

ADCETRIS® Combination Significantly Improves Overall Survival in Newly Diagnosed Patients with Advanced Hodgkin Lymphoma

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– Full Data from Phase 3 ECHELON-1 Clinical Trial to be Submitted for Presentation at Upcoming Medical Meeting –

BOTHELL, Wash.--(BUSINESS WIRE)-- [Seagen Inc.](#) (Nasdaq:SGEN) today announced that the phase 3 ECHELON-1 clinical trial demonstrated a statistically significant improvement in overall survival (OS) ($p=0.009$) in patients with advanced classical Hodgkin lymphoma (cHL) following treatment with ADCETRIS (brentuximab vedotin) in combination with chemotherapy. With approximately six years median follow up, patients receiving ADCETRIS plus doxorubicin, vinblastine, and dacarbazine (A+AVD) in the frontline setting had a 41 percent reduction in the risk of death (HR 0.59; [95% CI: 0.396 to 0.879]) compared with patients receiving doxorubicin, bleomycin, vinblastine, and dacarbazine (ABVD). The safety profile of ADCETRIS was consistent with previous studies and no new safety signals were observed.

"These groundbreaking results are important for patients with advanced classical Hodgkin lymphoma given that an improvement in overall survival has rarely been shown in frontline treatment of this disease," said Roger Dansey, M.D., Chief Medical Officer at Seagen. "We look forward to presentation of the results at an upcoming medical meeting."

ECHELON-1 is an open-label, international, randomized, phase 3 trial evaluating the safety and efficacy of frontline ADCETRIS plus AVD versus ABVD in 1,334 adult patients with stage III or IV cHL. Patients were randomly assigned to receive A+AVD or ABVD intravenously on days 1 and 15 of each 28-day cycle for up to six cycles. OS is the key secondary endpoint of the trial. The primary endpoint, modified progression free survival, served as the basis for global regulatory approvals.

Please see Important Safety Information, including BOXED WARNING, for ADCETRIS below.

ADCETRIS is approved for certain types of relapsed or refractory Hodgkin lymphoma (HL) including previously untreated Stage III/IV cHL and previously untreated peripheral T-cell lymphoma (PTCL). It has received marketing authorization in more than 75 countries and is being evaluated

globally in more than 70 corporate- and investigator-sponsored clinical trials across multiple settings in lymphoma and other diseases.

About Classical Hodgkin Lymphoma

cHL is a cancer of the blood. It starts when lymphocytes, a type of white blood cell, grow out of control. People with cHL have abnormal white blood cells called Reed-Sternberg cells in their lymph nodes. These cells usually have a special protein on their surface called CD30, which is a key marker of cHL. CD30 is present in approximately 95 percent of all cases of HL. In 2022, the American Cancer Society estimates that there will be about 8,540 new cases of HL and an estimated 920 people will die of this disease in the U.S.¹

About ADCETRIS

ADCETRIS is an antibody-drug conjugate (ADC) comprising an anti-CD30 monoclonal antibody attached by a protease-cleavable linker to a microtubule disrupting agent, monomethyl auristatin E (MMAE), utilizing Seagen's proprietary technology. The ADC employs a linker system that is designed to be stable in the bloodstream but to release MMAE upon internalization into CD30-expressing cells.

ADCETRIS is indicated for the treatment of adult patients with:

- previously untreated Stage III or IV classical Hodgkin lymphoma (cHL), in combination with doxorubicin, vinblastine, and dacarbazine,
- cHL at high risk of relapse or progression as post-autologous hematopoietic stem cell transplantation (auto-HSCT) consolidation,
- cHL after failure of auto-HSCT or failure of at least two prior multi-agent chemotherapy regimens in patients who are not auto-HSCT candidates,
- previously untreated systemic anaplastic large cell lymphoma (sALCL) or other CD30-expressing peripheral T-cell lymphomas (PTCL), including angioimmunoblastic T-cell lymphoma and PTCL not otherwise specified, in combination with cyclophosphamide, doxorubicin, and prednisone,
- sALCL after failure of at least one prior multi-agent chemotherapy regimen, and
- primary cutaneous anaplastic large cell lymphoma (pcALCL) or CD30-expressing mycosis fungoides who have received prior systemic therapy.

