MARCH / APRIL 2023 # 90

the Medicine Maker®

alcami | Masy BioServices an Alcami company

NAVIGATING THE

COLD CHAIN

WITH ALCAMI & MASY BIOSERVICES

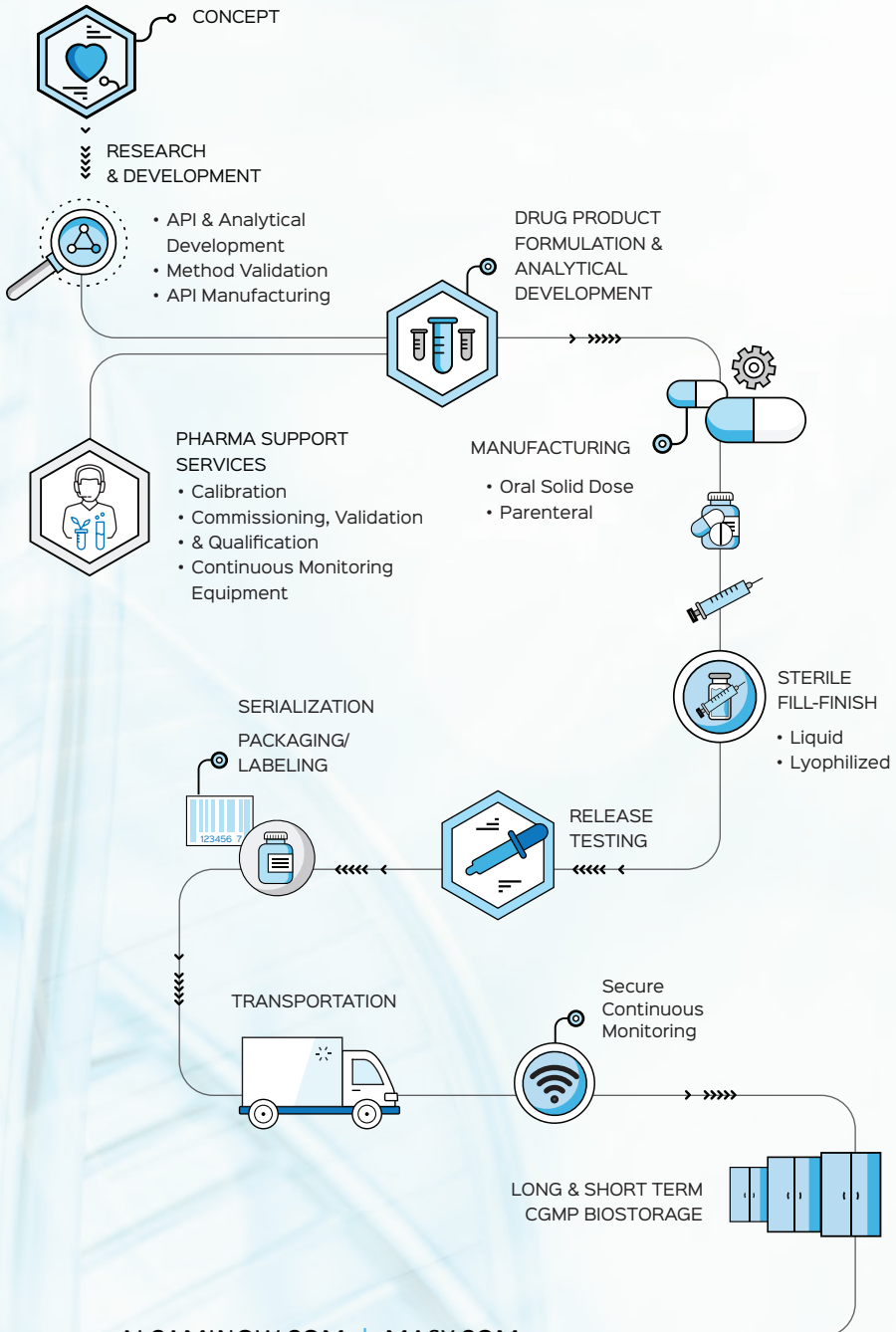
Ensure the quality and stability of your product at every point along the cold chain with expert solutions and services from Alcami and Masy Bioservices. Together we proudly offer world class contract development, manufacturing and analytical services, and a comprehensive suite of customizable and innovative pharma support solutions to advance your product through every stage of the development lifecycle.

ANALYTICAL SERVICES

DRUG PRODUCT DEVELOPMENT & MANUFACTURING

CGMP BIOSTORAGE

PHARMA SUPPORT SERVICES



ALCAMINOW.COM | MASY.COM

Let the Insulin Price Wars Begin

Eli Lilly, Novo Nordisk, and Sanofi all agree to lower insulin prices

There has been mounting anger amongst US patients for some time regarding the price of insulin. In an extreme example from 2022, some uninsured patients in the US were apparently paying over $1000 per month for insulin.

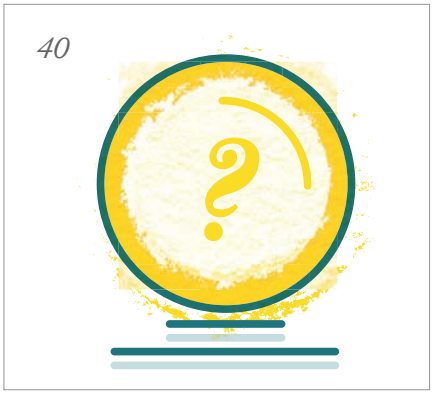
Political pressure had also been mounting for some time and the Inflation Reduction Act was passed in the US in 2022 to cap the price of insulin at $35 for Medicare patients. Efforts to introduce the insulin price cap in the private healthcare market were blocked, but insulin maker Eli Lilly appears to have "read the room." In March, Lilly dropped the price of its most commonly prescribed insulins by 70 percent in the US and expanded a program to immediately cap patient out-of-pocket costs at $35 per month. Its unbranded insulin lispro injection was priced at $25 per vial – which is less than the price of a Humalog vial in 1999. The price of Humalog will also be reduced by 70 percent in Q4 of 2023. Since Lilly's announcement, Sanofi and Novo Nordisk have announced their own price reductions.

It's also worth noting that Civica Rx – which has been shaking up the generic drug market with a nonprofit model – had its eyes on low-cost insulin before the Inflation Reduction Act. The company announced plans in March 2022 to manufacture and distribute insulins at significantly lower prices than competitors, which could have acted as a warning shot to major insulin makers. In March 2023, Civica Rx signed an agreement with California's CalRx Biosimilar Initiative to produce insulin that will be priced at no more than $30 a vial and $55 for a box of five pre-filled pens.

The price reductions are fantastic news for patients. Though it's true that the pharma industry needs huge revenues to survive, the high prices of insulin have been difficult to justify. Famously, the scientists who discovered and purified insulin (Frederick Banting, Charles Best, JJR Macleod, and James Collip) sold their patents to the University of Toronto for $1. At the time, Banting said, "Insulin does not belong to me, it belongs to the world."

Stephanie Sutton
Editor

Contents



On The Cover

Celebrating top hitters in the pharma industry, from individuals to companies

Core Topics

Business

NextGen

Sitting Down With

the Medicine Maker

ISSUE 90 - MARCH / APRIL 2023

Feel free to contact any one of us:
first.lastname@texerepublishing.com

Content Team
Group Editor - Stephanie Sutton
Rob Coker (Deputy Editor)
Jamie Irvine (Associate Editor)

Commercial Team
Head of Sales / Publisher - Helen Conyngham
Stacy Gaines (Business Development Manager, North America)
Chris Connolly (Business Development Manager)

Design Team
Marc Bird (Creative Director)
Hannah Ennis (Senior Designer - Commercial)

Digital Team
Head of Digital Operations – Brice Agamemnon
Digital Team Lead - David Roberts
Jody Fryett (Salesforce & Audience Sytems Manager)
Peter Bartley (Senior Digital Producer)
Jamie Hall (Audience Insights Analyst)
Shea Hennessey (Digital Producer)
Oliver Norbury (Digital Producer)
Seamus Stafford (Digital Producer)

CRM & Compliance
CRM & Compliance Manager - Tracey Nicholls

Commercial Services
Commercial Service and Social Media Manager - Matt Everett
Lindsey Vickers (Sales Support Manager)
Hayley Atiz (Sales Support Coordinator)
Julie Wheeler (Sales Support Coordinator)
Emily Scragg (Sales Support Coordinator)
Anna Harbottle (Video Producer)
Sophie Hall (Social Media Executive)

Marketing Team
Marketing Manager - Katy Pearson
Lauren Williams (Marketing Executive)
Charlotte Shaw (Marketing Executive)

Accounts Team
Kerri Benson (Assistant Accountant)

Human Resources
Human Resource Manager - Tara Higby

Management Team
Chief Executive Officer - Andy Davies
Chief Operating Officer - Tracey Peers
Senior Vice President (North America) - Fedra Pavlou
Financial Director - Phil Dale
Chief Commercial Officer - Richard Hodson
Content Director - Rich Whitworth
Creative Director - Marc Bird

Change of address info@themedicinemaker.com
Tracey Nicholls, The Medicine Maker, Texere Publishing Limited, Booths Park 1, Chelford Road, Knutsford, Cheshire, WA16 8GS, UK

General enquiries
www.texerepublishing.com | info@themedicinemaker.com
+44 (0) 1565 745 200 | sales@themedicinemaker.com

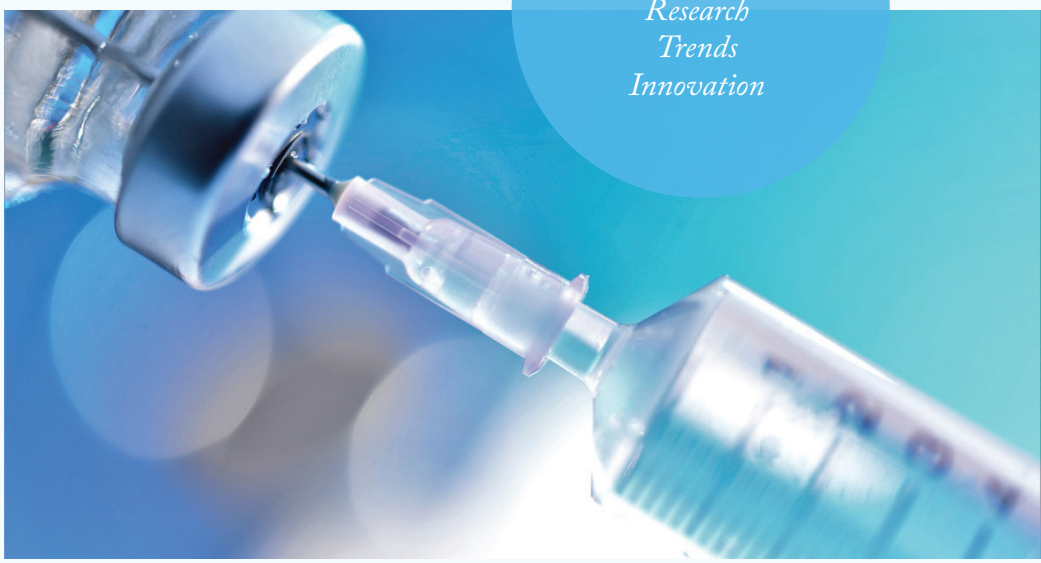
Distribution: The Medicine Maker (ISSN 2055-8201), is published bi-monthly by Texere Publishing Limited, Booths Park 1, Chelford Road, Knutsford, Cheshire, WA16 8GS, UK. Single copy sales £15 (plus postage, cost available on request info@themedicinemaker.com). Non-qualified annual subscription cost is £110 plus postage

Upfront

Research
Trends
Innovation

The Grand Winner

Which Innovation Award technology did readers select as our Grand Winner?



The wait is over. Voting for The Medicine Maker Innovation Awards has ended and we are delighted to announce our grand winner: Lubrizol Life Science Health's Apisolex Polymer.

This innovation is an injectable-grade excipient that can help enhance the solubility of BCS class II and IV APIs by around 50,000 fold. It is designed to work with simple formulation techniques, with a view to streamlining manufacturing and minimizing API loss with a high encapsulation rate. According to Lubrizol, the solubilizing excipient and API can be mixed in an aqueous-based solution followed by sterile filtration and lyophilization. The approach forms micellar structures that encapsulate the API during lyophilization, and the resulting formulation is stable and can be readily resuspended in common diluents for administration. In saline, the lyophilized drug product reconstitutes in less than 30 seconds.

You can look forward to finding out more about this technology in a future issue of The Medicine Maker.

Joey Glassco, Global Market Manager at Lubrizol Life Science, Health, said, "We are honored for Apisolex solubilizing excipient to be recognized by readers of The Medicine Maker for this prestigious innovation award. My hope is that winning this award will allow drug formulators struggling with water-insoluble APIs to learn about the polymer's benefits so that more life-changing medications can make it to market."

The Innovation Awards annually showcase new drug development and manufacturing technology that has hit the market. In 2022, we received a record number of nominations for new technologies. The top 12 was published in December 2022, but to decide our grand winner, we asked readers and visitors to The Medicine Maker website to vote for their favorite technology.

Honorable mentions go out to Terumo Blood and Cell Technologies Quantum Flex Cell Expansion System and Thermo Fisher Scientific's Direct Mass Technology Mode.

Nominations for the 2023 Innovation Awards will open soon. Keep your eyes peeled: www.themedicinemaker.com.

Pediatric Poisoning

Statistics show increase in child deaths from OTC and opioid drugs

The Children's Hospital of Philadelphia (CHOP) has released a report on the rising number of opioid-related deaths among children in the US. The research team, led by Christopher E. Gaw, analyzed data from the CDC's National Vital Statistics System and found the percentage of opioid poisonings leading to fatalities among children aged five and below had surged from 24.1 percent in 2005 to 52.2 percent in 2018 (1). The authors also noted that over-the-counter medications for pain, colds, and allergies were the second most common substances contributing to child poisoning deaths. Around one-third of children who died from poisoning were supervised by someone other than a biological parent.

The trend highlights the pressing need for comprehensive and targeted prevention measures to shield young children from opioids and other potentially harmful drugs.

Reference

1. *CE Gaw et al., Pediatrics (2023). DOI:10.1542/peds.2022-059016*

IMAGE OF THE MONTH

Microgravity Medicine

MicroAge II, led by the University of Liverpool, receives £1.4 million funding for the second part of its project investigating how the microgravity environment makes astronauts' muscles weaken in space in an accelerated way to how muscles get weaker as we age on Earth.

Would you like your photo featured in Image of the Month?
Send it to rob.coker@texerepublishing.com

QUOTE of the month

"Beauty is not just in fine arts or in music; it is everywhere in science. The intensity and guttural emotions of an artist should not be any different from those of a scientist. The patterns, the freedom of creativity, the process, the deductions leading to a great scientific journey are extremely beautiful and one must appreciate it."

Tirtha Chakraborty. See page 18

Pfizer's ADC Bet

Pfizer pays $43 billion to acquire Seagen and bolster its oncology pipeline

According to Pfizer, its recent acquisition of US biotech company Seagen could help accelerate breakthroughs in cancer through the development of antibody drug conjugates (ADCs). Pfizer will pay $229 per share and expects Seagen to contribute more than $10 billion in risk-adjusted revenues in 2030.

This strategic move gives Pfizer access to Seagen's four approved cancer therapies, as well as a promising array of ADCs in development that enable more precise targeting of tumors. The currently approved therapies are also being investigated for new indications in clinical trials. In a statement, Pfizer said, "Oncology continues to be the largest growth driver in global medicine, and this acquisition will enhance Pfizer's position in this important space and contribute meaningfully to the achievement of Pfizer's near- and long-term financial goals."

The transaction is expected to be finalized in late 2023 or early 2024.

When Outsourcing Goes Wrong

We ask Dean McAlister, Executive Vice President of Inizio Biotech, for his top tips for a good partnership

Sometimes outsourcing partnerships go wrong. What are the warning signs?

Major factors in an unsuccessful partnership include poor communication, a lack of therapeutic area expertise, quality issues, lack of local and cultural insights for new market expansions, and significant budget overruns.

