Lumanity

Cell and Gene Therapy

Pathways to successful commercialization

The promise and pace of cell and gene therapy innovation is hugely exciting and continues to accelerate. The nature of these advances, however, creates unique risks related to regulatory, manufacturing, valuation assessment and commercialization. The practical components of progressing cell and gene therapies to market launch and optimizing commercial success require equally innovative solutions across everything from indication selection and development strategy, to supply chain and patient access.

Navigating this complex journey through the commercial launch planning window requires early and ongoing collaboration across multiple stakeholders to ensure that these therapies are available to patients rapidly at the point of approval.

In our Q2 2022 Pharma Progress webinar, we explored the commercial readiness challenges and practical realities of driving a successful launch in this space, covering:

- Unexpected challenges along the commercialization journey and how these can be navigated
- Avoiding pricing pitfalls: the organizational and market readiness aspects you must get right
- Considerations when forecasting uptake and how this is evolving
- Navigating undefined regulatory standards and policy
- Recognizing the paradigm shifts in payer approvals and what this means
- Internal and external considerations that need to be addressed for successful launch
- Importance of shaping the environment for future success

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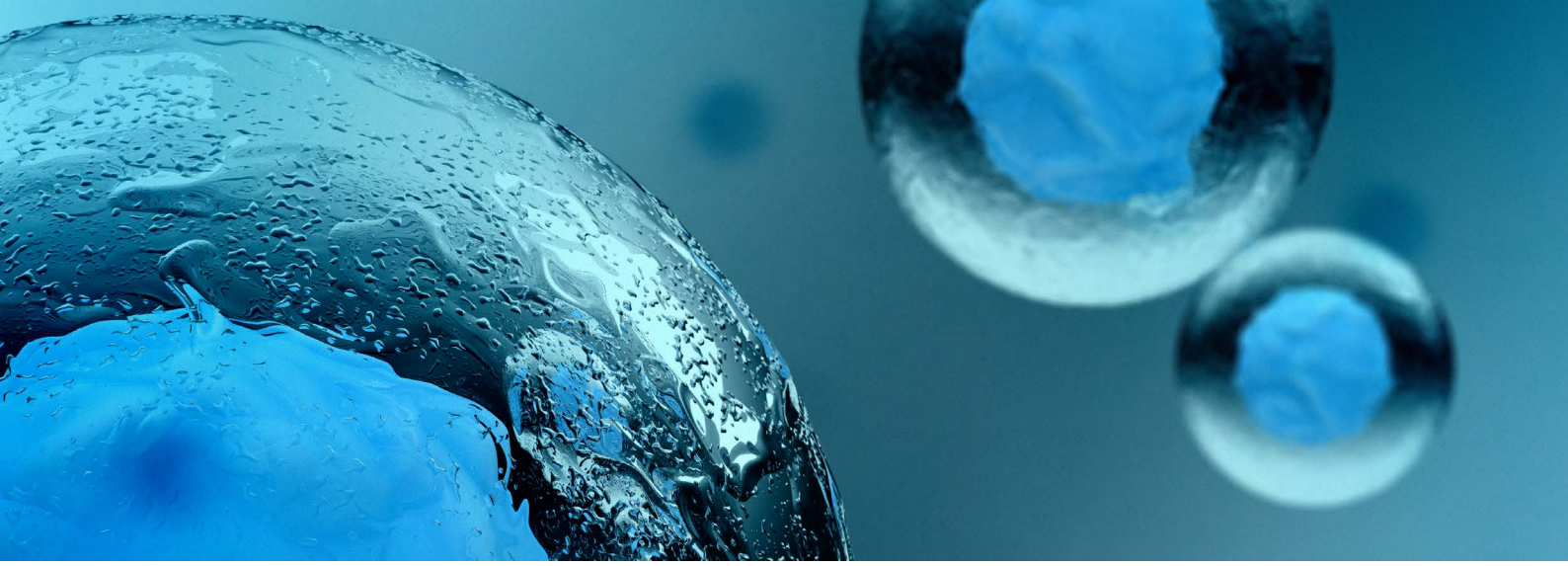
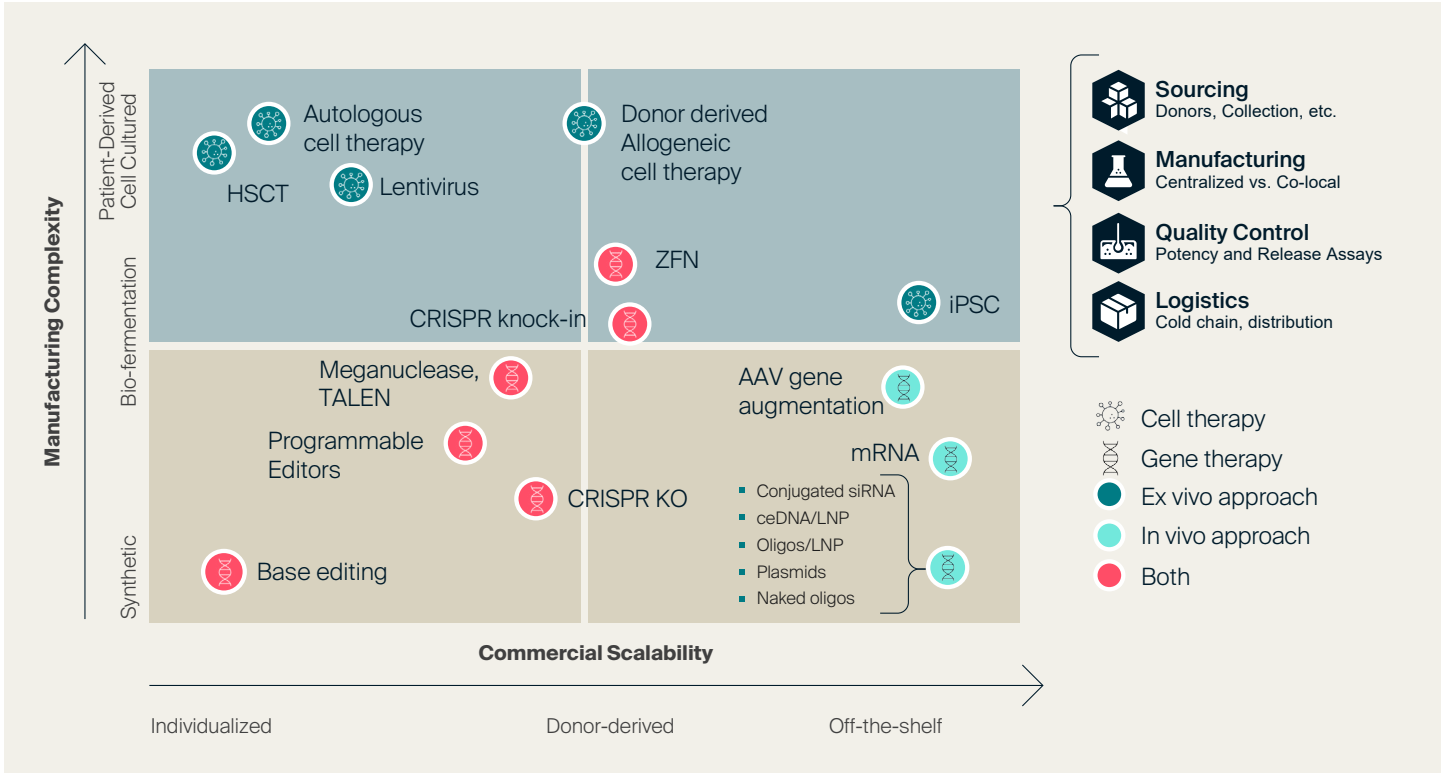


The cell and gene therapy landscape requires diverse commercialization models depending on complexity, scalability, infrastructure, and resource requirements.

