ADC Therapeutics Announces FDA Approval of ZYNLONTA™ (loncastuximab tesirine-lpyl) in Relapsed or Refractory Diffuse Large B-Cell Lymphoma

First and only CD19-targeted antibody drug conjugate (ADC) as a single-agent treatment for adult patients with relapsed or refractory (r/r) diffuse large B-cell lymphoma (DLBCL)

ZYNLONTA addresses an unmet need across a broad population of third-line (3L)+ r/r patients, including patients with DLBCL not otherwise specified, DLBCL arising from low grade lymphoma and high-grade B-cell lymphoma

ZYNLONTA demonstrated 48.3% overall response rate, 24.1% complete response rate and durable responses in heavily pretreated patients in pivotal LOTIS-2 trial

Investor conference call and webcast to be held Friday, April 23rd at 4 p.m. ET

LAUSANNE, Switzerland, April 23, 2021 – ADC Therapeutics SA (NYSE: ADCT) today announced that the U.S. Food and Drug Administration (FDA) has approved ZYNLONTA™ (loncastuximab tesirine-lpyl) for the treatment of adult patients with relapsed or refractory (r/r) large B-cell lymphoma after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified (NOS), DLBCL arising from low grade lymphoma and high-grade B-cell lymphoma.[1] ZYNLONTA, a CD19-targeted antibody drug conjugate (ADC), has been granted accelerated approval by the FDA based on overall response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

"There is a significant unmet need for treatment options for patients with r/r DLBCL, including those who have been heavily pretreated and have difficult-to-treat disease," said Paolo F. Caimi, MD, University Hospitals Cleveland Medical Center and Case Comprehensive Cancer Center, Case Western Reserve University. "Single-agent ZYNLONTA demonstrated clinically important outcomes in the pivotal LOTIS-2 study across several disease subtypes. Notably, this included transplant eligible and ineligible patients and patients who previously received stem cell transplant or CAR-T cell therapy."

The FDA approval was based on data from LOTIS-2, a large (n=145) Phase 2 multinational, single-arm clinical trial of ZYNLONTA for the treatment of adult patients with r/r DLBCL following two or more prior lines of systemic therapy. Results from the trial demonstrated an overall response rate (ORR) of 48.3% (70/145 patients), which included a complete response (CR) rate of 24.1% (35/145 patients) and a partial response (PR) rate of 24.1% (35/145 patients). Patients had a median time to response of 1.3 months and the median duration of response (mDoR) for the 70 responders was 10.3 months (inclusive of patients who were censored). In a pooled safety population the most common adverse reactions (≥20%) were thrombocytopenia, gamma-glutamyltransferase increased, neutropenia, anemia, hyperglycemia, transaminase elevation, fatigue, hypoalbuminemia, rash, edema, nausea and musculoskeletal pain. In LOTIS-2, the most common (≥10%) grade ≥3 treatment-emergent adverse events were neutropenia (26.2%), thrombocytopenia (17.9%), gamma-glutamyltransferase increased (17.2%) and anemia (10.3%).

"The FDA approval of ZYNLONTA is an exciting advancement for patients with r/r DLBCL and a transformational event for ADC Therapeutics," said Chris Martin, Chief Executive Officer of ADC

Therapeutics. “We extend our deepest gratitude to the patients who participated in our LOTIS-1 and LOTIS-2 clinical trials, their families, the study investigators and our employees, as their commitment made this important milestone possible.”

DLBCL, the most common type of non-Hodgkin lymphoma in the United States, is a rapidly progressing, aggressive disease that is heterogeneous with multiple subtypes.[2] More than 40% of first-line DLBCL treatments fail.[3] For patients who fail first-line therapy, prognoses are poor, worsening with each line of therapy as the chance for cure or long-term disease-free survival diminishes.[4,5]

ZYNLONTA will be commercially available in the United States shortly. ADC Therapeutics has launched the Advancing Patient Support Program, a comprehensive patient support program offering financial assistance, ongoing education and other resources to eligible patients who are prescribed ZYNLONTA.

