European Biotechnology

Spring 2021

Bioprocessing

Special

©Novartis

MERCK

BETTER, FASTER, SAFER

Vaccine Production

Improving Access to vaccines. Everywhere. Together.

Collaborate with our Process Solutions experts to **Accelerate** Vaccine Manufacturing.

Learn more at: MerckMillipore.com/vaccines

Millipore®
Preparation, Separation, Filtration & Monitoring Products

SAFC®
Pharma & Biopharma Raw Material Solutions

BioReliance®
Pharma & Biopharma Manufacturing & Testing Services

The life science business of Merck operates as MilliporeSigma in the U.S. and Canada.

Full books of producers!

BIOPROCESSING COVID-19 vaccine hoarding and capacity expansion in the market for cell and gene therapy or vaccine vectors currently fill the books of CDMOs. Also, Pharma giants such as Novartis most recently opened own production site at Kundl, Austria, for plasmid DNA, the raw material for RNA production and viral vector construction.

The current high demand for the mRNA-based COVID-19 vaccines from BioNTech and Moderna, and adenoviral vector vaccines from AstraZeneca, the Gamaleja Institute in Moscow and Johnson & Johnson (JNJ) has fueled the production of plasmid DNA. Plasmid DNA is required for both mRNA in vitro transcription and vector construction, even for non-COVID-19 purposes such as gene and cell therapies. While the vaccine market until 2025 is projected to make US$20bn in revenues, the gene and cell therapy currently suffers from the COVID-19 pandemic.

Analysts from Research & Markets expected the global cell and gene therapy market to lower its speed of growth from $6.68bn in 2019 to $6.92bn in 2020 at a compound annual growth rate (CAGR) of 3.61% mainly due to the COVID-19 outbreak that has disrupted the entire supply chain, impacting the market negatively. However, the experts expect the market to recover and reach $13.23bn in 2023 at a CAGR of 24.1%.

Huge market push

However, experts from Europe's gene and cell therapy hub, the CGT Catapult in Stevenage, UK, drew a different picture for UK-based gene and cell therapy trials. According to the Catapult's 2020 Advanced Therapy Medicinal Product (ATMP) clinical trials database and report, there was a 15% increase in 2019 and a 20% growth in 2020 in the number of ATMP clinical trials across the UK.

Picture: Novartis

A bird's view on Novartis centre in Kundl, Austria

As plasmid DNA is the prerequisite for manufacturing of RNA-based vaccine that provided their market proof in December 2020, 25 years after companies such as CureVac, BioNTech and Moderna pioneered its development, Big pharma companies and service providers have begun ramping up capacities for DNA plasmid and viral vector production with an eye on the larger and more durable gene and cell therapy market.

New modalities

In February, Rentschler Biopharma, the CDMO producing commercial lots of BioNTech's mRNA vaccine BNT162b2 and CureVac's Phase III candidate CVnCOV, announced that it will ramp up its mRNA production capacity at its Laupheim headquarters by 50% (see interview on page 50). Additionally, the company rented production space in Europe's most important gene and cell therapy hub, the CGT Catapult in the UK, to produce plasmids and vectors for ATMPs.

The same is true for service providers such as PlamidFactory, which received funding in February to expand its manufacturing space for minicircle plasmids that are required for RNA in vitro transcription carried out by CDMOs as well as for viral vector construction for ATMPs.

Big Pharma move

Even in November, Novartis AG, inaugurated a Centre of Excellence for gene and cell therapy production at its Austrian Kundl site, which will be used to produce plasmids – the most important basic material for cell and gene therapies – in Austria for the study medication of gene therapy pipeline programmes of the Swiss pharma giant. The rapidly growing global demand for plasmids for marketed and internal development programmes is to be covered substantially from Kundl from 2021 onwards. Novartis announced, by mid-2021, it will invest a total of US$20.4m in nucleic acid production lines at the site, and will create 45 new jobs for this purpose. At the Kundl site, Novartis has already invested US$15.7m this year in the new plasmid DNA production facility. Another US$4.7m will be used to build another facility for the production of mRNA by mid-2022.

AdeXis Inc, acquired by Novartis in 2018 for $8.7 billion, has developed a gene therapy for spinal muscular atrophy (SMA). This therapy is already approved in the U.S., Japan, the EU, Brazil and Israel. Additional approval processes are underway in nearly three dozen countries. Regulatory decisions are expected in Switzerland, Canada, Australia, Argentina, Taiwan and South Korea in early 2021. Novartis' AAV-based pipeline includes therapy candidates for the treatment of Rett syndrome, a genetic form of amyotrophic lateral sclerosis (ALS) caused by mutations in the superoxide dismutase 1 (SOD1) gene, and Friedreich's ataxia. With more than 90,000 square meters of space, Novartis has the world's largest production area for gene therapies. ■

t.gabrielczyk@biocom.eu

Gene therapy production at Novartis

Picture: Novartis

Your One-Stop-Shop CDMO for Biopharmaceuticals

Biovian's concept of a One-Stop-Shop is to provide clients with GMP CDMO services from gene to finished vial and from the laboratory bench to the clinic.