Seagen and Takeda are jointly developing ADCETRIS. Under the terms of the collaboration agreement, Seagen has U.S. and Canadian commercialization rights and Takeda has rights to commercialize ADCETRIS in the rest of the world. Seagen and Takeda are funding joint development costs for ADCETRIS on a 50:50 basis, except in Japan where Takeda is solely responsible for development costs.

ADCETRIS (brentuximab vedotin) for injection U.S. Important Safety Information

BOXED WARNING

PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY (PML): JC virus infection resulting in PML and death can occur in ADCETRIS-treated patients.

Contraindication

ADCETRIS concomitant with bleomycin due to pulmonary toxicity (e.g., interstitial infiltration and/or inflammation).

Warnings and Precautions

- **Peripheral neuropathy (PN):** ADCETRIS causes PN that is predominantly sensory. Cases of motor PN have also been reported. ADCETRIS-induced PN is cumulative. Monitor for symptoms such as hypoesthesia, hyperesthesia, paresthesia, discomfort, a burning sensation, neuropathic pain, or weakness. Institute dose modifications accordingly.
- **Anaphylaxis and infusion reactions:** Infusion-related reactions (IRR), including anaphylaxis, have occurred with ADCETRIS. Monitor patients during infusion. If an IRR occurs, interrupt the infusion and institute appropriate medical management. If anaphylaxis occurs, immediately and permanently discontinue the infusion and administer appropriate medical therapy. Premedicate patients with a prior IRR before subsequent infusions. Premedication may include acetaminophen, an antihistamine, and a corticosteroid.
- **Hematologic toxicities:** Fatal and serious cases of febrile neutropenia have been reported with ADCETRIS. Prolonged (≥ 1 week) severe neutropenia and Grade 3 or 4 thrombocytopenia or anemia can occur with ADCETRIS.

Administer G-CSF primary prophylaxis beginning with Cycle 1 for patients who receive ADCETRIS in combination with chemotherapy for previously untreated Stage III/IV cHL or previously untreated PTCL.

Monitor complete blood counts prior to each ADCETRIS dose. Monitor more frequently for patients with Grade 3 or 4 neutropenia. Monitor patients for fever. If Grade 3 or 4 neutropenia develops, consider dose delays, reductions, discontinuation, or G-CSF prophylaxis with subsequent doses.

- **Serious infections and opportunistic infections:** Infections such as pneumonia, bacteremia, and sepsis or septic shock (including fatal outcomes) have been reported in ADCETRIS-treated patients. Closely monitor patients during treatment for bacterial, fungal, or viral infections.
- **Tumor lysis syndrome:** Closely monitor patients with rapidly proliferating tumor and high tumor burden.
- **Increased toxicity in the presence of severe renal impairment:** The frequency of \geq Grade 3 adverse reactions and deaths was greater in patients with severe renal impairment compared to patients with normal renal function. Avoid use in patients with severe renal impairment.
- **Increased toxicity in the presence of moderate or severe hepatic impairment:** The frequency of \geq Grade 3 adverse reactions and deaths was greater in patients with moderate or severe hepatic impairment compared to patients with normal hepatic function. Avoid use in patients with moderate or severe hepatic impairment.
- **Hepatotoxicity:** Fatal and serious cases have occurred in ADCETRIS-treated patients. Cases were consistent with hepatocellular injury, including elevations of transaminases and/or bilirubin, and occurred after the first ADCETRIS dose or rechallenge. Preexisting liver disease, elevated baseline liver enzymes, and concomitant medications may increase the risk. Monitor liver enzymes and bilirubin. Patients with new, worsening, or recurrent hepatotoxicity may require a delay, change in dose, or discontinuation of ADCETRIS.

