Autolus Announces Initiation of the AMELIA and ALEXANDER Studies for AUTO3: Phase I/II Studies in paediatric ALL and DLBCL

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AUTO3 is the first dual targeting CAR-T cell therapy to enter clinical studies targeting CD19 and CD22 with independently-acting CARs

Autolus Limited, a clinical-stage biopharmaceutical company focused on the development and commercialisation of next-generation engineered T-cell therapies, today announced initiation of both the AMELIA and ALEXANDER phase I/II studies of its novel, dual-targeting, AUTO3 Chimeric Antigen Receptor (CAR) T-cell therapy.

AUTO3 is an autologous T-cell product, genetically modified to express two separate CARs which recognise CD19 and CD22; two antigens expressed by cancer cells in B-cell leukaemia and lymphoma. AUTO3 is designed to minimise the risk of relapse due to antigen loss, a key mechanism of resistance shown in single antigen targeting CAR-T therapies.

The AMELIA and ALEXANDER Studies are dose-escalation phase I/II studies in paediatric Acute Lymphocytic Leukaemia (ALL) and adult Diffuse Large B-Cell Lymphoma (DLBCL) in which cohorts of patients receive ascending doses of AUTO3 to determine the maximum tolerated dose and establish a recommended dose. The second part of the study is an expansion phase where patients receive AUTO3 to further evaluate the safety, tolerability and clinical activity at this recommended dose. In addition to the effects of AUTO3 alone, combination with short-duration use of a checkpoint inhibitor is also being evaluated in the ALEXANDER study.

Dr Martin Pule, Autolus' Founder and Chief Scientific Officer said:

> "Our approach at Autolus is to understand how tumours defend against T-cells and then design and programme CAR-T cell products which specifically address those defence and escape mechanisms. The AUTO3 programme seeks to overcome two limitations of current therapies by introducing dual targeting CARs and addressing checkpoint mediated inhibition."

Professor Persis Amrolia, Professor of Transplantation Immunology, Great Ormond Street Hospital, London commented:

> "The advent of CD19 CAR-T cell based therapy is an exciting and revolutionary advancement in the treatment of children with relapsed ALL. However, in approximately a third of the patients the disease reoccurs by losing CD19 antigen. AUTO3, a dual targeting CAR, addresses this challenge by independently targeting CD19 and CD22 antigen, which has the promise of reducing antigen escape."

Dr Anas Younes, Chief, Lymphoma Service at Memorial Sloan Kettering Cancer Center, New York commented:

> "CD19-directed CAR-T cell therapies already offer the possibility of an important new treatment option for patients with relapsed and refractory DLBCL. AUTO3 is a novel approach which simultaneously targets a second clinically relevant antigen, CD22. The field is looking forward to seeing how patients respond to AUTO3 in clinical trials and whether dual antigen targeting CAR-T cell therapy offers the possibility of deeper initial and more sustained responses."

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Notes for Editors:

About Autolus

Autolus is a clinical-stage, biopharmaceutical company, focused on the development and commercialisation of engineered T-cell immunotherapy products to combat cancer. Utilising its advanced cell programming and manufacturing technologies, Autolus has a pipeline of products in development for the treatment of both haematological malignancies and solid tumours. For further information please visit the Company's website

at: www.autolus.com

About AUTO3

AUTO3 is an autologous T-cell product, genetically modified to express two separate chimeric antigen receptors (CARs) which recognise CD19 and CD22 antigens expressed by cancer cells in B-cell leukaemia and lymphoma. It is believed to be the first dual-targeting CAR-T cell product to enter clinical development with both CARs delivered from a single retroviral vector during production.

Clinical studies with anti-CD19 CAR T cells have demonstrated efficacy in treating ALL and DLBCL patients; however, a significant proportion of patients relapse due to CD19 downregulation. CD22 is another B-cell antigen that is expressed on B-cell lymphomas and leukaemias, and expression of CD22 is maintained on cancer cells that have lost CD19. By targeting both CD19 and CD22 simultaneously, AUTO3 may decrease relapse rates by reducing the risk of the cancer cells evading treatment by loss or downregulation of a single antigen.

AUTO3 was the subject of a presentation at the International Congress on Malignant Lymphoma, Lugano, 2017: http://www.lymphcon.ch

About the AMELIA study

This is a single arm, open-label, multi-centre, phase I/II study evaluating the safety and clinical activity of AUTO3 in paediatric and young adult patients with relapsed or refractory B-Cell Acute Lymphoblastic Leukaemia. The phase I part of the study is evaluating the optimal dose in relapsed or refractory B-cell ALL patients. Phase II is an expansion phase where patients receive AUTO3 at the recommended dose to further evaluate the safety, tolerability and clinical activity at this recommended dose. The study will initially enroll patients at several sites in the UK, with further sites in Europe and the US added later.

Further details of the AMELIA study can be found at: https://www.clinicaltrialsregister.eu

About the ALEXANDER study

This is a phase I/II, open-label, multi-centre study to evaluate the safety and efficacy of AUTO3 administered by intravenous infusion in adult DLBCL patients. The phase I, dose escalation, is designed to identify the optimal dose in relapsed or refractory DLBCL patients. Phase II is an expansion phase where patients receive AUTO3 at the recommended dose to further evaluate the safety, tolerability and clinical activity at this recommended dose. In addition to evaluating the effects of AUTO3 alone, the study will also evaluate the effects of AUTO3 in combination with short-duration use of a checkpoint inhibitor. The study will initially enroll patients at several sites in the UK, with further sites in Europe and the US added later.

Further details of the ALEXANDER study can be found at: https://www.clinicaltrialsregister.eu

About paediatric Acute Lymphoblastic Leukaemia (ALL)

ALL is a cancer of the bone marrow and blood, in which the body makes abnormal white blood cells (lymphocytes). The disease progresses quickly and is the most common childhood cancer in the US and Europe. The National Cancer Institute (NCI) estimates that approximately 3,100 patients aged 20 and younger are diagnosed with ALL each year in the US alone. ALL can be of either T- or B-cell origin, with B-cell the most common. ALL usually gets worse rapidly if it is not treated and can be fatal within a few months; therefore, it is critical for patients to start treatment soon after diagnosis. Although the majority of B-cell ALL patients respond well to conventional treatment, the prognosis for patients that relapse is poor and novel therapies to treat these patients are urgently needed.

About Diffuse Large B-cell Lymphoma (DLBCL)

DLBCL is an aggressive type of non-Hodgkin lymphoma (NHL) that develops from the B- cells in the lymphatic system. The B-cells are a type of white blood cells responsible for producing antibodies. The disease develops when the body makes abnormal B-lymphocytes – the lymphoma cells. It is a rapidly growing blood cancer, which can occur in lymph nodes or outside of the lymphatic system, in the brain, bone, breast, skin, thyroid, gastrointestinal tract, and testes. According to the American Cancer Society, NHL accounts for about four percent of all cancers in the United States, making it one of the most common cancers diagnosed. DLBCL is the most common form of the disease, accounting for one out of every three cases of NHL.

About The Study Names

AUTO3 - AMELIA and ALEXANDER: are named after pioneers who achieved significant accomplishments in 1922; AMELIA for Amelia Earhart, the American aviator who set the altitude record for a woman by flying to 14,000 feet, and ALEXANDER, for Alexander Fleming, the famous Scottish physician and pharmacologist, who isolated lysozyme in the same year.