FORTE BIOSCIENCES

FB102 prevents histological damage and mitigates gluten challenge-induced symptoms in a celiac disease Phase 1b study

A. JAMES DAVESON[1], JENNIFER SCHAFER[1], VICTORIA SIRIETT[2], PAUL HAMILTON[3], DEAN QUINN[4], VINCENT HO[5], JORMA ISOLA[6], FRED DE LOOZE[7], SCOTT SCHOEMAN[8], PAUL WAGNER[9], THOMAS STOCK[9], BARBARA FINCK[9], DAVID JORDAN[9], JASON A. TYE-DIN[10,11]

1) WESLEY RESEARCH INSTITUTE, QLD, AUSTRALIA

2) PCRN WAIKATO (LAKELAND CLINICAL TRIALS), HAMILTON, NEW ZEALAND

3) PCRN AUCKLAND, TAKAPUNA, AUCKLAND

4) MOMENTUM PUKEKOHE, PUKEKOHE, NEW ZEALAND

5) CAMPBELLTOWN HOSPITAL, NSW, AUSTRALIA

6) JILAB, TAMPERE, FINLAND

7) MOMENTUM, NORTH SHORE HEALTH HUB, NSW, AUSTRALIA

8) ROYAL ADELAIDE HOSPITAL, ADELAIDE, AUSTRALIA

9) FORTE BIOSCIENCES, DALLAS TX, US

10) THE ROYAL MELBOURNE HOSPITAL, VICTORIA, AUSTRALIA

11) IMMUNOLOGY DIVISION, WEHI, VICTORIA, AUSTRALIA

DISCLOSURE

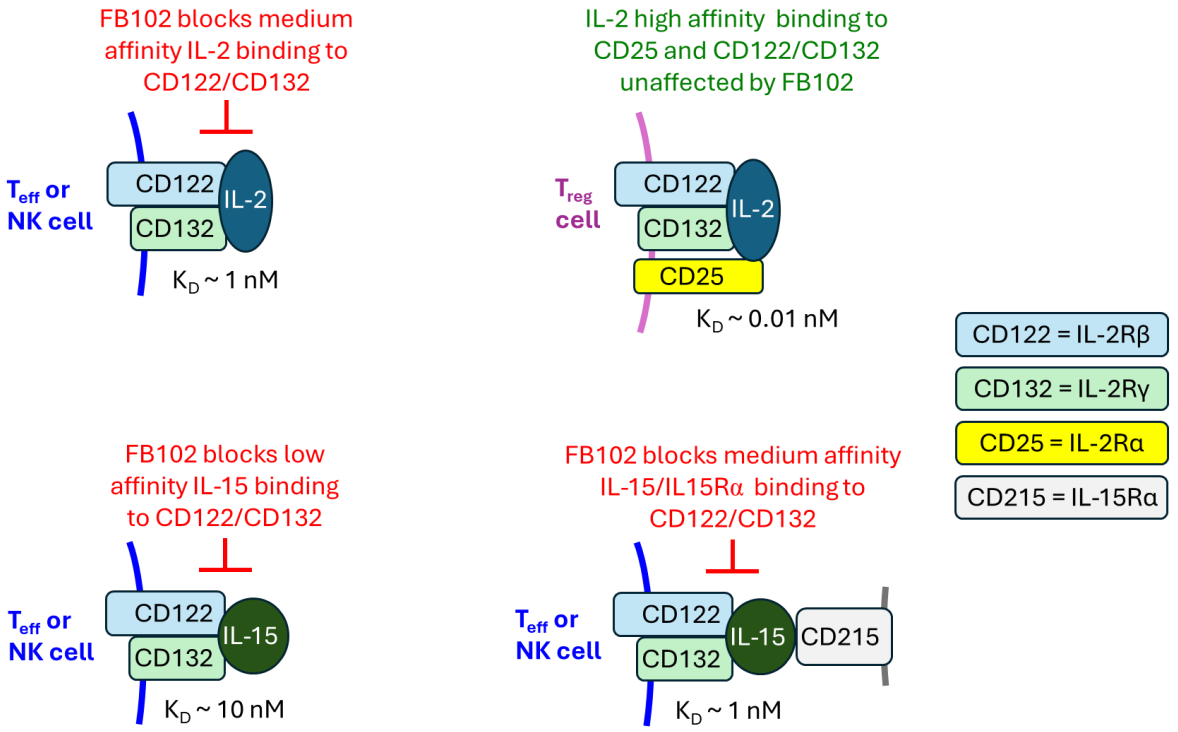
I have the following relevant disclosures:

- Consultant for Forte Biosciences
- Principal Investigator on the FB102 Phase 1B trial

FB102 (ANTI-CD122) OVERVIEW

CD122 is a subunit of the intermediate affinity IL-2/IL-15 receptor expressed on NK cells, certain T cell subtypes and is a subunit of the high affinity IL-2 receptor expressed on Tregs

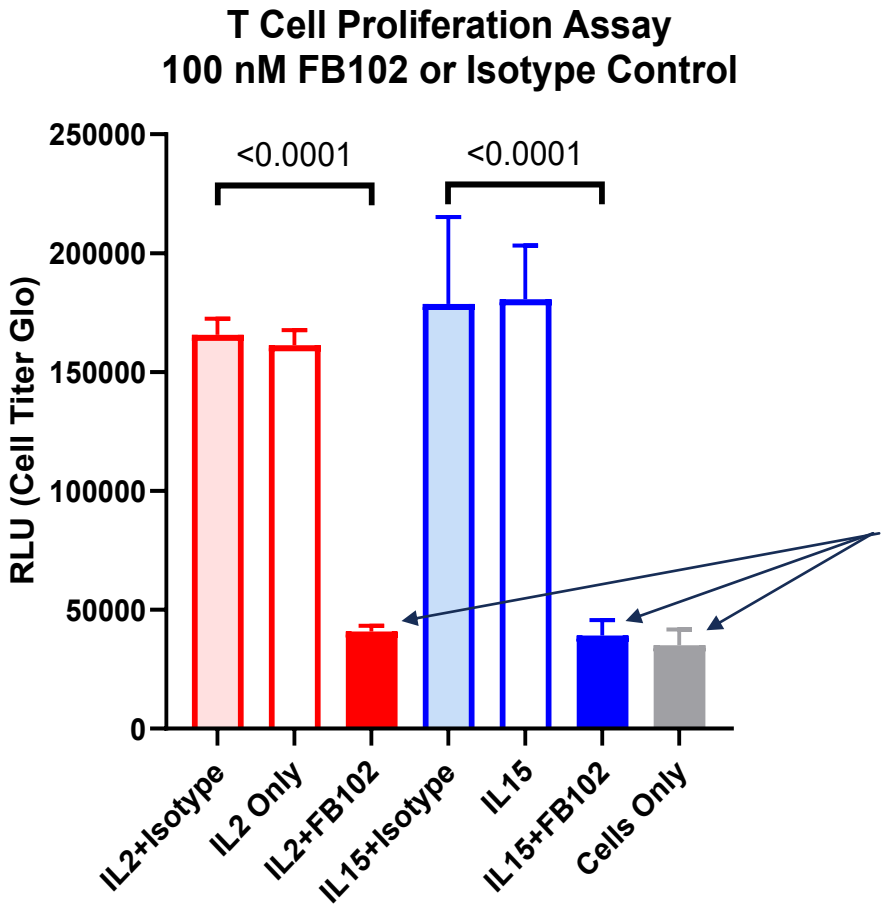
FB102 (Forte's anti-CD122 antibody) is designed to mediate <u>both</u> the IL-2 and the IL-15 induced proliferation and activation of pathogenic NK cells, certain T cell subtypes without effecting the IL-2 biology of beneficial Tregs