ONE-STOP-SHOP services

- Viral Vector production – AAV, Adenovirus etc.
- Plasmid DNA production
- Microbial production
- Cell Bank and Virus Seed Stock
- Aseptic Fill and Finish
- Process Development
- Quality Assurance and Quality Control

New modalities

CDMO Supporting both German mRNA-based COVID-19 vaccine developers BioNTech SE and CureVac N.V., Rentschler Biopharma SE has not only expanded into the promising field of RNA manufacturing. European Biotechnology spoke with Senior Vice President Global Business Development Federico Pollano about the company's recent expansion into the cell and gene therapy market.

EuroBiotech_Mr Pollano, with CureVac, Rentschler Biopharma recently received its second order from a COVID-19 mRNA vaccine manufacturer. What is your company doing to eliminate the perceived bottleneck in the production of COVID-19 vaccines criticised by politicians?

Pollano_*Rentschler Biopharma is contributing our know-how and competence in process development, process optimisation and cGMP production. We are supporting the downstream processing of the BioNTech vaccine Comirnaty. The process transfer from clinical to industrial scale was established in record time. Production started as early as September 2020 after discussions in April. Through close cooperation with international regulatory authorities, we were able to start manufacturing the vaccine even before market approval. We have just increased our capacities for BioNTech by +50% to meet the growing demand. For the CureVac vaccine CVnCoV, we are responsible for manufacturing, downstream processing and formulation. Our team is in the middle of process optimisation to ensure higher yield and is ramping up manufacturing in parallel. We are doing everything in our power to produce as much vaccine as possible within demanding timelines.*

EuroBiotech_Usually, it takes 12 months or more to set up a new production process that is approved as cGMP compliant. What made it possible to be faster under the conditions of the pandemic?

Pollano_*That is correct. Three things contributed to the fast process transfer: a close exchange with our clients, Rentschler Biopharma's longstanding experience as a full-service provider and, last but not least, our established working relationship with the regulatory authorities. Ultimately, for priority COVID-19 vaccine projects, time-to-market has to go hand in hand with the highest quality, as we need to ensure the safety and stability of therapeutics.*

FEDERICO POLLANO, joined the CDMO Rentschler Biopharma SE in 2018 as Senior Vice President, Business Development from Polpharma Biologics. Prior to Polpharma, he was Managing Director at Richter-Helm-BioTec and Executive Manager Pharmaceuticals at Helm Pharmaceuticals, the generics business of Helm AG. Earlier in his career, he was Head of Business Development of BioGeneriX AG and worked at Glaxo Wellcome GmbH.

EuroBiotech_Why then is there no talk of process transfer in record time, but rather permanent public claims that vaccine production has started too slowly?

Pollano_*It is but human mentality to be anxious in these unprecedented times and to highlight things that may not seem optimal, in comparison to those that are. Let us not forget that when considering the complexity of both the vaccine and the manufacturing process, it is simply not possible to ramp up production at the push of a button. Hence, I cannot fully comprehend the public perception of vaccine production being too slow. The biotech industry and regulatory authorities have in fact broken all records in terms of innovative collaboration and shortening of timelines. This achievement cannot be underestimated.*

EuroBiotech_Smaller biotech manufacturers of second-generation COVID-19 vaccines in particular say that production capacities for CDMOs are virtually sold out at the moment. How does Rentschler Biopharma see the market situation and the impact of COVID-19 on the market for CDMOs?

Pollano_*If you talk to the right providers, more is possible than you think. New technologies and formats always present opportunity. We have been monitoring new modalities closely. Hence, we could immediately transfer our knowledge and experience when it came to an mRNA-based vaccine. At the same time, we have been committed to ensuring a reliable supply of essential therapeutics to patients with life-threatening diseases beyond COVID-19. Of course, additional production capacities can be built up.*

Picture: ©RentschlerBiopharma SE

Picture: Rentschler Biopharma SE

But that takes time. Experienced manufacturers like Rentschler Biopharma are prepared to meet this challenge on rather short notice.

EuroBiotech_Rentschler Biopharma is world-renowned as an antibody producer. What does the expansion into the field of in vitro transcription of RNA mean in terms of corporate strategy?

