Roland Berger Focus

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Regenerative medicine

The next generation of therapeutic products is set to shake up the pharmaceutical world

Roland Berger

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navigating complexity

Management summary

Regenerative medicine is an exciting and multifaceted new development in the world of medical treatment. It promises novel therapeutic approaches to replace or restore the original functions of tissues, functional systems or even entire organs. The field also includes stem-cell and gene therapies, tissue engineering and materials science. Indications range from wound healing and tissue transplantation to curing damaged organs and even entire diseases, such as cancers, genetic disorders and autoimmune diseases.

Stem-cell and gene therapies represent a major revolution in medicine. They also represent a revolution for patients, shifting the focus from treatment to healing. While, for now, the bulk of the innovation will continue to come from chemical and biological compounds, we see a growing pipeline of stem-cell and gene therapies that will play a role in the pharmaceutical market of the future. Clearly desirable from a human perspective, these new approaches are also highly attractive from both a scientific and a commercial perspective.

But this revolution in medicine raises many questions and hurdles. Big Pharma is currently less active in the field of stem-cell and gene therapies than other players, and a real risk exists of them missing out on this opportunity. Alongside biotechnology ("biotech") companies and university hospital research centers, a new type of player has emerged in the field: medical technology ("medtech") companies. Medtech's role is to provide the framework for administering the stem-cell and gene therapies, and to engineer the desired tissue matrices for transplantation.

Once regenerative medicine has become mainstream, the entire healthcare ecosystem will have to adapt. Regenerative medicine requires special patient settings for application and new forms of reimbursement. Healthcare systems, payers and society need to decide how much they are willing to spend for patients to be healed of deadly diseases.

Pharmaceutical companies, for their part, must prepare themselves for the coming revolution, ensuring that they are able to integrate and launch the new therapies as and when they emerge. This will involve strengthening their "innovation radar" and scouting capabilities, reviewing their R&D and commercial models, establishing a supply chain for regenerative medicine, training physicians, developing digital services to support the use of the new products and generate real-life data, and shaping new market-access models in partnership with payers.

One thing is beyond question: Regenerative medicine is on course to transform the pharmaceutical world. By following our practical recommendations, Big Pharma can ensure that it is not left behind in the process.

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Chapter 1:

Regenerative medicine is poised to expand

Will Big Pharma miss the boat?

Regenerative medicine is currently limited to very few specialist clinics and trial situations. The majority of clinicians today know little about regenerative medicine and its potential. But regenerative medicine is set to transform the future of healthcare. We expect the global market to expand from a value of around EUR 18 billion in 2016 to somewhere in the region of EUR 130 billion by 2025. → A

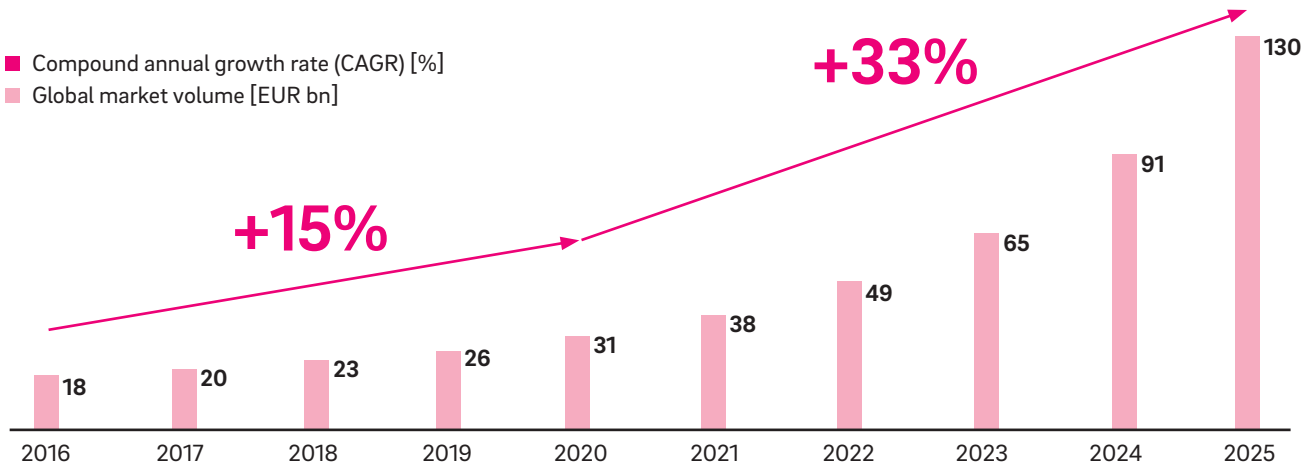
Stem-cell and gene therapies are on the rise, and their pipeline is growing. The reason these new treatments are so important is that they offer a potential cure for diseases rather than long-term treatment, shifting the focus from treating to healing. The current industrial pipeline is packed, with around 300 stem-cell and gene therapies in development registered in public databases. We estimate that a further 10 to 30 percent of stem-cell and gene therapies are currently in development outside the industry at academic institutions such as universities and scientific centers.

