Conventional cytokines like interferon-γ and tumor necrosis factor-alpha are important in anti-tumor immune response. However, the activity of IL-18 is partially blocked by a high affinity endogenous binding protein (IL-18BP), which is induced in myeloid cells. This upregulation in myeloid cells and IL-18BP's blocking activity is dose-dependent and abrogates the activity of IL-18. IL-18BP binds IL-18 with high affinity and inhibits its activity in HEK293 reporter system. IL-18BP binds IL-18 with high affinity and inhibits its activity in TME and expressed across multiple human cancer indications. Anti-IL-18BP antibody demonstrates monotherapy activity across murine syngeneic tumor models. Anti-IL-18BP antibody demonstrates combi activity with anti-anti-PD-L1 Ab in E0771 tumor model. Anti-IL-18BP Ab increases the expansion of proinflammatory myeloid populations and cytokine secretion in the TME. Anti-IL-18BP Ab increases IFNγ production by NK cells in the presence and absence of COM503 (10ug/ml). Anti-IL-18BP Ab increased IFNγ production, especially within subpopulation of IFNγ+CD8+ cells.