Pollano_*mRNA has been in our focus for a long time. It will now receive an enormous boost. We are convinced that the mRNA-based therapies, which were approved for the first time in December for the prevention of infections with SARS-CoV-2, will also gain importance in other, for example, oncological indications and represent a growth field.*

EuroBiotech_Recently, your company announced a collaboration with the CGT Catapult to play in the market for cell and gene therapies. What are your strategic goals here?

Pollano_*Our entry into the cell and gene therapy field was driven by our corporate strategy to make new and innovative modalities available to our clients, using space at the Cell and Gene Therapy Catapult facility in Stevenage, UK, the leading hub for cell and gene therapy companies in Europe. With this new venture, we will establish development and manufacturing capabilities in ATMPs. In the long-term, we want to accelerate the development of the vital infrastructure and skilled jobs needed to meet the rising demand for manufacturing capacity in the UK and globally.*

EuroBiotech_In addition to thematic expansion, how is Rentschler Biopharma's geographic expansion progressing and where are the next milestones?

Pollano_*Our Milford site near Boston is performing well, as evidenced by the collaboration with Genmab to produce bispecific antibodies using Genmab's DuoBody® technology platform, agreed at the end of May 2020. Furthermore, we are offering early formulation development directly out of our Milford site with our strategic partner Leukocare, since January 2021. The aim is to better support our U.S clients with this unique combination of profound know-how in biopharmaceutical formulation development with in-house biostatistics and artificial intelligence expertise.* ■

t.gabrielczyk@biocom.eu

A simple change delivers faster study start-up

CRO Study start-up is a chaotic time. There are lots of moving parts. Lots of decisions to make and processes to establish. Lots of room for error. Mistakes can quickly derail a trial – and delays are endemic. That all represents a potential waste of time and resources – just at a moment when speed is of the essence. In many cases, the problem comes down to spreadsheets.

› Kristin Mauri, Director of Solution Services, Remarque Systems

Life science industry reports indicate that early stages of study start-up take twice as long today as they did five years ago. As trials have grown in complexity, so too have data collection activities related to site identification, feasibility ranking, and site selection, as well as the masses of paperwork related to IRB and ethics committee approvals. The processes used to gather, organise and share all this information are largely unchanged. In a recent survey, fewer than a quarter of operations teams report using site portals – and more than 81% admit to still using spreadsheets to plot their start-up process.

Spreadsheets are a suboptimal study start-up solution for several reasons. Manual processes are not only time-consuming, but they are susceptible to human error, difficult to troubleshoot, and obstructive to regulatory compliance. Furthermore, paper-based information exchange methods require multiple document handoffs between study partners, lacking immediacy that slows decision making.

Operations teams are grasping the value of automating key components of study start-up by turning to products like Remarque Study Start-up, which combine the ease of spreadsheets with an approach specifically designed for activity tracking and project management. Such systems eliminate the issues with paper-based approaches and deliver additional transformative advantages.

Remarque Systems was put to the test when a pharmaceutical company raced to begin phase III trials for a potential COVID-19 therapy. With the pandemic as a catalyst, the team harnessed technology to accelerate their processes and turned to Remarque for solutions. Remarque was able to supply solutions in an easily implemented, technology-agnostic platform. In short order, the sponsor was able to identify and onboard sites with active onsite clinical research staff, active IRB with rapid turnaround, and a significant caseload of COVID-19 patients. Critically, they moved to launch in under a month.

Configurable technology can simplify and speed every aspect of study start-up and deliver a project management-driven approach to site start-up. By seamlessly handling all the inherent intricacies from concept to launch – faster and more efficiently than the traditional spreadsheet-based methods – can have a striking impact on study timelines. As trial start-ups face more complex demands and industry frustration grows, adopting such technology seems like the wise move. ■

Picture: Premier Research

All for one, one for all!

BIOCOM CARD Europe Individual

- European Biotechnology Magazine Subscription
- European Biotechnology Guide 2021
- Guide to German Biotech Companies 2021
- conveniently accessible ePapers
- Discount for BIOCOM events for 1 person
- additional partner offers

Price: **80 Euro p.a.** (incl. VAT)
Students 50% discount (subject to proof of enrolment)

BIOCOM CARD Europe Corporate

- European Biotechnology Magazine Subscription
- European Biotechnology Guide 2021
- Guide to German Biotech Companies 2021
- conveniently accessible ePapers
- Discount for BIOCOM events for 2 persons
- additional partner offers

Price: **120 Euro p.a.** (plus VAT)

european-biotechnology.com/card

BIOCOM®

Biopharma partnerships – a key to success

DSP Innovators at Rentschler Biopharma are continuously developing new processes for biopharmaceutical production to tackle life-threatening diseases. Two of them, Dr Birgit Ehrenberg, Process Manager, and Monika Häußler, Quality Control (QC) Manager, shared insights into their latest projects and how close collaboration with chromatography experts from Tosoh Bioscience helped them develop robust, scalable, and economically viable downstream processes, as well as corresponding reliable bioanalytical methods.

