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Abstract # 60

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Background:
• BCMA (B Cell Maturation Antigen) is a plasma cell specific surface molecule attractive as an antibody target in multiple myeloma.
• T-cell engaging bispecific antibodies are well suited to low density targets like BCMA.
• The Teneobio antibody platform uses fully human VH domains and an NGS-based discovery pipeline (Figure 1A).
• We developed a novel BCMA x CD3 antibody (TNB-383B) that selectively activates T-cell subsets with reduced cytokine secretion

Figure 1: BCMA x CD3 development A. TNB-383B is a hybrid of fixed light chain (αCD3, FlicAb) and heavy chain only (αBCMA, UniAb) antibody arms. B. TNB-383B is composed of two αBCMA moieties in sequence on one arm, a single αCD3 arm, and a silenced IgG4 Fc.

Figure 2: TNB-383B Lyses BCMA-positive tumor cells (H929) but not BCMA-negative tumor cells (K562) with an EC50 ~2 logs higher than a pan-T-cell anti-CD3 containing bispecific (+ control); the maximum achievable lysis is identical.

Figure 3: TNB-383B tumor lysis and T-cell activation are consistent across multiple donors and multiple cytokines A. T-cells from 10 donors lyse myeloma cells (NCI-H929, BCMA-positive) in the presence of TNB-383B, but not K562 cells (BCMA-negative). B. T-cells exposed to TNB-383B and BCMA-positive cells secrete lower levels of cytokines than those exposed to a pan T-cell activating bispecific.

Figure 5: TNB-383B preferentially activates effector T-cells (CD4/CD8) over Tregs. Human T-cells from healthy donors were incubated either fresh or after high-density culture (48h) together with drug and plate-bound BCMA for 24h. CD69 was measured by flow cytometry.

Conclusions:
• TNB-383B binds to tumor cells in a BCMA-dependent manner.
• TNB-383B mediates T-cell dependent tumor cell lysis and T-cell activation in vitro.
• TNB-383B has the half-life of a conventional IgG4.
• TNB-383B clears tumor cells in a BCMA- and T-cell dependent manner in vivo.
• TNB-383B induces less cytokine secretion than a conventional T-cell engaging bispecific in vitro, without reduction of tumor cell kill in vivo (Figures 3-5).

Future Directions:
• Preliminary tissue cross reactivity studies show absence of nonspecific staining by TNB-383B in human tissues.
• TNB-383B is well tolerated in preliminary Cynomolgus tolerability studies.
• IND Filing is anticipated in Late 2018.