Autolus Therapeutics Announces FDA Approval of AUCATZYL® (obecabtagene autoleucel – obe-cel) for adults with relapsed/refractory B-cell acute lymphoblastic leukemia (r/r B-ALL)

November 8, 2024 at 4:24 PM EST

- *AUCATZYL is the first CAR T therapy approved by the FDA with no requirement for a REMS program (Risk Evaluation Mitigation Strategy)*
- *Approval based on FELIX clinical trial of obe-cel in adult patients with r/r B-ALL*
- *Conference call to be held on November 11 at 08:30 am EST/13:30 pm BST: conference call participants should pre-register using the link at the bottom of this press release*

LONDON, Nov. 08, 2024 (GLOBE NEWSWIRE) -- Autolus Therapeutics plc (Nasdaq: AUTL), an early-commercial stage biopharmaceutical company developing next-generation programmed T cell therapies, today announces the U.S. Food and Drug Administration (FDA) has granted marketing approval for AUCATZYL® (obecabtagene autoleucel) for the treatment of adult patients with relapsed or refractory B-cell precursor acute lymphoblastic leukemia (r/r B-ALL).

“Adult ALL is an extremely aggressive cancer, and there is a high unmet medical need that exists in the treatment of patients with this disease once they relapse, where historically they suffer from poor outcomes,” **said Elias Jabbour, MD, U.S. lead investigator of the FELIX study and professor of Leukemia, ALL Section Chief, at The University of Texas MD Anderson Cancer Center, Houston, Texas**. “This milestone approval, based on the demonstrated clinical benefit of AUCATZYL, brings new hope for adult patients with relapsed/refractory B-ALL.”

AUCATZYL was approved by the FDA based on results from the FELIX clinical trial of obe-cel in adult patients with r/r B-ALL. In the morphological disease cohort, 94 patients received at least one infusion of AUCATZYL of which 65 patients had ≥ 5% blasts in the bone marrow after screening and prior to the start of lymphodepletion therapy and received a conforming product, qualifying them as efficacy evaluable. In the efficacy evaluable patients (n=65), 63% achieved overall complete remission (OCR[1]) which includes 51% of patients with CR at any time and 12% patients with CRi at any time. The major efficacy outcome was complete remission within 3 months, which was achieved in 42% patients, and the median duration of remission (DOR) was 14.1 months. AUCATZYL showed low levels of Cytokine Release Syndrome (CRS), with 3% Grade 3 events, and no Grade 4 or 5 events. Grade ≥ 3 Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS) was reported in 7% of patients. No REMS was required by the FDA for AUCATZYL.

The safety of AUCATZYL includes a boxed warning for CRS, neurologic toxicities, and secondary hematological malignancies. ICANS, including fatal or life-threatening reactions, occurred in patients receiving AUCATZYL. T-cell malignancies have occurred following treatment of hematologic malignancies with BCMA- and CD19-directed genetically modified autologous T-cell immunotherapies. In the FELIX trial, the most common non-laboratory adverse reactions (incidence ≥ 20%) included CRS, infections-pathogen unspecified, musculoskeletal pain, viral infections, fever, nausea, bacterial infectious disorders, diarrhea, febrile neutropenia, ICANS, hypotension, pain, fatigue, headache, encephalopathy, and hemorrhage.

“Based on the experience in the FELIX trial AUCATZYL is highly active and can be well managed, offering an attractive risk benefit profile for B-ALL patients,” **said Dr. Claire Roddie, MD, PhD, FRCPath, Lead investigator of the FELIX study and Associate Professor of Haematology at the University College London (UCL) Cancer Institute**. “In the FELIX trial AUCATZYL has shown long term persistence and deep responses which we believe are critical for long term remissions in B-ALL.”

