# A Novel Mechanism of Action for FS118 and the Potential to Overcome PD-(L)1 Resistance Published in Clinical Cancer Research

**Cambridge, UK and Cambridge, MA, April, 16, 2020 –** F-star Therapeutics Ltd., a clinical-stage biopharmaceutical company focused on transforming the lives of patients with cancer through the development of innovative tetravalent bispecific antibodies (mAb$^{2}$™), today announces the publication in *Clinical Cancer Research* of preclinical data highlighting the potential novel mechanism of action of its wholly-owned lead clinical asset FS118, a LAG-3/PD-L1-targeting tetravalent bispecific antibody.

FS118 is currently in a Phase 1 study in patients with late-stage solid tumors who have relapsed following prior successful PD-(L)1 therapy.

Despite advances with therapies targeting the highly immuno-suppressive molecules PD-1 (programmed cell death protein 1) or its ligand, PD-L1, many cancer patients are refractory to, or relapse following treatment. Relapse is associated with upregulation of other checkpoint inhibitor receptors such as LAG-3 (Lymphocyte Activation Gene 3). FS118 was selected for development based on its ability to overcome immunosuppression mediated by both LAG-3 and PD-L1 in cancer patients.

The *in vitro* and *in vivo* studies reported in *Clinical Cancer Research* demonstrated that FS118 simultaneously bound LAG-3 and PD-L1 with high affinity. FS118 showed a greater enhancement in T cell activity, and reversal of LAG-3 and PD-L1 immunosuppression, than the combination of the single component parts of the bispecific antibody. The authors concluded that targeting both LAG-3 and PD-L1 in a single tetravalent bispecific antibody can work synergistically to overcome inhibition of T cell activation.

In tumor mouse models, a bispecific antibody targeting LAG-3/PD-L1 significantly suppressed tumor growth. The anti-tumor immune response was greater than using PD-L1 or LAG-3 antibody monotherapy and was also more effective than a combination of those monotherapies. These data demonstrated that a LAG-3/PD-L1 targeting tetravalent bispecific antibody can provide dual blockade of LAG-3 and PD-L1 *in vivo* and can enhance the anti-tumor immune response.

The authors concluded that the study demonstrated a benefit from FS118, not observed with the combination of single PD-L1 and LAG-3 monoclonal antibodies, to drive a potent anti-tumor response, supporting the further development of FS118 for the treatment of patients with cancer.

**Neil Brewis, Chief Scientific Officer of F-star, said:** *"These data are the foundation for our confidence in FS118 and its potential to overcome cancer immune resistance. Currently only the minority of patients realize durable benefit from immunotherapy, so there remains a huge need to develop more effective options. At F-star we are developing antibodies with an innovative tetravalent bispecific format and the potential to elicit better biological responses compared to traditional antibodies or*

*combinations. We believe FS118, with its novel approach to overcoming resistance to PD-(L)1 blockade will be an important part of the exciting next wave of checkpoint therapies. We look forward to providing additional data from our ongoing Phase I study to validate our approach later this year."*

A link to the full study, entitled "FS118, a bispecific antibody targeting LAG-3 and PD-L1 utilises a novel mechanism to enhance T cell activation resulting in potent anti-tumor activity" can be found here.

**About FS118**

Currently in a Phase 1 study at four clinical sites in the United States, FS118 is a potentially first-in-class medicine for the treatment of resistant and refractory cancer. This tetravalent, bispecific antibody is developed to overcome tumor evasion mechanisms promoted by two highly immuno-suppressive molecules: LAG-3 (Lymphocyte-Activation Gene 3) and PD-L1 (Programmed Death-Ligand 1). By simultaneously blocking both inhibitory pathways, FS118 has preclinically demonstrated a potent anti-tumor growth activity as well as a highly differentiated mechanism of action when compared to checkpoint monotherapies alone or in combinations. In April 2018, a Phase 1 clinical study started in patients who have relapsed following a prior PD-(L)1-containing therapy. Information about the trial is available on clinicaltrials.gov NCT03440437. FS118 is manufactured at 2000L scale using standard mAb manufacturing processes.

**About F-star Therapeutics Ltd**

F-star is a leading clinical-stage biopharmaceutical company delivering tetravalent bispecific antibodies for a paradigm-shift in cancer therapy. By developing medicines that seek to block tumor immune evasion, the Company's goal is to offer patients greater and more durable benefits than current immuno-oncology treatments. Through its proprietary tetravalent, bispecific antibody (mAb²™) format, F-star is generating first- and best-in-class drug candidates with monoclonal antibody-like manufacturability. Building on the combined expertise of its world-class management team and scientific leadership, F-star is poised to deliver the next breakthrough immunotherapies for patients with cancer. For more information visit www.f-star.com.

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