Lodolce 2002 Cytokine Growth Factor Rev. PMID 12401478
Ross 2018 Annu Rev Immunol. PMID 29677473

FB102 INHIBITS CD4+ AND CD8+ T CELL PROLIFERATION

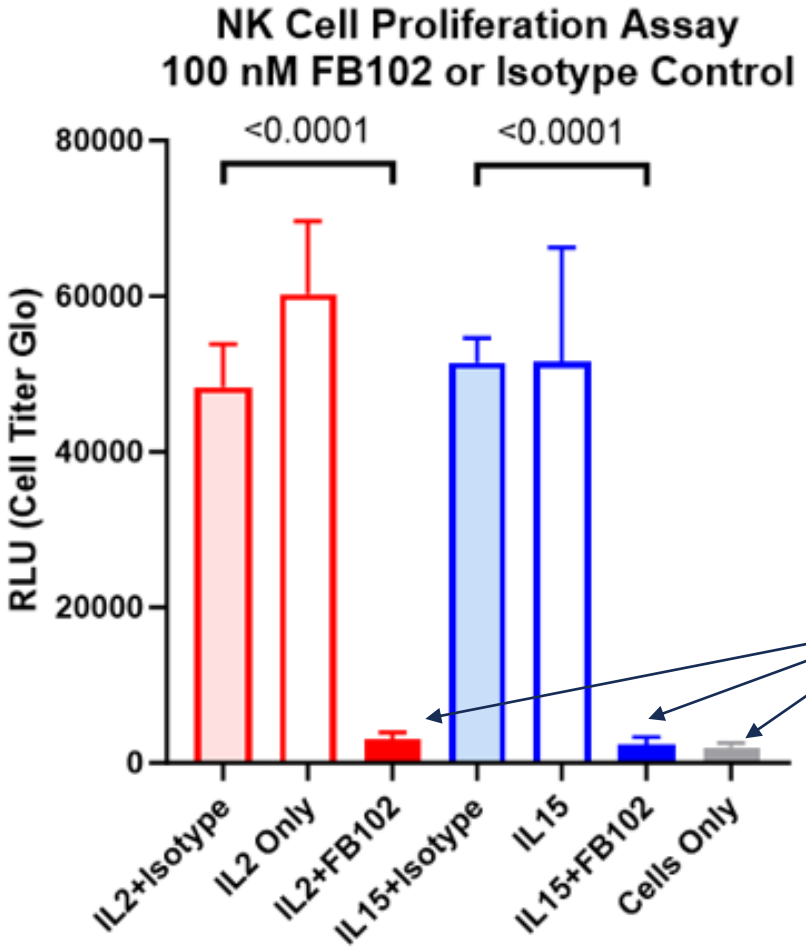
	Fold Reduction Isotype/FB102
IL-2	4.1
IL-15	4.6



FB102 inhibits IL-2/IL-15 signaling back to baseline levels of the unstimulated cell only

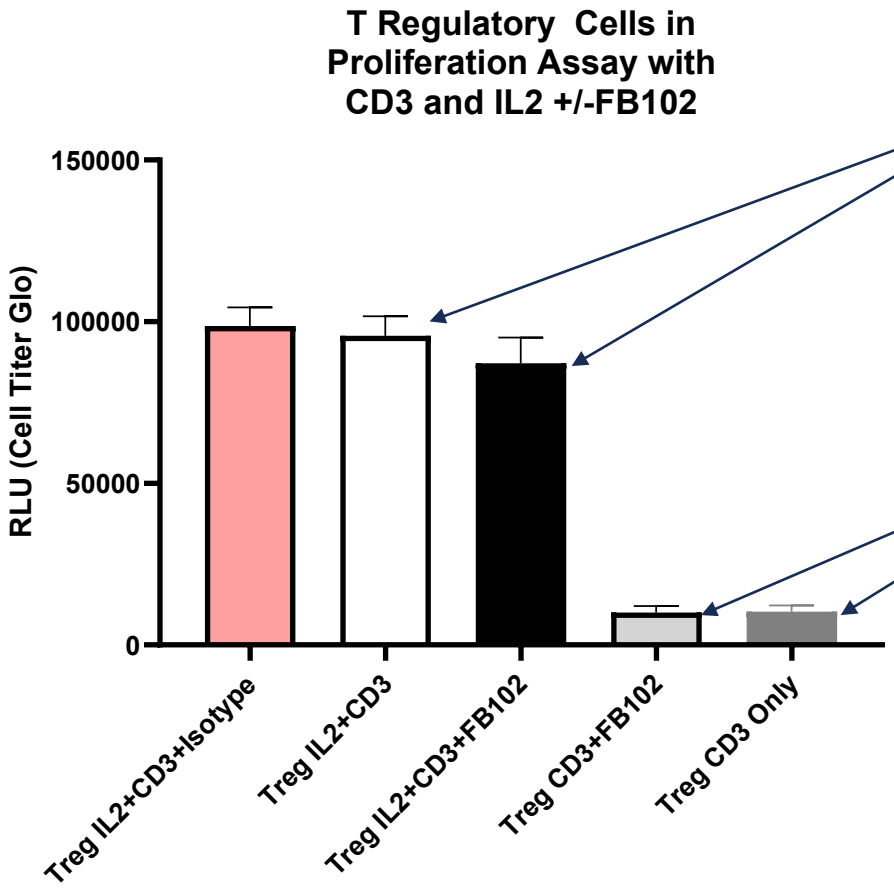
FB102 INHIBITS NK CELL PROLIFERATION TO BASELINE LEVELS

	Fold Reduction Isotype/FB102
IL-2	15.8
IL-15	21.8



FB102 inhibits IL-2/IL-15 signaling back to baseline levels of the unstimulated cell only

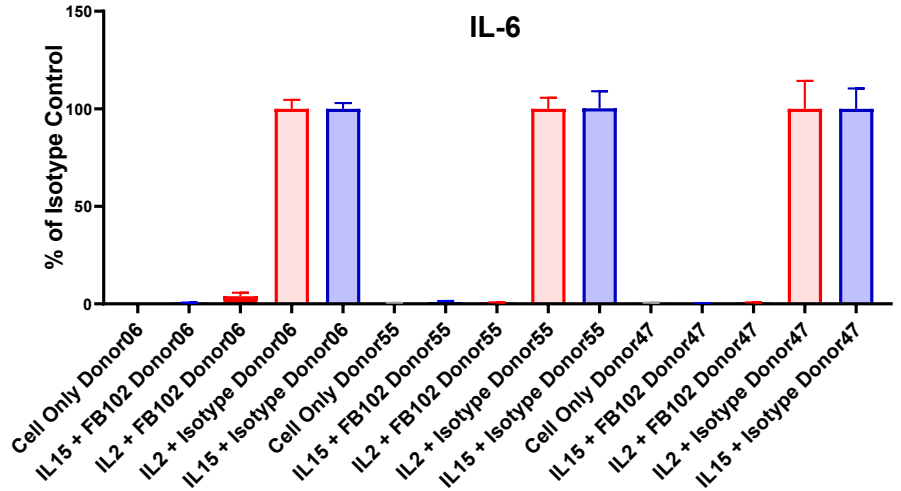
FB102 DOES NOT INHIBIT REGULATORY T CELL PROLIFERATION

