WHITE PAPER

The value of engaging a single CDMO for comprehensive biologics services from discovery to GMP manufacturing

Partnering with a single CDMO can increase speed to market, ensure production capacity and avoid costly and time-consuming tech transfers.

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Emerging biopharma companies at early discovery stages can benefit from a partner that can evolve with their molecule. A full-service CDMO can do that with the expertise to solve early-phase challenges, satisfy clinical timelines, plan for the next round of development and ensure smooth tech transfers into the clinic. Small companies do not possess the necessary infrastructure in-house and are underserved by the current CDMO landscape to meet early-phase challenges.

Speed to clinic is essential for startups with promising biologics

A majority of biologics are in either discovery, preclinical or early clinical stages, and are mostly aimed at oncology and infectious diseases.[1] There is promising growth in these areas, driven by increased funding for biologics, and growing demand for these treatments.

The mRNA market subsegment, for example, emerged to combat COVID-19 and, in recent years, cell and gene therapies have also matured, with multiple product launches serving as inflection points for continued growth in that market. In the midst of these shifts, innovators are racing to get to the clinic as quickly as possible as delays in getting a promising drug candidate to clinical trials can be expensive, delay patent filing and increase competitive threats.

The continued growth within the biologics market comes with supply and demand challenges. Unlike many large biopharmaceutical manufacturers, which have in-house capacity and are looking to a CDMO as a secondary source of supply, startups lack the internal expertise and are looking for support in the discovery and preclinical stages to accelerate movement into the clinic. The challenge is that most CDMOs tend to prioritize high-scale, late-stage projects, leaving the high-growth, early-stage, small-company pipeline behind. This further constrains small companies that are heavily reliant on external funding from investors who want to see a future-state manufacturing plan in place.

SUPPORT FOR STARTUPS FROM DISCOVERY TO GMP MANUFACTURING

Curia supports discovery, development and drug substance and drug product manufacturing for biologics modalities, including antibodies, proteins and mRNA therapeutics.

We prioritize the needs of small companies as a crucial part of our capacity allocation strategy to ensure the emerging molecule pipeline continues to move to clinic uninterrupted, offering better therapies for the future. We serve as a full-scale, sole-source partner evolving with your molecule and developing scalable processes from the start with commercial readiness in mind. We help streamline discovery to get to the preclinical stage faster and, as you approach the clinic, we become your manufacturing partner with the capacity to grow with you. Additionally, our commercial scale capabilities across a range of therapeutic types, along with our expansive network and commitment to growth, inspire confidence in our clients' funding partners as they pitch their innovative molecule.

THE BENEFIT OF WORKING WITH A SOLE-SOURCE SUPPLIER OF BIOLOGICS SERVICES

Engaging multiple CDMOs, for different process workflows, challenges the critical need of innovators looking for speed to clinic and market. Transferring a process step from one CDMO to another can be slow and may be hampered by proprietary concerns or transparency in communication. Instead, a holistic approach, in which the partnership continues from discovery to clinic with one CDMO, removes communication bottlenecks and allows quicker movement through the drug phases. At Curia, we streamline movement of your molecule and deliver success on your timelines by establishing an integrated network, integrated teams, structured governance and stage-gate process. Our complete network from discovery to clinical scale in biologics brings diverse talent together as one team, with a culture that works with a patient mindset each day.

Integration of teams streamlines development

The integration of our analytical, process development and manufacturing teams — regardless of whether at the same site or in different regions — smooths the transition between functions. Our global infrastructure is operationally agnostic and designed to meet rapid timelines irrespective of where manufacturing or process development occurs.

Customers appreciate our scientific capabilities and the depth of experience of our cross-trained teams, as evidenced by the many case studies we are able to share with them. Our transparent style of communication gives them a comprehensive view of how we will manage their program.

CASE STUDY

ANTIBODY DRUG TARGET OPTIMIZATION AND HUMANIZATION

SCOPE

A small company collaborating with two academic research institutes and one large pharmaceutical company was looking to optimize antibody leads. They needed a CDMO with integrated discovery services to run a diverse panel of monoclonal antibodies (mAbs) to optimize difficult targets and develop humanized models to fully human antibodies.

