The Journal of Clinical Oncology Publishes Five-year Analysis of Amtagvi® (lifileucel) in Patients with Advanced Melanoma

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One-time Amtagvi Treatment Continues to Show
Deep, Durable Responses and Meaningful Survival

One Third of Responses Remain Ongoing without Subsequent Treatment after Five Years

Simultaneous Presentation at ASCO 2025

SAN CARLOS, Calif., June 02, 2025 (GLOBE NEWSWIRE) -- Iovance Biotherapeutics, Inc. (NASDAQ: IOVA), a commercial biotechnology company focused on innovating, developing, and delivering novel polyclonal tumor infiltrating lymphocyte (TIL) therapies for patients with cancer, today announced that the *Journal of Clinical Oncology* has published the final analysis from the Phase 2 C-144-01 clinical trial evaluating the individualized T cell therapy Amtagvi® (lifileucel) in patients with advanced melanoma. These five-year follow-up results are being simultaneously presented during an oral session today at the 2025 American Society of Clinical Oncology (ASCO) Annual Meeting.

This five-year analysis of the C-144-01 trial represents unprecedented durability and duration of follow-up in advanced melanoma patients previously treated with anti-PD-1 and targeted therapy, where applicable. The analysis includes 153 patients from cohorts 2 and 4 of the C-144-01 trial.

One-time Amtagvi treatment demonstrated long-term benefit in heavily pretreated patients, including deep and durable responses, meaningful overall survival without further treatment, and no new or late-onset adverse events at a median follow-up of 57.8 months. The objective response rate was 31.4% with a median time to response of 1.4 months and a median duration of response of 36.5 months. Nearly one third of responders (31.3%) completed the five-year assessment with ongoing responses. The median overall survival (mOS) was 13.9 months with a five-year survival rate of 19.7%. Survival outcomes were consistent among responders, regardless of time of onset of response to Amtagvi therapy.

The observed safety profile was consistent with that of nonmyeloablative lymphodepletion and interleukin-2 administration. The incidence of AEs decreased rapidly within the first two weeks after Amtagvi infusion, and there were no new or late-onset treatment-related AEs.

Theresa Medina, M.D., medical oncologist at the University of Colorado Cancer Center on the Anschutz Medical Campus, stated, “Amtagvi has demonstrated long-term benefit and meaningful overall survival in a difficult-to-treat melanoma patient population resistant to immune checkpoint inhibitor therapy. Five years following one-time Amtagvi treatment, responses persisted or deepened during an extended treatment-free interval for some patients. Amtagvi offers a new standard of care for the advanced melanoma community and sets a new bar for one-time cell therapies with curative intent in solid tumors.”

In February 2024, the U.S. Food and Drug Administration granted accelerated approval to Amtagvi for the treatment of adult patients with unresectable or metastatic melanoma previously treated with a PD-1 blocking antibody, and if BRAF V600 mutation positive, a BRAF inhibitor with or without a MEK inhibitor. The approval was based on overall response rate and duration of response from the C-144-01 clinical trial. With this approval, Amtagvi became the first one-time T cell therapy for a solid tumor cancer as well as the first approved treatment option for patients with advanced melanoma after anti-PD-1 and targeted therapy. Iovance is also conducting TILVANCE-301, a Phase 3 trial in frontline advanced melanoma to confirm clinical benefit.

About the C-144-01 Clinical Trial

C-144-01 is a global, multicenter Phase 2 study in which patients received treatment with lifileucel. The study enrolled patients with metastatic melanoma who were previously treated with at least one systemic therapy, including a PD-1 blocking antibody, and if BRAF V600 mutation positive, a BRAF inhibitor or BRAF inhibitor with MEK inhibitor. Efficacy was established on the basis of objective response rate (ORR) and duration of response (DOR) by Independent Review Committee (IRC) per Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1. The pivotal Cohort 4 and supportive Cohort 2 of Study C-144-01 enrolled patients that met the same primary eligibility criteria, had the same assessments, and had received the same regimen and AMTAGVI that was produced using the same manufacturing process, and product formulation. The final five-year analysis of C-144-01 was published in the *Journal of Clinical Oncology* in 2025.

About Amtagvi®

AMTAGVI is a prescription medicine used to treat adults with a type of skin cancer that cannot be removed surgically or has spread to other parts of the body called unresectable or metastatic melanoma.

AMTAGVI is used when your melanoma has not responded or stopped responding to a PD-1 blocking drug either by itself or in a combination, and if your cancer is BRAF mutation positive, a BRAF inhibitor drug with or without a MEK inhibitor drug that has also stopped working.

The approval of AMTAGVI is based on a study that measured response rate. Continued approval for this use may depend on the results of an ongoing study to confirm benefit.

Important Safety Information

What is the most important information that I should know about AMTAGVI?

You will likely be in a hospital prior to and after receiving AMTAGVI.

Before taking AMTAGVI, tell your healthcare provider about all of your medical conditions, including if you:

- Have any lung, heart, liver or kidney problems
- Have low blood pressure
- Have a recent or active infection or other inflammatory conditions including cytomegalovirus (CMV) infection, hepatitis B or C or human immunodeficiency virus (HIV) infection
- Are pregnant, think you may be pregnant, or plan to become pregnant
- Are breastfeeding
- Notice the symptoms of your cancer are getting worse
- Have had a vaccination in the past 28 days or plan to have one in the next few months
- Have been taking a blood thinner

Tell your doctor about all the medications you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

How will I receive AMTAGVI?