“We are so pleased to now be able to offer AUCATZYL, our first commercial product, to adult r/r B-ALL patients in the U.S. This approval would not have been possible without the support of all the patients, their families and caregivers, their treating physicians and the nurses and investigators at the treatment centers – thank you,” **said Dr. Christian Itin, Chief Executive Officer of Autolus**. “This milestone is the culmination of many years of hard work, the foundational work by our partners at UCL and the unwavering commitment of our internal team, our external partners and shareholders. This is a proud day for Autolus.”

AUCATZYL will be manufactured at Autolus’ dedicated commercial manufacturing site, the Nucleus, in Stevenage, UK. The site was granted a Manufacturer’s Importation Authorization (MIA) and a GMP certificate from the U.K. Medicines and Healthcare products Regulatory Agency (MHRA) in March 2024, and was inspected as part of the FDA approval process. No major or critical observations were identified by either the MHRA or FDA during the site inspections. The Nucleus will supply AUCATZYL globally, with Cardinal Health serving as Autolus’ commercial distribution partner in the U.S. Autolus will now engage with existing treatment centers to complete the onboarding process and initiate the first scheduling of patients to make AUCATZYL commercially available in the U.S.

ALL is an aggressive type of blood cancer that can also involve the lymph nodes, spleen, liver, central nervous system and other organs. Approximately 8,400 new cases of adult ALL are diagnosed every year in the US and EU, with around 3,000 patients in the relapsed refractory setting.[1] Survival rates remain very poor in adult patients with r/r ALL, with median overall survival of eight months.[2] In frontline treatment for adult r/r B-ALL, up to 50% of patients will ultimately relapse, and the standard-of-care treatment can trigger severe toxicities and may be burdensome for some patients.[3,4]

Marketing authorisation applications (MAAs) for obe-cel in adult r/r ALL are being reviewed by the regulators in both the EU and the UK, with a submission to the European Medicines Agency (EMA) accepted in March 2024, and a submission accepted by the UK MHRA in August 2024.

Conference Call

Management will host a conference call and webcast on November 11 at 8:30 am EST/1:30 pm BST to discuss the AUCATZYL approval. Conference call participants should pre-register using this link to receive the dial-in numbers and a personal PIN, which are required to access the conference call.

A simultaneous audio webcast and replay will be accessible on the events section of Autolus' website.

About Autolus Therapeutics plc
Autolus is a biopharmaceutical company developing next-generation, programmed T cell therapies for the treatment of cancer and autoimmune disease. Using a broad suite of proprietary and modular T cell programming technologies, Autolus is engineering precisely targeted, controlled and highly active T cell therapies that are designed to better recognize target cells, break down their defense mechanisms and eliminate these cells. Autolus has an FDA approved product, AUCATZYL, and a pipeline of product candidates in development for the treatment of hematological malignancies, solid tumors and autoimmune diseases. For more information, please visit www.autolus.com

About AUCATZYL® (obecabtagene autoleucel, obe-cel, AUTO1)
AUCATZYL is a B-lymphocyte antigen CD19 (CD19) chimeric antigen receptor (CAR) T cell therapy designed to overcome the limitations in clinical activity and safety compared to current CD19 CAR T cell therapies. AUCATZYL is designed with a fast target binding off-rate to minimize excessive activation of the programmed T cells. AUCATZYL was approved by the FDA for the treatment of adult patients with relapsed or refractory B-cell precursor acute lymphoblastic leukemia on November 08, 2024. In the EU a regulatory submission to the EMA was accepted in April 2024, while in the UK, an MAA was submitted to MHRA in July 2024.

INDICATION

AUCATZYL® is a CD19-directed genetically modified autologous T cell immunotherapy indicated for the treatment of adult patients with relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL).