Mike Rice opened the webinar speaking about the importance of recognizing diversity in this space – highlighting different technologies of therapeutic approaches that have vast applications across many monogenic diseases.

"We often hear investors or transactors lumping these therapies into one category; cell and gene therapy, advanced therapeutics, but not really realizing that this is a diverse set of technologies that have very different business models based on how off the shelf they are."



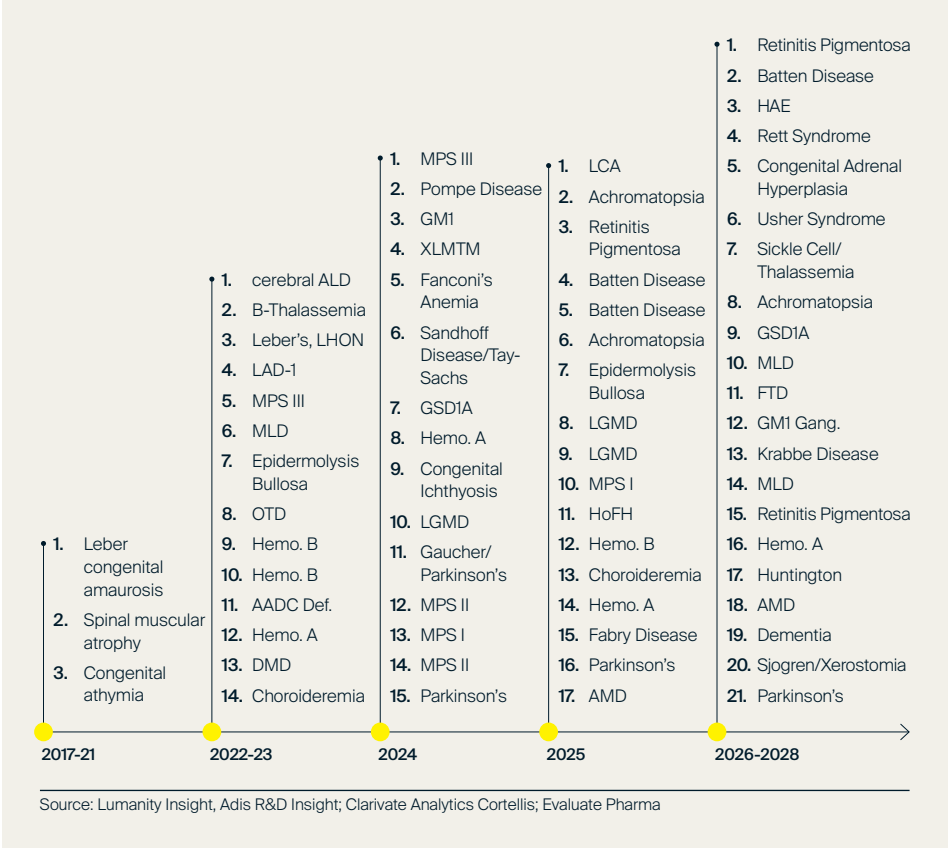
The health sector is anticipating a rapid increase in regulatory approval filings for novel cell and gene treatments in the coming years across a vast spectrum of therapy areas and diseases / conditions. The appreciation of what is required to bring these innovations to market however is lacking, and the clock is ticking.

Mike spoke about legacy programs such as LentiGlobin/Zynteglo), which took a long time to develop from inception, whereas some of the more recently approved drugs, Adeno-Associated Viral (AAV) gene therapies, Zolgensma, and the RNAi technologies seem to have a very rapid drug development pipeline, particularly for liver-targeted diseases.

"Companies seeking to develop and commercially launch cell and gene therapies need to think through a myriad of additional considerations to those normally addressed for launch. Go-to-market strategies from market shaping and education through to internal and external ecosystem development require extensive stakeholder engagement to effectively prepare for commercialization."

Mike highlighted that through RMAT [Regenerative Medicine Advanced Therapy] designation, FDA or PRIME status [EMA], an accelerated timeline can potentially be obtained for drug approval, but it doesn't necessarily mean being able to launch right away, particularly if organizations have not taken the necessary step to 'prepare the market' and engaged the right stakeholders in the right way.

