



PRESS RELEASE

Collectis Publishes Article in *Frontiers in Immunology* Unveiling Pre-Clinical Data on a Novel Treatment Paradigm for Successful CAR T Immunotherapy Against Stroma-rich Solid Tumors

May 12, 2023 - New York, NY – Collectis (the “Company”) (Euronext Growth: ALCLS - NASDAQ: CLLS), a clinical-stage biotechnology company using its pioneering gene-editing platform to develop life-saving cell and gene therapies, today published an article in *Frontiers Bioengineering*, demonstrating the efficacy of its TALEN® engineered FAP UCART-cells in cancer-associated fibroblast (CAF) depletion, reduction of desmoplasia and tumor infiltration.

Adoptive cell therapy based on chimeric antigen receptor-engineered T (CAR-T) cells has proven to be lifesaving for many cancer patients.

However, its therapeutic efficacy has so far been restricted to only a few malignancies, with solid tumors proving to be especially recalcitrant to efficient therapy. Poor intra-tumor infiltration by T cells and T cell dysfunction due to a desmoplastic, immunosuppressive microenvironment are key barriers for CAR T-cell success against solid tumors.

Cancer-associated fibroblasts (CAFs) are critical components of the tumor stroma, evolving specifically within the tumor microenvironment (TME). The CAF secretome is a significant contributor to the extracellular matrix and a plethora of cytokines and growth factors that induce immune suppression. Together they form a physical and chemical barrier which induces a T cell-excluding ‘cold’ TME. CAF depletion in stroma rich solid tumors can thus provide an opportunity to convert immune evasive tumors susceptible to tumor-antigen CAR T-cell cytotoxicity.

Collectis used its TALEN®-based gene editing platform to engineer non-alloreactive, immune-evasive UCAR T-cells targeting the unique CAF marker Fibroblast Activation Protein, alpha (FAP) to test whether FAP UCAR T-cell pre-treatment can make ‘cold’ tumors susceptible to subsequent tumor-antigen targeting CAR T-cells. Collectis also generated non-alloreactive CAR T-cells against the tumor associated antigen (TAA) Mesothelin which is overexpressed in most solid tumors including mesothelioma and large sub-sets of ovarian, breast, pancreatic and lung adenocarcinomas. The combination treatment strategy was tested in a pre-clinical mouse model of triple-negative breast cancer (TNBC), an aggressive, stroma-rich breast cancer sub-type with poor prognosis and very limited treatment options at present.

“Over 90% of epithelial cancers including breast, colorectal, pancreatic and lung adenocarcinomas express the CAF-specific surface marker, fibroblast activation protein α (FAP), which makes it a promising CAR T-cell target. In this study, we propose a novel and versatile approach of combination CAR T-cell therapy that can be extended to most stroma-rich cold tumors with relevant tumor-antigen targeting CAR T-cells which otherwise are recalcitrant to cell therapy”, said Shipra Das, Ph.D., Senior Scientist & Team Leader at Collectis.

Preclinical data showed that :

- In a mouse xenograft model, successful implantation of injected CAFs in the tumors was confirmed by positive staining of spindle-like cells with human-specific FAP antibody, recapitulating a physiologically relevant TNBC tumor with tumor and stromal compartments.
- FAP UCART-cells alone significantly reduced tumor growth.
- *In vitro* and *in vivo* results show that FAP UCART-cells enable the reprogramming of the cold, stroma-rich triple negative breast cancer (TNBC) TME, making the tumor susceptible to subsequent Meso UCAR T infiltration and cytotoxicity and improving the overall antitumor activity of the treatment.
- In the context of combination therapy with anti-PD1 checkpoint inhibitor, maximal anti-tumor activity and survival benefits were observed upon FAP UCAR T-cell treatment followed by Meso UCAR T-cell treatment.

This article is available on Frontiers Bioengineering website by clicking on this [link](#)

About Collectis

Collectis is a clinical-stage biotechnology company using its pioneering gene-editing platform to develop life-saving cell and gene therapies. Collectis utilizes an allogeneic approach for CAR-T immunotherapies in oncology, pioneering the concept of off-the-shelf and ready-to-use gene-edited CAR T-cells to treat cancer patients, and a platform to make therapeutic gene editing in hemopoietic stem cells for various diseases. As a clinical-stage biopharmaceutical company with over 23 years of experience and expertise in gene editing, Collectis is developing life-changing product candidates utilizing TALEN®, its gene editing technology, and PulseAgile, its pioneering electroporation system to harness the power of the immune system in order to treat diseases with unmet medical needs. Collectis' headquarters are in Paris, France, with locations in New York, New York and Raleigh, North Carolina. Collectis is listed on the Nasdaq Global Market (ticker: CLLS) and on Euronext Growth (ticker: ALCLS). For more information, visit www.collectis.com. Follow Collectis on social media: @collectis, LinkedIn and YouTube

Forward-looking Statements

This press release contains “forward-looking” statements within the meaning of applicable securities laws, including the Private Securities Litigation Reform Act of 1995. Forward-looking statements may be identified by words such as “anticipate,” “believe,” “intend,” “expect,” “plan,” “scheduled,” “could,” “would” and “will,” or the negative of these and similar expressions. These forward-looking statements, which are based on our management’s current expectations and assumptions. Forward-looking statements include statements about the potential of the innovations of the Company. These forward-looking statements are made in light of information currently available to us and are subject to numerous risks and uncertainties, including with respect to the numerous risks associated with biopharmaceutical product candidate development. With respect to our cash runway, our operating plans, including product development plans, may change as a result of various factors, including factors currently

unknown to us. Furthermore, many other important factors, including those described in our Annual Report on Form 20-F and the financial report (including the management report) for the year ended December 31, 2022 and subsequent filings Collectis makes with the Securities Exchange Commission from time to time, as well as other known and unknown risks and uncertainties may adversely affect such forward-looking statements and cause our actual results, performance or achievements to be materially different from those expressed or implied by the forward-looking statements. Except as required by law, we assume no obligation to update these forward-looking statements publicly, or to update the reasons why actual results could differ materially from those anticipated in the forward-looking statements, even if new information becomes available in the future.

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