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How Emerging Biotechs can Benefit
by Partnering with a CDMO for Early Stage Development

The partnership between CDMOs and emerging biotech companies in early-stage development can be mutually beneficial. In this exchange, Dr. Raymond Donninger, Senior Director, Commercial Development, Early Development Services, and Dr. James Berrie, Technical Director, Global Process Development both at Lonza explore how the expertise, efficiency, and scalability a CDMO can provide is crucial for efficiently and cost-effectively delivering new therapeutic candidates for an investigational new drug (IND) filing and first-in-human (FIH) trials.

Why is expertise and resource sharing beneficial for emerging biotechs?

RD: Small biotechs can sometimes be short of internal resources which can range from not having the right equipment to lack of regulatory expertise at the other end of clinical development. Gaps in their infrastructure and knowledge are what a well-resourced and experienced CDMO such as Lonza can plug.

JB: In early development for example, Lonza has years of technical expertise and experience with an extensive range of different molecule formats, which a small biotech would not have access to in-house. This would benefit emerging biotechs by gaining access to these expertise and capabilities enabling them to optimize their lead candidates and de-risk their molecules against potential manufacturing and immunogenicity issues later in development.

What benefits does risk mitigation bring to a small biotech?

RD: Drug development work is often not linear. Sometimes you go two steps forward and one step back, a scenario which is more likely if drug developers haven't done a sufficiently robust risk assessment early. For example, Lonza can highlight risks in a project at the very early development stage and this benefits a biotech company and its investors with the comfort and confidence that the project is less likely to be derailed by unforeseen setbacks later when a significant amount of resource and time has already been committed and costs are therefore much higher to put a manufacturing or safety issue right.

What kind of risk mitigation does Lonza do in early stage development?

JB: Lonza has sites in the UK and now the US that are dedicated to early stage development. There we use our Epibase® in silico and in vitro platform to predict potential immunogenicity risk and our in silico manufacturability platform to identify whether a therapeutic candidate could have manufacturability issues, for example, hydrophobicity.

RD: Using in-silico predictive tools is an inexpensive and rapid way to screen multiple therapeutic candidates. Often within a couple of weeks we can rank several candidates in terms of manufacturability and immunogenicity safety to rank which are the best ones to take forward into clinical development. Identifying these risks early in the program means that at Lonza we don't just identify the problem, but we can also offer solutions to it. For example, we can either assist with the redesign of a candidate molecule using protein engineering or suggest an upstream or downstream process that will take account of any potential manufacturing or safety risks.

RD: At Lonza, we have helped hundreds of customers/clients de-risk their early development programs. There are dozens of candidates in clinical development that were initially not viable because they had several potential issues which have all been fixed by using early stage in-silico tools and protein engineering.

JB: The early development material prior to tox material provision, can provide proof-of-concept data which helps to understand where the issues may arise in manufacturing, and this means a biotech can then eliminate or mitigate for those risks before the costs are too high or the timelines too

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long because of the need to change an upstream or downstream process.

Speed to FIH and costs - why are these so important for emerging biotechs?

RD: It's not so much about speed as efficiency. Getting to an IND filing or FIH trial as efficiently as possible is key for small biotechs because they have limited resources and cannot afford to waste them. Therefore, they don't want to have to repeat any steps because they often don't have the funding to do this.

RD: For many small biotechs the molecule they are developing can also be very personal. It is not unusual for the biotech company to have been set up to develop a therapy for a family member or based on decades of personal scientific research so they want to get to clinic as soon as possible. Lonza understands this urgency and we want to help them reach their development milestones as efficiently as we can.

JB: An IND filing is often linked to a funding milestone for small biotechs. Therefore, getting to IND faster also releases the next tranche of investment and can be the difference between continuing their development journey or not. Additionally, we can deliver monoclonal antibody (mAb) material with associated analysis for toxicology studies in three to four months, so much earlier than has traditionally been offered.

Scalability and flexibility how do these benefit emerging biotechs?

RD: If a biotech uses platform processes that are scalable, this can reduce costs and risks in manufacturing. For example, if they develop their molecule in a cell line such as GS-CHO that has a track record of performing equally well at lab scale or a manufacturing scale bioreactor and is well-known to regulators then their chances of producing a good chemistry manufacturing and controls (CMC) dossier for an IND filing are much higher. If they express their molecule in one cell line in the lab and then change to another cell line for manufacturing this could add significant amounts of development re-work and time to ensure that the characteristics of the molecule at lab scale are comparable to the characteristics of the clinical manufacturing scale molecule.

Additionally, a change of cell line may need to be discussed with the regulator which all adds delays and expense.