IMPORTANT SAFETY INFORMATION

WARNING: CYTOKINE RELEASE SYNDROME, NEUROLOGIC TOXICITIES, and SECONDARY HEMATOLOGICAL MALIGNANCIES

- **Cytokine Release Syndrome (CRS) occurred in patients receiving AUCATZYL. Do not administer AUCATZYL to patients with active infection or inflammatory disorders. Prior to administering AUCATZYL, ensure that healthcare providers have immediate access to medications and resuscitative equipment to manage CRS.**
- **Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS), including fatal and life-threatening reactions, occurred in patients receiving AUCATZYL, including concurrently with CRS or after CRS resolution. Monitor for neurologic signs and symptoms after treatment with AUCATZYL. Prior to administering AUCATZYL, ensure that healthcare providers have immediate access to medications and resuscitative equipment to manage neurologic toxicities. Provide supportive care and/or corticosteroids, as needed.**
- **T cell malignancies have occurred following treatment of hematologic malignancies with BCMA- and CD19-directed genetically modified autologous T cell immunotherapies.**

WARNINGS AND PRECAUTIONS

Cytokine Release Syndrome (CRS)
Cytokine Release Syndrome (CRS) occurred following treatment with AUCATZYL. CRS was reported in 75% (75/100) of patients including Grade 3 CRS in 3% of patients. The median time to onset of CRS was 8 days following the first infusion (range: 1 to 23 days) with a median duration of 5 days (range: 1 to 21 days). The most common manifestations of CRS included fever (100%), hypotension (35%), and hypoxia (19%).

Prior to administering AUCATZYL, ensure that healthcare providers have immediate access to medications and resuscitative equipment to manage CRS. During and following treatment with AUCATZYL, closely monitor patients for signs and symptoms of CRS daily for at least 14 days at the healthcare facility following the first infusion. Continue to monitor patients for CRS for at least 4 weeks following each infusion with AUCATZYL. Counsel patients to seek immediate medical attention should signs or symptoms of CRS occur at any time. At the first sign of CRS, immediately evaluate the patient for hospitalization and institute treatment with supportive care based on severity and consider further management per current practice guidelines.

Neurologic Toxicities
Neurologic toxicities including Immune Effector Cell-associated Neurotoxicity Syndrome (ICANS), which were fatal or life-threatening, occurred following treatment with AUCATZYL. Neurologic toxicities were reported in 64% (64/100) of patients, including Grade ≥ 3 in 12% of patients. The median time to onset of neurologic toxicities was 10 days (range: 1 to 246 days) with a median duration of 13 days (range: 1 to 904 days). Among patients with neurologic toxicities, the most common symptoms (> 5%) included ICANS (38%), headache (34%), encephalopathy (33%), dizziness (22%), tremor (13%), anxiety (9%), insomnia (9%), and delirium (8%).

Immune Effector Cell-associated Neurotoxicity Syndrome (ICANS)
ICANS events occurred in 24% (24/100) of patients, including Grade ≥ 3 in 7% (7/100) of patients. Of the 24 patients who experienced ICANS, 33% (8/24) experienced an onset after the first infusion, but prior to the second infusion of AUCATZYL.
The median time to onset for ICANS events after the first infusion was 8 days (range: 1 to 10 days) and 6.5 days (range: 2 to 22 days) after the second infusion, with a median duration of 8.5 days (range: 1 to 53 days).
Eighty-eight percent (21/24) of patients received treatment for ICANS. All treated patients received high-dose corticosteroids and 42% (10/24) of patients received anti-epileptics prophylactically. Prior to administering AUCATZYL, ensure that healthcare providers have immediate access to medications and resuscitative equipment to manage ICANS.

Counsel patients to seek medical attention should signs or symptoms of neurologic toxicity/ ICANS occur. At the first sign of Neurologic Toxicity /ICANS, immediately evaluate patients for hospitalization and institute treatment with supportive care based on severity and consider further

management per current practice guidelines.

Effect on Ability to Drive and Use Machines
Due to the potential for neurologic events, including altered mental status or seizures, patients receiving AUCATZYL are at risk for altered or decreased consciousness or coordination in the eight weeks following AUCATZYL infusion or until resolution of the neurological event by the treating physician. Advise patients to refrain from driving and engaging in hazardous occupations or activities, such as operating heavy or potentially dangerous machinery, during this initial period.

