

BYN-002 (TL-001), A NEXT-GENERATION ANTI-TL1A ANTIBODY DEMONSTRATING POTENT NEUTRALIZATION, EXTENDED PHARMACOKINETICS, DURABLE TL1A SUPPRESSION AND FAVORABLE IMMUNOGENICITY: INTERIM PHASE 1 SAD/MAD RESULTS

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BACKGROUND

TL1A contributes to intestinal inflammation and fibrosis and is a clinically validated target in inflammatory bowel disease (IBD). BYN-002 (TL-001) is a humanized anti-TL1A IgG1 monoclonal antibody incorporating YTE substitutions for half-life extension and LALA substitutions to minimize Fc-mediated effector functions. We report selected preclinical findings and interim safety, pharmacokinetic (PK), pharmacodynamic (PD), and immunogenicity results from the first-in-human study TL-001-101 (NCT06867796).

METHODS

Preclinical studies evaluated BYN-002 neutralization of TL1A signaling in vitro relative to first-generation anti-TL1A antibody analogues. In an ongoing randomized, double-blind, placebo-controlled phase 1 study, healthy volunteers received intravenous single ascending doses (SAD; BYN-002, n=24; placebo, n=8) or three administrations in multiple ascending-dose cohorts (MAD; BYN-002, n=12; placebo, n=4). Assessments included safety, serum PK, free and total soluble TL1A, and anti-drug antibodies (ADA). SAD follow-up was available through day 169 or day 253, depending on cohort; MAD and cross-cohort ADA analyses were available through day 85.

SAFETY

No treatment-related serious adverse events, infusion reactions, deaths or treatment-related discontinuations were reported

SAD cohorts

- No Grade ≥3 TEAEs, SAEs, TRAEs or IRRs; all TEAEs resolved
- Most frequent TEAEs: upper respiratory tract infection and headache

MAD cohorts

- TEAEs mostly Grade 1–2; one Grade 3 and one Grade 4 TEAE, both unrelated
- TRAEs, SAEs and TEAEs leading to discontinuation in 4, 2 and 1 participants; no IRRs. SAEs and the TEAE leading to discontinuation were considered not treatment-related

TEAE incidence and severity were comparable to pbo in both parts.

RESULTS

Figure 1. Neutralization of hTL1A-induced NFκB activation in TF-1-NFκB-luc cells (RLU)

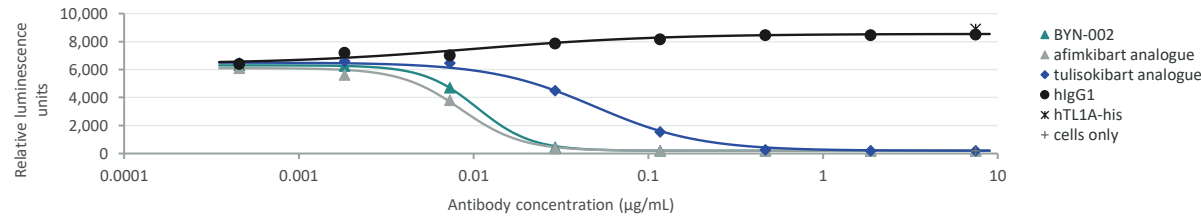
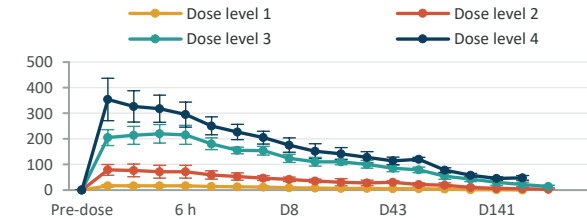
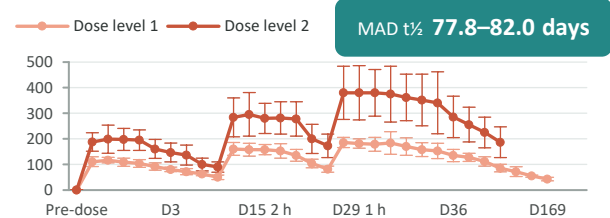


Figure 2. Mean (±SD) serum BYN-002 concentration (μg/mL, linear scale)

A SAD, single dose



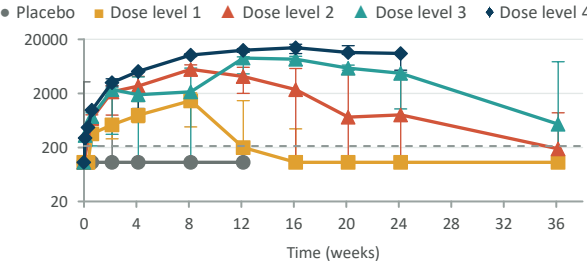
B MAD, doses on Days 1, 15 and 29



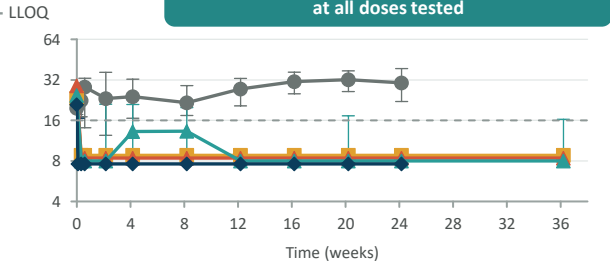
Cmax and AUC increased in a dose-proportional manner; t½ ranged from 35.7 to 78.2 days (SAD) and 77.8 to 82.0 days (MAD).

Figure 3. Median (IQR) total and free soluble TL1A, SAD cohorts (pg/mL, log scale)

A Total TL1A



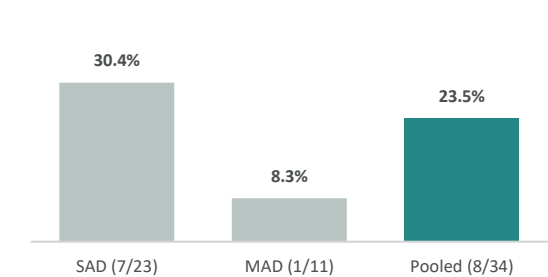
B Free TL1A



Total TL1A rose with dose, peaking between Day 57 and Day 113; free TL1A fell below the LLOQ at every dose level (placebo medians 19.7–34.8 pg/mL).

IMMUNOGENICITY

Figure 4. ADA incidence through Day 85 (% , n/N)



<10%

immunogenicity at predicted therapeutic doses

ADA responses were concentrated in lower-dose SAD cohorts; no treatment-enhanced ADA responses occurred.

CONCLUSIONS

BYN-002 demonstrated potent TL1A neutralization, prolonged PK, durable suppression of free soluble TL1A, and favorable interim tolerability and immunogenicity in healthy volunteers. Although terminal half-life estimates remain preliminary, these findings support potential for every-3-to-6-month maintenance dosing and support further clinical development in IBD and in other TL1A driven diseases

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Abbreviations: ADA, anti-drug antibody; AUC, area under the curve; Cmax, maximum concentration; IQR, interquartile range; IRR, infusion-related reaction; LLOQ, lower limit of quantification; MAD, multiple ascending dose; SAD, single ascending dose; SAE, serious adverse event; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event; t½, terminal half-life.

