Lonza
Biologics

Executive Summary

Lonza Shapes Biotherapeutics Development Programs Around Different CMC[1] Paths

Flexibility and Customization are Key for Successfully Realizing Clinical and Funding Milestones

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As protein engineering and manufacturing technologies evolve, small biotech and major pharma companies alike need flexible, customized strategies that balance cost, speed and risk to accelerate drug development and approval of biotherapeutics that could address unmet medical needs.

A Flexible Partner

Getting to the clinic is a major milestone for biopharmaceutical companies. The drug development journey is long, expensive, resource straining, and risky due to high attrition rates. A large amount of data must be generated, collected, interpreted and correctly integrated for the First-in-Human (FIH)-enabling data package. When developing more complex formats such as bispecific antibodies, fusion and recombinant proteins, you are probably facing even tougher technical challenges which can lead to longer timelines. As a biopharmaceutical company, you also face fierce competition from hundreds of other firms. How can you help your lead candidates get ahead of the pack? Joining forces with an experienced, yet flexible development and manufacturing partner could help your drug candidate reach those all-important milestones on time and on budget.

At Lonza, we understand that each journey to the clinic is unique and building optimal paths that balance risk with time and costs is complex. This is why we offer a flexible approach to shape together a program that is in sync with your molecule's profile, company and investors' needs.

Build your development and manufacturing path to IND: 3 paths shaped around your IND application for total flexibility

Firstly, if your priority is to speed up your path to the clinic, we offer bespoke integrated drug substance and drug product programs for any molecule type. We deliver your molecule format from DNA to IND[2]/IMPD[3] in as little as 11 months for monoclonal antibodies (mAbs), 13 months for bispecific antibodies (bsAbs) and 14-18 months for the most complex proteins*.

To help you find any adverse safety issues before you make potentially costly mistakes when scaling up to GMP[4] production, you can also have TOX drug substance for testing in just 5 months for mAbs, 7 for bsAbs and 10 for non-Fc recombinant proteins.

Secondly, if you are not yet ready for a full program, we offer flexibility to support your journey from DNA to the clinic. This means you can build your CMC strategy step by step, taking a break after key milestones to select a lead candidate to progress or secure more funding.

Thirdly, you can also bring in your own cell line at any stage of your journey.

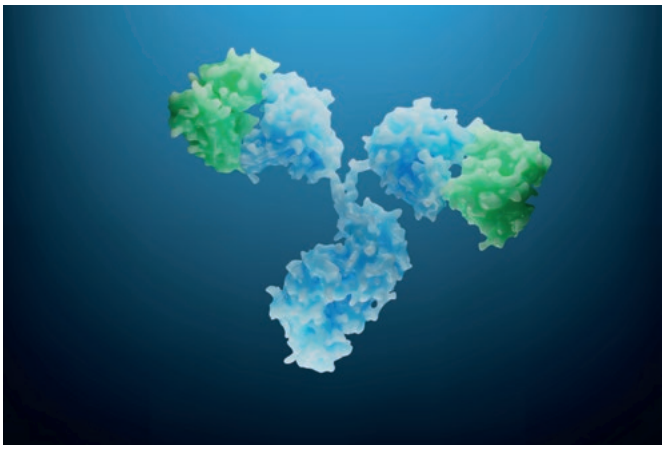


Figure 1
Three Paths Shaped Around Your IND for Total Flexibility

Integrated DS & DP DNA to IND Programs Speed | Quality | Bespoke	**Build your Manufacturing Path IND to match your pre-clinical milestones** Flexible | Milestone-based | Bespoke	
1	2	3
Speed up your path to clinic	**Rely on Lonza's expression platform and process to develop your DNA sequence**	**Drop-In your cell line/process at any stage depending on where you are in your journey**
Monoclonal Antibodies 11 months DNA to IND*	**A few examples of what is possible:**	**A few possible starting points:**
Bispecific Antibodies 13 months DNA to IND*	• Vector construction & manufacturability assessment • DNA to RCB or MCB • DNA to Tox DS ot DP Batch	• Customer vector system/cell line • Established RCB/MCB • Established process • Drug substance/Bulk purified product
Scaffolds & other Recombinant Proteins 15–18 months DNA to IND*		
Fabs & Fusion Proteins 14–16 months DNA to IND*		

How can we deliver in such competitive time?