If left unchecked, these issues can result in an unsuccessful launch.

Recognizing red flags early on can help companies take corrective action at pivotal points to prevent the partnership from going wrong. If these concerns persist after actions have been taken, terminating the partnership and finding a new partner that can better meet the company's needs may be necessary.

Finding the right partnership requires robust due diligence. Companies should carefully evaluate potential partners to ensure they have the necessary skills, culture, experience in their therapeutic area, and resources to meet their needs and ultimately maximize the value of their assets.

And what separates a good outsourcing partner from a bad one?

A good commercialization partner needs to bridge scientific knowledge and commercial understanding – and have the technical expertise their partner needs to deliver. Clear communication, reliability, and flexibility, while also being a cultural fit with their partners, are also a must. They should work with their partners to offer transparent and cost-effective pricing structures, but they should also be willing to negotiate terms to ensure a mutually beneficial relationship.

Overall, a good partner should be a reliable and responsive extension of their partner's team.

What are your top tips for ensuring a smooth relationship?

First, select your strategic partner as early as possible in your emerging biotech journey. When realistic expectations are set early on, and both parties remain transparent in their communications as the project progresses, they are able to effectively build trust and respect on their shared mission

to deliver life-saving therapies to patients. Ultimately, this alignment will help ensure the successful completion of the project.

Looking at the big picture – what are the major trends in outsourcing?

Right now, we're seeing significant demand for support across development projects treating age-related illnesses, chronic diseases, cancers, and other rare conditions. Cell and gene therapy is an area where we're seeing a notable uptick, with thousands of therapies in various stages of development.

In the biopharma industry as a whole, a key driver of growth is the rise of small start-ups and scale-ups, with more and more drug approvals coming from emerging biotechs.

Calling All Young Professionals

AstraZeneca launches its 2023 global R&D postdoctoral challenge

AstraZeneca's annual initiative challenges aspiring scientists across the world to devise research projects focused on innovative and practical solutions to current healthcare problems. Submissions that "push the boundaries of science in [AstraZeneca's] focus areas of cardiovascular, renal & metabolic diseases, respiratory & immunology, common infectious & rare diseases" are likely to do well. But the company is also interested in technologies that can improve development of novel therapeutics. Applicants must be in their final year of graduate studies (MD and/or PhD) or working as a postdoctoral researcher within three years of receiving their advanced postgraduate degree by December 31, 2023. Following rigorous evaluation on scientific merit, originality, and societal impact, the selected winners will be awarded a fully funded two-year postdoc research position with AstraZeneca.

The submission deadline is June 30, 2023; shortlisted applicants will have the chance to pitch their research ideas to a panel in September 2023. For further information, visit bit.ly/astrazenecachallenge

SK pharmteco

End-to-End CDMO Services

Your partner in...

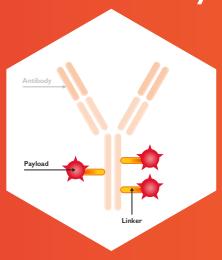
Research & Development

Continuous Processing

Chromatography, Batch & SMB

HPAPI

ADC Linkers & Payloads

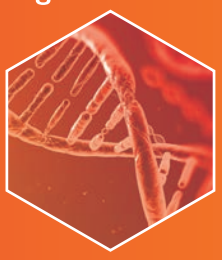


Particle Engineering, Spray Drying & Micronisation

Analytical Services

Cell Therapy Manufacturing

Oligonucleotides



Viral Vector Manufacturing

Plasmid Manufacturing

Regulatory Services

US | Korea | Ireland | France **info@skpharmteco.com** **www.skpharmteco.com**

In My View

Experts from across the world share a single strongly held opinion or key idea.

How Data Sharing Can Upgrade AI for Pharma

AI for drug discovery has enormous potential; to unlock it, we need to reset our mindset

By Robin Röhm, Co-founder and CEO, Apheris

It feels like we have been talking about the world-changing possibilities of using AI in drug discovery for decades. Yes, machine learning could potentially transform the way new medicines are developed – but it is fair to say that progress has been slow.

Discussions around AI typically focus on the technology and the need for more data to build the applications that can drive drug discovery forward. Although this is true up to a point, it is also misleading. To truly unlock the power of AI, we need to see a general shift in the collective mindset around data collaboration. The issue is not a shortage of data, but rather accessibility to the data that does exist. There are terabytes of high-quality data that could advance the application of AI in the drug discovery process. The problem is that much of this information is siloed in pharmaceutical companies or in clinical research organizations. In my view, we need more collaboration to accelerate the use of AI in the industry.

It goes without saying that the better and more diverse the data, the better the results – and the more efficient the entire drug discovery process becomes (with better outcomes for patients too). According to frequently-cited research from the Tufts Center for the Study of Drug Development,(1) it takes up to 15 years to develop a new medicine, and costs around $2.6 billion from initial discovery through to approval. Worse still, only a small fraction of the drugs in development ever make it to patients.

Research from McKinsey found that the efficiencies attainable from scaling the impact of advanced analytics were the equivalent of between 15 percent and 30 percent of EBITDA (a measure of profit) over five years (2). This positive impact increased to 70 percent over the course of a decade thanks to "predictive modeling in discovering and optimizing new blockbuster therapies".

Enhanced data analytics through greater data collaboration could have a dramatic effect at the preclinical stage. For example, instead of using animal models, researchers could use more accurate prediction models that combine molecular and clinical data. This approach would allow medicine makers to more accurately plan clinical studies and glean, at an earlier stage, whether trials might fail. To get there, we need collaboration between pharma companies that have already staged clinical trials – unfortunately, that's when commercial rivalry becomes a serious problem.

Despite these challenges, we are seeing more collaboration across the industry. For example, the MELLODY project brought together 10 of the biggest pharmaceutical companies to "enhance predictive machine learning models on distributed data in a privacy-preserving way," while the Pistoia Alliance has been advocating for greater collaboration since 2009. The alliance, which has more than 100 members including Pfizer, AstraZeneca and GlaxoSmithKline, has created a Centre of Excellence in AI to help the pharmaceutical industry overcome the obstacles such as access to data and skills as they continue to incorporate AI into their businesses.

However, these examples are still relatively isolated. Why? Failure to collaborate is typically the result of fears over privacy or the sharing of commercially sensitive data with rivals, but the cost and time commitment required to share data across multiple jurisdictions can also be a factor.

Federated data platforms for the creation of collaborative data ecosystems would enable multiple organizations to share and extract value from each other's decentralized datasets in a way that helps them overcome regulatory, technical, and commercial challenges. In a healthcare context, this means organizations can safely work using each other's data – including sensitive information from patients – without it ever leaving its secure environment. For example, take a pharma company in partnership with a genomic laboratory that uses data from all over a certain jurisdiction. Much of this data can't be shared because of patient privacy laws. However, use of a federated data platform would mean that the data in question never leaves its own secure server, and thus the two partners could develop models to better identify targets for new medicines. In the next stage on the value chain – lead generation – collaboration enables researchers to better predict target structure and binding using external data and proprietary models to complement their existing libraries, reducing the extent of trial and error and, therefore, cutting time and cost.

Access to this data – whether sourced from pharma companies, genomic laboratories, or hospitals – allows filtration and prioritization. Advanced analytics are necessary to recognize patterns and identify the information contained in the various data points, but to properly understand what matters we need varied and high quality datasets. That's where multiple data sources are advantageous.

Participating in a data ecosystem enables companies to work on more data than they have in-house, which supports their AI and analytics programs. And by using federated data platforms, it is possible to collaborate in a controlled way, opening up possibilities for commercial rivals and organizations to work together, while ensuring that the owner of the data has granular control of who has access and for what purpose. Data collaboration during clinical trials can help pharma companies to identify the most suitable patients and understand where on the globe it will be most effective to test. Such clinical operations data can help businesses understand their patients better and plan accordingly.

In short, enhanced access to data will drive AI analytics development, improving the drug discovery process and building a better healthcare ecosystem for all.

References

1. *Asher Mullard, "New drugs cost US$2.6 billion to develop", Nat Rev Drug Discov, 13, 877 (2014). DOI: https://doi.org/10.1038/nrd4507.*
2. *Lucia Darino et al, "How pharma can accelerate business impact from advanced analytics", (2018). Available at http://bit.ly/3DfQi5W*

30

Celebrating 30 influential and inspirational leaders across small molecule, biopharmaceutical, and advanced medicine development and manufacture

BY STEPHANIE SUTTON, ROB COKER, AND JAMIE IRVINE

The Medicine Maker is what it is because of its connection and collaboration with a vast network of industry experts. Whether speaking with seasoned CEOs, academic experts, or bench scientists, we are here to share stories and perspectives on what the industry could become – for patients and the planet.

Working alongside both new and ongoing challenges, including the COVID-19 pandemic and emerging threats to global health, online and media scrutiny, climate change, and a charged political worldscape, inspirational thought leaders continue to emerge and change the ways in which the pharma industry operates.

We asked readers to nominate the people enabling progress in the small molecule, biopharmaceutical, and advanced therapy spaces. Now, we invite you to join us as we celebrate the top 10 leaders in each.

Full profiles can be found online at www.themedicinemaker.com

SMALL MOLECULES

Marc Brown

CO-FOUNDER, MEDPHARM

Marc Brown has over 200 publications and 26 patents describing his work. He has been involved in the development of more than 80 products on the market in Europe, America, and Japan. He holds honorary and visiting professorships at the University of Reading, King's College London, and De Montfort University in the UK, and the status of Professor Emeritus of the University of Hertfordshire.

"As knowledge in molecular biology and genetics grows, the biopharma potential market increases, but so does that for small molecule drugs because of the discovery of new 'druggable targets.' I would argue that these two pathways need each other to maintain their growth in the future."

Francis Burrows

SENIOR VICE PRESIDENT, TRANSLATIONAL RESEARCH, KURA ONCOLOGY

Francis Burrows is a drug discovery and development scientist with a focus on the biology of disease. Previously as Senior Director of Oncology Discovery at Biogen, he was responsible for one clinical, two preclinical, and four discovery programs. He also initiated efforts to use Hsp90 inhibitors in neurodegenerative and autoimmune conditions.

"With every new small molecule discovery and approval alike, we get smarter and better at developing and maximizing them for patient benefit. I don't see the small molecule field slowing down any time soon and am eager to see what we as an industry can create and develop for cancer and other devastating diseases."

Matt Clark

CEO, X-CHEM

A recognized innovator and leader in the DNA-encoded library (DEL) field and part of X-Chem's founding team, Matt Clark has helped the company develop from a niche chemical discovery platform to a drug discovery engine serving the wider biopharma industry. With experience at GlaxoSmithKline and Praecis Pharmaceuticals, Clark has numerous patents and key DEL publications to his name. He holds a PhD in chemistry from Cornell University and has conducted postdoctoral studies at MIT.

"Small molecule therapies remain the only way to modulate intracellular pathways with a convenient dosing method that the patient can administer in their home. I think that the field is absolutely wide open in terms of opportunities."

Rebecca Guntern

VICE PRESIDENT, MEDICINES FOR EUROPE, HEAD OF EUROPE, SANDOZ

Rebecca Guntern-Flückiger is a purpose-driven leader and a regular contributor to industry discussions and initiatives. She is keen to drive debate and reform, and is particularly passionate about the accessibility and affordability of off-patent medicines.

As well as appearing in our previous Power List, she was named among the Top 100 Women in Business in Switzerland.

"My call to all players across all sectors: let's work together to create a sustainable environment for the generic medicines industry. We have the opportunity to jointly optimize the market and regulatory environment – and it's in the best interests of all of us."

Edward Hæggström

CEO, NANOFORM

A former Harvard visiting professor with an academic portfolio consisting of over 400 papers and 25 patents/patent applications, Hæggström co-founded Nanoform in 2015, launching a nanoparticle engineering technology for small molecule APIs. Nanoform's CESS technology was recently leveraged by Portuguese biotech company TargTex for a glioblastoma treatment study that showed promising results.

"We should explore new opportunities for scientists to leverage AI to improve current processes and innovate new methods for pharmaceutical development and manufacturing [but] we still need bright new minds to carry on innovating for the future."

Robert Lee

PRESIDENT, LUBRIZOL LIFE SCIENCES – CDMO DIVISION

Robert Lee holds more than two dozen issued patents or provisional patent applications and, through more than 30 years' experience in pharmaceutical research and development, he maintains strong academic ties as Adjunct Associate Professor of Pharmaceutical Chemistry at the University of Kansas. Lee also works as a reviewer and is on the editorial boards of several prestigious journals.

"There is plenty of innovation in the small molecule space, including computational methods that may lead to better target molecules with exquisite selectivity… Small molecule drug development isn't going anywhere soon."

Alexander Mullen

CO-FOUNDER AND CHIEF SCIENTIFIC OFFICER, FITABEO THERAPEUTICS

In addition to his roles at Fitabeo Therapeutics, Alexander Mullen is also a Professor of Pharmacy at the University of Strathclyde and a GPhC UK registered pharmacist. He is responsible for the design and development of an extensive portfolio of pharmaceutical products, and his academic activities have resulted in more than 50 papers, five patents, and four book chapters.

"The superior oral bioavailability of small drug molecules, compared with biologics that often require administration by an invasive parenteral route, is an important distinguishing clinical feature that should not be overlooked."

Anne Phelan

CHIEF SCIENTIFIC OFFICER, BENEVOLENTAI

Anne Phelan, who is also site head for the company's Cambridge Laboratories, has built BenevolentAI's drug discovery portfolio. She has worked on all stages from early discovery to late-stage development and brings experience from Mission Therapeutics and Pfizer, where she held the role of UK COO and was responsible for the generation of primary and secondary data to support the portfolio.

"The biggest weakness of biopharma and cell and gene is cost of goods, which is where small molecules can remain competitive. For diseases with high numbers of patients that are also non-life threatening, small molecules will often be the only viable route of treatment that payers are willing to accept."

Sharon L. Rogers

CEO, AMYRIAD

Sharon Rogers brings the strength of 35 years of pharma experience to AmyriAD, where she is best known as the world leader in and development strategist behind the Alzheimer's treatment, donepexil (Aricept), which has been the standard of care for more than 25 years.

"Because of advances in genetic research, small molecule drug development is on the cusp of a breakthrough moment. We are learning more every day about how to manipulate signaling pathways in selective and highly specific ways. Small molecule intervention in cell communication will become scientifically elegant, sophisticated and generate significantly more cost-effective therapeutics."

Christopher J. Schaber

CHAIRMAN, PRESIDENT, AND CEO, SOLIGENIX

Christopher Schaber has over 30 years of experience in the pharmaceutical and biotechnology industry. He also serves on the board of directors of the Biotechnology Council of New Jersey and the Alliance for Biosecurity. He has been a member of the corporate councils of both the National Organization for Rare Diseases and the American Society for Blood and Marrow Transplantation. Schaber received his BA from Western Maryland College, his MS in Pharmaceutics from Temple University School of Pharmacy, and his PhD in Pharmaceutical Sciences from the Union Graduate School.

BIOPHARMACEUTICALS

Akintunde "Tunde" Bello

VP CLINICAL PHARMACOLOGY AND PHARMACOMETRICS, BRISTOL MYERS SQUIBB

Joining BMS in 1998, Akintunde "Tunde" Bello spent five years working on the development of anti-infective and oncology therapeutics before 11 years as Pfizer's clinical pharmacology group leader. Returning to BMS in 2015, he now holds key responsibilities for the development, approval, and life cycle management of eight marketed drugs. Bello has authored and co-authored more than 70 peer reviewed abstracts and journal manuscripts, and is a member of the ASCPT, the AAPS, and the ASCO.

"My initial degree was in the biomedical sciences, a course that was focused on developing hospital laboratory scientists that ran diagnostic tests. I did not know that my entire career trajectory would change thanks to a job posting I saw in New Scientist. That post led to my first job in the pharmaceutical industry and has expanded my horizons in the drug development space."

Eric Dube

PRESIDENT, CEO, AND DIRECTOR, TRAVERE THERAPEUTICS

Eric Dube has served as the president and head of North America at ViiV Healthcare and spent more than 18 years working in roles of increasing leadership at GlaxoSmithKline across the US, Europe, and Japan. In his current role, Dube works on developing life-changing therapies for people living with rare diseases. He has won several awards, including being named one of 100 OUTstanding LGBT+ Executives in the Financial Times.