Prolonged Cytopenias
Patients may exhibit cytopenias including anemia, neutropenia, and thrombocytopenia for several weeks after treatment with lymphodepleting chemotherapy and AUCATZYL. In patients who were responders to AUCATZYL, Grade ≥ 3 cytopenias that persisted beyond Day 30 following AUCATZYL infusion were observed in 71% (29/41) of patients and included neutropenia (66%, 27/41) and thrombocytopenia (54%, 22/41). Grade 3 or higher cytopenias that persisted beyond Day 60 following AUCATZYL infusion was observed in 27% (11/41) of patients and included neutropenia (17%, 7/41) and thrombocytopenia (15%, 6/41). Monitor blood counts after AUCATZYL infusion.

Infections
Severe, including life-threatening and fatal infections occurred in patients after AUCATZYL infusion. Non-COVID-19 infections of all grades occurred in 67% (67/100) of patients. Grade 3 or higher non-COVID-19 infections occurred in 41% (41/100) of patients. AUCATZYL should not be administered to patients with clinically significant active systemic infections. Monitor patients for signs and symptoms of infection before and after AUCATZYL infusion and treat appropriately. Administer prophylactic antimicrobials according to local guidelines.
Grade 3 or higher febrile neutropenia was observed in 26% (26/100) of patients after AUCATZYL infusion and may be concurrent with CRS. In the event of febrile neutropenia, evaluate for infection and manage with broad-spectrum antibiotics, fluids, and other supportive care as medically indicated.
Viral reactivation, potentially severe or life-threatening, can occur in patients treated with drugs directed against B cells. There is no experience with manufacturing AUCATZYL for patients with a positive test for human immunodeficiency virus (HIV) or with active hepatitis B virus (HBV) or active hepatitis C virus (HCV). Perform screening for HBV, HCV and HIV in accordance with clinical guidelines before collection of cells for manufacturing.

Hypogammaglobulinemia
Hypogammaglobulinemia and B-cell aplasia can occur in patients after AUCATZYL infusion. Hypogammaglobulinemia was reported in 10% (10/100) of patients treated with AUCATZYL including Grade 3 events in 2 patients (2%).
Immunoglobulin levels should be monitored after treatment with AUCATZYL and managed per institutional guidelines including infection precautions, antibiotic or antiviral prophylaxis, and immunoglobulin replacement.
The safety of immunization with live viral vaccines during or following treatment with AUCATZYL has not been studied. Vaccination with live viral vaccines is not recommended for at least 6 weeks prior to the start of lymphodepleting chemotherapy treatment, during AUCATZYL treatment, and until immune recovery following treatment with AUCATZYL.

Hemophagocytic Lymphohistiocytosis/Macrophage Activation Syndrome (HLH/MAS)
HLH/MAS including fatal and life-threatening reactions occurred after treatment with AUCATZYL. HLH/MAS was reported in 2% (2/100) of patients and included Grade 3 and Grade 4 events with a time of onset at Day 22 and Day 41, respectively. One patient experienced a concurrent ICANS events after AUCATZYL infusion and died due to sepsis with ongoing HLH/MAS that had not resolved. Administer treatment for HLH/MAS according to institutional standards.

Hypersensitivity Reactions
Serious hypersensitivity reactions, including anaphylaxis, may occur due to dimethyl sulfoxide (DMSO), an excipient used in AUCATZYL. Observe patients for hypersensitivity reactions during and after AUCATZYL infusion.
Secondary Malignancies
Patients treated with AUCATZYL may develop secondary malignancies. T cell malignancies have occurred following treatment of hematologic malignancies with BCMA- and CD19-directed genetically modified autologous T cell immunotherapies. Mature T cell malignancies, including CAR-positive tumors, may present as soon as weeks following infusion, and may include fatal outcomes. Monitor lifelong for secondary malignancies. In the event that a secondary malignancy occurs, contact Autolus at 1-855-288-5227 for reporting and to obtain instructions on the collection of patient samples for testing.