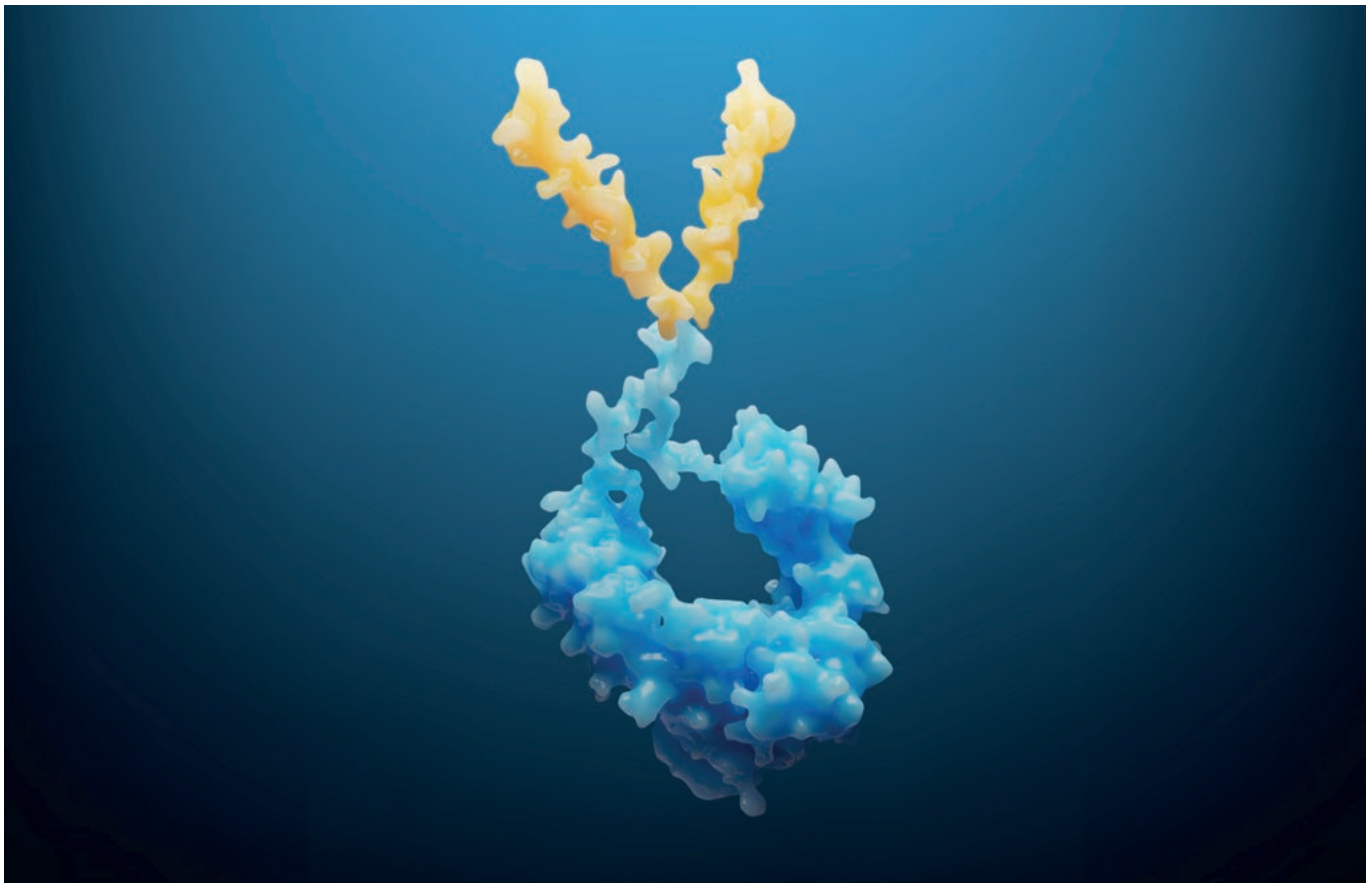
We proactively identify and mitigate technical risks at every stage. We are experts at that because we have an unrivalled depth of experience in developing and manufacturing biotherapeutics for hundreds of companies. Before proceeding with vector assembly and expression, we use Epibase® in-silico and in-vitro tools to ensure your molecule does not contain any unpleasant surprises and assess your lead candidates to predict your stand-out candidates. If your lead candidate still looks like it will have immuno-safety or manufacturability issues, we can re-engineer it.

