ANB033 (CD122 antagonist)

Investor Event

Oct. 14, 2025

AnaptysBio

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Intention to separate into two independent, publicly traded companies to unlock and maximize value

Biopharma Co

Focus on developing and potentially commercializing therapeutics for autoimmune diseases

Rosnilimab
(Pathogenic T cell depleter)

P2b complete in Rheumatoid Arthritis

P2 in Ulcerative Colitis

ANB033
(CD122 antagonist)

P1b in Celiac Disease (CeD)

ANB101
(BDCA2 modulator)

P1 in Healthy Volunteers

Research-driven • R&D capabilities with preclinical pipeline of immunology targets

Royalty Management Co

Focus on protecting and returning value of the royalties to shareholders

- Hold and continue to manage rights to
  - Potential substantial *Jemperli* royalties from GSK
  - Imsidolimab milestones and royalties from Vanda
- Expect minimal infrastructure and staff
- Anticipate will retain Anaptys' net operating loss (NOL) carryforwards

GSK Jemperli (dostarlimab-gxly) Injection 500 mg

VANDA PHARMACEUTICALS INC.

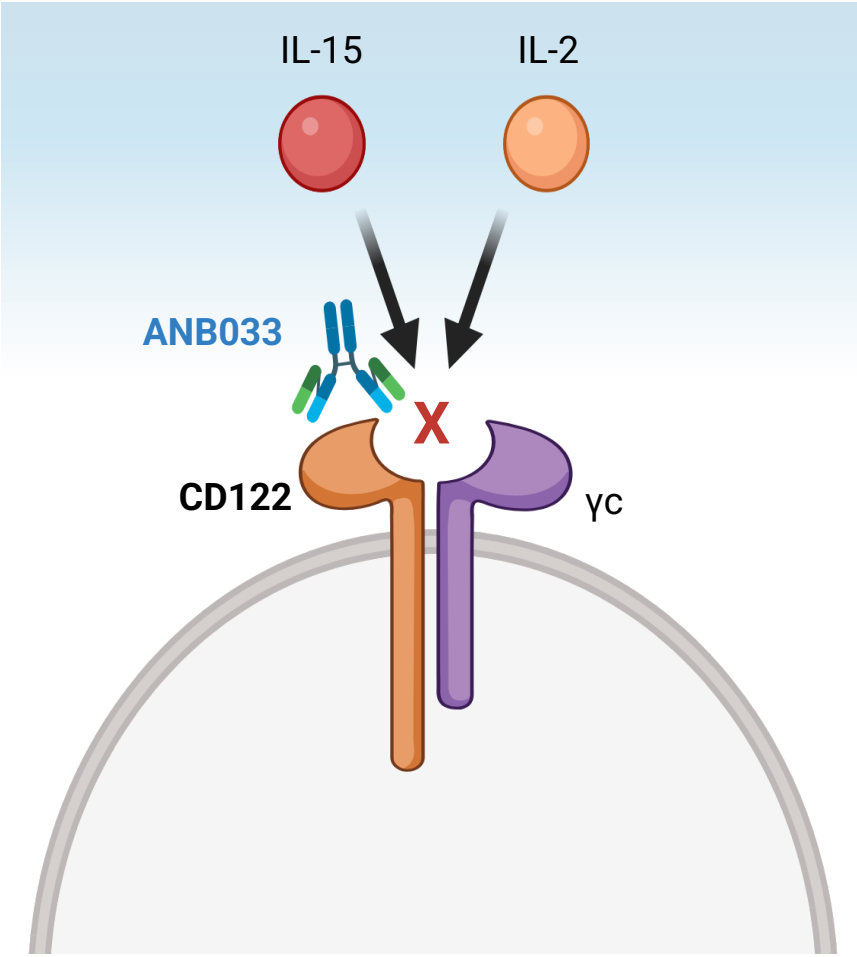
Note: Q2 2025 cash: ~$294MM. Anaptys expected cash runway through YE: 2027 includes GSK $75MM milestone for *Jemperli* $1B annual WW sales. Biopharma Co. to launch with adequate capital to fund operations for at least two years through significant potential corporate milestones. Cash runway excludes significant royalty potential from GSK or Vanda.

Targeting CD122 has strong biologic rationale

Why target CD122?

- Targeting only the IL-15 cytokine addresses inflammation, but may allow pathogenic cell survival through alternative escape mechanisms
- CD122 is the shared receptor subunit through which both IL-15 and IL-2 signal
- IL-15 and IL-2 are central cytokines in pathogenic inflammation across broad inflammatory diseases
  - Overactive signaling drives proliferation and survival of cytotoxic CD8+ and CD4+ T cell subsets and NK cells
  - Inflammatory Th1 and Th2 cytokine secretion during T cell activation

ANB033: potential best-in-class CD122 antagonist with optimized dual IL-15 and IL-2 signaling inhibition



ANB033 designed for high potency

- Specific binding epitope engineered for high affinity
- Inhibit both IL-15 and IL-2 signaling

Targets pathogenic cells in inflamed tissue

- Subsets of activated T cells
  - Cytotoxic CD8+ T cells
  - Memory CD4+ Th1/Th2 T cells
  - IELs
- ILC2s
- NK cells

Subcutaneous dosing

Broad therapeutic potential across autoimmune and inflammatory diseases

Gastroenterology	***Dermatology***	**Other Areas**
Celiac Disease	Atopic Dermatitis	Asthma
Crohn's Disease	Alopecia Areata	Multiple Sclerosis
Eosinophilic Esophagitis (EOE)	Hidradenitis Suppurativa	Psoriatic Arthritis
Ulcerative Colitis	Lichen Planus	Type 1 Diabetes
	Vitiligo	Solid Organ Transplant

Clinical-stage drugs targeting IL-15 or CD122

NOVARTIS	IL-15	• P1b PoC in CeD • P1b PoC in EoE
teva	IL-15	• P2a in CeD • P2a in vitiligo
Incyte	CD122	• P1b in vitiligo
FORTE	CD122	• Positive P1b in CeD (P2a ongoing) • P1b in vitiligo and alopecia areata • Assessing T1D

ANB033 has pipeline-in-a-product potential

ANB033: initiated initial P1b in CeD

- Multiple pathogenic drivers of disease
- Inflamed cells in CeD respond to both IL-15 and IL-2
- Targeting IL-15 / CD122 is clinically validated

Expansion opportunities

- GI, dermatology and other therapeutic areas
- Assessing potential to treat EoE

CeD Market[1]

- >250k diagnosed U.S. non-responsive CeD patients
- Gluten-free diet highly restrictive; ~50% of patients suffer anemia and fatigue
- No approved therapies
- $4 – 5bn U.S. market for CeD patients non-responsive to gluten-free diet
- Global pharma interest

1. Trinity Life Sciences Commercial Assessment HCP Primary Market Research (2025). CeD sizing reflects future US market in 2030 assuming growth in diagnosis rate based on historic trends and projected growth with entrance of novel therapies.

Agenda: ANB033 (CD122 Antagonist)

TOPIC	SPEAKER
CD122 biology and preclinical data	Martin Dahl, Ph.D., Senior Vice President, Research
Phase 1a in healthy volunteers	John Kwon, M.D., Ph.D. Vice President, Clinical Development
Drug development for CeD	Joseph Murray, M.D. Professor of Medicine Mayo Clinic College of Medicine, Rochester, MN
Phase 1b in CeD	Paul Lizzul, M.D., Ph.D. Chief Medical Officer
Commercial opportunity and next steps	Dan Faga Chief Executive Officer
Q&A	All

ANB033 blocks CD122 to inhibit pathogenic immune cells

CD122 is the beta subunit (IL-2Rβ) of the receptor for IL-15 and IL-2

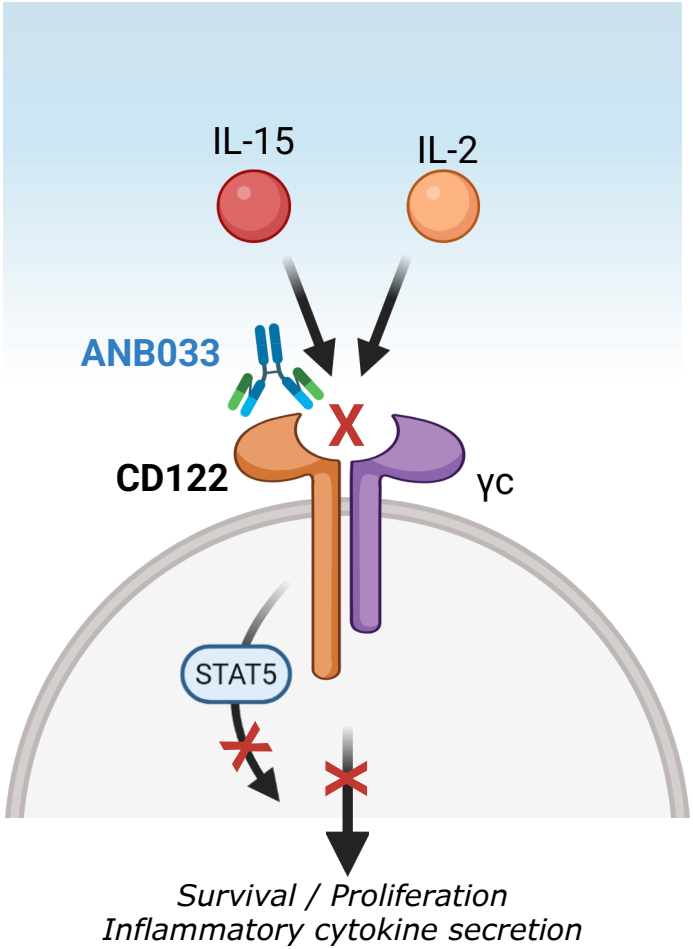
- Expressed on subsets of CD8+ and CD4+ T cells and NK cells

CD122 antagonism reduces these immune cell subsets

- Dependent on IL-15 and/or IL-2 for maintenance, proliferation and survival

Overexpressed in select diseases, including CeD gut or EoE

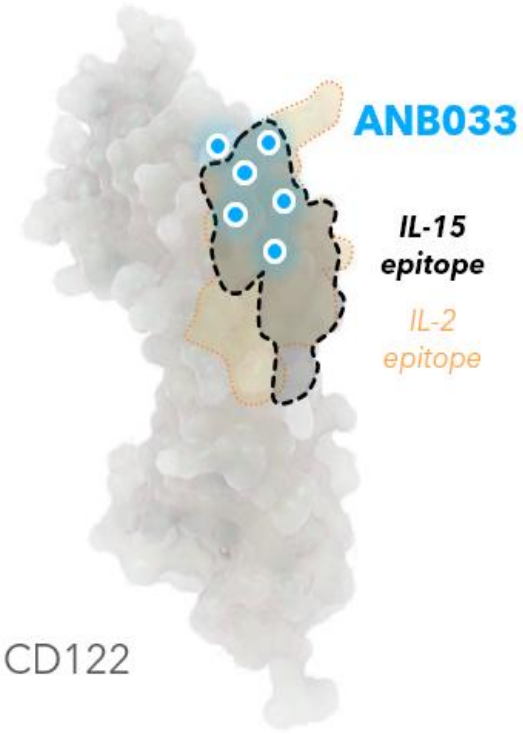
- CeD: IELs, including cytotoxic CD8+ and NK cells
- EoE: ILC2s



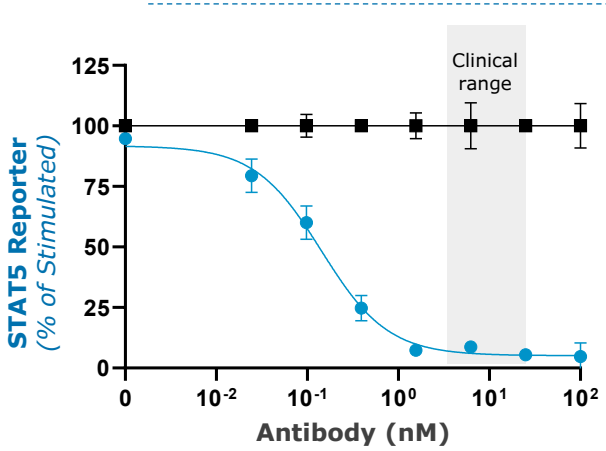
Richards et al, Cell Rep. 2025 Jul 21;44(8):116039.

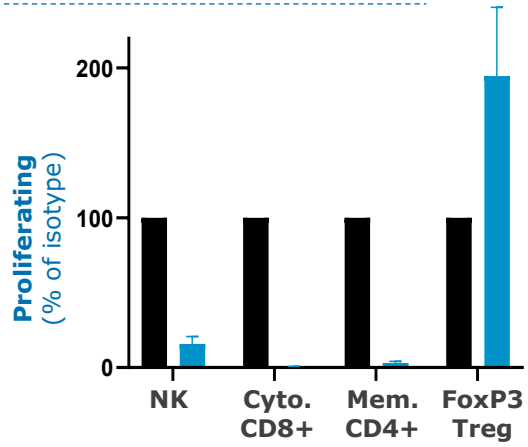
ANB033's optimized epitope and high affinity lead to differentiated inhibition of IL-15 and IL-2 signaling

ANB033 epitope sits squarely within IL-15 and IL-2 binding footprint

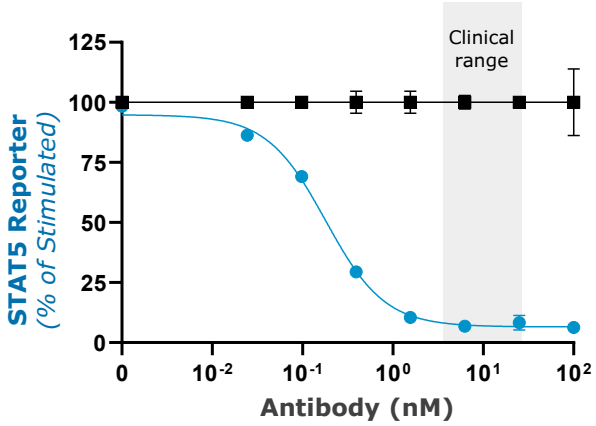


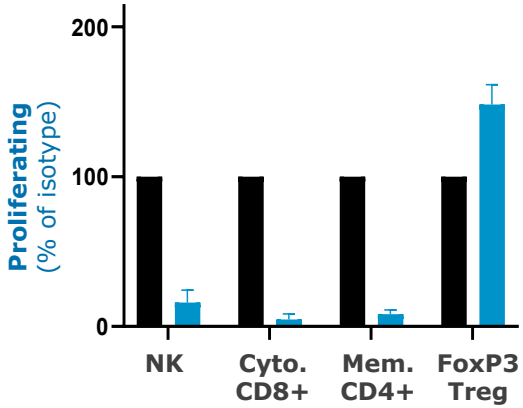
IL-15 stimulation





IL-2 stimulation



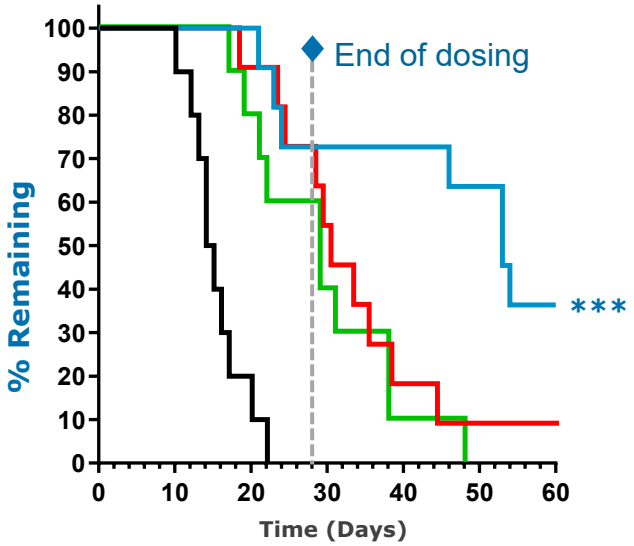


ANB033 Isotype Control

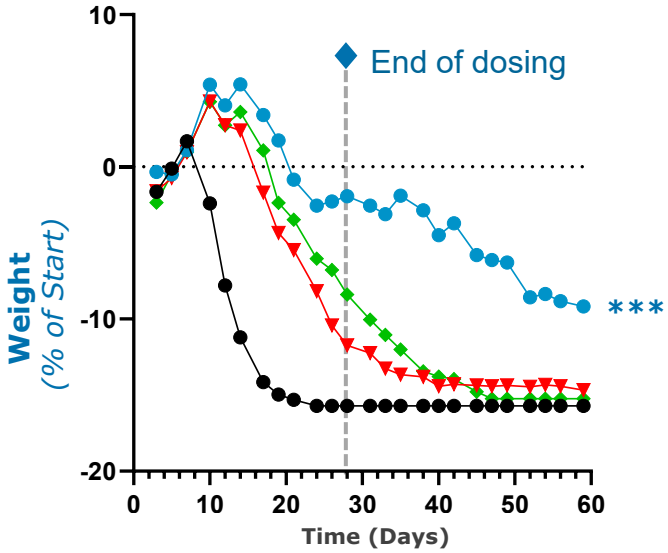
STAT5 luciferase reporter assay run in HEK293 cells that express CD122 and CD132, stimulated with IL-15 or IL-2; Cyto. = cytotoxic; Mem. = memory; Normal donor PBMC measuring proliferation (Ki67 staining) after stimulating with IL-15 or IL-2 for 7 days with isotype or ANB033 at 28 nM (N=4 donors).