What is striking, however, is the current lack of involvement of Big Pharma in regenerative medicine. Only around 50 of the 300 or so stem-cell and gene therapies currently on the way – less than 20 percent – are being developed by Big Pharma. → C

Big Pharma has, by and large, chosen a strategy of in-licensing new technologies at a relatively advanced development state. This approach is driven by precaution and the desire to bet only on sound, proven concepts. While this makes sense from a risk perspective, the danger is that Big Pharma will miss out on major opportunities and potential "hidden stars." Major pharmaceutical companies need to decide whether to play an active role in the emerging business of regenerative medicine or to stand on the sidelines. At the same time, they must be aware that new developments in regenerative medicine may cannibalize drug innovations that have a more traditional mode of action.

A: Get ready for growth

The market for regenerative medicine [EUR billion]



Source: Roland Berger

Chapter 2:

The pharmaceutical industry is evolving before our eyes

Players must redefine their roles and evolve from drug-product manufacturers to providers of therapeutic interventions.

We believe that both Big Pharma and biotechs will have to evolve from drug-product manufacturers to providers of therapeutic interventions. Stem-cell and gene therapies are much more difficult to integrate into the pharmaceutical value chain than previous innovations as they require a controlled process, from intervention by doctors to application in patients.

By comparison, when biopharmaceuticals, or "biologics" – drugs manufactured from biological sources – appeared on the scene some decades ago, only the early development steps had to be changed, from screening compound libraries to engineering the molecules needed. Nevertheless, it took about two decades for Big Pharma to incorporate biologics into their product portfolio. Even today, many pharmaceutical companies prefer to partner with a biotech to in-license products in early clinical development stages rather than conduct early development on their own.

Stem-cell and gene therapeutics affect all steps along the pharmaceutical value chain. Early development is different from chemicals and biologics as the interactions of numerous parameters need to be optimized, such as gene expression, cell viability and matrix. Not only that, clinical development and the relevant regulatory guidelines must be adapted to meet the specific requirements of these new therapies. What, for example, is the dose of a cell product?

Even when a stem-cell or gene therapy product is approved, it can't merge seamlessly with the established processes. Production of stem-cell and gene products not only requires completely different skills and technology, it needs to be located closer to physicians and patients. It will not be enough for companies to simply establish a production site somewhere in the world to serve global demand. Stem-cell and gene therapies are mostly patient-specific with a batch size of one unit.

Physicians need to be incorporated into the production process early on, as it generally falls to them to deliver the patient's stem cells or analyze their genetic predisposition. Other specialists such as clinical chemists or geneticists will then apply a procedure to the material obtained to give it the desired effects, or process the information obtained, and turn it into a pharmaceutical therapy before it can be readministered to the patient.

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PROTECTING INTELLECTUAL PROPERTY

Another key issue concerns protecting intellectual property. It will not be possible to base protection on the ingredients, as is the case with conventional pharmaceuticals. Instead, it will have to be based on the process of converting a patient's stem cells or genes into a favorable therapy. This is also where the value that a pharmaceutical company can add to such a form of therapy lies: it can simplify and standardize the use of highly complex procedures along the processing chain for stem cells or genes, thus providing the tools, techniques and agents required to conduct such procedures at any given hospital.

A NEW KID ON THE BLOCK: MEDTECH

But is it certain that Big Pharma will be the ones to take over next-generation products? Maybe Big Pharma is unable integrate stem-cell and gene therapeutics into its current operations. Maybe a different mindset is needed to cope with products of such high complexity. Or maybe new business models are required to generate profit with such products.

