A Novel Monoclonal Antibody Drug Candidate SPY001 Targeting Integrin α4β7 for the Treatment of IBD Demonstrates Prolonged Half-Life in Non-Human Primates

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**Background**

- Antagonism of the interaction between the cellular adhesion integrin α4β7 and MADCAM-1 by vedolizumab is safe and effective in the treatment of IBD. Additional benefit may be gained from an α4β7 antagonist administered via the subcutaneous (SC) route at extended intervals (e.g., every 8 to 12 weeks).
- **SPY001** binds to the same α4β7 epitope as vedolizumab and includes a YTE modification within the Fc region to increase its serum half-life (see Poster P587).

**Methods and Results**

α4β7 blockade is a validated therapeutic mechanism in IBD

**Figure 1:** Binding of SPY001 (or vedolizumab) to α4β7 prevents its association with MADCAM-1 and is anticipated to inhibit leukocyte trafficking across the endothelium and reduce GI inflammation. Created with BioRender.com.

**Figure 2:** YTE modification extends half-life by increasing IgG binding affinity to FcRn at low pH, increasing antibody recycling and reducing lysosomal degradation (1). Adapted from “extracellular vesicles” by BioRender.com (2023).

**Figure 3:** Determination of SPY001 and vedolizumab (Vedo) concentration in serum from Tg276 transgenic mice expressing human FcRn following a 10 mg/kg IV dose.

**Figure 4:** Measurement of SPY001 and vedolizumab (Vedo) serum concentration in cynomolgus monkeys (NHPs) following a single SC dose of 50 mg/kg.

**Figure 5:** Simulation of SPY001 and vedolizumab (Vedo) serum concentrations based on dosing on SPY001 at W0 and W2 during induction and Vedo as per label (3-5).

**Figure 6:** Simulation of SPY001 and vedolizumab (Vedo) serum concentrations based on dosing at the indicated intervals (3-5).

**Conclusions**

- **SPY001** is a novel humanized monoclonal IgG1 with an extended half-life over that of vedolizumab in Tg276 mice and cynomolgus monkeys.
- **SPY001** offers the potential for effective and safe treatment of CD and UC as a monotherapy or combination backbone, with the advantage of convenient SC dosing. First-in-human studies are planned for 2024.

**References**


**Disclosures**

EZ, DR, RV, HS, and JO are employees of Paragon Therapeutics. JF, DN, and AS are employees of Spyre Therapeutics. All authors own equity in Paragon Therapeutics and/or Spyre Therapeutics.

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