BIOPHARMA CDMO SUCCESS REQUIRES TECHNICAL LEADERSHIP AND PROBLEM-SOLVING CAPABILITIES

> BY **FEDERICO POLLANO,** RENTSCHLER BIOPHARMA SE

Biologics command a growing position in the biopharmaceutical market. As more antibody and other advanced therapies reach the commercialization stage, branded biologic and biosimilar development companies are increasingly turning to outsourcing partners that provide holistic solutions. CDMOs today must offer more than manufacturing support; they must be solution providers that can support clients from concept to market. Rentschler Biopharma has a long track record of innovation designed to support rapid development and commercialization.

EXPANDING MARKET

Since their introduction, biologic drugs have shown great potential to treat diseases not possible to remedy with traditional small-molecule drugs. As successes are achieved and our understanding of the physiology of diseases deepens, biologics are attracting even more attention. The advent of biosimilars and the expansion of the middle class in many emerging markets are further fueling the growth of the biopharmaceutical sector.

According to Transparency Market Research, the global biologics market will be valued at $479.7 billion by 2024 and is expanding at a compound annual growth rate (CAGR) of 10.9%.[1] Variant Market Research pegs the market as growing at a CAGR of 10.3% from 2016 to 2024, reaching a value of $394 billion by the end of the period.[2]

The Business Research Company estimates there are currently more than 1,000 biologic drugs in development and predicts that the U.S. FDA's focus on reducing time to market will lead to an increase in year-on-year growth of the biologic market from a recent 5.4% to 9.6%.[3]

PERIOD OF EVOLUTION

The first biologic drugs were hormones and simple proteins. Today, more complex monoclonal antibodies (mAbs) and recombinant proteins dominate. The market is dynamic, however. It is expanding in value and volume and broadening with respect to the types of disease mechanisms and disease classes being tackled.

Currently, treatments for autoimmune disorders, diabetes and cancer account for nine of the top ten marketed drugs; over 50% of generated revenue and 70% of market growth since 2010.[4] New therapies are, however, being developed to treat a host of other indications. More than 50% of biologics in development target diseases for which no or only a few biologics have previously been brought to market.[4]

According to QuintilesIMS, 25% of biologic pipeline candidates target diseases for which there are large patient populations that have mostly seen only small molecule therapies which can be improved upon and are now highly genericized.[4] The firm notes that "biologic agents entering these indications will be transformative not only because of their disease modifying efficacy in clinical trials, but also because of the rapid change in disease market size and growth that would follow a successful launch."

GREATER NEED FOR CDMOS

The evolution of the biologics market has resulted in increased complexity of development and manufacturing. Biologic drug substances are highly complex and more challenging to produce. Advances in automation and process analytics are leading to the generation of massive quantities of data that must be processed. Regulatory requirements are increasing while development timelines are decreasing, making project management more challenging.

Many branded biologic and biosimilar companies are, as a result, more frequently relying on contract development and manufacturing organizations (CDMOs) that have the capabilities, expertise and experience needed to rapidly move projects from concept to market.

From 2014 through 2017, the global biopharmaceutical contract manufacturing market grew at a much higher CAGR of 13% than was predicted (typically 8-10%) and included growth in both clinical and commercial manufacturing, according to HighTech Business Decisions.[5] Going forward, Future Market Insights estimates that the global biopharmaceutical contract manufacturing market will expand at a CAGR of 10.6% from a value of $5.625 billion at the end of 2017 to $15.468 billion by the end of 2027.[6]

BUILT BY TAKING BOLD STEPS

Founded in 1927 as a privately held pharmaceutical company, Rentschler Biopharma entered the biologics space in 1974 and is thus one of the pioneers in the development of biologics in the world. The company began working with recombinant cell lines in 1979 and was the first to receive market approval for a natural Interferon-β (Fiblaferon) in 1983. Approval of a recombinant Interferon-γ (Polyferon) followed in 1989.

Rentschler Biopharma became a 100% CDMO in 1997 and expanded its manufacturing capacity from 2008-2012, adding a 3000L stainless steel and two 1000L single-use (SU) bioreactors. Our proprietary TurboCell™ technology platform was first employed in 2014, and the first manufacturing runs in a 2000L SU bioreactor were

OUR **TURBOCELL™ CHO-K1 CELL-LINE** TECHNOLOGY ALLOWS IDENTIFICATION OF PREDICTABLE, ROBUST AND SCALABLE CHO CELL LINES.

completed in 2015. Another expansion in 2016 added two 3000L twin bioreactors and a second 2000L SU bioreactor. In 2017, the company established a strategic alliance with Leukocare AG in Munich, Germany in formulation development and a strategic partnership with Rentschler Fill Solutions GmbH in Rankweil, Austria.

When Rentschler Biopharma introduced its first 1000L SU bioreactors, we were the first CDMO to introduce disposable technology at this scale – and won a "Facility of the Year" award in 2012 for our modular and flexible single-use solution. We are a pioneer in single-use bioprocessing and have performed more than 120 batches in fed-batch or continuous mode. Rentschler Biopharma was also an early adopter of downstream disposable technologies, installing SU chromatography, tangential flow and viral filtration systems in 2010 and a second SU chromatography system in 2015.

ESTABLISHING STRATEGIC ALLIANCES AND PARTNERSHIPS

Rentschler Biopharma has responded to the growing needs of its clients with the establishment of strategic partnerships designed to expand its portfolio of services and capabilities.

Through our strategic alliance with Leukocare, we are able to offer advanced formulation development capabilities, with formulation issues considered at every step of the development and manufacturing process. Leukocare's proprietary SPS® formulation technology (SPS® = Stabilizing and Protecting Solutions) enables the development of cost-efficient dry and liquid protein formulations with significant improved stability at room temperature, even at high concentrations.