ANB033 shows strong survival benefit and reduced cytolytic gene expression in aggressive GvHD mouse model

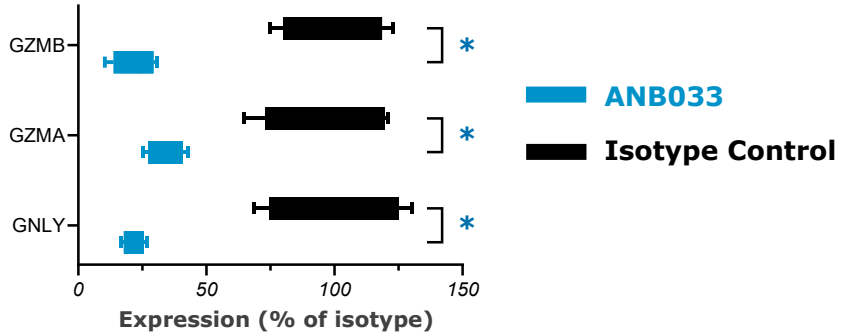
Survival



Body weight loss (carried)

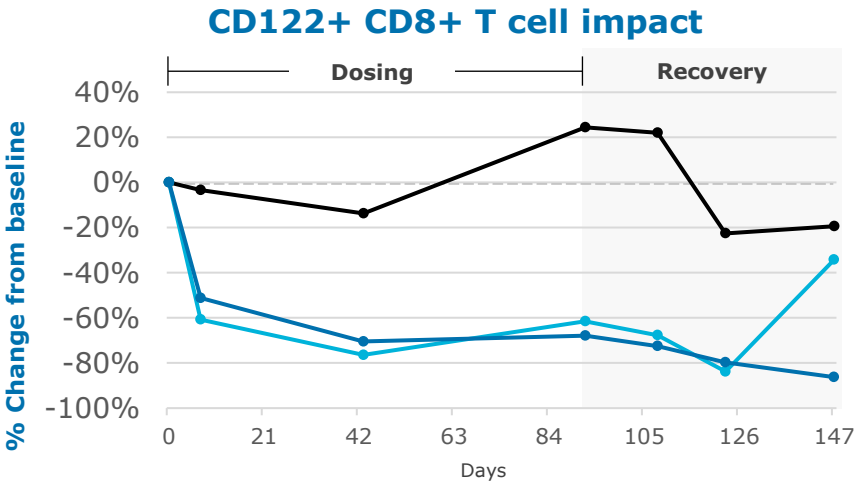


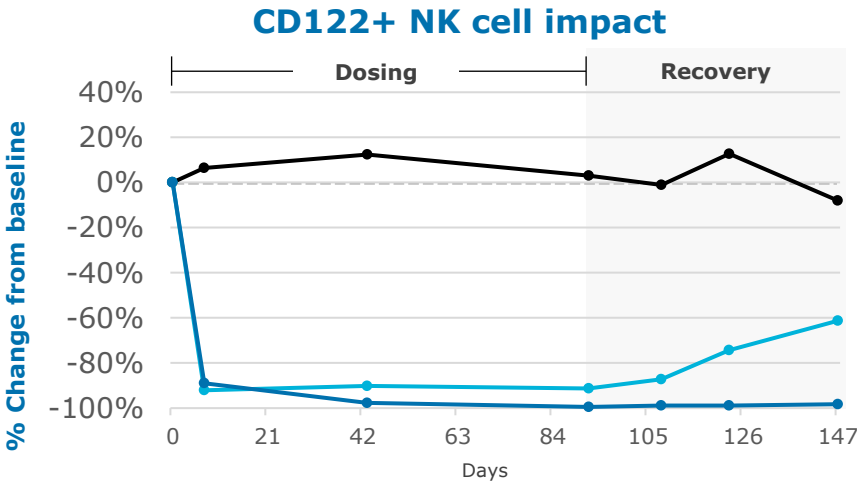
Cytolytic gene expression (Day 17)

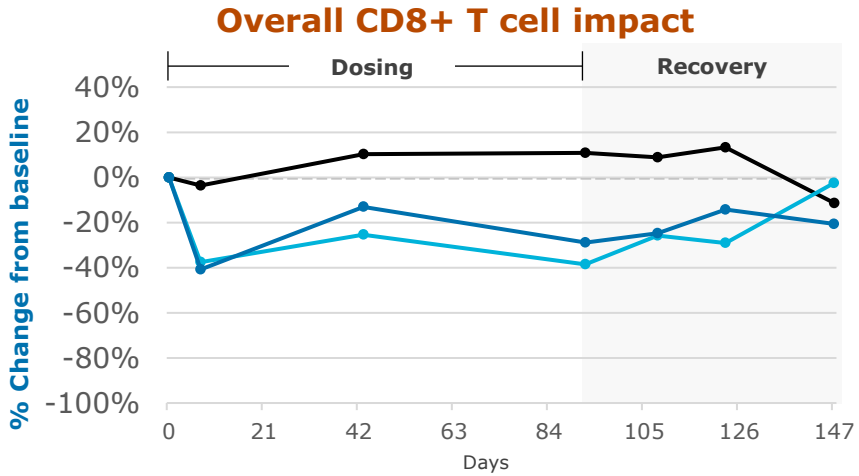


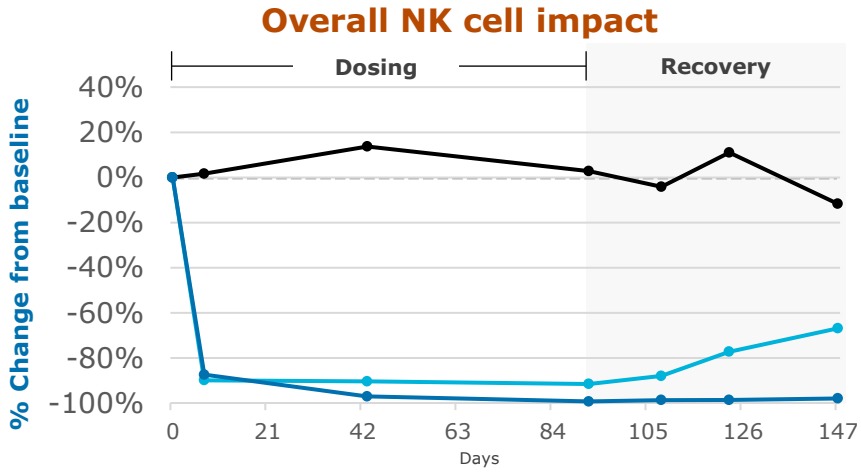
GvHD (severe phenotype) model using human IL-15 transgenic mice that support human T cell and NK cell engraftment. 60-day study. Mice dosed 3 mg/kg BIW (belatacept 75 µg TIW) through Day 28. N=10 per group (isotype control and Belatacept) or 11 per group (test articles). *** Survival: ANB033 statistically significant vs isotype control (P<0.0001), Belatacept (P=0.003), Forte anti-CD122 (first achieved on Day 38, p=0.031, with significance deepening through Day 60, P=0.0032) log-rank Mantel-Cox test; Body weight loss: ANB033 statistically significant vs isotype control (p<0.001), Belatacept (p=0.0016), Forte anti-CD122 (first achieved on Day 28, p=0.037, with significance deepening through Day 60, P=0.0003), Unpaired Student's t-tests. Gene expression data generated from purified human immune cells isolated from spleen on day 17. * p<0.05 Unpaired Student's t-tests.

ANB033 reduces key CD122+ target cells in cynomolgus monkeys







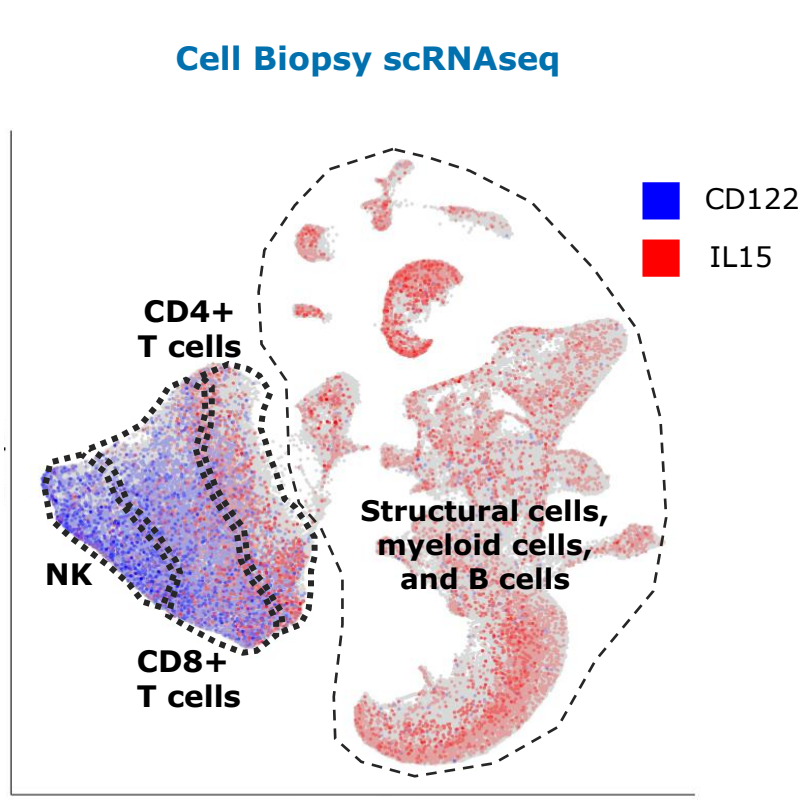


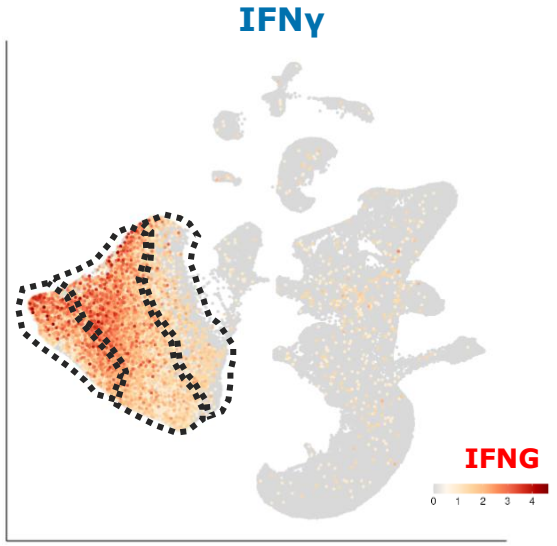
Vehicle ANB033 – 10mg/kg SC ANB033 – 100mg/kg SC

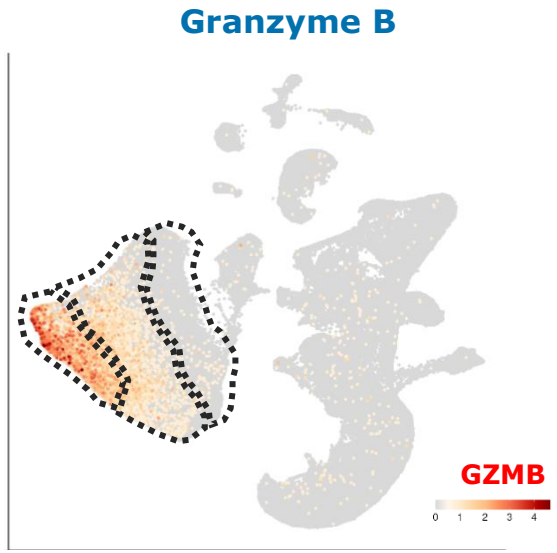
- 10-fold safety margin from cyno monkey toxicology to human in "clinical range" of dosing

Cyno NK cells identified by expression of CD159a, which unlike in humans, virtually all are CD122+.

CeD is characterized by a dense infiltration of inflammatory CD122+ immune cells







Dense CD122 expression by infiltrating immune cells

- IFNγ expression: cytotoxic CD8+ T cells, CD4+ T cells, NK cells
- Granzyme B expression: CD8+ T cells, NK cells

CD122+ cells are increased 50-150% compared to healthy

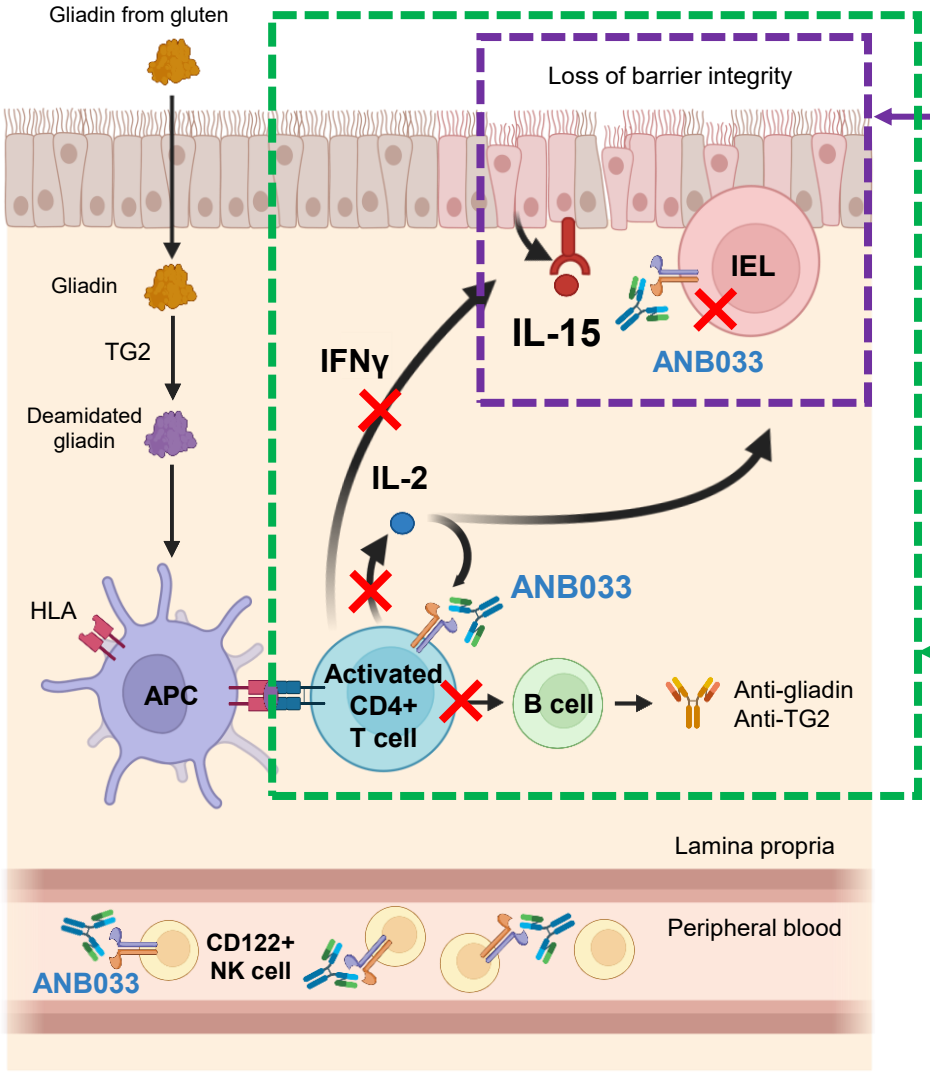
Broad IL15 expression by structural cells

- Epithelial cells, myeloid cells and lymphocytes

Richards et al, Cell Rep. 2025 Jul 21;44(8):116039; UMAP of single-cell RNA-seq data from celiac disease (CeD) intestine, colored by co-expression of gene pairs: Expression values are SCTransform-normalized; a color scale is used: red or blue: high gene expression, gray = low expression.

ANB033's MOA ideal fit for targeting CeD inflammation

CeD marked by excessive IL-15 and IL-2 production which perpetuates disease



Inhibition of IL-15 signaling

- IL-15 induces proliferation of IELs
  - Majority of IELs are CD122+ T cells
- Inhibiting IL-15 signaling reduces IELs
  - Reduces epithelial cell destruction
  - Restores barrier integrity

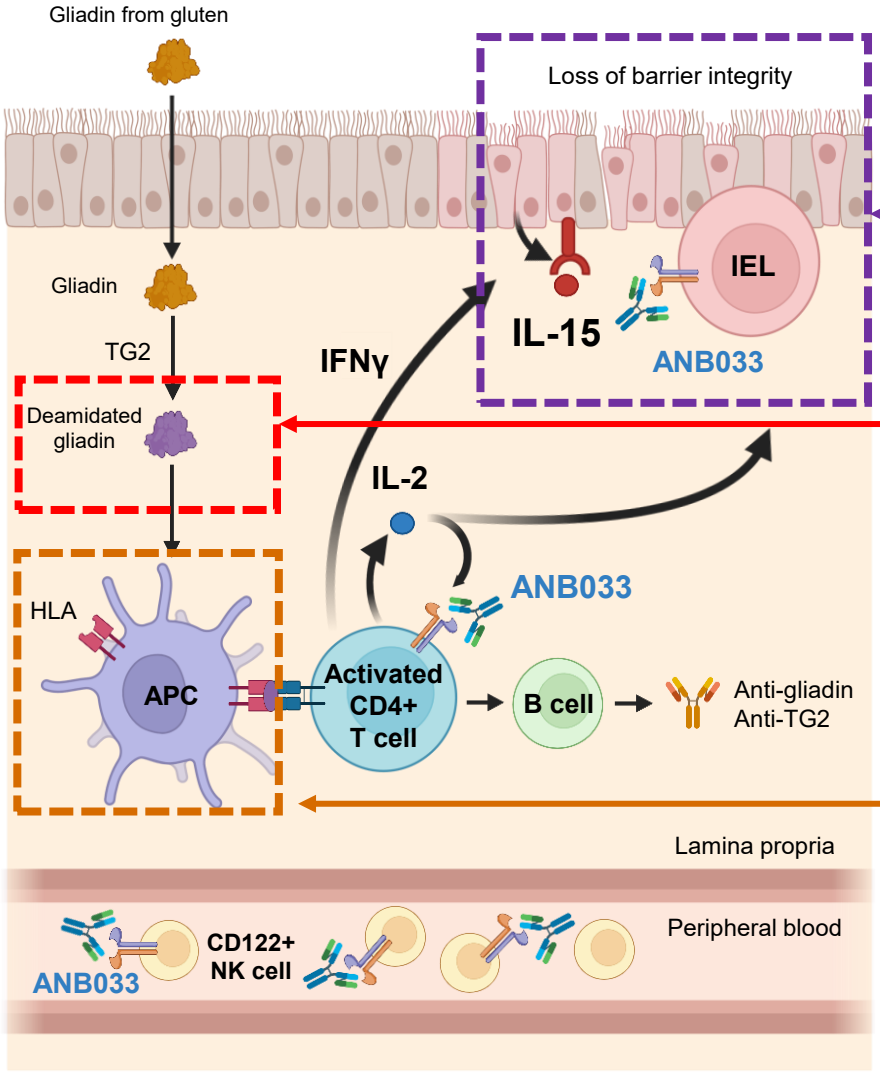
Inhibition of IL-2 signaling

- IL-2 stimulates
  - CD4 effector memory T cell activation and proliferation
  - IFNγ production leading to IL-15 secretion
- Inhibiting IL-2 signaling reduces
  - Gluten-responsive CD4 T cell expansion
  - Inflammatory cytokine secretion
  - Downstream B cell-mediated antibody responses

Adapted from Dieckman et al. (2022) Curr. Opin. Pharmacol. 66:102268.

