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Biologics

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For mAbs, a Small Biotech Recognizes the Value in Lonza's Expertise and Track Record

– William B. Jones, Ph.D., Senior Vice President of Pharmaceutical Development, Corvus Pharmaceuticals

CORVUS PHARMACEUTICALS

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Dr. Jones was Director of Global Regulatory Affairs in Sanofi U.S.'s oncology business unit from December 2012 to December 2014. From 2008 to March 2012, he was Director of Project Management & Regulatory at Pharmacyclics, where he played a principal role in the development of ibrutinib. Prior to Pharmacyclics, he was Associate Director of Development at Plexxikon and Senior Project Manager at Vertex Pharmaceuticals. Dr. Jones earned a B.S. and a Ph.D. in chemistry from the University of Cincinnati and completed a post-doctoral fellowship at the University of Oxford.

William B. Jones, Senior Vice President of Pharmaceutical Development at Corvus Pharmaceuticals, discusses how Lonza's reputation for quality and its experience with antibodies were the driving forces in his company's selection of CDMO for its CPI-006 antibody program, which is currently under development as an oncology drug and investigation as a therapeutic for immune disorders and infectious diseases.

Early Focus on Oncology

Corvus Pharmaceuticals is a clinical-stage immunology-focused biopharmaceutical company developing drugs that target the most critical cellular elements of the immune system. We focus on bringing cleverly designed medicines to patients with difficult-to-treat cancers, immune disorders, and infectious diseases.

Corvus was started by a group of people previously involved with Pharmacyclics, including Richard Miller, one of the founders of both Pharmacyclics and IDEC. I joined the company in late 2014, shortly after Series A funding was raised that year. We in-licensed CPI-444 (ciforadenant), a small-molecule adenosine 2A receptor antagonist, that we are developing as a cancer immunotherapy. Our research group created and we are developing CPI-818, a small-molecule ITK inhibitor for treatment of T cell lymphomas and autoimmune disease. We are developing a humanized monoclonal anti CD73 antibody for cancer therapy and for infectious disease. This agonistic antibody activates immune cells, particularly B cells and stimulates antigen

specific humoral immunity. We were the first group to identify this novel mechanism of action.

Looking to a Partner with Experience

As a small biotech — we were 25 people in the first year and approximately 40 today — with experience in small molecules and immunology, we knew we needed to outsource our mAb manufacturing, and we needed a partner that had a lot of experience developing, manufacturing, and commercializing antibodies.

We sent out a request for proposal to several companies — mostly larger, well-established firms. The companies responded with similar timelines and costs. Some quotes were a little higher than others, but the differences were small enough that it wouldn't significantly factor in the selection of a partner.

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Selection Centers on Quality and Reputation

The differentiating features were experience developing and manufacturing mAbs and a good reputation for quality, and that's how we ended up choosing Lonza. Its track record in producing monoclonal antibodies (mAbs) is exceptional, and that went a long way for us. I had experience working with Lonza when I was working with previous companies, as did one or two of my colleagues. Corvus' consultant was also part of the decision to select Lonza.

What made the difference to us was Lonza's reputation for quality and its expertise in the antibody space. It's a well-known CDMO that has been inspected routinely by many major health authorities worldwide. The company has an excellent track record, with demonstrated ability to get drugs approved. Beyond maximizing the likelihood of advancing the project, there is also value in the regulatory support. The authorities know Lonza well, so selecting Lonza helped Corvus mitigate risk and promote speed.

Lonza's brand name is another crucial factor that is particularly valuable for smaller biotechs — it lends credibility and provides comfort to investors and regulators that high quality antibody skills will be implemented. Lonza as our partner inspires confidence in our collaborators and investors, as they are typically very familiar with Lonza's reputation.

As mentioned, Lonza's depth of experience with antibodies was the biggest driver in the CDMO selection process. Corvus is developing a unique, engineered IgG1 antibody, so it made sense to look at a partner with deep experience manufacturing antibodies. The fact that CPI-006 fitted Lonza's antibody platform and processes so well gave us tremendous confidence in their ability to efficiently manufacture Corvus' mAb.

In fact, the three GMP lots we've made for clinical trials have been virtually indistinguishable from one another, along with the 250-L lot produced to initiate our pre-clinical studies and even the earlier 10-L and 15-mL lots made in the lab. That's important to an emerging company like Corvus, because we need reliability and efficiency. We have a high level of confidence that when our antibody is made it will be the exact same antibody we made before, and this consistency ultimately helps our timelines of course.

Not Just Corvus Driving the Decision

We talk about our selection process, but what was equally

gratifying was Lonza's appetite for our project and interest in creating the parameters to take it on. Lonza was very busy at the time but showed desire for our business and flexibility to start our project quickly. Lonza completed cell line development at its Singapore facility and transferred the cell line development to its Slough, UK facility to establish the master cell bank, develop the manufacturing process, manufacture, and test CPI-006.