In her latest work, Birgit focused on the polishing of antibody-based molecules using ion-exchange chromatography in Rentschler Biopharma's purification platform. The two pivotal reasons for her to implement the innovative salt-tolerant resins from Tosoh Bioscience, TOYOPEARL® Sulfate-650F and TOYOPEARL NH2-750F, were their unique performance and the professional support she received during method development.

Birgit Ehrenberg: TOYOPEARL Sulfate-650F demonstrated superior polishing capabilities during the process development for a new antibody fragment design. These properties were not provided by other conventional cation exchange resins that were tested in parallel. The resin demonstrated sufficient protein binding capacity at elevated ion strength while removing aggregates in bind-elute mode, accomplishing 98% or higher monomer content as determined by HPLC.

Additionally, the different and unique selectivity of TOYOPEARL NH2-750F anion exchanger was evaluated during the polishing step in the purification process of yet another designer molecule. Not only did it demonstrate sufficient high protein binding capacity at elevated ion strength, but it was also successful in removing aggregates in bind-elute mode at a pH close to its isoelectric point. We did face some challenges during process evaluation. For example, we quickly realized that buffer fine-tuning would be necessary to optimize aggregate removal. To this end, we optimized conditions to develop a robust process step. Tosoh's customer support and the Application Note publication provided relevant information which aided our decision-making. When it came to implementation, we also appreciated the detailed Regulatory Support Files (RSF) in case of product contact in addition to the Certificate of Analysis. This is important for the extraction of the data supporting pharmaceutical toxicology evaluation or sanitization options. To summarize, the Tosoh Bioscience product quality, customer service, and fast supply chain ensured a very productive collaboration. Additionally, support was extended immediately by a very knowledgeable technical team. I would like to take this opportunity to thank Tosoh for its professional expertise.

Picture: Rentschler

Reliability and reactivity

Other projects at Rentschler Biopharma focus on antibody fragments, one of the most promising new antibody classes for therapeutic applications. After the Downstream Processing (DSP) team developed a purification platform based on TOYOPERL AF-rProtein L-650F, Monika's team assessed the Protein L leaching in the product pool after capturing. Due to the low level of leaching using the stable Protein L resin from Tosoh Bioscience, Monika needed to ensure that the ELISA method was accurate, robust, and sensitive.

Monika Häußler: Reliability is a key factor while making the decision to implement a new method in our toolbox. Other factors such as the guaranteed delivery

Meet Rentschler Biopharma's experts

Dr Birgit Ehrenberg is a process manager in the MSAT (Manufacturing Science & Technology) team. She oversees DSP processes and chaperones client Active Pharmaceutical Ingredients (APIs) throughout the complete product life cycle. Together with her team, she always aims to develop robust, scalable, and economically viable downstream processes to maximize product potential. This includes the design and documentation of process qualification and validation at manufacturing scale within demanding clinical and commercial timelines. Additionally, she is responsible for establishing control strategies and continued process verification to ensure the highest quality in biopharmaceutical production.

Dr Birgit Ehrenberg (left), Monika Häußler (right)

Monika Häußler is a QC Manager in the quality control development department. With her team, she is responsible for the International Council for Harmonization (ICH)-conform establishment, qualification, and validation of bioanalytical methods that will later be used to release cGMP (Good Manufacturing Practice) batches. Rentschler Biopharma's bioanalytical laboratory regularly applies ELISA-based methods, such as potency determination of the API or quantification of process-related impurities like Host Cell Protein (HCP) or Protein L. Monika also conducts quantitative polymerase chain reaction (qPCR), cell-based assays and analytical techniques for new API formats such as mRNA-based vaccines.

She applies a quality by design approach – a scientific, risk-based approach, focusing on integrating high-quality into a product right from the beginning. Furthermore, she is constantly implementing new state-of-the-art methods and products into Rentschler Biopharma's portfolio, such as the aforementioned mRNA-based vaccines.

of reagents and materials of consistently high quality over a long time are essential. Tosoh Bioscience made three of their Protein L-T36 Kits available to us for testing, free-of-charge, allowing us to evaluate the reproducibility of the method. We aimed to build on our existing know-how and experience during testing to give feedback for potential improvements for the kits. Tosoh accepted our suggestions and implemented them promptly. We were also offered an advantage from the logistics perspective as the delivery time of the kits was shortened by stocking up on some kits in Europe, thereby circumventing shipment from Japan.