Previous approaches have not addressed multiple pathogenic drivers of CeD

However, a CD122 antagonist targets both key pathogenic drivers of CeD



IL-15 antagonists: Clinical PoC

- teva — *P2 ongoing*
- NOVARTIS — *P1b PoC*
- AMGEN — *Lacked potency*

Non-immune cell targeting

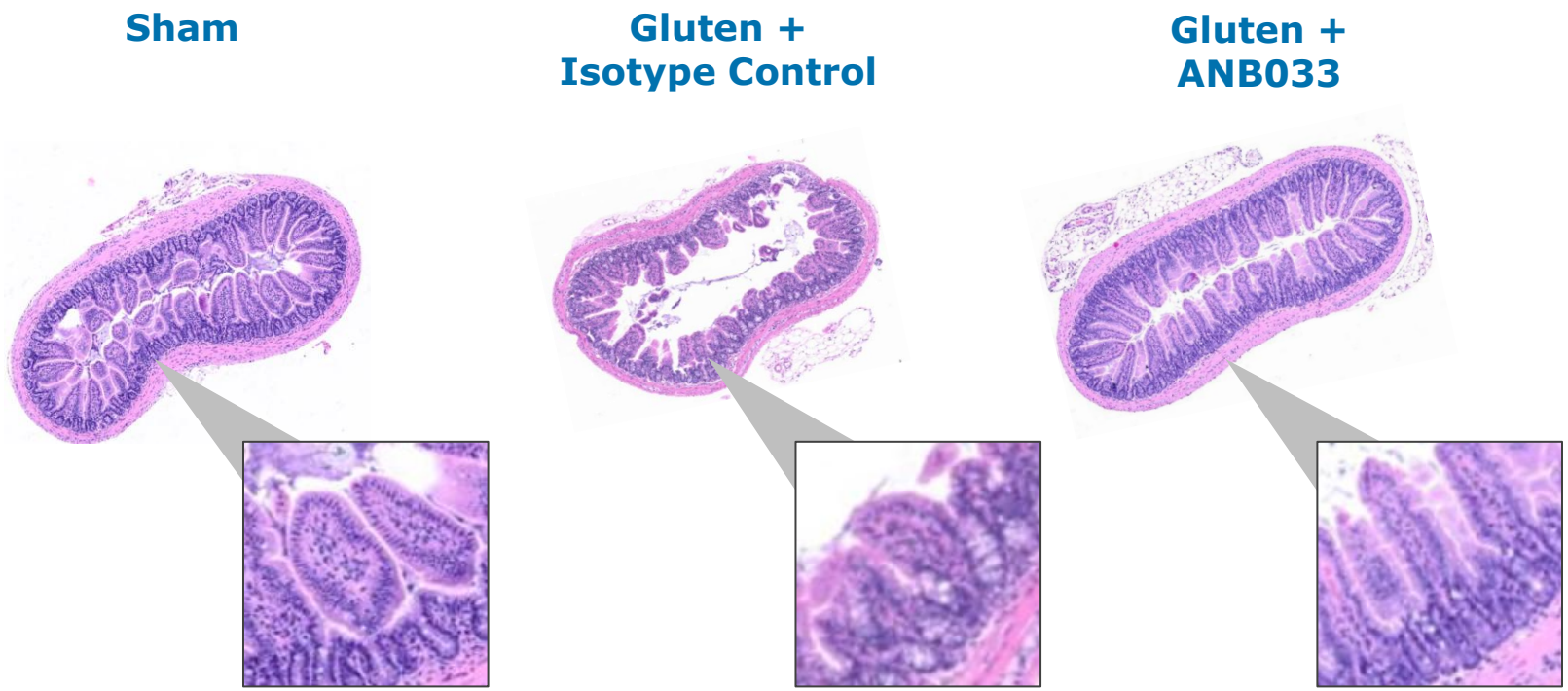
- Takeda — *P2 ongoing* — *Gluten tolerance*
- astellas — *Discontinued* — *Gluten tolerance*
- Roche — *P1 ongoing* — *HLA-DQ2.5 gluten peptide complex*
- Immunic THERAPEUTICS — *P1 ongoing* — *SIRT6 modulator*

OX-40L antagonist

- sanofi — *P2 ongoing*

Adapted from Dieckman et al. (2022) Curr. Opin. Pharmacol. 66:102268.

ANB033 prevents key CeD histologic manifestation of gluten-induced villous atrophy



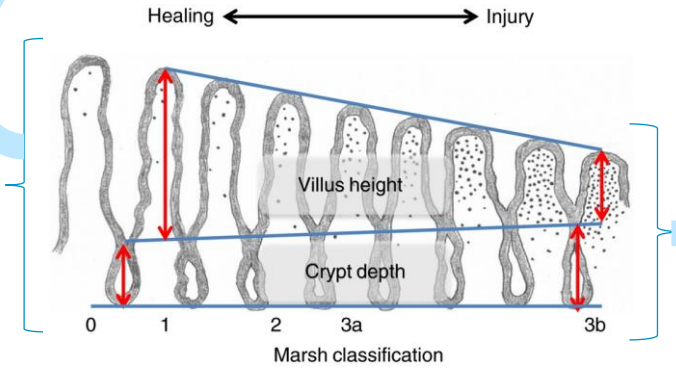
ANB033 treatment shows improved histology:
preserves villus height and crypt depth (Vh:Cd) in CeD mouse model

Note: HuDQ8-D^d-villin-IL-15tg mice on a gluten-free diet are challenged with gluten, and CeD features are analyzed on day 30. The treatment regimen includes a sham (no gluten), isotype control and ANB033 surrogate antibody (anti-mouse CD122 antibody with similar epitope and affinity to ANB033) administered at 10 mg/kg BIW.

ANB033 significantly prevents reduction of Vh:Cd ratio compared to control

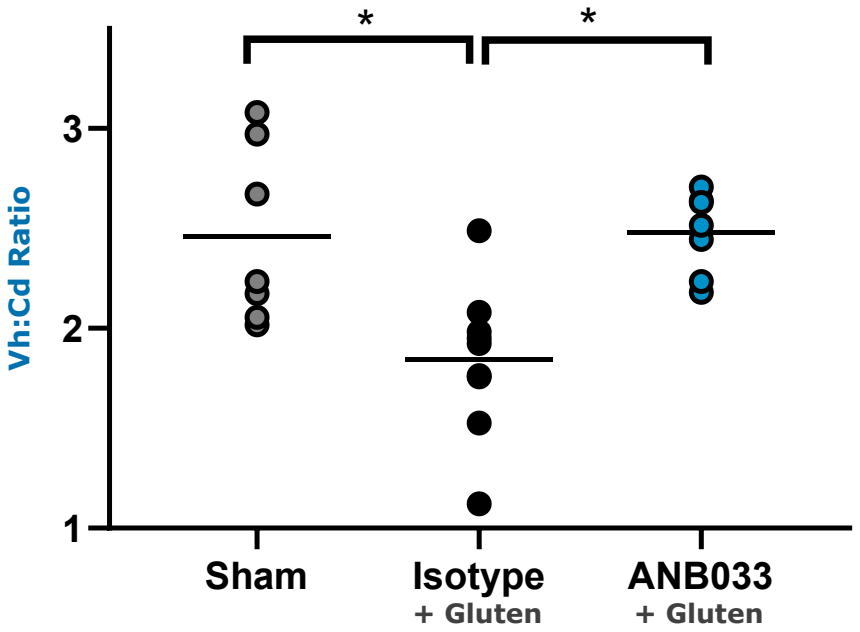
Vh:Cd ratio

Healthy tissue:
High villus height, lower crypt depth



CeD tissue:
Reduced villus height, extended crypt depth

ANB033 impact on Vh:Cd ratio



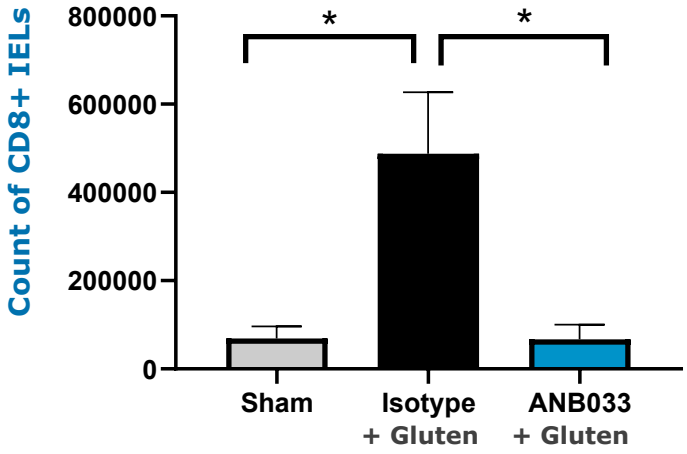
ANB033 treatment shows improved histology: preserves villus height and crypt depth (Vh:Cd) in CeD mouse model

Note: HuDQ8-D^{d}-villin-IL-15tg mice on a gluten-free diet are challenged with gluten, and CeD features are analyzed on day 30. The treatment regimen includes a sham (no gluten), isotype control and ANB033 surrogate antibody (anti-mouse CD122 antibody with similar epitope and affinity to ANB033) administered at 10 mg/kg BIW. * $p<0.05$.

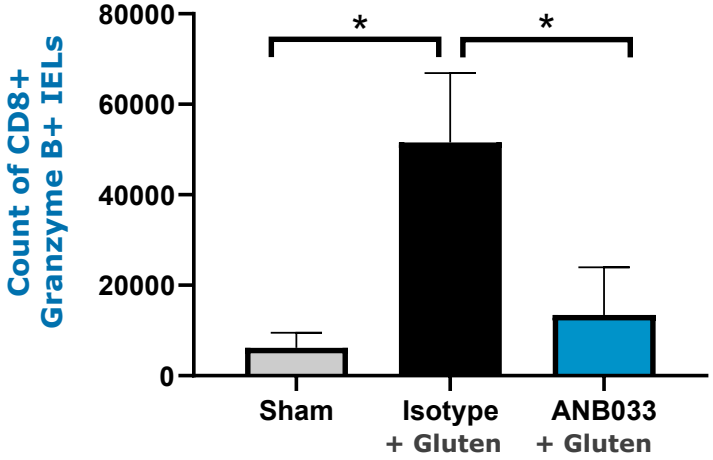
ANB033 prevents gluten-induced intestinal inflammation

Epithelial layer of small intestine

No increase in CD8+ IELs

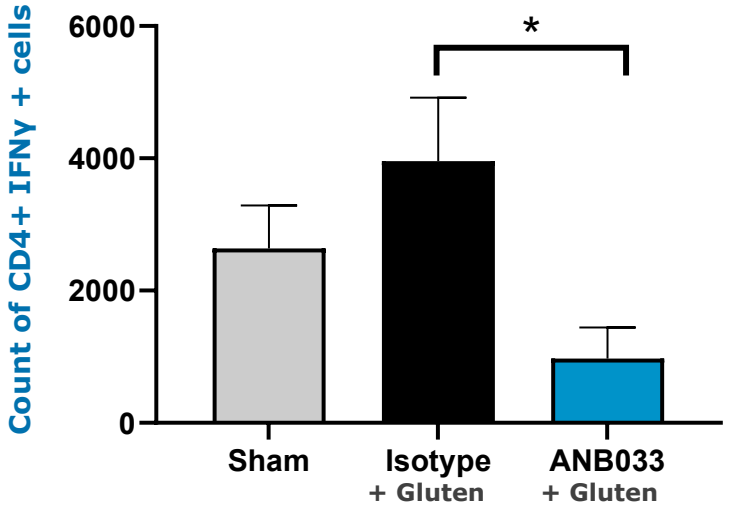


No increase in Granzyme B+ IELs



Lamina propria (LP)

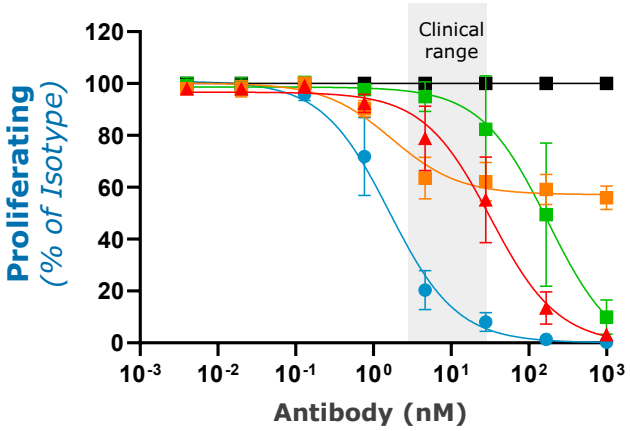
No increase in CD4+ IFNγ + T cells



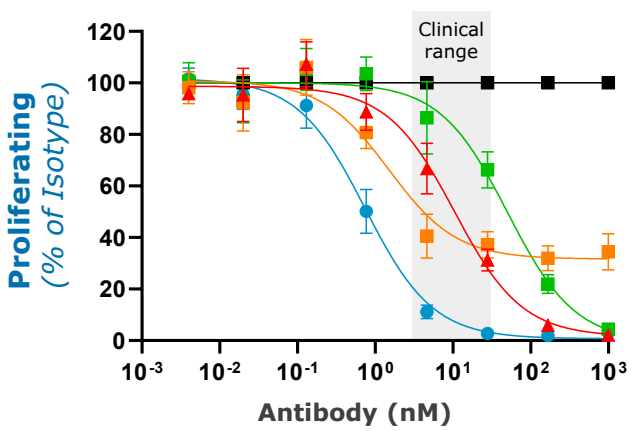
Note: HuDQ8-D^{d}-villin-IL-15tg mice on a gluten-free diet are challenged with gluten, and CeD features are analyzed on day 30. The treatment regimen includes a sham (no gluten), isotype control and ANB033 surrogate antibody (anti-mouse CD122 antibody with similar epitope and affinity to ANB033) administered at 10 mg/kg BIW. IFNγ + CD4 T cells and GrzB+ CD8+ T cells enumerated by intracellular flow cytometry.

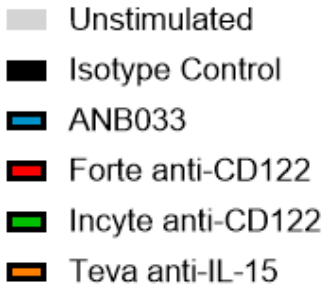
ANB033 shows differentiated impact in CeD patient-derived PBMCs compared to competing anti-IL-15s and CD122s

Cytotoxic CD8+ T cells

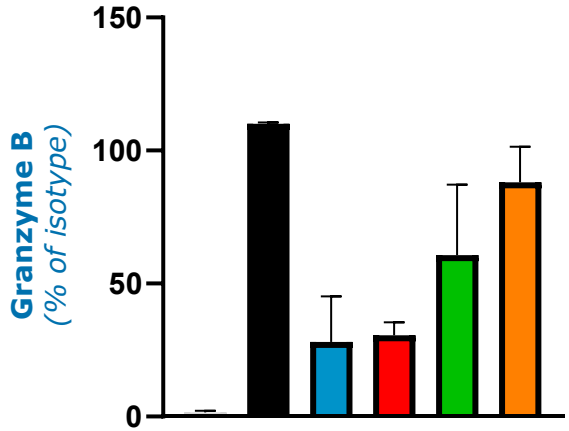


CD4+ Th1/Th2 T cells

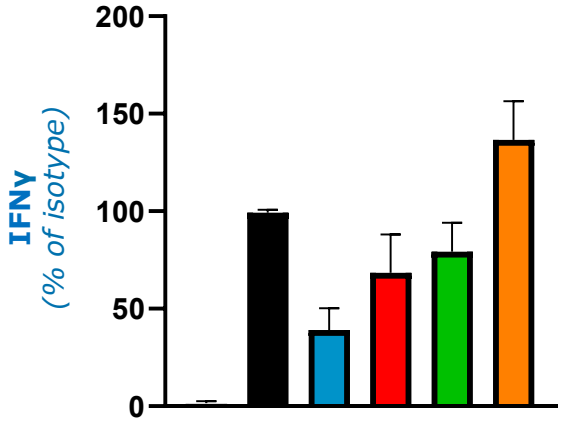




Granzyme B secretion



IFNγ secretion



Top Panel: PBMC from CeD donors measuring proliferation (Ki67 staining), stimulated for 7 days with IL-15 + IL-2 (N=4 donors).
Bottom Panel: PBMC from CeD donors stimulated for 3 days with anti-CD3 and anti-CD28 (N=4 donors).

Broad therapeutic potential across autoimmune and inflammatory diseases

Gastroenterology

Celiac Disease

Crohn's Disease

Eosinophilic Esophagitis (EoE)

Ulcerative Colitis

Dermatology

Atopic Dermatitis

Alopecia Areata

Hidradenitis Suppurativa

Lichen Planus

Vitiligo

Other Areas

Asthma

Multiple Sclerosis

PsA

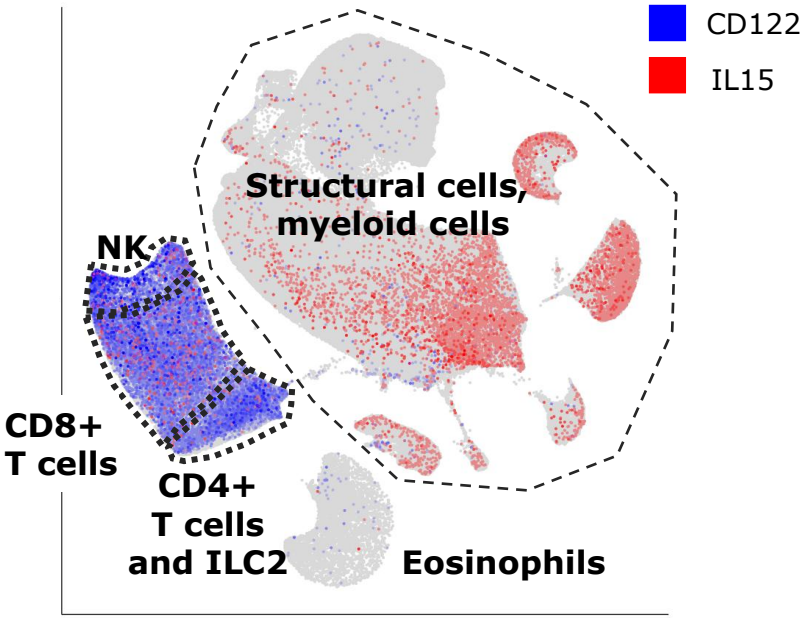
Type 1 Diabetes

Solid Organ Transplant

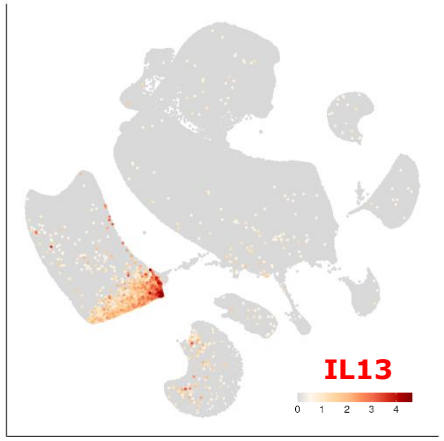
Assessing ANB033's potential to treat EoE

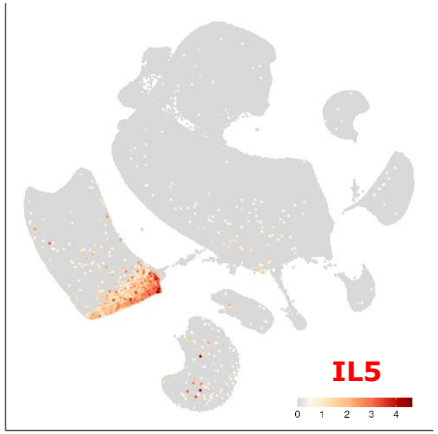
EoE is also characterized by a dense infiltration of immune cells presenting CD122+ expression

