ISSN 2364-2351 | A 60711 | BIOCOM

European Biotechnology

Life Sciences and Industry Magazine

Autumn Edition 2020 | Volume 19 | 20 €

Interview

Rainer Krüger, European Cannabis Association, explains how to establish product and process standards for medicinal cannabis.

FREE EXCERPT

Tumour Offensive

Striking from within

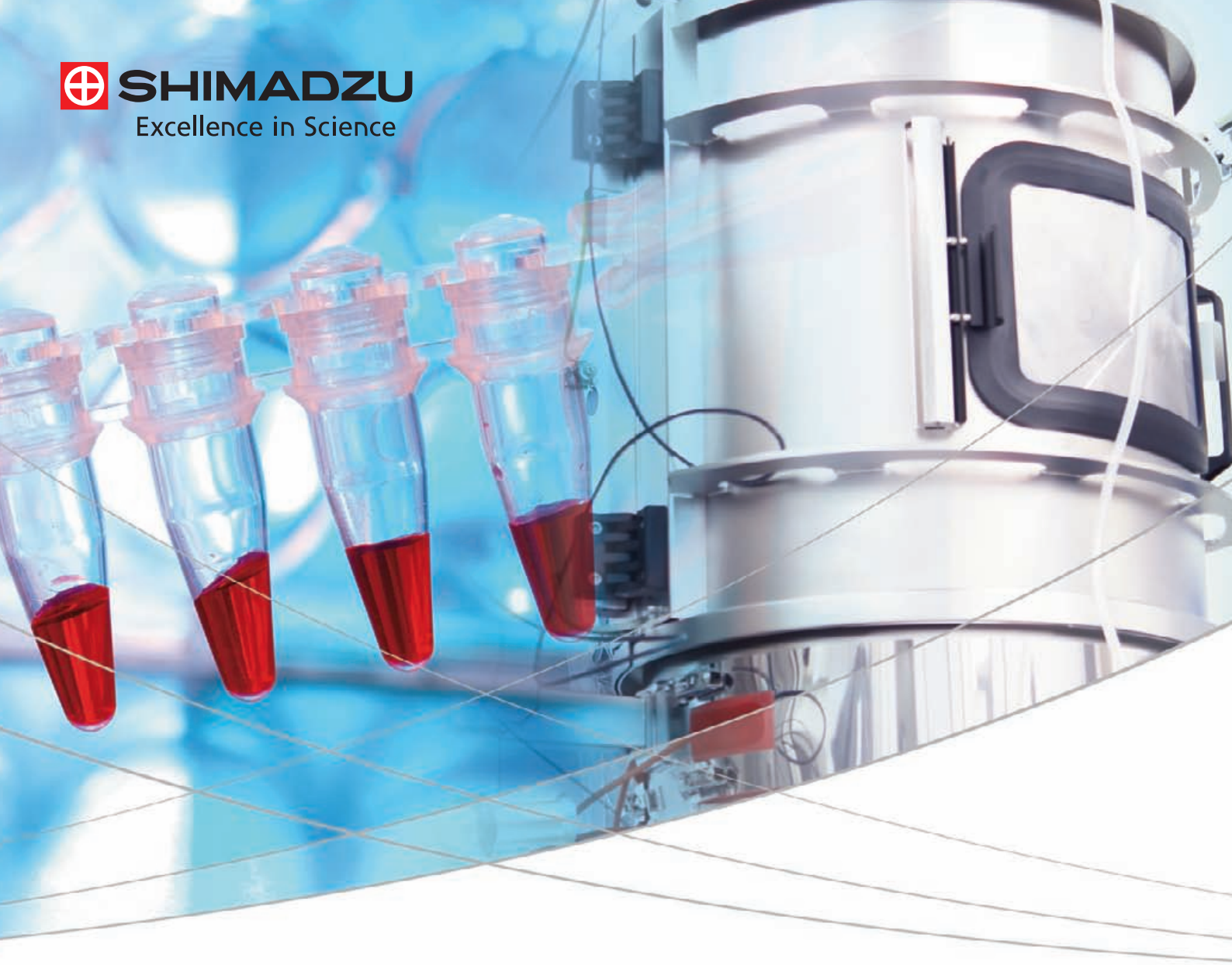
The AMR threat
Fighting the ever-growing peril of antimicrobial resistance

Bioeconomy
Biotech strategies for establishing a post-fossil hydrogen economy

CROs & CDMOs
How COVID-19 is triggering pharma outsourcing growth

BIOCOM

SHIMADZU
Excellence in Science



Don´t prepare. Just be ready.

C2MAP-2000 – 1 method, 17 mins, 95 media components

The new C2MAP-2000 automates all steps from pretreatment to measurement without any human intervention. It simplifies the workflow for optimizing cell culture conditions. There is no need to prepare. Just be ready.