A new competitor has emerged on the scene: medtech companies. Some medtech companies are already one step ahead of Big Pharma. Indeed, the medtech industry seems to be better positioned to profit from regenerative medicine. Medtech companies do not depend on single blockbuster products but generate profits with a large product portfolio. These players are also used to designing customer-specific solutions and adapting them to individual needs, as is the case with surgical instruments.

Most of all, medtech is already a partner in regenerative medicine, where combination products such as engineered tissues are produced. In many applications, cells only work when the environment – the matrix – provides appropriate living conditions. For example, ACTs (autologous chondrocyte transplants) only became a product in clinical routine when suitable matrices were developed to harbor cartilage cells.

Future therapies involving regenerative medicine will require tools, techniques and agents that can be used in-house to ensure their broad availability and use. Specific machines, devices, toolkits and process steps involving instruments and agents will be needed, and will be provided by the medtech industry.

Will the medtech industry be happy to act as a third-party manufacturer of specific tools and instruments, and take a secondary role as supplier to the pharmaceutical industry? Or will peer-to-peer collaboration models with Big Pharma succeed? Today, the race seems open – and it also involves competing biotech companies and leading research-driven healthcare providers.

ALL PARTIES NEED TO JOIN FORCES

Healthcare ecosystems consist of different types of players. → **B** While hospitals and healthcare professionals are responsible for delivering treatments, regulatory authorities and insurance companies are responsible for remunerating the parties involved. Pharmaceutical, biotech and medtech companies supply the system and have mainly driven innovation in the past. Now all parties will need to join forces to ensure broad, high-quality patient access using different means of integration, such as digital platforms and new reimbursement schemes. Real-life tracking of therapeutic success will be more important than ever, as healthcare systems will only pay for performance.

Substantial changes are likely on the operations side. Regenerative medicine, unlike current off-the-shelf pharmaceutical treatments, requires individualized manufacturing of tailored therapies. For many therapies, cellular material must first be sourced from blood, bone marrow, liquor or organ biopsies taken from the patient. This will be done locally at hospitals by healthcare professionals such as physicians and surgeons.

Once derived from the human body, stem cells and genes are fragile products that require immediate processing. This is unlikely to take place at the manufacturing sites of pharmaceutical companies. Instead, initial processing will probably occur at the bedside in the hospital, in a hospital pharmacy or at a clinical laboratory connected to the hospital. The procedure involved will require special training and investment in the necessary instruments and manufacturing devices.

While some new therapies may be simple injections, others may require interventional or even surgical implantation into the patient's body. A significant level of investment both in infrastructure and in the education and training of qualified personnel is therefore required if patients are to be treated with regenerative medicine on a broad basis.

What is regenerative medicine?

Regenerative medicine is a new and valuable treatment option for more and more acute and chronic clinical conditions. Using different types of regenerative medicine, it is possible to significantly improve such chronic conditions as cartilage defects or malignant melanomas. It is even possible to cure certain diseases, such as some types of leukemia and a rare genetic form of lipoprotein lipase deficiency. In terms of transplants, scientists have managed to tissue engineer the first autologous organ parts when donors were lacking. They have successfully constructed bladders, blood vessels, skin grafts, tracheal parts and even corneal skin from patients' own cells and tissues.

