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INSIGHT BRIEF

Realizing a New Approach to Allogeneic Cell Therapy Process Development

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As cell and gene therapies continue to gain traction in the larger pharmaceutical development pipeline, innovations enabling more "off-the-shelf" advanced therapeutics are likewise gaining steam. Increasing investment in pursuing allogeneic therapies, as well as the process-level advancements and automation necessary to achieve commercial scale, are paving the way for a more streamlined, standardized cell therapy development and manufacturing paradigm.

Allogeneic cell therapies have the potential to greatly improve the economies of scale associated with cell therapy production when compared to the autologous cell therapies more commonly pursued today. By working to standardize the cell therapy process steps and tools common across both allogeneic and autologous applications, operators can enable greater speed and reduce the potential for error during later phases of development and scale-up. Balancing this standardization with the flexibility necessary to support unique assets and applications requires both expertise and experience in closing cell therapy processes. It also requires successfully navigating a new era in global cell therapy regulations and the skills and experience in dealing with regulatory authorities. For many biopharmaceutical companies, this necessitates identifying a contract development and manufacturing organization (CDMO) that can support process intensification comprehensively to help an asset achieve faster development and optimized scaling.

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Enabling Standard Approaches for Bespoke Therapeutics

The relative novelty of many assets in the broader cell and gene therapy space, and the proliferation of technologies designed to support them, have created a landscape far from the kind of standardization seen in other pharmaceutical manufacturing sectors. While the complexity and fragility of these drug products precludes the same levels of standardization and automation as other modalities, there exists significant opportunity for drug developers and CDMOs to establish processes that reduce manual work and improve the analytical and data management approaches supporting these workflows. A typical cell process development workflow,

regardless of indication, cell type, growth media, or an asset's designation as autologous or allogeneic, incorporates several unit operations that are highly similar from unit operation to unit operation. By identifying the common denominators in various cell therapy workflows, manufacturers can establish a standard foundation to build out the customizations necessary for an individual asset.

Achieving scalable, flexible process standardization is especially crucial for allogeneic cell therapy applications, which are intended to represent a more accessible, "off-the-shelf" alternative to autologous therapies. The path to widely accessible allogeneic therapies is beset with its unique considerations, and finding suitable approaches to avoid an immune response in a wide range of patients is one of the primary hurdles that can hinder development. Even for applications that have validated the foundational science supporting an asset, challenges are often linked to the discrepancy between instruments used at varying scales. For example, an equipment vendor may not offer GMP-grade bioreactors at small sizes, impacting how quickly and at what volumes a developer can pursue its next scale-up phase. While a wide array of instruments and equipment is designed to support cell therapy development and manufacturing, this diversity can create challenges when trying to identify suppliers that can support these modalities reliably and consistently. Securing a supply chain and identifying equipment that can support a range of cell therapy products are critical to enabling standardization for a process and its unit operations.

Streamlining Cell Therapy Process Development to Improve Scale and Economics

The challenges that accompany cell therapy process development and manufacturing are numerous, and include closing process steps, securing supply chains, achieving optimal yields, accounting for donor variability, introducing automation, and identifying reagents suitable for GMP-grade processing. The nascence of allogeneic cell therapies has also meant that many innovations that might help further streamline specific processes, such as the pursuit of immortalized cell lines, are still in early research. However, the proliferation of technologies designed to support these processes has resulted in a degree of parity among many of the instruments on the market today, creating opportunities

for process standardization for manufacturers able to take most of what differentiates many cell therapies from a process standpoint, such as media and reagents, and map those unique elements against validated, state-of-the-art technologies and instruments.

Balancing standardization and customization will be the key to enabling sufficient scale for many cell therapies. While a typical cell therapy asset comes out of the laboratory having undergone a considerable degree of selection and customization, certain variables, such as the vectors most often used, have already begun to see standardization — the majority of applications in development currently utilize lentiviral vectors, adeno-associated viral vectors, or lipid nanoparticle systems. For other steps like cryopreservation, a deeper understanding of how best to protect cells from the brunt of adverse effects associated with traditional cryoprotectants is likely to promote greater standardization, as will the DMSO-free alternatives being pursued by research and vendors today. As best approaches continue to emerge and more data is amassed, having a manufacturing partner that can proactively adapt, while introducing new efficiencies to a process, will be crucial in an evolving cell therapy landscape.

Contact FUJIFILM Biotechnologies to accelerate your cell therapy product development and commercialization strategy.

About the Author

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Sara Miller is Director, Commercial Technical Lead – Advanced Therapies at FUJIFILM Biotechnologies, supporting the dedicated cell therapy facility in Thousand Oaks, CA and the viral and gene therapy facilities in College Station, TX and Darlington, UK. Prior to this role she was Associate Director, Manufacturing Services for Atara Biotherapeutics, an allogeneic cell therapy company that received the first approval of an allogeneic T-cell immunotherapy. Prior to Atara, Sara worked as a Senior Manager in External Quality for Cognate BioServices, and she began her career as a scientist in various roles at Emergent BioSolutions. Sara holds a Bachelor of Science from Grand Valley State University and a Master of Science from Johns Hopkins University.

About FUJIFILM Biotechnologies

FUJIFILM Biotechnologies, a subsidiary of FUJIFILM Corporation, is a world-leading contract development and manufacturing organization (CDMO) for the development and manufacture of biologics, advanced therapies, and vaccines. The company operates a global network with major locations in the United States of America, the United Kingdom and Denmark, offering end-to-end services including drug substance, drug product, and finished goods services. It is also building a new manufacturing site in Holly Springs, North Carolina, USA, scheduled to be operational in 2025. FUJIFILM Biotechnologies has over thirty years of experience in developing and manufacturing drug substance of recombinant proteins, monoclonal antibodies, vaccines, among other large molecules, viral products and medical countermeasures expressed in a wide array of microbial, mammalian, and host/virus systems. We have drug product filling capabilities to support both clinical and commercial demands. Our finished goods services, supported by more than 15 years of experience, can accommodate commercial products for more than 65 countries around the world. The company offers a comprehensive list of services from cell line development using its proprietary pAVEway™ microbial and ApolloX™ cell line systems to process development, analytical development, clinical and FDA-approved commercial manufacturing. For more information, go to: **fujifilmbiotechnologies.fujifilm.com**

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