Autolus Therapeutics announces publication describing its small molecule-regulated CAR T cells

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Tetracycline and minocycline controllable CAR T cell system to manage toxicities

LONDON, Nov. 10, 2021 (GLOBE NEWSWIRE) -- Autolus Therapeutics plc (Nasdaq: AUTL), a clinical-stage biopharmaceutical company developing next-generation programmed T cell therapies, today announced the publication of an article in Nature Scientific Reports describing a controllable CAR T cell system (TetCAR), designed to reversibly dampen the activity of the programmed T cells by the administration of the licensed and widely available antibiotics tetracycline and minocycline.[1]

Management of toxicities is a critical step in the successful application of programmed cell therapies. TetCAR is one of a number of approaches developed at Autolus that use a pharmacological agent to selectively control or eliminate cell therapies in the event a patient experiences severe adverse side effects from the treatment.

Safety switches, like Autolus' Rituxumab and Rapamycin controlled systems (RQR8 [2] and RapaCasp9[3]), are designed to selectively eliminate a programmed cell therapy following administration of a pharmacological agent, whilst controllable systems, like the TetCAR approach described in this publication, are designed to allow the activity of a CAR T cell therapy to be dialed down following administration of a pharmacological agent to a patient and then subsequently restored on clearance of the pharmacological agent from the patient.

"While many such systems have been described, most require use of experimental small molecules for control. Our TetCAR, RQR8 and Rapacasp9 approaches, all use licensed and widely available drugs, offering practical application of these systems in the clinic," said Dr. Martin Pule, chief scientific officer of Autolus. "We are excited to highlight this new publication which underscores the strong technology and IP base that we are using to develop the next generation of programmed cell therapies, both in-house and in partnership."

1. TetCAR: Hotblack A, Kokalaki E, Palton M, Weng-Kit Cheung G, Williams I, Manzoor S, Grothier T, Piapi A, Fiaccadori V, Wawrzyniecka P, Roddy H, Agliardi G, Roddie C, Onuoha S, Thomas S, Cordoba S and Pule M. Tunable control of CAR T cell activity through tetracycline mediated disruption of protein–protein interaction. Nature Scientific Reports, 2021 Nov 9. https://doi.org/10.1038/s41598-021-01418-9

2. RQR8: Philip B, Kokalaki E, Mekkaoui L, Thomas S, Straathof K, Flutter B, Marin V, Marafioti T, Chakraverty R, Linch D, Quezada SA, Peggs KS, Pule M. A highly compact epitope-based marker/suicide gene for easier and safer T-cell therapy. Blood. 2014 Aug 21;124(8):1277-87. https://doi.org/10.1182/blood-2014-01-545020

3. RapaCasp9: Maria Stavrou, Brian Philip, Charlotte Traynor-White, Christopher G. Davis, Shimobi Onuoha, Shaun Cordoba, Simon Thomas and Martin Pule. A Rapamycin-Activated Caspase 9-Based Suicide Gene. Molecular Therapy. 2018 May 02; 26(5): 1266-76. https://doi.org/10.1016/j.ymthe.2018.03.001

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 RQR8
Rituximab Safety Switch (RQR8) - The RQR8 safety switch is designed to selectively eliminate the programmed T cells by the administration of the commercially available monoclonal antibody rituximab. Once administered, rituximab binds to the engineered CD20 epitopes on the surface of the T cell and triggers cell death.

About Rapacasp9
Rapamycin Safety Switch (RapaCasp9) - The rapaCasp9 safety switch is designed to selectively eliminate the programmed T cells by the administration of the commercially available drug rapamycin. Once administered, rapamycin heterodimerises caspase 9 via FRB and FKBP to activate a cell death cascade and selectively eliminate the programmed T cells. Rapamycin is a small molecule drug, which we expect will have the benefit of better tissue penetration and may require less time to take effect as compared to a monoclonal antibody-activated safety switch.

About TetCAR
Tetracycline Controllable CAR (TetCAR) - TetCAR is a controllable CAR T cell system designed to reversibly dampen the activity of the programmed T cells by the administration of the commercially available antibiotic tetracycline. Once administered, tetracycline temporarily dislocates the CAR signaling domain from the cancer antigen binding domain leading to deactivation of the T cell therapy. The system is designed to be reversable, and on clearance of tetracycline from the patient, the interaction between the signaling domain and binding domain is restored and the programmed T cells

are reactivated. Controllable CAR T cells are intended to be used to manage a patient through a period of severe toxicity whilst also allowing for the subsequent reactivation of programmed T cells and the possibility of persistence and sustained anti-tumor activity.

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 future clinical development, efficacy, safety and therapeutic potential of obe-cel, including progress, expectations as to the reporting of data, conduct and timing and potential future clinical activity and milestones; expectations regarding the initiation, design and reporting of data from clinical trials. 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 4, 2021, 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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