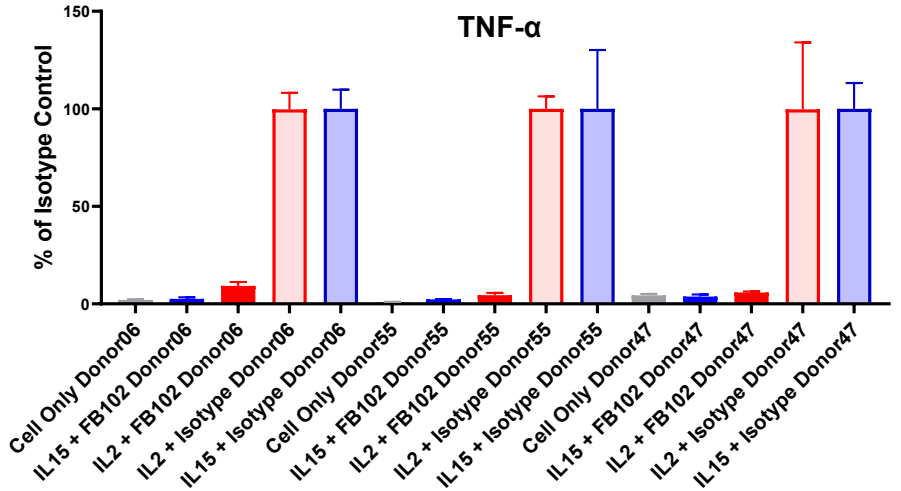


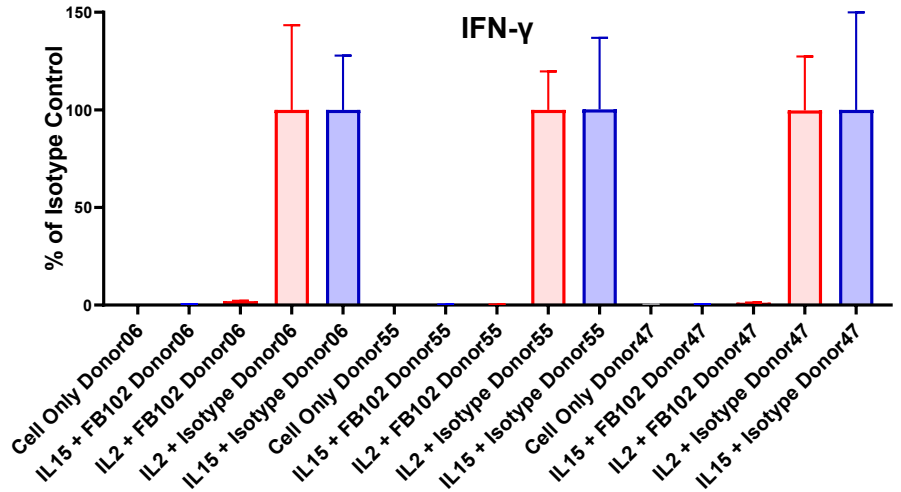
FB102 does not inhibit high affinity IL-2 signaling of Tregs

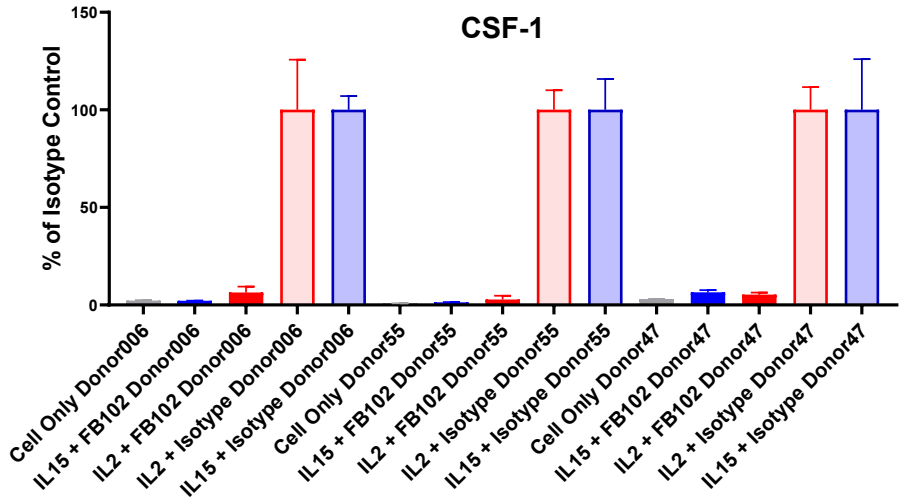
In the absence of IL-2 stimulation, FB102 does not impact cell viability and is comparable to unstimulated cell

