



Autolus Therapeutics Announces Publication Describing Novel Cell Programming Technology

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- Publication describing a novel technology that provides for very low levels of expression of one programming module relative to another programming module¹
- Method for expressing stable low levels of a toxic gene - technology deployed in Autolus' approach for the treatment of solid tumors
- Highly restricted IL-12 release increases CAR T activity in an immunocompetent mouse model without systemic toxicity

LONDON, March 03, 2022 (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 *BioTechniques* describing a novel technology that provides for very low levels of expression of one gene module, while maintaining high levels of expression of other gene modules expressed from the same promotor¹.

This technical paper describes a method of achieving very low levels of transgene expression in multi-cistronic mammalian expression systems. This is achieved via the insertion of a stop codon and translational readthrough motif (TRM) between the transgenes of an mRNA encoding a multi-cistronic cassette. The TRM helps to suppress the stop codon, facilitating continued translation of the downstream transgene at reduced levels compared with the upstream transgene. This system addresses a fundamental challenge in cell therapy when highly potent receptors, cytokines or toxins are expressed, which, at normal levels of expression, would be unsafe for patients.

"Throughout the history of gene-therapy the primary focus was on engineering mammalian expression cassettes driving high levels of transgene expression," said **James Sillibourne, director of synthetic genomics at Autolus**. "However, with a very potent or toxic transgene, you need a very low level of expression. Up until now, an easy way of achieving this was not available. Building on mechanisms known from bacteria and viruses, we have developed a reliable way of tightly controlling low levels of transgene expression."

IL-12 is a potent anti-tumor cytokine. However, the majority of clinical studies involving treatment of patients with IL-12 have been associated with severe systemic side effects and significant toxicities for patients.

"Our approach to solid tumors combines multiple gene modules in CAR T cells to drive the desired set of properties we believe are essential to maximize anti-tumor activity without increasing toxicity. Selectively adjusting expression levels became an important technology to establish therapeutic windows," added **Martin Pule, chief scientific officer and founder of Autolus**. "In this paper we successfully applied this technology for highly restricted IL-12 release which increases CAR T anti-tumor activity in an immunocompetent mouse model without inducing systemic toxicity."

1. *Sillibourne JE, Agliardi G, Righi M et al. A compact and simple method of achieving differential transgene expression by exploiting translational readthrough. BioTechniques doi: 10.2144/btn-2021-0079 (2022) (Epub ahead of print)*. The full publication in *BioTechniques* 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.

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 Autolus' development of the obe-cel program; the future clinical development, efficacy, safety and therapeutic potential of its product candidates, including progress, expectations as to the reporting of data, conduct and timing and potential future clinical activity and milestones; and 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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