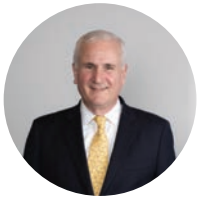
"We will only make progress if we are willing to reframe problems and place an increased focus on collaboration. Healthcare is often compared to an ecosystem. If we are going to function like one, we need every player in the system to collaborate."

Seth Lederman

CEO, TONIX PHARMACEUTICALS

Lederman is a renowned physician and entrepreneur with significant contributions to drug discovery. By addressing the unmet need of patients with painful neurological conditions, Lederman's focus is on developing novel therapies and vaccines to prevent and treat central nervous system disorders.

In a recent article with The Medicine Maker, Lederman wrote, *"Declaring definitive victory over any communicable disease may well be a thing of the past. At the same time, great progress is still possible. With our hard-earned pandemic lessons, we should be stepping up to the challenge."*



Hanns-Christian Mahler

CEO, TEN23 HEALTH

Hanns-Christian Mahler has worked in leadership roles at Merck, Roche, and Lonza since 2000. He studied pharmacy and toxicology at the University of Mainz, and obtained a venia legendi from the University of Frankfurt.

"Pharmaceutical sciences remain full of urban myths and beliefs. Many controlled studies are lacking in some fundamental considerations, such as what is an acceptable subcutaneous injection volume? My motivation is and always has been to question textbook knowledge, to assess based on primary studies and information, and to generate such studies in lieu of publicly available research."

Alessandro Maselli

PRESIDENT AND CEO, CATALENT

Alessandro Maselli has held key positions in global operations, corporate oversight, and strategy, as well as leading two manufacturing facilities in Italy and the UK. Prior to Catalent, Maselli held leadership roles at Alstom and SGS. He earned a master's degree in electronic engineering from the University of Rome (La Sapienza).

"CRISPR-CAS9, while only a decade old, shows the potential that DNA editing has to become a cure for previously incurable conditions… There is a lot of work still to be done, not least on the morality and ethics of gene editing, but it is no exaggeration to suggest that it will become safe and routine – and revolutionary."

Andrew Moore

GLOBAL GENERAL MANAGER, PFIZER CENTREONE

Andrew Moore's first year at Pfizer CentreOne saw him navigate the company through sweeping change forced by the pandemic. Under his leadership, the company now has a new toolkit and a new mindset when it comes to development and manufacturing. He is credited with reinvigorating Pfizer CentreOne's focus on genuine partnership and commitment to its core mission.

"Industry trends, such as personalized medicine, gene therapies, and complex vaccines, demand more agility and a culture of continuous improvement, with responsive investment in infrastructure and more flexible commercial approaches."

Mike Rea

CEO, IDEA PHARMA

A self-styled innovation protagonist/antagonist and "geek," Mike Rea is an established author who has been appearing in our Power List since 2017. Creator of the annual Pharmaceutical Innovation Index, Rea is Senior Fellow, FasterCures, at Milken Institute; Advisor, BioEthics International; and Owner and Chief Musical Officer of Medical Records, an indie record label.

"Although we have doubled the number of pharma companies worldwide in the past 20 years, and tripled the number of biotechs, we are still seeing no rise in the number of approved new drugs. The priority needs to be the re-evaluation of innovation and its process."

Paul-Peter Tak

PRESIDENT AND CEO, CANDEL THERAPEUTICS

Paul-Peter Tak is ranked among the global top 150 scientists in immunology. He was elected Fellow of the Academy of Medical Sciences, UK, and has served as Senior Vice President, Chief Immunology Officer, and Global Development Lead at GSK. As co-founder Sitryx Therapeutics and former CEO of Tempero Pharmaceuticals and Kintai Therapeutics, Tak has brought together a world-class executive team at Candel that has recently presented proof of concept for its viral immunotherapies across multiple solid tumors.

Jan van de Winkel

CEO, GENMAB

Jan van de Winkel co-founded Genmab in 1999 with the goal of unlocking the power of antibodies. Through his leadership, Genmab's innovations have powered six approved medicines to treat cancer and other serious diseases. Van de Winkel is also passionate about young scientists and teaches an annual immunotherapy course at Utrecht University.

"As an industry, we must be nimble and mobilize quickly to meet patients' needs in the coming years. This includes discovering novel disease targets, utilizing next-generation technologies to develop better targeted therapies, and utilizing AI and data sciences to shorten time lines."

Robert O. Williams

DIVISION HEAD AND PROFESSOR OF MOLECULAR PHARMACEUTICS AND DRUG DELIVERY, UNIVERSITY OF TEXAS

Robert Williams has co-founded several pharmaceutical companies, and pioneered drug delivery research for the development of novel drug delivery systems and topical applications, novel particle engineering technologies for low molecular weight drugs, and innovative dry powder applications for biologics. His current research focuses on refining particle engineering techniques including thin film freezing, a proprietary technology he invented that transforms medicines into a potent dry powder for better efficacy, safety, and stability.

ADVANCED MEDICINE

David Backer
CEO, CURATE BIOSCIENCES

David Backer joined Curate Biosciences as CEO to guide the commercial launch of its Curate Cell Processing System for cell therapy starting materials. He has decades of commercial experience in the cell and gene therapy space, most recently as Chief Commercial Officer at Oxford Biomedica, as well as leadership roles at ElevateBio. Backer also founded and led the successful sale of Molecular Medicine BioServices to Sigma-Aldrich's SAFC division, leading to an extensive career at Sigma-Aldrich SAFC and MilliporeSigma.

"For those patients that suffer from rare diseases, there is finally a potential treatment for diseases that were previously long ignored. The challenge is how to scale."

Alan Boyd
CEO, BOYDS

Alan Boyd is globally recognized as a pioneer in gene-based therapies, having led the development of Cerepro – the first gene therapy to be submitted to the EMA for approval as a prescription medicine. Founding Boyds in 2005, he and his team have been involved in the development of nine approved cell and gene therapies.

"When I start working with a new client on an advanced therapy, I tell them from the start they will have issues with their potency assay and other aspects of the product – such as purity. So they must prepare for this to happen and bring in the right skills to help."

Tirtha Chakraborty
CHIEF SCIENTIFIC OFFICER, VOR BIOPHARMA

Tirtha Chakraborty's career has been built on challenging the status quo and continuously pushing the boundaries in cell and gene therapy research. He began his career as an RNA biologist and immunologist, and quickly became a pioneer in the CRISPR industry after paving the way for the first clinical trial in the space. His vision to expand Vor Bio's technological expertise and accelerate its research towards the clinic resulted in his appointment as Chief Scientific Officer.

"Beauty is not just in fine arts or in music; it is everywhere in science. The intensity and guttural emotions of an artist should not be any different from those of a scientist. The patterns, the freedom of creativity, the process, the deductions leading to a great scientific journey are extremely beautiful and one must appreciate it."

Fabian Gerlinghaus
CO-FOUNDER AND CEO, CELLARES

Fabian Gerlinghaus is driven by a strong sense of purpose and is passionate about building the future of cell therapy manufacturing. Prior to Cellares, he was Chief Innovation Officer at Synthego and co-invented the company's RNA synthesizer technology.

"Collective industry expertise has led to so many remarkable breakthroughs, but there are several things we can learn from other industries. For example, we ought to accelerate the adoption of automation and allow pharmaceutical companies to reduce their development and manufacturing costs, timelines, and realize improved product quality and consistency."

Queenie Jang
CEO, INTERNATIONAL SOCIETY FOR CELL AND GENE THERAPY

Under Queenie Jang's leadership, the International Society for Cell and Gene Therapy (ISCT) has seen tremendous growth and now operates across five regions, with almost 3,000 members. The society mobilizes its global community to connect and collaborate with guidance from leading academic, regulatory, and industrial experts.

"Workforce development continues to be one of the most significant challenges facing the cell and gene therapy sector. The field has seen exponential growth, which has outpaced the rate at which new professionals enter."

Catherine Jomary

ATMP LEAD, IPS-INTEGRATED PROJECT-SERVICES

Catherine Jomary is an expert in the field of ATMPs with over 20 years' experience in cell and gene therapy and regenerative medicine research across academic, biotechnological, CDMO, and pharmaceutical sectors. Her accolades include the UK Wellcome Trust Value in People Award, a Marie Curie Fellowship, a Medical Research Council of Canada Fellowship, and a Fondation Recherche Médicale Française post-doctoral research fellowship.

"The biggest challenges for new genome editing therapeutics are the specificity of delivery, control of their activity, detection of potential off-target mutations, and their inherent immunogenicity."

Sheila Mikhail

CO-FOUNDER, ASKLEPIOS BIOPHARMACEUTICAL (ASKBIO)

Sheila Mikhail co-founded AskBio in 2001. The company was an IP holding company until 2017, when it was repositioned as an operating company. Mikhail has advanced several programs into the clinic and grown the company to over 800 employees across five countries. She was CEO until March 2023, but now serves as an advisor. In 2018, she co-founded the Columbus Children's Foundation.

"I have been in the gene therapy field for over 20 years. There have been several cycles of difficult periods where gene therapy was out of vogue and funding dried up, followed by several periods of unbridled optimism. The key is to focus on solving the fundamental problems, including more efficient manufacturing, repeat administration, and durability of therapeutic benefit."

Dirk Nagorsen

CHIEF MEDICAL OFFICER, AFFINI-T THERAPEUTICS

For over 20 years, Dirk Nagorsen has pioneered precision immunotherapies that have transformed patients' lives. He was one of the first scientists to describe naturally occurring T-cell responses against cancer, and led the development of the first FDA-approved bispecific T-cell engager, Blincyto. As CMO of Affini-T Therapeutics, he leads the development of TCR-T cell therapies for the most intractable solid tumors driven by oncogenic driver mutations, beginning with KRAS G12V and KRAS G12D.

"Embrace the fact that you are working on the forefront of science and paving the way for a whole new generation of medicines. Keep and spread the excitement!"

Angela Osborne

CEO, EXMOOR PHARMA

Angela Osborne has supported the development of cell and gene therapy, and biopharmaceutical businesses, processes, and facilities for over 30 years. Prior to founding eXmoor, she was Senior Vice President of Pharmaceuticals at Aker Kvaerner, an engineering multinational, where she was responsible for the pharmaceutical business in Europe. Osborne is also a keen supporter of the UK's BioIndustry Association, co-founder of the AMC (ATMP Manufacturing Community), and an active contributor to the UCL Masters course in cell and gene manufacturing.

"It takes a truly multidisciplinary team to bring a cell and gene therapy product to market, and being part of that team will be hugely beneficial and a great learning experience. Focus on building that experience before starting to worry about job titles and positions."

Victor Vinci

VICE PRESIDENT, GLOBAL PRODUCT DEVELOPMENT, CELL, GENE AND PROTEIN THERAPIES, CATALENT

Victor Vinci joined Catalent following the company's acquisition of Cook Pharmica. He has led FDA QbD collaborations and was responsible for Catalent's development teams through the onboarding, tech transfer, and scale-up of the Moderna, J&J, and AstraZeneca COVID-19 vaccines across multiple sites.

"There is more confidence to investigate different applications of gene therapy beyond genetic disease. For cell therapy, we're seeing therapies being investigated and gaining approvals as earlier treatments."

the Medicine Maker

COMPANY OF THE YEAR

CELEBRATING *Eight Companies Ahead of the Rest*

Which pharma companies and service/system providers have impressed the most over the last 12 months? We asked you to vote…

And vote you did! For each category, we selected top contenders based on market research – but we also gave readers the opportunity to nominate other impressive companies. We'd like to thank everyone for taking the time to vote; the resulting winners – and the honorable mentions – do a wonderful job of showcasing why the pharma industry is such an exciting place.

Why did we launch the Company of the Year Awards? Well, a huge amount of effort and investment goes into drug development and manufacturing – and though our annual Power List shines a light on individuals making big waves and big decisions, it takes a "village" – sometimes a virtual city – to raise a therapeutic.

Now, without further ado, we present the Company of the Year Awards 2023!

BEST BIG PHARMA COMPANY: *Pfizer*

Pfizer retains its crown this year as your number one big pharma company. In 2022, the company's revenues hit an all time high of $100.3 billion (an increase of 23 percent compared with 2021) – but it's worth noting that the majority of this growth has been driven by the company's Comirnaty vaccine and Paxlovid antiviral drug. Now that demand for COVID-19 products is beginning to wane, what will happen next? Profits could be significantly lower in 2023. That said, the company still boasts a healthy pipeline with around 23 products in phase III trials – and that's alongside more approved products than we can count in dozens of indications.

As a quick reminder of Pfizer's history, the company was founded in 1849 in New York by Charles Pfizer and Charles Erhart. The company initially focused on fine chemicals but pivoted to more research-based pharmaceuticals in the 1950s.

RECENT NEWS:

Expands work with An Accord for a Healthier World to offer even more medicines and vaccines (around 500) on a not-for-profit basis for certain lower income countries

Submits supplemental Biologics License Application to FDA for its 20-valent pneumococcal conjugate vaccine candidate for infants and children

Phase III BENEGENE-2 study for hemophilia B gene therapy meets primary endpoint

KEY FACTS

Global HQ: New York, USA

Number of employees: *79,000*

Sales Revenue in 2022: *$100.3 billion*

HONORABLE MENTION: MERCK, SHARP & DOHME

BEST API SUPPLIER: *BASF*

Credit: U.S. designundfotoart / Pixabay.com

When it comes to excipients and active ingredients, readers voted BASF Pharma Solutions as the best company for the job. It's hardly a surprise, given that BASF is one of the leading manufacturers in the world in this field, with solutions for numerous applications including orals, topicals and parenterals, as well as a portfolio of biopharma ingredients and ingredients for improving solubilization. The company also boasts a global team of industry experts and digital solutions, such as the Virtual Pharma Assistants, to support customers in developing efficient, cost-effective and reliable formulations.

The company was founded in 1865 as Badische Anilin- und Sodafabrik in Mannheim, Germany. One of the company's most famous innovations is PVP, which was first used as an additive in the textile industry due to its great affinity to dyes, and as a binder and thickening agent. However, by the end of 1940, BASF's Kollidon PVP gained its first medicinal application as a synthetic blood plasma substitute.

Of note, the company has made major steps forward in terms of sustainability – and has even developed a digital tool that can provide transparency to customers about the carbon footprints of BASF products such as ibuprofen.

RECENT NEWS:

Excipient accepted into FDA Pilot Program for novel excipients

Announces plans for neopentyl glycol plant at Zhanjiang Verbund site in China

Calculates individual carbon footprints of a large part of its chemical intermediates portfolio

KEY FACTS

Global HQ: Ludwigshafen, Germany

Production sites worldwide: *238*

Number of employees: *111,047*

Sales Revenue in 2022: *$78.6 billion*

HONORABLE MENTION: DOW

BEST BIOPHARMA EQUIPMENT COMPANY: *Merck*

Merck is one of the oldest pharmaceutical companies in the world – its origins date back to 1668, when Friedrich Jacob Merck took over a pharmacy in Darmstadt, Germany. After World War I, the company lost subsidiaries abroad (including the US subsidiary, which today is the independent company Merck, Sharp & Dohme) and underwent structural changes. It debuted on the Frankfurt Stock Exchange in 1995, but the Merck family still owns the majority of the company's shares.

Today, the company has three divisions: healthcare, life sciences, and electronics. The life science division is a leading provider of equipment, solutions, and services for the biopharma industry, including end-to-end solutions, single-use technologies, raw materials, and more. The company has also created the M Lab Collaboration Centers, where customers can try out new ideas and technologies alongside Merck scientists.

