



Istari Oncology Announces First Patient Dosed in the LUMINOS-102 Phase 2 Clinical Trial of PVSRIPO With and Without Immune Checkpoint Blockade in Advanced PD-1/L1 Refractory Melanoma

DURHAM, NC, March 31, 2021 – Istari Oncology, Inc., a clinical-stage biotechnology company, today announced that the first patient was dosed in the LUMINOS-102 phase 2 clinical trial, which will assess the safety and efficacy of PVSRIPO alone or in combination with a programmed death receptor-1/ligand 1 (PD-1/L1) inhibitor in patients with melanoma who are resistant to these checkpoint therapies.

PVSRIPO is a novel viral immunotherapy that activates the innate and adaptive immune system to stimulate the production of a functional, systemic anticancer CD8+ T cell response. Following positive phase 1 results,¹ the phase 2 trial will further explore PVSRIPO's impact on this population of patients in severe need of additional therapeutic options.

"Anti-PD-1/L1 therapies have been a major advancement in melanoma treatment, however, many patients develop resistance or never respond in the first place," said Matt Stober, President and Chief Executive Officer at Istari Oncology. "We are very optimistic about the prospects for the phase 2 trial. PVSRIPO monotherapy has already shown clinical activity in this population, and its mechanism is synergistic with anti-PD-1/L1 therapies, so we believe the combination may provide even more benefit."

"As the use of anti-PD-1/L1 therapies has grown, so too has the need for new treatments as patients experience primary or acquired resistance and must resort to therapeutic approaches with a high incidence of serious adverse events," said Garrett Nichols, MD, MS, Chief Medical Officer at Istari Oncology. "Our goal is to address this unmet need, and LUMINOS-102 will be a critical step in determining whether PVSRIPO can rekindle antitumor responses in the PD-1/L1 refractory population without adding any significant toxicity."

LUMINOS-102 is an open-label, phase 2, multicenter randomized trial ([NCT04577807](https://clinicaltrials.gov/ct2/show/study/NCT04577807)) in patients with melanoma that have progressed on anti-PD1/L1 therapy and will characterize the safety, tolerability and initial efficacy of PVSRIPO intratumoral injection alone (Arm 1) and in combination with a PD-1 inhibitor (Arm 2). An interim analysis is planned once 20 patients have been randomized and treated for 3 months. Patient outcomes, including objective response

rates (by RECIST criteria), durability of responses, progression free survival and overall survival will be measured over a 24-month time frame.

LUMINOS-102 builds upon a successful [phase 1 trial](#) of PVSRIPO monotherapy in anti-PD-1 refractory advanced melanoma presented by Dr. Georgia Beasley and colleagues at the Society for Immunotherapy of Cancer (SITC) 2020 Annual Meeting and in-press for an upcoming issue of the Journal for ImmunoTherapy of Cancer (JITC). In the phase 1 study, the overall response rate in subjects who received three single intratumoral injections 3 weeks apart (the maximum number administered in the study) was 67% (4/6), suggesting PVSRIPO was able to initiate or rekindle responses in patients who have failed anti-PD-1 therapy. Responses were observed in both injected and noninjected tumors, suggestive of an abscopal response. No serious adverse events or dose-limiting toxicities were observed.

“Being based on the poliovirus vaccine, our team was intrigued by the potential for PVSRIPO to leverage an immunological recall response to fight cancer in patients who have been vaccinated against polio. This and other unique mechanisms as well as the responses seen in the phase 1 trial encouraged us to get involved in LUMINOS-102,” noted Ding Wang, MD, Director of the Phase 1 Program and Associate Director of Clinical Trials Office at Henry Ford Cancer Institute, Detroit, MI. “LUMINOS-102 will build on these data and further evaluate the ability of PVSRIPO to generate a systemic immune response, important for patients with unresectable anti-PD-1 refractory melanoma. We’re proud to be the first site to treat a participant and looking forward to continuing enrollment.”

The LUMINOS-102 phase 2 trial will be conducted across more than 20 research sites across the US including Henry Ford Cancer Institute.

For more information about Istari Oncology and their ongoing clinical trials, visit www.istarioncology.com.

About PVSRIPO

PVSRIPO is an investigational immunotherapy based on the live attenuated Sabin type 1 poliovirus vaccine that has been genetically modified for safety. PVSRIPO has a distinct target (the poliovirus receptor, CD155), which is expressed on virtually all solid tumors and antigen-presenting cells. Via CD155, PVSRIPO targets tumors with two primary mechanisms: 1) direct damage to and killing of cancerous cells; and 2) engaging innate and adaptive antitumor immune responses via nonlethal infection of antigen presenting cells in the tumor, which stimulates a specific signaling pathway resulting in a sustained, robust type-I/III interferon-dominant response, with minimal release of unwanted cytokines. Its effects are potentiated by prior vaccination against poliovirus. PVSRIPO has been granted Breakthrough Therapy Designation and Orphan Status by the FDA in recurrent glioblastoma. PVSRIPO has also been granted Orphan Status by the FDA for advanced melanoma.

About Melanoma

There are estimated to be over 12,000 new and recurrent cases of advanced, unresectable melanoma diagnosed in the U.S. each year, and around 7,000 deaths. While immune checkpoint inhibitors have dramatically improved the outlook for advanced melanoma patients today, most patients treated with these immunotherapies are either primary nonresponders or eventually develop immune-refractory progressive disease and require additional therapy.

About Istari Oncology

Istari Oncology, Inc., headquartered in Research Triangle Park, North Carolina, is a privately held clinical-stage biotechnology company focused on novel immuno-oncology and immunotherapy platforms for the treatment of glioblastoma and a wide variety of tumors. The company was founded by Darell Bigner, MD, PhD and Matthias Gromeier, MD, of Duke University Medical Center in 2016. Istari licensed a broad range of patents and patent applications from Duke University and has access to additional intellectual property to continue clinical and commercial development of these technologies. The company's primary platform currently in clinical development is PVSRIPO. For more information, please visit www.istarioncology.com.

References

1. Beasley GM, Nair SK, Farrow NE, et al. A phase I trial of intratumoral PVSRIPO in patients with unresectable, treatment-refractory melanoma. *J Immunother Cancer*. 2021 [in press].

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