Finally, the collaboration with Tosoh was very pleasant and professional. We were always supported in a friendly, open-minded, interactive, supportive, and prompt manner.

Changes and expectations

During our interview, Birgit and Monika shared their thoughts about the future of the biopharmaceutical industry and, more specifically, downstream processing and biomolecule analytics.

Monika Häußler: The biopharmaceutical industry has always been very innovative and will undoubtedly come up with many new targets and products in the near future. An excellent example of this is messenger RNA (mRNA)-based biopharmaceuticals that are relatively new to the market. Working with new molecules and formats means having to improvise and innovate continuously. The analytical industry must be equally innovative to foster and support the growth of these new modalities. This will be vital in ensuring high product quality and patient safety. In general, higher throughput with optimum efficiency could be facilitated by the increased incorporation of automation through the usage of minimum material and closer linkage between the analytics and purification steps.

Birgit Ehrenberg: Complex biomolecules demand increasing flexibility of all parties involved. A continued modular and versatile capacity management along the supply chain will be extremely significant in the years to come. Besides, a supportive IT landscape for just-in-time-delivery and growing databases for rapid communication will be key to translating scientific research into outstanding biopharmaceuticals. As biopharmaceutical formats grow more complex, it is crucial that downstream processing and biomolecule analytics keep pace to ensure the highest quality. This is of utmost importance to our work here at Rentschler Biopharma.

Contact
Patrick Endres, Junior Manager Application Development at Tosoh Bioscience GmbH
patrick.endres@tosoh.com

Dr. Romain Dabre, Senior Product Manager at Tosoh Bioscience GmbH
romain.dabre@tosoh.com

Rentschler Biopharma:
communications@rentschler-biopharma.com

Picture: Rentschler

A very "cool" topic in the pharmaceutical industry

DRUG STORAGE The current debates regarding vaccine production and logistics have also made it clear even to the layman: Pharmaceutical production depends on cold. Temperatures below –80°C are just as common as the requirement to freeze precursors such as blood plasma within a specified time period. Refrigeration specialists with pharmaceutical know-how are in demand for these challenging tasks.

› from Dipl.-Ing. Christoph Wiemer, L & R Kältetechnik GmbH & Co KG, Sundern, Germany

Absolutely reliable provision of ultra-low temperatures: This is a requirement in many pharmaceutical production plants. Cooling systems installed in large production sites can reach a cooling capacity in the megawatt range and are 100% fail-safe thanks to redundant refrigerating circuits.

A current trend in the sensitive task of supplying process media and energy is the desire for high energy efficiency, which can be met by advanced drives and control systems, among other things. Equally important is the use of high quality components (pumps, heat exchangers, etc.) with very high efficiency. Central energy consumers such as compressors and pumps can either be speed-controlled or divided into several circuits to be switched on and off in a staggered manner.

The effects of the EU-wide F-Gas Regulation, which calls for a gradual "phase-down" of the refrigerants used to date, are still a hot topic and the subject of much discussion. Companies in the pharmaceutical industry are pursuing various strategies for the use of future-proof and environmentally friendly refrigerants. Some use new refrigerants such as HFO blends, while others basically rely on natural refrigerants such as propane, propene, CO_2 or ammonia.

New concepts for cooling

As an alternative to "classic" product cooling in an ultra-low temperature environment, contact cooling is gaining acceptance in some areas of application, enabling faster and more precise freezing times. A typical example is the freezing of blood plasma in bags. Another trend is the replacement of deep freezers with walk-in deep freeze storage. Vaccine serums, stem cells, bone marrow and biomedical materials can be stored in them at temperatures typically ranging from –20°C to –80°C. Depending on each case, this solution achieves its economic break-even point when more than 10 to 15 of the usual deep freezers would otherwise have to be used.

L&R Kältetechnik (*www.lr-kaelte.de*) has been implementing all of these concepts for and with companies in the pharmaceutical industry for many years now. Based on this industry-specific know-how in refrigeration technology, an innovative system concept has recently been developed that specifically addresses vaccine logistics. The basic idea: A well-insulated storage cell of –20°C to –80°C with an anteroom temperature of –10°C to –20°C is installed in an industrial container with corresponding redundant, multi-stage refrigeration technology in order to guarantee a suitable (and mobile) pharmaceutical storage option for millions of doses of vaccine.

Two highly efficient, redundant refrigeration systems are installed in the 20' or 40' containers. The interior equipment of the GMP-compliant facility is adapted to user requirements. And if the vaccine supply should be completed at the current location, the containers can fulfil the same or a different task at another location. The operator thus benefits from both a useful and sustainable long-term investment. ■

Picture: www.l-r@kaelte.de

eppendorf

Scale Up!