FB102 INHIBITS IL-2 AND IL-15 INDUCTION OF IL-6, TNF-ALPHA, IFN-GAMMA, AND CSF-1 WITH 3 DIFFERENT T CELL DONORS



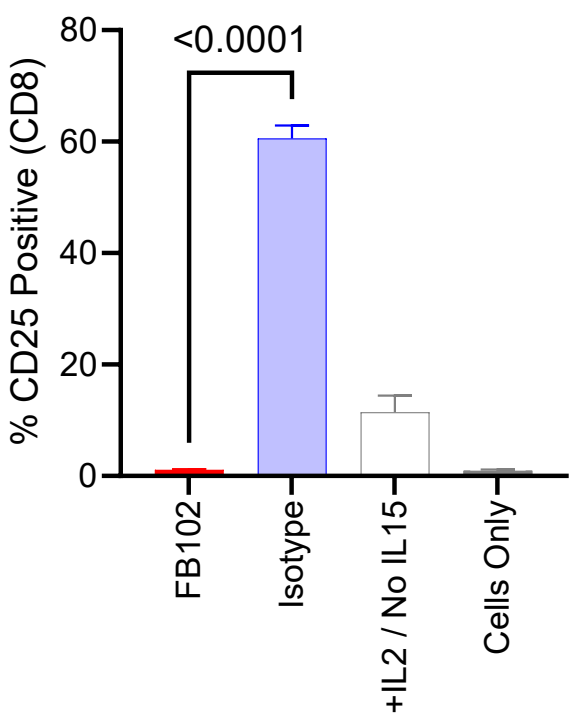




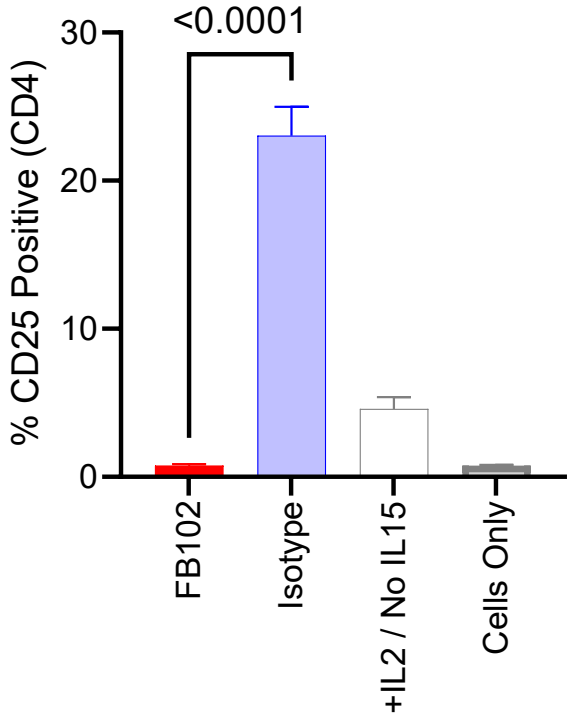


FB102 INHIBITS IL-2/IL-15 CD4+ AND CD8+ T CELL ACTIVATION IN IN VITRO DISEASE MODEL

- CD4+ and CD8+ T cells were treated with IL2 for 24 hours then with IL15 for 3 days, simulating disease activity in the presence or absence of FB102
- FB102 provides nearly complete inhibition of T cell activation

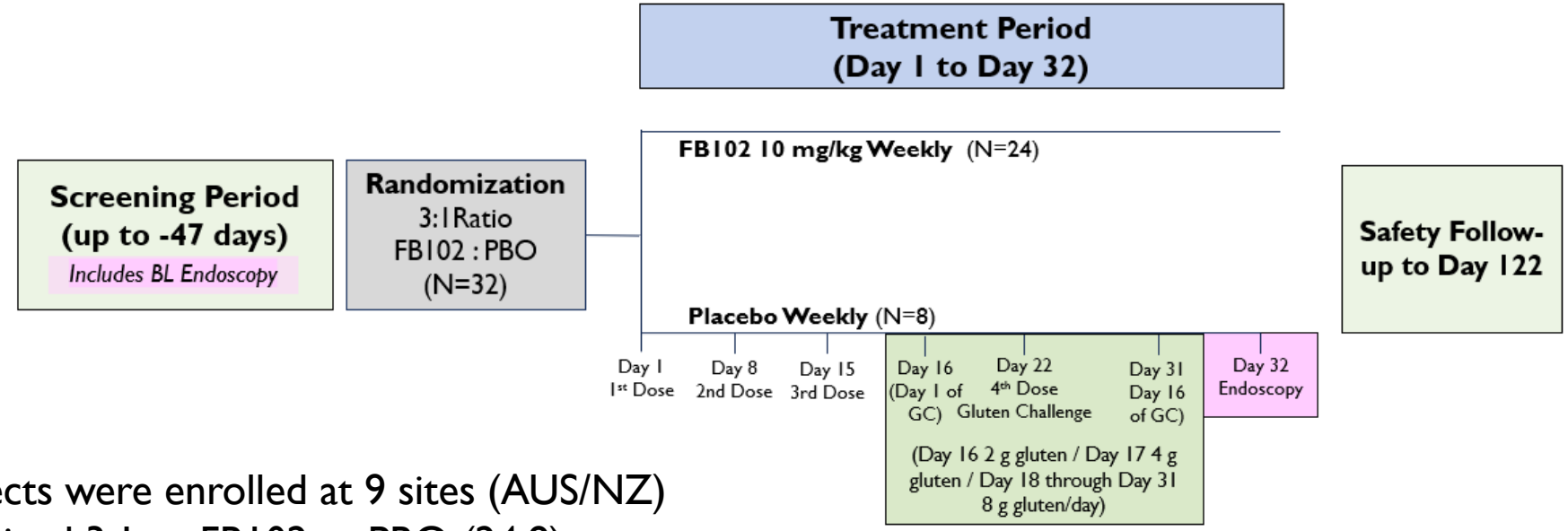


CD8+ T Cells



CD4+ T Cells

CELIAC DISEASE PHASE 1B DESIGN



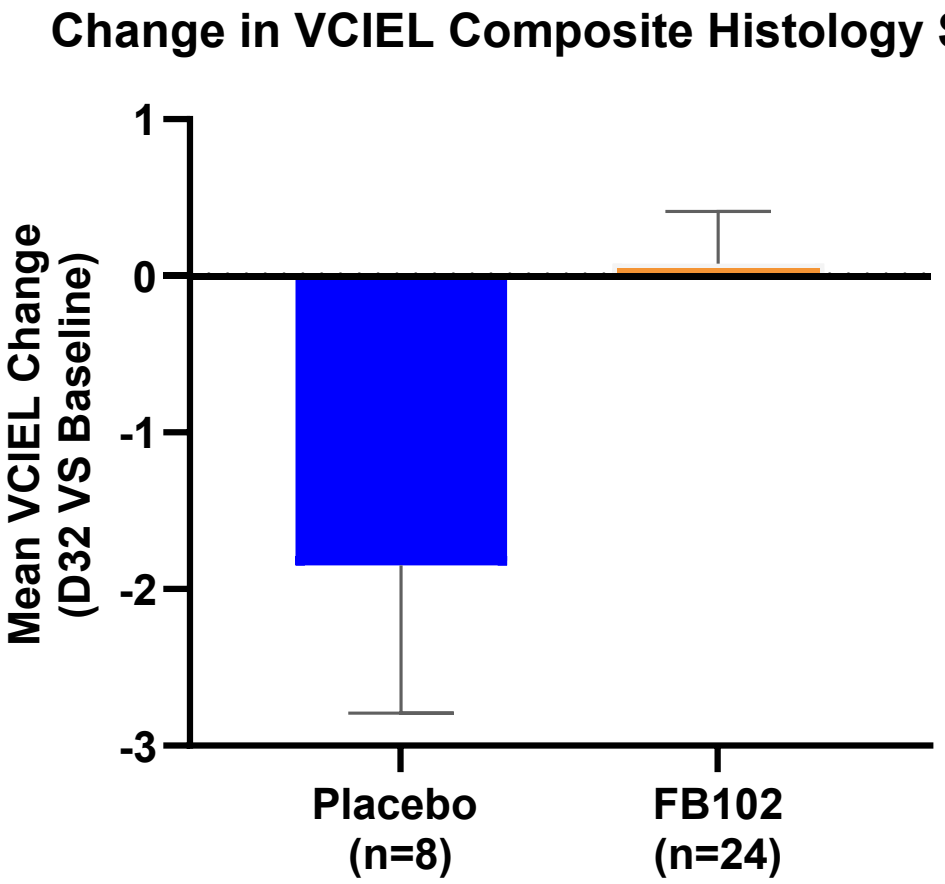
- 32 subjects were enrolled at 9 sites (AUS/NZ)
- Randomized 3:1 to FB102 vs PBO (24:8)
- Subjects received 3 of 4 doses of either FB102 (10mg/kg) or placebo then began 16 day gluten challenge (2g,4g, 8g for 14 days)
  - 4th dose of either FB102 or placebo on day 22
- Endoscopy/biopsy at baseline and at end of gluten challenge (central review of histology endpoints)
- Gluten challenge symptoms collected in patient diaries/AE reporting
- All subjects completed day 32 biopsy

