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Unique Demands of CGT Biomanufacturing Necessitate an Early-stage Collaboration Between Suppliers and Biomanufacturers

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A surge in pharmaceutical R&D has led to an increase in the number of Cell & Gene Therapy (CGT) candidates being developed. The goal has been to develop cost-effective and efficient cell and gene therapies while focusing on biomanufacturing innovations. It's now becoming essential to outsource manufacturing services that can leverage innovative cutting-edge biomanufacturing technologies to enhance efficiency and flexibility in CGT. **Narayana Rao, Vice President of Biopharma, Asia Pacific Middle-East Africa** at Avantor interacted with BioSpectrum Asia and shared his insights on Asia's CGT Biomanufacturing ecosystem. Edited excerpts;

- **What are your insights into the current state of biopharmaceutical R&D?**

The global biopharma market has been and continues to be one of the fastest-growing sectors in the healthcare industry. According to Fortune Business Insights, the global biopharmaceutical Contract Manufacturing Organisations (CMO) market is projected to reach $26.49 billion in 2028 with a compound annual growth rate (CAGR) of 12.6 per cent in the 2021- 2028 period.

In parallel with the evolution of the industry is the growth of the cell and gene therapy (CGT) platform as an avenue of innovation. The emergence and evolution of precision medicine today offers hope for treating previously incurable life-threatening diseases such as cancer. Moreover, the rising prevalence of chronic disorders coupled with an ageing population is expected to fuel the growth of the CGT market to almost $15.5 billion by 2025, further doubling to nearly $34 billion by 2030.

This trend suggests that these pharmaceutical companies are increasing their research and development (R&D) efficiencies through persistent investments as well as collaborative research efforts, with hopes to see greater returns on their investment

in the long run. The increase in pharmaceutical R&D has resulted in a sharp increase in the number of cell and gene therapy candidates under development.

This has made it necessary to outsource manufacturing services to develop cost-effective and efficient cell and gene therapies, while emphasising new biomanufacturing innovations.

- **Which emerging trends are shaping the future of biomanufacturing?**

Some of the key trends that have emerged in the pandemic era include the explosive growth of new modalities and the need for rapid industrialisation. New platforms such as cell therapy, gene therapy and mRNA are complementing more traditional platforms such as mAbs, and these labs are looking at more therapeutic areas such as Alzheimer's, Parkinson's and Infant Spinal Muscular Atrophy.

These sources of research and development, along with the usage of these platforms to support a wide landscape of therapeutic areas, lead to many intersections and overlaps that bring about opportunities to collaborate and transform the industry.

Ensuring launch excellence and strengthening resilience in end-to-end supply chains are two other factors that will be focused on in upcoming years. This is an area Avantor has increasingly been focusing on by investing in the latter. For example, to better serve its customers in the AMEA region, Avantor in May announced a new Manufacturing and Distribution Hub in Singapore, by integrating its existing distribution facility with new manufacturing operations. The new hub, which provides a range of services including quality control and inventory management expertise, aims to bring Avantor solutions closer to regional customers and strengthen global supply chain capabilities.

Lastly, digitalisation and rapid adoption of Industry 4.0 technologies will also revolutionise all aspects of biopharma. For example, cloud-based digital solutions can be tailored to the needs of the lab and can be used to track and document every stage of the scientific journey, making lab and inventory management efficient and easy to replicate. This can allow scientists the freedom to focus on their work while enhancing coordination between them.

- **What are the challenges that you anticipate in the CGT sector?**

Two main challenges in the CGT sector include scalability and manufacturability, which are prevalent throughout the industry. Despite the growth in the CGT sector, advanced-therapy capacity remains insufficient in the industry. According to BioPlan's 18th Annual Report and Survey of Biopharmaceutical Manufacturing Capacity and Production, an upcoming 'capacity crunch' will cause shortfalls for the CGT industry of up to 500 per cent and is looking to increase significantly over the next 5 years.

Rising shortages and lack of scale-up and inefficiencies in production can lead to hindrances in clinical potential. This includes a lack in ready-to-use packaged materials at an appropriate scale, as well as GMP availability of raw materials with supply chain visibility and controlled manufacturing. Other key constraints include the need for specific storage conditions and traceable logistics, sterile process environments, and the requirement for highly trained and efficient personnel.

- **How could biopharmaceutical companies in the CGT space overcome these challenges?**

Firstly, investing in high-quality materials and risk management processes can minimise upscaling risks. By implementing early risk assessment systems and eliminating manual steps as early as possible, manufacturers are better able to maintain optimised pharmaceutical quality systems.

Several upscaling risks can also be minimised by utilising single-use and closed-system processing. Customisable sampling platforms such as Avantor's OmniTop Sample Tubes system with an adjustable volume sampling system (AVSS) are beneficial in CGT due to the precision and control they offer while drawing the sample, eliminating the volume loss typically associated with these scenarios. On the other hand, the implementation of closed-system processing using ready-to-use sterilised solutions mitigates the risk of contamination and enhances speed and flexibility while facilitating automation.

Thirdly, coordination with suppliers can also assist with ensuring efficiency in production work environments. Technical expertise can be used to enhance services across key production service segments such as Design Consulting, Planning and Materials Management, Production Readiness and Critical Environment and Sanitation. On the whole, coordinating with an end-to-end supplier can help enhance every step of the CGT cascade ranging from consumables such as cGMP chemicals, single-use solutions, equipment and sera, production (upstream processing, downstream purification, final fill), logistics support, environmental control as well as staffing expertise.

- **How do you see the opportunities for Asia's Cell and Gene Therapy industry?**

In the coming years, rapid advancements in regenerative medicine are anticipated to provide more effective solutions for existing chronic conditions. A substantial number of companies in growing markets, such as China, India and South Korea are striving to capitalise on untapped opportunities in the market, thereby driving the market.

The sector's growth is additionally fuelled by fund and regulatory support from local government bodies and regulatory agencies. For instance, in August 2020, the government of South Korea passed an Act on the Safety and Support of Advanced Regenerative Medical Treatment and Medicine to establish a regulatory system for patient safety during quality control and clinical trials and to strengthen the regulatory support for regenerative medicine development. The implementation of the Act is expected to enhance clinical studies and approvals of regenerative medicine in South Korea.

Though CGT represents the next frontier in biomanufacturing, several capability gaps exist making upscaling of the therapies from the lab to the patient a challenge. The unique demands of CGT biomanufacturing necessitate an early-stage collaboration between suppliers and biomanufacturers to enable successful process implementation and regulatory compliance.

CGT manufacturers can collaborate with suppliers who are proficient in both the materials and single-use technology space to adopt technical, quality and regulatory best practices needed to facilitate consistent product quality. Through collaborative efforts between manufacturers and suppliers, resilient support systems can be established by incorporating innovative/flexible material workflows, reducing system-based risk and implementing robust formulation strategies.

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