

Understanding the Critical Impact of Logistics on Scale-Up & Commercialization



Sam Herbert is President of World Courier, a global specialty logistics company and a part of AmerisourceBergen. He leads a business that spans more than 140 company-owned offices in 50-plus countries. Prior to his role as President, Herbert was Chief Operating Officer, responsible for World Courier's global functions. Before joining World Courier in 2013 as Vice President of Strategy, Herbert was a partner in Oliver Wyman's Health and Life Sciences practice where he advised some of the world's leading pharmaceutical, healthcare and pharmaceutical services companies, including AmerisourceBergen. He is based in World Courier's global headquarters in London. Sam recently contributed to a white paper published by AmerisourceBergen, "Commercializing Cell and Gene Therapies."

Q What are the three key logistical challenges that need to be overcome to enable the commercialization of cell and gene therapies?

Executing the logistics of cell and gene therapies is a challenge like no other – after all, if you cannot deliver the therapy to the patient, its efficacy is irrelevant. The seamless integration of multiple suppliers is a critical issue for the field. As a therapy progresses from clinical development to commercial-scale manufacturing, you have to manage increasing throughput and the addition of new partners at different points across your supply chain. The key to making a successful transition is to seamlessly coordinate each step of the process across multiple contractors and suppliers. In order to do so, the key players in your supply chain must work together and provide integrated solutions that will ultimately make the patient and physician experience as streamlined as possible.

Scalability is another challenge, though it's not just about scaling up or out, it's about the increased complexity in your supply chain and managing multiple stakeholders at each point. Innovators should avoid making the process even more complex, as increased complexity generally leads to higher costs. The simplest way to mitigate the impact is to think ahead and have a vision for the commercial supply chain whilst in early clinical trials.

The cost of goods and the reimbursable price of your therapy will also make or break the commercial viability of your product. For early-stage companies, the primary focus is generating clinical data to underpin financing needs. As a result, some fall into the trap of designing their supply chains just to get through to the next clinical end-point. Then, once they progress to the next stage, they start to look at adapting their supply chain to suit the evolving needs. However, that process often results in very complicated and costly supply chains.

Even within an optimized supply chain, it's essential for suppliers to continue to find ways to innovate and drive down costs. It's clear that we need better economies of scale if these potentially transformative therapies are to become a mainstay of modern healthcare, and that will impact partnering decisions. Packaging is a good example of the need for innovation. Most of the dry shipper technologies currently available are large and bulky and often move a very small set of cells at one time, which is not cost effective. The logistics company and various partners should work together to help drive down that costs through innovation.

Finally, it's essential to consider the physician and patient experience. A number of these early stage cell and gene therapies are targeting similar, small niche patient populations. What factors are going to have the biggest impact on whether the physician prescribes one therapy versus another? Undoubtedly, their experience as a stakeholder in the supply chain will greatly influence their decisions. These therapies present new challenges for the prescribing physician versus the more traditional 'drug' and if one therapy has a simpler, streamlined supply chain that optimises the patient experience and treatment, that could be the commercial differentiator.

By understanding physicians' needs, logistics providers can leverage technology and data to develop innovative solutions to address such needs. For example, automatically repositioning a dry shipment once a patient is approved for reimbursement to expedite scheduling and pick up times, as the manufacturing process will require an apheresis sample.

Q What is needed from the industry as a whole to overcome these challenges?

From the supplier side, we need to get together and build integrated solutions for the innovators. The first wave of cell and gene therapy companies coming to market is similar to that of any new field: new science, new technology and in terms of supply chain and logistics, they are all designing their own solutions for their products. This has led to a scenario where multiple stakeholders in the supply chain are brought in at different stages in the commercial development process, which dramatically affects their integration and efficiency.

That's not a criticism – it's a common issue faced with any nascent field. But it means we are seeing highly customised, unique supply chains for each therapy, which ultimately results in increased expense and reduced economies of scale. Therefore, suppliers need to come together to devise an almost off-the-shelf logistics solution that caters to 80% of the supply chain requirements of a cell/gene therapy, requiring only 20% to be customized on a client-by-client basis. By doing this, there's a real opportunity for suppliers to dramatically contribute to the commercial viability of these products.

When looking at the innovator side, I think the most effective way to tackle the challenges in supply chain management is to start planning early – ideally 2–3 years before your product is on the market. When I talk about supply chain it's much more than logistics – you need to be looking at the technology you are going to use to manage the various stakeholders and data such as patient services, payment management and reimbursement. If we take CAR-T as an example, therapies are going to go from 'first in man' to market approval in under 5 years, which requires earlier than standard commercial planning.