Please see full Prescribing Information at www.adctherapeutics.com for ZYNLONTA.

Conference Call Details

ADC Therapeutics management will host a conference call and live audio webcast on Friday, April 23, 2021 at 4 p.m. ET. To access the live call, please dial (833) 303-1198 (domestic) or +1 914 987 7415 (international) and provide conference ID 6867157. The live webcast will be available under “Events & Presentations” in the Investors section of the ADC Therapeutics website at ir.adctherapeutics.com. The archived webcast will be available for 30 days following the call.

Important Safety Information

WARNINGS AND PRECAUTIONS

Effusion and Edema

Serious effusion and edema occurred in patients treated with ZYNLONTA. Grade 3 edema occurred in 3% (primarily peripheral edema or ascites) and Grade 3 pleural effusion occurred in 3% and Grade 3 or 4 pericardial effusion occurred in 1%.

Monitor patients for new or worsening edema or effusions. Withhold ZYNLONTA for Grade 2 or greater edema or effusion until the toxicity resolves. Consider diagnostic imaging in patients who develop symptoms of pleural effusion or pericardial effusion, such as new or worsened dyspnea, chest pain, and/or ascites such as swelling in the abdomen and bloating. Institute appropriate medical management for edema or effusions.

Myelosuppression

Treatment with ZYNLONTA can cause serious or severe myelosuppression, including neutropenia, thrombocytopenia, and anemia. Grade 3 or 4 neutropenia occurred in 32%, thrombocytopenia in 20%, and anemia in 12% of patients. Grade 4 neutropenia occurred in 21% and thrombocytopenia in 7% of patients. Febrile neutropenia occurred in 3%.

Monitor complete blood counts throughout treatment. Cytopenias may require interruption, dose reduction, or discontinuation of ZYNLONTA. Consider prophylactic granulocyte colony-stimulating factor administration as applicable.

Infections

Fatal and serious infections, including opportunistic infections, occurred in patients treated with ZYNLONTA. Grade 3 or higher infections occurred in 10% of patients, with fatal infections occurring in 2%. The most frequent Grade ≥3 infections included sepsis and pneumonia.

Monitor for any new or worsening signs or symptoms consistent with infection. For Grade 3 or 4 infection, withhold ZYNLONTA until infection has resolved.

Cutaneous Reactions
Serious cutaneous reactions occurred in patients treated with ZYNLONTA. Grade 3 cutaneous reactions occurred in 4% and included photosensitivity reaction, rash (including exfoliative and maculo-papular), and erythema.

Monitor patients for new or worsening cutaneous reactions, including photosensitivity reactions. Withhold ZYNLONTA for severe (Grade 3) cutaneous reactions until resolution. Advise patients to minimize or avoid exposure to direct natural or artificial sunlight including exposure through glass windows. Instruct patients to protect skin from exposure to sunlight by wearing sun-protective clothing and/or the use of sunscreen products. If a skin reaction or rash develops, dermatologic consultation should be considered.

Embryo-Fetal Toxicity
Based on its mechanism of action, ZYNLONTA can cause embryo-fetal harm when administered to a pregnant woman because it contains a genotoxic compound (SG3199) and affects actively dividing cells.

Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with ZYNLONTA and for 9 months after the last dose. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with ZYNLONTA and for 6 months after the last dose.

ADVERSE REACTIONS
In a pooled safety population of 215 patients (Phase 1 and LOTIS-2), the most common (>20%) adverse reactions, including laboratory abnormalities, were thrombocytopenia, increased gamma-glutamyltransferase, neutropenia, anemia, hyperglycemia, transaminase elevation, fatigue, hypoalbuminemia, rash, edema, nausea, and musculoskeletal pain.

In LOTIS-2, serious adverse reactions occurred in 28% of patients receiving ZYNLONTA. The most common serious adverse reactions that occurred in ≥2% receiving ZYNLONTA were febrile neutropenia, pneumonia, edema, pleural effusion, and sepsis. Fatal adverse reactions occurred in 1%, due to infection.