RECENT NEWS:

Signs MoU with Synplogen to accelerate development and manufacturing of viral vector based gene therapy applications

Acquires Erbi Biosystems – including leading perfusion micro bioreactor

Invests 290 million euros in US drug safety testing capacity

KEY FACTS

Global HQ:
Darmstadt, Germany

Number of employees: *60,000*

Sales Revenue in 2022: *$19.7 billion*

HONORABLE MENTION: THERMO FISHER SCIENTIFIC

BEST CDMO:
Thermo Fisher Scientific

Thermo Fisher Scientific was officially formed in 2006 following the merger of Thermo Electron and Fisher Scientific. Both companies had a rich history before then – and the combined entity has since gone on to acquire numerous other companies focused on instrumentation, services, and consumables for the life sciences industry. One notable acquisition was that of the CDMO Patheon in 2017.

Today, Thermo Fisher Scientific provides industry-leading pharma services solutions for drug development, clinical trial logistics, and commercial manufacturing to customers of all sizes through its Patheon CDMO brand. With more than 60 locations around the world, the company provides integrated, end-to-end capabilities across all phases of development, including API, biologics, viral vectors, cGMP plasmids, formulation, clinical trials solutions, logistics services, and commercial manufacturing, and packaging. The business has also won numerous CMO awards in multiple categories including capabilities, compatibility, expertise, quality, reliability and service.

RECENT NEWS:

Expands global biologics and sterile manufacturing capabilities in China

Collaborates with Celltrio to introduce fully automated cell line platform

Joins Momentum Labs as founding sponsor of new biotech hub in Alachua, Florida

KEY FACTS

Global HQ:
Waltham, MA, USA

Number of employees: *>125,000*

Sales Revenue in 2022: *$44 billion*

HONORABLE MENTION:
PFIZER CENTREONE

BEST PROCESSING & PACKAGING EQUIPMENT

Optima Packaging Group

Filling machines, closing machines, packaging machines, freeze drying machines, isolators, and more; Optima offers a huge portfolio of equipment for the pharma and life sciences industry, as well as process engineering services. The company's equipment can cope with highly potent products, biologics, and cell and gene therapies – which require highly flexible systems. Both custom and modular options are available, and the company also produces digital solutions for monitoring and optimizing processes, and format changes and troubleshooting.

This family-owned business was founded in 1922 by Otto Bühler as a manufacturer of filling scales for foodstuffs and everyday products. Large parts of the company were destroyed during World War II, but the company was reconstructed. By the 1970s, the company had a presence in over 40 countries. Several subsidiaries have been added over the years and today the company boasts an export share of over 85 percent.

RECENT NEWS:

Celebrated its 100th anniversary in 2022 and published annual review outlining recent investments

John Groth appointed vice president pharma at Optima Machinery Corp

Invests 290 million euros in US drug safety testing capacity

KEY FACTS

Global HQ: Schwaebisch Hall, Germany

Number of employees: *3000*

HONORABLE MENTION:

GEA GROUP

BIGGEST "TALKING POINT"

Regeneron

Which pharma company has been most discussed or lauded in the media? Readers voted for Regeneron, which has had a very vibrant year of innovation, with new approvals and promising results from clinical trials. In less positive news, the company did see a slump in revenues last year as demand decreased for COVID-19 products. At the same time, Eylea has been affected by competitor products. Nevertheless, the outlook for the company is far from negative. Revenues for 2022 were better than some analysts expected, and, at the time of going to print, Regeneron had already scored a handful of new approvals for 2023.

A little background on the company: Regeneron was founded by Leonard S Schleifer, an assistant professor at Cornell University Medical College in 1988. The company started with $1 million but by 1991 was trading publicly – an initial public offering raised $91.6 million. It received its first FDA approval for a drug (Arcalyst) in 2008. Today, the company works in a range of therapeutic areas and has proprietary technology to aid with antibody target discovery.

RECENT NEWS:

Eylea injection approved by the FDA as first pharmacologic treatment for preterm infants with retinopathy of prematurity

Dupixent approved by the European Commission as the first and only targeted medicine indicated for eosinophilic esophagitis

Libtayo approved in Japan for advanced or recurrent cervical cancer

KEY FACTS

Global HQ:
Tarry Town, USA

Number of employees: *9,000*

Sales Revenue in 2022: *$12.17 billion*

HONORABLE MENTION:
BAVARIAN NORDIC;
BLUEBIRD BIO

SMARTEST SUSTAINABILITY INITIATIVE:
GlaxoSmithKline

GSK was the only pharmaceutical company to appear in the gold class of the Dow Jones Sustainability Yearbook 2022, and has initiatives focused around climate, water, materials and waste, and biodiversity. In September 2022, the company launched its Sustainable Procurement Program for suppliers. From 2023, GSK will "require and support suppliers to take action on sustainability commitments and make improvements on emissions, energy, heat, transport, waste, water and biodiversity." According to GSK, 40 percent of its carbon footprint is located in the supply chain – with suppliers accounting for a substantial part of that share. The big pharma player says it will support its suppliers through education and the adoption of new environmental sustainability measures.

KEY SUSTAINABILITY GOALS:

100 percent renewable electricity by 2025

Net zero emissions across the full value chain by 2030

Zero impact API levels in water for all sites and key suppliers by 2030

100 percent of sites to achieve good water stewardship by 2025 and reduce overall water use by 20 percent by 2030

25 percent environmental impact reduction for products and packaging by 2030

Positive impact on biodiversity at all sites by 2030

HONORABLE MENTION:
BASF

BEST START UP:
ElevateBio

What about the smaller players in the industry – and particularly those just starting out? Added by popular demand, this category highlights a budding new start up. To be eligible for inclusion, the company must have been formed no earlier than 2016.

ElevateBio was founded in 2017 by David Hallal, Vikas Sinha, and Mitchell Finer. The goal was to help drug companies accelerate their cell and gene therapies through technologies, such as gene editing, induced pluripotent stem cells, and cell, protein, and vector engineering. The company has formed a number of partnerships, including with Affini-T Therapeutics, the California Institute of Regenerative Medicine, the University of Pittsburgh, and Boston Children's Hospital, with the company describing itself as an "ecosystem."

In 2020, the company's BaseCamp facility won an Award for operational excellence in the ISPE Facility of the Year Awards, with judges describing the facility as a "gamechanger for cell and gene therapy."

RECENT NEWS:

BaseCamp unveils its LentiPeak lentiviral vector platform

Partners with Affini-T Therapeutics to advance Affini-T's cell therapy programs targeting core oncogenic drivers

Collaboration with the University of Pittsburgh to create Pitt BioForge BioManufacturing Center at Hazelwood Greed to accelerate cell and therapy innovation

HONORABLE MENTION:
TEN23 HEALTH

Future-Proofing Aseptic Filling

How the thoughtful adoption of new technology can both problem-solve and future-proof critical processes in biomanufacturing

By Adam Pinkert, Site Quality Head, Alachua, Florida, at Resilience, and Áine Brennan, Manager, Technical Services, Aseptic Filling at Cytiva

For any forward-facing biomanufacturing service provider, it's crucial to keep on top of new technologies and be ready to meet new industry trends and challenges. Resilience is a technology-focused biomanufacturing service provider that can support end-to-end services for the development and production of biologics, vaccines, cell and gene therapies, and mRNA products. The company was established in 2020 with the aim of addressing two major challenges faced by the biopharma manufacturing industry: a shortage of manufacturing supply chains capable of withstanding disruptive shocks (a clear issue during the COVID-19 pandemic) and a lack of scientific advancements in biopharmaceutical manufacturing. Manufacturing has not kept pace with innovation in therapeutic discovery, which is preventing new modalities from reaching patients at speed. To address these challenges, Resilience focuses on implementing flexible technologies.

Resilience works in numerous therapeutic areas, including biologics, vaccines, nucleic acids, cell therapy, and gene therapy, spanning platform technology and development, process and analytical development, and cGMP manufacturing. With increasing demand for advanced therapeutics, Resilience has pivoted between products quickly and adapted to the ever-changing needs of clients.

Adopting the right technology

In its ongoing search for flexible solutions, Resilience recently invested in two Cytiva SA25 aseptic filling workcells, which are currently available and ready to use, for its manufacturing site in Florida.

Resilience was looking for a filling solution with a small footprint that could handle multiple products, with quick changeover times and high product quality output. After investigating several options, the company chose Cytiva's SA25 – a fully closed, gloveless, robotic isolator that can fill nested vials, syringes, and cartridges (from 0.5 mL to 50 mL) with high levels of accuracy and consistency. All material handling is robotic, with no conveyor belts or crimp capping, to help ensure the sterility of the environment.

The system is suitable for a wide variety of emerging therapeutics, including mRNA, biopharmaceuticals, and cell and gene therapies. And because the system operates within a closed, robotic aseptic filling workcell, the risk of product contamination is significantly reduced. The robotics eliminate the need for operators to intervene in the process with the use of traditional, and cumbersome, cleanroom gloves that limit dexterity. The use of robotics not only eliminates operator interventions, it increases filling accuracy and consistency, enabling higher product quality and yield.

Another key feature of the SA25 for Resilience was the speed of deployment. For any busy manufacturer, speed is key. Every SA25 machine is standardized with pre-qualified components that enable rapid machine changeovers (less than one hour) between runs, keeping the output rate high. It also means that any product validation work performed on one machine effectively validates every other machine because they are the same. Overall, these features help manufacturing service providers to move their customers' products to the clinic faster.

The design behind the system

Cytiva is a well-established provider of high-quality technologies and services for the biopharma drug development industry, covering drug development, drug substance, and drug product. In 2021, Vanrx became part of Cytiva, bringing its expertise in aseptic filling, the final step of the biomanufacturing process. By improving this process, biomanufacturers can bring their novel therapies to patients faster.

The design of the SA25 concentrates on the fundamentals of quantitative risk management: identify the risk and then remove the path to that risk. Over the years, aseptic filling has made significant advances, including the introduction of RABS and gloved isolators, but the SA25 goes a step further by completely eliminating the human operator from the core of the process. Given that human intervention in aseptic processing is the leading cause of contamination risk, a fully enclosed robotic system mitigates that significant risk.

The SA25 comprises two chambers. The first is the decontamination and

Key Questions Answered

What are the main advantages of the SA25?

i. Flexibility. The SA25 can fill a range of final product packaging, including nested vial, syringe, or cartridge formats ranging from 0.2 to 50 mL. Cytiva says that users can change between formats within around 45 minutes.
ii. Reduced risk. The integrated gloveless robotic isolator design intentionally removes the need for operator intervention. The intelligent automation oversees every aspect of the aseptic process and reduces the risk to drug product quality.
iii. Speed to market. The SA25 is a standardized system that can be installed quickly and easily adopted. Cytiva sees customers regularly reach GMP production within 15 months after purchase.

Can you use pre-sterilized and packaged vials?

Yes. Pre-sterilized and packaged vials, syringes, or cartridges are supplied in sealed tubs, usually sterilized with radiation or EtO2. Single-use components are compatible and standardized for the SA25.

How does the system remove the Tyvek lid?

When the components enter the filling chamber, they are handled by the tray-robot and a peel tool. This removes the Tyvek within the filling chamber. The system uses a vision process coupled with robotic handling to remove the first Tyvek layer, then a secondary action to remove the inner layer of the packaging, giving full access to the containers within.

What is the time from fill to storage?

At Resilience, as the tubs are coming off, they move directly into the visual inspection area prior to cold storage (or any other chosen storage conditions). Depending on the filling speed, and how fast the visual inspection is performed, the process usually takes between 4–8 hours from initial fill to storage.

Can the system accommodate PUPSIT testing?

The SA25 is designed to allow for PUPSIT testing of the external sterilizing filter. Cytiva also has a dedicated team that can help design alternative approaches to PUPSIT, if required.

staging isolator (DSI), which is a material transfer airlock designed and qualified to meet ISO 5 particle limits. The tubs of ready-to-use primary container enclosure units are loaded and external surfaces are decontaminated with hydrogen peroxide before entry into the filling chamber. The DSI carousel can hold 24 container tubs and eight closure tubs, depending on the chosen format. The second chamber is the fill isolator, the main aseptic processing unit, where the primary containers, closures, and drug products are combined in a controlled environment to preserve product sterility. The results include increased product and patient safety. For this reason, the SA25 has become a standard system for many leading biopharma companies and has been part of the journey to bring several clinical and commercial products to patients.

In addition, the system has been designed to take advantage of single-use/ready-to-use components (either standardized or customized) and a proprietary needle (available in sizes of 0.8 to 3.2 mm). An environmental monitoring swab sheath allows safe, non-aseptic installation of the flow path during batch set up, which maintains integrity prior to decontamination of the fill isolator.

Setting up for success

Speed and flexibility are essential for the success of a biomanufacturing service provider – and new technology can help achieve these important goals. Resilience believes that technology like the Cytiva SA25 can help the company remain agile and responsive to clients' ever-changing needs. The system is helping the company maximize valuable manufacturing space and increase production capacity, while improving process quality through a dependable assurance of sterility, reproducibility, use of high-grade components and, importantly, removal of human error via the robotics. Together, these characteristics promise high product quality and allow Resilience to face the future with confidence.

If you'd like to know more about this topic, then check out this webinar on future proofing aseptic filling https://resources.resilience.com/future-proof-your-aseptic-filling-ondemand-webinar

You can also contact:
Nithin Stephen, Director, Commercial Development - Drug Product at Resilience
nithin.stephen@resilience.com
Scott Harper, Head of Business Development, at Cytiva Aseptic Filling
scott.harper@cytiva.com

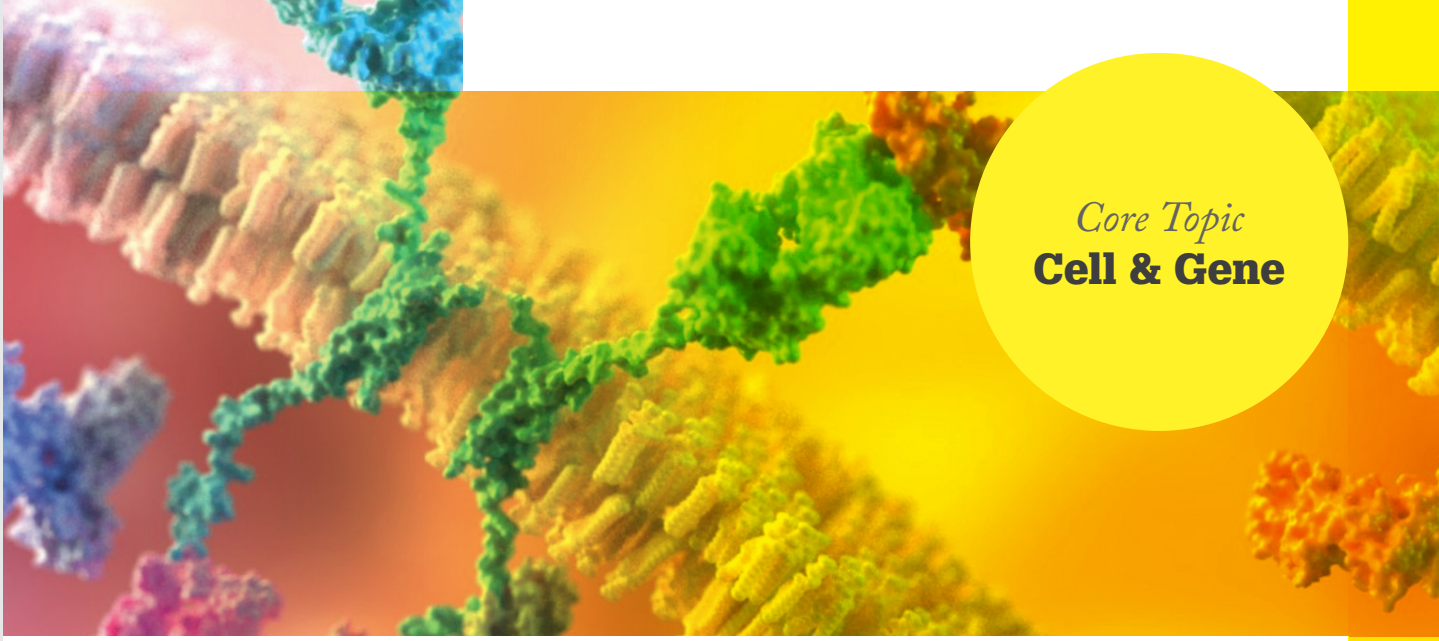
Advanced Therapy Solutions

CGT experience where it counts.

