Preclinical Characterization of the Bispecific EGF/CD16A Inmate Immune Cell Engager AFM24 for the Treatment of EGF-Expressing Solid Tumors

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Abstract S59

Introduction

- Elevated growth factor receptor (EGFR) is known to be overexpressed in several tumor types (e.g., colorectal cancer, non-small cell lung cancer, head and neck squamous cell carcinomas, glioblastomas, and triple-negative breast cancer), to obtain frequent drive in the EGFR signaling pathway, leading to resistance

- Current standard of care (SOC) therapies, including EGFR-targeting monoclonal antibodies (mAbs) and tyrosine kinase inhibitors (TKIs), are often the first line of treatment in patients that require second or third-line treatments

- A Ph4b trial recently demonstrated that a combination of afatinib and erlotinib resulted in a superior outcome compared to erlotinib alone in patients with EGFR mutations

- Although TKIs are reversible inhibitors of EGFR, they can be used to generate customized therapies targeting a new mechanism of action (MOA) that activates innate immunity, redirecting EGFR-expressing immune cells (e.g., effector macrophages) to EGFR-positive tumor cells

- AFM24 is a fully human recombinant bispecific IgG1 and IgG4 antibody, designed to redirect NK cells and macrophages to EGFR-expressing tumors

- AFM24 efficiently induces ADCC by human macrophages

- AFM24 is an EGFR-targeting innate cell engager inducing ADCC

- Highly cytotoxic potency of AFM24 in vitro is independent of EGFR density, BFA and KRAS mutation

- No correlation of EGFR density and origin of tested cell line for AFM24 potency

- Efficacy of AFM24 against A-431 tumours in humanized RNO mice

- AFM24 has anti-tumor efficacy and enhances tumor infiltration of immune cells

- AFM24 shows dose-dependent in vivo tumor growth inhibition in a therapeutic setting

- Pharmacokinetics (PK) of AFM24 in cytomolgous monkeys

- Summary & Conclusions

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