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European Biotechnology

Life Sciences and Industry Magazine

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Interview

Marco Rupp, Bio-based Industries Consortium, on how to make the circular bio-based economy a success.

FREE EXCERPT

Cellular Agriculture

Boom or exodus?

Targeted Therapies

Progress with antibody-drug conjugates against solid tumours

Manufacturing

Billion-euro expansion of new obesity blockbusters in Europe

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Attractive Life Sciences Events in the first half of next year

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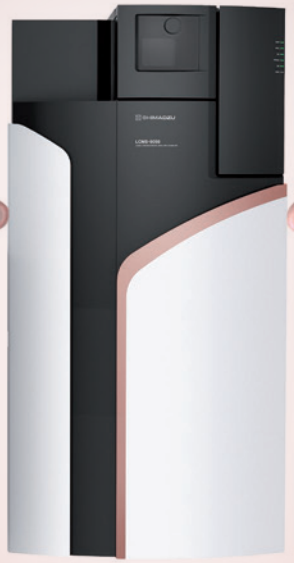

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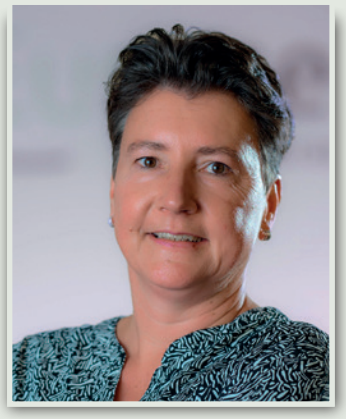
Plant breeding innovation reloaded?



PETRA JORASCH, holds a PhD in plant molecular biology from the University of Hamburg. She is an internationally recognised industry advocacy expert with more than 20 years of experience in plant science and breeding as well as relevant intellectual property protection systems and a deep knowledge of the relevant policy frameworks. Petra joined Euroseeds in February 2017 as the spokesperson of the EU plant breeding sector on modern plant breeding methods and innovative technologies.

The European Court of Justice ruling from 2018 which put the latest breeding methods under the EU GMO legislation was a huge push-back for plant breeding innovation in the EU. With the proposal for a new regulation for certain new genomic techniques (NGTs) published on 5 July 2023, some faith in a rebirth of plant breeding innovation may just start to return. The European plant breeding and seed sector welcomes that the Commission proposal finally recognises the need for a differentiated regulatory approach to certain NGTs from the burdensome GMO legislation.

The proposal establishes a verification process to confirm if a NGT plant is meeting the equivalence criteria to be categorised as conventional-like (Category 1). Consequently, those Category 1 plants should also be subject to the same regulatory requirements as conventional breeding products. It is therefore inconsistent that Category 1 NGT plants are considered GMOs for organic farming. This does not allow organic farming to benefit from any of the NGT-derived product innovations in plant breeding – specifically those that enhance environmental sustainability of crop production- that we expect in the years to come. Euroseeds welcomes that national competent authorities are the responsible bodies for conducting the verification procedure. This increases accessibility for SMEs. We nevertheless regret that the Commission took a very conservative approach in view of the limited numbers of genetic changes for an NGT-plant to be covered by the equivalence criteria for Category 1. This does not allow polyploid crops which include multiple copies of the same gene to benefit in the same way from the application of NGTs if each copy is counted separately.

Breeding companies invest up to 20% of their turnover in research & development and rely on legal certainty for their investments. The verification process should therefore be effective and predictable based on clear criteria and the scientific expertise of member states' competent authorities.

Euroseeds reiterates that any GMO-approach (Category 2) -even if it includes a lighter risk assessment- is unworkable, specifically for SMEs. We expect import approval applications for Category 2 plant products to be the same as for classical GMOs but we do not consider the GMO system suitable for cultivation approvals. This will again lead to a situation which allows for import of innovation but restricts the cultivation of such innovations for EU agriculture.

