beyond more effective medical treatments that can be applied routinely despite age, comorbidities, or disease severity, it also has the potential to cure many of today's "incurable" diseases and support healthcare systems to move towards a preventative model.

DELIVERING REGENERATIVE MEDICINE FROM LAB TO CLINIC

Today, regenerative medicine is largely confined to a research environment. In fact, according to a recent report, there were 1,028 clinical trials for regenerative therapies taking place globally at the end of 2018.

Regenerative medicine is poised to transform healthcare as we know it, offering potential cures for deadly diseases which before would require long-term treatment to manage. However, while billions are being spent on regenerative medicine research and clinical studies, little resource has, so far, been allocated to the management and delivery of innovative medical therapies at scale.

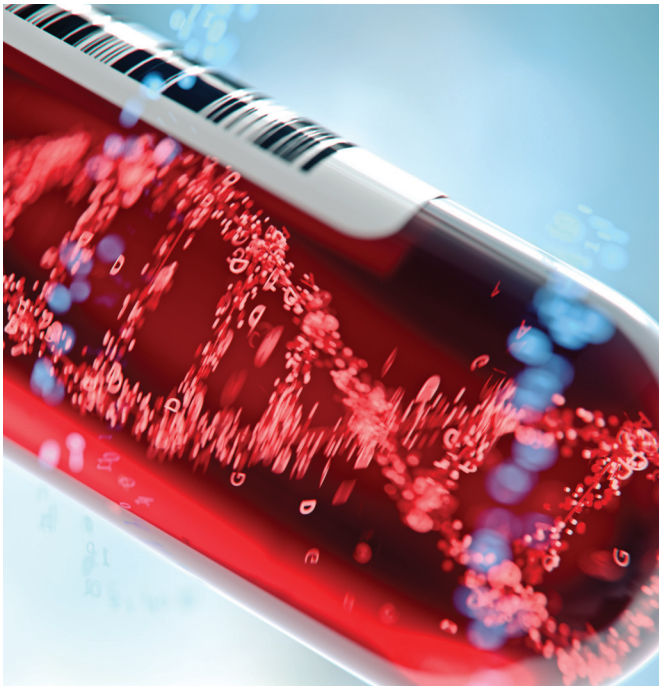
Currently, the race appears to be on between smaller Medtech companies and large multi-national pharmaceutical companies to see who wins first-mover advantage in the regenerative medicine market. Today, many established pharmaceutical companies prefer to partner with Medtech startups to in-license products in early clinical development stages as opposed to conducting early development on their own which comes at a huge cost. This is a risk-reduction tactic, but it could mean big pharma misses the boat.

The question remains unanswered as to whether a peer-to-peer collaborative model will prosper where Medtech companies—who are in some instances one step ahead of big pharma in terms of drug development—are happy to be a third-party provider to big pharma who have the budgets and networks to truly deliver the regenerative medicine revolution.

Regulation is, and will continue to, play a hugely important role in delivering regenerative medicines from a lab setting to a clinical setting. Only recently, the FDA announced a new policy framework for the development of regenerative medicine products, taking into account the dynamic and fast-moving nature of the field.

Ultimately, the government's aim is to "protect patients from products that pose potential significant risks, while accelerating access to safe and effective new therapies" according to Former FDA Commissioner Dr. Scott Gottlieb. The FDA plans to achieve this over the coming years by driving stakeholder engagement with the developing regulatory framework in order to efficiently advance access to safe and effective regenerative medicine advanced therapies.

However, so far, progress by the pharma industry in coming into compliance with FDA's regulations for regenerative medicines has been slow, despite the grace period set by the FDA before it fully exercises enforcement fast approaching (ending in November 2020).



> “The clinical supply chains required to deliver these therapies are arguably the most complex the industry has seen so far, even more so than for biologic medicine.”

In order to speed up the process of bringing novel medicines to market, the FDA is toying with the idea of fast-tracking products that are deemed low risk to patients if sponsors have engaged with the regulatory process and demonstrated responsibility by filing Investigational New Drug Applications (INDs).

