



Iovance's AMTAGVI™ (lifileucel) Receives U.S. FDA Accelerated Approval for Advanced Melanoma

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AMTAGVI is the first FDA-approved T cell therapy for a solid tumor cancer and first treatment option for advanced melanoma after anti-PD-1 and targeted therapy

AMTAGVI deploys patient-specific immune cells that recognize and fight cancer

SAN CARLOS, Calif., Feb. 16, 2024 (GLOBE NEWSWIRE) -- Iovance Biotherapeutics, Inc. (NASDAQ: IOVA), a biotechnology company focused on innovating, developing and delivering novel polyclonal tumor infiltrating lymphocyte (TIL) cell therapies for patients with cancer, today announced that the U.S. Food and Drug Administration (FDA) has approved AMTAGVI™ (lifileucel) suspension for intravenous infusion. AMTAGVI is a tumor-derived autologous T cell immunotherapy indicated 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. This indication is approved under an accelerated approval based on overall response rate (ORR) and duration of response. Iovance is also conducting TILVANCE-301, a Phase 3 trial to confirm clinical benefit.

AMTAGVI is the first and the only one-time, individualized T cell therapy to receive FDA approval for a solid tumor cancer. The proposed mechanism for AMTAGVI offers a new cell therapy approach that deploys patient-specific T cells called TIL cells. When cancer is detected, the immune system creates TIL cells to locate, attack, and destroy cancer. TIL cells recognize distinctive tumor markers on the cell surface of each person's cancer. When cancer develops and prevails, the body's natural TIL cells can no longer perform their intended function to fight cancer.

AMTAGVI is manufactured using a proprietary process to collect and expand a patient's unique T cells from a portion of their tumor. AMTAGVI returns billions of the patient's T cells back to the body to fight their cancer.* Authorized Treatment Centers (ATCs) will administer AMTAGVI to patients as part of a treatment regimen that includes lymphodepletion and a short course of high-dose PROLEUKIN® (aldesleukin).



[A Media Snippet accompanying this announcement is available by clicking on this link.](#)

"The accelerated approval of AMTAGVI™ is the first step in realizing lovance's ambition to usher in the next generation of cell therapy by bringing this breakthrough to patients with advanced solid tumors," said Frederick Vogt, Ph.D., J.D., Interim Chief Executive Officer and President of lovance. "Given the significant unmet needs in the advanced melanoma community, we are proud to offer a personalized, one-time therapeutic option for these patients. We are continuing our development efforts to address additional unmet medical needs in patients with solid tumor cancers, making our novel cell therapies available to more patients with melanoma and other types of cancers."

Each year, approximately 8,000 people in the U.S. die from melanoma.¹ Until now, there have been no FDA-approved treatment options for patients with advanced melanoma whose disease progressed following initial treatment with an immune checkpoint inhibitor and, if appropriate, targeted therapy.

"The approval of AMTAGVI™ offers hope to those with advanced melanoma who have progressed following initial standard of care therapies, as the current treatment options are not effective for many patients," said Samantha R. Guild, J.D., President, AIM at Melanoma Foundation. "This one-time cell therapy represents a promising innovation for the melanoma community, and we are excited by its potential to transform care for patients who are in dire need of additional therapeutic options."

The FDA approval is based on safety and efficacy results from the C-144-01 clinical trial. C-144-01 is a global, multicenter trial investigating AMTAGVI in patients with advanced melanoma previously treated with anti-PD-1 therapy and targeted therapy, where applicable. AMTAGVI demonstrated deep and durable responses. The primary efficacy analysis set included 73 patients from Cohort 4 who received the recommended AMTAGVI dose from an approved manufacturing facility. Among the 73 patients, 31.5% achieved an objective response by Response Evaluation Criteria in Solid Tumors (RECIST 1.1) with a

median duration of response not reached at 18.6 months follow-up² (43.5% of responses had a duration greater than 12 months). Additionally, the supporting pooled efficacy set included a total of 153 patients from Cohort 4 and Cohort 2. Among the 153 patients, 31.4% achieved an objective response by RECIST 1.1 with a median duration of response not reached at 21.5 months follow-up² (54.2% of responses had a duration greater than 12 months). The detailed results of clinical trial C-144-01 are published in [The Journal for ImmunoTherapy of Cancer](#) (Chesney 2022).

AMTAGVI is for autologous use only. AMTAGVI has a boxed warning for treatment-related mortality, prolonged severe cytopenia, severe infection, and cardiopulmonary and renal impairment. Warnings and precautions include treatment-related mortality, prolonged severe cytopenia, internal organ hemorrhage, severe infection, cardiac disorder, respiratory failure, acute renal failure, and hypersensitivity reactions. Please see Important Safety Information and Prescribing Information below.