- AMTAGVI is made from your surgically removed tumor. Tumor derived T cells are grown in a manufacturing center at the end of which they number in the billions of cells.
- Your tumor tissue is sent to a manufacturing center to make AMTAGVI. It takes about 34 days from the time your tumor tissue is received at the manufacturing center until AMTAGVI is available to be shipped back to your healthcare provider, but the time may vary. Your AMTAGVI will be provided in 1-4 patient-specific infusion bag(s) containing 100 mL to 125 mL of viable (alive) cells per bag.
- After your AMTAGVI arrives at your treating institution, your healthcare provider will give you lymphodepleting chemotherapy to prepare your body.
- Approximately 30 to 60 minutes before you are given AMTAGVI, you may be given other medicines including:
    - Medicines for an allergic reaction (anti-histamines)
    - Medicines for fever (such as acetaminophen)
- Your AMTAGVI will be provided in 1 to 4 infusion bag(s) containing 100 mL to 125 mL of viable cells per bag. When your body is ready for AMTAGVI infusion, your healthcare provider will give AMTAGVI to you by intravenous infusion. This usually takes less than 90 minutes.

After getting AMTAGVI

Beginning 3 to 24 hours after AMTAGVI is given, you may be given up to 6 doses of IL-2 (aldesleukin) every 8 to 12 hours via intravenous infusion. Your doctor may discontinue IL-2 (aldesleukin) infusion any time if you have severe side effects.

You will have to stay in the hospital until you have completed the IL-2 (aldesleukin) treatment and you have recovered from any serious side effects associated with the AMTAGVI treatment.

You should plan to stay within 2 hours of the location where you received your treatment for several weeks after getting AMTAGVI. Your healthcare provider will check to see if your treatment is working and help you with any side effects that occur.

What are the possible side effects of AMTAGVI?

The most common side effects of the AMTAGVI treatment include chills, fever, low white blood cell count (may increase risk of infections), fatigue, low red blood cell count (may cause you to feel tired or weak), fast or irregular heartbeat, rash, low blood pressure, and diarrhea.

These are not all the possible side effects of the AMTAGVI treatment. Talk with your healthcare provider for more information about AMTAGVI. You can ask your healthcare provider for information about AMTAGVI that is written for healthcare professionals.

You may report side effects to Iovance at 1-833-400-4682, or to the FDA, at 1-800-FDA-1088 or at www.fda.gov/medwatch.

Please see Full Prescribing Information and Patient Information, including Boxed Warning, for additional Important Safety Information.

About Iovance Biotherapeutics, Inc.
Iovance Biotherapeutics, Inc. 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. The Iovance TIL platform has demonstrated promising clinical data across multiple solid tumors. Iovance's Amtagvi® is the first FDA-approved T cell therapy for a solid tumor indication. 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 http://www.iovance.com/.

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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"). 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,” “can,” “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 U.S. 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 risks related to our ability to successfully commercialize our products, including Amtagvi, for which we have obtained U.S. Food and Drug Administration (“FDA”) approval, and Proleukin, for which we have obtained FDA and European Medicines Agency (“EMA”) approval; the risk that the EMA or other ex-U.S. regulatory authorities may not approve or may delay approval for our marketing authorization application submission for lifileucel in metastatic melanoma; the acceptance by the market of our products, including Amtagvi and Proleukin, and their potential pricing and/or reimbursement by payors, if approved (in the case of our product candidates), in the U.S. and other international markets and whether such acceptance is sufficient to support continued commercialization or development of our products, including Amtagvi and Proleukin, or product candidates, respectively; future competitive or other market factors may adversely affect the commercial potential for Amtagvi or Proleukin; the risk regarding our ability or inability to manufacture our therapies using third party manufacturers or at our own facility, including our ability to increase manufacturing capacity at such third party manufacturers and our own facility, may adversely affect our commercial launch; the results of clinical trials with collaborators using different manufacturing processes may not be reflected in our sponsored trials; the risk regarding the successful integration of the recent Proleukin acquisition; the risk that the successful development or commercialization of our products, including Amtagvi and Proleukin, may not generate sufficient revenue from product sales, and we may not become profitable in the near term, or at all; the risks related to the timing of and our ability to successfully develop, submit, obtain, or maintain FDA, EMA, or other regulatory authority approval of, or other action with respect to, our product candidates; whether clinical trial results from our pivotal studies and cohorts, and meetings with the FDA, EMA, or other regulatory authorities may support registrational studies and subsequent approvals by the FDA, EMA, or other regulatory authorities, including the risk that the planned single arm Phase 2 IOV-LUN-202 trial may not support registration; 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 risk that 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, EMA, or other regulatory authorities; the risk that our interpretation of the results of our clinical trials or communications with the FDA, EMA, or other regulatory authorities may differ from the interpretation of such results or communications by such regulatory authorities (including from our prior meetings with the FDA regarding our non-small cell lung cancer clinical trials); the risk that clinical data from ongoing clinical trials of Amtagvi will not continue or be repeated in ongoing or planned clinical trials or may not support regulatory approval or renewal of authorization; the risk that unanticipated expenses may decrease our estimated cash balances and forecasts and increase our estimated capital requirements; the risk that we may not be able to recognize revenue for our products; the risk that Proleukin revenues may not continue to serve as a leading indicator for Amtagvi revenues; the risks regarding our anticipated operating and financial performance, including our financial guidance and projections; the effects of global pandemic; the effects of global and domestic geopolitical factors; and other factors, including general economic conditions and regulatory developments, not within our control. Any financial guidance provided in this press release assumes the following: no material change in our ability to manufacture our products; no material change in payor coverage; no material change in revenue recognition policies; no new business development transactions not completed as of the period covered by this press release; and no material fluctuation in exchange rates.

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