Adverse Reactions
The safety of AUCATZYL was evaluated in the FELIX study in which 100 patients with relapsed or refractory B-cell acute lymphoblastic leukemia (B-ALL) received AUCATZYL at a median dose of 410×10^6 CD19 CAR-positive viable T cells (range: 10 to 480×10^6 CD19 CAR-positive viable T cells with 90% of patients receiving the recommended dose of 410×10^6 +/- 25%).

The most common serious adverse reactions of any Grade (incidence ≥ 2%) included infections-pathogen unspecified, febrile neutropenia, ICANS, CRS, fever, bacterial infectious disorders, encephalopathy, fungal infections, hemorrhage, respiratory failure, hypotension, ascites, HLH/MAS, thrombosis and hypoxia. Nine patients (9%) experienced fatal adverse reactions which included infections (sepsis, pneumonia, peritonitis), ascites, pulmonary embolism, acute respiratory distress syndrome, HLH/MAS and ICANS. Of the 9 patients, five patients who died from infections had pre-existing and ongoing neutropenia prior to receiving bridging therapy, lymphodepletion chemotherapy treatment and/or AUCATZYL.

Please see full **Prescribing Information,** including **BOXED WARNING** and Medication Guide.

Forward-Looking Statements
This press release contains forward-looking statements within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995. Forward-looking statements are statements that are not historical facts, and in some cases can be identified by terms such as "may," "will," "could," "expects," "plans," "anticipates," and "believes." These statements include, but are not limited to: statements regarding the market and therapeutic potential of for AUCATZYL for adult r/r B-ALL; Autolus' development and commercialization of its product candidates; the expected clinical benefits of AUCATZYL; Autolus' manufacturing, sales and marketing plans for AUCATZYL, including expectations regarding the timing of commercial launch in the United States and the ability to reach patients in a timely manner; the amount and timing of milestone payments under Autolus' collaboration and license agreements; and future development plans of AUCATZYL, including the timing or likelihood of expansion into additional markets or geographies and related regulatory approvals. Any forward-looking statements are based on management's current views and

assumptions and involve risks and uncertainties that could cause actual results, performance, or events to differ materially from those expressed or implied in such statements. Actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of various risks and uncertainties, which include, without limitation: Autolus' ability to maintain regulatory approval of AUCATZYL; its ability to execute its commercialization strategy for AUCATZYL; its ability to develop, manufacture and commercialize its other product candidates and the timing or likelihood of expansion of AUCATZYL into additional markets or geographies; Autolus' ability to establish and expand a commercial infrastructure and to successfully launch, market and sell AUCATZYL; actions of regulatory agencies, which may affect the initiation, timing and progress of clinical trials or future regulatory approval; the labelling for AUCATZYL/obe-cel in any future indication or patient population, if approved; the potential for payors to delay, limit or deny coverage for AUCATZYL; Autolus' ability to obtain, maintain and enforce intellectual property protection for AUCATZYL or any product candidates it is developing; the results of clinical trials are not always being predictive of future results; the cost, timing and results of clinical trials; that many product candidates do not become approved drugs on a timely or cost effective basis or at all; the ability to enroll patients in clinical trials; and possible safety and efficacy concerns. For a discussion of other risks and uncertainties, and other important factors, any of which could cause Autolus' actual results to differ from those contained in the forward-looking statements, see the section titled "Risk Factors" in Autolus' Annual Report on Form 10-K filed with the Securities and Exchange Commission, or the SEC, on March 21, 2024 as well as discussions of potential risks, uncertainties, and other important factors in Autolus' subsequent filings with the Securities and Exchange Commission. All information in this press release is as of the date of the release, and Autolus undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events, or otherwise, except as required by law. You should, therefore, not rely on these forward-looking statements as representing Autolus' views as of any date subsequent to the date of this press release.

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*Rate of Overall Complete Remission "At Anytime" includes Complete Remission (CR) and Complete Remission with incomplete hematologic recovery (CRi) "At Anytime"