The sector is anticipating a rapid increase in regulatory filings for approval of novel treatments focused on both underserved populations with rare or ultra-orphan conditions through to those diseases with large prevalent populations wanting the right to explore new therapeutic options.

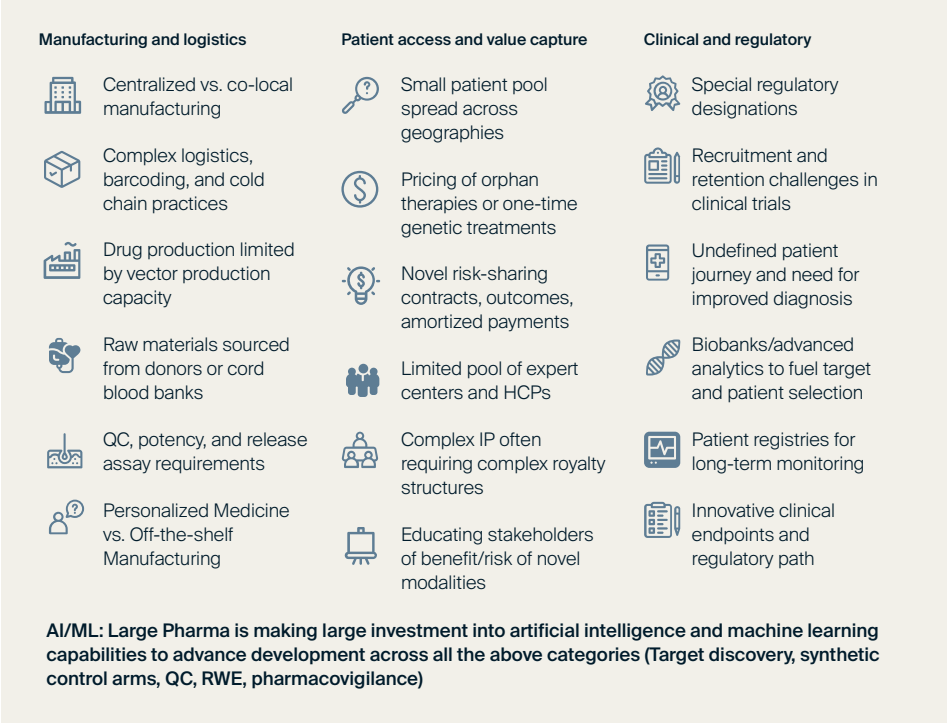


Source: Lumanity Insight, Adis R&D Insight; Clarivate Analytics Cortellis; Evaluate Pharma

Mike spoke to the number of potential therapies that we are likely to see come before the FDA and EMEA and the increasing proportion that serve previously unaddressed (and chronic) diseases.

"We're rapidly going to be looking at addressing white space and high unmet need, but also in the next several years we're going to be actively testing the acceptance of gene therapies in the broad chronic markets, not only for the clinical and safety profiles but also for the pricing models that might make them more attractive in broad, chronic diseases."

Gene and cell therapy platforms bring about a number of healthcare delivery considerations not encountered in conventional therapeutics. The often-bespoke nature of the platforms can have very complex chains of custody and logistics behind them, so that manufacturing and logistics could be a big change in the way that healthcare is delivered to patients.



Mike spoke about the nascent nature of these therapy platforms and the additional complexities involved in delivering these therapeutics to market.

"It's a massive challenge to reduce cost and get these therapies to patients that are in need, and some of them don't have time, some patients don't have 20, 30, 70 days to wait for their treatment."

On the clinical regulatory side there's a lot of innovation looking at how we review all these different applications.

"We're seeing a tidal wave of applications. How does the FDA and the EMA feel about all these applications and respond to them, process them in a proper time?"

Finally, Mike highlighted issues with recruitment and retention in clinical trials and dealing with the undefined patient journeys for diseases where natural history registries aren't available to be a comparator.

