Autolus Therapeutics Announces Update on its Novel CAR T Cell Program for Peripheral T Cell Lymphoma (PTCL)

December 1, 2018 at 9:16 PM EST

-First patient dosed in Phase 1/2 trial of AUTO4 in TRBC1-positive peripheral T cell lymphoma-

-Preclinical data for AUTO5 targeting TRBC2-positive peripheral T cell lymphoma presented at the 60th Annual American Society of Hematology (ASH) Meeting-

LONDON, Dec. 1, 2018 /PRNewswire/ -- Autolus Therapeutics plc (Nasdaq: AUTL), a clinical-stage biopharmaceutical company developing next-generation programmed T cell therapies for the treatment of cancer, today announced that the first patient has been dosed in its Phase 1/2 LibrA T1 clinical trial of AUTO4, a developmental therapy for the treatment of relapsed or refractory TRBC1-positive peripheral T cell lymphoma (PTCL). In addition, the company also announced that data on the preclinical sister program, AUTO5 targeting TRBC2-positive lymphoma, were presented at the 60th American Society of Hematology (ASH) Annual Meeting, San Diego. Autolus' T cell program comprises a companion diagnostic to determine whether the PTCL is TRBC1- or TRBC2-positive and two novel CAR T cell product candidates AUTO4 and AUTO5. PTCL is a rare and heterogeneous form of non-Hodgkin lymphoma, currently estimated to affect approximately 2,900 patients in the United States, annually.[1]

"There are limited treatment options for patients with relapsed and/or refractory peripheral T cell lymphoma. We are particularly excited to participate in the LibrA T1 trial of AUTO4, a novel CAR T cell therapy for this aggressive cancer," said Dr. Kate Cwynarski, Principal Investigator, Consultant Haematologist at University College London Hospital and Honorary Senior Lecturer at University College London.

"Effective systemic treatment for peripheral T cell lymphomas remains a challenge. CAR T therapies selectively targeting TRBC1-positive and TRBC2-positive T cell lymphomas have the potential to be major therapeutic advances," said Steven T. Rosen, M.D. provost and chief scientific officer of City of Hope and director of the Beckerman Research Institute of City of Hope.

On December 2 at the 60th ASH Annual Meeting in San Diego, the company presented data from preclinical studies of AUTO5 targeting TRBC2. TRBC1 and TRBC2 are virtually identical in sequence, and antibody binders had to be designed to differentiate TRBC1 from TRBC2 extracellular domains by selectively recognizing a single inversion of two amino acids. Employing a structural biology approach and molecular modelling techniques, a binder was generated that could bind TRBC2 without binding to TRBC1, and when included in a CAR T approach, selectively eliminated TRBC2-positive cells.

Structure guided engineering of highly specific Chimeric Antigen Receptors for the complete treatment of T cell lymphomas (Abstract number 1661, poster presentation from 6:15 PM PST- 8:15 PM PST, on Saturday, December 1, 2018.)

About LibrA T1 P1/2 Clinical Trial
The LibrA T1 trial is a single-arm, open label, multi-center, Phase 1/2 trial evaluating the safety and efficacy of AUTO4, a single dose intravenous CAR T cell treatment targeting TRBC1 in patients with relapsed or refractory TRBC1-positive selected PTCL. The trial will consist of a Phase 1 portion, or dose escalation phase, and a Phase 2 portion, or expansion phase. The Phase 1 portion of the trial, which is expected to enroll up to 25 patients, is designed to evaluate up to three dose levels, beginning with a low dose of 25 million AUTO4 cells in cohorts of three to six patients. If no dose limiting toxicities are observed, the dose escalation phase of the trial will continue to higher doses of 75 million AUTO4 cells and 225 million AUTO4 cells. Once a recommended dose has been identified in the Phase 1 portion of the trial, up to 30 patients will be enrolled and treated in the Phase 2 portion.