Cell Biopsy scRNAseq

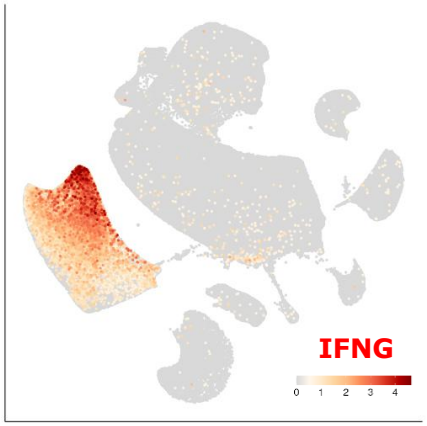


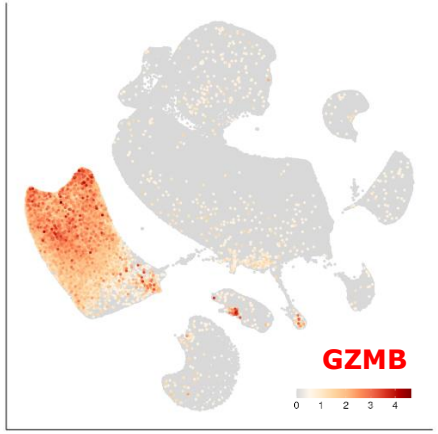
CD4+ and ILC2
(dupilumab-sensitive pathway)





CD8+ and NK
(dupilumab-insensitive pathway)





Dense CD122 expression by infiltrating CD8+ T cells, CD4+ T cells, NK cells

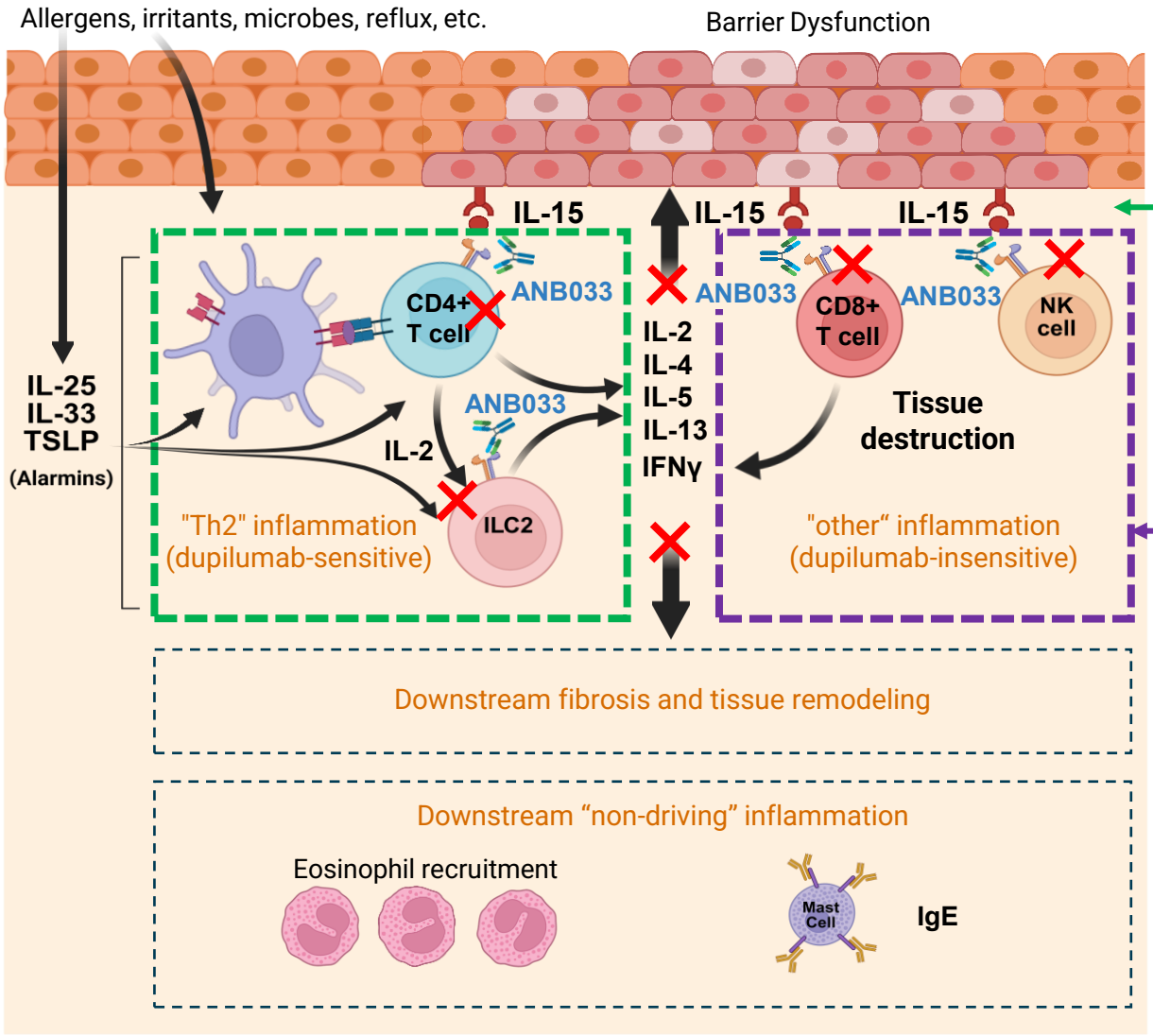
- Across both dupilumab-sensitive and insensitive mechanisms

Broad IL15 expression by structural cells

- Epithelial cells, myeloid cells and lymphocytes

Ding et al, Nature Commun. 2024 Apr 18;15(1):3344; UMAP of single-cell RNA-seq data from EoE biopsies, colored by expression of gene pairs: Expression values are SCTransform-normalized; a color scale is used: red or blue = high gene expression, gray = no expression.

Similar to CeD, ANB033 targets multiple drivers of EoE biology addressing both dupilumab sensitive and insensitive pathways



CD4+ and ILC2 (dupilumab-sensitive)

- Reduces CD4+ T cell proliferation
- Reduces IL-5/13 from CD122+ ILC2 and CD4+ T cells

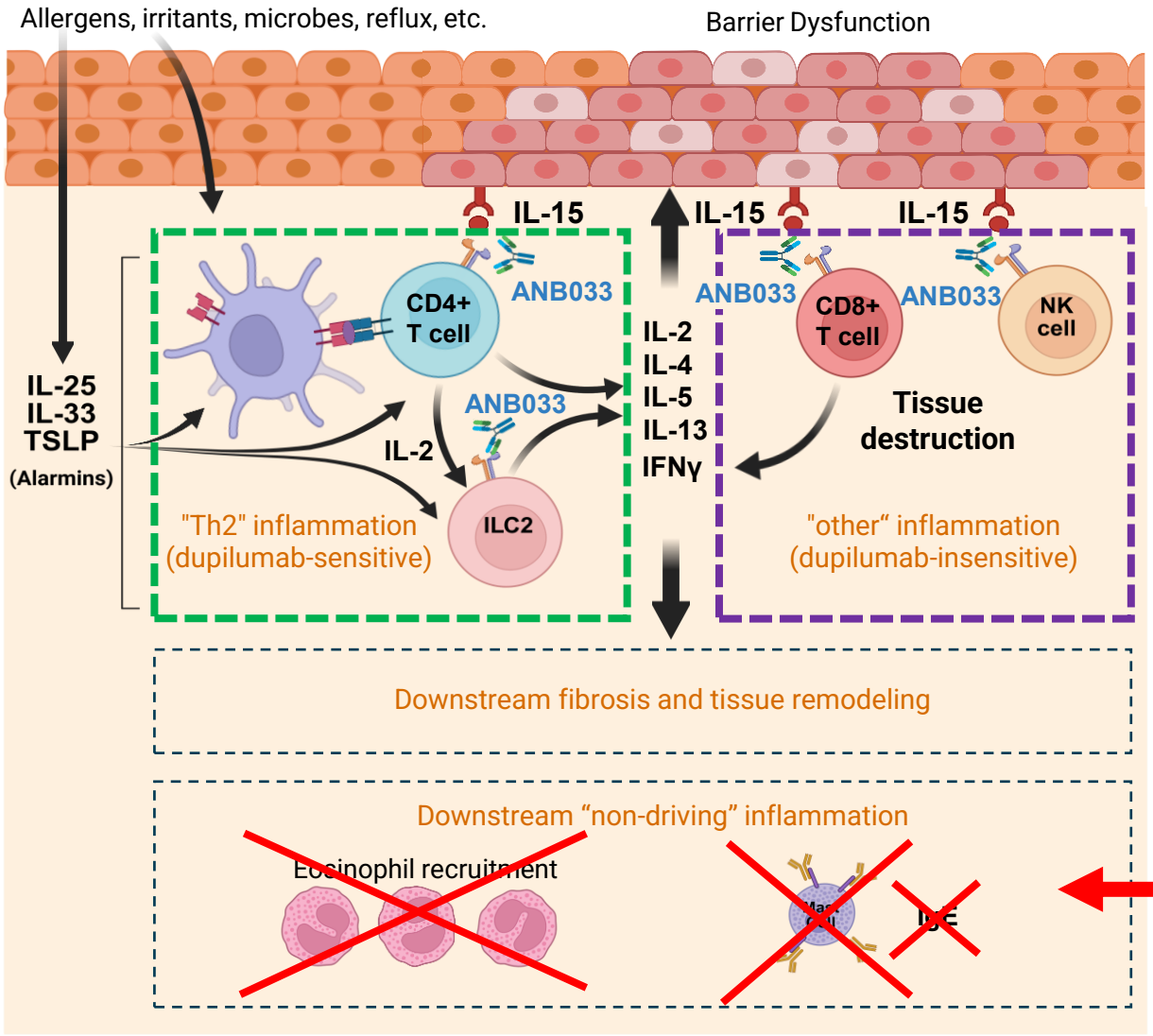
CD8+ and NK (dupilumab-insensitive)

- Inhibiting IL-15 signaling reduces –
  - IFNγ
  - Granzyme B
  - CD8+ T cell proliferation
  - NK cells

Upstream pathways lead to downstream eosinophilic infiltration into tissue

Adapted from Discepolo et. al. Gastroenterology. 2024; 167:90-103.

Mechanisms that target only downstream signals of inflammation have not been successful in EoE



Approved

sanofi

Dupilumab (anti-IL-4Ra)

Has PoC

NOVARTIS Calypso biotech

GIA-632 (anti-IL-15)

Ongoing

AMGEN

tezepelumab (anti-TSLP)

Failed mechanisms

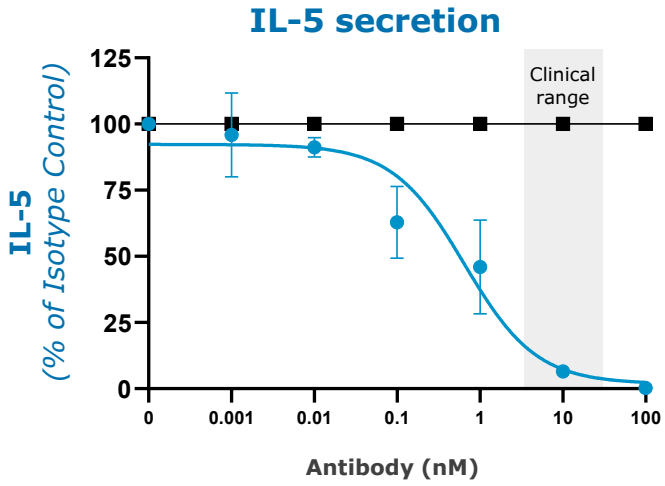
anti-cKIT, anti-IL-5Ra, anti-IgE

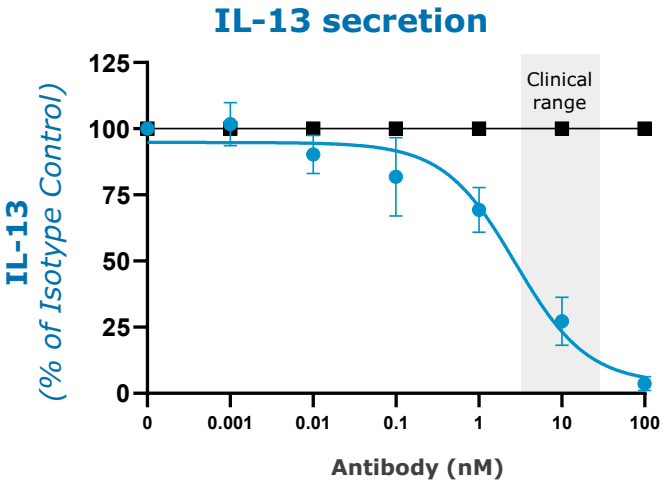
Celldex Genentech AstraZeneca

Adapted from Discepolo et. al. Gastroenterology. 2024; 167:90-103.

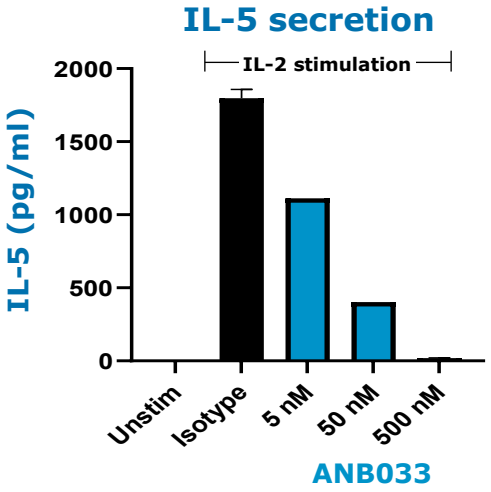
ANB033 reduces CD4+ T cell and ILC2 derived Th2 cytokines, proven drivers of EoE pathology

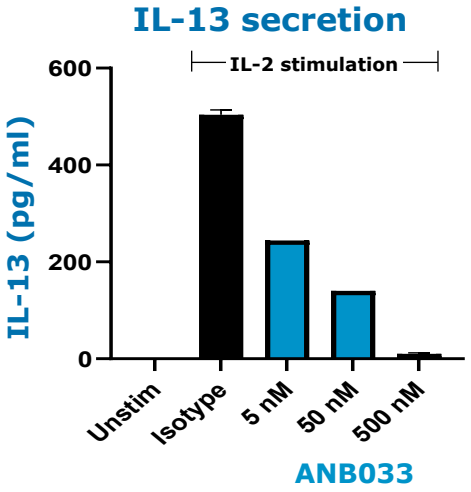
PBMC





ILC2

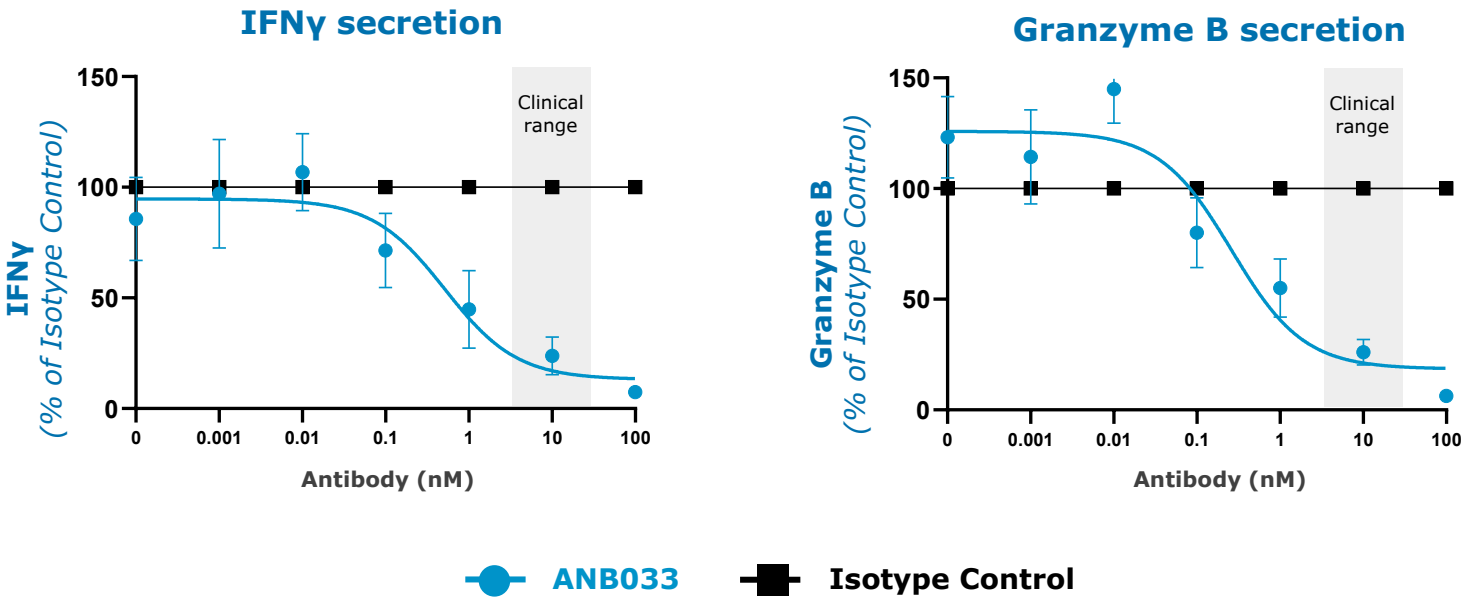




ANB033 Isotype Control

Top Panel: Human healthy PBMC were activated by anti-CD3/CD28 for 3 days; n=4 donors shown.
Bottom Panel: Purified human whole blood-derived ILC2 maintained in IL-33 were stimulated with IL-2 for 3 days; 1 of 6 similar representative donors shown.

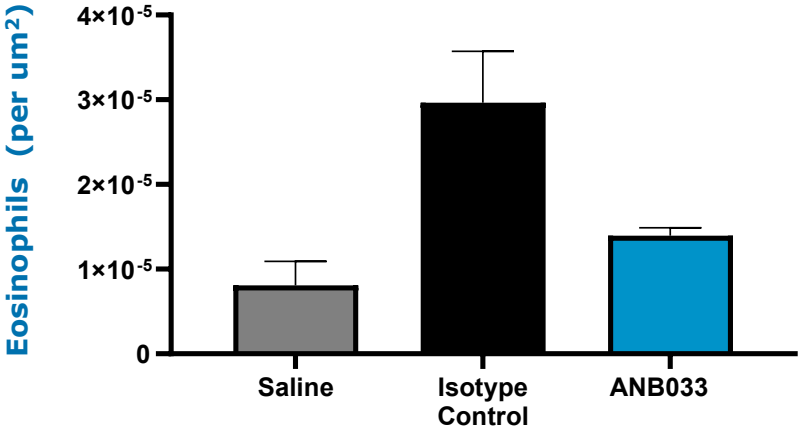
ANB033 reduces CD8+ T cell and NK cell derived Th1 cytokines and cytolytic markers



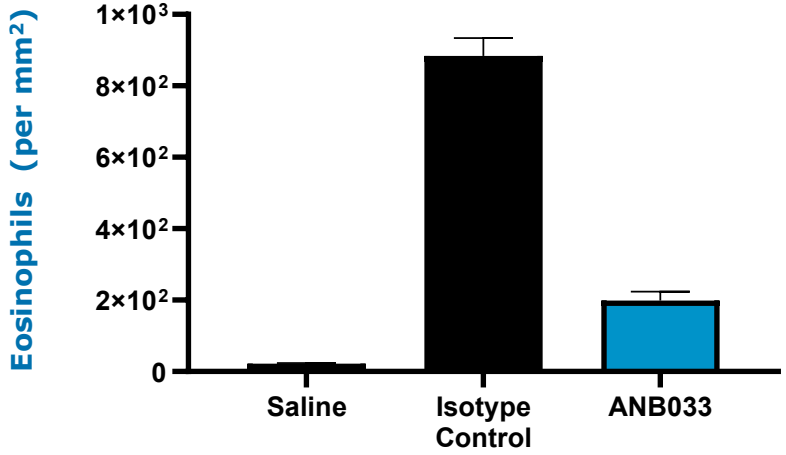
Human healthy PBMC were activated by anti-CD3/CD28 for 3 days; n=4 donors shown.