Complete LCMS solution for cell culture analysis
combining the C2MAP-2000 pretreatment module with ultra-fast LCMS-8060

Highly efficient
through cutting culture media analysis time by 80 percent

Monitoring of up to 95 components
including amino acids, metabolites, sugars, vitamins and organic acids

Changes at a glance
with C2MAP-TRENDS viewer software visualizing temporal changes of components

C2MAP-2000 – Complete LCMS solution

www.shimadzu.eu/c2map

AMR – the silent pandemic that can still be contained

MARC GITZINGER Marc Gitzinger is Chief Executive Officer and co-founder of BioVersys. He has over 10 years of experience in the biotech industry, having launched a university spin-off in the field of antimicrobial resistance and growing it into a multi-asset early clinical stage company. He is also vice-president of the board of the BEAM Alliance, a European association representing over 70 European and international SMEs active in antimicrobial research and development.

The COVID-19 pandemic is having a devastating effect on global health and an unprecedented impact on the economy. As the world struggles with the challenges brought on by this pandemic, the threat of the next one is already looming in the form of AMR. AMR is already responsible for an estimated 750,000 deaths worldwide on an annual basis and is predicted to cause 10 million deaths by 2050.

Many of the reports that analysed the AMR crisis gave policy guidance on how to prevent AMR from becoming a global phenomenon. One pillar in this guidance was to increase grant funding (Push) for SMEs. This Push funding has resulted in a solid early-stage pipeline of novel approaches combatting AMR. The newest addition to the Push funding is the US$ 1bn AMR Action Fund that was created by over 20 of the largest pharma companies.

The successes of the Push funding notwithstanding, the fundamental problem of the broken economics of the global market for antibiotics remains. If this is not resolved, the billions invested in Push funding will go to waste as none of these innovative drugs will ever reach patients.

Rightly so, valuable life-saving antibiotics are reserved for last resort purposes. However, pricing and reimbursement policies are still configured globally as if novel antibiotics would still be high volume products. This deliberate misalignment between years of R&D involving billions of investments and commercial non-viability is what prevents newly approved antibiotics from reaching patients in dire need.

This is evidenced by four of the most recently FDA-approved antibiotics consciously not being commercialised in Europe as they will never be profitable. This deprives European citizens of the newest life-saving antibiotics. The global lack of urgent political will to address this is scandalous. The UK and Sweden are two positive exceptions testing novel reimbursement mechanisms.

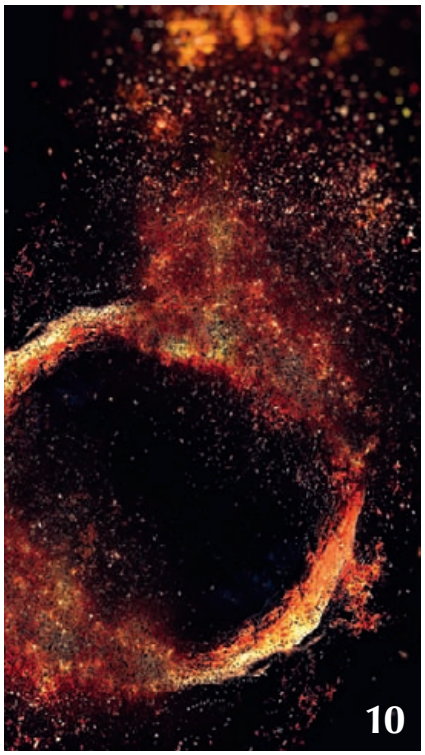
A recent Call to Action that was published by the BEAM Alliance, supported by a global alliance of stakeholders in AMR, calls for immediate action by the European Commission, Parliament and member states to implement a new Pull incentive framework as part of the upcoming EU Pharmaceutical Strategy.

The underlying effort that is needed by the G20 countries and in particular by the EU is to create a marketplace that ensures a collective global Pull incentive over a time period of 10 years of $3-4 billion for a novel antibiotic that saves lives and addresses a high unmet medical need caused by resistant infections. This is a small price to pay compared to the predictions highlighting an economic burden of $100 trillion globally by 2050. ■

Picture: BioVersys AG

FREE EXCERPT

COVER STORY



Some like it hot

Since the first approval of a checkpoint blocker in 2011, immune therapy has revolutionised cancer treatment. However, most tumours are still able to evade the immune response by creating an immunosuppressive tumour microenvironment that blocks full activation of dormant T killer cells. A new generation of targeted cytokines is now on the cusp of helping us overcome that problem. The field looks set to change the treatment landscape in oncology in dramatic ways, and is providing new hope to those who contract cancers that are currently difficult or impossible to treat effectively.

