MBK-103, a potent novel conjugation platform-based antibody-drug conjugate, changing therapeutic options in folate receptor alpha positive cancer patients

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INTRODUCTION

Folate receptor alpha (FRα) is a clinically validated target that is overexpressed extracellularly in numerous solid malignancies with a high unmet medical need. Ovarian, non-small cell lung, breast, and colorectal adenocarcinomas are among indications with the highest frequency of FRα-positive patients, with one out of two patients showing upregulated topoisomerase I expression.

MBK-103, an ADC targeting FRα, is based on Mablink’s proprietary PSAIRink® hydrophilic drug-linker platform. It is comprised of:

1. An Fc-fusion humanized IgG1 monoclonal antibody (MBK-103.1), that selectively binds to FRα with low mAb affinity,
2. A polysaccharide hydrophobic masking entity enabling a high homogeneous drug-to-antibody ratio (DAR) of 8, while improving the pharmacokinetics and tolerability of the conjugate; and
3. A proprietary orthogonally embedded dipeptide (Val-Ala)-clayable unit;
4. exetacan, a potent topoisomerase I inhibitor.

RESULTS

MBK-103 binds specifically to FRα, internalizes rapidly and exerts potent in-vitro efficacy

MBK-103 shows excellent in-vivo antitumor activity in colorectal and ovarian carcinoma models

MBK-103 is well tolerated upon repeated administration in cynomolgus monkeys, with a favorable PK profile

MBK-103 shows excellent DAR stability ex-vivo and in-vivo

MBK-103 induces less inflammation/lung toxicity in mice compared to Enherba®

CONCLUSIONS

- MBK-103 demonstrates strong and specific cell binding to FRα, fast internalization into target-expressing cells upon binding, and low mAb IC50 cell killing potencies.
- Favorable PK profile were observed in rodents, with prolonged half-life (above 9 days) and total mAb/tot al ADC curves of similar shapes and slopes.
- MBK-103 was efficacious in various in-vivo PDX and in-vivo CDOX models at doses in the range of 1-3 mg/kg. MBK-103 consistently outperformed the comparator mitoxantrone/soravtansine ADC at similar doses. MBK-103 was able to induce immunological memory (NK-dependent) that prevented tumor re-growth in IGR01-v ovarian cancer CFD mice.
- Cynomolgus HSNID was 3 times 50 mg/kg (IV) administered every 3 weeks, in a non-GLP dose-range-finding study.
- MBK-103 exhibited excellent ex vivo and in vivo DAR stability (approx. 90% DAR stability ex-vivo at day 8 and approx. 75% DAR stability in cynomolgus at day 21).
- Liner-payload used to construct MBK-103 caused less lung toxicity (potential interstitial lung disease) than that of Enherba® in a fully immunocompetent mouse model.
- Phase I clinical trial evaluating MBK-103 is planned for early 2024.