TIMELINE AND OUTCOME

- Successful discovery and optimization of potent, target-specific and humanized mAbs.
- Select the appropriate animal strains, and implement advanced proprietary approaches for immunizations of DNA, protein and cellular immunogens, generating and screening thousands of hybridomas.
- Humanize mAbs from client programs.
- Implement proven screening methods, custom antibody characterization assays and state-of-the-art binding studies.
- Ten successful campaigns in three years delivered on time and in full.

BENEFIT TO CUSTOMER

- Expansion of client pipeline with abundance of preclinical and clinical targets.
- Integration and close coordination between various teams to holistically build and execute on lead discovery and optimization strategy.

Balancing the science of discovery with the engineering of manufacturing

Our end-to-end capabilities mean we're able to handle complexity and can do much more than the minimal engineering requirements to perfect processes, ensure reproducibility and manufacture a biologic once you get into the clinic. Our discovery capabilities mean we can manage the scientific complexity that arises prior to having a well-developed process. We have worked with many customers as early as identifying hits and optimizing leads. Then, once the projects move into preclinical, we are able to shift our strategy to reproducibility, engineering and manufacturing.

What follows is a brief overview of our capabilities in discovery, process development and GMP manufacturing across all biologics modalities.

Discovery

Curia's drug discovery capabilities are beyond the scope of most premier CDMOs. Offering discovery services allows us to partner with you early and adapt to your evolving needs from the beginning of your molecule's journey.

FIRST-TO-HUMAN ANTIBODY DISCOVERY AND OPTIMIZATION

Our efficient and comprehensive services identify, optimize and characterize new monoclonal antibody (mAb) hits, turning them into leads in as little as 90 days. We deliver molecules with the right function, selectivity and cross-reactivity.

Antibody discovery uses hybridoma, phage display and yeast display. Our PentaMice® platform, combined with single B cell screening with the Berkeley Lights Beacon® Optofluidic system, usually requires no further optimization. This First-to-Human antibody discovery can reduce development time to its bare minimum, producing leads in as little as six months. For a detailed workflow, see our white paper, Antibody-based drug discovery at the speed of light.

ANTIBODY PRODUCTION: "START IN CHO, STAY IN CHO"

Curia has extensive experience using mammalian platforms for antibody production, including HEK293 cells. Alternatively, rapid re-expression of variable region genes (V_H and V_L) in TunaCHO℠, Curia's proprietary platform for CHO transient production, delivers milligram quantities for analysis of select leads. Beginning with CHO cells eases the transition to stable, high-yield GMP clinical manufacturing of mAbs, which uses Curia's proprietary and royalty-free CHO-GSN cell line. To learn more, see our white paper, Leveraging efficiency from cell line development to clinical manufacturing of monoclonal antibodies.

PROTEIN ENGINEERING AND PRODUCTION

We offer a complete range of services for molecular design, construction and expression purification and characterization. With more than a decade of experience, our sites work with mammalian, microbial and baculovirus systems.

Development

PROTEIN PROCESS DEVELOPMENT

Upstream process development services optimize cell productivity in single-use bioreactors (SUBs). Upstream process development for mAbs includes:

- Testing leads with the Sartorius Ambr 15 Cell Culture Bioreactor System, which is able to parallel test up to 48, 15-mL cell cultures. This small-scale evaluation is an efficient and cost-effective way to optimize the process.
- Cell line scalability is tested in multiple 2-L SUBs.
- A confirmation run is then done in a 50-L SUB.
- Further scale up to 200–2,000-L SUBs allows delivery of kilogram quantities of clinical phase material.

Downstream process development includes protein-based technologies to engineer purification processes for manufacturing. Curia has developed purification processes for hundreds of unique proteins for preclinical toxicology studies. This is done concurrently with upstream process development and in parallel with analytical services to reduce time between development and toxicology studies.