INSIGHT EUROPE

ECONOMY

REGIONAL NEWS

SCIENCE & TECHNOLOGY

SERVICE

IMPRINT European Biotechnology (ISSN 2364-2351) is published quarterly by: BIOCOM AG, Lützowstr. 33–36, D-10785 Berlin, Germany, Tel.: +49-30-264921-0, Fax: +49-30-264921-11, Email: service@european-biotechnology.com, Internet: www.european-biotechnology.com; Publisher: Andreas Mietzsch; Editorial Team: Thomas Gabrielczyk (Editor in Chief), Derrick Williams (Co-editor), Sandra Wirsching, Nicolas Goffette; Advertising: Oliver Schnell, +49-30-2649-2145, Christian Böhm, +49-30-2649-2149, Andreas Macht, +49-30-2649-2154; Distribution: Lukas Bannert, +49-30-2649-2148; Graphic Design: Michaela Reblin; Production editor: Benjamin Röbig; Printed at: Königsdruck, Berlin; European Biotechnology Life Sciences & Industry Magazine is only regularly available through subscription at BIOCOM AG. Annual subscription BIOCOM CARD Europe: €80 for private individuals (students €40) incl. VAT, €120 plus VAT for corporates. Prices includes postage & packaging. Ordered subscriptions can be cancelled within two weeks directly at BIOCOM AG. The subscription is initially valid for one year. Subscriptions will be renewed automatically for one more year, respectively, unless they are cancelled at least six weeks before the date of expiry. Failures of delivery, which BIOCOM AG is not responsible for, do not entitle the subscriber to delivery or reimbursement of pre-paid fees. Seat of court is Berlin, Germany. As regards contents: individually named articles are published within the sole responsibility of their respective authors. All material published is protected by copyright. No article or part thereof may be reproduced in any way or processed, copied and proliferated by electronic means without the prior written consent of the publisher. Cover Photo: k_yu/stock.adobe.com; Supplement: Sino Biological Europe GmbH; ® BIOCOM is a registered trademark of BIOCOM AG, Berlin, Germany.

Picture: k_yu/stock.adobe.com

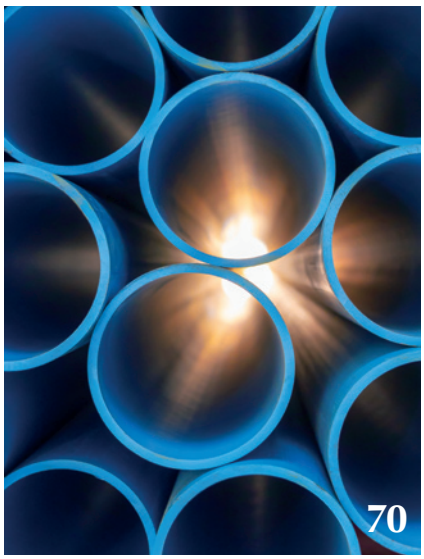
FREE EXCERPT

ANTIMICROBIAL RESISTANCE

EU needs strategies

During this year's five-day digital AMR Conference, stakeholders said that unless incentives to improve market conditions aren't instituted in Europe soon, more innovators in the space might have trouble just surviving, much less providing desperately needed novel antibiotics and diagnostics. Discussions on how to change this are ongoing.

DATA MANAGEMENT



A hydrogen economy

As part of its Green Deal climate protection programme, the European Commission is for the first time focusing on hydrogen as a wide-scale future energy source. The plan is to have the climate-neutral gas produced primarily via electrolysis. But biotechnological processes also offer sustainable alternatives. What opportunities do biotech solutions provide?

