BIOPHARMA THOUGHT LEADERS

OFFERING INDEPENDENCE THROUGH PARTNERING

Opportunities are rising for small biotech companies but so are challenges in scaling. In the first of our Thought Leader series, ***Marc Funk***, ***CEO of Lonza***, talks to us about the new business models and technology the company is developing to help companies remain independent.

WHAT DO YOU THINK THE CURRENT SITUATION OF THE DRUG DISCOVERY AND DEVELOPMENT MARKET IS?

This is an extremely exciting time in the drug discovery and development area. First, innovation is coming increasingly from small companies; emerging companies patented over two-thirds of new drugs in 2018. In some areas, such as cell and gene therapy, this number is even higher; around 80% of our customers are small biotech companies. We're seeing that many small companies now want to launch their drug, instead of being acquired.

Second, there is increasing complexity in the therapies themselves; standard monoclonal antibodies are less present in development pipelines, and we are now seeing a move toward more diverse and complex protein formats, such as bispecifics. Even more complex is the emerging cell and gene therapy market, which presents new challenges from a manufacturing and logistics perspective.

WHAT CHALLENGES DO SMALL COMPANIES DEVELOPING BIOLOGICS FACE?

Small biotechs have internal and external challenges. From an internal perspective, many small companies want to stay small and agile. They often do not want to invest heavily in manufacturing capabilities straight away, so they need strong partners who can share risk with them as they grow.

Externally, small companies face a couple of challenges; the first is time pressure. Many programs are on expedited regulatory pathways, putting manufacturing on a critical path, which is not always simple. The second challenge is funding. Although the funding climate is still good, there is increasing competition for funds. In that respect, companies need full visibility of their costs and they need to manage their investments in phase with their funding milestones. That can be difficult.

Manufacturing can pose an additional challenge, especially for companies that are in phase 2 and taking their products toward commercial launch. In a short timeframe, they need to cover many different scenarios and be able to ramp up quickly if successful. If we were to combine all the different scale-up strategies that we've worked on with small or mid-sized biotech companies, we can clearly see that there is no single way of doing things and that all asset strategy options need to be available.

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>
> Marc Funk, CEO, Lonza

HOW ARE YOU TACKLING THIS PROBLEM WITH THE DEVELOPMENT OF NEW BUSINESS MODELS AT LONZA?

From a business model perspective, we have changed the way we partner with companies; previously, contract manufacturers were just a support to our client's procurement team, but now if we look closely at the journey taken, and the challenges faced by, the young companies we work with, we can see that the traditional contract manufacturing organization business model is too complex and too transactional.

We needed business models that simplify the path to commercialization and avoid the complexity of juggling many suppliers. Therefore, last year, we launched two programs, Ibex Design and Ibex Develop, to provide solutions that are in line with the biotech's development programs.

Ibex Design offers a set package that covers gene to investigational new drug (IND). For our part, we commit to delivering 1 kg of drug substance and final drug product in less than 12 months. This means that small companies get more clarity and can stage gate their investment and reduce risk.

The second model, Ibex Develop, covers the next phase of clinical development and the transition to the commercial stage. Again we offer a time commitment: from the start of process characterization to biologics license application (BLA) in 22 months or less. For this package we also offer support for regulatory filing. In total, we have managed seven fast-track BLA filings, so we really know what the risks are and the areas that regulatory bodies are looking for. Providing the drug substance and product in one location is absolutely key to simplifying the supply chain and avoiding the need for costly technology transfer. We are building a new biopark at our site in Switzerland to accommodate these new offers using single-use technology and a high level of automation to further reduce costs and risks. The first program will start mid-2020.

YOU ALSO MENTIONED COMPLEXITY WAS A TREND—CAN YOU TALK A LITTLE BIT MORE ABOUT THIS?

Our industry has become really good at manufacturing therapeutic proteins at scale, but now we're seeing whole new families of protein formats based on antibody molecules. For example, bispecifics (where you may need three or four genes) or bioconjugates (that require non-

native linkers) can be harder molecules to produce at scale. We're seeing that around 26% of early-phase pipelines are focused on these molecules. We're developing new technologies to prepare for this demand and it is keeping us very busy.

CAN YOU DESCRIBE HOW YOUR TECHNOLOGY WORKS IN A LITTLE BIT MORE DETAIL?

We have a robust expression system called the GS Gene Expression System, which has been used for many years by Lonza and other companies. More than 50 biological products have been approved from this platform, including Synagis and Soliris. A lot of data are available on the GS System and many regulatory bodies are familiar with its use. Now, we're using it as our base for developing a new toolbox and we're building a range of different vectors to meet specific challenges, such as site-specific conjugation for bioconjugates or multigene vectors for bispecifics.

We are also partnering with innovative companies in the gene-editing space to find new technologies with applications in biomanufacturing. For example, we acquired rights from Transposagen to develop their piggyBac jumping gene technology so that we can preferentially insert large DNA payloads into stable regions of the genome. We are also working with a UK company, called Synpromics, to use its inducible promoters to turn gene expression on and off. This could allow improved control of the expression of proteins, in particular those that are toxic to the cell line or that are unstable.