BASELINE DEMOGRAPHICS

Parameter		Placebo N=8	FB102 N=24	Overall N=32
Age (Years)	Mean	38.3	40.8	40.1
Sex [n (%)]	Female	5 (62.5%)	19 (79.2%)	24 (75.0%)
	Male	3 (37.5%)	5 (20.8%)	8 (25.0%)
Ethnicity [n (%)]	Hispanic or Latino	0	0	0
	Not Hispanic or Latino	7 (87.5%)	23 (95.8%)	30 (93.8%)
	Not Reported	1 (12.5%)	1 (4.2%)	2 (6.3%)
	Unknown	0	0	0
Body Mass Index (kg/m2) at Screening	Mean	25.61	24.8	25
Baseline Villus height to Crypt depth ratio	Mean	2.756	2.818	
	Standard error of mean	0.1398	0.1099	
Baseline CD3 positive IELs per 100 enterocyte	Mean	25.6	23.5	
	Standard error of mean	3.83	1.68	

RESULTS

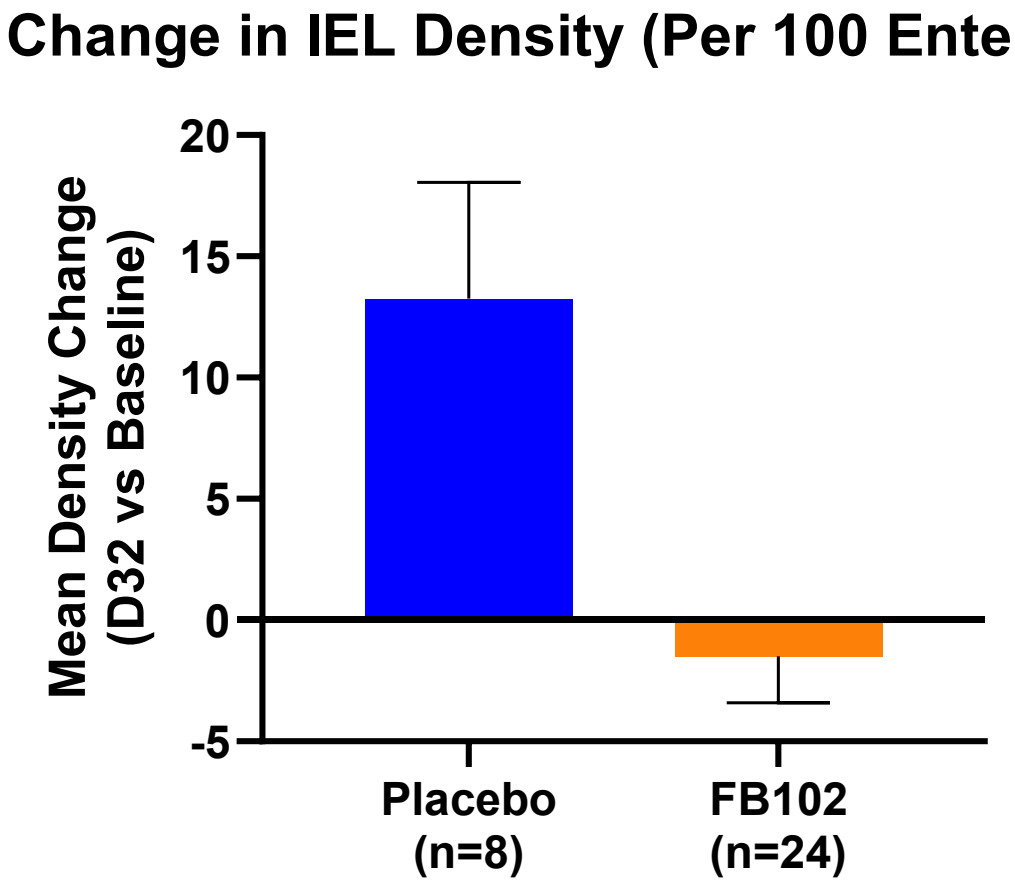
FB102: SIGNIFICANT DIFFERENCE IN COMPOSITE HISTOLOGY



Day 32 vs baseline VCIEL composite score –1.849 for PBO compared to 0.079 for FB102 treated subjects
•(p=0.0099) *

* Based on analysis of variance of changes from baseline

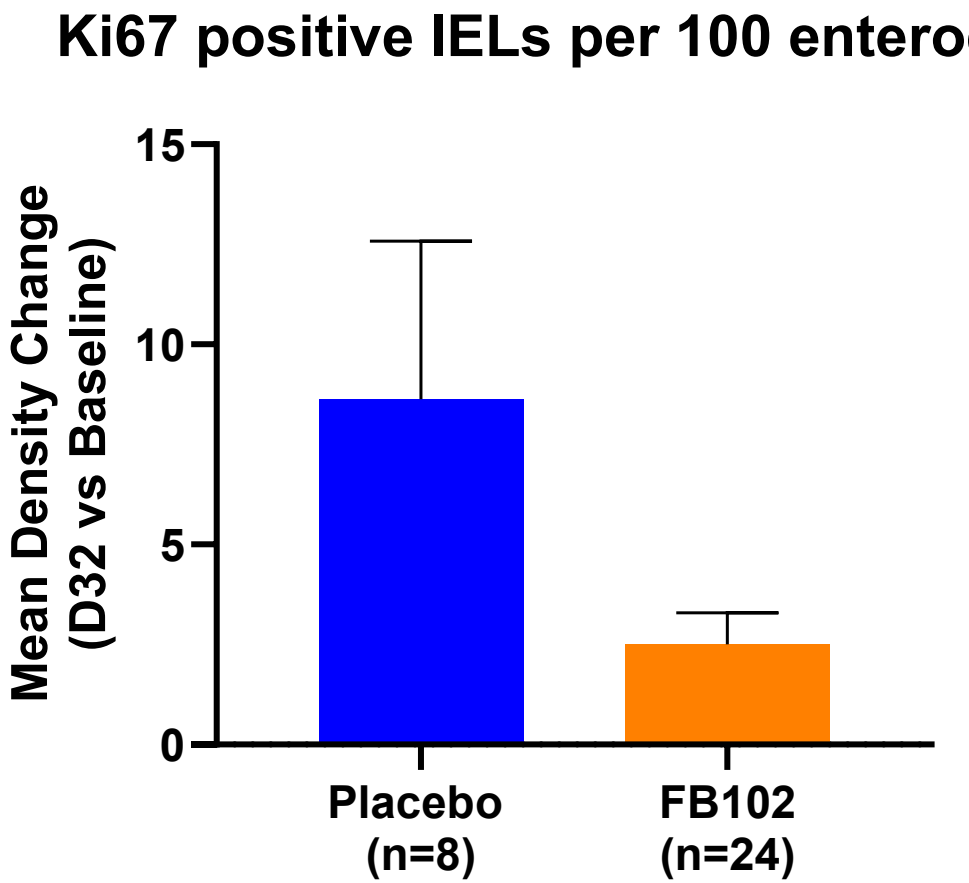
FB102: SIGNIFICANT DIFFERENCE IN CHANGE IN IEL DENSITY



•Day 32 vs baseline mean IEL density increase of 13.3 for PBO compared to a decrease of 1.5 for FB102 treated subjects (p=0.0035)*