Having set out the exciting promise as well as some of the unique challenges across cell and gene therapy innovation, Nicola Redfern was brought into the discussion to reflect on her real-world experience, starting with a reflection of the challenges she faced in her role at bluebird bio. From there she covered a number of critical internal and external factors that need particular attention and solutions to ensure successful commercialization.

The experiences of bluebird bio demonstrate the very real challenges of bringing new cell and gene therapies to market in Europe – despite enormous clinical potential for underserved patients.

Nicola reflected briefly on the withdrawal of gene therapies Zynetglo and Skysona in Europe – despite the positive data and science, and the exciting potential of bringing these therapies to patients.

"It's been one of my worst industry experiences having to contact the hospital clinicians, and even more so the patient advisory groups – to tell them that treatments they knew the regulators were saying yes to, and where the data supported the therapies being introduced to the market, weren't going to become accessible and part of routine practice."

Nicola went on to discuss the mismatch in a payer's definition of value and a significant need to bridge that gap.

"I would go as far as to say there is even a gaping hole between what the payers are prepared to invest, what the industry and the investors have already invested, and the ongoing manufacturing and cost of goods that then have to come into play when you're looking at a viable commercial scenario."

From an internal organizational perspective, there are a number of aspects that need to be in sharp planning focus, to ensure the best chance of successful commercialization in this space. These include the manufacturing and production piece as well as consideration of the overall service and treatment pathway.

Nicola spoke about a need in some scenarios to manufacture treatments in the space rapidly, highlighting that in some conditions patients can deteriorate during the complex treatment pathway from time of the conversation starting as to when they are actually treated.

"We have to be able to manufacture quickly and efficiently, but we also have to be able to do it at a price the payers will pay. So that whole piece, compared to previous industry experience is much more profound and front of mind. If you're in a general manager position for example, you really have to find ways to marry those two things in order to balance a P&L."

Nicola also highlighted the need to pay attention to how services in this space will be delivered. Thinking about the large number of new therapies coming through, there has to be a strong grasp and early analysis around how hospitals and laboratories will deliver to patients in the real world.

"How do we standardize what we're doing company by company in order to make it simpler at the provider point – so that they don't become overburdened, make errors or incur delays in the system? From a cross-industry perspective, we need to monitor what's going on across different companies in the cell and gene therapy space, not just those we might immediately consider competitors. And we need to be speaking to the providers and the patient organizer much, much earlier to make sure that what we're bringing to market is viable and practical for the system."

Nicola also referenced the importance of collecting real-world evidence and natural history data sets on the current standards of care and the current experience of families, stating this needs to be done in parallel with clinical trial research.

"If you don't have a data set that explains clearly what reality is today, it's very difficult to then build a strong value proposition."

A cell or gene therapy is typically unique and necessitates a tailored approach in defining the optimal value proposition. There is also a pressing need for drug manufacturers to play their part in shifting payer perceptions in how value should be assessed.

Nicola spoke about the challenges caused by some of the media hype surrounding cell and gene therapies – being seen as universally curative which isn't necessarily the case.

"We know that some important innovations on the horizon are not curative but still offer a significantly better quality of life, or life extension by slowing down or halting disease progression. We therefore need to be ultra-clear on what we are delivering with these treatments and the associated value proposition. How much do we improve a patient's quality and quantity of life? How do we improve the service infrastructure and make savings for a payer or for a hospital, so that we improve the overall situation across the healthcare system? And in the wider world, how do we get people back to school or back to work?"

Because there are significant differences product by product, disease by disease Nicola believes it can be a disservice for industry to talk about and address cell and gene therapies as a class.

"We are fueling generalized expectations, yet they are all so varied. I think about parallels in the oncology world where initially we all talked about cancer – then we evolved into a world where we talked about in which part of the body the cancer presents and now, we talk about targeting the type of cancer and where it's from, its hormonal status, what receptors it emits etc."

When it comes to a more tailored approach to defining treatment value in this space, Nicola advises a number of required shifts, that start with the overall payer mindset.

