Iovance Biotherapeutics Announces Updated Clinical Data for Lifileucel in Advanced Melanoma at Society for Immunotherapy of Cancer (SITC) Annual Meeting

November 10, 2022

31% Objective Response Rate (ORR) and Median Duration of Response (mDOR) Not Reached at 36.5 Months Median Study Follow Up in C-144-01 Trial (Cohorts 2 and 4)

42% of Responses Lasted for 24+ Months

SITC Update and KOL Panel Webcast Thursday, November 10 at 4:30 pm ET

SAN CARLOS, Calif., Nov. 10, 2022 (GLOBE NEWSWIRE) -- Iovance Biotherapeutics, Inc. (NASDAQ: IOVA), a late-stage biotechnology company developing novel T cell-based cancer immunotherapies (tumor infiltrating lymphocyte, TIL, and peripheral-blood lymphocyte, PBL), today announced updated clinical data for lifileucel in advanced melanoma during a rapid oral presentation at the Society for Immunotherapy of Cancer (SITC) Annual Meeting.

Amod Sarnaik, M.D., Professor of Cutaneous Oncology and Immunology at H. Lee Moffitt Cancer Center, presenting author and lead C-144-01 trial investigator, stated, “We are excited to present the comprehensive clinical data on behalf of the C-144-01 investigators. The trial demonstrated a robust and clinically meaningful response rate and long-term durability following one-time treatment. Patients in this study were difficult to treat and lacked approved therapies after current standard of care. We hope to offer lifileucel to many more patients after initial progression on immune checkpoint inhibitors.”

The oral presentation for the C-144-01 trial included efficacy data from 153 patients with advanced melanoma enrolled in Cohort 2 (n=66) and Cohort 4 (n=87) with a median study follow up of 36.5 months (data cut off July 15, 2022). All patients had progressed on or after immune checkpoint inhibitor (ICI) therapy and targeted BRAF/MEK inhibitor therapy where appropriate. There are no treatments approved by the U.S. Food and Drug Administration (FDA) for the C-144-01 study population. The current available care is chemotherapy (4-10% ORR; median overall survival [mOS] of 7-8 months).[1-4]

SITC C-144-01 Data Highlights for Pooled Analysis (36.5 Months Median Study Follow Up)

- **Heavily Pretreated Patient Population with Substantial Disease Burden:** Patients had received a median of 3 lines of prior therapy (range 1-9), including anti-PD-1 therapy in 100% of patients (median: 2 lines, range 1-7) and anti-CTLA-4 therapy in 81.7% of patients, with prior combination anti-PD-1 and anti-CTLA-4 therapy received in 53.6% of patients. Baseline disease characteristics were generally similar between Cohorts 2 and 4. However, Cohort 4 patients showed both a higher disease burden (> 3 lesions: 83.9% vs. 65.2%) and a higher proportion of patients with elevated lactate dehydrogenase (LDH; 64.4% vs 40.9%), a well-known negative prognostic factor in melanoma.[5]

- **Clinically Meaningful Response Rate and Durability**
  - **Clinically Meaningful ORR and Deepening of Responses Over Time**: The ORR assessed by an independent review committee (IRC) using RECIST v1.1 was 31.4% (95% CI: 24.1%-39.4%), with 9 complete responses (CRs) and 39 partial responses (PRs). The median time from lifileucel infusion to best response was 1.5 months, and responses deepened over time. Initial PRs converted to CRs in 7 patients, as late as 2+ years post-lifileucel, including 1 conversion to CR in approximately 10 months since the initial data analysis in the abstract.

  - **mDOR (Not Reached) and Durability at 2+ Years:** The mDOR was not reached (estimated by Kaplan-Meier, or KM, method). Responses lasted for 24 months or greater in 41.7% of responders (47.8% of responders in Cohort 2; 36.0% of responders in Cohort 4).