* Based on analysis of variance of changes from baseline using log-transformed data

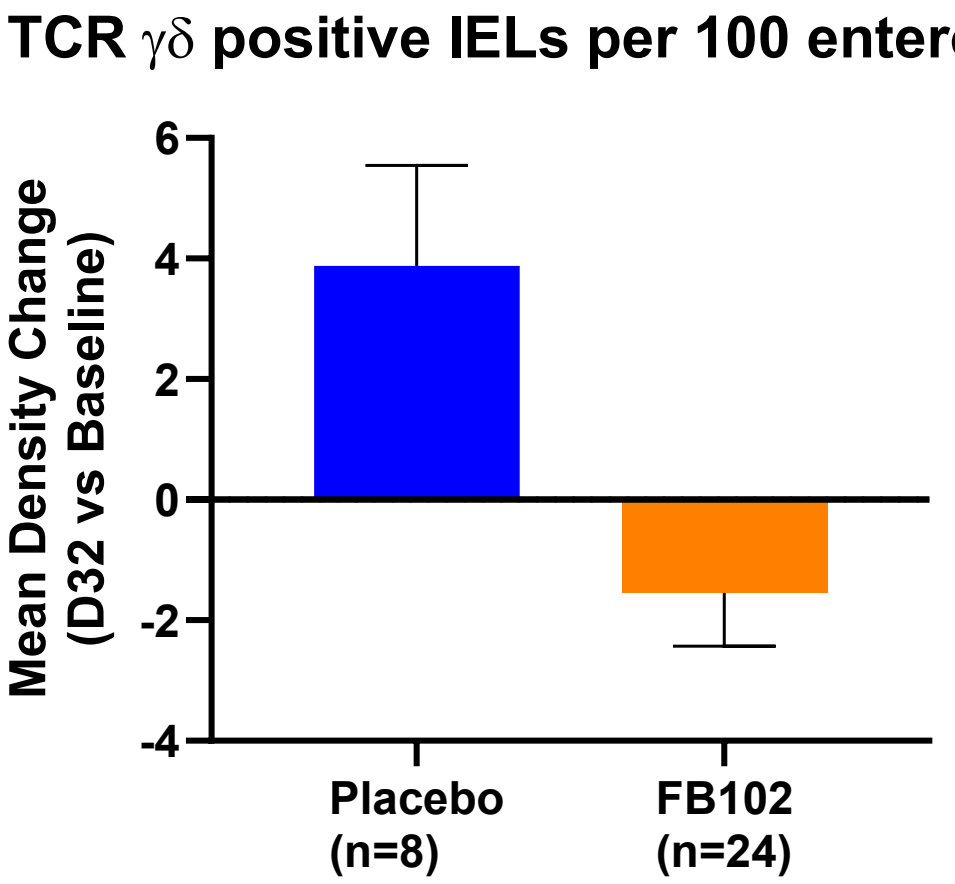
FB102: SIGNIFICANTLY LESS KI67 ACTIVATION IN IELS



- Ki67 is a marker of proliferation (inflammation) on gluten challenge in celiac disease.
- FB102 treated subjects had statistically significantly less Ki67 activation in IELs after gluten challenge vs placebo (p = 0.0006)*

* Based on analysis of covariance of changes from baseline with baseline value as covariate

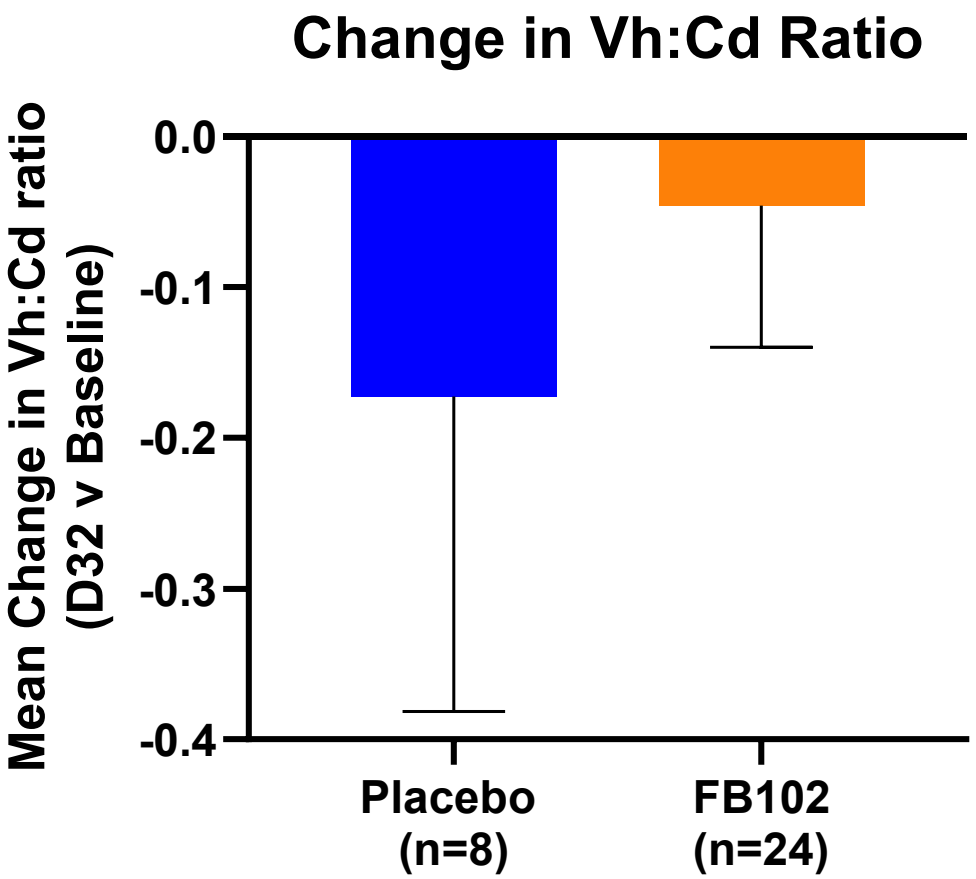
FB102: TCR γδ CELLS SIGNIFICANTLY REDUCED



- Gluten interacts with the receptors on TCR γδ IELs resulting in the activation to cytotoxic T cells
- FB102 treatment led to statistically significantly lower TCR γδ cells vs placebo following gluten challenge (p = 0.0007)*