Seamlessly transition your process to the next level

Many engineering parameters need to be considered to ensure a successful tech transfer from bench to pilot and production scale.

Efficient and reliable scale-up is no hurdle anymore with the BioFlo® 720 bioreactor control system*.

> **Scalability:** Compatible with the Thermo Scientific™ HyPerforma™ 5:1 Single-Use Bioreactors (S.U.B.)
> **Efficiency:** Intuitive software tools such as *Auto Calibrate* and *Auto Inflate*
> **Application Driven:** Documentation packages available to help assist qualification into cGMP biomanufacturing environments

www.eppendorf.com/bioflo720

* BioFlo 720 is not a medical device as defined by the Food and Drug Administration or other regulatory authorities.

AAV vectors from a CDMO that cares about SMEs

AAV VECTOR MANUFACTURING The future of AAV vector-based therapies holds great promise if manufacturers can cope with the demand. While in-house manufacturing may be an option for so me companies, partnering with a CDMO can be the best choice for others. Teaming up with a One-Stop-Shop CDMO can make it easier to achieve the project goals. There are many reasons for this.

› from Magnus Gustafsson, Head, Global Business Development; Artur Padzik, AAV Production Manager; Biovian Oy, Turku, Finland

GMP manufacturing of AAV vectors for medicinal human use is a highly regulated process. The production facility needs to be designed for both GMP and biosafety, and certifications from regulatory authorities are required for compliance verification. Setting up the infrastructure from the start and hire of experienced scientists and operators can be a challenge for drug developers as time frames are tight. Not to mention capital investment that may be out of reach, especially for small and medium enterprises, SMEs.

Biovian is a One-Stop-Shop CDMO, which means that the offered AAV vector services span from the laboratory bench to the clinic. The 4000 m^2 facilities and processes are EMA certified and FDA inspected. Switching providers at various stages could cause costly delays and risks, so Biovian is licensed for GMP production of both investigational drugs and commercial gene therapy products. Part of the One-Stop-Shop concept of Biovian is to source or produce GMP-grade materials, such as plasmids and cell banks to get you started. We also provide access to the newest production platforms through our partnerships. To complete the service chain, an aseptic filling is provided under the same roof. Full GMP documentation and detailed batch records are provided, and our Qualified Persons are at your service to ensure that products are certified for clinical use before shipping.

Caring for the needs of SMEs

How to secure a production slot? The AAV vector manufacturing capacity at Biovian has more than doubled since the opening of the new state-of-the-art production facility. Forming a partnership with us at an early stage helps us design a production road map for you. Biovian has gained the reputation as a CDMO that provides premium services to small and mid-sized companies - those are at the core of innovation but often find themselves overrun by bigger clients when reserving CDMO resources. We understand that early-stage trials require fast response, a high degree of customization and flexibility in production. Net Promoter Score as high as 72 in client satisfaction speaks for itself.

Flexibility and Scalability

The rapid growth in the development of AAV vector-mediated gene therapy products has increased the need for small to medium-sized batches. Biovian responds to the need through flexible process development or efficient technical transfer, depending on the starting point. At the same time, the importance of scalability can't be overemphasized. Our processes are built with scale-up in mind to minimize the need for process changes and for studies required to demonstrate equivalence.

To summarise, the main goal of a CDMO is to manufacture AAV vectors efficiently and cost-effectively to support client success. Biovian's One-Stop-Shop service concept is designed to provide flexibility in all clinical phases. In this way, Biovian supports SMEs as they take their valuable AAV vectors through the development and onto the market. ■

Picture: Biovian

How do I find a new job or a new employee? Now, there is an easy solution: **eurobiotechjobs.net,** the Europe-wide job market for biotechnology and the life sciences. Presented by the European Biotechnology Network.

Photo: Freepik.com

eurobiotechjobs.net

Don't bet only on vaccines!

COVID-19 THERAPY First emergency approvals of vaccines and antibody drugs in less than a year are great achievements of modern biotechnology in our battle against the COVID-19 pandemic, but we still have no efficient therapeutics to cure severe COVID-19. Millions of lives remain at risk until we control the pandemic, and what if we will never reach herd immunity? Waiting for others to do the job cannot be the strategy, as well as betting only on vaccines.

› Dr Thomas Schirrmann, CEO, YUMAB GmbH

One year has passed after World Health Organisation (WHO) declared COVID-19 a pandemic. Back then, no one ever expected, how much the new coronavirus SARS-CoV-2 would impact the entire world not only our societies and economy but also our individual lives. As of the end of February, the WHO recorded more than 110 million infections and about 2.5 million deaths world-wide. According to the United Nations (UN), the global economy is expected to lose nearly $8.5tr in output over the next two years due to the pandemic.

