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European Biotechnology

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Interview

Kurma Partners Daniel Parera (r.) and Peter Neubeck explain how good data finds attention and money even in difficult times.

FREE EXCERPT

Cell & Gene Therapy

Getting Europe rolling

Cellular agriculture
The Netherlands pave the way for access to lab-farmed protein

CDMOs & CROs
Post-pandemic, new formats are powering market growth

Featured country
The biotechnology sector in Spain is burning up the track

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NOVARTIS | Reimagining Medicine

Building a new industry and medicine thanks to biotech

Picture: Ion Arocena, CEO of AseBio, the Spanish Bioindustry Association

ION AROCENA is the CEO of AseBio, the Spanish Bioindustry Association. He holds a Bachelor's degree in Biology from the Complutense University of Madrid, graduating with honours (2003), and a Master's degree in Business Administration from EOI (2010). He worked in a life sciences venture capital firm for almost a decade before joining AseBio in 2016.

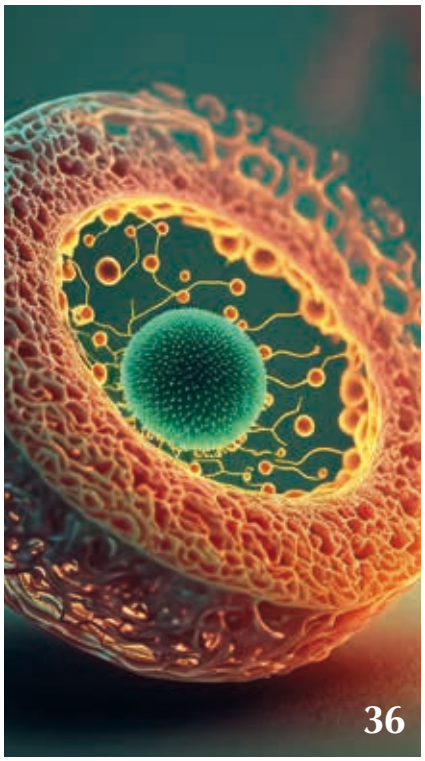
Biotechnology is helping us tackle challenges such as emerging diseases, the impact of ageing in healthcare, population growth, climate change, and the green transition of the economy. Precision medicines, advanced therapies, mRNA and gene editing technologies are transforming the way diseases can be diagnosed and treated, providing life-saving solutions. Biotechnology is also at the forefront of building a sustainable economy, developing better crops, providing new protein sources, and producing bio-based materials.

It's time to place biotechnology at the core of a new, more sustainable European growth model. Since July 1st, Spain holds the Presidency of the Council of the EU with a programme focused on four key pillars: re-industrialisation of the EU and ensuring its strategic autonomy, advancing in the green transition, promoting greater social and economic justice, and strengthening European unity. Biotechnology can play a fundamental role in achieving these objectives. The COVID-19 pandemic highlighted both the vulnerabilities and strengths of the EU life sciences ecosystem. It may be too late or costly to revert some of the latter, but with the lessons learnt in mind, we could still strengthen our capabilities in key technologies for the medicines of tomorrow, such as biologics, cell and gene therapies. While the EU remains a scientific powerhouse in these areas, we struggle to develop technology, launch ventures and grow them into global players. Europe needs to boost investment in R&D and enabling infrastructure, generate and grow more innovative companies, and increase biomanufacturing capacity in this space. On the other hand, biotechnology is crucial for the green transition. New Genomic Techniques (NGTs) are very precise and efficient, allowing us to modify the genome of plants and microorganisms specifically. NGTs are key tools for developing plant varieties that can be climate resilient, pest resistant, require fewer fertilisers and pesticides, or ensure higher yields, contributing to the goals of the green deal and meeting the increasing demand. Their application in microorganisms can also lead to new strains to produce raw materials for other industries, reduce the demand for natural or fossil resources and contribute to the green transition.

Europe is clearly at a turning point that will determine our competitiveness and resilience for the next generation. Legislative proposals affecting the biotech ecosystem are currently under discussion. To mention two, the EC launched a proposal for a new regulation on plants obtained by NGTs paving the road to enable the use of NGTs in Europe. Secondly, the proposal of the Commission for the revision of the EU Pharmaceutical Legislation includes provisions aimed at improving the EU's regulatory framework and promoting 'novel technologies, although some may undermine the predictability and stability of EU's incentives regime and may hamper the industry's ability to innovate. It is a critical moment for Europe to establish regulatory frameworks which are fit for purpose and enable innovations to happen, allowing their potential to be fulfilled. Only by doing so will Europe be able to lead in global innovation and transition towards a more sustainable economy, thereby strengthening its strategic autonomy. ■

FREE EXCERPT

COVER STORY



ATMPs: Capitalising on Europe's strengths

Cell and Gene Therapies (CGTs) have emerged as one of the fastest growing sectors in the life sciences industry, even though supply chains in the field are more complex than in traditional pharma. That's because CGTs for rare diseases mostly can't be produced centrally, and still require a lot of hands-on work, including directly in clinics. For firms to take advantage of Europe's excellent science base, networking stakeholders and safe reimbursement are proving to be crucial factors. The EU has some catching up to do.