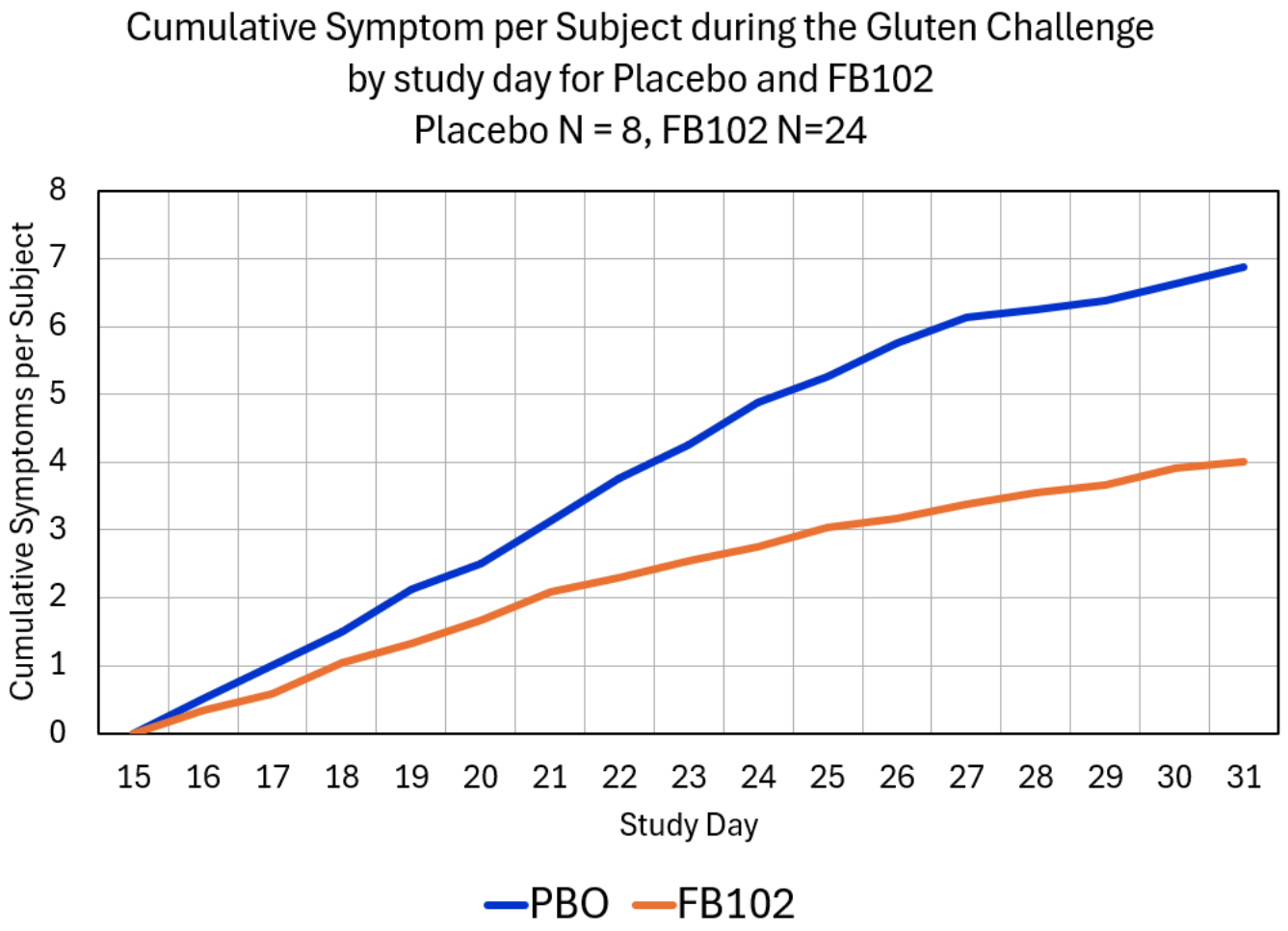
* Based on analysis of covariance of changes from baseline with baseline value as covariate

FB102: VH:CD RATIO IMPROVEMENT



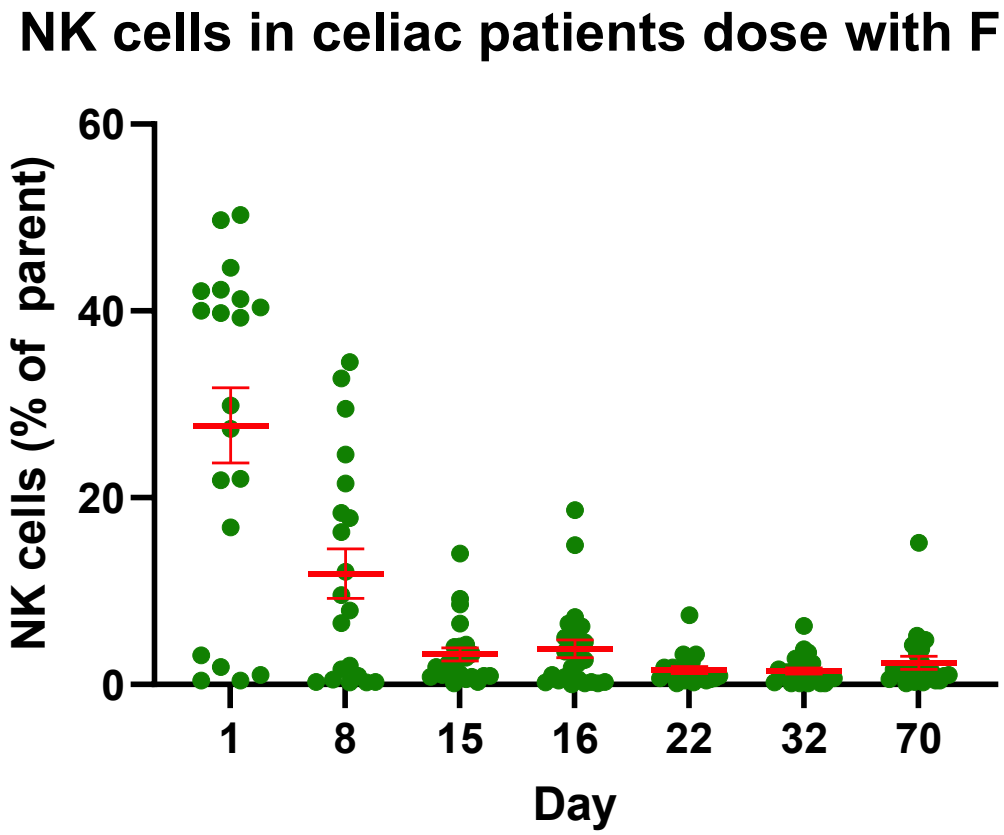
- Day 32 vs baseline Vh:Cd ratio improvement of 73% for FB102 (-0.046) compared to PBO (-0.173)

