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What you need to know about Regenerative Medicine in 2022: Industry and Tech Trends

GROWTH IN THE REGENERATIVE MEDICINE FIELD

The regenerative medicine sector is on track for another watershed year where clinical progress, continued growth, and segmentation into new disease areas affecting larger patient populations is anticipated. With over 2,600 active clinical trials in 2021, the clinical pipeline is maturing at a rapid pace. Forty three percent of all product candidates are in late-stage testing (Phase III), according to the Alliance for Regenerative Medicine[1]. It is an exciting time in the field with global regulatory approvals for several investigational therapeutics expected by the end of 2022.

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Regenerative medicine is a diverse field that includes cell and gene therapies (cell therapy, gene therapy, gene-modified cell therapy) and tissue engineering intended to correct hereditary defects, to replace or rebuild vital tissues, organs and metabolic processes in the body. Researchers in the regenerative medicine space aim to tackle the underlying root cause of diseases. Regenerative medicine's applications range from treating cancers, neurological and cardiovascular disease, wound healing, degenerative to genetic disorders, and more. The diversity of therapeutic indications under evaluation showcases the enormous scope regenerative medicine could achieve to revolutionize patient care.

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ADVANCING REGENERATIVE MEDICINE ACROSS THE GLOBE

The curative potential and unprecedented clinical results of these novel therapies has driven explosive growth in the field. Globally, regulatory agencies have responded to support the pace of innovation and advancements by providing expedited approval pipelines for regenerative medicine products[2]. As part of the 21st Century

Cures Act, the US FDA uses the regenerative medicine advanced therapy (RMAT) designation to allow for faster, more streamlined approvals of regenerative medicine products. In the European Union (EU), regenerative medicines are classified as advanced therapeutic medicinal products (ATMPs) that may be fast-tracked for approval through the European Medicines Agency's (EMA) priority medicines (PRIME) pathway. In Asia-Pacific, Japan is one of the leading countries in embracing and adopting regenerative medicines. Its regulatory body, the Pharmaceuticals and Medical Devices Agency (PMDA), has a dedicated, expedited approval stream tailored to reviewing regenerative medicinal products as per the Pharmaceuticals and Medical Devices Act.

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KEY CHALLENGES

Industry experts cite manufacturing capacity, supply chain security and product sustainability as key challenges to address in the coming years as the scope of disease indications and the size of target patient populations expands. More development and growth in the allogeneic space is expected in 2022, as clinical data for the efficacy and safety of early product candidates becomes available. Here are a few trends and advancements that are expected in the coming year.

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INDUSTRY TRENDS

The unparalleled speed of innovation and inherent complexities and challenges associated with cell and gene therapies has led to some progressive approaches to accelerate the transition from the bench to bedside patient care. Traditionally, as an ecosystem of siloed knowledge, the industry has recognized the need to work together to advance clinical development and address manufacturing capacity shortages. For example, the Accelerating Medicines Partnership® has established the **Bespoke Gene Therapy Consortium (BGTC)**, which includes stakeholders from the public, private, and nonprofit sectors with a mandate to create a standardized operational playbook that could be accessed by academics and commercial companies in the industry. One main focus will be defining common viral vector platform technologies with standardized manufacturing templates and master regulatory files to streamline the path towards commercialization for investigational gene therapies.

As one of only a few clinical-grade suppliers, AllCells is rising to meet the capacity challenge by proactively expanding its infrastructure to support the growing requirements for clinical-grade hematologic tissues.

As more allogeneic therapies come online, an increased demand for scalable supply of donor-sourced tissues—like bone marrow and apheresis material—will put pressure on the supply chain. As one of only a few clinical-grade suppliers, AllCells is rising to meet the capacity challenge by proactively expanding its infrastructure to support the growing requirements for clinical-grade hematologic tissues. At the end of 2021, AllCells announced the expansion of its FDA-registered GMP production capacity at both the Alameda, California and Quincy, Massachusetts facilities. In 2022, AllCells opened a brand-new donor collection facility in Houston Texas to further increase its capabilities. Continued diversification of the **clinical portfolio**, which includes **GMP-compliant Bone Marrow**, **GMP-compliant Fresh Leukopaks**, **GMP-compliant Cryopreserved Leukopaks**, as well as upcoming product launches including GMP-compliant Mobilized Leukopaks.

TECHNOLOGY TRENDS

Gene therapies are paving the way for regulatory approvals in the coming few years, with several highly anticipated approval decisions to be made by global regulatory agencies. **BioMarin's** Roctavian is set to be the first market approved gene therapy to treat hemophilia A (an X-linked recessive hereditary blood disorder) with regulatory approval from the FDA and EMA pending this year. UniQure and **CSL Behring** released promising endpoint data for their Phase III clinical trial for etranacogene dezaparvovec (EtranaDez), an investigational adeno-associated virus five (AAV5)-based gene therapy for the treatment of patients with severe to moderately severe hemophilia B. The European Medicines Agency began an accelerated review of EtranaDez for possible approval as a first gene therapy for hemophilia B in March 2022, with a decision likely by early fall. uniQure and CSL Behring expect to soon file a similar approval request with the U.S. Food and Drug Administration (FDA).

The momentum of CAR-based therapies continues with CAR-T therapies still dominating the field— over 500 active CAR-T clinical trials[3] globally. However, CAR-based strategies are expanding to other T cell subpopulations (i.e., gamma delta (γδ) T cells[4,5]) and other immune cell types (i.e., NK cells[3,4,6] macrophages[4,7]) as part of efforts to improve safety profiles, persistence and achieve efficacy in solid tumor indications where current CAR-T therapies have not been as effective.

Data from early clinical phases will evaluate the safety and efficacy of several allogeneic therapies in 2022. After a brief pause in 2021, **Allogene** was given the green light by the FDA to resume Phase 1 clinical trial evaluation of their gene-edited allogeneic CD19-CAR T products ALLO501 (**NCT03939026**) and ALLO501A (**NCT04416984**) to treat relapsed/refractory non-Hodgkin lymphoma (NHL). **Nkarta Therapeutics** is on track to present clinical data from their Phase 1 trial (**NCT05020678**) for their experimental therapy NKX019 (allogeneic CD-19 CAR NK cells) targeting relapsed/refractory NHL, chronic lymphocytic leukemia (CLL) or B cell acute lymphoblastic leukemia (B-ALL). Also, **Gamida Cell** is on track to complete the Biologics License Application (BLA) submission in the second quarter of 2022 for its omidubicel cell therapy. If approved, it has the potential to be the first FDA advanced cell therapy product for allogeneic stem cell transplants.

For 2023, the sickle cell disease treatment developed by Vertex Pharmaceuticals and CRISPR Therapeutics (**CTX001**), will be considered by the FDA in the US among many others in the global pipeline. It certainly feels as if the industry is on the cusp of some pivotal breakthroughs, particularly in the cell and gene therapy arena, which will continue to shape the future of the industry and provide new ways to treat diseases that will ultimately benefit patients worldwide.

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