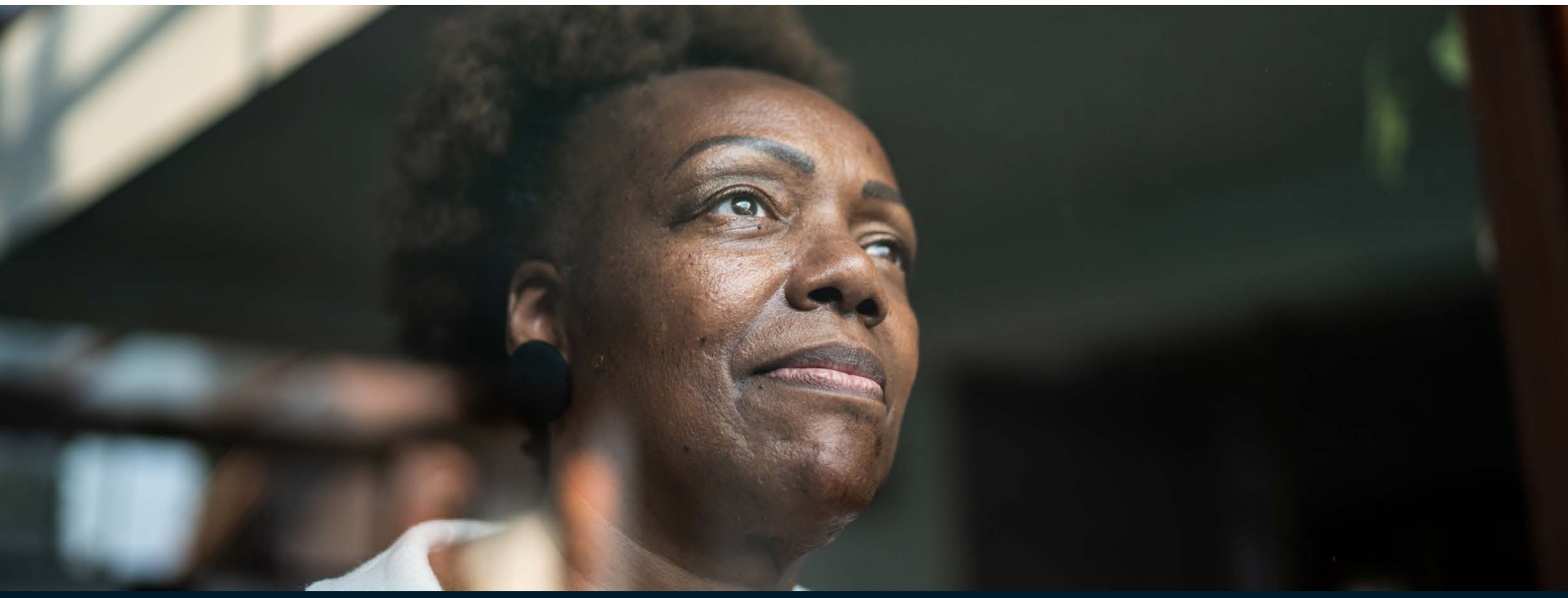
"Of course, we have to be realistic as industry, as in most countries including the US and across Europe – they have very established mechanisms in how they assess value. As drug developers we can make our initial assessments based on clinical trial assumptions of where the data is going to land, as to what the cost-effectiveness might be or what that value proposition might generate in context of the net pricing that we might be able to realize. I think understanding those pieces early from an industry point of view is hugely important to understand if you have a viable proposition"

Nicola used an example of a person who has a short-term life expectancy or a terminal diagnosis, as having much more emotional impact on decision-making than a chronic disease situation where there are already options available that manage the condition on an ongoing basis, such as haemoglobinopathies or haemophilia. Here is where there needs to be an evolved payer mindset that considers the quality-of-life improvements for those patients as well as the positive impacts on public health.

