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# Tuning the Myeloid Compartment with a Best-in-Class CDMO

– Alicia Levey, Chief Operating Officer  
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Alicia Levey and Kiren Khanduja of Pionyr Immunotherapeutics — a San Francisco-based biotech with a pipeline of first-in-class clinical-stage cancer immunotherapies targeting the tumor microenvironment — discuss the basis for selection of Lonza to meet Pionyr’s goals to rapidly develop a third lead candidate from the start and to scale-up manufacturing of two clinical-stage immuno-oncology treatments after tech transfer.

## A Different Type of Immuno-Oncology Drug

Pionyr Immunotherapeutics was one of the first companies in the immuno-oncology space to look beyond the T-cell and focus on targeting immunosuppressive myeloid cells as an anti-cancer therapeutic strategy. Building on work initially conducted in Max Krummel’s laboratory at UCSF, Pionyr has built a target discovery platform and pipeline of next-generation immuno-oncology therapeutics targeting immunosuppressive myeloid cells (monocytes, macrophages and neutrophils) with unique mechanisms of action (depletion, activation and reprogramming).

## Pionyr’s Approach

Pionyr’s Myeloid Tuning™ approach enhances the immune system’s anti-tumor response by specifically altering the immunosuppressive myeloid infiltrate in the tumor microenvironment. We are currently advancing PY314 and PY159 — Fc-engineered monoclonal antibodies targeting TREM2 and TREM1, respectively — in Phase I dose-escalation and expansion studies in the clinic. PY314 selectively



Alicia Levey, Ph.D.  
Chief Operating Officer

Dr. Alicia Levey currently serves as Chief Operating Officer at Pionyr Immunotherapeutics. Dr. Levey joined Pionyr in July 2019 and leads business development, business operations, portfolio strategy, and program management, in addition to managing intellectual property and legal functions. Dr. Levey was instrumental in architecting and closing a transformational staged acquisition of Pionyr by Gilead Sciences in 2020 and currently leads Alliance Management for the ongoing collaboration between the two companies. Dr. Levey earned a Ph.D. in Cancer Biology from the Stanford University School of Medicine.

depletes Tumor Associated Macrophages (TAMs) expressing TREM2, clearing a path for T-cells and pro-inflammatory myeloid cells to infiltrate the TME and destroy tumor cells. PY159 “re-programs” immunosuppressive monocytes, TAMs and TANs (Tumor Associated Neutrophils) to shift intracellular signaling to a pro-inflammatory state and subsequent further immune cell recruitment and tumor destruction.

Our third program, PY265, has a target and mechanism of action distinct from either PY314 and PY159 and is at the Development Candidate stage. We also continue to leverage our platform and deep expertise in the myeloid space to progress additional first-in-class programs at earlier

would really allow Pionyr to optimize our resources and remain lean.

Pionyr’s Chief Technical Officer, Evan Greger, knew Lonza from relationships while at other companies, and his consequent familiarity with several Lonza sites and experience working with the company influenced a view of Lonza as one of the best providers in its class. Similar experience among several Pionyr board members was another important factor.

The internal team at Pionyr worked to ensure the company conducted a thorough CDMO selection process that considered both technical and business criteria. We initially

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development stages. Each of these therapies has the potential to be a transformational addition to the immunotherapy armamentarium due to their broad applicability in multiple tumor types and likely synergy with first-generation checkpoint inhibitors.

#### **Unifying to a Full-Service CDMO**

For our first two candidates, PY314 and PY159, Pionyr partnered with a Europe-based CDMO to produce Phase I material. This partner is excellent but does not currently have the capability to support projects through commercialization. We consequently focused on finding a best-in-class provider across the entire value chain from cell line development to commercialization, who could support our third pipeline project and also transfer our two assets already progressing through the clinic. As a startup company, we felt that a partnership with a single CDMO that has a fully integrated, end-to-end solution and strong technical capability

evaluated CDMOs worldwide but quickly narrowed to providers in Europe because it would allow us to leverage our existing European network.