The FDA has also promised to strengthen its enforcement action against drug developers who are marketing unapproved products, prioritizing cases where the threat to patient health and safety is largest.

For example, last November the FDA stepped in where a Californian business was selling stem cell products using umbilical cord blood for the treatment of arthritis and other conditions, despite this form of treatment not having FDA approval for that particular use. Several patients (at least 12) undergoing this treatment were hospitalized after developing infections of the bloodstream and joints, as well as abscesses along the spine and skull.

In summary, one of the FDA’s central aims over the coming years is to drive stakeholder engagement with the developing regulatory framework for regenerative medicine advanced therapies in order to efficiently advance access to safe and effective new products.

ESTABLISHING AN EFFICIENT SUPPLY CHAIN FOR REGENERATIVE MEDICINE

The promise of regenerative medicine requires an innovative look at the complete product lifecycle, including the development of an efficient distribution network.

Once these novel drugs become mainstream, the entire healthcare ecosystem will have to adapt. Regulatory approval for any drug relies on it safely and successfully fulfilling its medical intent. As such, information about supply chain management needs to be submitted to the regulator after the completion of phase three clinical trials, including packaging, labeling, storage and distribution.

The clinical supply chains required to deliver these therapies are arguably the most complex the industry has seen so far, even more so than for biologic medicine. That’s because, unlike many mass-market drugs, regenerative medicine is either personalized or matched to a unique donor-recipient.

The distribution of regenerative medicine therapies is further complicated by the fact they are also extremely sensitive to exogenous factors like time and temperature. Therefore, there are strict conditions under which these therapies must be transported and received.

Advanced IT solutions and monitoring systems are being developed and employed to ensure end-to-end traceability across the pharma supply chain. These are giving clinicians access to view the progress of therapies and their distribution in real-time and allow users to automatically schedule or amend material collections in line with manufacturing capacity, helping to keep the supply chain as agile as possible and avoid costly wastage.

The live tissues and cells which form the basis of regenerative medicine products are highly sensitive and some have a shelf life of no more than a few hours, making distribution a complex task. Therefore, materials need to be transported from the site of harvest to manufacturing facilities, and from manufacturing facilities to medical institutions under strictly controlled conditions, within certain time periods and temperatures, according to different cell and tissue requirements which can vary from product to product.

Temperature-controlled logistics solutions are vital to ensure a safe, effective and financially viable supply chain network for these high-value shipments. Cryopreservation is one technique increasingly being used to deliver medicines at optimum temperature using vapor phase nitrogen, however, many clinical settings remain ill-equipped to handle such equipment.

Onsite production is an alternative manufacturing arrangement, particularly for autologous products which are derived from a patient’s own cells. However, this throws up a number of compliance and infrastructure challenges, as the hospital would need to comply with a host of regulations including installing a licensed clean room which may not be possible given budget restrictions and limited space onsite.

As a first-generation technology, stakeholders will have a greater tolerance for higher pricing, but only for a limited time period. By streamlining the currently very expensive manufacturing process and improving supply chain management, yields will automatically get larger and costs will slowly come down.

While there are many challenges in the road ahead, 2019 certainly appears to be the start of regenerative medicine’s move to the big time. Just like big data and artificial intelligence is transforming the practice of medicine, regenerative medicine holds the promise of extending the body’s natural ability to replenish, replace and rejuvenate itself.

If the global health industry can work collaboratively on overcoming the challenges presented by delivering safe and effective advanced therapies, a dramatic extension of the human healthspan is possible. We may even reach the point where no disease is considered “incurable”, transforming healthcare as we know it. **CP**

RICH QUELCH is an experienced global marketer within the healthcare and pharmaceutical sector. He has led the development of the Origin brand, positioning it as a world-leading supplier of innovative and ground-breaking pharmaceutical packaging devices, as well as offering a unique supply chain model which is disrupting the pharma industry.

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