A Small Biotech with Two Complex Bispecific Antibody Candidates Benefits from Lonza's Blend of Expertise and Flexibility

– Craig Parker, President & CEO, Surrozen

Surrozen's President & CEO, Craig Parker, discuss how the expertise, resources and flexibility of Lonza have been fundamental in advancing its novel and complex bispecific antibody candidates that target the WNT pathway.

Targeted Regeneration

The ability of tissues to regenerate and maintain the structures of certain organs and systems is attributed to a fundamental biological pathway referred to as the Wingless-INT (WNT) signaling pathway. Although the WNT pathway has been studied for decades, no one has ever been able to intervene in this pathway and take advantage of its regenerative potential. Surrozen is a California-based small biotech working to change that paradigm.

Surrozen's founding scientists contributed to a deeper understanding of the underlying biology of the WNT pathway and its role across diverse [normal and diseased] tissues. They identified the gene and explored the concept of targeting the pathway with non-naturally occurring molecules to initiate natural responses. Driven by this, Surrozen is developing bispecific antibodies that potently activate the WNT pathway, but in a very targeted manner and only in diseased tissue. We are excited to be advancing these first-in-class, novel molecules into the clinic for the first time in 2022.

SURROZEN

Craig Parker, MBA
President & CEO, Surrozen

Craig Parker has over 25 years of science and business experience from leadership positions in biopharmaceutical and financial companies. Prior to Surrozen, he was Senior Vice President of Corporate Development at Jazz Pharmaceuticals, and also held senior roles at Geron Corporation and Human Genome Sciences. In his early career, he was a top-ranked biotechnology research analyst on Wall Street. Mr. Parker has a bachelor's degree in biological sciences from the University of Chicago, an MBA from the University of Michigan, and attended Georgetown University School of Medicine.

A Need for the Right CDMO Partner

Approximately two years ago, Surrozen's data in models of liver injury proved quite promising and suggested that our first bispecific antibody could ultimately be a clinical candidate. Although we were still performing antibody engineering work, we wanted to quickly get started on process development and manufacturing. We contracted with a cell line development company first, and then, with the aid of a consultant, embarked on a full evaluation of several CDMOs that might have the necessary expertise to help Surrozen.

One of our first requirements was that the CDMO have experience developing and producing bispecific antibodies and fusion proteins. Because we were starting the project at such an early development point and the structures were so novel, we didn't know if they would be stable, whether they could be formulated, or what quantities we might need manufactured.

As a result, we needed a CDMO with a combination of strong technical expertise, flexibility and capacity. We were concerned not only with manufacturing, but also formulation development and aspects such as scheduling. The right CDMO would need a full suite of capabilities and also the infrastructure to offer real flexibility to support our unique needs – and in some cases unknowns at that point.

Consultant Support and Other Input

Surrozen engaged the help of a consultant for the CDMO selection process because although our team had some experience working with CDMOs, it was limited and not recent in many cases. The consultant constructed a very technically-specific RFP and sent it to a group of CDMOs identified as having as many of the characteristics we were seeking as possible – bispecific and fusion protein experience, GMP manufacturing capacity above 1,000 L, and other factors. Some of these companies were small, while others were the typical larger players in the CDMO space.

In addition to the consultant's work, we sought input from various experts within the local biopharma ecosystem in the south San Francisco area about their experiences with the various CDMOs we were canvassing. We consistently heard about Lonza's reputation for extensive, expert capabilities, their experience, and presence in multiple geographies, but also that we should expect their proposal to be considerably more expensive than some of the lower bids. The other input we got was not to underestimate the challenges of coordinating meetings and dealing with issues with CDMOs located in Asia.

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On the basis of input we received, we viewed Lonza as a highly desirable CDMO partner, but one that we may not be able to afford. There was no doubt that they had the experience, technical knowledge, scale and capacity in suitable locations to meet our needs.

Responsive and Competitive

We quickly received responses to our RFP, and were pleasantly surprised to find that Lonza's proposal was actually very cost competitive. Not only this, but there were other indications that Lonza was very motivated to work with Surrozen. They appeared to have a great appetite for the

novel science we were working on, which was encouraging because they are a CDMO with valuable technical know-how that they could bring to our project.

As our shortlist of CDMOs was quickly narrowed, we visited the key candidates. The meeting with Lonza took place at its Slough, UK site and our team was introduced to the senior scientists we would be working with. The Lonza team was very well prepared. The fact there were 10-12 people in the room who clearly understood what we were doing, the key characteristics of our molecules, and some of the uncertainties, made it feel more like a kick-off meeting than a pre-selection visit. Lonza further demonstrated in that meeting that they were approachable and wanted to work with Surrozen.

the second program, and laid the foundation for a very meaningful strategic relationship.

Open-Minded Scientific Team

Another key driver in the relationship developing was the flexibility that Lonza conveyed in the initial interactions – a factor we felt would be crucial to our development program, as there were some unknowns in terms of milestone timing and volumes. We knew that Lonza had tried and tested platform approaches and methods, but we found the scientists to be open minded and willing to listen to us. Our concern was actually not with any limitations of a large CDMO but rather that smaller CDMOs with limited technologies would lack the capability and resources to be adaptable.