"This landmark FDA approval reflects significant advancements in TIL cell therapy since we initially showed that TIL cells isolated from patients with metastatic melanoma could be expanded in the lab and returned to the patient to mediate cancer regression," said Steven Rosenberg, M.D., Ph.D., Chief, Surgery Branch, National Cancer Institute, and a TIL and immunotherapy pioneer. "This approval is transformative for the entire research field and supports continued investigation of TIL cell therapy across additional types of solid tumors."

"One-time treatment with AMTAGVI™ offered clinically meaningful and deep, durable responses in the Phase 2 clinical trial, and I am excited by its potential as a much-needed new treatment option for the many advanced melanoma patients who progress on the current standard of care," said Dr. Alexander N. Shoushtari, Melanoma Oncologist & Cellular Therapist at Memorial Sloan Kettering Cancer Center. "This welcome news represents an important step forward in harnessing cell therapy to treat solid tumors," added Dr. Jae Park, Chief of Cellular Therapy Service at Memorial Sloan Kettering Cancer Center.

AMTAGVI will be manufactured in Philadelphia at the Iovance Cell Therapy Center (iCTC), with capacity for up to several thousand patients annually, including a nearby contract manufacturer. Additional expansion at iCTC is underway, which will significantly increase this capacity over the next few years. iCTC is the first FDA-approved, centralized, and scalable manufacturing facility dedicated to producing TIL cell therapies for patients with solid tumors. AMTAGVI must be administered in an ATC, and more than 30 ATCs are prepared to collect and ship tumor tissue from patients for AMTAGVI manufacturing.

Iovance is dedicated to providing access to AMTAGVI for patients with advanced melanoma. A comprehensive support program, IovanceCares™, is now available for patients and ATCs throughout the treatment journey. IovanceCares will also offer copay support, financial assistance, and travel and lodging assistance for eligible patients during AMTAGVI therapy. For more information, physicians and patients may call 833-400-IOVA (4682) or visit www.iovancecares.com.

Iovance is investigating AMTAGVI in frontline advanced melanoma in the Phase 3 confirmatory trial, TILVANCE-301, as well as additional solid tumor types, which represent 91% of the cancers in the U.S.¹ For more information, please visit: <https://www.iovance.com/clinical-trials/>.

¹ National Cancer Institute Surveillance, Epidemiology and End Results (SEER) Program. 2023 Estimates. <https://seer.cancer.gov>. Accessed February 2024.

² Kaplan-Meier estimate of median potential follow-up for duration of response.

* A single dose of AMTAGVI contains 7.5×10^9 to 72×10^9 viable cells.

Webcast and Conference Call

Iovance will host a conference call and live audio webcast today to discuss the FDA approval of AMTAGVI. Details will be shared in a subsequent announcement.

About the C-144-01 Clinical Trial

C-144-01 is a global, multicenter Phase 2 study in which patients received treatment with lilelucel. 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 detailed results of C-144-01 were published in [The Journal for ImmunoTherapy of Cancer](#) in 2022.

What is AMTAGVI (lilelucel)?

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 lovance 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 lovance Biotherapeutics, Inc.

[lovance Biotherapeutics](#) aims to be the global leader in innovating, developing and delivering tumor infiltrating lymphocyte (TIL) cell 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 [lovance TIL platform](#) has demonstrated promising clinical data across multiple solid tumors. lovance'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, which may be a promising option for patients with cancer. For more information, please visit www.lovance.com.

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Forward-Looking Statements

Certain matters discussed in this press release are "forward-looking statements" of lovance 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, including, without limitation, the statements by Frederick Vogt, Ph.D., J.D., Samantha R. Guild, J.D., Steven Rosenberg, M.D., Ph.D., Dr. Alexander N. Shoushtari, and Dr. Jae Park, 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 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 obtain U.S. Food and Drug Administration ("FDA"), European Medicines Agency ("EMA"), or other regulatory authority approval; the risk that the EMA or other regulatory authorities may not approve or may delay approval for our biologics license application ("BLA") submission for lileucel in metastatic melanoma; the acceptance by the market of our products, including AMTAGVI, 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, or product candidates, respectively; our ability or inability to manufacture our therapies using third party manufacturers or at 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, may not generate sufficient revenue from product sales, and we may not become profitable in the near term, or at all; the risk that future competitive or other market factors may adversely affect the commercial potential for AMTAGVI; 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 effects of the COVID-19 pandemic; and other factors, including general economic conditions and regulatory developments, not within our control.

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A photo accompanying this announcement is available at <https://www.globenewswire.com/NewsRoom/AttachmentNg/b01f4de7-8dc3-47e6-bada-df2a7ec36604>



Source: Iovance Biotherapeutics, Inc.

AMTAGVI (lileucel) Product Shot



