CASE STUDY: BUILD OR BUY DECISION FOR CGT COMPANIES THAT MUST BE EXPERTS IN MULTIPLE TECHNOLOGIES

Dave Backer, Chief Commercial Officer at Oxford Biomedica

SITUATION

Cell and gene therapy (CGT) manufacturing differs from standard MAbs manufacturing in a few significant ways. First, the batch sizes are smaller for cell and gene therapies, as they tend to be in earlier phases, so from a viral standpoint, the batches range from 100s of litres to 2000 litres. Also, it's always advantageous to use single-use technology as the viruses are treated as an infectious product; it's much easier from a cleaning validation standpoint and change over to utilise disposables. However, they are generally limited to a couple of thousand litres.

ABOUT

Dave Backer has been in the cell and gene therapy (CGT) industry for over 20 years, giving him a long-term view of the differences and similarities of manufacturing CGTs vs monoclonal antibodies (MAbs) and how that plays out in terms of tech transfer and scale-up.

In this case study, Dave shares his experiences and necessary considerations when scaling up AAV manufacturing.

To manufacture CGT products, like many products, there are incoming raw materials, including the virus itself (as it's often not the final product) and plasmids, either GMP plasmids or near GMP, based on whether it's for a final product or not. There's been a big pinch point in the industry around these raw materials. We talk about supply chain issues because of Covid-19 but there's been a pinch point around plasmids side for some time due to the tremendous growth in the number of compounds that are in CGT pipelines.

This scenario involves an immuno-oncology company with an autologous cell therapy, which is similar to Kymriah. They were subject to the same pinch points as the rest of the industry and faced a decision of whether to build or buy manufacturing space.

The manufacturing and supply chain process is complex; plasmids are required to create the lentivirus product, so there's plasmid and lentivirus production to consider, as well as the final autologous product. The process involves taking the lentivirus with the gene of interest, transducing selected cells that are apheresed from the patient and then the manufacturing process that is release tested and reintroduced into the patient.

CHALLENGES

There are challenges in getting slots with CDMOs if you're a small company for the plasmids, the virus and the cells. The venture companies that are putting in big money and need returns in an appropriate amount of time are being held up by these 12, 18, even 24-month lead times that are necessary to getting manufactured in the CDMO space.

The company had to think about the financial side of things, as venture money is expensive and it's not always sensible to put it into real estate, but the supply chain challenges were making budling a more attractive option. You could build a 20,000 sq ft facility but then need to determine what to manufacture – the plasmids, the virus, the cells? These three different technologies should be considered as separate, as well as the manufacturing of the technologies and the skillset of the people can be quite different.

The other challenge is that while the plasmids can be multi-use and the virus can be multi-use, each batch is for one specific patient, at least from an autologous standpoint. This means the company needed to consider the need to scale out rather than up.

So, there were actually many factors that went into the final decision making of whether to build or to buy - price, timeline, technology, the employee base, i.e. who can make what and what are those required skillsets.

SOLUTIONS

The options were really to build, to outsource or some type of hybrind set up, which could take many forms. In the end, the decision making was bi-modal, first, the customer wanted to protect their IP and the decision was made to build and focus on the autologous therapy final product then work with CDMOs for the plasmids and the lentivirus. Even for the cell therapy there were still CDMO partnerships that came into place, but the actual build and design of the facility was geared towards the autologous cell therapy. There was some fallow area incorporated that could be used for other products.

The second factor was a strong desire to be as close as possible to the patient, as this was a cell therapy-driven company, with the vector and plasmids being raw materials. The company did select a CDMO that had both plasmid and virus capabilities in separate parts of the company but there was a streamlining of relations and they picked the CDMO because of this and it did increase the importance of the company, as there were two different technologies and products that they were buying from the CDMO rather than one and it also helped with timelines.

The most interesting part was that the company realised that the product they were designing for was probably not going to be the same as the products they had in the pipeline five years, so they designed it originally around autologous cell therapy with the fallow area to provide some flexibility in the event they moved into allogeneic, or they could have used that space for vectors. They did not go completely in house because they didn't have the capabilities on the different technologies and so they remain reliant on CDMO partnerships.

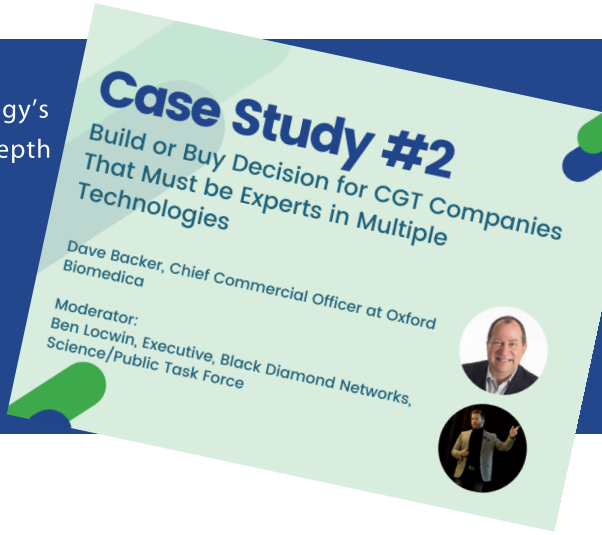
LESSONS

Companies can be somewhat short-sighted when they build, and the natural intent is to take everything in house and avoid having to deal with outside entities. The company wisely decided to reduce their reliance on CDMOs in certain areas but not to completely cut off CDMOs. That was based on price, speed and the fact they wanted good strong partnership relationships in place and that doesn't happen if you cut that process off. They saw that with an expanding pipeline they were going to run out of space and need these relationships in place in the future.

This case study was presented at a recent virtual event 'Technology's Evolution and Impact on Mnaufacturing', which included six in depth case studies and networking sessions.

Details of future events can be found here.

You can watch Dave's case study in full and on demand here



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