Autolus Therapeutics Announces Publication in Molecular Therapy

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- Dual targeting of CD19 and CD22 against B-ALL using a novel high-sensitivity aCD22 CAR

- AUTO1/22 may reduce CD19 negative escape in children with B-ALL, and may have broader applications in improving outcomes in other B-cell malignancies

LONDON, April 04, 2023 (GLOBE NEWSWIRE) -- Autolus Therapeutics plc (Nasdaq: AUTL), a clinical-stage biopharmaceutical company developing next-generation programmed T cell therapies, today announced the publication of a paper in *Molecular Therapy* titled '*Dual targeting of CD19 and CD22 against B-ALL using a novel high-sensitivity aCD22 CAR.*' [1]

While CD19 CAR T cell therapy has had remarkable success in the treatment of B-cell malignancy, a proportion of patients may relapse with CD19 negative escape. Relapses due to antigen escape are a common cause of treatment failure in pediatric B-ALL. A solution to this is the co-targeting of a 2nd B-lineage antigen. CD22 is expressed early in B-cell development up until plasma cell differentiation and is expressed broadly by B-cell malignancies. Co-targeting of CD19 and CD22 is challenging for two reasons. Firstly, CD22 is a difficult CAR target being bulky and expressed at low density. Secondly, the optimal way of designing a CAR T cell which targets two antigens simultaneously has not been established.

In this paper, the Autolus research team first develop a highly sensitive CD22 CAR which can recognize target antigen even if CD22 is expressed at low density. Secondly, they explore a co-transduction approach with the clinically proven Autolus CD19 CAR, Obecabtagene autoleucel (obe-cel). The advantage of a co-transduction approach is that expression of neither obe-cel nor the new CD22 CAR are perturbed. This new CD19/CD22 CAR T cell therapeutic (AUTO1/22) was found to be effective in a mouse model of B-Cell Acute Lymphoblastic Leukemia (B-ALL) with CD19 negative escape.

AUTO1/22 is currently being tested in a pediatric study of relapsed/remitting (r/r) B-ALL [NCT02443831].

"CD22 targeting and CD19/CD22 co-targeting are challenging technical problems in the field," **said Martin Pule, Chief Scientific Officer, and Founder of Autolus**. "Development of AUTO1/22 in this paper represents the state-of-the-art with a high-sensitivity CD22 receptor and efficient co-targeting."

"I am delighted to see publication of the pre-clinical data for AUTO1/22," **added Christian Itin, Chief Executive Officer of Autolus**. "This work builds on our success with CD19 targeting with obe-cel and represents a significant evolution of our obe-cel platform. AUTO1/22 may reduce CD19 negative escape in children with B-ALL and may have broader applications in improving outcomes in other B-cell malignancies."

[1]. *Evangelia Kokalaki, Biao Ma, Mathieu Ferrari et al. Dual targeting of CD19 and CD22 against B-ALL using a novel high-sensitivity aCD22 CAR. Molecular Therapy.* The full publication can be viewed here.

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. For more information, please visit www.autolus.com.

About obe-cel (AUTO1)
Obe-cel is a CD19 CAR T cell investigational therapy designed to overcome the limitations in clinical activity and safety compared to current CD19 CAR T cell therapies. Designed to have a fast target binding off-rate to minimize excessive activation of the programmed T cells, obe-cel may reduce toxicity and be less prone to T cell exhaustion, which could enhance persistence and improve the ability of the programmed T cells to engage in serial killing of target cancer cells. In collaboration with Autolus' academic partner, UCL, obe-cel is currently being evaluated in a Phase 1 clinical trials for B-NHL. Autolus has progressed obe-cel to the FELIX trial, a pivotal trial for adult ALL. [NCT04404660]

About AUTO1/22
AUTO1/22 is a novel dual targeting CAR T cell based therapy candidate based on obe-cel. It is designed to combine the enhanced safety, robust expansion and persistence seen with the fast off rate CD19 CAR from obe-cel with a high sensitivity CD22 CAR to reduce antigen negative relapses. This product candidate is currently in a Phase 1 clinical trial for patients with r/r pediatric ALL. [NCT02443831]

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 the continued development of Autolus' obe-cel program including timing of and expectations regarding planned readouts as well as expectations that the final data set will be confirmatory of the data from the interim analysis; expectations the trial will result in sufficient data to support the utility of obe-cel across the full range of disease burden; the status of clinical trials (including, without limitation, expectations regarding the data that is being presented, the expected timing of data releases and development, as well as completion of clinical trials) and development timelines for the Company's product candidates; the planned submission of a Biologics License Application for obe-cel by the end of 2023; the expected benefits of the Company's collaborations and partnerships as well as the anticipated receipt of milestone payments; and the sufficiency of the Company's cash resources and its

anticipated cash runway into 2025. 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; possible safety and efficacy concerns; and the impact of the ongoing COVID-19 pandemic on Autolus' business. 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 20-F filed with the Securities and Exchange Commission on March 10, 2022, 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.

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