We remain committed to contribute and to advocate for a system of intellectual property rights that takes the needs of all stakeholders involved in the development of innovative technologies and products into account. Such system needs to successfully balance effective protection and fair, broad access, to the benefit of Europe's agri-food sector and society. ■

Picture: © Euroseeds

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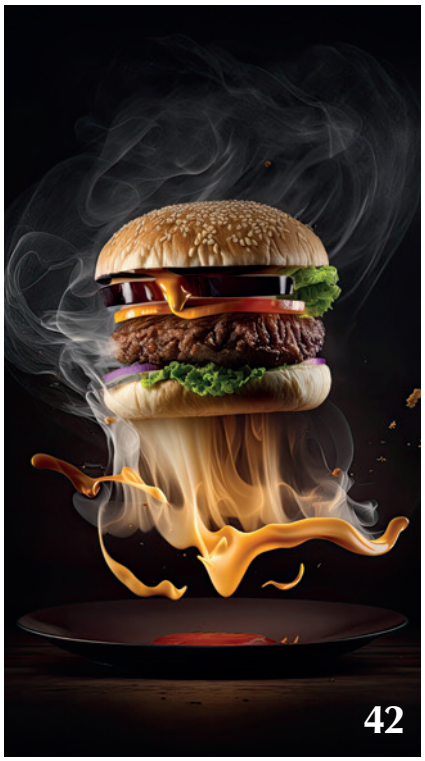
COVER STORY



A looming EU foodtech exodus?

Will Europe once again grow dependent on the US and Asia – this time in the potential billion-dollar market for cultivated meat, fish and dairy products? Over 90% of EU biotechs with a corresponding product range decide to have their products approved in Singapore or the US because of slow responses from an unmotivated EU food authority and hesitant investment in industrial production facilities. Dubai is also trying to attract EU innovators with big equity investments.

INSIGHT EUROPE

ECONOMY

REGIONAL NEWS

SCIENCE & TECHNOLOGY

PICK & MIX

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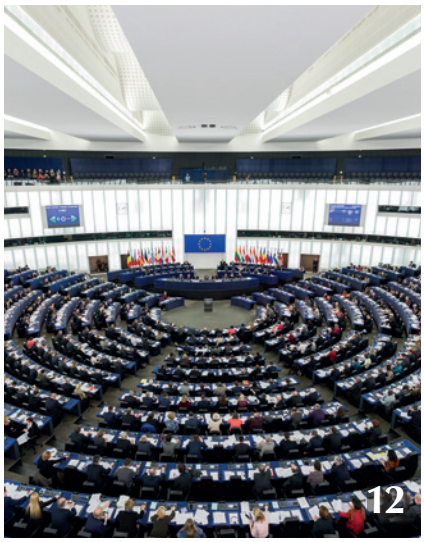
ADC

Take your best shot

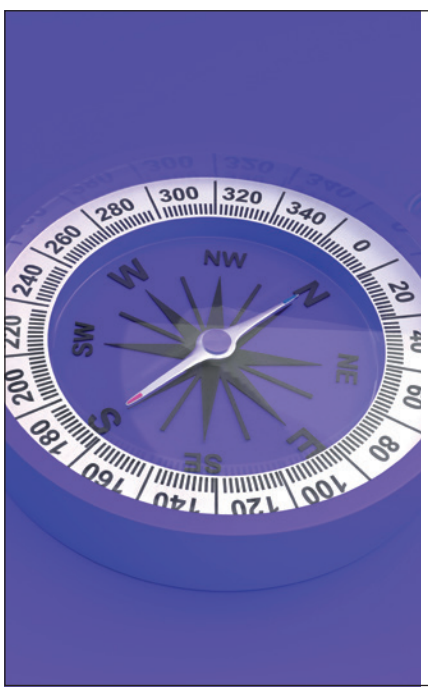
It has taken two decades, but the field of antibody-drug conjugates is finally hotting up – underlined by Pfizer's mega-takeover of Seagen for over US$40bn, as well as other deals that are making headlines. Clinical data in the area show better-than-ever results, while interesting moves in the field and new payloads are drawing lots of attention.