Our tailored solutions and dedication to continuous innovation uniquely allow us to help biopharma pioneers successfully bring cell and gene therapies to the people that need them most.

Learn more about Advanced Therapy Solutions

CardinalHealth™



Credit: Shutterstock

Core Topic
Cell & Gene

Treating DMD. Is the first gene therapy for Duchenne muscular dystrophy in sight? Sarepta Therapeutics (working in collaboration with Roche) submitted SRP-9001 for accelerated approval with the FDA in Q4 last year. The FDA initially said it would not be holding an advisory panel meeting for the drug, but has since done a u-turn. The final decision on the therapy is expected in Q2 this year. According to Sarepta CEO and President Doug Ingram, the FDA has confirmed there are no significant safety concerns. Sarepta is now preparing for scheduled pre-approval inspections and making plans for launch.

Not for autism. The NeuroGen Brain and Spine Institute in India has had its license revoked for advertising and selling stem cell therapies to treat autism. India's Association of Child Neurology has issued a position statement on the use of stem cell therapy as a treatment for autism – stressing that there is "insufficient evidence" that it works and that it is not recommended. India-based experts have expressed concern and warned about indiscriminate promotion and predatory marketing of stem cell therapies causing false hope and unrealistic expectations. The statement adds that the promotion and advertisement of such therapies for autism will be treated as "professional misconduct."

DREAM heart boost. Researchers from the Texas Heart Institute have carried out the largest cell therapy trial to date for patients with chronic heart failure from low ejection fraction. The procedure used a special immunomodulatory cell-type called MPC (mesenchymal precursor cells) developed by Mesoblast Inc, which is sponsoring the studies (DREAM-HF), and involved modifying cells to enhance regenerative properties, and reduce the risk of cardiovascular death, myocardial infarction, or strokes. In a statement, lead researcher, Emerson C. Peri, said, "The cells appear to work by reducing inflammation, increasing microvascular flow, and strengthening heart muscle." The results have been published in the Journal of the American College of Cardiology.

Parkinson's Transplant. Researchers from Skåne University Hospital, Sweden, have successfully administered a transplant of stem cell-derived nerve cells for a patient with Parkinson's. Originally developed by researchers at Lund University, the procedure replaced defunct dopamine cells with new ones manufactured from stem cells that have the potential to differentiate into mature dopamine-producing neurons. "The brain region that the cells are transplanted into in this trial can be as narrow as four millimetres. The surgical instrument has a very high level of precision, and we are greatly helped by modern imaging techniques" said consultant neurosurgeon, Hjálmar Bjartmarz.

IN OTHER NEWS

Rosalind Franklin University neuroscientist Daniel Peterson receives funding for gene therapy involving reprogramming non-neural glial cells to replace lost neurons

University of Tennessee Science Center receives funding from US Department of Defense for DNAzymes research focusing on frontotemporal dementia

BioMarin Pharmaceutical announces extension of FDA review for ROCTAVIAN gene therapy for adults with hemophilia A

Adaptimmune acquires rival cell therapy company TCR2 Therapeutics to advance research on reengineering immune cells to fight cancer

Moderna and Life Edit Therapeutics enter strategic collaboration to accelerate development of in vivo mRNA gene editing therapies

Between Two Worlds: Doing Business as a Cell and Gene Academic

The pharmaceutical industry depends on academia, but that relationship – and its points of interchange – could be improved

By Stuart Curbishley, Head of Business and Project Development – Advanced Therapies at the University of Birmingham, UK

Stuart Curbishley

Medicine making for cell and gene therapy is a tripod; its three legs are academia, business, and the state. Pull out one leg and it falls. Without university laboratories, we would not have a single therapy for the market. And without state support through institutions such as the UK'S Cell and Gene Therapy Catapult, cell and gene companies would not perform at their best. For the foreseeable future, we can expect these things to remain true.

However, I do think that, if funding worked differently, the academic leg could stand on its own for longer. The problem is that academics simply cannot set out to raise, say, £150 million to fund the commercialization of a therapy. This is where the private sector steps in, turning the pure science of academia into viable IP.

Conversely, I seriously doubt that the private sector leg could ever stand entirely on its own. Although certain big pharma companies have set up cell therapy development teams, I expect that these companies are far more likely to release new iterations of existing products than truly novel therapeutics. This is where business needs academia.

I believe that we would be able to advance the field far more quickly if we could establish a way to distribute industry's financial resources to academic programs earlier. If we could lead big pharma to fund the bakery, rather than buy the bread, we would shave years off the development process.

Though I would not claim to have all the answers to what is certainly a very difficult and inflexible problem, I would insist that new and better bridges be built between pharma and academia. You don't need to take it on faith. I'm living proof.

This is my journey…

In 1999, I launched my academic career with a Master's research degree at the University of Birmingham, UK. I stayed on to undertake a PhD on how chemokines drive inflammation and inflammatory liver disease. After completing that, I stayed on again, this time in a postdoctoral position researching monocyte myeloid cell biology with a view to developing dendritic cells as a primary liver cancer therapy. It was at this job that I first worked on a cell therapy program. It eventually led to my first involvement with a cell therapy trial, treating end-stage liver cancer with a dendritic cell vaccine. That trial reached its target and

closed during the COVID-19 pandemic, ultimately yielding positive results.

Across the last half-decade, I have taken over running GMP activity for the University of Birmingham as a whole. We've grown from a small, self-enclosed facility to one with a variety of academic and commercial partners. Today, we manufacture a wide range of cell types and run a wide range of GMP services for the university.

Adding commercial viability to academic centers could transform the offer to early-stage startups. This is where academic CDMOs tend to falter; they are simply not designed with commercial questions such as speed and contracting in mind. Juxtaposition with appropriate commercial partners could smoothly speed the transition of academic programs to the world of privately financed cell therapy trials.

As a sector, academic CDMOs need to show a way out for people stuck in the rut of trying to build a therapy entirely on grant funding. After all, the moves that win you a grant are usually not the moves that will help you set up a robust, sustainable business. We need to spare these people from an imperative to regularly reinvent the wheel just to keep moving forward.

… and this is my bridge

In the case of my own company's transition to the market, I don't expect a massive change in our basic function – a CDMO with a strong focus on development. We will continue to work with commercial partners and focus on how they can complement our academic program. There are partial precedents for this here in the UK, where we have seen people take academic programs into our government-funded Cell and Gene Therapy Catapult and go on to raise impressive capital investments. However, in many instances, there is a lack of preparation and a lack of understanding of what is needed to commercialize. Often, the company's processes require expensive development that comes far too late, after the company has already moved into rented manufacturing space.

Sensible commercial partnerships should help ease such transitions. We need to leverage the proximity of academic CDMOs to patient treatment centers and their populations of key opinion leaders at centers of clinical excellence. Our goal should be to work closely with early-stage therapy developers to get the product and the process right first time.

Skeptics may ask: doesn't coupling with commercial partners introduce new problems, swapping the games of academia for the games of business? These are valid concerns, but all I can say in response is that, if we are careful in our establishment of key partnerships, we can still make a difference for patients. In business, of course, we have to deliver a return on investment – but the right market exists and is receptive, as we can see from the sector's ongoing acceleration. In my university role, I am expected to make my current facility break even, but I am not being pushed to make returns to shareholders. Developing a commercial strategy would mark a change in my work, but I don't see it as a major challenge.

Centers with no center

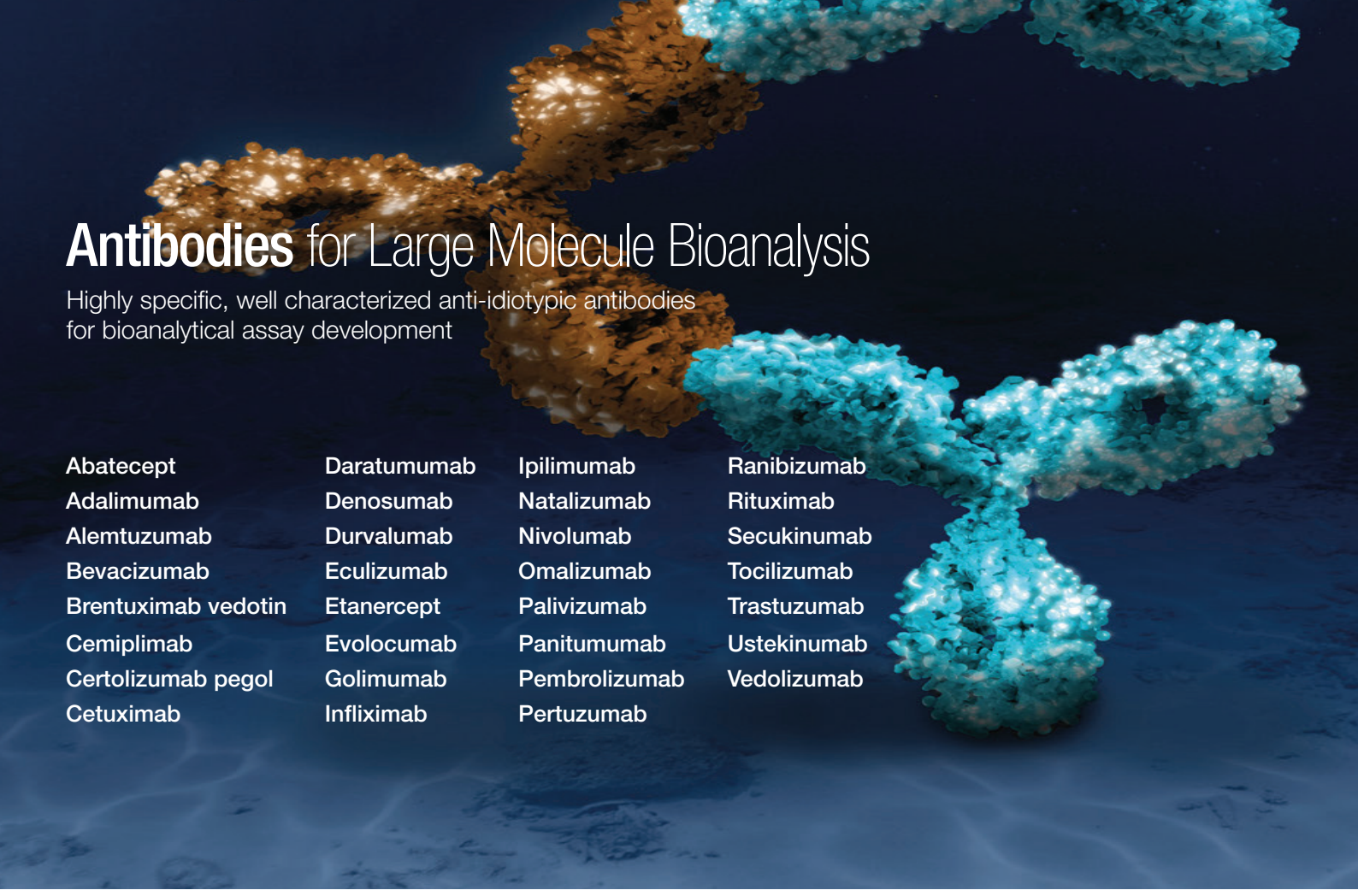
One of the factors we need to consider is scale. Academic CDMOs must take advantage of economies of scale to become profitable because there are huge costs involved in running a GMP facility. If we can create a network of academic centers with the right industry partnerships, the initial cost of setting up this cooperative enterprise will pay for itself down the line. For example, you can achieve a certain degree of leadership and quality oversight remotely – so these elements can be dispersed across your network, rather than replicated at every node. Therefore, the larger your network is, the more you can dilute these aspects of your running costs.

"If we could lead big pharma to fund the bakery, rather than buy the bread, we would shave years off the development process."

A dispersed network is also well suited to delivering autologous therapies to patients because it helps avoid the current situation. Right now, we ship materials thousands of miles to factories in the middle of nowhere only to then ship them back again. This is a bad economic practice, bad environmental practice, and adds an unnecessary high risk to your process.

To sum up…

Companies like mine must play a significant role in providing GMP manufacturing for cell and gene therapy clinical development post-grant-funding. We want to provide a bridge in manufacturing provision for smaller institutions who wish to develop cell and gene therapies, but do not have either the resources or the need to engage a large CDMO. This will enable more cell and gene therapies from a wider group of specialist organizations to progress to the clinic and potentially reach an even wider group of patients than may currently benefit from therapies in development.



Antibodies for Large Molecule Bioanalysis

Highly specific, well characterized anti-idiotypic antibodies
for bioanalytical assay development

Abatecept	Daratumumab	Ipilimumab	Ranibizumab
Adalimumab	Denosumab	Natalizumab	Rituximab
Alemtuzumab	Durvalumab	Nivolumab	Secukinumab
Bevacizumab	Eculizumab	Omalizumab	Tocilizumab
Brentuximab vedotin	Etanercept	Palivizumab	Trastuzumab
Cemiplimab	Evolocumab	Panitumumab	Ustekinumab
Certolizumab pegol	Golimumab	Pembrolizumab	Vedolizumab
Cetuximab	Infliximab	Pertuzumab	

Could your bioanalytical method development benefit from a secure, consistent supply of critical antibody reagents for PK and immunogenicity assays?

Imagine how good it would feel to save time and increase your success rates.

- You have easy, long-term access to highly specific recombinant antibodies
- You can design and optimize a selective and sensitive assay
- Your results are translatable and reproducible

Join our customers in global biopharma companies and CROs, and buy from our industry-leading range of pre-made antibodies against marketed blockbuster biologic drugs.

Visit bio-rad-antibodies.com/biotherapeutics to learn more.

BIO-RAD

Credit: Shutterstock

Core Topic
Bioprocessing

Heat-stable vaccine. A phase I trial of a freeze dried, temperature-stable TB vaccine has shown promising results. The vaccine was developed by the Access to Advanced Health Institute (AAHI) and supported by the NIH. The subunit vaccine is made from four proteins of Mycobacterium tuberculosis bacteria and combined with an adjuvant, GLA-SE, to stimulate an immune response – and proved to be well-tolerated and effective in recipients, with robust T-cell responses and high levels of antibodies. According to the team, a lyophilized vaccine has clear advantages in ease of administration, transport, and sustainability for regions with limited resources for cold-chain vaccine storage.

Lung cancer collaboration. The Lung Cancer Research Foundation (LCRF) is collaborating with Daiichi Sankyo and AstraZeneca to fund up to three research grants focusing on using ADCs to improve outcomes for patients with lung cancer. Specifically, the collaboration aims to "support research to study HER2 directed and TROP2 directed ADCs including mechanism of action, biomarkers, and resistance mechanisms." LCRF Scientific Advisory Board Chair Katerina Politi said, "The specific focus of this grant program is to further study ADCs and how they might be applied to lung cancer treatment. It is an exciting and promising area in lung cancer research."

mRNA breakthrough. The FDA has granted breakthrough treatment designation to Moderna's personalized mRNA cancer vaccine combined with MSD's Keytruda. The vaccine (mRNA-4157/V940) generates specific T-cell responses based on the unique mutational signature of a patient's tumor to stimulate an immune response, while Keytruda works to increase the body's immune system to fight tumor cells. Moderna President Stephen Hoge said, in a statement, "mRNA-4157/V940 in combination with Keytruda provided the first demonstration of efficacy for an investigational mRNA cancer treatment in a randomized clinical trial and potentially represents a new frontier in treating melanoma and other cancers."

The rectal route. Infliximab suppositories for rectal biologic delivery have the potential to improve treatment options for patients with IBD, according to a study published in the International Journal of Pharmaceutics. Exploring the use of 3D printing technology to manufacture suppositories with a uniform shape and dosage, researchers from UCL, University of Santiago de Compostela, and FabRx believe that the approach increased accuracy and consistency in drug delivery. The rectal route allows the drug to be localized at the disease site, which improves integrity and bioactivity. The study also provides proof of concept for using 3D printing as a novel manufacturing platform for biologics.