"My ask for payers would be that they invest appropriate time understanding the varied conditions better before making their decisions. My personal experiences in the discussions we had around thalassemia, was that there is a huge chasm between the payer's perception of what was acceptable versus patients' actual lives. Often there were misconceptions built up by what payers read on the patient group websites about the good news stories of when somebody has managed to climb a mountain or obtain a PhD. The general patient reality though is very different – being required to take a huge number of drugs and requiring blood transfusions every two or three weeks – getting side-effects from those blood transfusions and generally feeling very sick."

Nicola summarized this point stating that as an industry, we need to empower patient groups to give an accurate perspective of what living with these conditions is like, and we need to better collaborate and partner to do that. She also believes we need the clinical community to stand up and be more vocal about why new innovations are important and needed. From her experience, the doctors in the field can be reticent in advocating for new innovations publicly. A stronger voice from clinicians however is likely to have tangible impact with payers.

"Ultimately, it's about working earlier and more effectively with payers so that they take appropriate time to accurately assess the impacts of these rarer conditions and the value that these treatments will bring."



New approaches and payment models could have the potential to make a difference in payer discussions, resulting in greater reimbursement. However, many countries are not yet ready to adopt more novel approaches.

Drawing on her experiences at bluebird bio, Nicola felt that an outcomes-based payment model approach was pursued in the hope it would help address anticipated customer concerns around uncertainty, affordability, and budget management.

"There was a clear aspiration to help, collaborate and be flexible in our approach, recognizing that paying for one-time treatments can be perceived as a challenge. In the main however, this approach didn't work out and dialogue was time consuming and challenging."

"Whatever we launch as an industry, we never really know what the outcome and impact is going to be in 5, 10, 15, 20 years' time. I think the focus in the cell and gene world has brought that even more into view, because it's sometimes a one-off treatment with all the cost up-front. That makes people more nervous because you can't stop it if it isn't working out. You've already incurred the full cost before you know for certain how the outcome and impact will play out longer term."

Nicola spoke about many countries not being ready to adopt these new payment models, although some are more open than the UK. In the UK for example, it would mean that treasury rules would need to change, as well as how payers approach budgeting, and track payments in the system.

"This conversation has become quite complex and tied into discussions on the voluntary scheme, and levies/ paybacks. It is therefore sadly being linked – and consequently delayed – to conversations on how much the NHS spends on industry innovations as a whole. If you talk to the companies with an interest in cell and gene therapies in the UK, there is very much an aspiration that we can work with the Department of Health, the NHS and the Treasury to open up discussions further and make new options viable, both to address the affordability when they see that as an issue, and also to help underwrite uncertainty and give greater confidence when conditional licenses are given. All of this takes time to build and shape."

Expanding on her point about mitigating uncertainty Nicola explained that cell and gene therapies are coming to market making quite bold claims about long-term benefits without long-term data.

"If by offering a solution in the way the treatments are paid for, with a commitment to refund when it doesn't work, we underwrite the uncertainty and by making people more confident that enables us to bring these things to market – it then becomes a choice that the patient makes rather than a payer blockade."

Summary Reflections

Nicola believes we owe it to people living with genetically based conditions to fully explore and enable these new approaches to become part of routine clinical offerings across the globe and to ensure that Europe can be as successful as the USA in making these a success.

"Governments across Europe have invested in the data collection and infrastructure to support the cell and gene therapy advances, but we still have hurdles in getting the success stories to patients."

Nicola reflected further on aspects of her personal experience at bluebird bio, with other companies since, and through multiple industry group discussions – she highlighted additional challenges and need for change in this space, with tangible examples.

Sharing insights and approaching commercialization of cell and gene therapies as an aligned industry.

Nicola's first ask would be to build focus on sharing insights and approaching commercialization of these therapies as an aligned industry.

"If we all ask for different changes nothing will evolve. Bringing together the voices of ARM, EFPIA, ABPI, BIA and catapult [in the UK] and others will be essential."

Making therapy delivery simpler for those on the front line.

Service redesign is something Nicola re-iterated as being increasingly important.