Permanent treatment discontinuation due to an adverse reaction of ZYNLONTA occurred in 19% of patients. Adverse reactions resulting in permanent discontinuation of ZYNLONTA in ≥2% were gamma-glutamyltransferase increased, edema, and effusion.

Dose reductions due to an adverse reaction of ZYNLONTA occurred in 8% of patients. Adverse reactions resulting in dose reduction of ZYNLONTA in ≥4% was gamma-glutamyltransferase increased.

Dosage interruptions due to an adverse reaction occurred in 49% of patients receiving ZYNLONTA. Adverse reactions leading to interruption of ZYNLONTA in ≥5% were gamma-glutamyltransferase increased, neutropenia, thrombocytopenia, and edema.

You may report side effects to the FDA at (800) FDA-1088 or www.fda.gov/medwatch. You may also report side effects to ADC Therapeutics at 1-855-690-0340.

About ADC Therapeutics

ADC Therapeutics (NYSE: ADCT) is a commercial-stage biotechnology company improving the lives of cancer patients with its next-generation, targeted antibody drug conjugates (ADCs). The Company is advancing its proprietary PBD-based ADC technology to transform the treatment paradigm for patients with hematologic malignancies and solid tumors.

ADC Therapeutics' CD19-directed ADC ZYNLONTA™ (loncastuximab tesirine-lpyl) is approved by the FDA for the treatment of relapsed or refractory diffuse large B-cell lymphoma after two or more lines of systemic therapy. ZYNLONTA is also in late-stage clinical trials in combination with other agents. Cami (camidanlumab tesirine) is being evaluated in a late-stage clinical trial for relapsed or refractory Hodgkin lymphoma and in a Phase 1b clinical trial for various advanced solid tumors. In addition to ZYNLONTA and Cami, the Company has multiple PBD-based ADCs in ongoing clinical and preclinical development.

ADC Therapeutics is based in Lausanne (Biopôle), Switzerland and has operations in London, the San Francisco Bay Area and New Jersey. For more information, please visit https://adctherapeutics.com/ and follow the Company on Twitter and LinkedIn.

Forward-Looking Statements

This press release contains statements that constitute forward-looking statements. All statements other than statements of historical facts contained in this press release, including statements regarding our future results of operations and financial position, business and commercialization strategy, products and product candidates, research pipeline, ongoing and planned preclinical studies and clinical trials, regulatory submissions and approvals, addressable patient population, research and development costs, timing and likelihood of success, as well as plans and objectives of management for future operations, are forward-looking statements. Forward-looking statements are based on our management's beliefs and assumptions and on information currently available to our management. Such statements are subject to risks and uncertainties, and actual results may differ materially from those expressed or implied in the forward-looking statements due to various factors, including those described in our filings with the U.S. Securities and Exchange Commission. No assurance can be given that such future results will be achieved. Such forward-looking statements contained in this document speak only as of the date of this press release. We expressly disclaim any obligation or undertaking to update these forward-looking statements contained in this press release to reflect any change in our expectations or any change in events, conditions, or circumstances on which such statements are based unless required to do so by applicable law. No representations or warranties (expressed or implied) are made about the accuracy of any such forward-looking statements.

ZYNLONTA™ is a trademark of ADC Therapeutics SA.

References

1. ZYNLONTA™ Prescribing Information. ADC Therapeutics SA.

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3. Coiffier B, Thieblemont C, Van Den Neste E, et al. Long-term outcome of patients in the LNH-98.5 trial, the first randomized study comparing rituximab-CHOP to standard CHOP chemotherapy in DLBCL patients: a study by the Groupe d'Etudes des Lymphomes de l'Adulte. *Blood*. 2010;116:2040-2045.
4. Crump M, Neelapu SS, Farooq U, et al. *Blood*. 2017;130:1800-1808.
5. Klink AJ, Nabhan C, Lee CH, et al. *J Clin Pathways*. 2020;6:44-53.

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