FB102: GLUTEN CHALLENGE SYMPTOM EVENT BENEFIT



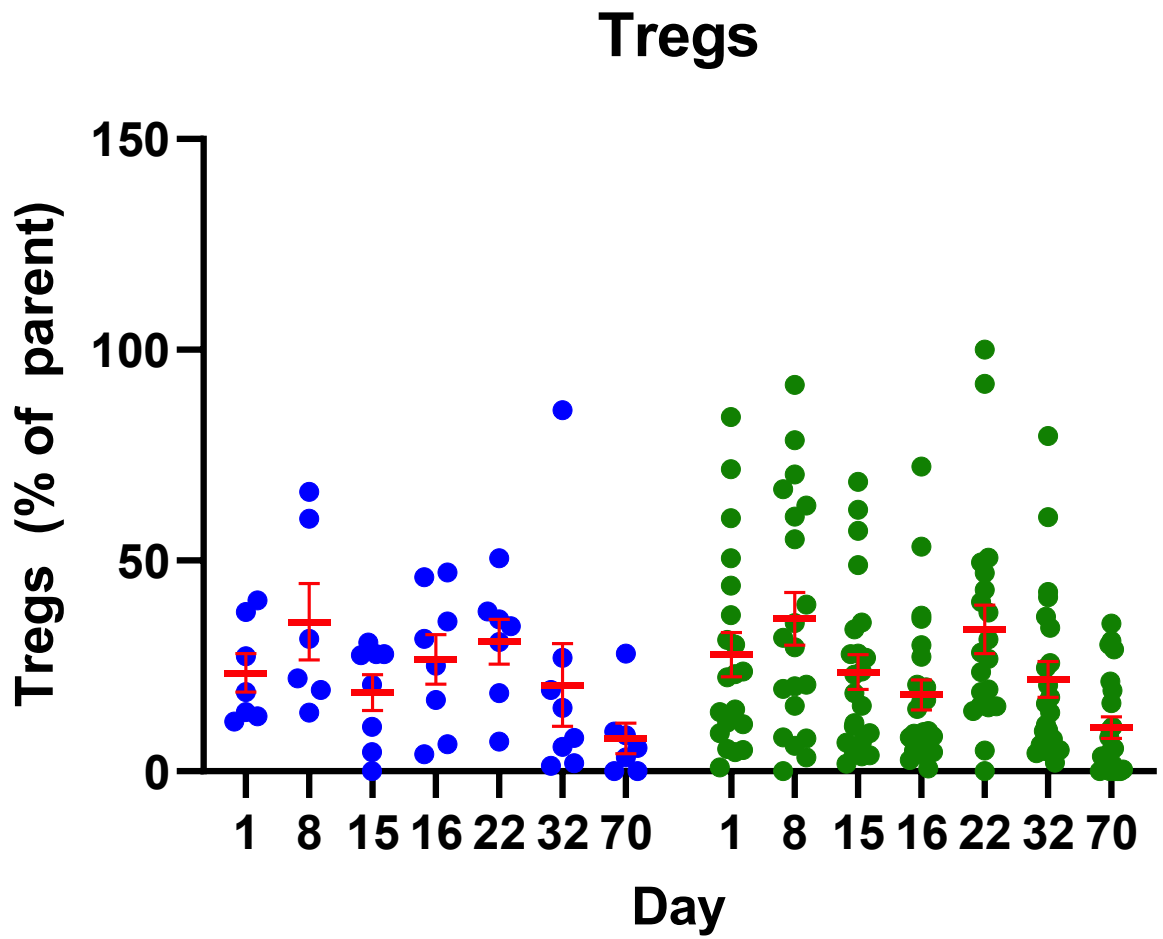
- Gluten challenge (GC) symptoms reported in patient diaries/AE collection
- GC induced GI symptoms tracked: nausea, diarrhea, vomiting, abdominal pain, abdominal bloating
- Through the 16-day gluten challenge FB102 demonstrated a 42% symptom benefit vs placebo (average of 6.9 events per subject on placebo compared to 4.0 events per subject on FB102)

FB102 DECREASES CD56+ BRIGHT NK CELLS IN PATIENTS



Day	% Lymphocyte	% Change
1	27.7	-
8	11.9	-57%
15	3.2	-88%
16	3.8	-86%
22	1.5	-95%
32	1.5	-95%
70	2.3	-92%

TREGS DO NOT CHANGE WITH FB102 TREATMENT



- Placebo (N=8)
- 10 mg/kg FB102 (N=24)

No Statistically Significant Difference in Treg FB102 vs PBO at any timepoint

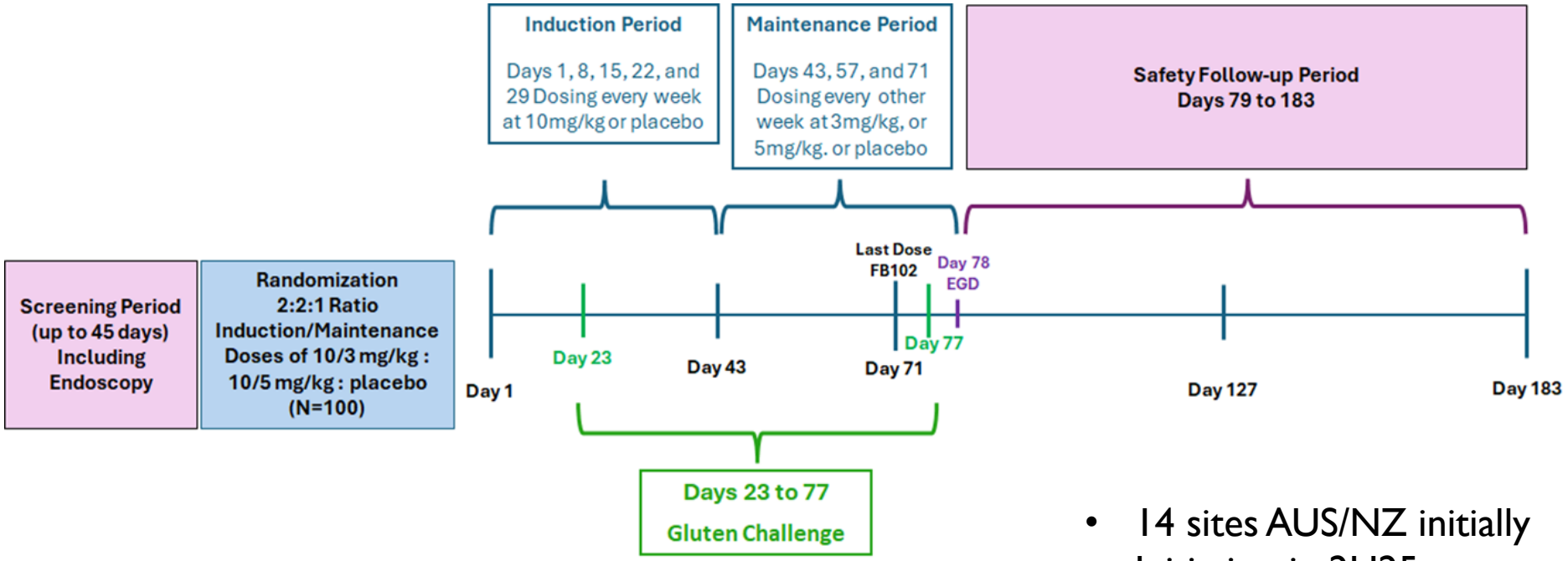
FB102 GENERALLY SAFE AND WELL TOLERATED

Treatment Emergent Adverse Events By Grade

	Placebo (N=8)		FB102 (N=24)		Overall (N=32)	
	n (Participant Count)	%	n (Participant Count)	%	n (Participant Count)	%
All Any Grade	8	100.0%	23	95.8%	31	96.9%
Grade 1 (Mild)	8	100.0%	22	91.7%	30	93.8%
Grade 2 (Moderate)	6	75.0%	9	37.5%	15	46.9%
Grade 3 (Severe)	1	12.5%	0	0.0%	1	3.1%

WHAT'S NEXT?

CELIAC DISEASE PHASE 2 TRIAL



Study Day	Amount of Gluten (grams)
Day 1 to 22	0 grams of gluten per day
Days 23 to 36	8 grams of gluten per day
Days 37 to 77	3 grams of gluten per day
Day 78	EGD

- 14 sites AUS/NZ initially
- Initiation in 2H25
- US IND expected late 2025/early 2026
- Topline data readout expected in 2026

THANK YOU