"When I joined bluebird bio, I was told that we were going to give each of the hospitals a printer to generate their labels. How they were going to print the labels, and the label size for example, actually ends up in your detailed submission to your regulators, so the detail is important and that is what you are then expected to do. Imagine though, with the number of therapies coming through, what it would be like for a hospital to try and manage multiple printers for multiple drugs – it's not realistic."

In this example, Nicola highlights the importance of engaging in conversations on labeling standardization – changing the rules to create specific procedures and specifications for industry to follow, which will be more realistic for providers.

"If we don't think early about cartridge size, fridge temperatures, using the same registries where it makes sense, and unless we start to join that up across the industry and come together in what our asks are and what we want to shape, we're just going to cause confusion and delays, and any one company is going to struggle to achieve their goals."

Nicola spoke about the welcome changes that NHS England have now made, appointing a specific team to help navigate the complexities of setting up services at hospital level – working out how many hospitals need to be initiating treatment, given the size of population impacted, where the expertise lies, and ensuring viable reach for families so they get the best possible care.

"The Advanced Therapies Treatment centers have also explored lots of areas where improvements can be made and are sharing these priceless insights via the Cell and Gene therapy catapult. Organizations like ARM equally are helping spread best practice and share insights across the globe. It will only be by working together we iron out some of the early challenges and improve adoption timelines in clinical practice. This is such a complex cross functional arena within industry, for decision makers and for providers."

Maintaining patient centricity and establishing realistic timelines to bring about change.

For Nicola, this isn't about abandoning aspirations or accepting the status quo, but about being patient centric and moving forwards positively in a way that will benefit people's lives and society as a whole. Nicola believes there are a number of aspects that industry need to change – although these can differ by geography there is certainly a significant degree of commonality.

"Reimbursement is a big challenge in most countries and taking this amazing science into routine practice really isn't very profitable – if at all – in the early days. This cannot however be an ongoing block for evolution of health care. We have to be realistic however as industry on how long this is going to take, and what's realistic from a net pricing point of view. If we want to change policy, we need people on the ground shaping conversations, probably three years before you want that new policy to be in place if not longer, and others advocating for more flexibility."

Nicola also pointed out the challenges for individual organizations where companies and products are coming through quickly, being bought into organizations quite late, or have competing products and portfolio considerations.

"It's important for the individual company to be realistic about how much the environment can be influenced by the time a drug comes to market versus able to commercialize something successfully in the existing environment. The science is followed closely by the community living with many of these conditions and delayed access to things that work is a tragedy, wherever in the system or by which ever organization. Honest, open conversations early as an organization and across the different stakeholder groups are essential, so everyone knows how optimistic to be. Scientists, Royal Colleges, industry associations, patient organizations and clinicians therefore need to continue to battle this and drive change."

Given the number of commercial sensitivities and complexities in this space, commercial partners can play a significant role steering cell and gene assets to reach their potential and help change patients' lives.

"For me, having external partners and bringing people in that can slow down your recruitment, is going to be really important as the temptation is to over-build your teams too soon. Also, if you bring partners in to support the strategy planning work and add to the commercial thinking and marketing planning, that's going to augment the team resource and importantly augment the level of relevant experience of your team. Partners bring fresh insights because they work across multiple companies. There's not actually that many of us out there who have worked in this space, especially at the early commercialization stages."

Lumanity has the experience and expertise to navigate the complex journey to commercialization, offering expert guidance through the clinical journey and the commercial launch planning window – putting you on a clear path to delivering value and changing patients' lives.

Find out more here:
lumanity.com/cell-gene

Lumanity applies incisive thinking and decisive action to cut through complex situations and deliver transformative outcomes to accelerate and optimize access to medical advances. With deep experience in medical, commercial, and regulatory affairs, Lumanity transforms data and information into real-world insights and evidence that powers successful commercialization and empowers patients, providers, payers, and regulators to take timely and decisive action.

Contact us to learn more about how Lumanity can support your unique challenge.

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