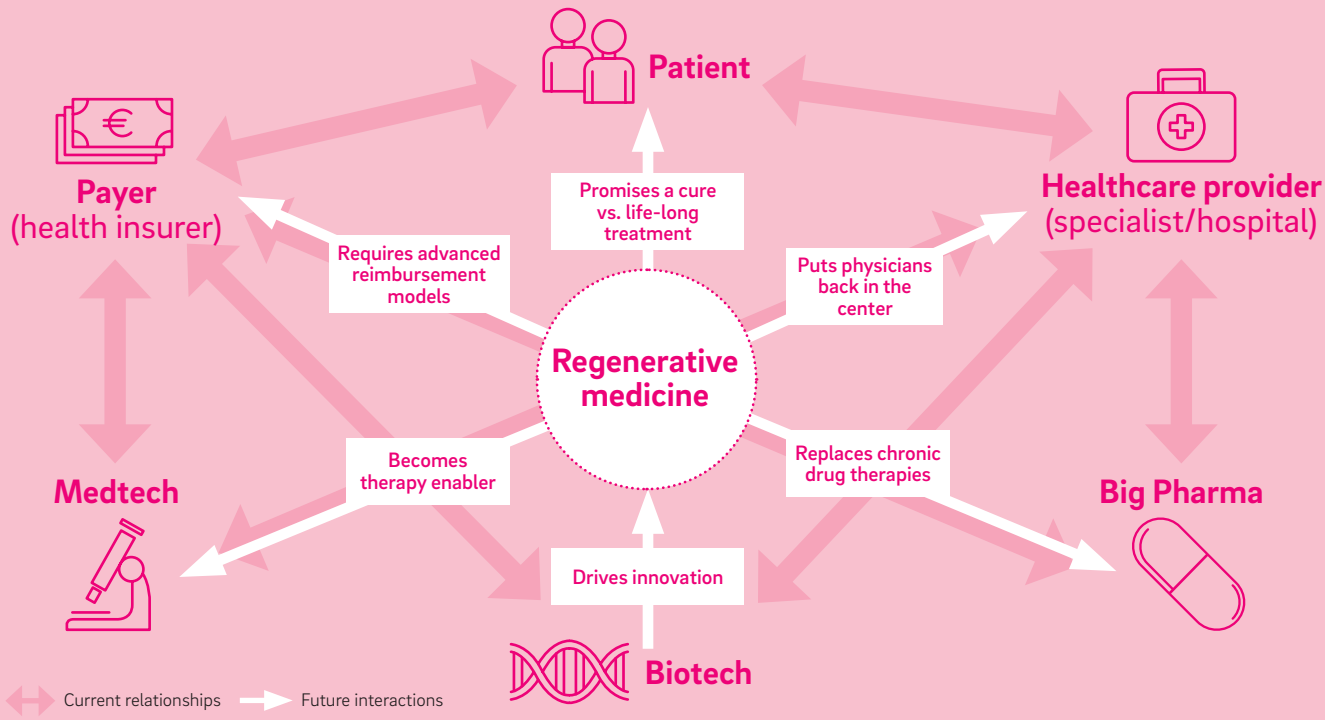
Examples: The first **ex-vivo stem-cell gene therapy** to treat patients suffering from a very rare disease called ADA-SCID (severe immunodeficiency caused by a lack of adenosine deaminase) received marketing authorization in April 2016. The product, Strimvelis was developed by San Raffaele Telethon Institute for Gene Therapy and GlaxoSmithKline. The price for the therapy was set at approximately EUR 600,000 – double the annual cost of enzyme replacement therapy.

An ex-vivo gene therapy approach has also been chosen by another partnership between academia and industry. The consortium HemAcure addresses a far more frequent disease, hemophilia A, which represents a major pharmaceutical market worth almost USD 8 billion. HemAcure consists of academic groups from Germany, Italy and the United Kingdom, and uses a medical device supplied by a Canadian medtech company.

One European biotech company is even further along the road, with an **allogenic stem-cell injection** currently in the approval process. The manufacturer plans to launch the product this year. The treatment aims to cure anal fistulas in patients with inflammatory bowel diseases (IBD) via a onetime injection of pluripotent human stem cells sourced from the donor's fat cells and cultivated in the lab prior to injection. The treatment is able to significantly reduce the time of fistula closure and saves the patient and the healthcare system an average of five to seven complex surgeries.