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A Multiproduct Proposal

In fact, not only did Lonza want to work on the original project we discussed, they were intrigued by the novel and complex nature of our range of molecules. Surrozen was starting out with a molecule targeting liver disease, but our class of regenerative antibodies has the potential to repair a broad range of tissues and organs damaged by serious diseases, so there are many applications, and this includes a second program that was being explored to target inflammatory bowel disease.

A multiproduct deal was consequently discussed, and Lonza agreed to apply the favorable terms and flexibility proposed for the first program to both. This symbiotic approach would benefit both parties. For Surrozen, it meant avoiding repeating the whole CDMO evaluation process for each molecule, defined known economics for development of

One good example of process flexibility was Lonza adapting to our approach in the management of salt concentration. Surrozen is typical of a small biotech with no manufacturing capability, but there is considerable protein science expertise in the organization. One of our scientists had developed a particular technique relating to salt concentration in our liver disease candidate. Lonza found that a typical process and salt concentration didn't work, so they implemented Surrozen's recommendations, which was successful. This was early on in the relationship and set the tone for scientific collaboration and flexibility.

Crucial elements of flexibility were not merely exhibited by one individual at Lonza. The entire scientific team proved very open minded. Our first molecule turned out to be challenging in many unexpected ways, even in steps that we had assumed would be fairly standard. Lonza's scientists did

a lot of debugging and modified several basic steps once the relationship began.

It was clear that the Lonza's scientists had expertise in the inherent variability of molecules made by living cells. The company is clearly driven by science and is willing to follow the direction suggested by data. Lonza has also been very proactive. The team often presents experimental results on a Monday in response to ideas discussed at a meeting on the preceding Thursday.

Establishing Manufacturability

When we first selected Lonza, we did not even know if novel, bispecific, multivalent antibodies –– with their unprecedented structures –– could actually be reliably manufactured, particularly at scale. We had conducted research at Surrozen, but only on a very small scale. Questions remained about the ability to express these molecules at large scale at concentrations high enough to make them commercially viable, as well as question marks over their stability and ability to be formulated.

Fortunately, the molecules proved to be very stable and were able to be formulated like typical antibodies. While this can be attributed to the nature of the molecules themselves, there is no doubt that Lonza's work on the development of an effective cell line, process development, and scale-up – including upstream cell culture and product expression and downstream purification and formulation development – significantly reduced the risks for our molecules.

This part of the project was extraordinarily successful thanks to Lonza's technical strength. We are now starting with very high concentrations of our antibody, which helps to facilitate every step downstream. If you don't start in a good place, you're definitely not going to end up in a good place. We are in a strong position with the titers that Lonza has been able to achieve for both molecules. Lonza's capabilities also enabled rapid screening of typical antibody formulations to quickly identify optimum formulations.

Promising Preclinical Data

Everything that has happened in preclinical development between when Surrozen signed the deal with Lonza and today has been positive. We continue to see outstanding efficacy in animal models of the diseases we are pursuing, including disease modification, for which there was no precedent with current treatments. So, we are excited about these early results.

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For inflammatory bowel disease — target of our second candidate — anti-inflammatory therapies can lead to some healing of inflammation in the gut of a minority of patients. Our bispecific antibody, at least in animal models, is directly stimulating mucosal healing. If this effect can be achieved in humans and is durable, patients could manage their condition rather than just the symptoms, and the FDA could potentially make a determination of disease modification.

For our liver molecule, we are first targeting severe alcoholic hepatitis (SAH), a disease associated with chronic alcoholism in which binge drinking or infection leads to rapid destruction of hepatocytes, the functional cells of the liver. Typical patients are 40-45 years of age, and 30% die within 90 days. We have shown that our bispecific antibody rapidly stimulates the proliferation of hepatocytes in rodent models of liver injury, with manifestations of SAH reduced in three

days. If we see strong activity in humans in this disease, we will take this molecule into other potentially more chronic indications, such as diseases that cause cirrhosis.

Good Prospects for an Ongoing Collaboration

Partnering with a CDMO, in a truly collaborative manner, demands that a biotech recognizes the challenges and business needs of the CDMO. Sometimes, it is necessary to be understanding, while at others, there is a need to be more demanding. However, it always means being driven by the data. Good CDMOs are not basic service providers – the relationship should be a scientific collaboration.

Surrozen and Lonza have taken this approach together, and the relationship has been successful. Surrozen has benefited from a pre-existing relationship between our head of technical operations and Lonza's project manager, which provided a fundamental comfort level. They conduct regular project team meetings and introduce subject matter experts as needed. Lonza is also quick to set up special meetings with additional experts if there is a problem that requires more specific scientific knowledge. It has also been very responsive in terms of additional data. With the time difference between Slough and California, the Lonza team is working when we are sleeping, and sometimes that has benefitted us with really short turnaround times to get those results.

Returning to the theme scheduling flexibility, our liver bispecific is a challenging molecule, and, despite the best efforts of our teams, the project has not always progressed as anticipated. In these cases, Lonza has always found an alternative slot for us when things have had to change. They have a lot of customers with many different projects to manage, but that also gives them some freedom and flexibility that is not available to a smaller CDMO. We have had a number of anticipated but unplanned delays, however,in every case Lonza has found a way to minimize the overall impact.

We are close to producing the first vial of GMP material, which is very exciting and a testament to both the relationship and the combined expertise of Lonza and Surrozen. With the success we are having with our first two programs, we hope to soon collaborate with Lonza on a third molecule.