**AFM24 is a novel, highly potent, tetravalent bispecific EGFR/CD16A-targeting Innate Cell Engager (ICE®) designed for the treatment of EGFR-positive malignancies**

**INTRODUCTION**
- **AFM24** is a tetravalent bispecific ICE® binding CD16A and epidermal growth factor receptor (EGFR) [Figure 1].
- **AFM24** engages CD16A (FcγRIIIA) on natural killer (NK) cells and macrophages with a much higher affinity than monoclonal antibodies and triggers NK cell-mediated antibody-dependent cell-mediated cytotoxicity (ADCC) and macrophage-mediated antibody-dependent cellular phagocytosis (ADCP) responses directed at EGFR-expressing cancer cells.
- EGFR is frequently overexpressed in a broad range of solid tumors, including colorectal cancer (CRC), head and neck squamous cell carcinoma, and non-small-cell lung carcinoma (NSCLC).
- **EGFR** overexpression in tumors is a strong prognostic factor associated with reduced recurrence-free or overall survival.
- Clinically approved EGFR signaling inhibitors have limitations such as:
  - i. specific toxicities related to the inhibition of EGFR signaling in healthy tissues, particularly skin and gastrointestinal linings.
  - ii. Intrinsic and unavoidable acquired resistance.
- Mouse monoclonal models allow for screening of 1 to 2 regimens and can provide guidance towards promising therapeutic combinations, such as with NK cell products.
- The unique MOA of **AFM24** and its favorable preclinical safety profile promise to overcome the limitations of existing EGFR-targeted therapies and to provide additional therapeutic options to patients with EGFR-expressing tumors who do not respond to these therapies.

**RESULTS**
- **AFM24** exhibits high binding capacity to enriched primary human NK cells in the presence of competing IgGs
- **AFM24** shows a favorable preclinical safety profile due to its minimal interaction with 10 mg/mL hIgG.

**CONCLUSIONS**
- **AFM24** with its unique MOA has the potential to change the treatment paradigm for patients with various EGFR-expressing solid tumors.
- **AFM24** induces high ADCC activity in the presence of competing IgGs.
- **AFM24** shows a favorable preclinical safety profile due to its minimal interaction with 10 mg/mL hIgG.

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**Key points**
- **AFM24** is a tetravalent bispecific EGFR/CD16A fusion antibody (IgG1-FcγRIIIA) with high ADCC activity.
- **AFM24** shows a favorable preclinical safety profile.
- **AFM24** demonstrates high ADCC activity in vitro.
- **AFM24** induces in vivo ADCC against tumor cells expressing TNBC MDA231 cells.
- **AFM24** is currently being investigated in Phase 1/2a study in patients with different EGFR-expressing tumors.

**References**

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