  - **Long-Term Benefit from One-Time Lifileucel Therapy:** The DOR and overall survival (OS) KM plots show plateaus characteristic of immunotherapy, supporting the potential for long-term benefit from lifileucel therapy. Median (mOS) had not been reached (95% CI: 30.4-NR) in patients who achieved a response at first assessment (6 weeks). mOS in all patients was 13.9 months (95% CI: 10.6-17.8).

- **Responses Across All Subgroups:** Responders to lifileucel included patients with ICI primary-resistant disease, those who received prior anti–CTLA-4 therapy and/or targeted therapies, and responses were observed regardless of PD-L1 status. LDH and target lesion sum of diameters (SOD; tumor mass across locations) were correlated with ORR (P=0.008). Higher odds of response with lower tumor burden suggest that early intervention with lifileucel after ICI may maximize

benefit.

- **Safety**: Treatment-emergent adverse events (TEAEs) were consistent with the underlying disease and known AE profiles of nonmyeloablative lymphodepletion and interleukin-2 (IL-2). Incidence of TEAEs decreased rapidly within the first 2 weeks after lifileucel infusion.

- **94.7% Manufacturing Success Rate:** All patients in both cohorts received the same lifileucel treatment using Iovance's proprietary 22-day manufacturing process (Gen 2). Lifileucel was manufactured within specification in 94.7% of patients across Cohorts 2 and 4.

Friedrich Graf Finckenstein, M.D., Chief Medical Officer of Iovance, stated, "Our C-144-01 trial is the largest clinical trial of a cell therapy in advanced melanoma following anti–PD-1 therapy and the basis for our rolling BLA submission for lifileucel. We observed responses across the spectrum of patients with advanced melanoma, including early responses and deepening responses over time, following anti-PD-1 and anti-CTLA-4 therapy, and regardless of mutation and PD-L1 status. Given the correlation of lower tumor burden and response, we believe there is a strong rationale for treatment with lifileucel as soon as possible after initial progression on anti–PD-1 therapy. The potential for long-term benefit from one-time treatment with lifileucel is promising, as the overall survival data show the desired plateau of maintained benefit with immunotherapy, and include patients who are alive five years after treatment."

The C-144-01 results are available in the oral presentation slide deck on the Iovance corporate website. Data from the pivotal Cohort 4, supportive data from Cohort 2 and the pooled analysis of Cohorts 2 and 4 are part of a rolling Biologics License Application (BLA) submission to the FDA for lifileucel in advanced melanoma, which Iovance initiated in August 2022.

Investor Webcast on Thursday, November 10, 4:30 p.m. ET
Iovance will host a webcast on Thursday, November 10 at 4:30 p.m. ET to discuss clinical data updates for lifileucel in advanced melanoma. Iovance senior leadership will be joined by the following key opinion leaders and principal investigators in Iovance clinical studies: Amod Sarnaik; Allison Betof Warner, M.D., Ph.D., Assistant Attending Physician and Melanoma Medical Oncologist, Memorial Sloan Kettering Cancer Center; Miguel Perales, M.D., Chief, Adult Bone Marrow Transplant Service, Memorial Sloan Kettering Cancer Center; and Martin McCarter, M.D., Surgical Director for the Esophageal and Gastric Multidisciplinary Clinic, Vice Chair for Strategy and Program Development Department of Surgery, UCHealth Cancer Care - Anschutz Medical Campus - University of Colorado Cancer Center. The live and archived webcast can be accessed in the Investors section of the company's website here: https://ir.iovance.com/events/event-details/sitc-investor-webcast

About Iovance Biotherapeutics, Inc.
Iovance Biotherapeutics aims to be the global leader in innovating, developing and delivering tumor infiltrating lymphocyte (TIL) therapies for patients with cancer. We are pioneering a transformational approach to cure cancer by harnessing the human immune system's ability to recognize and destroy diverse cancer cells in each patient. Our lead late-stage TIL product candidate, lifileucel for metastatic melanoma, has the potential to become the first approved one-time cell therapy for a solid tumor cancer. The Iovance TIL platform has demonstrated promising clinical data across multiple solid tumors. We are committed to continuous innovation in cell therapy, including gene-edited cell therapy, that may extend and improve life for patients with cancer. For more information, please visit www.iovance.com.