EU POLICY



EU STEPs back

In response to biotechnology being prioritised in the US under the Inflation Reduction Act, EU Commission President Ursula von der Leyen wanted to hit back with the €360bn STEP initiative – but Member States were only willing to provide €10bn. MEPs are now lobbying for €13bn.



SPECIAL

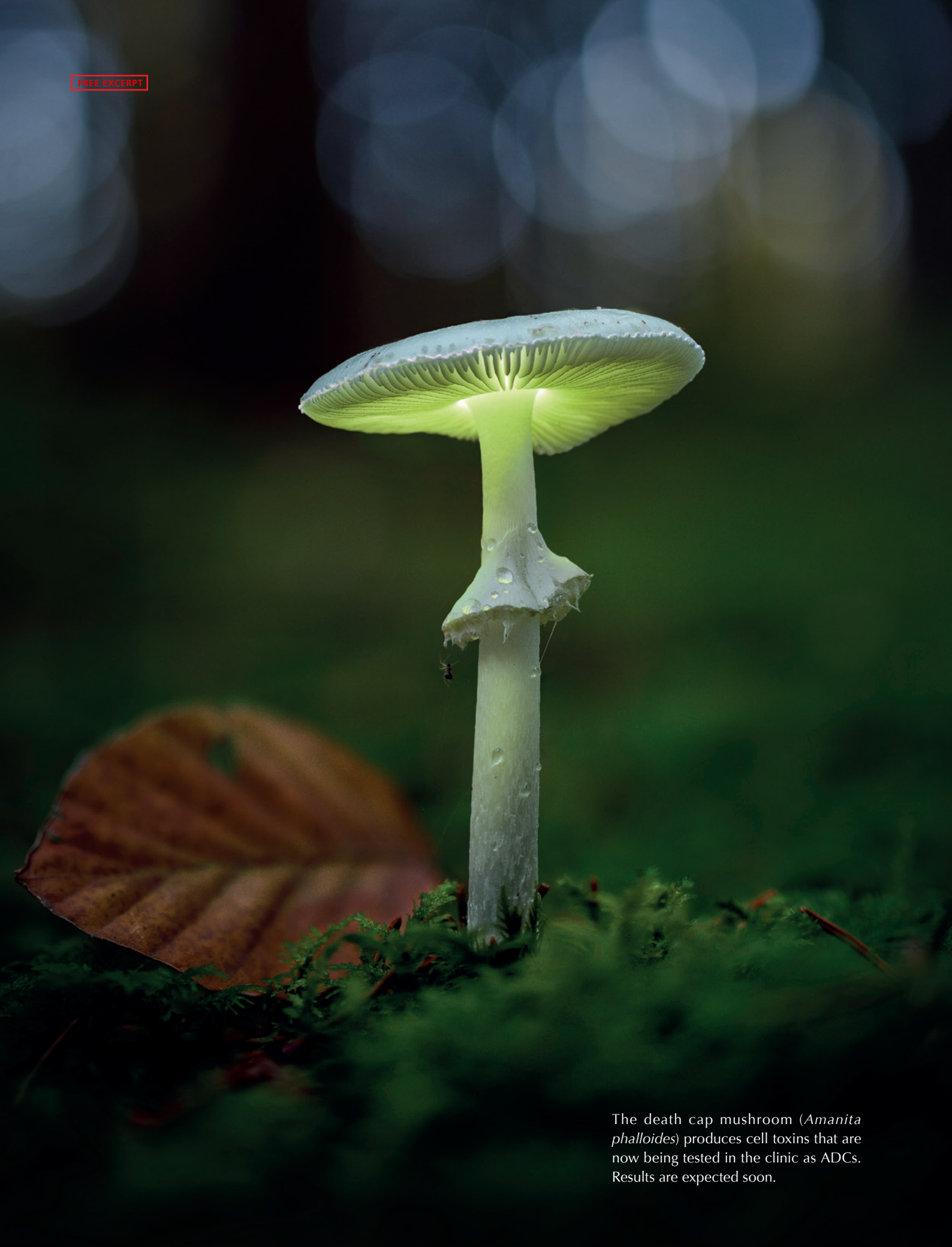
Biofairs Compass

EDITORIAL

Move or not?