FOCUS

CROs & CMOs

EDITORIAL

Plan B

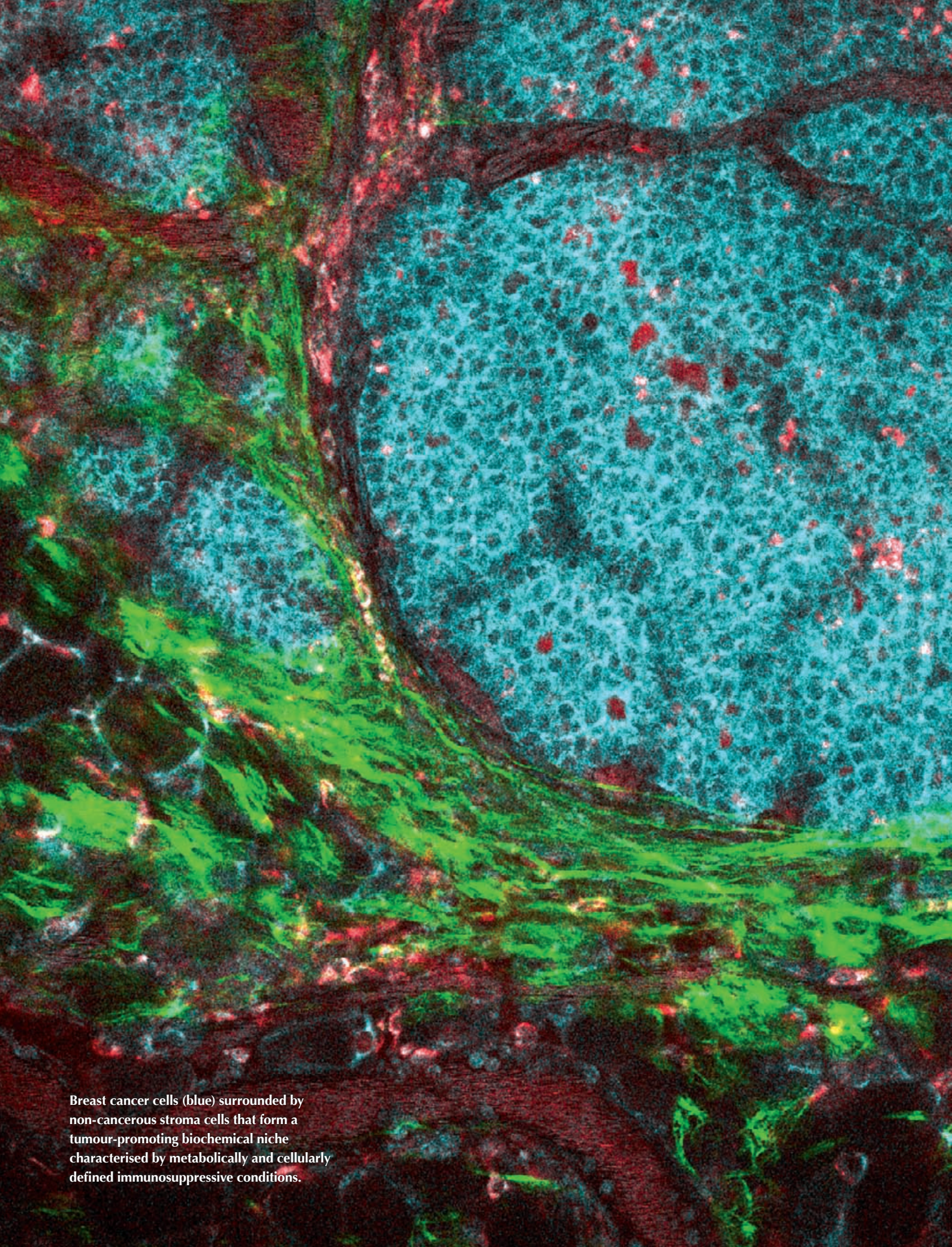
In mid-September, the head of the Indian Serum Institute Adar Poonawalla tweeted a prediction targeting the COVID-19 vaccine nationalism of rich nations unleashed by US President Donald Trump. If the current pre-production of pandemic vaccines were to continue, said the head of the world's largest vaccine supplier, then large parts of the world's population should not be expected to be vaccinated before the end of 2024.

What does that mean? A return to a halfway-open economy only appears possible if G20 countries establish therapeutics as an additional pillar alongside social distancing and vaccination. Until we can protect the uninfected with a vaccine, people will die, and we have to try to treat them. The EU's huge investment of more than US$10bn in COVID-19 jab preorders (see p. 22) ignores the fact that in the past, just 6% of vaccine projects have succeeded. Additionally, even if we have a vaccine that protects 60% of the elderly against infection with SARS-CoV-2, we still face potentially 20 million deaths due to the disease.

While the US-BARDA has set up a funding mechanism for adaptive Phase II/III trials called "ACTIVE" of monoclonal antibodies that can be used to fight viremia, as well as for passive vaccination of the immunocompromised, the EU has yet to do the same. A Plan B is urgently needed if efforts to find an effective COVID-19 vaccine fail.

Thomas Gabrielczyk
Editor-in-Chief

Pictures: noppadon/stock.adobe.com (top), iLexx/istockphoto.com (left), HartmutBösener, IDT Biologika GmbH (bottom left), BIOCOM AG (bottom right)



Breast cancer cells (blue) surrounded by non-cancerous stroma cells that form a tumour-promoting biochemical niche characterised by metabolically and cellularly defined immunosuppressive conditions.

FREE EXCERPT

Some like it hot

CANCER Since the first approval of a checkpoint blocker in 2011, immune therapy has revolutionised cancer treatment. However, most tumours evade the T cell attack triggered by PD-1/PD-L1 blockers by creating an immunosuppressive tumour microenvironment that blocks full activation of dormant T killer cells in the tumour, along with infiltration. A second generation of targeted cytokines now herald a turnaround. By activating tumour-restricted IL-2 signalling without its side effects, they promise to overcome tumour escape tactics. Can they change the mostly non-inflamed tumour phenotype to hot?