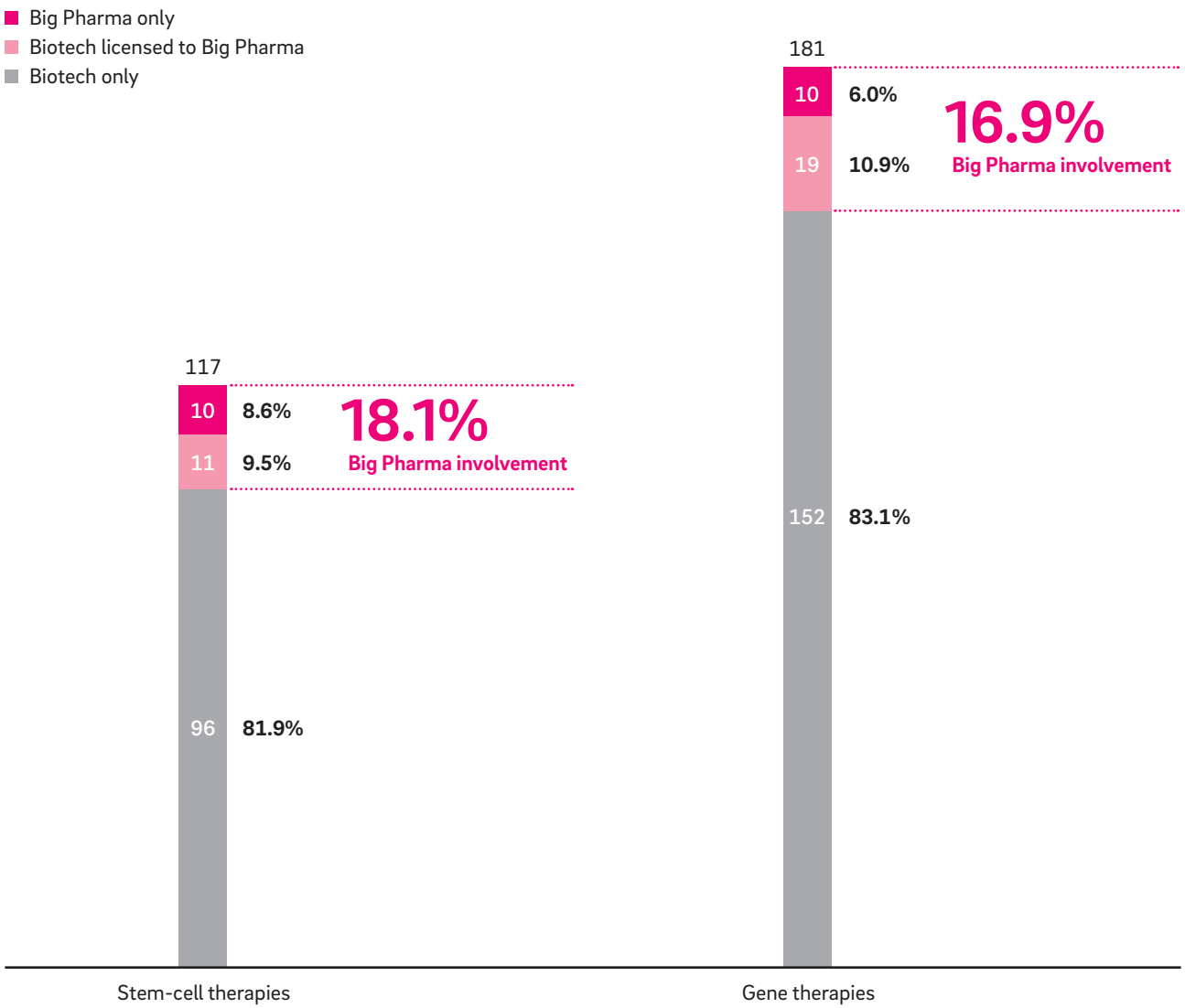
Regenerative medicine is revolutionary in that it potentially cures diseases, or prevents them from occurring in the first place. Ultimately it may replace palliative treatments for the chronically ill. In fact, it is not impossible that we will see diseases become extinct for which patients used to take daily medication for decades.

B: Regenerative medicine is set to transform the healthcare ecosystem



C: Big Pharma, small player

Active pharmaceutical ingredients currently in clinical development



Source: Citeline, Roland Berger

A NEW OPERATING MODEL AND NEW REIMBURSEMENT MODELS ARE REQUIRED

The level of investment required by the promise of achieving breakthrough results in the therapy of chronic or life-threatening diseases raises an uncomfortable question: What are cures actually worth? Or rather, what costs can society handle? The question must be answered separately for each treatment, based on the target population size and the severity of the disease. However, the problems it raises and the need for negotiation between payers and providers of such therapies will be the same in each case.

Currently, the most expensive therapies cost around USD 100,000 per patient per year and prolong life for only a couple of months on average. This gives pharmaceutical companies a justification for demanding USD 1 million or more per patient where they are able to provide therapies that have the potential to cure a disease. Unfortunately, this is not the way pharmaceutical remuneration works. Healthcare systems will simply not be capable of paying such linear extrapolations of prices for gained lifetime. At some point, the financial value will grow more slowly than the value the therapy provides to the patient.

The truth is that current reimbursement models are not ready for regenerative medicine. Roland Berger foresees far more complex and integrated commercial remuneration models developing for regenerative medicine in the future. We believe that, before a complex regenerative therapy enters the market, it must have a sound commercial model behind it. This may be the only way to ensure that the providers of the therapy are sufficiently reimbursed to keep them committed to it in the long run.

