Autolus Therapeutics Presents Clinical Data Updates at the 2025 Tandem Meetings

January 17, 2025 at 7:00 AM EST

LONDON, Jan. 17, 2025 (GLOBE NEWSWIRE) -- Autolus Therapeutics plc (Nasdaq: AUTL), a commercial-stage biopharmaceutical company developing, manufacturing and delivering next-generation programmed T cell therapies, announces an oral presentation and three poster presentations accepted to the 2025 Tandem Meetings | Transplantation & Cellular Therapy Meetings of ASTCT and CIBMTR, being held from February 12-15, 2025, in Hawai'i Convention Center, Honolulu, HI.

"Building on our data presented at ASH in December, we come to Tandem with an updated health economic cost model directly comparing the cost of adverse events of AUCATZYL® versus other CAR-T cell therapies, which demonstrates that the shorter duration and lower incidence of CRS and ICANS contributes to a reduction in healthcare costs," **said Dr. Christian Itin, Chief Executive Officer of Autolus.** "We also show the effectiveness of AUCATZYL® versus non CAR-T standard of care therapies, and have an oral presentation update on the hematotoxicity model and poster presentation on the impact of deep molecular remissions on clinical outcomes, which were both announced in December."

Oral:
Title: Risk Factors Associated with Sub-Optimal Outcomes and Hematotoxicity Following Obecabtagene Autoleucel (obe-cel) for Relapsed/Refractory B-Cell Acute Lymphoblastic Leukemia (R/R B-ALL)
Session Name: Oral Abstract - Session A - Leukemia and Relapse
Session date and time: Wednesday, February 12, 2025, 3:15 PM

Presenting Author: Karamjeet S. Sandhu, MD

Summary: Risk-stratification for hematotoxicity, using pre-LD clinical parameters together with disease burden, has potential use for identifying patients more likely to benefit from obe-cel treatment and experience reduced toxicity. Patients with low-risk hematotoxicity scores had consistently better outcomes than patients with high-risk hematotoxicity scores.

Abstract 24949 - Poster:
Title: An Economic Model Comparing the Costs Associated with Cytokine Release Syndrome (CRS) and Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS) Among Patients Treated with Chimeric Antigen Receptor (CAR) T-Cell Therapies for Relapsed/Refractory B-Cell Acute Lymphoblastic Leukemia (R/R B-ALL)
Session Name: Engineered Immune Cells (CAR-T, NK, TCR): Clinical - Immune Effector Cells for Heme Malignancies
Session date and time: Thursday, February 13, 2025, 6:45 PM
Presenting Author: Aaron C. Logan, MD

Summary: A decision tree economic model was developed using rates and median durations of AEs reported in the FELIX (NCT04404660; n=127) and ZUMA-3 (NCT02614066; n=55) trials. Obe-cel was associated with lower CRS- and ICANS-related healthcare costs versus brexu-cel, primarily due to lower rates of Gr 3/4 AEs and faster resolution of these events. These results suggest that obe-cel improves resource utilization and reduces healthcare costs versus other CAR T-cell therapies for R/R B-ALL.

Abstract 26113 – Poster:
Title: Comparison of Obecabtagene Autoleucel (obe-cel) Versus an External Control Arm (ECA) in Adult Patients (pts) with Relapsed/Refractory B-Cell Acute Lymphoblastic Leukemia (R/R B-ALL)
Session Title: Acute and Chronic Leukemia (AML, MDS, MPD ALL, CML,) - Clinical
Session date and time: Thursday, February 13, 2025, 6:45 PM
Presenting Author: Karamjeet S. Sandhu, MD

Summary: The study was designed to report efficacy and safety outcomes of obe-cel in FELIX patients vs. patients treated with non-CAR T-cell standard of care (SOC) therapies in a matched External Control Arm. Obe-cel demonstrated higher ORR and longer OS and EFS vs. SOC in matched ECAs. Safety was comparable between treatment groups, demonstrating a positive benefit-risk profile of obe-cel for treatment of adult R/R B-ALL.

Abstract 26366 – Poster:
Title: Deep Molecular Remission Predicts Better Clinical Outcomes in Adults with Relapsed/Refractory B-Cell Acute Lymphoblastic Leukemia (R/R B-ALL) Treated with Obecabtagene Autoleucel (obe-cel)
Session Name: Engineered Immune Cells (CAR-T, NK, TCR): Clinical - Immune Effector Cells for Heme Malignancies
Session date and time: Thursday, February 13, 2025, 6:45 PM

Presenting Author: Aaron C. Logan, MD

Summary: Among obe-cel responders for whom measurable residual disease (MRD) by next-generation sequencing could be analyzed, 84% achieved MRD $<10^{-6}$ leukemic cells, which was associated with more durable responses, and higher EFS and OS rates than patients with MRD $\geq 10^{-4}$ and MRD between 10^{-4} and 10^{-6} leukemic cells. Patients who did not achieve MRD $<10^{-6}$ had poorer outcomes.

About Autolus Therapeutics plc
Autolus Therapeutics plc (Nasdaq: AUTL) is a commercial stage biopharmaceutical company developing, manufacturing and delivering next-generation 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 obe-cel FELIX clinical trial
Autolus' Phase 1b/2 clinical trial of obe-cel enrolled adult patients with r/r B-precursor ALL. The trial had a Phase 1b component prior to proceeding to the single arm, Phase 2 clinical trial. The primary endpoint in the pivotal cohort was overall response rate, and the secondary endpoints included duration of response, MRD negative complete remission rate and safety. The trial enrolled over 100 patients across 30 of the leading academic and non-academic centers in the United States, United Kingdom and Europe. [NCT04404660].

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 16, 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 Autolus' development and commercialization of its products and product candidates. 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. These risks and uncertainties include, but are not limited to, the risks that Autolus' preclinical or clinical programs do not advance or result in approved products on a timely or cost effective basis or at all; the results of early 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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