Forward-Looking Statements
Certain matters discussed in this press release are "forward-looking statements" of Iovance Biotherapeutics, Inc. (hereinafter referred to as the "Company," "we," "us," or "our") within the meaning of the Private Securities Litigation Reform Act of 1995 (the "PSLRA"). All such written or oral statements made in this press release, other than statements of historical fact, are forward-looking statements and are intended to be covered by the safe harbor for forward-looking statements provided by the PSLRA. Without limiting the foregoing, we may, in some cases, use terms such as "predicts," "believes," "potential," "continue," "estimates," "anticipates," "expects," "plans," "intends," "forecast," "guidance," "outlook," "may," "could," "might," "will," "should" or other words that convey uncertainty of future events or outcomes and are intended to identify forward-looking statements. Forward-looking statements are based on assumptions and assessments made in light of management's experience and perception of historical trends, current conditions, expected future developments and other factors believed to be appropriate. Forward-looking statements in this press release are made as of the date of this press release, and we undertake no duty to update or revise any such statements, whether as a result of new information, future events or otherwise. Forward-looking statements are not guarantees of future performance and are subject to risks, uncertainties and other factors, many of which are outside of our control, that may cause actual results, levels of activity, performance, achievements and developments to be materially different from those expressed in or implied by these forward-looking statements. Important factors that could cause actual results, developments and business decisions to differ materially from forward-looking statements are described in the sections titled "Risk Factors" in our filings with the Securities and Exchange Commission, including our most recent Annual Report on Form 10-K and Quarterly Reports on Form 10-Q, and include, but are not limited to, the following substantial known and unknown risks and uncertainties inherent in our business: the effects of the COVID-19 pandemic; risks related to the timing of and our ability to successfully develop, submit, obtain and maintain U.S. Food and Drug Administration ("FDA") or other regulatory authority approval of, or other action with respect to, our product candidates, and our ability to successfully commercialize any product candidates for which we obtain FDA approval; whether clinical trial results from our pivotal studies and cohorts may support registration and approval by the FDA; preliminary and interim clinical results, which may include efficacy and safety results, from ongoing clinical trials or cohorts may not be reflected in the final analyses of our ongoing clinical trials or subgroups within these trials or in other prior trials or cohorts; the risk that enrollment may need to be adjusted for our trials and cohorts within those trials based on FDA and other regulatory agency input; the changing landscape of care for cervical cancer patients may impact our clinical trials in this indication; the risk that we may be required to conduct additional clinical trials or modify ongoing or future clinical trials based on feedback from the FDA or other regulatory authorities; the risk that our interpretation of the results of our clinical trials or communications with the FDA may differ from the interpretation of such results or communications by the FDA (including from the recent pre-BLA meeting with the FDA); the risk that the rolling BLA submission for lifileucel in metastatic melanoma may take longer than expected; the acceptance by the market of our product candidates and their potential reimbursement by payors, if approved; our ability or inability to manufacture our therapies using third party manufacturers or our own facility may adversely affect our potential commercial launch; the results of clinical trials with collaborators using different manufacturing processes may not be reflected in our sponsored trials; the risk that unanticipated expenses may decrease our estimated cash balances and forecasts and increase our estimated capital requirements; and other factors, including general economic conditions and regulatory developments, not within our control.

[1]Keytruda USPI accessed Mar 2022
[2]Weber et al., Lancet Oncol 2015
[3]Kirchburger et al., Eur J Cancer 2016
[4]Goldinger et al., J Clin Oncol 2018
[5]Claps et al., Nat Rev Clin Oncol 2022

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