For example, we have seen a number of players who picked a logistics partner for their early-stage trials in the USA, and when they looked to transition to a larger number of sites, or across different countries, the partner was not able to support their needs. As a result, the companies then had to transfer and reset their processes, which can cost time, resources and ultimately money. At World Courier, our precise global logistics planning, rigorous quality standards, innovative transport systems and flawless execution have driven more than half of the active cell and gene therapy innovators to trust us with their personalized supply chain. In fact, we helped Novartis overcome the unique logistical hurdles associated with commercializing Kymriah.

Currently, there's a lot more money flowing into this space than in previous years – a trend spurred by the clinical data of the front-runner therapies, such as the CAR-T products. As such, we're starting to see a shift toward earlier planning with companies recognizing the need to select partners who can support and help navigate the challenges on the path to commercialization. Innovators must identify a GxP-compliant logistics partner that offers critical services – from coordinated peripheral scheduling and pinpoint pickup to real-time product tracking and advanced cryoshipping technologies – and is capable of developing advanced contingency plans to safeguard against unforeseen challenges (hurricanes, donor unable to donate, etc.) to allow patients to be treated effectively.

Q How do these issues compare for allogeneic versus autologous therapies, and what are the implications for the evolution of the sector?

From a logistics perspective, you can have very different supply chains not only between autologous and allogeneic products, but also within those categories. For example, the patient specific modality, which from a logistics standpoint is a hybrid of the autologous and

allogeneic paradigms with storage challenge of allogenic but the traceability of autologous. It's often not as straightforward as 'this product is autologous therefore its supply chain looks like this'. For example, the Argos Therapeutics' Rocapuldencel-T, is a batch manufactured autologous therapy that is then stored as part of a multi-dose supply chain. That storage requirement adds a level complexity to the supply chain but also reduces the risk of product loss. Conversely, there are examples of allogeneic therapies that aren't batch manufactured.

The 'typical' allogeneic supply chain profile is seen as potentially more straightforward and cost efficient, as innovators are able to follow the more traditional manufacturing model, with storage at distant distribution sites. However, that involves more partners in the supply chain. We are working with a company that is looking to commercialize an allogeneic product in the USA, Europe, Canada and Australia. Logistically, of course, this is possible. But it's important to understand the level of complexity associated with inventory management across multiple countries, and with different partner relationships.

From the autologous perspective, it's interesting to see the different models emerging that look at manufacturing hubs close to clinical sites, or point of care manufacturing versus centralised manufacturing.

Q What new approaches are being taken to address these issues and with what results?

More and more companies are starting to think about their supply chain logistics earlier in the process. It is hugely encouraging to step back and recognize that companies are planning for success when they are still at a preclinical stage. Proactive planning is critical, as it allows innovators to establish scalable processes that support patient, provider and payer requirements and drive commercial success and most importantly, enhanced patient outcomes.

We are also seeing genuine innovation across the supply chain. For example, a number of suppliers are innovating in dry shipper design – a crucial piece in the point of care logistics strategy, which has the potential to impact cost of goods and commercial success. We are also seeing the emergence of software companies such as TrakCel – one of our cell therapy supply chain integration partners – that identify ways to leverage technology and data to help manage the chain of custody, chain of identity, and the overall supply chain process.

Ultimately, it's the combination of innovators thinking about the commercial component earlier in the process and suppliers working to develop new solutions. Today, more and more suppliers are working together on these challenges, which will ultimately create more integrated solutions and hopefully reduce the constant 'reinvention of the wheel'.

Q What impact are logistics decisions having on the scale-up and commercialization of cell and gene therapies?

Some companies make supply chain decisions early in their therapy's development based on the pre-commercial requirements and then have to reinvent their logistics strategy as they scale to commercialization. Innovators must recognise that all the different components of logistics are as important as the manufacturing processes and have an impact on cost. A poorly planned supply chain may push the cost over the reimbursement threshold and stop it from being a viable therapy. Dry shippers are one such example. In some cases, complicated supply chains might require three or four dry shippers for each patient – a move that is not cost effective or optimal at the point of care. In other cases, the company supplying your dry shipper might use a specific courier to ship to your required depot, while you use a different courier to manage the delivery of that shipper to the clinical sites. As a result, this creates additional points of potential failure that could be avoided by improved planning and a streamlined logistics strategy.