Even when Sanofi's R&D Chief John Reed headed Roche's pRED department, he believed that a more targeted and side-effect free use of the immune messenger interleukin-2 (IL-2) could help to significantly increase the number of cancer patients responding to immune checkpoint blockers. As early as the 1990s, when Chiron/Novartis' recombinant IL-2 aldesleukin received FDA approval in kidney cancer, it was known that the short-lived, pro-inflammatory cytokine amplified anti-tumour immunity, both in the tumour itself and in the surrounding immunosuppressive tumour stroma. But its serious side effects – including vascular leakage syndrome – and concurrent activation of immunosuppressive regulatory T cells (Tregs) through binding to the IL-2-receptor α (CD25) subunit prevented its wider application.

"Cytokines are emerging as a fundamental backbone in immuno-oncology"

"We set out to answer how we could engineer cytokines to better use their powerful immune-stimulating properties while minimising their known side effects," recalls Pablo Umaña, Head of Roche's Cancer Immunotherapy Discovery in Schlieren. Protein engineers under Christian Klein developed an IL-2 version (IL-2v) at Roche pRED that can't bind to IL-2Rα, and fused it to a monoclonal antibody that specifically homed in on fibroblast activation protein-α (FAP) – a tumour protein not found on healthy cells. The resulting immunocytokine (RO6874281) is currently being tested in a Phase II basket trial in combination with Roche's PD-L1 antagonist atezolizumab (Tecentriq®) against a range of solid tumours.

John Reed, MD, PhD
Global Head of Research & Development, Sanofi

? What does Sanofi's US$2.5bn takeover of Synthorx mean for cancer immune therapy?

! *Synthorx's exceptionally novel discovery platform has already produced a molecule that has the potential to become a foundation of the next generation of immuno-oncology combination therapies. By selectively expanding the numbers of effector T cells and natural killer cells in the body, THOR-707 can be combined with our current oncology medicines and our emerging pipeline of immuno-modulatory agents for treating cancer.*

In February 2020, two years after Reed left Roche, his new company acquired a programme with the same goal. Closing a US$2.5bn takeover of US company Synthorx Therapeutics Inc., Sanofi added Phase I/II lead asset THOR-707 (SAR444245) to its pipeline, and set out to test it alone and in combination with several checkpoint blockers. THOR-707 uses a base bair of synthetic amino acids built into the IL-2 DNA sequence to attach a polyethylene glycol (PEG) molecule to IL-2 that sterically shields it from binding to IL-2Rα, stopping the unwanted Treg effect while boosting the immunostimulatory cytokine effect.

Huge market potential

Besides pharma majors Roche and Sanofi, seven biotech companies and many other academic groups in the EU and the US are seeking to boost the immunostimulatory effect of IL-2 in the tumour microenvironment through binding the cytokine to IL-2Rβγ and decreasing binding to IL-2Rα (see table, p. 18).

Most advanced is Nektar Therapeutics' bempegaldesleukin (NKTR-214), in Phase III testing in combination with Bristol Myers Squibb's PD-1 blocker nivolumab against renal cell carcinoma and malignant melanoma. The recombinant […]

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

Pictures: NCI (left), Sanofi (right)

Methicillin-resistant Staphylococcus aureus (MRSA) is a bacterium responsible for several difficult-to-treat infections in humans

FREE EXCERPT

Calls for Europe to take a leading role

ANTIMICROBIAL RESISTANCE During this year's five-day digital AMR Conference, around 450 international experts once again discussed how to ramp up the fight against antimicrobial resistance. Stakeholders said that unless incentives to improve market conditions aren't instituted in Europe soon, more innovators in the space might have trouble just surviving, much less providing desperately needed novel antibiotics and diagnostics. However, the event also highlighted a range of new initiatives, and showed that some progress has been made this year by companies, regulatory agencies and investors.

During the virtual closing session of the 4th Antimicrobial AMR conference at the end of August, Renu Swarup from the Indian Ministry of Research hit the nail on the head when she emphasised that "resistance is global, and we will only get a grip on it in the long-term." Representing a country that is currently being hit badly by the COVID-19 pandemic, she also underlined the need for global cooperation and a growing role for developing countries: "The COVID-19 crisis shows us that we can build structures together and join forces globally. This is the way we should also fight antibiotic resistance."

We must prepare now so that the slow crisis does not hit us with even greater force than COVID-19.