Italy's right-wing government under Giorgia Meloni has made a decision about foodtech. In mid-November, it became the first country in the world to ban the industrial production of food based only on cells rather than vertebrates (see p. 6). Instead, the government is standing behind farmers, who fear biotechnological food production could replace traditional agricultural methods. Specialists for cellular agriculture say the area has a huge number of advantages: less water, pesticide, land and fertilizer consumption, and over 90% reduction in CO_2 emissions (see p. 42). Italy's decision also reveals a flaw in EU policy. In an era when Asia, China and the US are increasingly relying on biotech, the EU promise of jobs AND growth no longer works, because job-making agriculture will remain low-tech as long as Member States block new genomic techniques (NGT, see p. 50) or food biotech. The bureaucracy involved highlights the problem. EU food authority EFSA can check the safety of novel foods for up to three years, and in the end a political vote by Member States can extend waits to 4-6 years. In innovation-hungry nations, the whole process can take as little as nine months. The situation could end with an exodus of European innovators. Instead of complaining about backlogs, EU decision makers should curtail the endless discussions and streamline authorisation. The potential is there.

Thomas Gabrielczyk
Editor-in-Chief



The death cap mushroom (*Amanita phalloides*) produces cell toxins that are now being tested in the clinic as ADCs. Results are expected soon.

Cancer: Hit it with your best shot

THERAPEUTICS After decades of development, antibody-drug conjugates (ADCs) are increasingly making headlines, although the earliest authorisations were somewhat less successful than theory predicted. Researchers now finally appear to be mastering the interplay between antibody, linker and toxin. The next wave of ADCs is just around the corner

When the first antibody-drug conjugated co-therapy was approved, euphoric observers viewed it as a breakthrough. Modified ADCs loaded with a cytotoxic payload have long been a goal in the field. The initial hopes proved to be misplaced, however, and practical experience has since revealed that the fragile complex of a protein-chain antibody – usually coupled to a cytotoxin via a linker – interacts with the body's physiology in ways that are still far from being sufficiently understood. If toxins detach from their antibody transport system too early and unspecifically, it can affect healthy cells and tissue close to the targeted tumour. This 'collateral damage' could mean high toxicity, and was a fundamental reason the first wave of approvals disappeared from treatment schedules.

The first ADC to be approved back in 2000 was Mylotarg, which was pulled from the market in 2010 because death rates actually increased under medication. It was relaunched in 2017, but meaningful traction really only set in when the technology for each component improved and second-generation ADCs were introduced, among them Takeda's Adcetris in Hodgkin lymphoma (2011) and Genentech/Roche's toxin-coupled variant of trastuzumab, Kadcyla (2013). Since then, clinical and commercial wins have continued to rack up, including for programmes combining ADCs with checkpoint inhibitors (i.e. Padcev/Keytruda).

The field of developers has subsequently split even more into those specialised in coupling the toxin to the antibody and those who test and optimise a range of cytotoxins from nature – or known chemotherapy cytostatics – in tissue-specific delivery to the tumour. A smaller fraction of companies and development projects in Big Pharma companies is focused on antibody variants, along with smaller fragments and their various modifications, to see whether they could be made even better at specifically delivering toxins to a desired target site, generally due to better penetration of tumour tissue.