ANB033 prevents eosinophilia by targeting upstream inflammation

Esophageal eosinophils



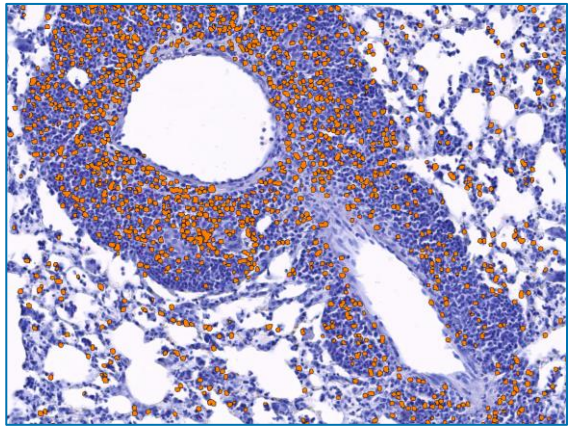
Lung eosinophils



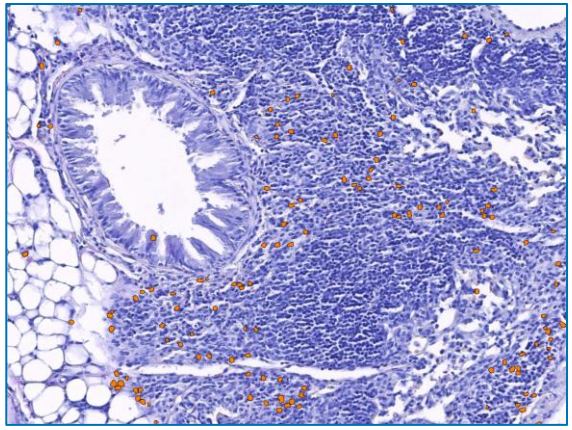
Aspergillus-induced eosinophilia

(Lung sample shown)

Isotype Control



ANB033



Model of eosinophilic inflammation: Balb/c mice were challenged intranasally with *Aspergillus fumigatus* TIW for 3 weeks. The treatment regimen includes a saline, isotype control, and ANB033 surrogate antibody (anti-mouse CD122 antibody with similar binding epitope and affinity to ANB033, administered at 10 mg/kg BIW for 3 weeks. Tissues were stained with H&E for histopathology assessment.

Agenda: ANB033 (CD122 Antagonist)

TOPIC	SPEAKER
CD122 biology and preclinical data	Martin Dahl, Ph.D., Senior Vice President, Research
Phase 1a in healthy volunteers	John Kwon, M.D., Ph.D. Vice President, Clinical Development
Drug development for CeD	Joseph Murray, M.D. Professor of Medicine Mayo Clinic College of Medicine, Rochester, MN
Phase 1b in CeD	Paul Lizzul, M.D., Ph.D. Chief Medical Officer
Commercial opportunity and next steps	Dan Faga Chief Executive Officer
Q&A	All

ANB033 Phase 1a trial ongoing in healthy volunteers

Objectives

- Safety and tolerability
- Evaluate PK and immunogenicity

Design

- All healthy volunteers have been dosed
  - ANB033: n=60
  - Placebo: n=20
- Administered both IV and SC dosing
- 10 cohorts: Four SAD IV, three SAD SC and three MAD SC
- Follow-up to ~7 months*

* The first 4 lowest SAD dose cohorts are followed through day 85; the three higher SAD dose cohorts are followed for 197 days; all MAD cohorts are followed through 218 days.

ANB033 demonstrated favorable safety, tolerability and PK profile in Phase 1a

Phase 1a results to date

✓ Safe and well tolerated

✓ No unexpected findings

✓ PK and PD support SC dosing

Favorable safety and tolerability

- No safety concerns at any dose
  - No SAEs, severe AEs, or discontinuations
  - Any adverse events mild or moderate
- No unexpected lab abnormalities
- No signs of viral infections
- No clinical pharmacology findings of concern

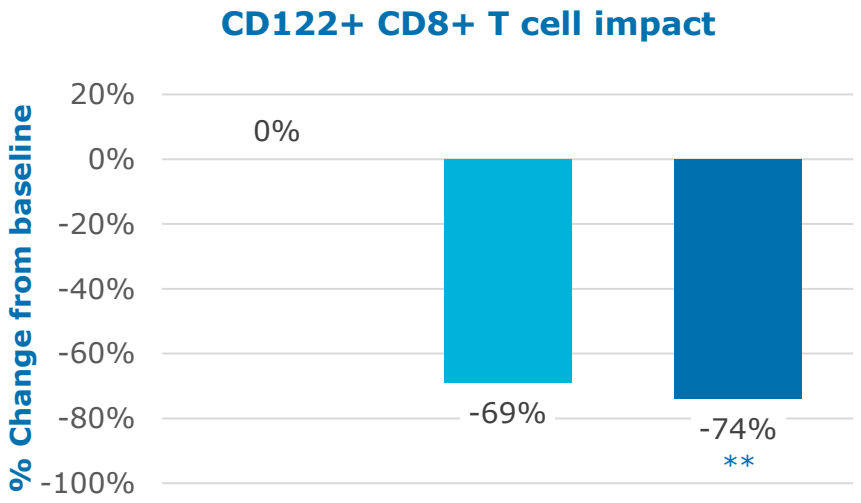
Rapid and sustained PK profile

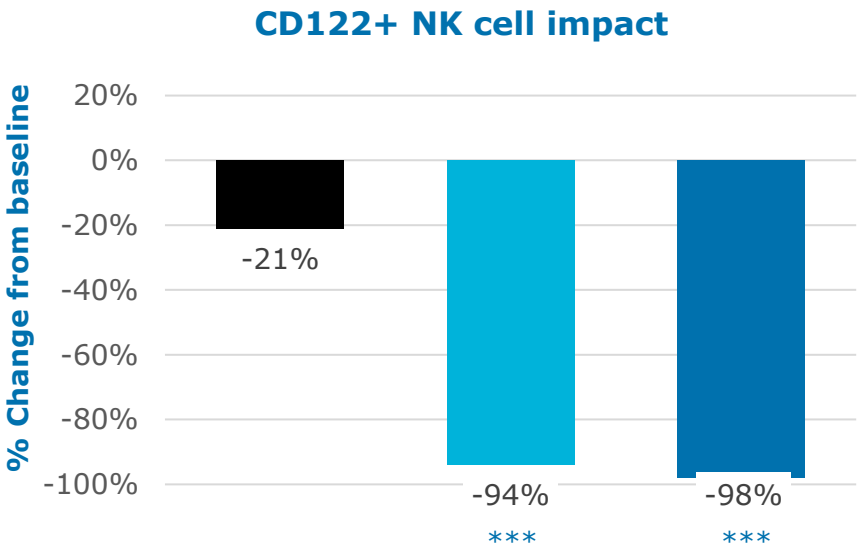
- Favorable 2 to 3-week half-life with IV and SQ dosing
- Full receptor occupancy (RO) within hours and maintained for >30 days
- Dose response observed
- Modeled to achieve >IC90 on CD8+ T cells subsets in GI tissue
- Overall, no impact on peripheral total Treg counts

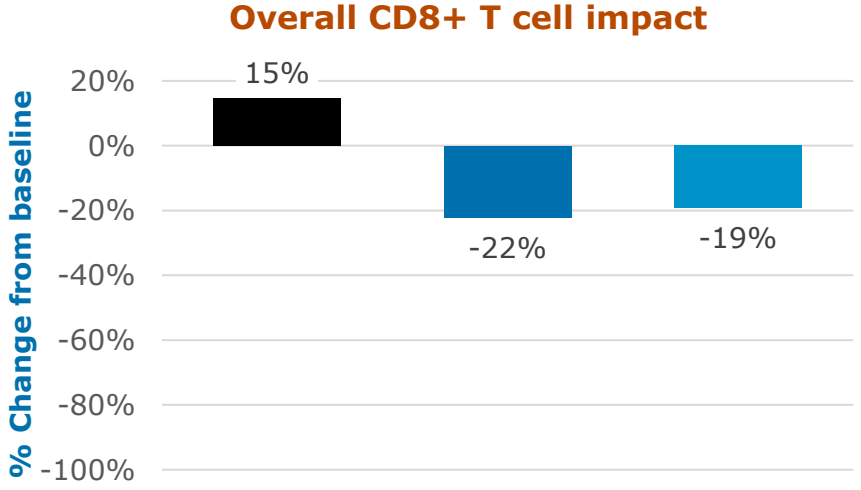
SAE = Serious adverse event

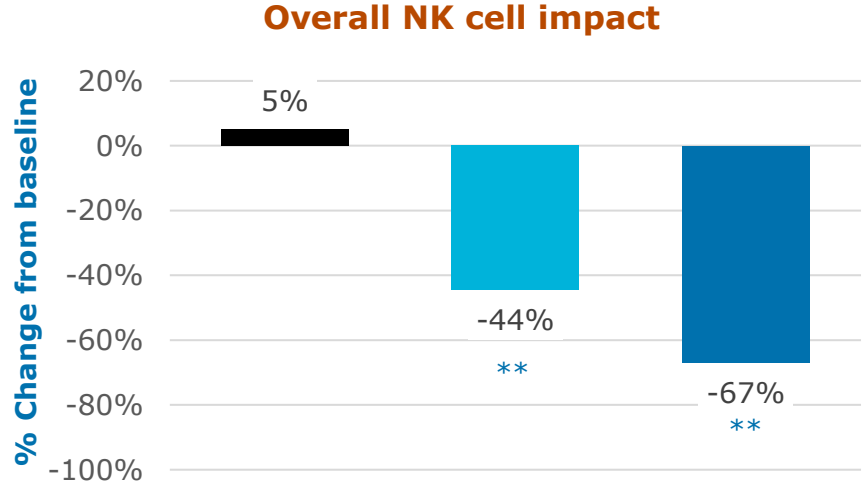
ANB033 significantly reduces CeD relevant CD8+ T cells and NK cells after single dose

Effect of ANB033 is limited to CD122 expressing cells





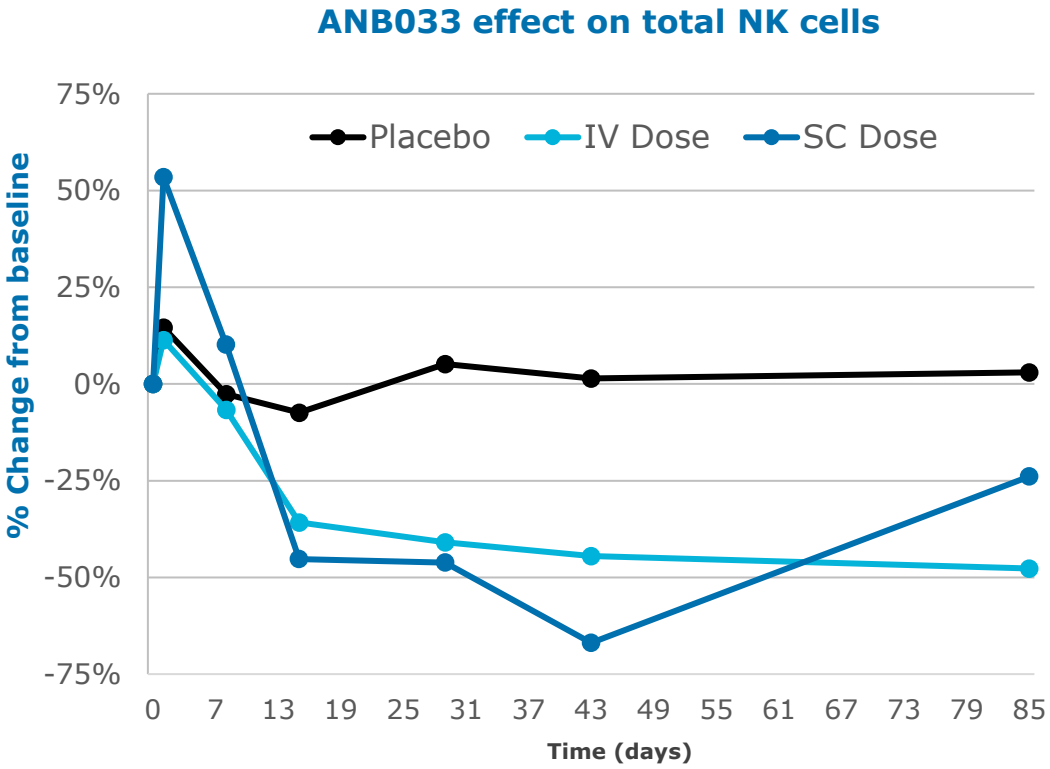


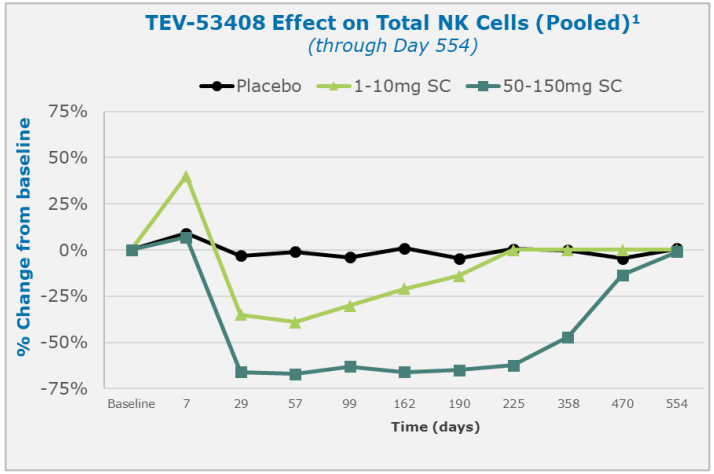


Placebo ANB033 – IV Dose ANB033 – SC Dose

Graphs reflect SAD data and maximum reductions were achieved within the first 43 days. *** p<0.001 **p<0.01

Anti-IL-15 and CD122 therapies have demonstrated sustained reduction in CD122+ NK cells with no observed safety issues





No safety signals observed in any CD122 or IL-15 trials to date after NK cell reduction

- ANB033 >50% <u>peak</u> total NK cell reduction with return towards baseline within 3 months
- TEV-53408: >50% <u>sustained</u> total NK cell reduction for 1 year with return to baseline over 18 months

1. Schnir et. al; Developing TEV-53408 for the Treatment of Celiac Disease: Summary of Preliminary Results from the First-in-Human Phase 1 Study in Healthy Volunteers, Single SC doses, DDW, May 2024. Phase 1a, single dose, study completed (n=60 TEV-53408, n=19 placebo). Moved into Phase 2a CeD trial in 48 adults while undergoing gluten challenge; primary trial completion in Sept. 2026.

Agenda: ANB033 (CD122 Antagonist)

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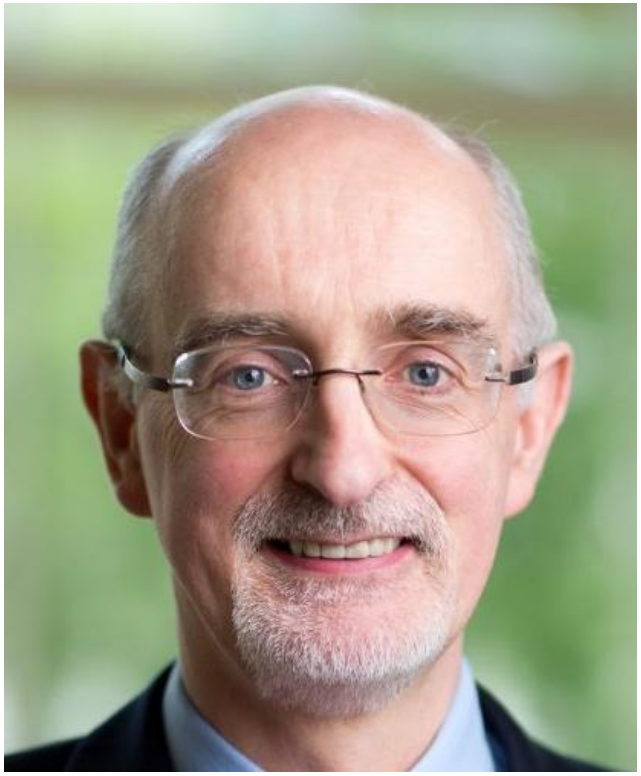
Commercial opportunity and next steps	Dan Faga Chief Executive Officer
Q&A	All

KOL discussion



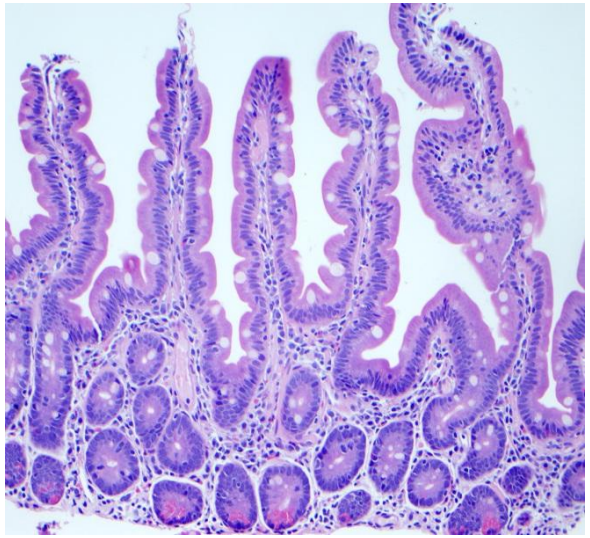
Joseph A. Murray, M.D.,
Professor of Medicine, Director, Celiac Disease Research, John and Shirley Berry Professor of Gastrointestinal Sciences, Division of Gastroenterology and Hepatology, Department of Internal Medicine, Mayo Clinic, Rochester, MN

- Co-founder and past president of North American Society for Study of CeD
- Contributed to 2013 guidelines and 2019 AGA practice update on diagnosing and monitoring CeD
- Published more than 450+ peer-reviewed papers on CeD
- Past chair of AGA's Intestinal Disease Section
  - Broad experience with GI disorders, including EoE

Gluten and Celiac Disease (CeD)

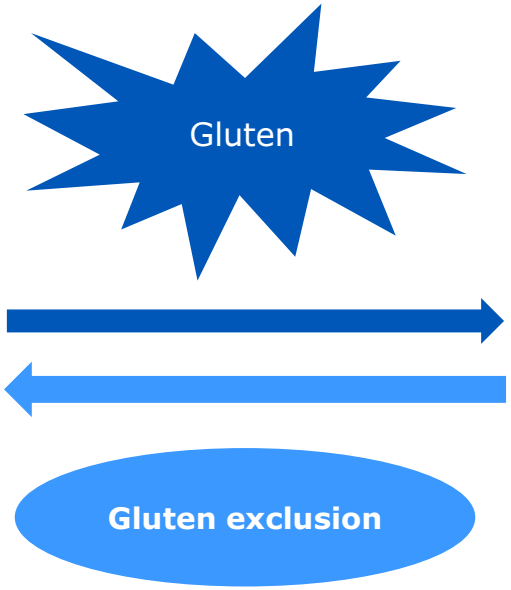
- Genetic predisposition
- Permanent intolerance to gluten