Optimized workflow using PentaMice and the Beacon system

The CHO-GSN℠ development platform is used for the generation of a research cell bank and future use as a manufacturing cell line for high-level expression of commercial products. It includes a proprietary, royalty-free CHO cell line, custom stable expression vectors and glutamine synthetase (GS) selection. CHO-GSN cell lines are stable for at least 80 generations. Our platform process is designed to maximize purity and yield, while minimizing the time between development and toxicology studies.

PROCESS DEVELOPMENT FOR mRNA VACCINES AND THERAPEUTICS

With the success of the COVID-19 mRNA vaccines, the number of clinical trials for RNA-based therapeutics has skyrocketed, the bulk of which are mRNA drug products.[2] Curia is well positioned to serve this need, with process development capabilities for mRNA therapeutics including mRNA synthesis, lipid manufacturing and the formulation of lipid nanoparticles (LNPs). For more detail, see our white paper, The current and future value of mRNA vaccines and therapeutics.

ANALYTICAL METHOD DEVELOPMENT AND SERVICES

A wide range of molecular, biochemical and cell-based bioassays optimize assay design, capacity and execution. Our comprehensive analytical development and quality control includes analytical, bioassay and microbiology services, all of which adhere to USP and FDA guidelines. Our expertise supports discovery, development and cGxP therapeutic testing campaigns across all service types.

Curia's assays and analytics for mAbs are listed in our white paper, Leveraging efficiency from cell line development to clinical manufacturing of monoclonal antibodies. More information on the analytical assays applied to mRNA drug products can be found in our white paper, The current and future value of mRNA vaccines and therapeutics.

FORMULATION DEVELOPMENT

Our fully integrated formulation development programs emphasize defining critical quality attributes with an eye on ICH stability guidelines and manufacturability. This accelerates timelines by preventing the need for reformulation and streamlines tech transfers.

Manufacturing

DRUG SUBSTANCE: ANTIBODY, mRNA AND PROTEIN MANUFACTURING

Our ISO 13485:2016 certified facilities provide biomanufacturing services for GMP production of mRNA, antibody and protein therapeutics and vaccines. Our established quality systems support production of early-phase bulk drug and diagnostic products. mRNA manufacturing, large-scale production of proteins and antibodies, in-process testing and batch release and fill-finish of LNPs are all performed in ISO 7 suites with GMP-compliant single-use equipment.

DRUG PRODUCT: mABS, PROTEINS, mRNA MANUFACTURING AND FILL-FINISH

Our sterile drug product manufacturing expertise spans early clinical stage through large-scale commercial production. Curia offers a complete suite of services for all sterile dosage forms — liquid, suspension and lyophilized. We cover a broad range of therapeutics in mRNA, proteins, mAbs, peptides and oligonucleotides to deliver large-scale fill-finish needs.

Support from discovery to GMP manufacturing

The discovery of new biologics is exciting, but getting them into the clinic takes expertise in process development and manufacturing most smaller companies don't have. Partnering with a CDMO capable of taking your biologic from discovery to GMP manufacturing is the most efficient and successful way to cross the finish line first.

ABOUT CURIA

Curia is a Contract Development and Manufacturing Organization with over 30 years of experience, an integrated network of 29 global sites and over 3,500 employees partnering with customers to make treatments broadly accessible to patients. Our biologics and small molecule offering spans discovery through commercialization, with integrated regulatory and analytical capabilities. Our scientific and process experts and state-of-the-art facilities deliver best-in-class experience across drug substance and drug product manufacturing. From curiosity to cure, we deliver every step to accelerate and sustain life-changing therapeutics. ***Learn more at curiaglobal.com***

References

1 GlobalData.com. Biologics report. 11 Oct 2022.

2 Webb C, Ip S, Bathula NV, et al. Current Status and Future Perspectives on MRNA Drug Manufacturing. *Mol Pharm.* 2022;19(4):1047–1058. https://pubs.acs.org/doi/10.1021/acs.molpharmaceut.2c00010

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