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REGIONAL NEWS

SCIENCE & TECHNOLOGY

PICK & MIX

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CELLULAR AGRICULTURE

Steak hollandaise 2.0

Biotech start-ups that want to completely decouple protein production from agriculture due to environmental and animal protection benefits have been blocked by the EU's stubbornly slow Novel Food Regulation. This summer, the Dutch Government paved the way to giving consumers early and rapid access to cellular agriculture products through unique tasting events.

AGRIBIOTECH

Ending the deadlock?

Except in Spain and Portugal, the commercialisation of biotech crops stalled in Europe for about 15 years. In July, the EU Commission tabled a draft regulation, backed by agriculture ministers at an informal meeting to incentivise researchers and farmers to make use of new genomic techniques in plant breeding.

SPECIAL

CROs & CDMOs

Pictures: Xxxxxxxxxx (left); xxxxxxxx (middle); BIOCOM AG (right); Xxxxxxxxxx

EDITORIAL

Survival training

Survival of the fittest – that's how Charles Darwin formulated the idea that the species best adapted to prevailing environmental conditions will win out. In the fastest-growing field in the pharma biotech sector – cell and gene therapy – China now looks set to overtake the US, the biotech world market leader – at least as far as clinical trials are concerned. And Europe? The bloc continues to suffer from a lack of communication/networking and seemingly ineradicable bureaucratic hurdles when it comes to bringing ideas from bench to bedside – with exceptions such as the UK or Spain (see Country Focus, p. 57). Biotech entrepreneurs want to turn that around with historic opportunities for reform of the EU's pharmaceutical legislation (see. p. 36).

Their biotech colleagues in the boom market of cellular agriculture and precision fermentation – in short, vegan protein substitutes – feel the same. This summer, the Netherlands opted out of the EU system, and will now allow pre-approval tastings of novel sustainable foods (see. p. 12).

The EU Commission has already moved on the issue of biotech breeding, and was able to get a majority in the EU Council of Agri-Ministers behind its proposal to create the most liberal set of regulations in the world for approving crops produced with new techniques (see p. 6). Now we have to see how adaptable Europe is in other fields.

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Thomas Gabrielczyk
Editor-in-Chief

FREE EXCERPT

The novel food sector has gotten a boost in The Netherlands. Tasting has grown much easier, helping start-ups get customer feedback early on – a seemingly simple but important step.

FREE EXCERPT

Steak hollandaise 2.0

PRECISION FERMENTATION As plant-based alternatives to meat increase market share substantially, novel foods are no longer looking so novel – even when it comes to those grown in the lab. Many start-ups are now pursuing the lab-based development of milk, meat or fish. What's missing is the customer experience. The Netherlands is now seizing a position at the centre of the novel food movement in Europe by opening the door on early tasting events.

Food is no longer just food. It may come from traditional agriculture, which now includes products from land that's extensively or intensively farmed with the digital help of drones to optimise pesticide use. But the term 'food' also covers products farmed according to dynamic-organic regulations that explicitly exclude chemistry, or ones that follow traditional methods, like planting and harvesting during certain phases of the moon. Not even to mention genetically modified crops. But much of the 'food' we buy from the supermarket may soon no longer require farmland at all. It can be blended in the laboratory into a product that outwardly resembles the original fruit, vegetable, meat, fish or milk.

Sounds disgusting, inhuman or unnatural? Well, it's already happening. It would just be a further step down a road that many foods in our industrialised world have taken. We often mix different ingredients and some natural raw materials to create products that taste like what is pictured on the packet. Just look at the ingredients list on the ice cream you buy in your favourite shop. Do you recognise them, or know what they are for?

The new movement of novel foods from the lab is actually in most cases aimed at giving consumers more insight, and talking openly about the processes of cultivation or fermentation. But the landscape is also hard to parse. On the one hand, there's a lot of investor interest in lab-grown meat, precision fermentation and cow-less milk or cheese. On the other, the sector is cooling down because the gulf between product and consumer is still pretty deep and wide. At least that's true in Europe, where regulation of novel food approvals coordinated by European Food Safety Authority (EFSA) is very slow, to say the least. Consumer experiences of lab-grown meat were first celebrated in London (2013), and have since also happened in Singapore. The cost of that complex first generation burger made of diced cellular matrices was a whopping €330,000.

MAARTEN BOSCH
CEO Mosa Meat

? Your comment about the new legislation in The Netherlands?