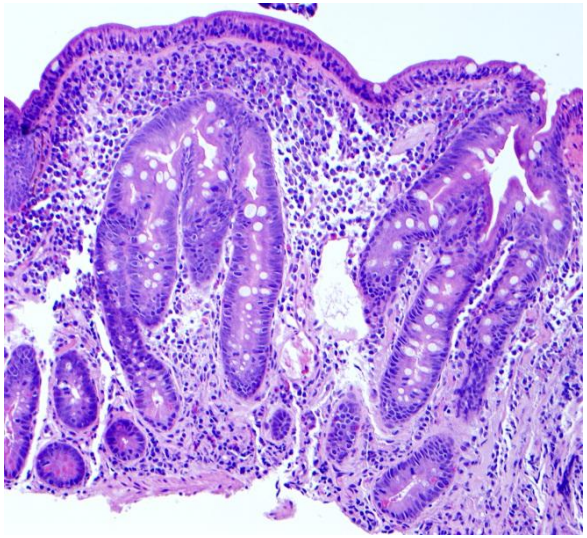
- Inflammation
- Villi destruction
- Crypt hyperplasia
- IEL proliferation



Normal histology

(Marsh 0)



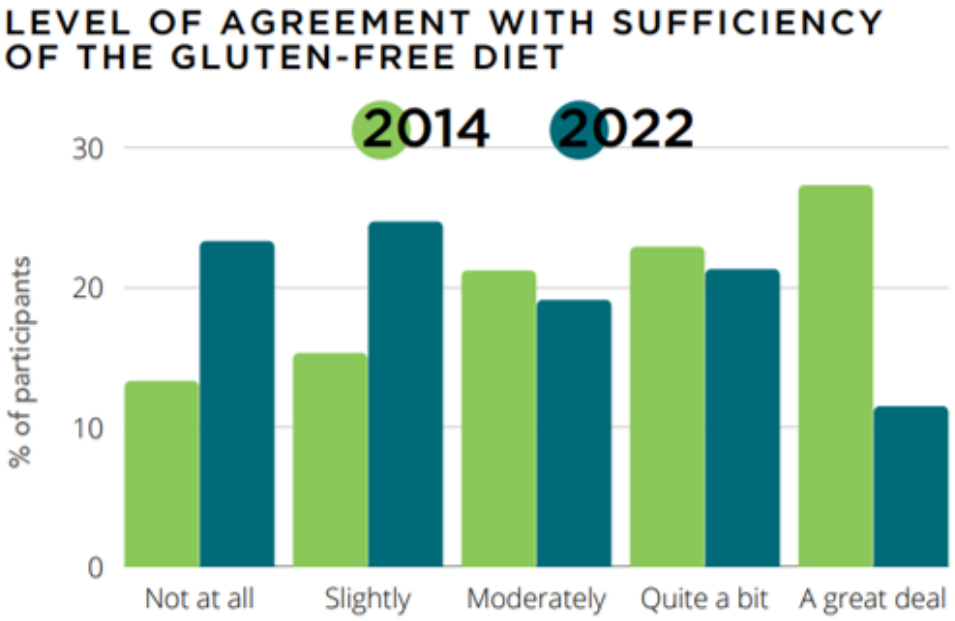


Total villous atrophy

(Marsh 3)

Note: Marsh score -- a histological grading system – classifies severity of intestinal damage by evaluating microscopic appearance (IELs and Vh:Cd) of a small intestine biopsy. Ranges from Marsh 0 (normal villi) to Marsh 3c (complete villous atrophy), with higher scores indicating progressively more severe damage

Majority of CeD patients desire new treatment options



There has been a significant decline in satisfaction over time

- In 2022, only 12% of participants agreed “a great deal” that a gluten free diet was a sufficient treatment, compared to 27% in 2014

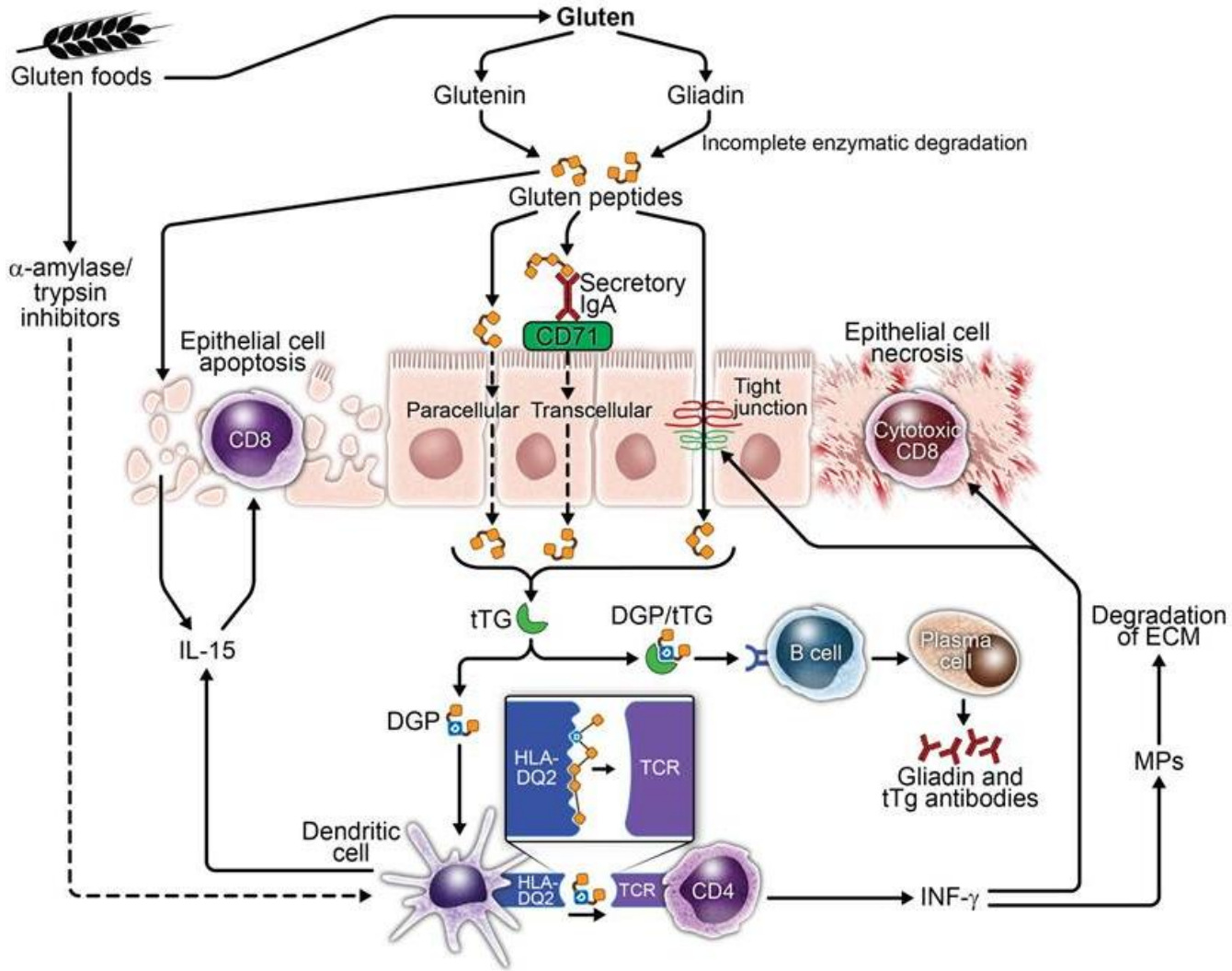
Consequences of persistent, chronic active CeD:

- GI symptoms: abdominal pain, diarrhea, constipation
- Severe malnutrition: vitamin deficiencies, anemia
- Reduced quality of life
  - Reduced social, emotional well being
  - Diminished physical functioning
- Osteoporosis
- Increased cancer risk: intestinal lymphoma, small bowel cancer

Regardless of gluten free diet, ~50% of patients suffer anemia or fatigue

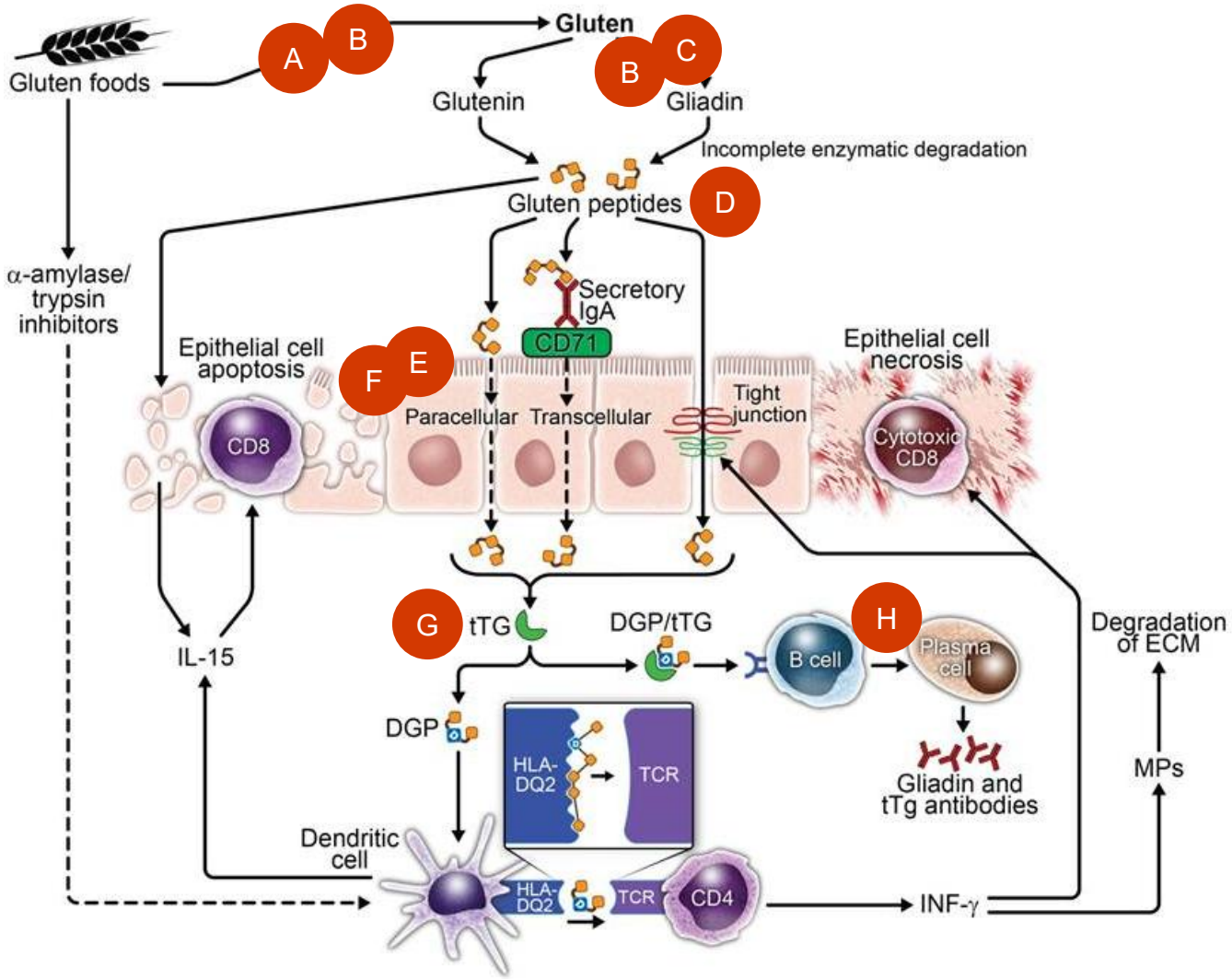
Adams et al Gastroenterology 2024;167:51-63; 1460 and 1140 CeD participants completed survey in 2014 and 2022

CeD has a multi-cell pathology



- Immune scarring is present in treated CeD
  - Epithelial-stromal-immune impacts / interactions
- IL-2, produced by CD4 T cells, elevates following gluten ingestion
  - Starting 2 hrs. after exposure
- Stressed epithelial cells express IL-15 (olmesartan)
- Key role of IL-15 contributes to:
  - Expansion of T cells, particularly IELs
  - Expansion and activation of NK cells

Some mechanisms that have been tried in CeD…



A — Toxic wheat → Non-toxic wheat

B — Enzymes + Wheat → Gluten peptide fragments

C — Protease supplement (IMGX003), Kumamax (TAK-062), and Allergan

D — Polymeric gluten binder

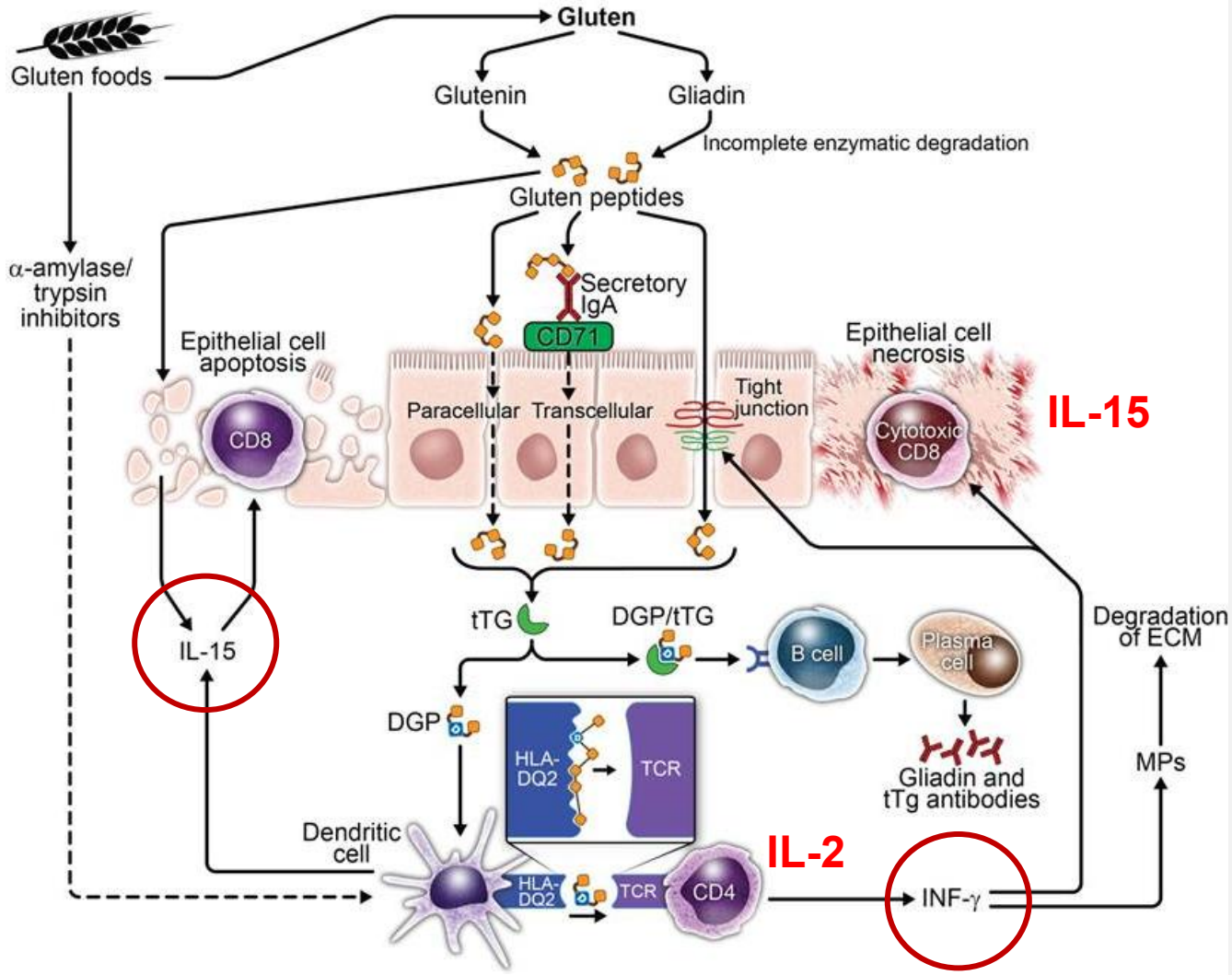
E — Probiotics (B. infantis)

F — Permeability inhibitor (larazotide acetate)

G — AntiTTG (ZED1227)

H — Nexvax

Rationale in targeting CD8 and CD4 T cells to broadly impact CeD inflammation

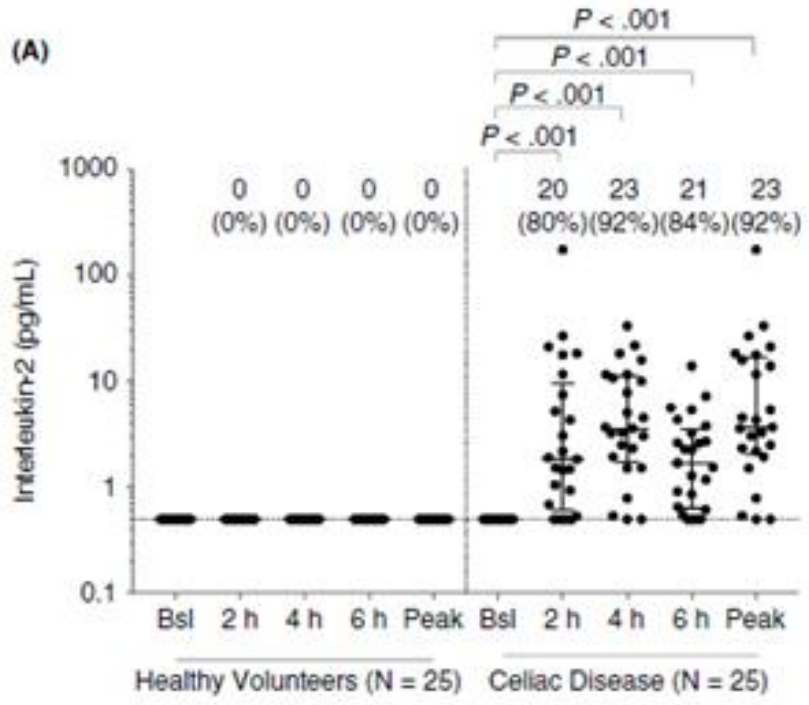


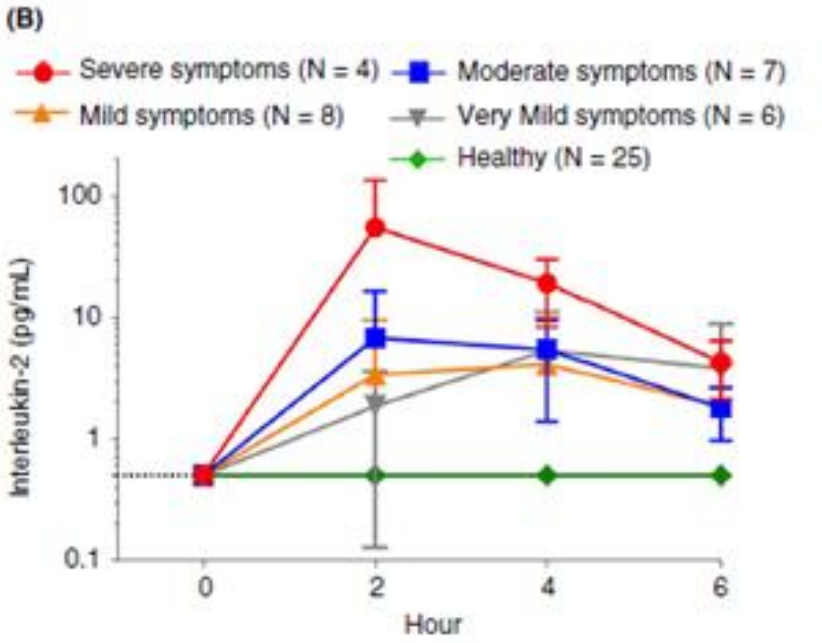
- Overactive IL-15 and IL-2 signaling drives pathogenic immune cell expansion and inflammation effects
- IL-15 is inflammatory cytokine
  - Expressed by stressed epithelial cells
  - Supports T cell and NK cell homeostasis and expansion
  - Binds intercellularly
  - IL15/IL15R transported to cell surface by stromal cells and APCs
- IL-15 expression in epithelium (mid villi), crypts and LP increased in CeD patients
- IL-2 stimulates CD4 Tem cell activation and proliferation and IFNγ production, leading to IL-15 secretion