In December 2020, the first vaccine achieved emergency approval in a record time. This success feels like the light at the end of the pandemic tunnel, but without efficient cure of severe COVID-19 cases, millions of people are still at risk and before we reach herd immunity – if we ever will reach it. Patients often lose neutralising antibody titers soon after convalescence, which could make them again susceptible to re-infection. We can argue that vaccines stimulate immune protection stronger, but there are only data available from a few months. No one can predict, how the situation will look like in 12 months. Meanwhile, the virus changes, adapts and develops new properties continuously.

Changing virus

First SARS-CoV-2 mutations led to increased infectivity and reduced the efficacy of some vaccines. We need to stay alerted and continue to develop better vaccines and more importantly, we need an efficient treatment option to save lives as soon as possible.

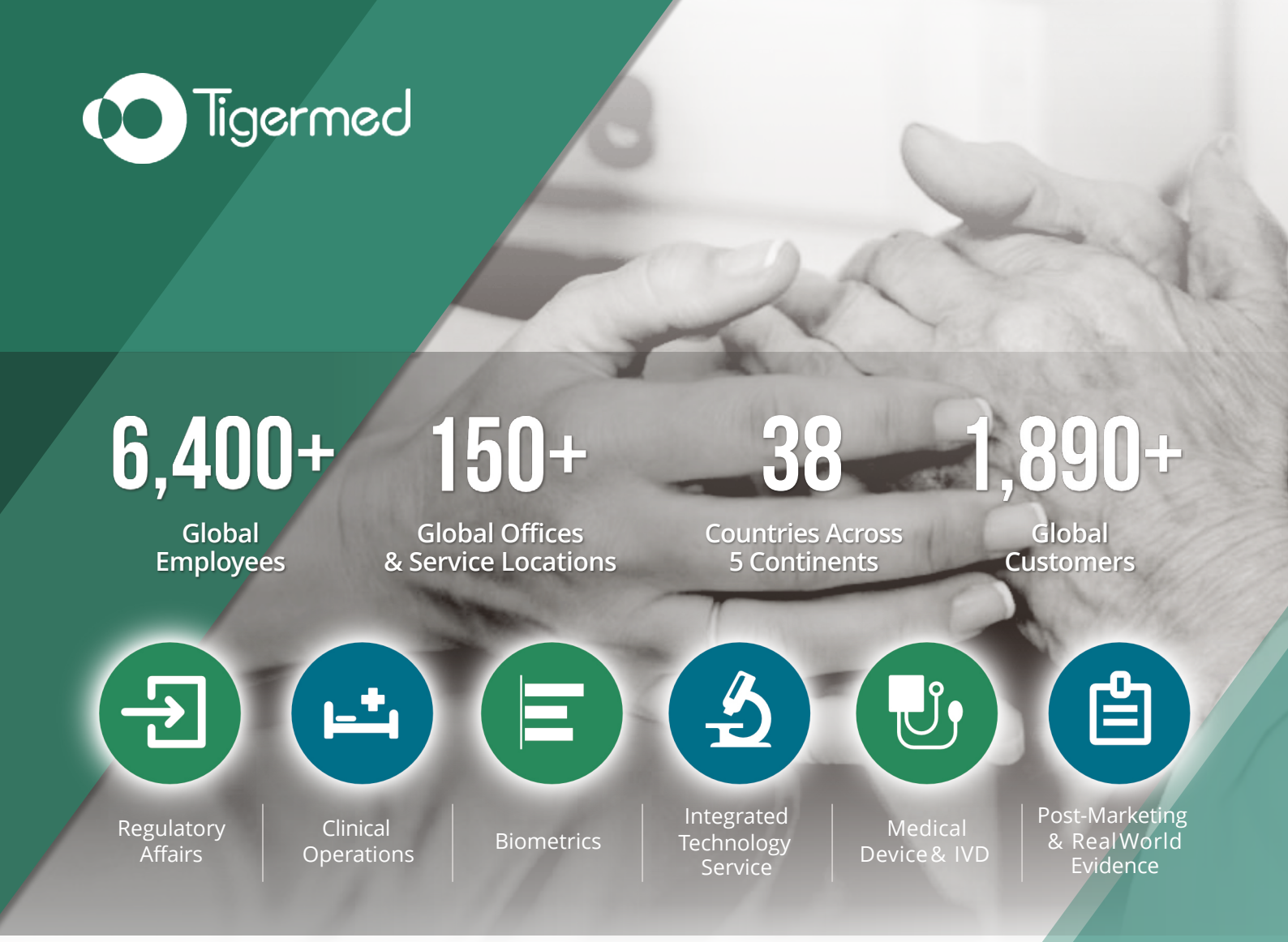
Picture: Yumab

Unlike vaccines, virus-neutralising antibodies can stop the virus after infection. Thanks to robust industrial processes, large manufacturing capacities, but also smaller clinical cohorts, antibody development even beat the timelines of the novel vaccine platforms.