IN OTHER NEWS

Sandoz will invest approximately $400 million in a new state-of-the-art biologics manufacturing facility in Slovenia to meet global demand for biosimilar medicines

AstraZeneca looks to advance its gastric cancer research through the acquisition of KYM Biosciences and its ADC drug CMG901 Claudin-18.2

Valneva receives FDA priority approval for VLA1553 – its single-shot, live-attenuated monovalent vaccine candidate for chikungunya

Eli Lilly's solanezumab fails prevention trial for Alzheimer's disease, with both primary and secondary trial end points not met

Gilead Sciences pairs lenacapavir with teropavimab and zinlirvimab as a potential twice-yearly treatment for HIV

Welcome to the CRISPR Powerhouse

Why 2023 is the year that antibody manufacturers should embrace CRISPR gene editing

By Eric Rhodes, CEO at ERS Genomics, Ireland

It's incredible how far the mAb industry has come. The first therapeutic mAb was approved in 1986. Now, the global market for mAbs is anticipated to grow to $451.89 billion by 2028 from an already-impressive $178.50 billion in 2021 (1). We are also seeing the emergence of increasingly complex antibody therapeutics, including bi-and multi-specific antibodies, as well as small-format single domain VHH antibodies originally derived from camelids.

But while the pace of innovation in antibody therapeutics is accelerating, the challenges of manufacturing them at the scale required to meet demand remains a bottleneck. For a start, antibody bioproduction is a relatively low yield process, with each liter of bioreactor volume typically producing around 10 doses of a mAb compared with 1,400-2,000 doses of a viral vaccine (2). Furthermore, antibody production can affect cell growth and viability, even triggering apoptosis. There can also be issues with expression, post-translational modification, folding and purification, adding further layers of complexity to the manufacturing process.

Antibody manufacturers are continually looking for ways to improve and optimize production. So at this point I'd like to turn everyone's attention to CRISPR/Cas9 – the gene editing technology invented by Nobel prizewinners Emmanuelle Charpentier and Jennifer Doudna. As many of you may know, CRISPR/Cas9 (often just referred to as CRISPR) is a standalone genetic modification tool used to delete, add, or alter specific regions of the genome with high precision. It can be used in a wide range of cell types and species, including the commonly-used bioproduction workhorses of HEK293 (derived from human embryonic kidney) and CHO cells.

Unsurprisingly for such a flexible and useful technology, CRISPR gene editing could improve antibody manufacturing processes in a number of areas, including regulating apoptosis and cell cycle progression to enhance growth, engineering cells to grow at lower temperatures or in cheaper media to reduce manufacturing costs, and modifying the biological pathways within cells to ensure correct expression, post-translational modification, and folding of the resulting products (3).

At a broad level, CRISPR can be used for genome engineering of host cells to create lines that are optimized for large-scale cell antibody production. Industry leader Lonza is among a group of companies that have taken a license from ERS Genomics to use CRISPR for just this purpose.

Zooming in on the antibody production process, CRISPR can also be used to precisely control the insertion of an antibody cassette into a specific location or multiple locations within the genome of the cell. This approach reduces the likelihood of epigenetic silencing effects and helps guarantee high levels of stable gene expression. It also facilitates the rapid development of new antibody producing lines by cutting down the time required to clonally isolate high-producing cells.

CRISPR can be used to engineer the molecular chaperones that are responsible for ensuring correct protein folding, which is particularly useful for increasing the yield of antibodies that are more difficult to express (4). Similarly, genome engineering can be used to modify the enzymes involved in post-translational modification, such as the addition of N-glycan sugars, which have an important role in antibody activity, efficacy, and safety.

Unwanted binding of endogenous proteins is another problem in bioproduction. These proteins can affect antibody secretion or co-purify with the antibody being produced, causing problems during purification or downstream processing, adding time and cost to manufacturing. CRISPR can remove or alter these problematic proteins.

Another potential application of CRISPR exists in the area of antibody-drug conjugate (ADC) development. With a global market expected to reach $13.8 billion by 2028 (5), ADCs offer a more precise way of treating cancer, improving efficacy and reducing side effects. However, the addition of therapeutic payloads can disrupt antibody stability and affinity, and it can also be difficult to control the number of drug molecules that are added to each antibody. Precision engineering of modification sites using CRISPR can result in more efficient and reliable drug conjugation – and far faster and more accurately than conventional antibody engineering techniques (6).

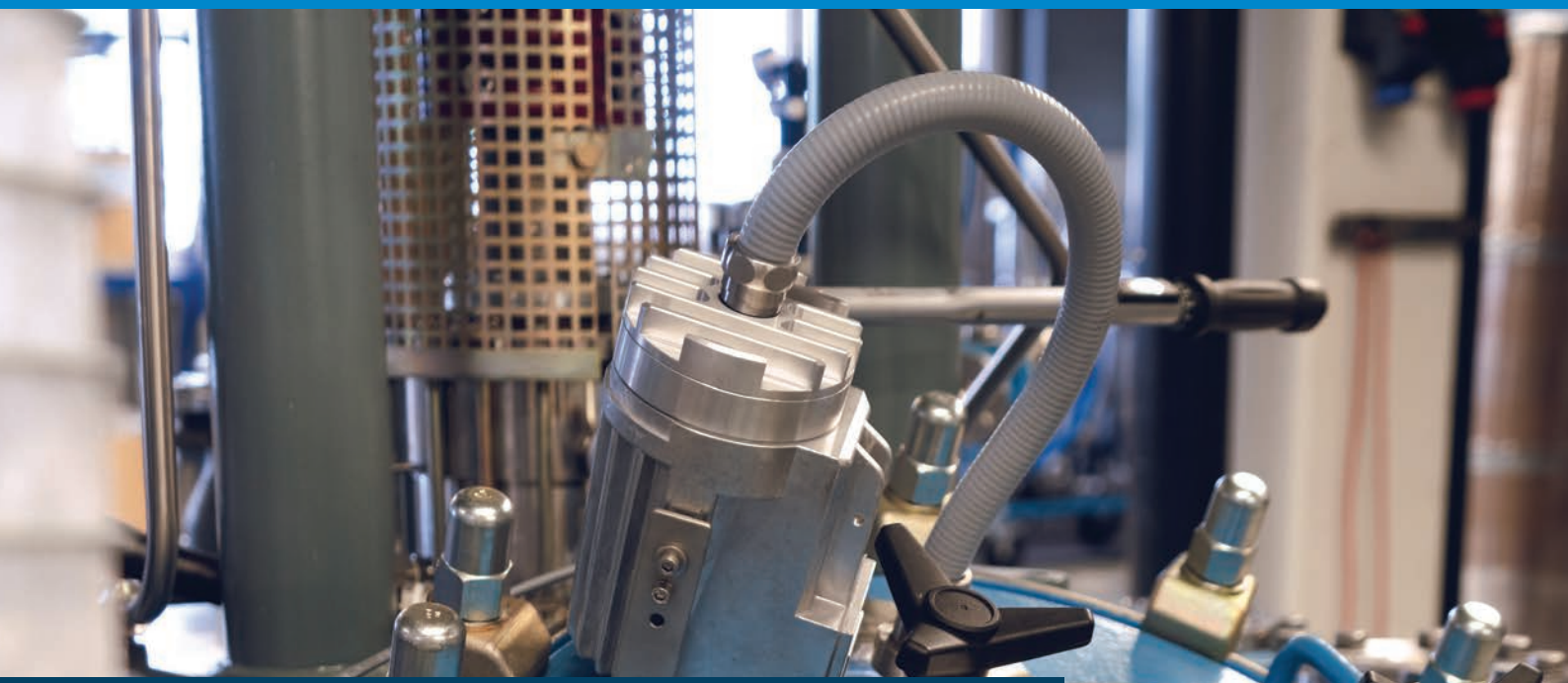
That's just a snapshot of the possibilities. The past decade has seen exceptional growth in the market for antibody therapeutics, and this trend is only set to continue. As the demand for these next-generation biotherapeutics continues to grow at pace, manufacturers should start embracing the great potential of CRISPR.

References

1. *Fortune Business Insights, "Monoclonal Antibody therapy Market Size, Share and COVID-19 Impact Analysis" (2021) Available at https://bit.ly/3ii7KiY*
2. *AstraZeneca, "Understanding the Complexities of Monoclonal Antibody Development and Manufacturing" (2022) Available at https://bit.ly/3vEvYXR*
3. *AK Dangi et al., Front Pharmacol., 12 (2018) Jun 12;9:630. DOI: 10.3389/fphar.2018.00630*
4. *LP Pybus et al., Biotechnol Bioeng., 111, 372–385 (2014). DOI: 10.1002/bit.25116*
5. *Research and Markets, "Global Antibody Drug Conjugates (ADC) Market Analysis Report 2022: A $13.8 Billion Market by 2028 – Increased Investments by Key Industry Players" (2022). Available at https://bit.ly/3XaFRse*
6. *M Khoshnejad et al., Sci Rep., 29 (2018). DOI: 10.1038/s41598-018-19784-2*

BIOSYNTH®

Securing Life Science Supply Chains



Small Molecule Manufacturing Services

- **Custom Synthesis**
- **Large Scale Manufacture**
- **GMP Manufacture**
- **CDMO Services**
- **Experts in Complex Chemicals**

Our end-to-end manufacturing services take you from the first idea to the finished product. Scale and Quality to secure your supply chain with ISO and GMP capability.

www.biosynth.com **sales@biosynth.com**

Credit: Shutterstock

Core Topic

Small Molecule Manufacture

Migraine melody. Pfizer has received FDA approval for its Zavzpret (zavegepant) nasal spray, a CGRP receptor antagonist for the treatment of migraine. Phase III study results, published in The Lancet Neurology, showed that the drug was statistically stronger than placebo on co-primary endpoints, significantly improving pain freedom in patients as early as 15 minutes after use. In a statement, Pfizer's Chief Commercial Officer Angela Hwang said, "The FDA approval of Zavzpret marks a significant breakthrough for people with migraine who need freedom from pain and prefer alternative options to oral medications." The drug should be available in US pharmacies by July 2023.

Gates funding. The Bill & Melinda Gates Foundation has granted Finland-based drug delivery technology developer DelSciTech funding to establish long-acting injectable formulations that improve and ensure the slow release of HIV vaccines. Using silica matrix technology to control long-acting drug release without interfering with therapeutic function, DelSciTech's research will work to enable parenteral delivery of complex immunogens and adjuvants, as well as mRNA encoding protein immunogens. This is the third such grant that DelSiTech has been awarded by the Bill & Melinda Gates Foundation since 2018. DelSiTech CEO Lasse Leino said, "the realization of this project will help shape a new era for vaccine development."

SMA development. Data from the SUNFISH study, conducted by Roche, shows promising long-term results for Evrysdi (risdiplam) in people aged 2-25 years with spinal muscular atrophy (SMA). Results show that an increase in motor function from baseline observed during the first year of the study was maintained through the fourth year of treatment with Evrysdi, as measured by changes in motor function measure 32 (MFM-32) and revised Upper limb module (RULM), which Roche says reinforces the long-term efficacy and safety of Evrysdi. The study also reported continuous improvement and stabilization when independently performing everyday activities.

Antibiotics assemble. Scientists from RMIT University, Australia, have created an antibiotic that can rapidly self-assemble into viscoelastic hydrogels to avoid resistance by dangerous microorganisms. Developed by PhD candidate Priscila Cardoso, the tetrapeptide Fmoc-WWRR-NH2 – named Priscilicidin – uses a small molecular with programmable physicochemical properties that can disturb the microbial membrane and attack various forms of antimicrobial resistance. The team says the approach offers clear advantages for the future of natural antibiotics, and also has a quick and cost-effective production process.

IN OTHER NEWS

Researchers from the University of Texas at Arlington gain new understanding into how aspirin reduces inflammation, which could lead to alternatives with fewer side effects

FDA accepts Lilly's supplemental New Drug Application for Jardiance as a potential heart failure treatment

License agreement between AnnJi Pharmaceutical and Avenue Therapeutics aims to develop and commercialize AJ201 for Kennedy's Disease

FDA approves Pharming Group's Joenja (leniolisib) for APDS in adult and pediatric patients 12 years of age and older

Research from the Norwegian Institute of Public Health highlights causes of market failure and scarcity of development programs in the antibiotic pipeline

What Does the Future Hold for Excipients?

IPEC-Americas look at the hot trends in pharmaceutical excipients

IPEC-Americas' mission is to advocate, educate, innovate, and develop best practices for excipients, with a focus on patient safety. This industry association brings together diverse stakeholders that share a common objective: safe and effective production and use of excipients.

IPEC-Americas provides a source for reliable current and emerging excipient regulatory information, a structure for pharmaceutical industry collaboration, a seat at the table to discuss excipient issues, and a system for education.

What's hot at the moment in the excipients space? IPEC-Americas give their view – and also let us know what the association is focusing on at the moment.

TiO_2: The Precautionary Food Ban with a Potential for Formulation Chaos

The EU's decision to ban E171 for food uses and assess pharma uses in the future, even though there is no credible safety concern, is having significant global impact. Regulators in the UK, Canada, and Australia/New Zealand have performed a thorough scientific assessment and concluded that TiO_2 is safe. If the EU (and potentially other

Discussing Novel Excipients

Have you seen The Medicine Maker's roundtable video discussion with experts from IPEC-Americas? In September 2021, a Novel Excipient Review Pilot Program was launched by the FDA that would allow excipient manufacturers to get their novel excipient approved for use in pharmaceuticals prior to use. A number of excipients have since been accepted onto the program,

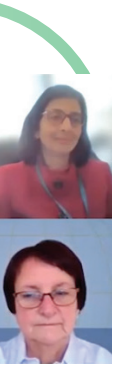
In this roundtable discussion, five experts from IPEC-Americas give their view on why the program is so important – and how it could transform the industry. Watch the discussion at: tmm.txp.to/ipecvideo

"IPEC is working to facilitate collaboration between excipient makers and users to develop a scientifically sound and consistent strategy."

countries) ban TiO_2 for pharma uses in the future, there will be negative consequences related to the availability and cost of drugs. IPEC-Americas is working with key stakeholders to provide scientific justification and advocacy for not banning TiO_2 in pharma uses.

Nitrosamines: Open Communication is Key

Nitrosamines continue to be a concern among regulatory agencies globally. Regulators require drug product manufacturers to identify products at risk for the presence of nitrosamines. The understanding of nitrosamine formation in drug products continues to evolve. Excipients are evaluated as potential risk factors during drug product risk assessments. Although there is no regulatory requirement for excipient manufacturers to complete nitrosamine risk assessments, it is in their interests to provide information that would facilitate the safe use of their excipients. IPEC has published a position paper (available at https://ipec-federation.org/position-papers/) and template (https://ipec-federation.org/nitrosamines-questionnaire/) to facilitate open communication and will continue to monitor future developments.



Co-Processed Excipients: Decoupling from Novel Excipients

Co-processed excipients, which have the ability to simplify and improve consistency and robustness of some drug manufacturing processes (e.g., continuous manufacturing) are considered as novel and face a perceived regulatory barrier for their adoption and use. IPEC-Americas is currently collaborating with industry to request the FDA to decouple co-processed excipients (meeting certain, defined criteria) from being classified as novel. This would allow greater usage of co-processed excipients in both innovator and generic drug products. Lifting the perceived regulatory barrier should also stimulate innovation and potentially allow for customization of co-processed excipients.

Microplastics: Plastics in Tablets. Really?

The European Chemicals Agency (ECHA) is moving forward with proposed restrictions focused on

synthetic polymer microparticles under the EU Restriction Evaluation Authorization of Chemicals (REACH) regulations. The extent of this regulation has the potential to create a significant compliance burden on large industry segments. Medicinal products are derogated from restrictions but subject to labeling and reporting requirements. ECHA's broad definition of microplastics will result in excipients and potentially whole tablets (< 5mm in size) being classified as a microparticle. IPEC is working to facilitate collaboration between excipient makers and users to developa scientifically sound and consistent strategy.

Latin America Working Group: Expanding Collaboration

IPEC-Americas formed a dedicated Latin America working group in Fall 2022. The working group will discuss regulatory issues related to regional and global practices for pharmaceutical excipients to determine appropriate advocacy actions. It will include manufacturers, importers, and distributors of pharmaceutical excipients as well as finished drug manufacturers in the region. It will also address hot topics and trends offering training and sharing latest industry knowledge.

