A LAG-3/PD-L1 bispecific antibody inhibits tumour growth in two syngeneic colon carcinoma models
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**ABSTRACT**
A bispecific antibody against murine LAG-3 and PD-L1 was generated which binds both antigens simultaneously with nanomolar affinities. The anti-LAG-3/PD-L1 bispecific antibody (mAb²) inhibits LAG-3 binding to MHC II and PD-L1 binding to PD-1 and CD80, thereby enhancing T cell activation in an in vitro assay. This potency translates into in vivo efficacy, where the anti-LAG-3/PD-L1 bispecific antibody decreased tumour burden in a MC38 colon carcinoma tumour model. At the end of the study tumour-free animals were more numerous in the LAG-3/PD-L1 bispecific group than in the group treated with a combination of anti-LAG-3 and PD-L1 mAb. Efficacy was also seen in a CT26 murine colon cancer model, where the anti-LAG-3/PD-L1 bispecific antibody also demonstrated more potent anti-tumour activity compared to the mAb combinations. Thus, the preclinical data supports developing an anti-human LAG-3/PD-L1 bispecific for the treatment of cancer patients.

**BACKGROUND**
F-star’s Modular Antibody Technology™ platform introduces a novel antigen binding site into the constant (Fc) region of an antibody to create a so-called Fcab™ (an Fc-domain with antigen binding activity).

The resulting Fcab is then used as a building block for other drug formats. In particular, an Fcab can be easily combined with the variable region (Fab) of an existing antibody to generate a full-length bispecific antibody or mAb²™.

This simple “plug-and-play” capability of F-star’s highly efficient discovery engine creates virtually limitless bispecific product opportunities.

**CONCLUSIONS**
The anti-mouse LAG-3/PD-L1 mAb² bispecific antibody:
- Maintains biological characteristics of IgG
- Co-engages both antigens at nanomolar affinities
- Potently activates T cells in vitro
- Inhibits tumour growth more efficiently than combination of two antibodies

**mAb² potently activates T cells in vitro**

**mAb² inhibits tumour growth in syngeneic colon carcinoma models**

**LAG-3/PD-L1 mAb² suppresses tumour growth in the MC38 syngeneic tumour model.**

**LAG-3/PD-L1 mAb² is superior to a combination of monoclonal antibodies in suppressing tumour growth in the CT26 syngeneic tumour model.**

**Figure 1:** MC38 Tumour Growth Curves

**Figure 2:** MC38 End Tumour Weights

**Figure 3:** C57 tumour cells were injected subcutaneously into BALB/c mice until a palpable tumour formed. Three doses of antibody were administrated to the mice between day 11 and day 14. The control group received saline. The anti-LAG-3/PD-L1 mAb² cohort a total of 20mg/kg (10mg/kg antibody A + 10mg/kg antibody B or IgG control) total antibody was administered.