TNB383B.0001: A Multicenter, Phase 1, Open-Label, Dose-Escalation and Expansion Study of TNB-383B, a Bispecific Antibody Targeting BCMA in Subjects with Relapsed or Refractory multiple Myeloma

Abstract #1874

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Introduction

- BCMA (B Cell Maturation Antigen) is a low-density surface molecule highly specific for plasma cells and well suited to T-cell engagement-based treatment of myeloma.
- The Teneobio antibody platform uses fully human VH domains and an NGS-based discovery pipeline.
- We identified a unique αCD3 moiety that induces T-cell dependent cytotoxicity of tumor cells with significantly reduced cytokine secretion
- We developed a novel BCMA x CD3 antibody (TNB-383B) that selectively activates T-cell subsets with reduced cytokine secretion (Figure 1).
- TNB-383B is now being studied in a Phase 1 Clinical Trial, TNB383B.0001 **(NCT03933735)**

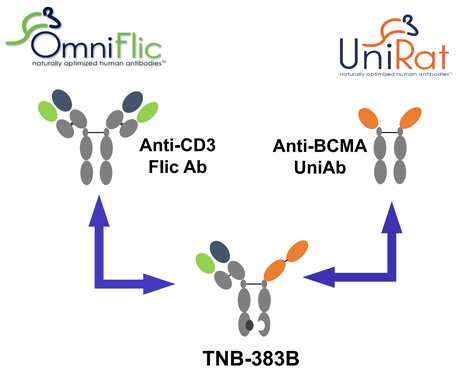

Figure 1: TNB-383B Development
TNB-383B is a fully human T-BsAb combining fixed-light-chain (FLC) and heavy-chain-only (HCO) arms paired using knobs-in-holes. The FLC arm weakly activates CD3. The HCO arm has two high-affinity anti-BCMA moieties.

Study Design and Dose Escalation

Table 1: Key Inclusion/Exclusion Criteria in TNB383B.0001

Key Inclusion Criteria	Key Exclusion Criteria
3 Prior Lines including a PI, an IMiD, and an anti-CD38 mAb	Prior BCMA-targeted Therapy
Adequate marrow function: • Absolute neutrophil count (ANC) ≥ 1000/mm^3 • Platelets ≥ 50,000/mm^3 • Hemoglobin ≥ 8.0 g/dL.	Other Cancer Drug within 21 days OR 5 half-lives, whichever is shorter
eGFR ≥ 30 mL/min	Neuropathy ≥ Grade 3
Measurable Disease	CNS involvement by their myeloma
Adequate archival bone marrow tissue or consents to a fresh biopsy	Plasma cell leukemia, POEMS, or amyloidosis
ECOG ≤ 2	Auto-SCT within 12 weeks or Allo-SCT within 12 months

Table 2: Key Design Features of TNB383B.0001

Key Design Features	Rationale
Fixed (as opposed to weight-based) Dosing	• Simple dose prep • Error reduction
Every 3 Week (Q3W) Dosing	• Dosing consistent with $T_{1/2}$ • Safety (CRS can set on as late as 2 weeks post-dose)
Bone Marrow Biopsies Optional	• Patient care/access
Confirmed BCMA expression is **NOT** required	• Lack of reliable diagnostics • Equivocal expression and efficacy correlation • Slow turn-around

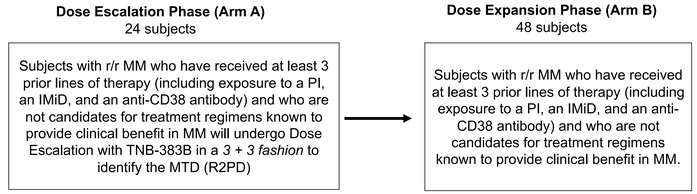

Figure 2: **TNB383B.0001 Study Design.** *A.* TNB383B.0001 consists of 2 phases, a Monotherapy Dose Escalation Phase (Arm A) and a Monotherapy Dose Expansion Phase (Arm B).
Abbreviations: IMiD = Immunomodulatory imide; MM = multiple myeloma; MTD = maximum tolerated dose; PI = proteasome inhibitor; PK = pharmacokinetic; RP2D = recommended phase 2 dose; r/r = relapsed / refractory.

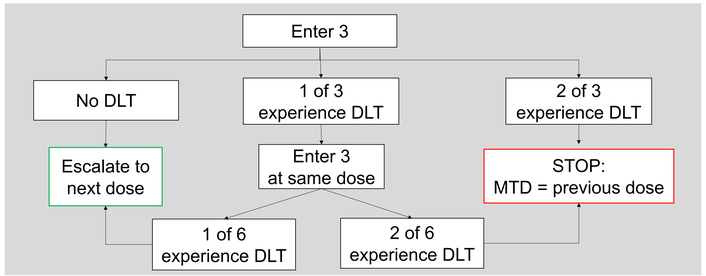

Figure 3: TNB383B.0001 Dose Escalation Scheme

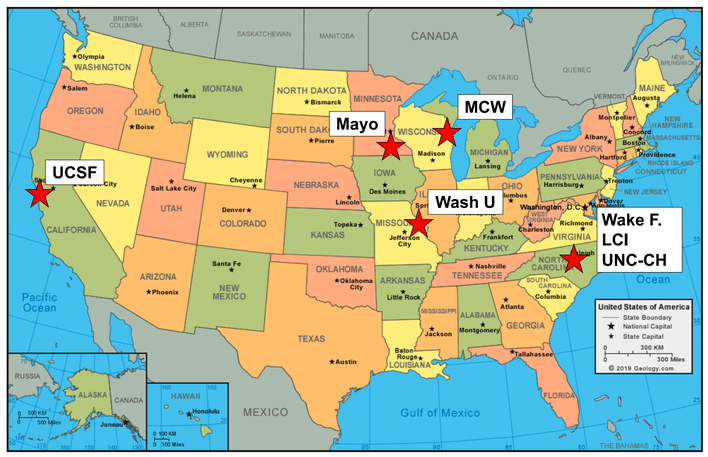

Figure 4: 7 US Centers Are Enrolling Arm A of TNB383B.0001

Statistical Methods and Study Endpoints

Safety
- Arm A: Dose-Limiting Toxicities
- Arm B: Unacceptable Adverse Events

Activity
- Overall Response Rate
- Progression-Free Survival
- Overall Survival
- MRD-negativity Rate
- Duration of Response
- Depth of Response

Pharmacokinetic
- C_{max}
- Time to C_{max}
- Area Under the Curve
- Clearance
- Terminal $T_{1/2}$

Summary:

- TNB-383B clears tumor cells in a BCMA- and T-cell dependent manner *in vitro, in vivo,* and *ex vivo.*
- TNB-383B induces less cytokine secretion than a conventional T-cell engaging bispecific *in vitro*, without reduction in tumor cell kill.
- TNB-383B has a predicted half-life of 3 weeks in humans.
- 12 Patients have been enrolled in the Dose Escalation Arm of TNB383B.0001
- TNB-383B has been well tolerated in all patients: no Grade 3+ Drug-associated AEs have been observed to date.
- The Dose Expansion Arm is anticipated to open Q3-Q4 2020.