#### **Lonza Stands Out in Evaluation Process**

Through our formal RFP process, Pionyr evaluated 13 different CDMOs using a scoring matrix, and Lonza scored highly. It has a strong footprint in Europe, as well as a global manufacturing network comprising large bioreactor capacity with scale-up capability, offering flexibility to adapt to market demand fluctuations.

For our internal experts, the conversations our team had with different Lonza SMEs across analytical and manufacturing (upstream / downstream drug substance and final drug product) areas stood out from other CDMOs — not just hearing about Lonza’s capabilities but also their thoughts on certain technical trends and how the company is responding

and incorporating new technologies into its offering.

### **De-risking the Manufacturing Process**

During the selection process, we were excited to learn that Lonza offered competitive pricing for its end-to-end offering, which made it clear that that Lonza could be an ideal partner for Pionyr. That, coupled with the company's experience, meant that Pionyr would be taking on less risk. We are a small company, so partnering with Lonza was a way to minimize manufacturing risk and shift the candidate development risk to where it should be, which is in the clinic itself.

The selection process happened to coincide with the COVID-19 pandemic and the travel restrictions it imposed,

There was a camaraderie in the process — as serious as the process is, the two teams laughed along the way, which made it an enjoyable experience for all concerned. And despite the depth and breadth that Lonza brought to the table, it was also helpful to have a single point of contact work with Pionyr through the entire proposal process, and that person is now our account manager, which provides continuity.

### **Ideal Platform Alignment**

When we first sought a new CDMO partner, we were not yet sure if our third candidate would be fucosylated or afucosylated. The fact that Lonza has the ability to produce both was therefore an important factor. The candidate turned out to have an IgG1 format, which slotted perfectly into Lonza's

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which was an added challenge, but Lonza was well organized and provided informative virtual tours of its sites. They were willing to do this as many times as we requested and also connected our team with key business and technical leaders from the sites relevant to Pionyr. Lonza's teams comprised many people with a wide range of expertise, so they were able to answer all the questions we had. They were also very responsive, turning documents around and providing answers to our questions quickly.

### **Understanding and Listening**

Overall, Lonza recognized that we needed a detailed understanding of its capabilities and the different sites to determine if it was truly a good fit. There was also an appreciation and recognition that Pionyr is a small but growing biotech with certain needs and the ability to tolerate some risks but not others, particularly with respect to manufacturing.

Just as importantly, Lonza was open and candid about the areas where they could be more flexible and less flexible.

Light Path technical platform — a great plus for Pionyr when we evaluated the entire proposal from start to finish because we knew we could leverage this platform from cell line development to IND.

The initial collaboration with Lonza aims to bring PY265 — directed against an undisclosed novel Myeloid Tuning™ target — into clinical development. Lonza is providing cell line development, process development, supply chain simplification and de-risking, as well as drug substance and drug product manufacturing. Another key indicator of Lonza's flexibility is its tailoring of the cell line development program to accommodate the specific needs of Pionyr. The cGMP batches of drug substance and drug product are expected to be completed in 2022.

We started the program in April 2021. By the end of November, things were progressing according to the project plan. There are points where we need to really align and pay close attention, but everything is going well and we are already

benefiting from the strength of Lonza's platform technology, which is enabling a fast path to IND.

#### **Well-Structured and Enjoyable Collaboration**

Lonza has a strong framework for our interactions throughout the project process. We have a biweekly joint project team meeting that has CMC representation, as well as different team members within our organization that interface with Lonza, such as toxicology, protein sciences and bioanalytical.

On alternate weeks, we have a one-on-one with our project manager that includes project management and technical representation. Lonza also brings in other SMEs for brainstorming sessions if we have technical questions, if we need to alter the scope of work, or if any other opportunities arise.

Lonza has exceeded our expectations in terms of technical depth, but has also been extremely receptive to our ideas and flexible in its approach.

Fundamentally, sticking to the timeline is one of the biggest priorities for Pionyr, and Lonza has aligned their approach with this need. There are always some hiccups in any project, but everything has moved forward without any impact on the timeline. A big part of that is the problem-solving capabilities within the Lonza team, which enables them to stay on task and move things forward.

