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Closing The Gaps In Gene Therapy Production

by

General Manager at Rentschler ATMP, Dr. Rob Panting, speaks to Scrip about his team's critical work in cell and gene therapy.

The growing pace of approvals in the advanced therapy medicinal products (ATMP) sector is testament to the impact this part of the biopharma industry is having on improving and saving patients' lives. But, the sheer "volume" of scientific ideas for therapeutic ATMP approaches is far exceeding the available production capacity - even for pilot-scale manufacturing. The result is a growing need for experts in both process development and manufacturing to ensure new ATMP therapies reach the market swiftly with no production hold ups during the clinical and regulatory processes.

Scrip spoke with Dr. Rob Panting, General Manager at Rentschler ATMP – a Rentschler Biopharma SE company – about the work he and his team are undertaking in Stevenage, UK; Europe's largest gene and cell therapy cluster.

Exceptional changes have occurred in the last 30 months for the biopharma sector based on technology advancements, resulting in a true paradigm shift in the industry. Without doubt, most striking was the fast development and approval of the mRNA-based COVID-19 vaccines. Also the flourishing of new therapeutic approaches in cell and gene therapies is a milestone in the sector. The term ATMP, groups together gene therapy medicinal products, somatic-cell therapy medicines, and tissue-engineered products. As recently as December 2014, the EMA recommended the first ATMP containing stem cells for approval in the European Union.

As of September 2022, eleven gene therapy medicinal products, three cell therapies and ten tissue-engineered products have received marketing authorization in the EU. The novelty of ATMPs is also associated with special characteristics in terms of development, production, approval and market access expertise. Especially so the development of efficient and reliable manufacturing processes for ATMPs can be complicated to design, develop and expand as need

requires.

Throughout Rentschler Biopharma's 150 years of history, the family-owned business has taken on the challenges of addressing unmet medical needs and continues to transform itself through innovation and international growth. Wherever there is a gap in addressing clients' needs in the area of biopharma development and manufacturing, Rentschler aims to fill these gaps.

In Germany, the company was able to swiftly set up, expand and continuously optimize a manufacturing suite for the downstream processing of mRNA to provide highly purified drug substance for the coronavirus vaccine.

In the Greater Boston area in Milford, MA, USA, the CDMO recently started the largest buildout in the company's history to double commercial cGMP capacity. Last but not least, in 2021, Rentschler Biopharma founded UK-based Rentschler ATMP in Stevenage, UK, to address gaps in production capacity and support for early-stage cell and gene therapy innovators.

With the founding of Rentschler ATMP, Rentschler has shown its understanding of paradigm shifts in medical science and meeting patient needs: The field of cell and gene therapy is quickly developing with over 450 companies worldwide, developing some 1,900 products in a broad spectrum of indications including autoimmune, cancer, and ophthalmic diseases. The sector is set to rapidly expand and the demand for manufacturing capabilities and support is growing along with it.

The number of authorized ATMPs in the EU has more than doubled in the last two years. While as of May 2020, only ten ATMPs had a central marketing authorization, by September 2022, the number had already grown to 24. Numbers have also exploded across the Atlantic. As of October 2022, the FDA lists 25 approved products licensed from the Office of Tissues and Advanced Therapies (OTAT). The Office is currently facing 3,000 Investigational New Drug (IND) applications. As a consequence, the OTAT is massively staffing up with an additional 100 employees planned over the next five years in order to manage the growing number of INDs in this field.

"The ATMP market is experiencing healthy and strong growth," summarized Dr. Robert Panting, General Manager at Rentschler ATMP. "In particular, we see a massive increase in pre and early clinical products in development. However, the sector is still early stage and there are challenges to be met in the safety of trials and reducing product development costs to make gene therapies more accessible to patients."

Addressing Current Limitations

At the basic level of all these potential therapies is the need for cGMP-compliant viral vectors. Small-scale manufacturing of Adeno-associated viruses (AAV) under cGMP poses a bottleneck

that affects the speed of development and manufacture of cell and gene therapies. Rentschler ATMP provides a highly experienced team, well-versed in viral vector process development and cGMP manufacturing and thereby actively contributes to opening existing bottlenecks. Rentschler ATMP counts on a tailored and collaborative experience to support its clients in getting products through clinical development and the regulatory process. With the experience, technology, analytical expertise, plus development and manufacturing capabilities, the company is supporting the unique needs of advanced therapies for tomorrow.

On the other hand, development and manufacturing costs are a sensitive topic, especially for innovators in the early development stages of new cell and gene therapeutics. Panting and his team are focusing on chemistry, manufacturing and controls (CMC) and how to make gene therapies less expensive in development and production. "Faster development and lower product costs are certainly two key factors in the overall success and availability of gene and cell therapies. The most important and initial step is the development and introduction of stable integrated gene expression and capsid cell lines. Just solving these limitations will enable a significant reduction in manufacturing costs and will enable the efficient scale up to larger batch sizes for clinical trials and eventually marketed products," said Panting.

Looking at 2023, Rentschler ATMP is preparing for big advancements. "Already, we provide the vital AAV services to our clients and are ready for process development. In addition to the cGMP-capable production suites, we have fully equipped laboratory space for process development and quality control, including cell cultures for process development and pilot-scale bioreactors. Very soon, though, Rentschler ATMP will also offer other types of gene vectors and will evaluate cutting-edge technologies to support the industry and help provide novel therapeutics to patients," Panting added.

Wasn't There A Minor Thing Called Brexit?

By 2019, before Brexit, many companies had relocated offices or business operations from Britain to continental Europe and Ireland. Now, for over 18 months, the UK has no longer been part of the EU single market and customs union. It has now been almost as long since Laupheim-based biopharma service provider Rentschler chose the UK as the location for its new cell and gene therapies production facility.

Unfortunate timing or was there a deeper insight? "The decision was driven by our corporate strategy to make new and innovative modalities available to our clients," explained Panting. "With the largest industry cluster for cell and gene therapies outside North America, the UK is an ideal location for us to establish our Centre of Excellence for cell and gene therapy. Additionally, the UK's life sciences sector is one of the strongest in the world. In 2021 the sector raised £4.5 billion in public and private financings, that is £1.7 billon more than the year before. And, on top of that, Stevenage is located strategically, right in the middle of the 'golden triangle' of the UK's high-profile/top-ranking university cities: Cambridge, Oxford and London with its Imperial

College and the University College. That is why Rentschler chose this location," he added.