Eli Lilly's antibody bamlanivimab received emergency approval for US patients on November 9th, 2020, followed by Regeneron's antibody cocktail REGN-COV2 two weeks later – both before any vaccine. The US government funded both antibody programs with more than US$800m. Unfortunately, both drugs do not help in cases of severe COVID-19. That is why we urgently need other therapeutics to save the lives of many patients. For example, CORAT Therapeutics' COR-101 antibody program employs a novel Fc design that avoids immunological safety risks of conventional antibody drugs. COR-101 was developed in less than eight months from discovery to GMP. The clinical phase Ib in patients with moderate to severe COVID-19 patients is planned for March 2021.

However, new therapeutic programs such as COR-101 have not been substantially supported by the German government, which leads to unnecessary delays just because of financial limitations. We urgently need the same support of drug development as we did for vaccines or we will always be one step behind the virus. ■

Tigermed



6,400+
Global Employees

150+
Global Offices & Service Locations

38
Countries Across 5 Continents

1,890+
Global Customers

Regulatory Affairs | Clinical Operations | Biometrics | Integrated Technology Service | Medical Device & IVD | Post-Marketing & Real World Evidence

Tigermed Group

Tigermed (Stock code: 300347.SZ/3347.HK) is a leading provider of innovative clinical research solutions across the full life cycle of biopharmaceutical and medical device products globally. With a broad portfolio of services and a promise of quality, from clinical development to commercialization, we are committed to moving our customers and patients through their development journey efficiently and cost-effectively, embracing challenges to fulfill our commitment to serve unmet patients' needs, and eventually saving lives.

Excellence In Every Trial For Every Patient

www.tigermedgrp.com
marketing@tigermedgrp.com

Advancing protein production with Pichia pastoris

RECOMBINANT PROTEIN PRODUCTION Effective bioprocess development starts with the targeted and time-saving generation of high-productivity strains already considering economic target values and regulatory requirements. The UNLOCK PICHIA technology platform comprises a large number of versatile expression tools for the generation and identification of effective industrial protein production strains without compromising development timelines.

› Dr Thomas Purkarthofer and Dr Evelyn Trummer-Gödl, VALIDOGEN GmbH

Recombinant DNA technology was initially applied in microbial hosts. The first commercial biopharmaceutical products, such as insulins, growth hormones, and interferons, were produced in bacteria or yeasts. Since then, the market demand has instigated the development of a number of different expression hosts including bacteria, yeasts, fungi, insect cells, mammalian cells and transgenic plants or animals.

Mainly driven by the commercial success of monoclonal antibodies (mAbs), mammalian cells have become the dominant recombinant protein production system for biotherapeutics. However, biologics pipelines are moving from standard mAbs to novel biotherapeutic formats such as small antibody derived formats, non-Ab scaffolds and bioconjugates with less complexity in terms of size and post-translational modification. The changing nature of biotherapeutic pipelines and the increased use of recombinant proteins in non-pharma applications strongly foster the development and optimisation of more cost-efficient microbial expression hosts.

Among these, the approved (FDA, EMA) and safe (GRAS, QPS list) expression host *Pichia pastoris (Komagataella phaffii)* features cost-efficiency, simple genetic modification and cultivation procedures as well as a powerful secretion capability and subcellular protein processing system that is required for post-translational modifications, which is an advantage over bacterial systems.

Picture: VALIDOGEN GmbH

To address today's bioprocessing needs and to allow for the exploitation of the growing market potential, access to high-productivity technologies ensuring competitive bioprocess development timelines is necessary.

With manufacturability in mind

VALIDOGEN is addressing these needs by early consideration of production strain and process requirements. The versatility of its UNLOCK PICHIA protein production platform provides the tools and genetic diversity necessary for fine-tuning protein expression.

Key to productivity and development speed is the targeted application of the full toolbox by high-throughput generation and comparison of thousands of combinations of different promoter variants, strain background, helper factors, secretion signals or production regimes.

All aspects of manufacturability from targeted debottlenecking for yield maximisation, to product quality (including glycosylation issues) and regulatory requirements (antibiotic-free strain selection) as well as process safety (methanol-free production) and process economy are considered and integrated at the earliest possible stage during strain development. Hence, high-speed industrial protein production strain generation is assured paving the way for economically viable processes. ■