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 mouse LAG-3 and PD-L1 was generated which binds both antigens simultaneously with nanomolar affinities. The anti-LAG-3/PD-L1 bispecific antibody (mAb) inhibits LAG-3 binding to MHC-I and PD-L1 binding to PD-1 and CD80, thereby enhancing T cell activation in an in vitro assay. This pathway translates into in vivo efficacy, where the anti-LAG-3/PD-L1 bispecific antibody decreased tumour burden in an MC38 colon carcinoma tumour model. At the end of the study tumour-free animals were most numerous in the LAG-3/PD-L1 bispecific group than in the groups treated with a combination of anti-LAG-3 mAb and anti-PD-L1 mAb, demonstrating more potent anti-tumour activity compared to the mAb combinations. Thus, the preclinical data supports developing an anti-human LAG/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 FFab™ (Fab-only chimeric antigen binding protein). The resulting Fab™ is then used to create a building block for other drug formats. In particular, an FFab™ can be easily combined with the variable region (Fab) of an existing antibody to generate a full-length bispecific antibody or antibody-drug conjugate.

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 mAb bispecific antibody:
  - Monitors biophysical characteristics of IgG
  - Co-engages both antigens at nanomolar affinities
  - Potentially activates T cells in vivo
  - Inhibits tumour growth more efficiently than combination of two antibodies

mAb* inhibits tumour growth in syngeneic colon carcinoma models

mAb* potently activates T cells in vivo

**anti-mouse mAb** binds both mouse LAG-3 and PD-L1 with nanomolar affinities

mAb* potently inhibits tumour growth in syngeneic colon carcinoma models