Autolus Therapeutics announces a publication in Nature Medicine on obe-cel in Pediatric Acute Lymphoblastic Leukemia

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- Long-term CAR T cell persistence is associated with durable responses in B-ALL
- Obe-cel CAR T cells can persist in patients at levels sufficient to allow their isolation from blood samples, even years after infusion
- Single-cell analysis of persisting obe-cel CAR T cells sheds light on the biology of long-term CAR T cell persistence

LONDON, July 06, 2023 (GLOBE NEWSWIRE) -- Autolus Therapeutics plc (Nasdaq: AUTL), a clinical-stage biopharmaceutical company developing next-generation programmed T cell therapies, today announced a publication in *Nature Medicine*[1] entitled: 'Transcriptional hallmarks of persisting CD19 CAR T-cells in children with leukaemia,' describing new findings from the original Obecabtagene autoleucel (obe-cel) study (CARPALL [2]) in Pediatric B-cell Acute Lymphoblastic Leukemia.

Long-term CAR T cell persistence is associated with durable responses in some cancers, including B-cell acute lymphoblastic leukemia (B-ALL). Obe-cel, Autolus' CD19 CAR, was designed to maximize CAR T cell persistence by tuning the affinity to CD19 to result in more physiological signaling.

The transcriptional mechanisms behind long-term persistence of antigen-specific T cells are not fully understood. The long-term persistence of obe-cel CAR T cells in patients allows their isolation by flow-cytometric sorting from peripheral blood at very late time-points (including several years) after infusion. This has enabled researchers at University College London, working in collaboration with the Wellcome Sanger Institute, to perform detailed single-cell analysis on long-term persisting CAR T cells from patients treated in the CARPALL study[2], the first clinical study of obe-cel in pediatric B-ALL.

Publishing her findings in *Nature Medicine* today, Dr Sara Ghorashian described how long-term persistence was associated with a particular T cell population which was CD4/CD8 double-negative, but expressed the transcription factor TOX and Granzyme K. This phenotype emerged across all clones and subsets of T-cells, suggesting that CAR T-cells converge transcriptionally to this state to maintain persistence. This finding fits with the newly described T_{PEX} sub-population found in chronic viral infections.

"Long-term CAR T cell persistence is required for durable responses in B-ALL but is not well understood," said **Dr Martin Pule, Chief Scientific Officer and Founder of Autolus:** "Dr Ghorashian has exploited the ability to isolate obe-cel CAR T-cells from patients at late time-points to further our understanding of which transcriptional states drive long-term persistence. These findings will allow us to work towards further refining CAR T manufacturing to favor these transcriptional states."

1. **Ghorashian, S. et al, Nature Medicine, 2023. DOI: 10.1038/s41591-023-02415-3**
2. **Ghorashian, S. et al. Nat. Med. 25, 1408–1414 (2019). DOI:10.1038/s41591-019-0549-5**

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 trial for B-NHL. Autolus has progressed obe-cel to the FELIX trial, a pivotal trial for adult ALL.

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, and the potential application of new findings to the Company's manufacturing and development activities. 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 7, 2023, 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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