With that said, it's understandable that historically the logistics piece is often the last to be looked at – the focus is on getting good clinical data as quickly as possible. In addition, some of the earlier companies found that there was not a significant number of contract manufacturing organisations (CMOs) that they could partner with. And the issue of technology transfer is never the easiest to tackle.

Again, I think as an industry we understand the cost implications and potential risks to the product that exist across 'our' specific parts of the supply chain. However, until we collaborate and take a more holistic approach, we're missing an opportunity to really create ready-made solutions that will dramatically impact the route to commercialisation in a positive way.

Q What's going to be the key driver for encouraging that partner collaboration in our industry?

There's certainly a move toward more collaboration and we are constantly looking at ways in which we can move the conversation forward. We recognize that there will be an increasing number of innovators moving through to commercialisation, asking us to devise and manage their logistics strategy while working with different partners across their supply chain. It's not cost efficient for us or the client to build a logistics plan from scratch each time so, as with any industry, cost will be a key driver for encouraging collaboration among partners.

We recognize that while a therapy is in clinical trials, it's all about needle-to-needle. As you transition to commercialization it's more a case of accountant-to-accountant. Before you get to the treatment you need to go through pre-authorization and insurance steps, and then after the treatment you're going to have to collect the payment from the relevant insurance body. We recognized this increasing complexity in logistics as companies move to commercialization and, as a large business with decades of experience, we believe there is a real opportunity to define and help lead the solution for this industry.

Q Do you think there's enough discussion and recognition within the sector of the importance of logistics?

I was at Cell and Gene Meeting on the Mesa last year and I think World Courier was the only logistics provider in attendance. There wasn't a great deal of content or discussion around this topic, in part, because I think innovators trust companies like World Courier to provide the solutions. But I also think the limited discussion reflects the stage of development most of the companies in this space are at – a lot of the companies are early stage, small, biotech companies whose primary focus is around the science. Their priority is getting the data they need with the funding they have, and not spending money on something that will not provide them with a perceived immediate value.

However, we are starting to see a shift in the industry. As more money flows into the sector, companies can start thinking about issues such as logistics earlier in the process. The same is true for the manufacturing piece – more time and money is being invested earlier in the product's development to try to mitigate risks and drive down costs through automation or integrated solutions. More and more, the trend is to view logistics as a key part of manufacturing; as without the delivery of a viable donation, there cannot be a manufacturing process.

As more products reach commercialization, it is going to be interesting to see how the focus and priorities shift as we start to grapple with the different manufacturing models and the distribution and logistics challenges that come with them. I think we need to focus much more on one crucial but often overlooked stakeholder group within the supply chain: the hospital sites. It's essential to understand the 'user' experience. For example, how will these clinical sites manage multiple different ordering procedures, tracking platforms, product storage and handling requirements, as well as staff training on how to administer each product? Standardization will be an essential piece in helping to alleviate the potential burden these therapies place on clinical sites. Certainly, we are seeing efforts to implement standardisation within manufacturing, but we're hoping that approach will also start to be applied to logistics. Part of that shift will be innovators recognising where their product is truly 'unique' and where there are actually similarities to other products, thus enabling economies of scale to be achieved through logistics.

Q Where do you see opportunities to continue to support the successful commercialization of cell and gene therapies over the next 5–10 years?

As these therapies mature and we resolve the logistics strategies for their commercialization, we must start to look at how we can expand access more broadly. Of course, the immediate focus is to achieve approval within North America and Europe. However, many of these treatments hold the potential to transform patient outcomes, so

we need to identify ways to expand access to these therapies in emerging markets and the developing world.

One key element will involve reducing costs down and maximising efficiencies through standardisation, automation and integrated solutions across the supply chain. However, it's not feasible to implement some of the manufacturing and treatment models for these therapies in emerging markets, particularly when you consider the clinical sites and infrastructure requirements.

As more of these therapies reach commercialization, such as Novartis' Kymriah, stakeholders across the industry will continue to learn valuable lessons that feed into the constant evolution of manufacturing and supply chain. Ultimately, stakeholders have a joint obligation to drive efficiencies across every part of the pathway to ensure that these life-changing therapies meet the key stakeholder (i.e., the patient).

AFFILIATION

Sam Herbert, President of World Courier

To learn more about the potential challenges to commercializing a cell or gene therapy and strategies for success, download the white paper at: www.worldcourier.com/cell-and-gene-therapies-whitepaper

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