! *We thank all 127 members of the Tweede Kamer who voted in favour of finding a way to make food from laboratories possible. Mosa Meat will use these controlled tastings to gather feedback, but also to educate stakeholders on the role that cellular agriculture can play in Europe to meet food sovereignty and sustainability goals.*

The field has come a long way since those early days. Professor Mark Post from the University of Maastricht in the Netherlands cultured that very first lab burger from muscle stem cells in fetal calf serum, so the method didn't meet slaughter-free expectations from the start. But Post and his team at Mosa Meat have since learned to use other ingredients for lab cultivation, and now guarantee results where no animal was harmed.

So far, only California-based Good Meat (formerly known as Eat Just) has managed to have a lab-grown meat product approved for public sale. Regulators in Singapore – until recently the only country in the world to allow the sale of such products – greenlighted their cultured chicken in December 2020. "Cultured meat is real meat, but you don't have to slaughter an animal," said Josh Tetrick, CEO of Good Meat, in a BBC interview.

Now his home country is following suit. At the end of last June, the US Department of Agriculture gave a first-ever approval for cell-cultured meat produced by two companies: Good Meat and Upside Foods. Both grow small amounts of chicken cells into slaughter-free slabs. It was the final regulatory thumbs-up the California-based companies needed to sell and serve their products in the United States. The approval came less than a year after the US Food and Drug Admin-

›› Read the full story in the printed issue.

Picture: © Good Meat Inc., Mosa Meat

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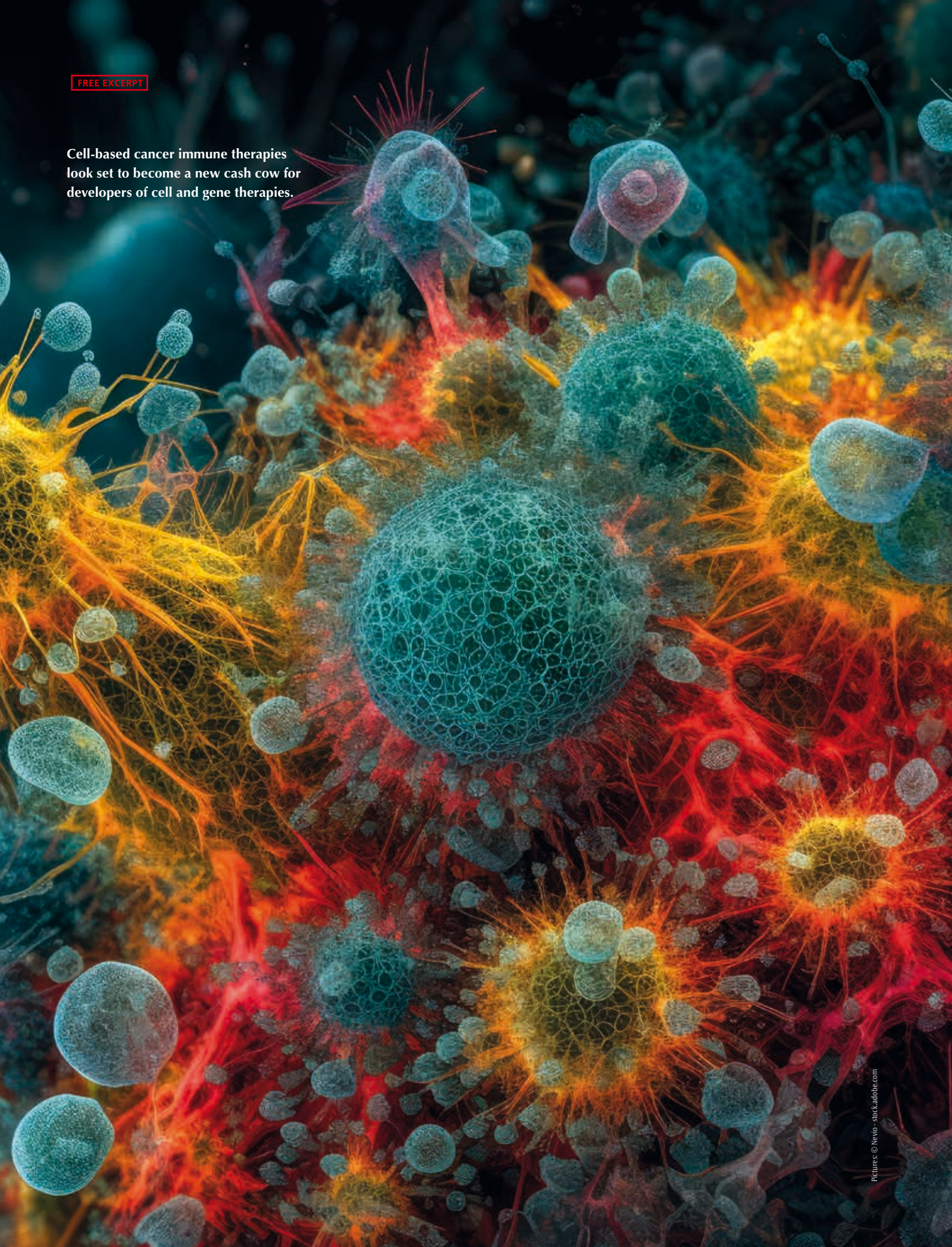
Cell-based cancer immune therapies look set to become a new cash cow for developers of cell and gene therapies.