The Indian government representative was among the 120+ speakers who provided insights during more than 20 sessions. The event drew representatives from a wide range of areas – from medium-sized companies in biotech or diagnostics, Big Pharma, diagnostics corporations, clinicians, human and veterinary medicine experts. But whether investor or scientist, the high-level panels and expert sessions proved an effective way to bring together major international players in the AMR space. For most of the infection research experts, one thing was clear: while COVID-19 is putting health systems under acute stress, the three-quarters of a million deaths caused annually by antimicrobial resistance is a slow pandemic in its own right – just one that doesn't draw the same headlines. "We must prepare now so that the slow and creeping crisis does not hit us with even greater force," emphasised Manica Balasegaram, director of the multi-government-backed global organisation GARDP. Rafael Cantón, the head of clinical microbiology at the Ramón y Cajal University Hospital in Madrid, mentioned that bacterial infections are growing increasingly common as secondary complications in severe cases of COVID-19, and that both pandemics are already closely linked in the clinical context. Stefanie Deinhardt-Emmer, a diagnostics expert from the Institute for Medical Microbiology at Jena University Hospital in Germany, added that "fast and valid diagnostics will play a decisive role in the fight against COVID-19 and the accompanying bacterial infections in the coming winter."

However, one of most important top […]

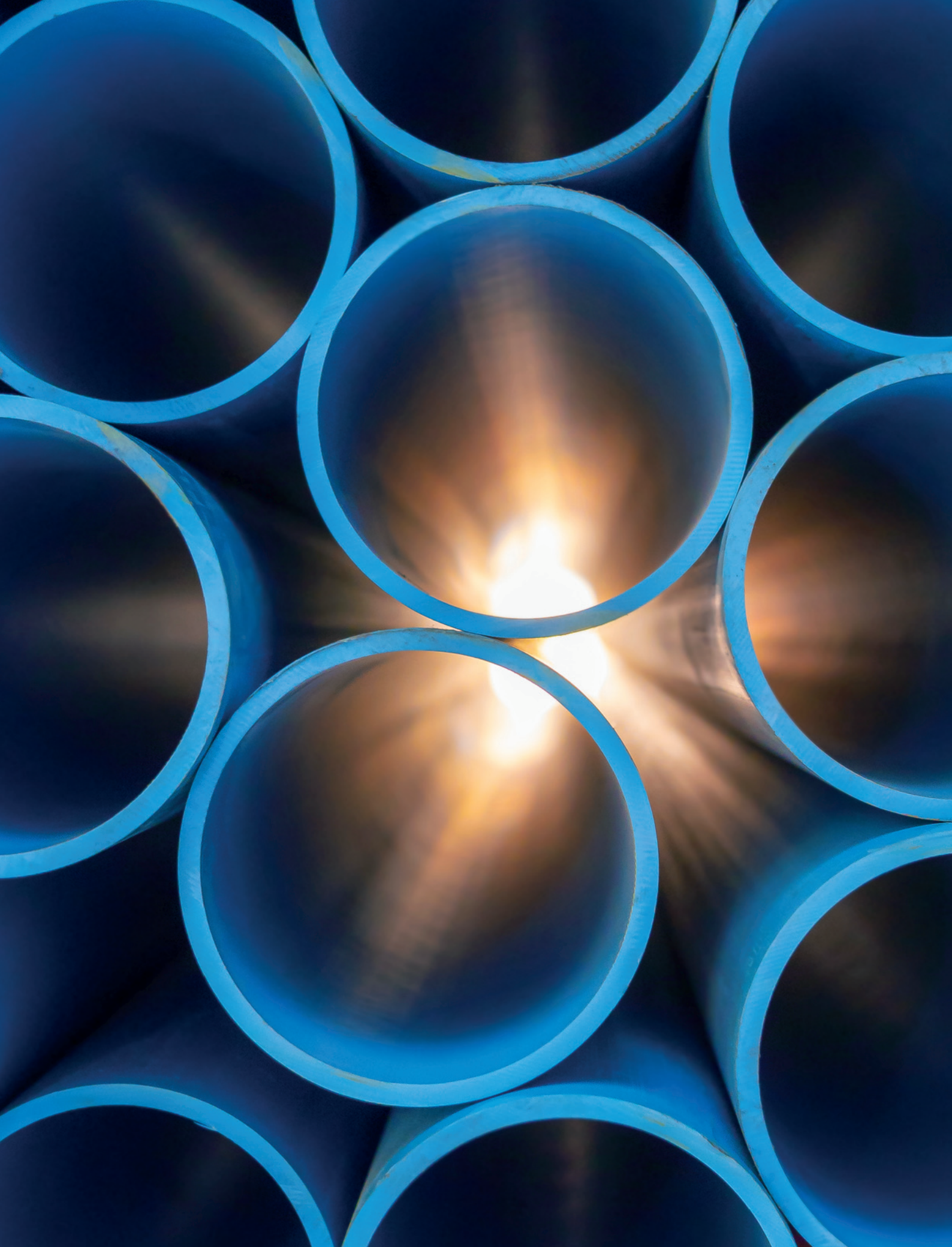
Manica Balasegaram
Executive Director, Global Antibiotic Research and Development Partnership (GARDP)

? What global health comparisons can you draw between the AMR crisis and COVID-19?