Possible remuneration models for stem-cell and gene therapies include shared cost models, special financing plans, milestone payment models and repayment models in the event of failure. Partnerships and incentives will also be needed for the clinical laboratories and hospital pharmacies involved in the event that therapies need to be partially delivered on site.

Current reimbursement models are not ready for regenerative medicine. We foresee far more complex and integrated commercial remuneration models.

Designing commercial models for these complex, costly therapies is likely to determine whether or not they are available in certain countries. It also represents an enormous chance for healthcare systems to work together with the pharmaceutical and medtech industry to develop sophisticated win-win models that benefit everyone: pharmaceuticals and medtech suppliers, payers, providers and, of course, patients.

Chapter 3:

Time for out-of-the-box thinking

Our recommendations for Big Pharma: reexamine your position and develop a fitting strategy.

The advent of regenerative medicine is a game changer for Big Pharma. Given the challenges it presents to their established business model, we recommend that companies carry out an audit to determine their "fit" with the new world of regenerative medicine.

This type of audit involves closely examining all aspects of the organization: the company's "innovation radar" and scouting capabilities, its clinical development model, its supply chain operating model, how it integrates external partners and alliances, its launch readiness processes, the proximity of its commercial operations to qualified clinical centers, the training and coaching it provides for applications, its digital tools (for monitoring the supply chain, generating and applying regenerative products, providing training, collecting clinical outcome data and so on) and its overall organizational model and people strategy. Further areas can be included as necessary, depending on the specific business and nature of the company. Based on the gaps identified in the audit, the company should then develop a strategy, an investment program and a schedule of activities.

Pharmaceutical companies have a number of aspects to consider. One of their key objectives must be to establish ways to identify threats from products with substitution potential for their own therapeutics. They should also establish a mechanism for identifying the right collaborations and strategic alliances. Equally important are searching for potential biochemical targets for drug interactions and enriching the pipeline with potential new regenerative products.

Another priority for Big Pharma is adapting their clinical development model. Companies can work with partners such as clinical centers, digital service providers and even artificial intelligence (AI) companies to bring their clinical development model into line with the specific requirements of regenerative medicine. Given the severity of interventions, they must place a special focus on long-term studies of safety.

Pharmaceutical companies should also adapt their organizational model and people strategy to ensure the availability of appropriate skills, capabilities and capacities in the new development, manufacturing and commercialization model required by regenerative medicine. Coping with decentralized manufacturing – managing complexity, securing supply and establishing close partnerships with clinical centers – will be challenging for pharmaceutical companies. They also need to develop the right value proposition and pricing or reimbursement model for payers, including systems for measuring success on a long-term basis.

Importantly, players should consider new strategic options and investments that go beyond the established pharmaceuticals model. Out-of-the-box thinking will be necessary to secure their position in the future world of regenerative medicine. They will need to find answers to some difficult questions: Should they expand their activities to include healthcare provision? How can they engage in outcome-based payer models? What is the best way to steer their regenerative medicine business in parallel with their traditional drug business? How can they engage more in sensors, devices and diagnostics? What tools should they provide to physicians and clinical staff to simplify medical treatments and the measurement of outcomes? What changes must be made to their legal structure or organizational setup?

If this array of questions seems overwhelming, companies should remember that the rewards for succeeding in the new world of regenerative medicine will be substantial. The time is right for pharmaceutical companies to reexamine their position and develop a fitting strategy. This is an opportunity they cannot afford to miss.

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WE WELCOME YOUR QUESTIONS, COMMENTS AND SUGGESTIONS

AUTHORS

Dr. Thilo Kaltenbach
Partner
+49 89 9230-8651
thilo.kaltenbach@rolandberger.com

Dr. Stephan Rapp
CEO, biovenco consulting GmbH
+49 174 5898485
s.rapp@biovenco.com

Dr. Bastian Eulenstein
Senior Consultant
+49 89 9230-8151
bastian.eulenstein@rolandberger.com

Morris Hosseini
Partner
+49 30 39927-3342
morris.hosseini@rolandberger.com

Martin Erharter
Partner
+49 89 9230-8414
martin.erharter@rolandberger.com

Koen Besteman
Principal
+31 20 796 0619
koen.besteman@rolandberger.com

Lennart Boesch
Principal
+49 30 39927-3541
lennart.boesch@rolandberger.com

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Publisher

ROLAND BERGER GMBH
Sederanger 1
80538 Munich
Germany
+49 89 9230-0