The strategic partnership with Rentschler Fill Solutions provides reliable full-service solutions and new state-of-the-art aseptic filling capabilities from a

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single source. The partnership unites two centers of excellence for the fast and efficient manufacturing of biopharmaceuticals with the Rentschler commitment to quality and enables optimally aligned processes to meet the client's time-to-market expectations.

MORE THAN MANUFACTURING

These investments in state-of-the art equipment, innovation and partnerships have made Rentschler Biopharma one of the global leaders focused on mammalian cell culture. We remain a medium-sized, family-owned company with a 100% focus on our clients' projects, which we support from gene to vial. Because we are fully dedicated to our customers and their projects, our clients have a clear advantage – their projects do not compete with any internal development efforts.

Our clients also benefit from our extensive experience in the manufacturing of a wide range of biomolecules, from monoclonal and bispecific antibodies to fusion proteins, enzymes, blood factors, cytokines and growth factors. Since 2000, Rentschler Biopharma has worked on more than 250 molecules and has produced more than 350 batches. Our TurboCell™ CHO-K1 cell line technology allows identification of predictable, robust and scalable CHO cell lines. With this platform – or a customized approach – we can provide cGMP-compliant manufacturing of master and working cell banks. With our platform technology we can produce material for screening studies within seven weeks and and up to 200g for tox studies within ten weeks, reducing development costs and timelines.

Overall, Rentschler Biopharma is a solution provider. We listen to our clients to understand their project objectives and specific challenges and find solutions where others don't even look. We can help customers solve problems with their biologic upstream and downstream processes, formulation and analytical development and optimization efforts. We help customers take their ideas from genetic engineering all the way through fill-finish, with cGMP production of both clinical and commercial quantities. Projects are supported by the elaboration of optimal global regulatory approval strategies from clinical studies to market approval, including compilation of all required documentation (IMPD/IND CMC-Parts, Module 3 of BLA/NDA/MAA).

RELIABLE GLOBAL PARTNER

With long-term expertise in development and manufacturing, Rentschler Biopharma has established itself as a reliable global partner and one of the world's leading biopharmaceutical CDMOs. We have worked with 130 clients worldwide since 1997, including 15 of the top 20 pharmaceutical companies, as well as emerging and medium-sized biotechnology firms. Half of those clients work with us on multiple projects, and 40% have relied on us for more than five years.

IDENTIFYING FUTURE SOLUTIONS

With the biopharmaceutical industry undergoing a significant transformation, it is essential that CDMOs serving the industry evolve to meet the changing needs of their customers. Rentschler Biopharma has always been a technology leader, and the implementation of our Strategy 2025 initiative will ensure that we continue to be a partner of choice for our customers.

Over the past two years, we have evaluated the key trends in the biopharmaceutical industry, talking with people across the sector and generating a vast data pool for in-depth analysis. The generated information gives Rentschler Biopharma a solid platform to determine the path the company should follow going forward.

We are considering important questions such as, "What will the treatment of rare and severe diseases look like in 10-20 years? Will mAbs continue to be the major therapies of choice? Or will the majority of treatments consist of cell and gene therapies?

The strategy will address all aspects of our development and manufacturing activities, from the platform technologies we need and determing how our people will work in the future to what our clients will expect from a company like Rentschler Biopharma. It is all about innovation and ensuring that Rentschler Biopharma remains a technology leader. P

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Passion for Performance

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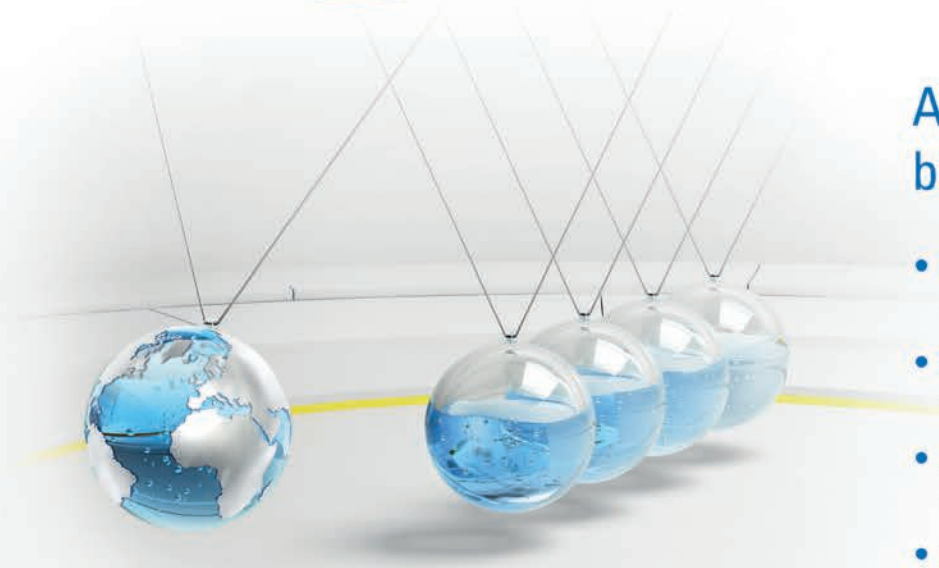

A world-class biopharmaceutical CDMO

- Experts in cell culture for bioprocess development and manufacturing
- Family-owned company, focused exclusively on our clients projects and made in Germany
- Biopharma pioneer with commitment for technology and innovation leadership
- Extensive track record and 40 years of experience

Our partnerships

Strategic Alliance with

LEUKOCARE BIOTECHNOLOGY

Best-in-class formulations provide significant competitive advantages

Strategic Partnership with

Rentschler Fill Solutions

Complete solutions with state-of-the-art fill and finish facilites

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