TEM= T effector memory

Serum IL-2, produced by CD4 T cells, elevated in CeD patients

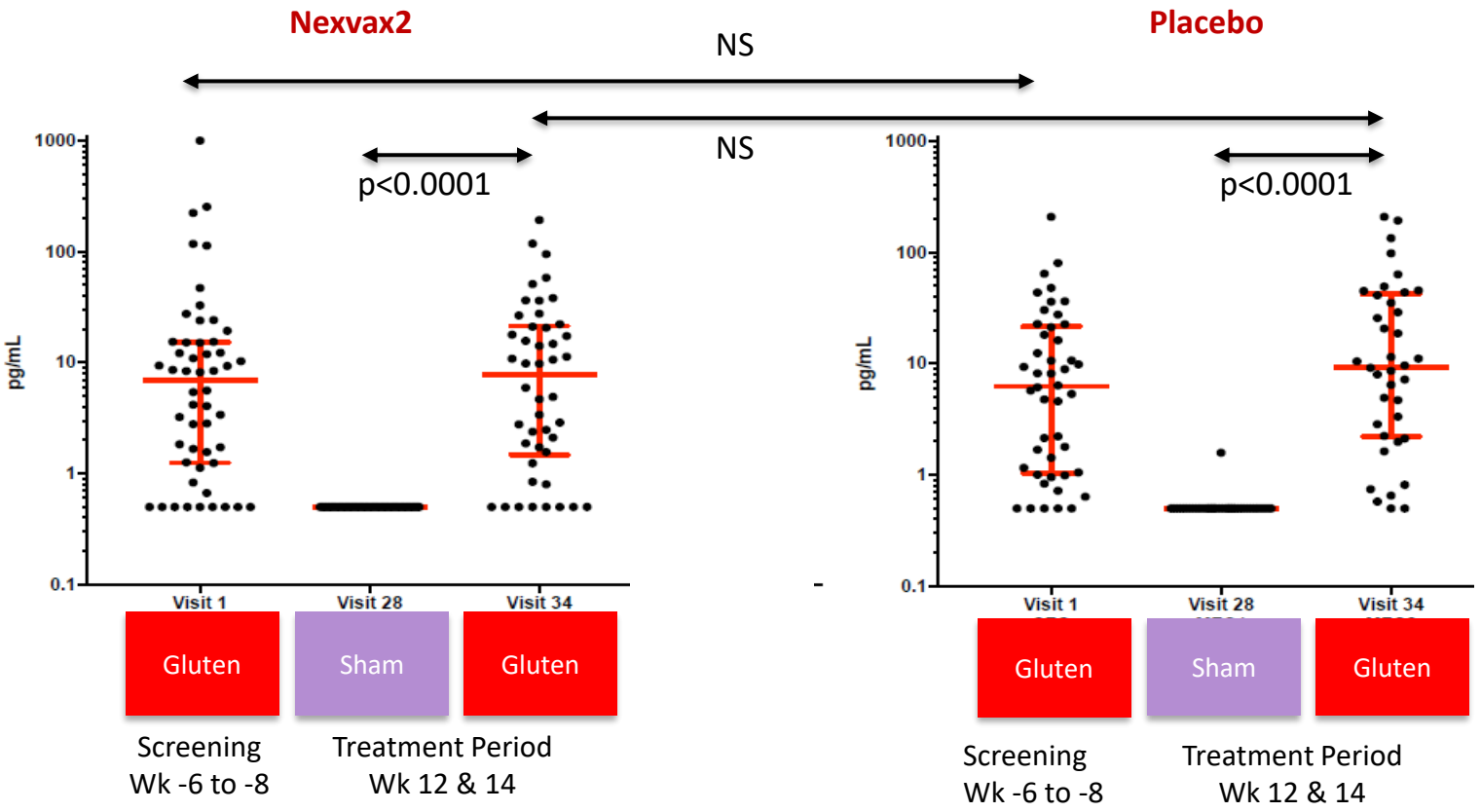
- Increase in IL-2 seen within two hours of gluten ingestion
- Magnitude of IL-2 response correlates with severity of symptoms
- IL-2 elevation key marker for central role of CD4 T cells
- IL-2 elevation is not observed in healthy controls, CeD patients provided sham GC or non-celiac gluten sensitivity[1,2]





1 Tye-Din et al Aliment Pharmocol Ther 2019;00:1-10
2 Cartee et al Am J Gastroenterol 2022; 117:319-326

Gluten exposure induces significant serum IL-2 increase vs. sham

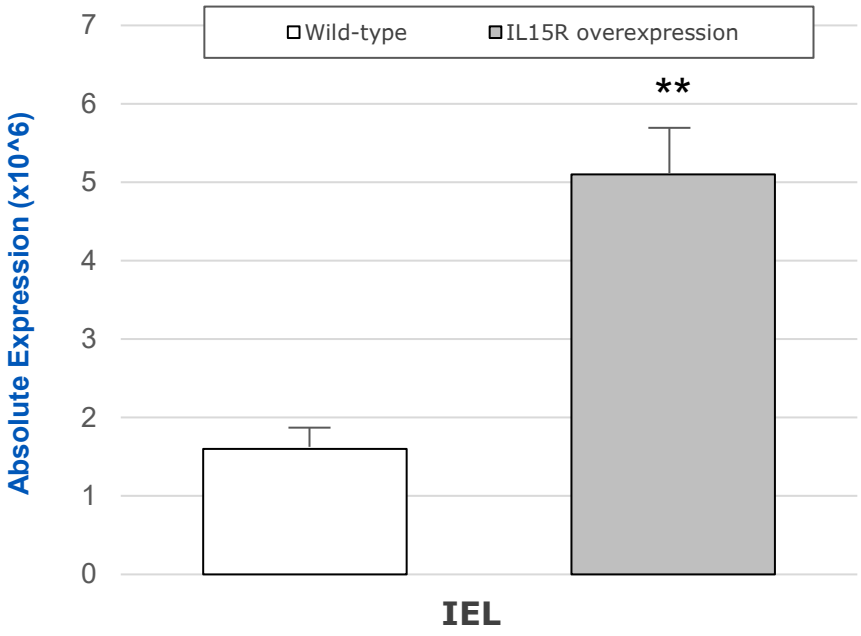


Immunotherapy aiming to restore tolerance in CD4+ T cells failed to reduce significant IL-2 induction from gluten challenge

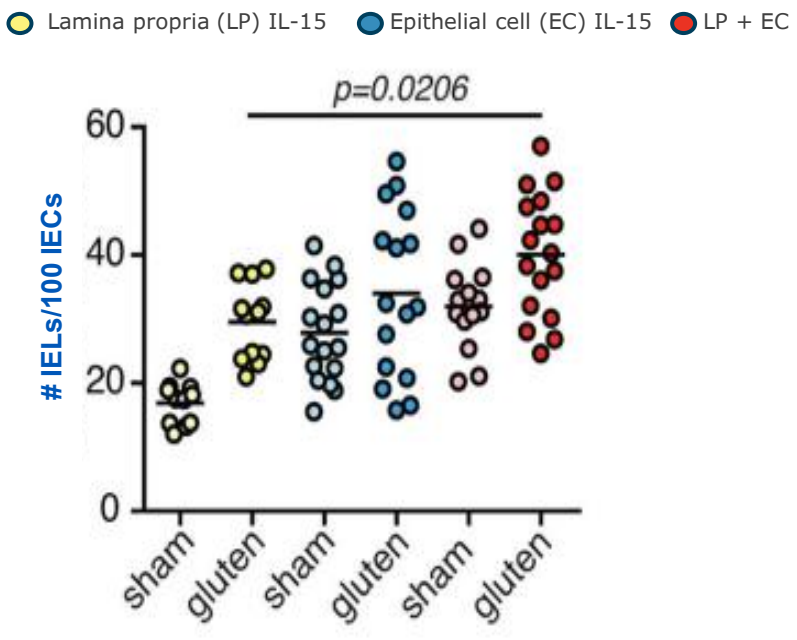
Note: Serum levels 4 h after.

IL-15 a key driver of IEL expansion

Mouse model overexpressing IL-15Rα



Three mouse models overexpressing IL-15

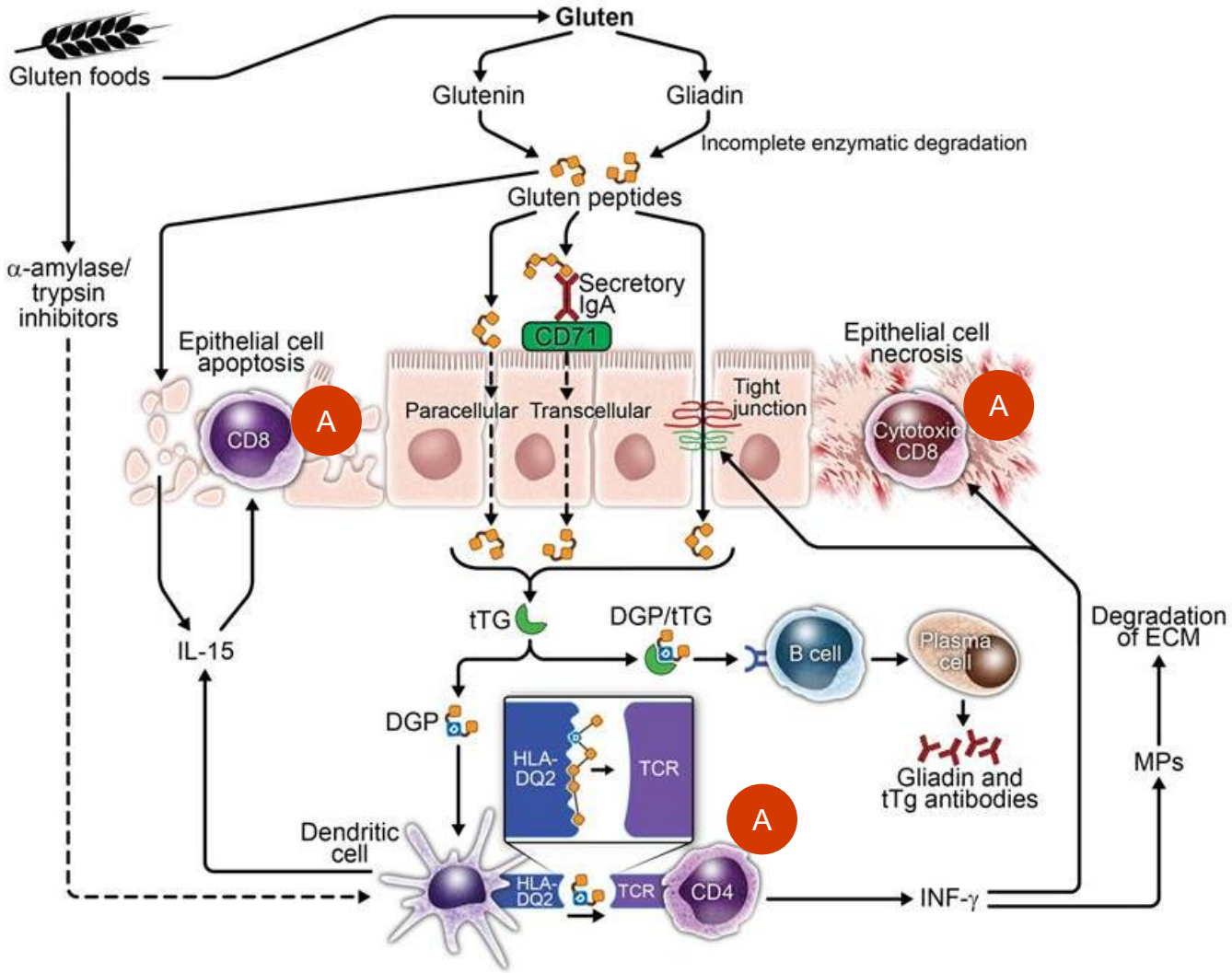


Intestinal epithelial IL-15 expression drives increases in IELs

IL-15 expression in gut drives gluten-induced increases in IELs

Left panel: Mouse model over-expressing IL-15Ra in the intestinal epithelial cell
Right panel: Mouse models with genetic predisposition to celiac disease (HLA-DQ8) and IL-15 expression driven in the epithelium and/or the lamina propria

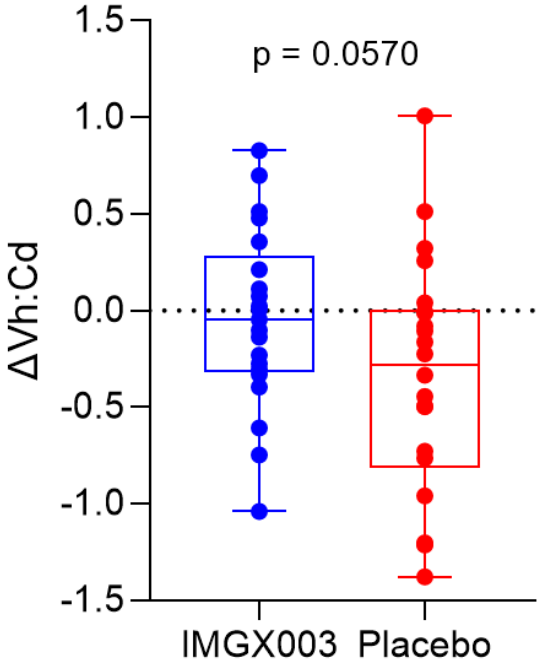
Inhibiting CD122+ CD4+ and CD8+ cells and signaling of IL-15 and IL-2



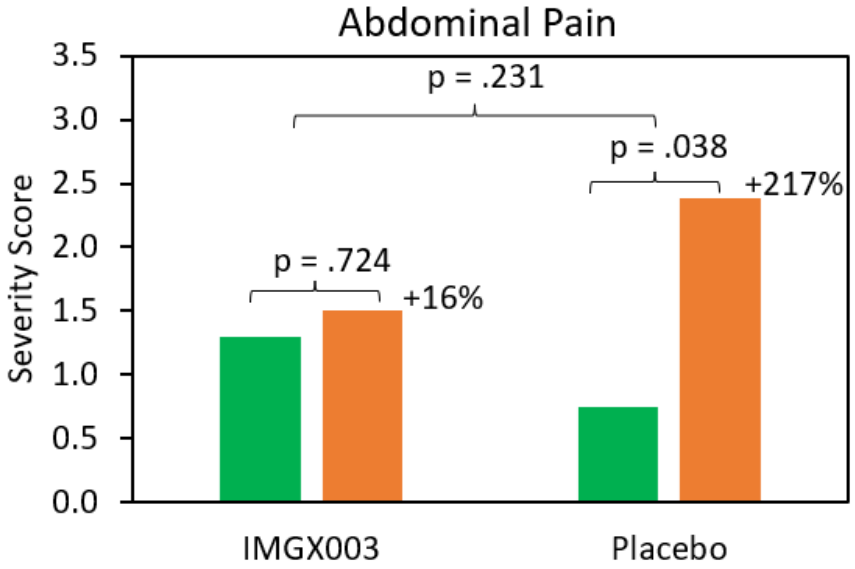
- CD122 shared receptor subunit through which both IL-15 and IL-2 signal
- Expressed on range of immune cells: CD8+ and CD4+ T cells, NK cells
- Inhibiting IL-15 and IL-2 signaling inhibits subsets of these cells, reducing inflammation and tissue destruction
- Targeting CD4 T cell activity leads to reduced inflammation and downstream immune responses, ultimately decreasing CeD consequences

A CD122 antagonist

Latiglutenase: MOA effective in preventing gluten induced injury in P1b but not in healing established disease



Latiglutenase attenuates mucosal damage by ~80% based on ratio of means for IMGX003 *vs.* placebo arms



Based on means latiglutenase attenuated abdominal pains for 2g gluten per day by 93%

This MOA was not predictive for symptomatic CeD patients with mucosal damage and failed P2 study

Oberhuber G, Granditsch G, Vogelsang H. The histopathology of celiac disease: time for a standardized report scheme for pathologists. Eur J Gastroenterol Hepatol. 1999;11(10):1185–1194