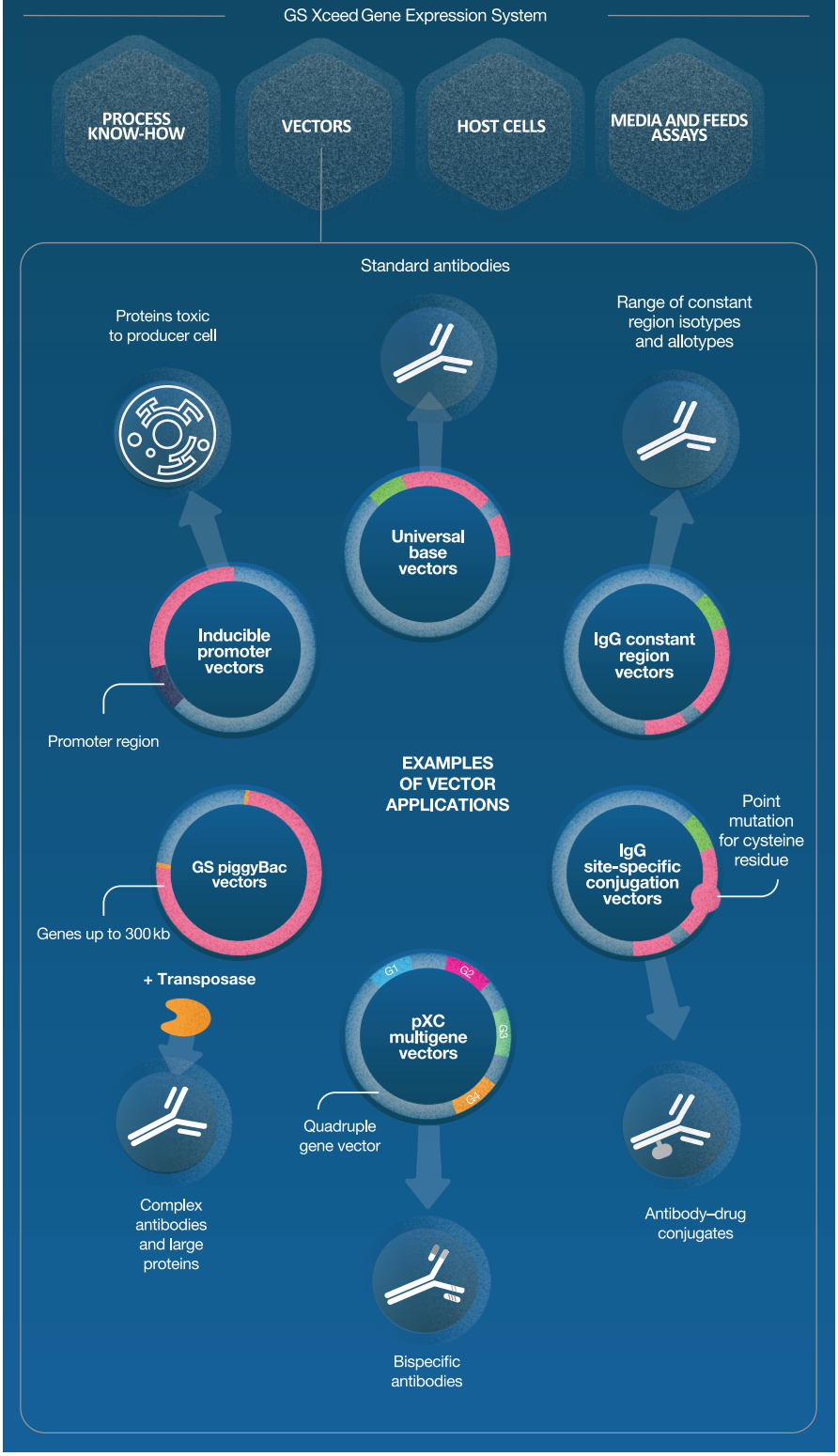
In-house, we have a number of our own research and development programs, and we just launched a new innovation center in Israel to foster biomanufacturing partnerships with universities and startups. Collectively, our goal is to offer solutions to support increasingly complex protein formats and any new discovery our customers develop.

WHY SHOULD SMALL BIOTECH COMPANIES CHOOSE LONZA?

It's about getting the right balance of experience—we've been manufacturing medicines for over 40 years—together with the right technology to support new molecular and cellular formats. Smaller companies need a partner to be an extension of their in-house team that can act as a trusted partner and share risk. They need development that can get them to the clinics fast, but with a process that is robust enough to scale. They also need the flexibility to manage fluctuations in demand. We believe Lonza is that partner, and I feel confident and optimistic about the current innovations that will define the development and manufacture of medicines of the future.

A PROCESS FOR EVERY PROTEIN

To support the growth of next-generation therapeutics, Lonza recently improved its stalwart GS Gene Expression System. The new GS Xceed System uses the improved CHOK1SV GS-KO host cell line and an expanded set of vectors and pairs them with an upgraded commercial platform process. The result is a system capable of rapidly and reliably producing high product titers, even in the case of complex proteins.



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