- **PML:** Fatal cases of JC virus infection resulting in PML have been reported in ADCETRIS-treated patients. First onset of symptoms occurred at various times from initiation of ADCETRIS, with some cases occurring within 3 months of initial exposure. In addition to ADCETRIS therapy, other possible contributory factors include prior therapies and underlying disease that may cause immunosuppression. Consider PML diagnosis in patients with new-onset signs and symptoms of central nervous system abnormalities. Hold ADCETRIS if PML is suspected and discontinue ADCETRIS if PML is confirmed.
- **Pulmonary toxicity:** Fatal and serious events of noninfectious pulmonary toxicity, including pneumonitis, interstitial lung disease, and acute respiratory distress syndrome, have been reported. Monitor patients for signs and symptoms, including cough and dyspnea. In the event of new or worsening pulmonary symptoms, hold ADCETRIS dosing during evaluation and until symptomatic improvement.
- **Serious dermatologic reactions:** Fatal and serious cases of Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) have been reported with ADCETRIS. If SJS or TEN occurs, discontinue ADCETRIS and administer appropriate medical therapy.
- **Gastrointestinal (GI) complications:** Fatal and serious cases of acute pancreatitis have been reported. Other fatal and serious GI complications include perforation, hemorrhage, erosion, ulcer, intestinal obstruction, enterocolitis, neutropenic colitis, and ileus. Lymphoma with preexisting GI involvement may increase the risk of perforation. In the event of new or worsening GI symptoms, including severe abdominal pain, perform a prompt diagnostic evaluation and treat appropriately.
- **Hyperglycemia:** Serious cases, such as new-onset hyperglycemia, exacerbation of pre-existing diabetes mellitus, and ketoacidosis (including fatal outcomes) have been reported with ADCETRIS. Hyperglycemia occurred more frequently in patients with high body mass index or diabetes. Monitor serum glucose and if hyperglycemia develops, administer anti-hyperglycemic medications as clinically indicated.

- **Embryo-fetal toxicity:** Based on the mechanism of action and animal studies, ADCETRIS can cause fetal harm. Advise females of reproductive potential of the potential risk to the fetus, and to avoid pregnancy during ADCETRIS treatment and for at least 6 months after the final dose of ADCETRIS.

Most Common (≥20% in any study) Adverse Reactions

Peripheral neuropathy, fatigue, nausea, diarrhea, neutropenia, upper respiratory tract infection, pyrexia, constipation, vomiting, alopecia, decreased weight, abdominal pain, anemia, stomatitis, lymphopenia, and mucositis.

Drug Interactions

Concomitant use of strong CYP3A4 inhibitors or inducers has the potential to affect the exposure to monomethyl auristatin E (MMAE).

Use in Specific Populations

Moderate or severe hepatic impairment or severe renal impairment: MMAE exposure and adverse reactions are increased. Avoid use. Advise males with female sexual partners of reproductive potential to use effective contraception during ADCETRIS treatment and for at least 6 months after the final dose of ADCETRIS.

Advise patients to report pregnancy immediately and avoid breastfeeding while receiving ADCETRIS.

Please see the full Prescribing Information, including BOXED WARNING, for ADCETRIS [here](#).

About Seagen

Seagen is a global biotechnology company that discovers, develops and commercializes transformative cancer medicines to make a meaningful difference in people's lives. Seagen is headquartered in the Seattle, Washington area, and has locations in California, Canada, Switzerland and the European Union. For more information on the company's marketed products and robust pipeline, visit www.seagen.com and follow [@SeagenGlobal](https://twitter.com/SeagenGlobal) on Twitter.

Forward Looking Statements

Certain statements made in this press release are forward looking, such as those, among others, relating to the therapeutic potential of ADCETRIS, its safety, efficacy and therapeutic uses, plans to present results at an

upcoming medical meeting, and anticipated and ongoing development activities for ADCETRIS, including clinical trial activities. Actual results or developments may differ materially from those projected or implied in these forward-looking statements. Factors that may cause such a difference include without limitation the level of utilization and adoption of the referenced treatment regimen by prescribing physicians, competitive conditions including the availability of alternative treatment regimens, the availability and extent of reimbursement, the risk of adverse events or safety signals, the possibility of adverse regulatory actions, the risk that data may not be selected for presentation at the referenced medical meeting; and the potential for delays or setbacks in product development and the regulatory review process. More information about the risks and uncertainties faced by Seagen is contained under the caption "Risk Factors" included in Seagen's Quarterly Report on Form 10-Q for the quarter ended September 30, 2021, filed with the Securities and Exchange Commission. Seagen disclaims any intention or obligation to update or revise any forward-looking statements, whether as a result of new information, future events or otherwise except as required by applicable law.

¹ <https://www.cancer.org/cancer/hodgkin-lymphoma.html>

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