A New Definition of Versatile

Looking for an adaptable screening approach for lipid nanoparticle R&D? KNAUER offers total flexibility with its new lab-scale system

Lipid nanoparticles are currently a hot topic in the industry. Here, we catch up with Svea Stephan, Application Scientist for Customized Solutions at KNAUER, to learn about the company's new benchtop system for lab-scale lipid nanoparticle production. The IJM NanoScaler allows researchers to screen for optimal process parameters for API and lipid nanoparticle formulations, presenting results that can be readily adapted for GMP-compliant small batch production.

What makes your role at KNAUER so interesting?

My role involves optimizing our lipid nanoparticle (LNP) production devices and systems, and adapting them to customer requirements. I have the opportunity to run system demos, whether at KNAUER or at customer sites, and publish results in collaboration with our partners. I take on a wide range of tasks, and there is great deal of variety in the customers I work with – and their requirements.

What's the story behind the IJM NanoScaler?

During the pandemic, the industry mainly focused on the rapid production of vaccines, but now companies are paying greater attention to R&D. KNAUER's NanoProducers are ideal for big batch vaccine production, but many of our customers wanted to screen through different APIs or find optimal lipid systems at small production scales. This demand inspired us to use our proven IJM technology to develop a system suitable for pre-clinical research and development.

The IJM NanoScaler is a highly versatile system that users can adapt to their needs in just a few seconds. Researchers can screen APIs, lipids, and process parameters to identify the optimal raw materials and process characteristics for their lipid nanoparticle formulation. Raw materials come with very high costs, so we've made sure that the system only requires very small quantities for screening – as little as 500 µL of API solution. Furthermore, if researchers wish to produce small batches up to 2 L, they can do so using the same system; by switching to GMP production mode, the system can be manually adapted in no time at all. Users can also connect and use their own mixing units.

Tell us about KNAUER's recent application note…

The application note was written in collaboration with Curapath (1), which helps companies to design, develop, and manufacture lipid-based formulations. Curapath used our IJM technology for preclinical R&D, and compared it with the traditional Herringbone mixer. We investigated the influence of the total flow rate on the LNPs produced, as well as any possible differences in single injection versus batch experiments. As well as experiments using mRNA, there were runs producing LNPs containing pDNA. We found that the NanoScaler can encapsulate mRNA and pDNA into LNPs with high reproducibility and efficiency. The resulting LNPs matched those of the traditional Herringbone, but with greater flexibility and control that can fine-tune LNP size by increasing or decreasing the total flow rate.

What feedback have you had from customers about the system?

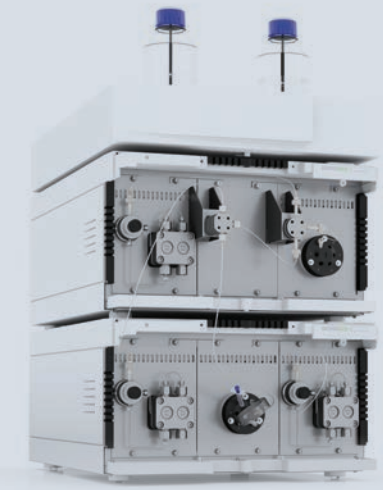
Our customers are very happy with the system and have commended the simplicity and flexibility. They are also very satisfied with the quality of the LNPs produced. By adding the IJM NanoScaler to our range, it allows customers to rely on the same IJM mixing technology for their R&D activities as their production process – and soon customers will be able to screen APIs and lipids in a fully automated manner. We are constantly in conversation with customers and we use their feedback to identify areas for improvement, as well as new innovations for the future.

What else is KNAUER working on?

We are building on our downstream purification expertise in fast protein liquid chromatography to address the need for mRNA purification. We will be investing heavily in this area over the next few years – particularly in laboratory and pilot scale systems. We want to ensure we can continue to meet customer demand for small-scale, GMP-compliant systems.

Reference

1. *KNAUER, "Development and optimization of LNP formulations – using the KNAUER NanoScaler," (2022). Available at https://bit.ly/3lCkdlB*



Business

Economic drivers
Emerging trends
Business strategies

The Golden Age of Drug Delivery

How are the last few years of pharmaceutical industry trends affecting the drug delivery landscape – and what opportunities should we grasp?

By Cornell Stamoran, VP of Corporate Strategy and Government Affairs, Catalent Pharma Solutions

I've spent more than three decades on the front lines in the drug delivery sector, including the last 10 years advocating for increased use of drug delivery to enhance patient outcomes. Looking at the current state of the industry from an end market perspective, I believe there has never been a better time to be in the drug delivery field! Pipelines are at their largest, healthiest point in history, and are more reliant than ever on enabling technologies to achieve desired patient outcomes.

New molecular entity approvals have continued their upward trend over the last decade. Based on my analysis of data available at Evaluate.com, in 2021, there were more than double the annual number of approvals versus 20 years ago. And more than 500 drugs are projected to be reaching registration stage over the next five years – clinical trial outcomes permitting.

This pipeline has been supported by strong industry R&D spend, which was estimated to be $270 billion for 2022 – almost four times the level of about 20 years ago. External funding has been strong in recent years; vibrant global venture capital and public equity markets have supported that spending expansion, investing almost $175 billion in early-stage companies across biopharma, discovery, services, and tools in the last five years. In that same period, almost $24 billion has been invested in emerging drug delivery platforms and manufacturing companies (based on data I have analyzed from Biocentury BCIQ).

Challenges, however, remain. The most obvious being the current economic environment in the wake of the global pandemic and other geopolitical challenges. Inflationary cost pressures are pervasively impacting our industry, driving up costs and leading to some recent softening of venture capital investments and new compound starts. Forecasted R&D spend growth over the next few years has also been revised downwards to low-to-mid single digits.

Other key challenges are ongoing shifts in expectations from regulators and payors. Clinical trial process expectations have continued to escalate, with more process steps/testing/data tracking/analytical needs driving up the costs per phase for drug developers and slowing down phase transitions for non-accelerated trials. Combined with rising expectations for truly representative genotypes and gender diversity in trial participants and the need for timely pediatric clinical trials (where relevant), clinical trials have grown more complex. Payors around the world are dealing with post-COVID-19 budget recovery and facing a rapidly expanding new modality pipeline of highly expensive drugs, which has led them to become even more aggressive in their control of market access and reimbursement.

We have also seen the retirement of a whole generation of leading drug delivery experts across industry, academia, and regulators. Combine this with the fast-growing need for expertise with newer large molecule modalities and vibrant new startup hiring, and we face key talent shortages across our industry.

New large molecule modalities drive delivery complexity

So, in light of the above challenges, why do I feel so positive about the future for drug delivery?

As mentioned earlier, the pipeline is very strong; based on Citeline's Pharmaprojects gold standard database, there are over 19,500 drugs in active development, with about 40 percent in the clinic. Just under half of these drugs are biologics from an ever-expanding range of modalities, each of which brings its own delivery and manufacturing challenges. Newer modality pipelines, such as viral vector-based gene therapy and autologous/allogeneic cell therapies, have reached critical mass and are growing at mid double-digit rates. Emerging modalities – such as mRNA-based therapies, non-viral vector-based gene therapies, exosomes, and microbiome treatments – are small today, but may be even faster growing if clinically successful. And proteins – monoclonal and multi-specific antibodies and fusion proteins in particular – form a large share of this pipeline.

Drug delivery for biologics, based on both pipeline and recent launches, remains primarily infused or injected, though there has been some limited progress in non-invasive delivery platforms. By reviewing historic trends in identified routes of administration there is a notable increase in the number of compounds targeted towards subcutaneous delivery, versus infusion or intramuscular methods. This trend suggests there is growing potential to reduce the total cost of treatment for such drugs in the future using patient self-administration including wearable devices.

Post-pandemic, there have been several medical professional organizations that have recommended the increased use of prefilled syringes (PFS) for in-patient infusion and injectable administration, with studies showing reduced dosing errors and improved treatment efficiency. Technologies enabling improved concentration, reduced viscosity, and sustained release of injectable formulations are gaining early ground; they will be important to support the evolution of this pipeline. And materials innovation, driven by the extreme cold chain requirements for the mRNA COVID-19 vaccines, may expand options for use of PFS and other components for compounds previously only distributed in vials.

The fast-growing new modality area brings its own opportunities and challenges for both innovators and drug delivery providers. Carriers, such as viral vectors, cells, and lipid nanoparticles, are required to deliver the therapeutic nucleic acid or other payloads. Each one influences treatment efficacy, and requires the right carrier design and formulation knowledge to select. Equally importantly, the manufacturability of these compounds continues to be challenging, while the regulatory expectations for advanced therapy medicinal products continue to evolve. Process innovation will remain critical to support these pipelines by ensuring scale-up of supply for patient populations and hopefully helping drive down production costs. The ultimate goal: reduced total cost of treatment.

Small molecule delivery challenges remain

The small molecule field is also expanding, with an increase of almost 10 percent in new oral programs alone. The mix of programs across the range of more widely used delivery routes remains relatively stable.

Bioavailability continues to be a key challenge for the new oral pipeline – particularly stemming from pipeline growth-driving mechanisms of action, such as kinase inhibitors, and from newer classes of drugs, such as protein degraders, which do not possess the optimal Rule of 5 characteristics. There are real opportunities here to advance – both in materials science, using enhanced excipients, polymers, and so on, and in predictive in silico science. Models and platforms can predict individual molecule characteristics – and perform some degree of excipient/API matching – but the process to determine the best solubility enhancement path for a given combination of patient usability and molecule still often involves compromises, which can lead to drugs with potentially suboptimal patient usability compared with what is actually – optimally – possible.

Additional effort focused on targeted delivery – less about controlling time/duration, more about site-specific release, bypassing first-pass effects, or site-specific accumulation – could potentially help create improved delivery options for both small and large molecules.

Turning opportunity into value

In my view, drug delivery is perfectly positioned to enhance the impact of new, evolving therapies. How?

First, through talent. Many companies have individual partnerships with universities and other educational establishments in an attempt to develop the workforce pipeline needed for both science and – importantly – cGMP manufacturing. There are opportunities for collaboration across boundaries, including innovators, CDMOs, and other technology providers to advocate for increased workforce development investment, starting with an increased focus on STEM education.

Secondly, harmonizing advanced technology development and regulatory acceptance. Though the FDA and other regulators have some programs that assist in early platform evaluation, advanced manufacturing and new delivery platforms need to be associated with a product filing before the FDA can devote any material degree of time and attention. However, this approach is not beneficial to support early development for delivery, device, or manufacturing platforms, which are especially important for emerging modalities. There has been some progress; for example, in December 2022 US Congress passed legislation that calls for the development of a broadly accessible advanced manufacturing technology pathway with the FDA, allowing for direct interaction with technology developers early and providing potential filing review efficiencies to sponsors who adopt those technologies, once the technology receives an advanced designation from the FDA. Working together and via our trade associations, we might be able to achieve even more support for advanced technologies in the future.

Collaboration is key – whether through new and better ways of working with academia to produce more translational research relevant to the near-to-medium needs of the industry's current pipeline or through industry working groups. The more open these collaborations are to all relevant industry stakeholders – including technology providers, not just innovators – the better. The goals for the industry as a whole remain the same: developing effective drugs that can be delivered appropriately and in a timely manner to the patient population.

I hope you share my excitement for the enhanced patient value that increased and more effective use of drug delivery will bring to today's pipeline – and tomorrow's!

NextGen

R&D pipeline
New technology
Future trends

Top Tips to Optimize Downstream Processes

From resins to buffers to single-use technologies – there are many opportunities to improve downstream processes

By Nandu Deorkar, Vice President, R&D, Biopharma; Jungmin Oh, Manager, New Product Development; Pranav Vengsarkar, Manager, Process Development; Jonathan Fura, Manager, R&D – all at Avantor

Emerging treatments, including cell and gene therapies, are exciting and are certainly starting to expand pipelines. However, traditional biologics (monoclonal antibodies) still dominate the world of biopharma. Research has shown that the clinical pipeline of antibody therapeutics grew by 30 percent over the past year (1) – excluding COVID-19 antibody therapies – highlighting the importance of these treatments and the need for their efficient production.

Given that 60–80 percent of mAb production costs can be attributed to downstream processing (2), removing downstream bottlenecks and improving yields will continue to be an important priority for mAbs manufacturers – especially amidst rising demand. Below, we offer a few suggestions.

Considering resins and buffers

In the capture step, protein A is the most widely used resin. Protein A is simple to implement as a standard purification process and holds a strong regulatory track record (3); however, the costs of the resin are substantial, making it important to optimize the process to maximize cost and efficiency. A key consideration in process optimization is understanding the role dynamic binding capacities (DBC) plays in overall protein A performance. Use of a resin with higher DBC can improve capture step productivity while maintaining column sizes and minimizing facility modification – especially when it comes to high titer cell culture processes.

To prove the point, we performed a simulation using BioSolve software, calculating the number of bind/elute cycles, process time, and volumes of buffer required for a 2000 L bioreactor

Cell culture volume	2000L
Titer	5g/L
Protein A column bed height	20cm
Protein A column volume	68.6L
Step yield	90%
Flow rate	150cm/hr
Protein A process phase	*Duration (Column Volume)*
Flush (WFI)	3CV
Equilibrium	5CV
Load	N/A
Wash	5CV
Elution	5CV
CIP (0.5M NaOH)	2CV
Storage	5CV

	Resin A	*Resin B*	*Resin C***
DBC	30g/L	40g/L	65g/L
# of Protein A cycle/batch	4	3	2
Protein A column size	68.6L	68.6L	68.6L
Process time	18.8 hours	15.8 hours	12.8 hours
Total buffer consumption per batch	4,365L	3,429L	2,496L

** 2000L Bioreactor providing 5g/L titer*

*** DBC value of Resin C was taken from experimental value (3)*

Table 1 (left): Process parameters used for simulation
Table 2 (above): Process output based on resin capacity

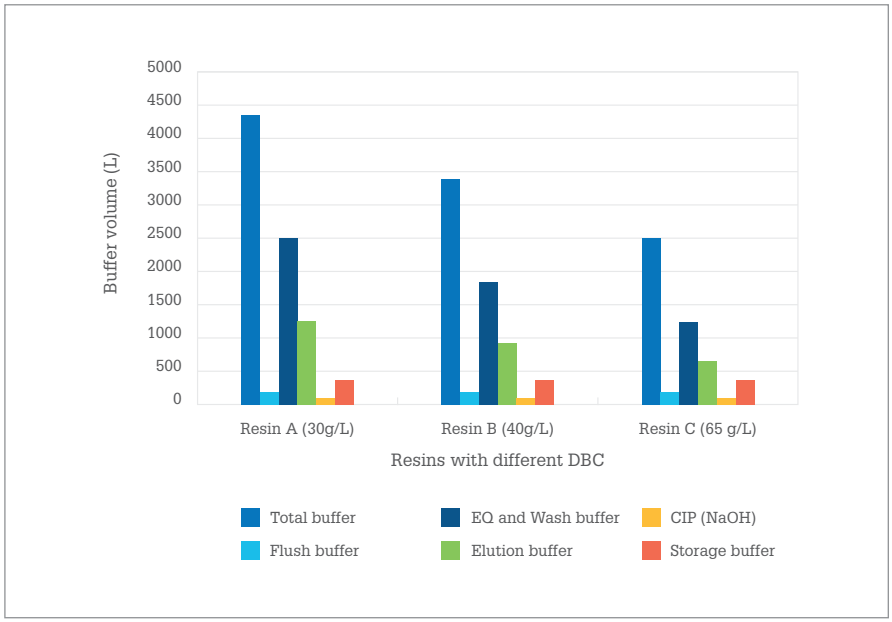


Figure 1: Buffer consumption of three protein A resins with different dynamic binding capacity (DBC) for processing of one 200L bioreactor batch

batch. We looked at three model resins with DBCs ranging from 30 g/L–65 g/L. Assumptions made for the calculations are summarized in Table 1. We maintained column size at 68.6 L for 2000 L cell culture reactor with 5 g/L titer value. We evaluated process productivity based on the number of cycles required per batch as well as process time.