There was a bit of uncertainty in how the process was going to work at the beginning, but Lonza worked hard to support Corvus from the outset. In the time since this project began, Lonza added its Hayward, California, and Visp, Switzerland sites, so it's clear there is an effort to offer flexibility and global capacity to serve the innovation coming out of small biotechs.

Understanding Small Company Challenges

While small companies need predictability from their CDMO partners, it is also really difficult for biotechs to predict what is going to happen over several years. This dichotomy can be challenging for CDMOs supporting startups and virtual companies.

challenge by being flexible about batch sizes and frequency. While they wanted to make a five-year plan, they understood our situation and we ended up producing three GMP batches for the clinic — one per year for three consecutive years. Now we are in a position to scale-up to larger batch sizes as more drug is required.

Responsive and Engaging

The project managers and scientists at Lonza have been very responsive to our requests. We initially had some small issues with continuity and communication between project managers at different facilities, but that has been resolved.

Currently, we are working with four different project managers and a business development person on different aspects of the project. These five Lonza people are our main points of contact, but they are also always willing to connect us with individual experts as needed. However, Corvus can contact subject matter experts such as the regulatory person directly to avoid delays.

It has been tremendously helpful to have all of the Lonza

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We have proven to be a prime example of this, since we are developing CPI-006 as an oncology agent and, based on research we have done along the way, as an immunotherapy for infectious diseases. Oncology requires high and frequent dosing, creating the need for many tens of grams of antibody per person. As a result of discoveries we made along the way regarding stimulation of the immune system, and influenced by the subsequent emergence of the SARS-CoV-2 virus, we are now exploring the potential of CPI-006 to modulate immunity in a variety of indications. Ultimately, this could lead to a big shift in manufacturing – from needing tens to hundreds of kilos of the antibody to less than ten kilos. Lonza has worked with us to manage this manufacturing

experts engaged in our projects. For example, when the idea of moving the CPI-006 project from Slough to another site was first raised, being able to talk to the scientific personnel at both sites helped us get a better understanding of what would be involved to transfer the process, including identifying the systems and equipment that would change, how the process would be modified, issues that may arise, and plans to mitigate the issues. In essence, Lonza helped us understand the biggest risks and how they could be managed. That openness has been invaluable.

Visibly Increasing Flexibility

During the first three years working with Lonza, the approach was more rigid with respect to the process and use of the

platform method. They work well, but there have been rare instances when the platform method didn't work perfectly for Corvus' mAb. Lonza's flexibility improved markedly over the last couple of years, and today there is much greater latitude to change methods.

That change has been accompanied by a shift in culture as well. There is more flexibility around scheduling and a willingness to take more unique approaches that better fit a smaller company like Corvus, which has a different perspective of risk than Lonza's larger customers.

Lonza has increased its willingness to adapt to complex and involved processes to reduce cost and or time by taking on calculated risks. In cases where the confidence level is high, savings could outweigh any slightly elevated risk.

Learning and Evolving Together

A lot has changed over the five years Corvus has been working with Lonza. CPI-006 was initially developed to target the CD73 enzyme, which converts adenosine monophosphate to adenosine. This is thought to play a major role in cancer. In fact, Corvus was one of the first companies and probably the leader in looking at adenosine in cancer.

In the fall of 2019, we discovered that CPI-006 also activated B cells and thus the immune system. We considered potential applications, including as a booster of immune responses in vaccines against various viruses. The COVID-19 pandemic emerged, which inspired us to explore the affect of CPI-006 in immune related indications in addition to cancer.

Corvus continues to focus on oncology trials with CPI-006, which are in phase II. What was exciting from our research into the activation of B cells is that CPI-006 may have applications outside of oncology. That could lead to additional increases in demand if approvals are received for other infectious disease indications.

Lonza was part of discussions to plan a strategy that would address this tremendous shift in our program. For instance, we elected to use 2,000-L reactors because Lonza has a large number of them, which will allow us to scale up or down as needed. It's another example of the flexibility Lonza is delivering for Corvus.

Lonza is helping us transfer the manufacturing process from its Slough, UK facility to the Visp, Switzerland facility this year to keep our project moving forward within budgetary constraints. With expanded production capabilities in Europe, the United States, and Asia, Lonza is well positioned to help Corvus meet all future requirements.

A Likely Long-Term Relationship

The investigation of CPI-006 as a treatment for viral infections has opened the door to many other possibilities. In addition to its potential as a treatment for infectious diseases, it is possible that CPI-006 could be effective against virally induced cancers. We are in the process of adapting to these possibilities and determining what the future will hold for Corvus.

Regardless, we expect Lonza to be a partner for the long term. We will need their manufacturing support if CPI-006 is commercialized for cancer as well as other indications. We have already initiated discussions with Lonza about pre-BLA activities. It is likely that Corvus will have a long-term relationship, certainly on this molecule and potentially others in our pipeline going forward.