! *"While COVID-19 puts the health system to an acute stress test in which ad-hoc solutions must be found, antibiotic resistance with around 750,000 deaths annually is a creeping, slow pandemic crisis that has long been there – but doesn't get the same attention."*

›› Read the full story in the printed issue.

Pictures: iLexx/istockphoto.com (left), GARDP (right)



FREE EXCERPT

Biotech weighs in on hydrogen debate

SUSTAINABLE ENERGY As part of its Green Deal climate protection programme, the European Commission is for the first time focusing on hydrogen as a wide-scale future energy source. The plan is to have the climate-neutral gas produced primarily via electrolysis. But biotechnological processes also offer sustainable alternatives. What opportunities do biotech solutions provide?

Back in July, Commission Executive VP Frans Timmermans, who is in charge of the Green Deal, said the new hydrogen economy could be a growth engine for overcoming the economic damage caused by COVID-19: "In developing and deploying a clean hydrogen value chain, Europe will become a global front-runner and retain its leadership in cleantech." According to the most ambitious version of the EC's 'Hydrogen Roadmap', which lays the foundation for achieving a sustainable pathway for Europe's energy transition, hydrogen could meet nearly a quarter of the bloc's total energy demand by 2050. Forecasts say the fuel and associated equipment sales could generate €130bn for EU companies by 2030, and hit €820bn by 2050. The long-term vision would put the EU on a path to reducing about 560 million metric tonnes of CO_2 – around half the required abatements needed to achieve the under-2°C scenario laid out in the Paris Agreement.

A hydrogen-powered world

Hydrogen has often been called the clean fuel of the future, but industrial production has not yet ramped up enough to have a real impact in environmental terms. To meet its objectives, the EC has said it intends to continue to rely on electrolysis – the electrochemical process that splits water into hydrogen and oxygen. But because it consumes large amounts of electricity and water, the technology historically has been far more competitive price-wise when run on fossil-based rather than renewable and low-carbon systems. To scale up to meet future hydrogen needs, the Commission is promoting solar and wind power sources for the generation of so-called 'Green Hydrogen', but has also come out in support of low-carbon technologies that are still fossil-based ('Blue Hydrogen').

> Converting solar energy into hydrogen for storage is especially promising

Bridging the gap between the costs of hydrogen technologies and their lowest cost low-carbon alternatives would necessitate a €70bn investment by 2030. "An ambitious vision for hydrogen's role in the future of energy is far from automatic," the Hydrogen Council says, "and requires investment above and beyond current commitments." While welcoming the focus on renewable hydrogen, the European Environmental Bureau (EEB) warned it could prove a double-edged sword. "Investing in fossil-based hydrogen, the production of which is already available on an industrial scale, risks making truly clean and fossil-free hydrogen uncompetitive for the EU market and creating stranded assets," says Barbara Mariani, the EEB's Senior Policy Officer for Climate and Energy. "It's a costly gamble that Europe cannot afford and could easily avoid." Requesting a clear timeline for a halt to investment in fossil fuel use, infrastructure and technology, she also added that "EU leaders must gear up for a complete phase-out of fossil gas by 2035, in line with the goal of limiting global warming to 1.5°C. This is not going to happen if we invest in false solutions such as fossil-based hydrogen and carbon capture technology, which together would create the perfect storm for deepening Europe's dependence on fossil fuels."

Hydrogen made by biotech

Against that political backdrop, some promising biotech-based processes that produce hydrogen are also in pipelines at European academic institutions.

"Converting solar energy directly into hydrogen for storage is particularly promising," says Dr Kirstin Gutekunst. The head of the 'Bioenergetics in Photoautotrophs' research group at Kiel University's Botanical Institute says that pathway "creates no CO_2, and the efficiency is very high due to the direct […]

›› Read the full story in the printed issue.

Pictures: noppadon/stock.adobe.com (left), ECDC (right)

FREE EXCERPT

SWISS BIOTECH™

Save the date!

SWISS BIOTECH DAY 2021

20 April 2021
Congress Center Basel

The Swiss Biotech Day has become the leading biotechnology conference in Switzerland and is a fixed date in the community's calendar. While the event could not take place this year due to the worldwide COVID-19 pandemic, we will bring the Swiss Biotech Day back on stage on 20 April 2021.

What you can expect in 2021:

- Meet senior experts from the life science industry from across Europe
- Exhibition throughout the day
- Delegations from various countries
- Presentation of the Swiss Biotech Report
- Swiss Biotech Success Stories Awards
- Innovative biotech start-ups and medium-sized biotech companies
- Thematically focused panel discussions
- Pre-scheduled one-to-one partnering meetings

Of course, we will adhere to all applicable hygiene and safety regulations on site to enable a safe and successful event for everyone.

Mark your calendar for the upcoming face-to-face event on 20 April 2021.

Sign in on our website at **www.swissbiotechday.ch** and stay updated on any news.