We hope to have all three of our programs at Lonza by the end of 2022. If things go well in the clinic, we will advance all three to commercialization, with plans to leverage Lonza's

## **“ We are already benefitting from the strength of Lonza's platform technology, which is enabling a fast path to IND. ”**

The mix of formal and informal interaction is beneficial in terms of keeping our project on track. From this point of view, it is also helpful that Lonza has a stable team and there is a great deal of personnel continuity.

Pionyr is also currently in discussions with Lonza about our two assets that are moving toward Phase II, evaluating how they will fit into Lonza's network. We are conscious that we are bringing in cell lines and analytical methods that were developed elsewhere, but so far there have been focused, productive discussions on strategy and the different approaches necessary from commercial and network flexibility perspectives.

#### **More Flexible Than Most Realize**

As a large CDMO, people tend to expect Lonza to be inflexible, but this has not been our experience. The adaptability and openness we have witnessed is what you would expect from an agile provider. The team at Pionyr has enjoyed the process.

network and expertise to scale from development to commercial production using processes that are well-defined, scalable and robust.

#### **Advice to Small Biotechs**

As a small biotech, one of the most important goals when selecting a CDMO partner is to choose one that will not introduce any upstream risk. The risk should not be in manufacturing — it should be in the clinic. From a technical perspective, the CDMO has to have a demonstrated history of success, combined with the expertise and capacity relevant to the program of interest. The ideal scenario is to work with a CDMO that is well-versed in the development lifecycle and positioned to support smaller biotechs from cell line development through commercialization. At the same time, it is important to be sure to select a CDMO that understands the unique needs and perspectives of small companies, and one that is willing to listen and collaborate.

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At the end of the day, our advice is to select a CDMO that can allow you to grow your programs to position for success. Our third pipeline asset, PY265, will leverage the Lonza platform from its inception through development as it advances. The assets we are transferring, PY314 and PY159, have potential to be transformative therapies in the immuno-oncology space, targeting multiple solid tumor indications, and we are confident in Lonza as a partner to help us advance these programs quickly — should it be required — and scale to meet demand.

### **Pionyr’s Myeloid Tuning™ Technology**

Pionyr Immunotherapeutics is a clinical-stage company developing cancer immunotherapies that target the tumor microenvironment to enhance the body’s antitumor immunity. Pionyr’s Myeloid Tuning™ technology builds on the discovery that altering the tumor microenvironment to favor immune-activating cells over immune-suppressing cells enhances the body’s ability to combat cancer. By targeting cellular subsets distinct to those of approved checkpoint inhibitors (CPIs), Pionyr’s Myeloid Tuning™ therapies represent an orthogonal and potentially synergistic approach to treatment with CPIs.

Each of Pionyr’s three lead programs is a first-in-class molecule. PY314 targets for selective depletion of a subset of tumor-associated macrophages (TAMs) that express the surface receptor TREM2. Depleting TREM2+ TAMs clears the way for activated T cells and proinflammatory myeloid cells to take control of the TME and destroy tumor cells. PY159 targets of TREM1+ immunosuppressive monocytes, neutrophils, and macrophages for cellular “reprogramming”. Upon PY159 binding to TREM1 on these cells, intracellular signaling shifts them into proinflammatory states, leading to tumor cell destruction. PY265 is another reprogrammer but operates by a totally different mechanism involving a unique target.

Beyond these lead programs, Pionyr has a pipeline of candidates leveraging the concept of tuning the myeloid compartment within the tumor, each operating by a unique mechanism.



**Kiren Khanduja**  
Associate Director, CMC

Kiren Khanduja is an Associate Director in the CMC Group at Pionyr Immunotherapeutics, and has over 10 years of experience working in the biotechnology industry. She joined Pionyr in December 2019 and manages outsourced development and manufacturing activities across various Contract Development and Manufacturing Organizations (CDMOs) for both Drug Substance and Drug Product. Kiren played a key role in establishing the company’s relationship with Lonza. Prior to Pionyr, Kiren worked on the CDMO side of the business at Boehringer Ingelheim, supporting late-stage clients. Kiren earned a B.S./M.S.E. in Chemical Engineering from Johns Hopkins University.