To achieve the best expression levels, we then use our industry standard GS Xceed® system combined with GS piggyBac® transposon system. We can additionally test factors such as gene copy number and order, which can improve titer and product quality, whilst enabling construction and expression of up to four genes in one vector. It is worth noting that our GS Xceed® expression system has been used in over 1300 preclinical, phase 1 and 2 molecules as well as in over 70 commercial biotherapeutics. Thus, it is well known to world-wide regulatory authorities, both at the clinical and commercial dossier level, which can help you save time with your regulatory filling. Combining these effective expression vehicles with specially designed media and feeds we can optimize cell growth, viability, and protein production with ease.

Once we have your clones growing well and producing the therapeutic protein, we use stable pools for early process optimization, whilst simultaneously performing high -throughput clone selection with state-of-the-art technologies such as the Beacon® Optifluidic System. Our extensive data shows that early pool material is representative of product produced from a clonal cell line, indicating that we can safely use this approach to deliver faster process and formulation development without increasing risk.

The combination of host cell line, vector and stringency of selection enables us to provide our customers with high-producing cell lines suited to fit a commercially relevant process.

As we optimize the upstream process, we continue de-risking the downstream one as well. For novel molecular formats, any standard plug-and-play purification platforms will require specialized customization. As a result, downstream processing can require extra time-consuming purification steps, and analytical methods need to be highly sensitive.

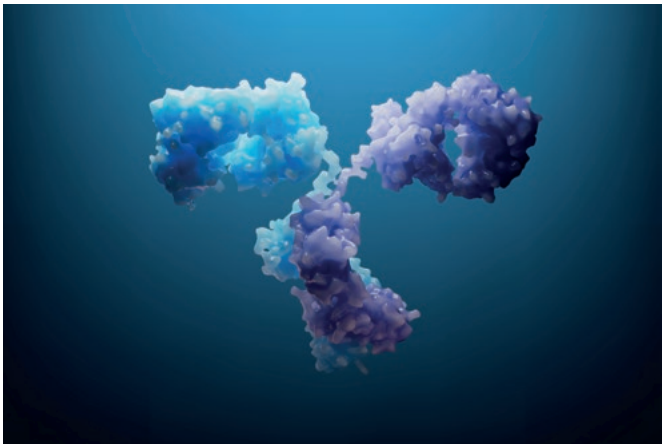


Our experience with new molecular format means we know how to handle these challenges and using high-throughput chromatography screening we can find the right resins, pH, and buffer combinations to balance PQAs[5] with the highest titers to deliver you a scalable process which produces safe and manufacturable complex biotherapeutics.

By utilizing state-of-the-art technologies and combining all our platform processes including stability studies, storage, and supply chain management, we can save time. Additionally, by running many of our process and formulation development activities in parallel, we can guarantee delivery of GMP quality drug substance to industry-leading timelines.

By optimizing your end-to-end process, we can help you deliver submission-ready CMC data for an IND, helping you progress any molecule type to clinic and funding milestones on time.

By offering flexibility at all stages of your biotherapeutic development to deliver customized lead candidates and processes, Lonza is your perfect partner for helping you progress on time and on budget to your clinical and funding milestones.



To discover more about our Cell Line Development Capabilities, visit: **Cell Line Development Services | Lonza**

Glossary

1. Chemistry, Manufacturing, and Controls
2. Investigational New Drug
3. Investigational Medicinal Product Dossier
4. Good Manufacturing Practice
5. Product Quality Attributes

*Subject to molecule assessment and terms and conditions.

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