Good ideas can take time

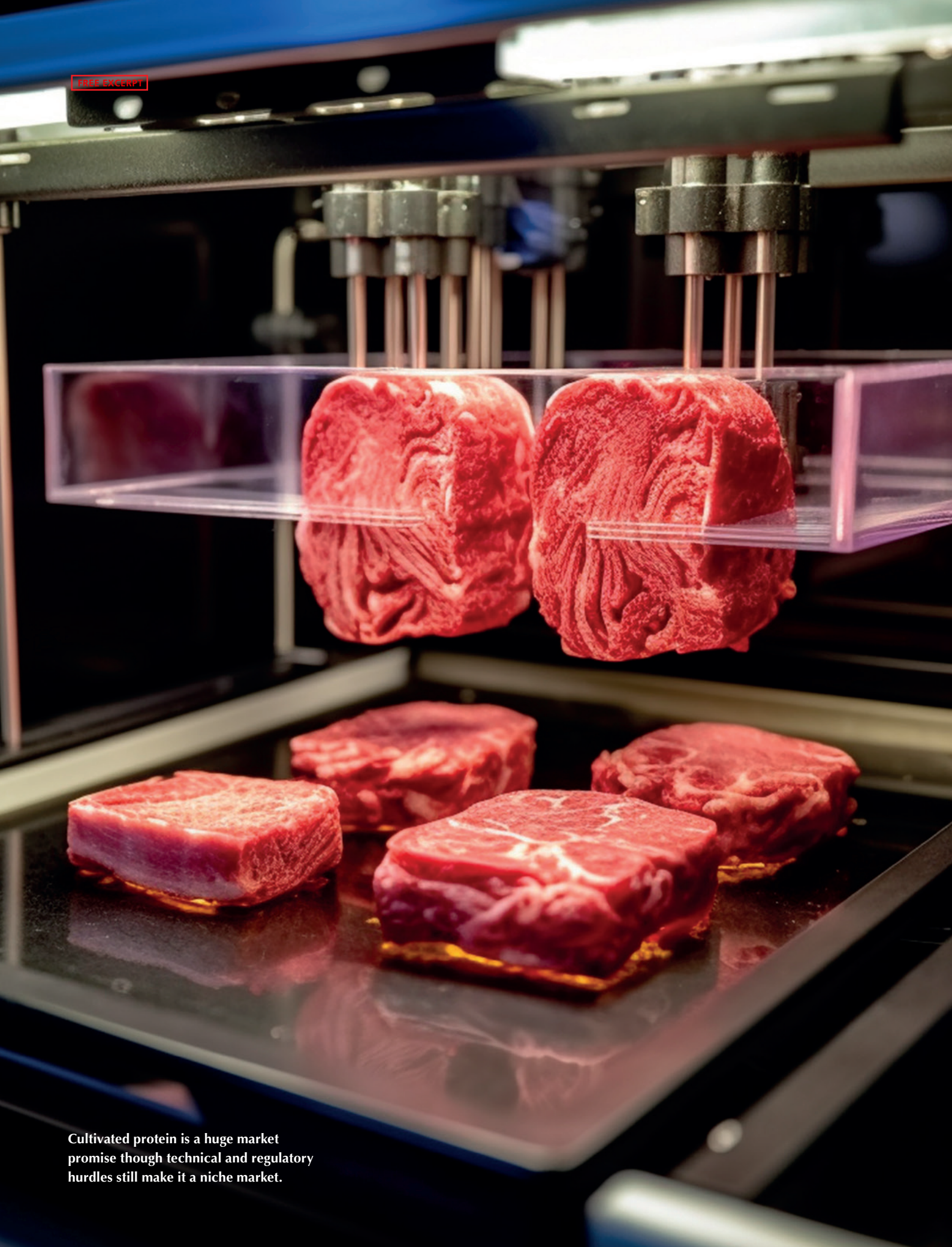
But smaller antibody derivatives have not yet proven to be more successful than their larger cousins. Faster degradation rates and other pharmacokinetic dynamic factors could be reduced with a number of space-taking attachments, but this also appeared to reduce penetration into tumour tissue – a hoped-for advantage of smaller fragments.

Experienced developers on the ADC front have now told European Biotechnology that the years of research have helped to clarify many outstanding issues. Specialisation in linker technology and cytotoxins has brought a lot of progress, while many licensing deals and acquisitions can now be seen in the area. Some were the subject of discussion at major partnering events like BIO-Europe 2023, which took place this time around in Munich.