What did we find? Higher DBC resins significantly reduce the number of cycles and total downstream processing time (see Table 2 and Figure 1). Notably, by reducing the number of cycles, one can also reduce operational risks and per-cycle costs for labor and consumables.

Similarly, a lower volume of buffer consumption not only reduces raw material cost, but also buffer preparation time, buffer tank size, and method of preparation. In our model, Resin C reduced total buffer consumption by approximately 40 and 30 percent when compared to Resin A and B, respectively.

Creating buffers in-house is a well-established method suitable for manufacturing large volumes; however, preparation of buffers often involves utilities and resources, such as Water for Injection (WFI), which may be constrained due to demand in other systems such as clean-in-place or other process lines. Further, the sheer number and volume of buffer solutions required for the entire downstream purification process may cause scheduling issues for the buffer prep team trying to meet the demands of the production schedule. Reduced buffer solution requirements offer additional flexibility as these operations require significant

"A lower volume of buffer consumption not only reduces raw material cost, but also buffer preparation time, buffer tank size and method of preparation."

Buffer preparation method	*Powder hydration in stainless-steel or single-use tanks*	*Multicomponent buffer concentrates with in-line dilution (or single component stocks with buffer stock blending)*	*Ready-to-use cGMP 1X buffers*
Workflow improvements	— Supply of pre-weighed cGMP powdered raw materials in pails and drums, or in single-use powder delivery systems, to eliminate solid subdivision steps and streamline pre-buffer prep operations and prevent damage to single-use buffer tanks — Delivery and use of free-flowing powdered raw materials to eliminate de-clumping steps and prevent damage to single-use buffer tanks — Supply of pre-weighed cGMP powdered raw materials in single-use powder delivery systems to enable faster charging into tanks and quicker turnaround time — Implementation of rapid ID systems in the warehouse to speed up incoming material release into production — Hot WFI usage in dissolution to speed up dissolution in single-use tanks with poor heat transfer rate (cooling or heating)	— Extractable & leachable data on single-use packaging which enables longer shelf life — Single-use in-line dilution systems to reduce cleaning validations and enable faster batch changeovers — Stability studies on buffers made using buffer concentrates to analyze shelf life — pH/conductivity sensitivity to temperature of buffers for in-line dilution system (for example, TRIS buffers are extremely sensitive to temperature) to reduce rejected buffers — Harmonized concentrates/stocks across unit operations to improve flexibility of concentrates — Robust supplier agreements and forecasting of demand to prevent supply chain issues — Standardized single-use connectors for process use to enable more flexibility across unit operations	— Stability studies available on buffers to analyze shelf life (for example, 1x buffers are typically susceptible to pH/conductivity changes over time, leading to shorter shelf life) — Robust supplier agreements and forecasting of demand to prevent supply chain issues — Implementation of rapid ID systems including refractive index and Fourier transform infrared (FTIR) testing for quick release of buffer solutions

Table 3: Workflow improvements for each of the three options

infrastructure, including warehouse space for holding raw materials prior to their use, a weighing and dispensing area for raw materials, and space to store the prepared solutions which are often stored in corridors due to lack of space. In addition, the stainless-steel tanks themselves can require a considerable footprint in the facility and frequently experience corrosion issues due to the caustic nature and high chloride content of commonly used buffers.

New developments in single-use technology have added flexibility in buffer preparation methods, allowing small- and medium-scale facilities to move to single-use tanks for buffer preparation. This has enabled faster changeovers in buffer preparation, saving both time and cost in manufacturing processes (4). Single-use fluid handling systems can help reduce bottlenecks, particularly in cell therapy manufacturing where downstream processing is often slowed by a lack of the suitable closed manufacturing systems. The closed, automated systems that are available are often unsuitable for large volumes of allogeneic cell therapies. If a biomanufacturer uses single-use equipment, a reputable supplier with a multiple-source supply chain is key to avoid disruptions.

A hybrid approach

Combining both in-house systems and outsourced buffers in a hybrid approach can help streamline downstream purification unit operations. Moreover, in-line dilution (ILD) systems can improve the efficiency of critical buffer component production.

- Clean-in-place solutions: Usually a fixed normality of NaOH, it can be prepared in-house using concentrate or purchased as a 1X concentration thanks to the smaller volumes needed, lowering safety concerns.
- Storage buffer: Due to low consistent volumes typically required (irrespective of resin DBC), storage buffers, such as 20 percent ethanol, can be managed in-house in the same way as the cleaning buffer.
- Equilibration and wash buffers: Volumes of these buffers (for example, 1X PBS or 50 mM Tris, pH 7) significantly decrease with an increase in resin DBC, as shown in Figure 1. Whether these buffers are prepared using in-house or single-use systems, high volumes can cause several operation challenges. When preparing these buffers, inline dilution (ILD) systems using multicomponent concentrates (for example, 10X PBS) can provide operational advantages. For example, ILD can help minimize facility footprint, reduce raw material management, and increase availability of buffer on demand.
- Elution buffers: Use of these buffers (for example, 0.1M acetate buffer, pH 3.4) can also be streamlined through the use of an in-line dilution system.

Workflow improvements in buffer preparation

Broadly, there are three options for

buffer prep system/process in downstream purification:

1. Single-use buffer prep reactors or chemical hydration in fixed stainless-steel tanks
2. Multicomponent buffer concentrates with in-line dilution or single component stocks with buffer stock blending
3. Ready-to-use cGMP 1X buffers

BioPhorum Operations Group (BPOG) and other industry organizations have offered insight into how buffer stock blending and in-line dilution generate overall improvements across unit operations (4, 5, 6). Choosing the right option will usually depend on an economic analysis of several factors, including scale, batches of drug produced per year, raw materials required, and other site attributes.

The flexibility and productivity of the mAb capture process step can be improved by using high DBC resins along with optimal buffer management. High-capacity resin decreases process time by allowing fewer numbers of cycles required per batch – saving cost, mitigating risk, and reducing labor costs.

In addition, implementing a high DBC resin decreases the volume of process buffers significantly, which allows the flexibility to adopt different buffer preparation processes based on facility requirements. Each facility and downstream process has unique requirements and bottlenecks, so having flexible process optimization options is important.

As innovative biologic treatments continue to emerge, manufacturers will almost certainly face even more hurdles – but, in every situation, the development of highly efficient, high yield manufacturing processes will be a key factor for success.

References

1. *H Kaplon et al., MAbs 14 (2022). DOI: 10.1080/19420862.2021.2014296*
2. *BioProcess International, "Key challenges and potential solutions for optimizing downstream bioprocessing production," (2019). Available at https://bit.ly/3GlBxzi*
3. *T Pabst, J Thai, A Hunter, Journal of Chromatography A 1554, 45-60 (2018). DOI: 10.1016/j.chroma.2018.03.060*
4. *P Vengsarkar, N Deorkar, BioPharm International 33, 17-20 (2020).*
5. *BioPhorum, "An economic evaluation of buffer preparation philosophies for the biopharmaceutical industry" (2019). Available at https://bit.ly/3GDKOUN*
6. *BioPhorum, "Nimble-Biophorum buffer stock blending system: A more advanced concept for buffer manufacturing" (2019). Available at https://bit.ly/3GJpgX6*

Time for (CAR) T

Sitting Down With… Carl June, Richard W. Vague Professor in Immunotherapy in the Department of Pathology and Laboratory Medicine; Director of the Center for Cellular Immunotherapies at the Perelman School of Medicine; Director of the Parker Institute for Cancer Immunotherapy, at the University of Pennsylvania – and 2018 TIME 100 honoree!

How did you feel when you were recently honored at Advanced Therapies Week with the Lifetime Achievement Award?

It is a huge honor – and really it's down to the team. In some cases, I've been working with people for 25 years who have been involved with this. It's great to have the recognition, particularly at such an exciting time for the field since it's the 10-year anniversary of when we started CAR T therapy in humans.

How far back in time do the roots of CAR T reach?

The first successful cell therapies in humans were bone marrow transplants in the 1980s. In this type of transplant, a donor's T cells are given to a patient with cancer, but the cells are not genetically modified. Around 1989, Zelig Eshhar at the Weizmann Institute of Science made something called "T bodies." He made the first T cell that worked with antibodies binding the target cells instead of a T cell receptor – and this is really at the heart of what a CAR is. With this work in place, it was acknowledged that T cells could be very potent for bone marrow transplants and work with an antibody redirection – a chimeric form of a cell between a B and a T cell. However, it took until 2017 to get FDA approval for a CAR T.

How did you get involved with this field?

I'm a medical oncologist and immunologist. After completing medical school, I trained in bone marrow transplantation and became interested in how T cells could activate and kill with "graft versus host disease." In the case of a bone marrow transplant, donor T cells can go out of control and cause severe damage. T cells are highly potent and research in this area has led to breakthroughs in CAR T therapy – but it's taken 25 years to get to this point.

Looking back to what first got you interested in the field, do you think the success of CAR T could have been predicted?

No one could have predicted what has happened in CAR T – for many reasons! For one thing, it actually worked a lot better in our initial trials in humans than it had worked in mice. That's a very unusual situation; over the years, many mice have been cured of cancer but there are still very few new therapies for humans. Also, back in the 1990s, there were only about five labs working on CAR T cells. There was no pharmaceutical industry involvement back then, and for the academics (including my own lab) that were working on the topic, it was more of an academic thought experiment: Could you redirect a T cell and use it to treat cancer? We weren't necessarily thinking it would or could ever be commercialized, but it worked. Back then, there was no cell therapy industry – but now there is. And the statistics are amazing.

You were in the movie Of Medicines and Miracles; how did that come about?

Ross Kauffman is an accomplished documentary filmmaker who has won Academy Awards. When he saw the first report in The New York Times about our CAR T cell therapies, he thought it would be an interesting story.

He got permission to make a three-minute documentary called Fire With Fire about Emily Whitehead's treatment, severe cytokine storm, and then recovery. That three-minute video went viral with about 25 million views, and it also served a really important purpose because it allowed people to see that cell and gene therapy had promise. It also helped increase research funding – which at the time had been difficult to obtain.

Ross Kaufman then decided to make a full-length documentary, which was released in 2022 at the Tribeca Film Festival. It's been an exciting time and I never thought in my career that I would end up in a film! I'm really glad that he has made Of Medicines and Miracles because it highlights the true benefits of these new therapies, and can help educate the public about the long-term need for funding basic science research.

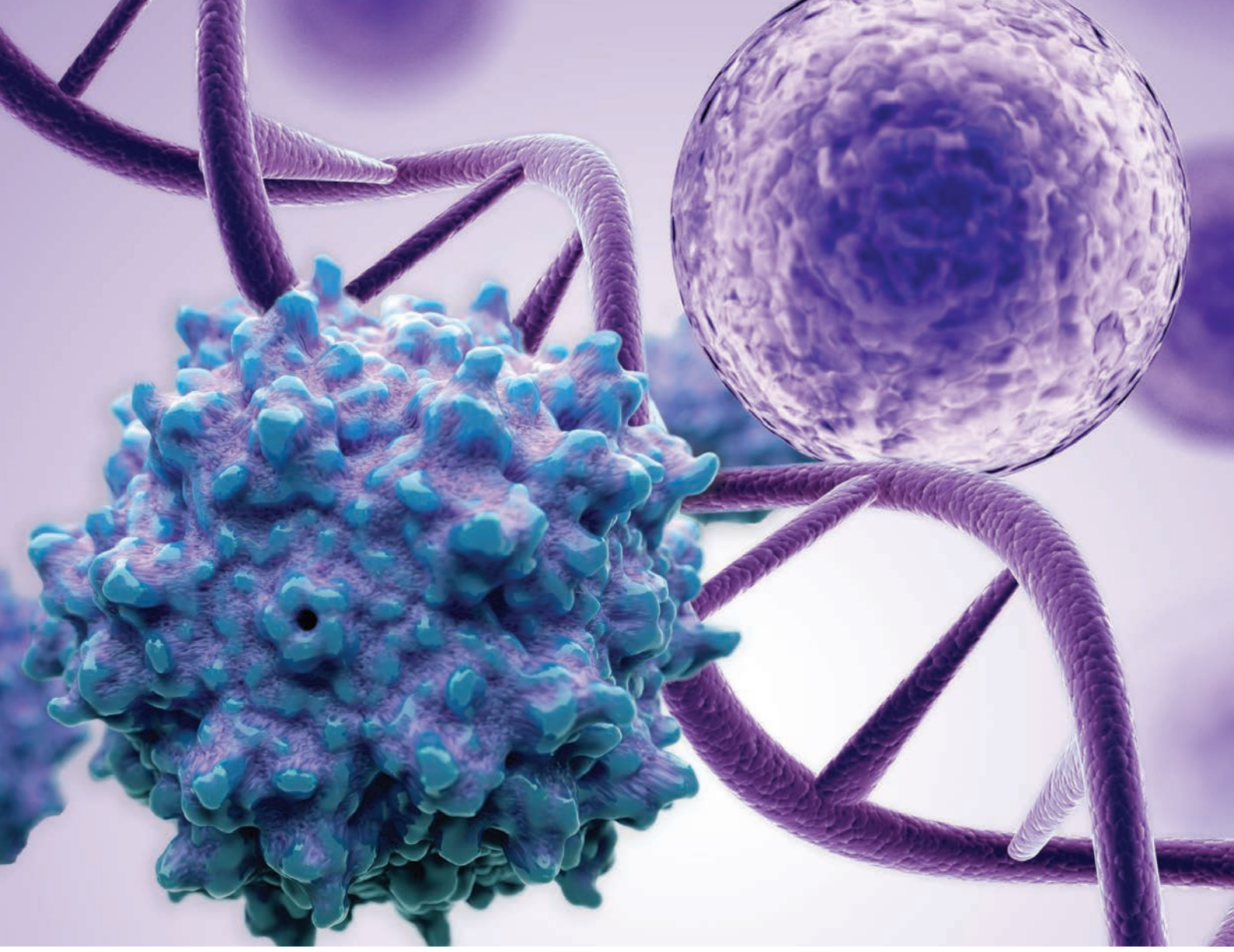
How has CAR T success affected the University of Pennsylvania?

Usually, new findings in academia at the bench get licensed and go into industry so there is a clear handover. Since there is a handoff, the academics don't really benefit from the growth or participate in new directions of the research. In the case of the CAR T cells, we worked with those first patients, and that caught the attention of Novartis, who then licensed the CAR molecule; we had a very vibrant research partnership with them.

The effect of that first CAR T trial has led us to become a center with broad experience and expertise. And that has led to new faculty, attracted very talented postdocs and graduate students, and led to huge growth and innovation at the university. But the real reason it happened is strategic planning. In the early 1990s, Penn made a strategic plan to bring in cell and gene therapy, which is how I got recruited to the university in 1999 to establish human immune therapy. Today, there is a large and diverse research portfolio at the university.

Are you emotionally affected by your work?

Personalized therapy is a unique experience because the therapy is made from the patient's own cells. When a pharmaceutical company usually makes a batch of drugs, the people who make that product never actually see the patients. But with cell therapy, it is hard baked into what we do. We get the blood from the patient and then a few weeks later the patient gets their treatment. The people in our group get to know our patients and it is hugely rewarding. We've seen cases where people are deathly ill but then they come back to our center and they are healthy: true Lazarus cases. When you are so involved with the patient, this experience is hard to put into words.



bench to commercial expertise in advanced therapeutics

Catalent is your global CDMO partner offering full-scale integrated solutions that can bring your next transformative cell and gene therapies to patients. From raw material to finished product for plasmid DNA, iPSC, mRNA, viral vector, and cell therapies, leverage our technical expertise, scale-up experience, and state-of-the-art facilities.

- AAV & LENTIVIRAL VECTORS
- PLASMID DNA & MRNA
- AUTOLOGOUS & ALLOGENEIC CELL THERAPY & IPSC
- INTEGRATED SOLUTIONS FROM PRECLINICAL TO COMMERCIAL

Catalent®
CELL & GENE THERAPY

DEVELOPMENT DELIVERY SUPPLY

Comprehensive solutions. Advanced technologies. Better biologics.

US + 1 888 SOLUTION (765-8846) **EUR** 00800 8855 6178 biologics.catalent.com