About AUTO4 and AUTO5
AUTO4 is a programmed T cell therapy product candidate being developed to leverage a new targeting approach based on the mutually exclusive expression of two subtypes of the T cell receptor beta chain: AUTO4 targets TRBC1, while another of the company's product candidates in development, AUTO5, targets TRBC2. Normal T cells contain both TRBC1 and TRBC2 compartments, whereas T cell lymphoma cells are derived from mature cells and express only TRBC1 or TRBC2. A companion diagnostic is used to identify if the T cell lymphoma is TRBC1 or TRBC2 positive. Unlike non-selective approaches targeting the entire T cell population that can lead to severe immunosuppression, this approach has the potential to eradicate a portion of T cells containing the malignancy, while preserving a healthy T cell sub-population to preserve cellular immunity.

For more information about this trial and the inclusion criteria, visit www.clinicaltrials.gov.

About Peripheral T Cell Lymphoma (PTCL)
Lymphoma is the most commonly occurring blood cancer. The two main forms of lymphoma are Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL). Lymphoma occurs when cells of the immune system called lymphocytes, a type of white blood cell, grow and multiply uncontrollably. Lymphomas can originate from two types of lymphocytes, B cells and T cells. T cell lymphoma is a rare and heterogeneous form of NHL, representing approximately 10 to 20% of NHL cases and 3 to 4% of all hematological malignancies

While T cell lymphoma is a smaller percentage of all lymphomas compared to B cell lymphomas, T cell lymphoma is an aggressive disease. Most T cell lymphomas are PTCL, and generally involve high-grade tumors, with a relatively high proportion of patients rapidly developing significant morbidity. The five-year survival rate ranges from 18% to 24%. The first-line treatment for PTCL consists of the combination chemotherapy CHOP, consisting of cyclophosphamide, vincristine, doxorubicin and prednisolone. However, treatment with chemotherapy introduces toxicity concerns, including low blood cell counts, nausea, vomiting, diarrhea, hair loss, mouth sores, and increased risk of infections. Additionally, with CHOP chemotherapy, complete response rates are lower than in DLBCL and relapse is more common. In many treatment centers, CHOP chemotherapy is consolidated with high-dose chemotherapy and autologous or allogenic stem cell transplantation. According to National Comprehensive Cancer

Network (NCCN) guidelines, participation in a clinical trial is the preferred option for all patients with T cell lymphoma with any stage disease.[2]

REFERENCES

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2. Horwitz SM, Ansell SM, Ai WZ, Barnes J, Barta SK, Choi M, Clemens MW, Dogan A, Greer JP, Halwani A, Haverkos BM, Hoppe RT, Jacobsen E, Jagadeesh D, Kim YH, Lunning MA, Mehta A, Mehta-Shah N, Oki Y, Olsen EA, Pro B, Rajguru SA, Shanbhag S, Shustov A, Sokol L, Torka P, Wilcox R, William B, Zain J, Dwyer MA, Sundar H. NCCN Guidelines Insights: T-Cell Lymphomas, Version 2.2018. J Natl Compr Canc Netw. 2018 Feb;16(2):123-135. doi: 10.6004/jnccn.2018.0007. PubMed PMID: 29439173.

About Autolus Therapeutics plc
Autolus is a clinical-stage biopharmaceutical company developing next-generation, programmed T cell therapies for the treatment of cancer. Using a broad suite of proprietary and modular T cell programming technologies, the company is engineering precisely targeted, controlled and highly active T cell therapies that are designed to better recognize cancer cells, break down their defense mechanisms and eliminate these cells. Autolus has a pipeline of product candidates in development for the treatment of hematological malignancies and solid tumors.

Forward-Looking Statement
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 progress, timing and results of the company's clinical trials and the anticipated clinical development of the company's 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. For a discussion of other risks and uncertainties, and other important factors, any of which could cause our actual results to differ from those contained in the forward-looking statements, see the section titled "Risk Factors" in the company's Annual Report on Form 20-F filed on November 23, 2018 as well as discussions of potential risks, uncertainties, and other important factors in the company's future filings with the Securities and Exchange Commission from time to time. All information in this press release is as of the date of the release, and the company 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.

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