PHASE 1 STUDY OF COM701 (A NOVEL CHECKPOINT INHIBITOR OF PVRIG) IN PATIENTS WITH ADVANCED SOLID TUMORS.

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BACKGROUND

• There is a high unmet medical need for the treatment of pts with relapse/refractory disease following treatment with checkpoint inhibitors.
• COM701 is a novel first-in-class checkpoint inhibitor and humanized IgG4 monoclonal antibody that binds with high affinity to poliovirus receptor related immunoglobulin domain containing (PVRIG) blocking its interaction with its ligand, PVRL2.
• In non-clinical experiments we have demonstrated that inhibition of PVRIG leads to enhanced activation of T and NK cells and that knockout of PVRIG results in tumor growth inhibition in mouse tumor models.
• We hypothesize that COM701 will be safe and tolerable and demonstrate antitumor activity in pts with R/R solid tumors.
• We have reported on safety/tolerability in initial dose level cohorts¹.

PVRIG IS A NOVEL CHECKPOINT IN THE TIGIT/DNAM-1 AXIS

Two Parallel Inhibitory Pathways

Tumor microenvironment

T-cell/NK cell

Dose level escalation

Patient selection criteria

Safety & Tolerability

PVRIG inhibition required for tumor growth inhibition in TIGIT KO mice

PVRIG INHIBITION REDUCES TUMOR GROWTH IN MOUSE CANCER MODELS

PVRIG KD MICE (MC58)

- Reduced tumor growth in KD mice
- Synergistic tumor growth inhibition with anti-PD1

Anti-PVRIG + anti-PD1 (CT26)

Anti-PVRIG + TIGIT KD (137)

METHODS

• NCT03667716 is an ongoing open-label first-in-human phase 1 study in pts with R/R solid tumors.
• We report on the initial part of this study (in red box) evaluating the safety and tolerability of escalating doses of COM701 monotherapy IV Q3 weekly.

PHASE 1a

Arm A

Monotherapy

Dosage escalation

Interim & final DLT window

All dose levels (escalating)

Arm B

Dual combination

PVRIG + TIGIT KO (B)

KEY INCLUSION CRITERIA

• Age ≥18 yrs
• Histologically or cytologically confirmed, locally advanced or metastatic solid malignancy, and has exhausted all the available standard therapy or is not a candidate for the available standard therapy
• ECOG performance status 0-1
• Prior anti-PD-1, anti-PD-L1, anti-CTLA-4,OX-40, CD137 permissible
• Adequate hematological, hepatic and renal function

EXPLORATORY OUTCOME MEASURES

• To evaluate preliminary antitumor activity of COM701 as monotherapy
• To assess any association of DNAM axis members with clinical outcome
• To explore evidence of COM701-mediated PD effect in blood as monotherapy as well as in combination with nivolumab

KEY EXCLUSION CRITERIA

• Active autoimmune disease requiring systemic therapy in the last 2 years prior to the first dose of COM701
• Symptomatic interstitial lung disease or inflammatory pneumonitis
• Untreated or symptomatic central nervous system metastases
• History of immune-related events that led to immunotherapy treatment discontinuation

ACCRUAL INFORMATION

• As of the date of this presentation the 5th dose level pt cohort has been filled
• No dose-limiting toxicities have been observed in the 5th dose level pt cohort and earlier dose level cohorts¹
• Clinical and laboratory assessment for safety and tolerability is ongoing for the 5th and earlier pt dosing cohorts

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REFERENCE