Deals that are making headlines

The ADC space has heated up in a big way in the last few years. Over US$125bn in partnerships and M&A have been reported since 2019, including this year's Pfizer US$43bn mega-acquisition of Seattle Genetics (Seagen) and a record US$5.5bn upfront deal between Merck (MSD) and Daiichi Sankyo. There are hundreds of assets across thousands of trials in the field in various indications. Eight approvals in the last five years (raising the number to 13 in total) have done more than crack open the door. Looking at pipelines and assets in later clinical phases, it seems more like a dam has broken. If you include the radiopharma space in the ADC landscape as well, as a closely related technology for delivering killing substances spatially in cancer, an overview of what is going on where becomes even more entangled.

›› Read the full story in the printed issue.



Cultivated protein is a huge market promise though technical and regulatory hurdles still make it a niche market.

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Boom or exodus?

FOOD BIOTECH Europe is the cradle of the cell-based meat sector. However, companies that have developed microbial, fungal and cell-based alternatives to conventional meat, fish or dairy products – or to plant-based protein alternatives, which are often expensive and not very tasty – face major hurdles when it comes to authorisation and production on the continent. Will companies soon begin leaving Europe for greener pastures?

Rarely have entrepreneurs and politicians around the world been so unanimous in their assessment of the emerging market for cell-based and microbially produced meat, fish and dairy product alternatives. On the occasion of the US market launch of its cell-based chicken product in June 2023, founder and CEO of manufacturer Upside Foods Uma Valeti called it "a dream come true" and said the market approval "marks a new era". Good Meat Inc, a company that was given FDA/USDA marketing permission the same day, had already received the world's first ever authorisation for a cell-based meat product in Singapore three years earlier. In addition to the 20 companies worldwide that cultivate meat and fish alternatives from muscle stem cells, 136 biotech companies are churning out completely animal-free alternatives produced in fermenters instead of through livestock farming. At the end of September, German Research Minister Bettina Stark-Watzinger confirmed Valeti's enthusiasm for this new way of producing food: "I am certain that these products will revolutionise our diet. Biotechnology is the key to this – whether in the production of animal-free beef or pea protein. There is a market worth billions waiting to be tapped."

So what's behind the enthusiasm, which has also gripped stock market analysts? According to the Food and Agriculture Organization of the United Nations (FAO), meat, fish and dairy products from factory farming are responsible for at least 15% of global CO_2 emissions and 40% of all global deforestation. And that isn't even counting the consequences that animal feed production has on soils and biodiversity. In contrast, the cultivation of protein or fat alternatives, which are often produced from waste sidestreams or directly from CO_2, promises carbon savings of 99% compared to conventional livestock farming. It demands neither agricultural land nor artificial fertilisers, antibiotics or pesticides, and requires much less water.

DR KLAUS PELLENGAHR
Managing Director, Corden Biochem GmbH, Frankfurt/Main

? What role do the comparatively high energy prices in Europe play for foodtech producers and CDMOs?

! *In Europe, especially in Germany, energy costs are far too high by global standards. We are seeing in biotechnology what we are already seeing in the chemical industry: there is a risk of a major exodus from Europe.*

In 2022, researchers from the Potsdam Institute for Climate Impact Research analysed the environmental land use impacts that substituting fermentation-derived microbial protein for ruminant meat would have. Replacing just 20% of per-capita beef consumption with microbial protein from sugar-fed fermentation by 2050 would reduce deforestation and related land-use change emissions by 50%. A group of researchers in Finland found that microbial protein obtained from hydrogen-oxidising bacteria results in environmental impacts 53%-100% lower than conventional meat.

Tailwinds for producers

That's reason enough for many governments to support the development financially. A month after Stark-Watzinger made her comments, the budget committee of the German Parliament earmarked €38m from its 2024 draft budget for the new biotechnological production methods and to set up a coordinating centre of excellence. "A great signal," stressed Tanja Bogumil, the Managing Director of Berlin-based Lovely Day Foods, which has developed Perfeggt, a bio-identical protein substitute produced by precision fermentation, "even if the sum is of course small if you want to set up an industrial production plant." That would cost a three-

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