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Europe's next steps are crucial

BIOMEDICAL RESEARCH Cell and Gene Therapies (CGTs) have emerged as one of the fastest-growing sectors in the life sciences industry. Supply chains in the field are more complex than in traditional pharma, due to the fact that CGTs for rare diseases mostly can't be produced centrally, and still require a lot of hands-on work. For companies to take advantage of Europe's excellent science base, networking stakeholders and safe reimbursement are proving to be crucial factors. Approaches in other regions have shown how to turn concepts into therapies.

Since Novartis received FDA approval for the very first (CAR-)T cell-based blood cancer therapy (Kymriah) in 2017, the Advanced Therapy Medicinal Products (ATMPs) that involve cell, tissue engineered and gene therapies have really come into their own – outperforming annual growth rates of the most lucrative indications three to fourfold (see Fig. 1). ATMPs, many of which have been optimised by researchers for at least 30 years, are now providing hope for cures to many diseases that in the past were difficult if not impossible to treat with conventional medications. Examples include patient-derived CAR-T cell therapies that have knocked out several blood cancers, as well as gene therapies against haemophilia A, spinal muscular atrophy or the heritable immune deficiency ADA-SCID.

However, due to both their nature and very small patient populations, CGTs face several challenges (see p. 39) compared to centrally manufactured biologics such as antibodies. These include scaleability and immune rejection of gene therapy vectors or administered cells, the many manual steps in engineering the cells suited to a patient's genetic make-up, and the logistics of autologous cells on the hospital site – to name just a few.

CGT developers in the EU have increasingly lost ground to the US and China when it comes to clinical development and funding in the field, despite a historically superior research base. But in an effort to advance the lucrative cellular immunotherapies for cancer, which make up the bulk of the clinical CGT pipeline, there are now at least good role models in Europe demonstrating what changes in the recently updated EU Pharmaceutical Legislation could help EU biotechs advance.

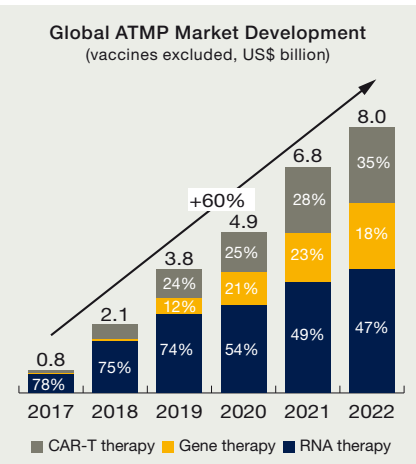

Fig. 1: Revenues with CGT including RNA, CRISPR, gene and cell therapeutics have been growing at an annual rate of 60% since 2017 – three to six times more than in the top 10 therapy areas by value (including the lucrative US$184bn cancer market). This also benefits GCT CDMOs, whose revenues are expected to grow from currently US$4.8bn to US$15.4bn by 2030.

UK taking the lead

In retrospect, when it comes to CGTs at least, the EU may regret Brexit. In the UK, remarkable things are currently happening in the rapidly evolving field – although China and the US remain far ahead of Europe in terms of numbers of preclinical and clinical CGT studies, investment and developers (see Fig. 2, p. 38). In June, for instance, UK-based Adaptimmune Therapeutics plc shook up the sector by completing its US marketing application for afami-cel, the world's first TCR-T cell therapy to treat solid tumours.

Access to a bull market

Solid tumours, unlike the blood cancers for which all engineered immune cell therapies (mostly T- or NK cell-based) have been approved, account for 90% of all cancers. That makes them a potential goldmine for Adaptimmune and the rest of the pack. Big news came in June with

›› **Read the full story in the printed issue.**

Picture: © BIOCOM, Source: IQVIA EMEA ThoghtLeadership

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Efficacy evaluation

CRO Antibody drugs including monoclonal antibodies (mAb), bispecific antibodies, antibody-drug conjugates (ADCs), and nanobodies have sparked a new surge in research and development.

The bioactivity of mAbs is often confirmed by rigorous testing of efficacy and potency. This forms an essential part of the antibody drug evaluation system and plays an important role in determining the mechanism of action (MOA) of drugs, providing a foundation for preparing investigational new drug (IND) submissions.

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