Media partners:

transkript

European Biotechnology
Life Sciences and Industry Magazine

LABORWELT

Organized by:

Swiss Biotech Association

BIOCOM®

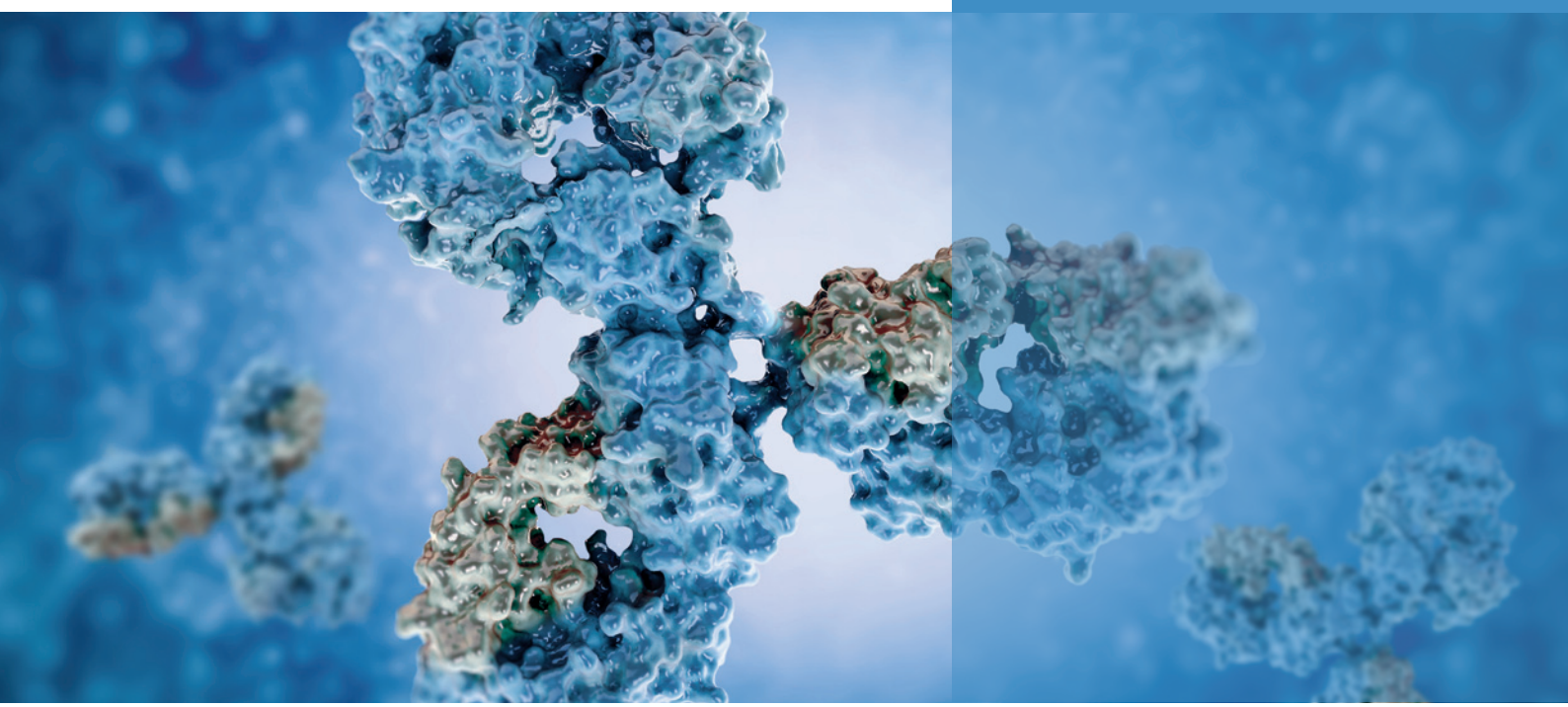
polpharma biologics

INTEGRATED BIOLOGICS DEVELOPMENT TO SUPPORT YOU FROM DISCOVERY TO COMMERCIAL SUPPLY

We have now integrated our Dutch based subsidiary, Bioceros, fully into Polpharma Biologics, enabling us to offer the complete spectrum of services from discovery to commercial supply.

The change means Polpharma Biologics can now additionally offer the development of high quality and high yield cell lines through our proprietary platform CHO$^{BC®}$, as well as comprehensive discovery, process development and analytical capabilities for the development of novel biologics and biosimilar.

- Antibody Discovery
- Antibody Optimization
- Cell Line Development
- Analytical Development and Characterization (USP and DSP)
- Formulation Development
- Process Scale-up
- Clinical DS and DP Manufacturing
- Process Validation and Commerical DS Manufacturing
- Fill & Finish (vial, PFS, cartridges, liquid and lyophized formulations)



www.polpharmabiologics.com