RD: Investors know that using scalable processes increases the chances of a successful IND filing and may therefore discount the amount they are willing to invest in a biologic if scalability is in question. For example, if there is a possibility of a change being required to different production systems or xenograft model studies having to be repeated, investors may offer less, delay funding for a molecule until bridging studies are completed or ask for a larger share in the company for the same investment due to the cost of having to generate bridging data. Therefore, if a biotech wants to maximize the amount of investment in their project, then choosing to partner with a CDMO such as Lonza which offers a scalable path to IND and FIH trials often makes sense scientifically and commercially.

RD: In terms of flexibility, at Lonza we can adapt quickly to any potential issues with our client's molecule. We also offer flexibility in our services, so for example some biotechs want to go from DNA to IND with us and others just want the in-silico early development services or at the other end of the development path they want in-vitro formulation studies. Being able to offer phase and stage appropriate services means small biotechs can break their work into more manageable campaigns with us according to their technical needs and the amount of funding they have available, or they can commit to a comprehensive development gene to IND program.

Why is access to global networks important?

JB: Working with a CDMO like Lonza that has many sites world-wide means that an emerging biotech can leverage a global team with many years of collective experience. We also have what we call Senior Technical Leads that can look at all the elements of a project from the perspective of the services that Lonza has to offer at all the different sites and suggest the best development path and sites for their program. For example, we don't just develop mAb-based therapies but are working with broad spectrum proteins and other modalities such as antibody drug conjugates (ADCs), so can make suggestions where development and manufacture would be best suited.

Additionally, because we have facilities in different places globally for developing drug substance (DS) and drug product (DP) we can start many activities in parallel. This optimizes the use of facilities and reduces timelines to IND filing, so that we can offer small biotechs developing standard mAbs, our Ibex® Design program that will take their molecule from DNA to IND in just 11 months*.

*For antibodies. From DNA transfection. Subject to terms and conditions.

Define collaborative innovation at Lonza and how it can help with early development strategies?

JB: For us collaborative innovation in the early development space involves always looking at our suppliers in terms of supply chain times, quality and operations. It also involves assessing what new technologies offer and where appropriate acquiring or licensing that technology to use in our programs or to offer our clients as a stand-alone service or product.

JB: For example, there has been a greater demand for development of bispecific antibodies recently. However, correct pairing of heterodimer heavy and light chains in a bispecific antibody has meant expression and manufacturability of these molecules can be inefficient. We assessed and developed bYlok® technology and now offer it as a service or as a licensed product. This technology offers up to 95% correct chain pairing, which if used by small biotechs at the early development stage can help produce more optimal molecules and reduce the cost of goods.

JB: Many small biotechs want to maximize their protein titers to reduce their manufacturing costs. So, we evaluated the piggyBac® technology and developed the GS piggyBac® system and this enables high protein expression of mAbs and bispecific antibodies.

Regulatory compliance, why is this an issue for small biotechs?

RD: Emerging biotechs may not be familiar with working with regulators and it can be quite daunting for them. Many are worried about their funding from month to month and don't have the time or the expertise in-house to worry about regulatory CMC dossiers. By working with Lonza they are going down a well-trodden path with helpful regulatory support.

JB: Many small biotechs make process changes to deliver more efficient and scalable production of biologics. However, they must notify Regulatory agencies in an updated filing. By partnering with a CDMO like Lonza, emerging biotechs can leverage our experience to help get their IND filings right first time. We offer plenty of regulatory support because we have vast experience of authoring regulatory submissions on behalf of clients. Additionally, we can send a Lonza representative with a small biotech to their meeting with the regulator, if they require extra support and alignment on process changes.

Long-term relationships and future opportunities – how can working with a CDMO on an early development program translate into later success?

JB: It is not unusual for us at Lonza to work for many years with a small biotech on multiple therapeutics to develop their portfolios to IND filing and FIH trials. Many become very emotionally attached to their molecules and rely on us throughout the development process and we often provide technical and regulatory support for them throughout. This is a huge responsibility for us because often these biotechs only have enough funding to develop perhaps one molecule to toxicology studies stage and we are very conscious of that, and we tailor our support to be as efficient as possible.

Summarize Lonza's market validation and credibility with relation to programs for small biotechs.

JB: We have over 35 years' experience developing biologics and have supported over 500 molecules on their pre-clinical and clinical journey. Many of these molecules have been developed in collaboration with emerging biotechs, so we understand the constraints under which they are working. This means we can personalize our partnerships and services to fit around their budget and skills or infrastructure gaps.

RD: Lonza is well-known for its expertise and innovation with both the biopharma industry and investors and is considered a preferred partner for small biotechs. We are also continually improving and expanding the support our clients need. For example, we have recently opened early development services facilities in the US, which will further help emerging biotechs by increasing our capacities to continue to deliver on critical timelines. At Lonza we want to work with small biotechs, because we enjoy seeing their novel therapies reach FIH trials and often even go beyond that to commercialization where they can be used to treat patients with chronic and life limiting conditions. ■

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