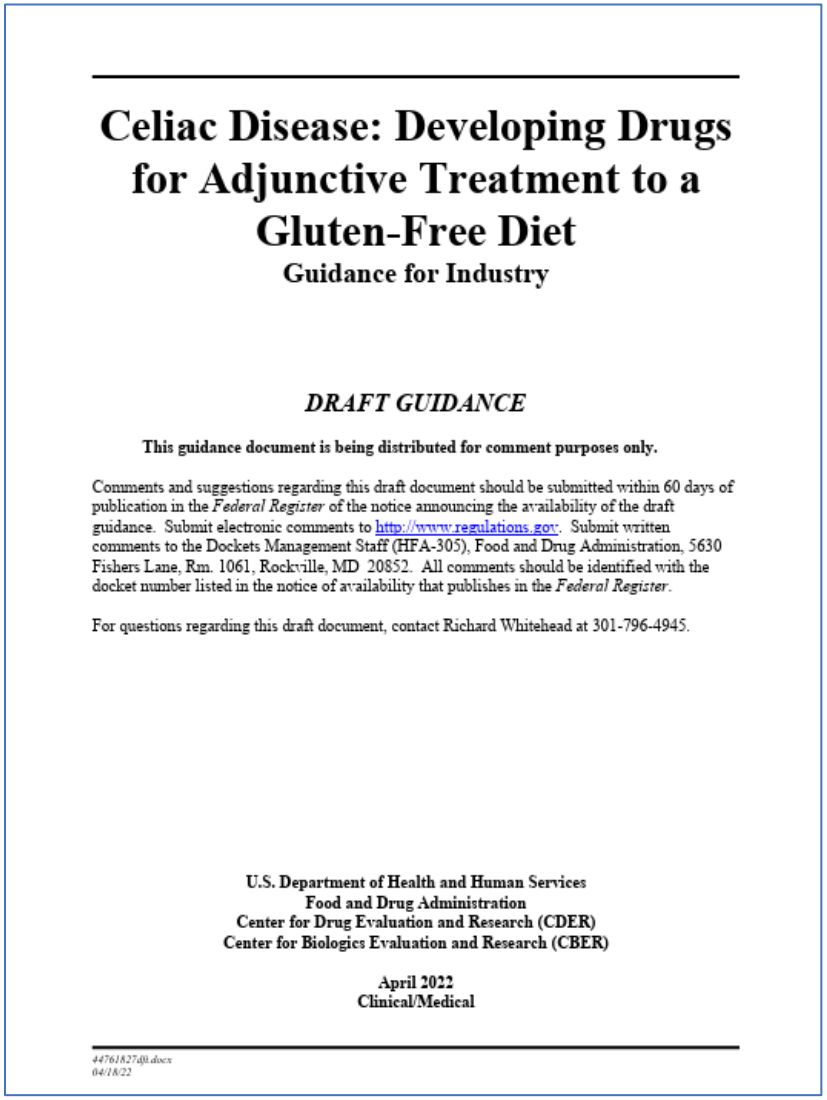
Considerations for Phase 1b CeD trial design

- Traditional P1b gluten challenge
  - Controlled symptoms and limited mucosal damage at baseline
- P2b and P3 population targets symptomatic CeD patients with mucosal damage
- Drugs whose MOA breaks down gluten (e.g., latiglutenase), have shown positive effects in P1b gluten challenge
  - Not predictive for P2b population
- For immunologic MOAs that treat inflammation, a P1b trial may be predictive of P2b
  - Could directly result in mucosal healing
- Tolerating gluten in P1b gluten challenge is difficult, leading to non-compliance

For drugs with upstream immunologic MOA, early P1b trial data that demonstrate mucosal healing and/or protection from gluten challenge, provide key foundation for further clinical development

Perspectives on FDA guidance for CeD

- GREAT Conference*
  - Significant public engagement at advocacy meetings (Beyond Celiac 2024)
- **Alignment on P2/P3 target population: symptomatic CeD despite a GFD***
  - **Need to prevent symptoms of gluten exposure in CeD patients and improvement of histologic injury**
- FDA DRAFT guidance available for registrational trials –
  - Inclusion criteria: evidence that disease is active and causing symptoms
  - Co-primary endpoints: both symptoms (PRO) **and** histology (various)
    - Both must be met as a whole



Celiac Disease: Developing Drugs for Adjunctive Treatment to a Gluten-Free Diet

Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to http://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document, contact Richard Whitehead at 301-796-4945.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

April 2022
Clinical/Medical

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04/18/22

GREAT Conference= The Group on Research, Education, and Training (GREAT) provides professional development to, and fosters the exchange of information and ideas among the faculty and administrative leaders of biomedical Ph.D., M.D.-Ph.D. and postdoctoral programs; GFD= Gluten free diet

Agenda: ANB033 (CD122 Antagonist)

TOPIC	SPEAKER
CD122 biology and preclinical data	Martin Dahl, Ph.D., Senior Vice President, Research
Phase 1a in healthy volunteers	John Kwon, M.D., Ph.D. Vice President, Clinical Development
Drug development for CeD	Joseph Murray, M.D. Professor of Medicine Mayo Clinic College of Medicine, Rochester, MN
Phase 1b in CeD	Paul Lizzul, M.D., Ph.D. Chief Medical Officer
Commercial opportunity and next steps	Dan Faga Chief Executive Officer
Q&A	All

Symptomatically controlled CeD patients present with range of histologic activity

Histology *(Vh:Cd ratio)*

Symptoms

Symptomatically controlled on GF diet

Gluten challenge
Phase 1 population

teva *(Phase 1b)*

NOVARTIS / Calypso *(Phase 1b)*

FORTE *(Phase 1b/2a)*

Nearly all P1b/P2a studies only assess ability **to prevent** gluten-induced mucosal injury

- Gluten challenge: patients with higher Vh:Cd ratios (>2.5 or >2.0)

Persistent mucosal damage despite paucity of symptoms

AnaptysBio *(Phase 1b)*

Added additional cohort to P1b **to inform on potential to heal mucosa** in patients with existing histologic mucosal damage and further derisk 2b

Symptomatic on GF diet

Non-responsive

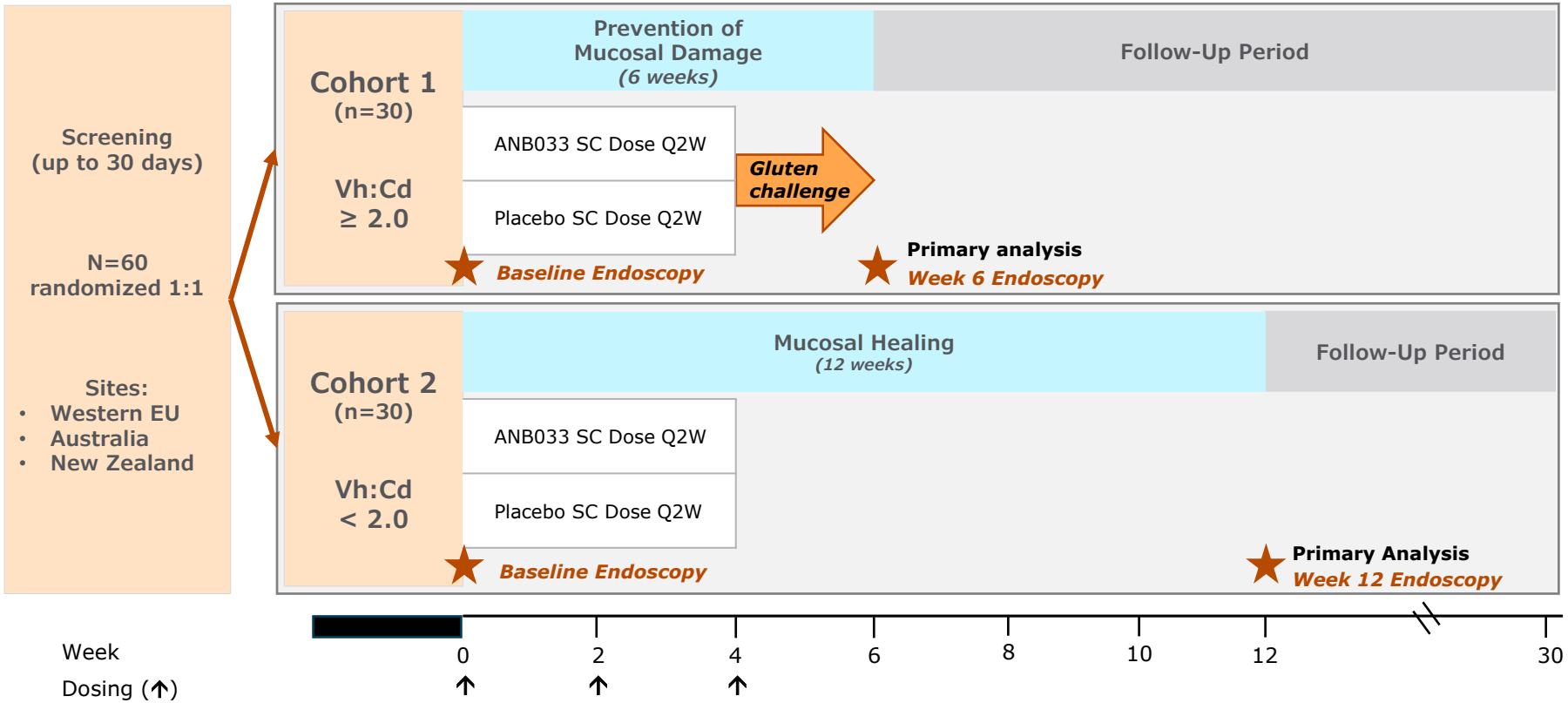
sanofi *(Phase 2b)*

Goal of P2b or P3 to assess if drug can heal damaged mucosa and restore normal symptomatology

GF diet = Gluten free diet.

ANB033 Phase 1b trial in CeD initiated

Anticipate top-line data by year-end 2026



Safety	Safety and tolerability in adult participants with well-controlled CeD
Clinical PK	PK and immunogenicity
Efficacy	• Change from baseline in Vh:Cd ratio • IEL count • PROs, including Celiac Disease Symptom Diary (CDSD)
Biomarkers	Characterize ANB033 effects on circulating biomarkers, including robust translational plan

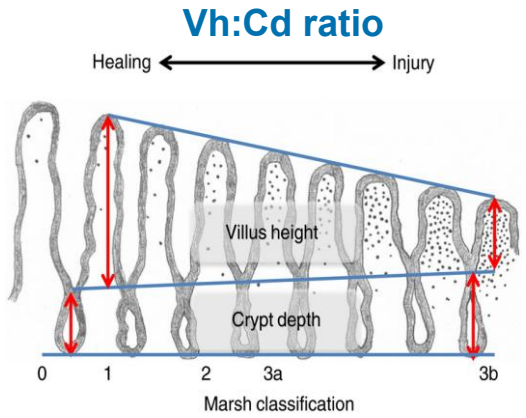
CeD quantitative histology and qualitative symptom assessments

Histology *(Vh:Cd ratio)*

3.5	2.5	2.0	1.5	1.0	0.1
Normal		Mucosal damage			Abnormal

Quantitative histology measures villus height (Vh), crypt depth (Cd) and intra-epithelial lymphocyte count (IEL per 100 enterocytes) to assess histologic changes

- Vh:Cd ratio
- IEL count

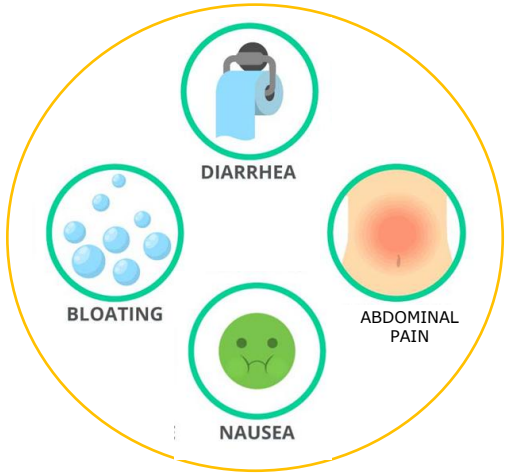


Symptoms

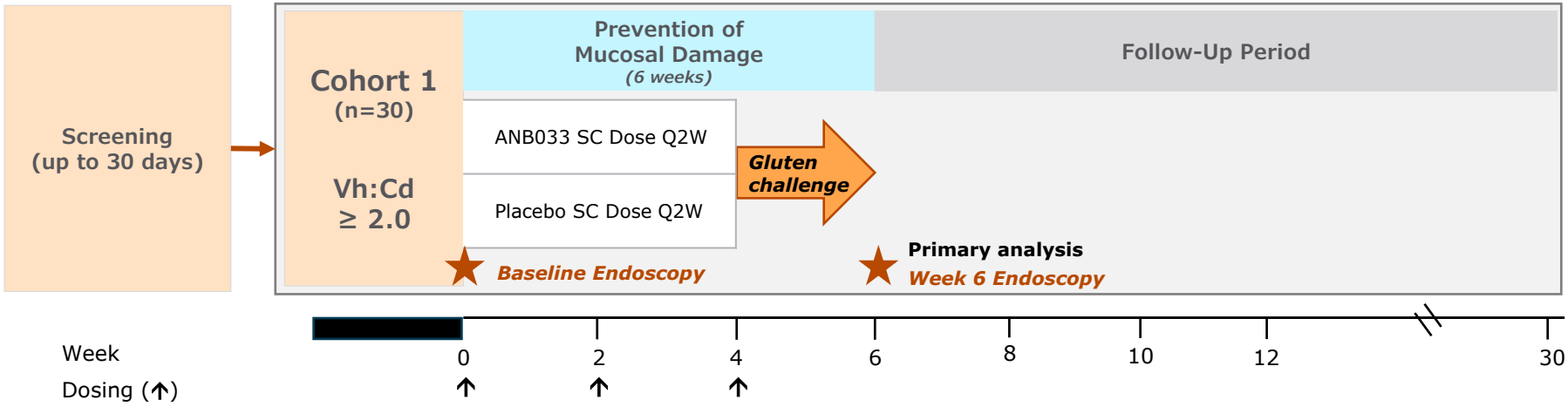
Asymptomatic	Symptom controlled	Poorly controlled

Qualitative evaluation to track changes during treatment or gluten exposure

- CeD Symptom Diary (CDSD) monitors symptoms, including
  - Severity: nausea, abdominal pain, tiredness, and bloating
  - Frequency: vomiting, diarrhea, and bowel movements



Cohort 1 (Vh:Cd ≥ 2.0) is a gluten-challenge to assess prevention of mucosal damage



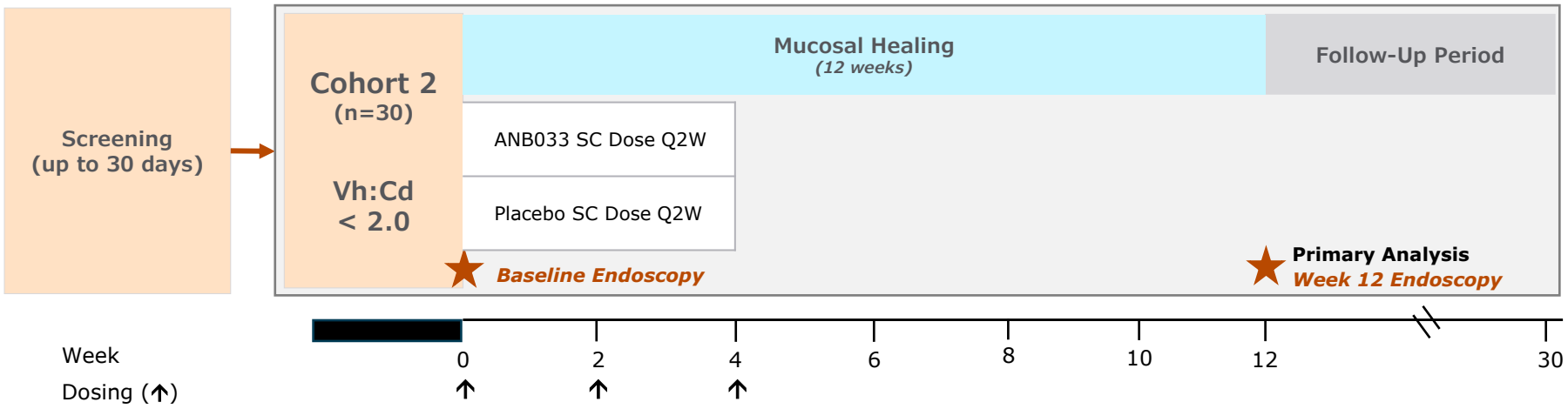
Minimal evidence of mucosal damage (Vh:Cd ≥ 2.0)

- Symptom-controlled CeD patients
- Receive GC after pre-treatment with ANB033 vs. PBO

- ANB033 dose at Week 0, 2, 4 (pre-treatment)
- Gluten challenge allows for controlled induction of mucosal damage
  - Beginning Week 4, 6g gluten dose daily (study supplied cookie) for two weeks through Week 6
- Endoscopy at Week 6
  - Assess prevention of gluten-induced mucosal damage

GC = Gluten challenge

Cohort 2 (Vh:Cd < 2.0) assesses ability to heal mucosal damage in symptom-controlled patients



Persistent evidence of histologic CeD activity (Vh:Cd < 2.0)

- Symptom-controlled CeD patients
- Substantial mucosal damage already present (no gluten-challenge)
- *Proxy: nonresponsive patients*

- ANB033 dose at Week 0, 2, 4
- Endoscopy at Week 12
  - Assess healing 8 weeks after last ANB033 dose
  - Maximize healing time given ANB033 prolonged tissue exposure and PD properties

GC = Gluten challenge

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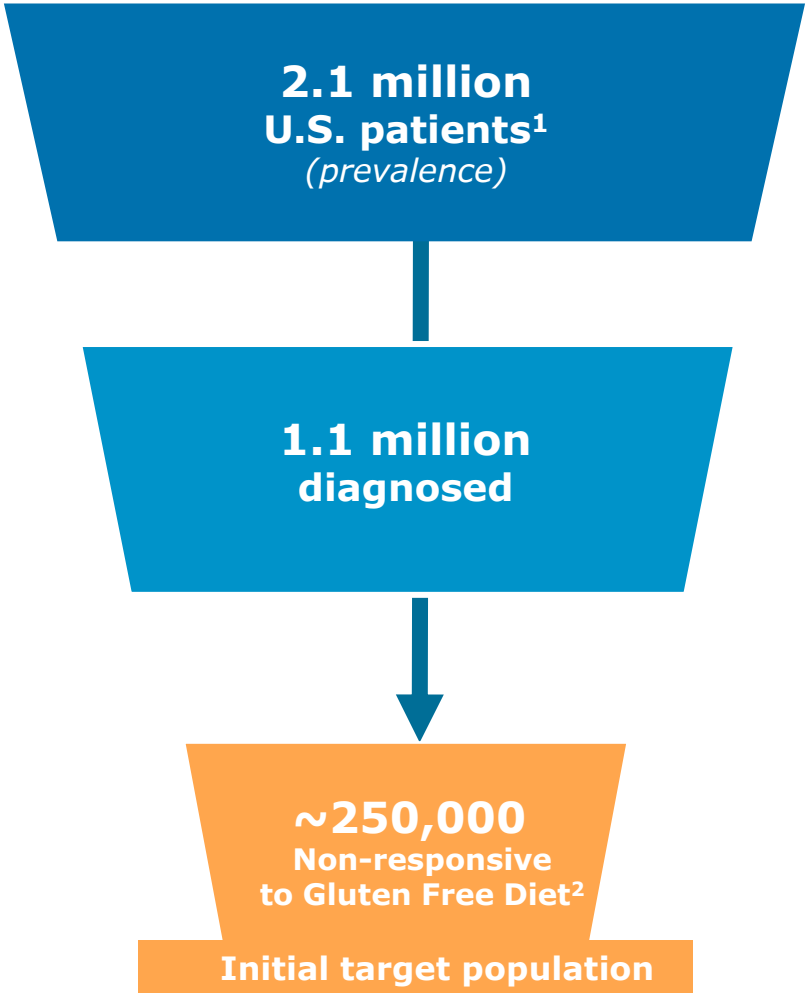
Potential blockbuster opportunity for ANB033 in non-responsive CeD



High disease burden

- Debilitating symptoms, social isolation
- Disease awareness driving growth
- No approved therapies

CD122s differentiated from other Tx in development

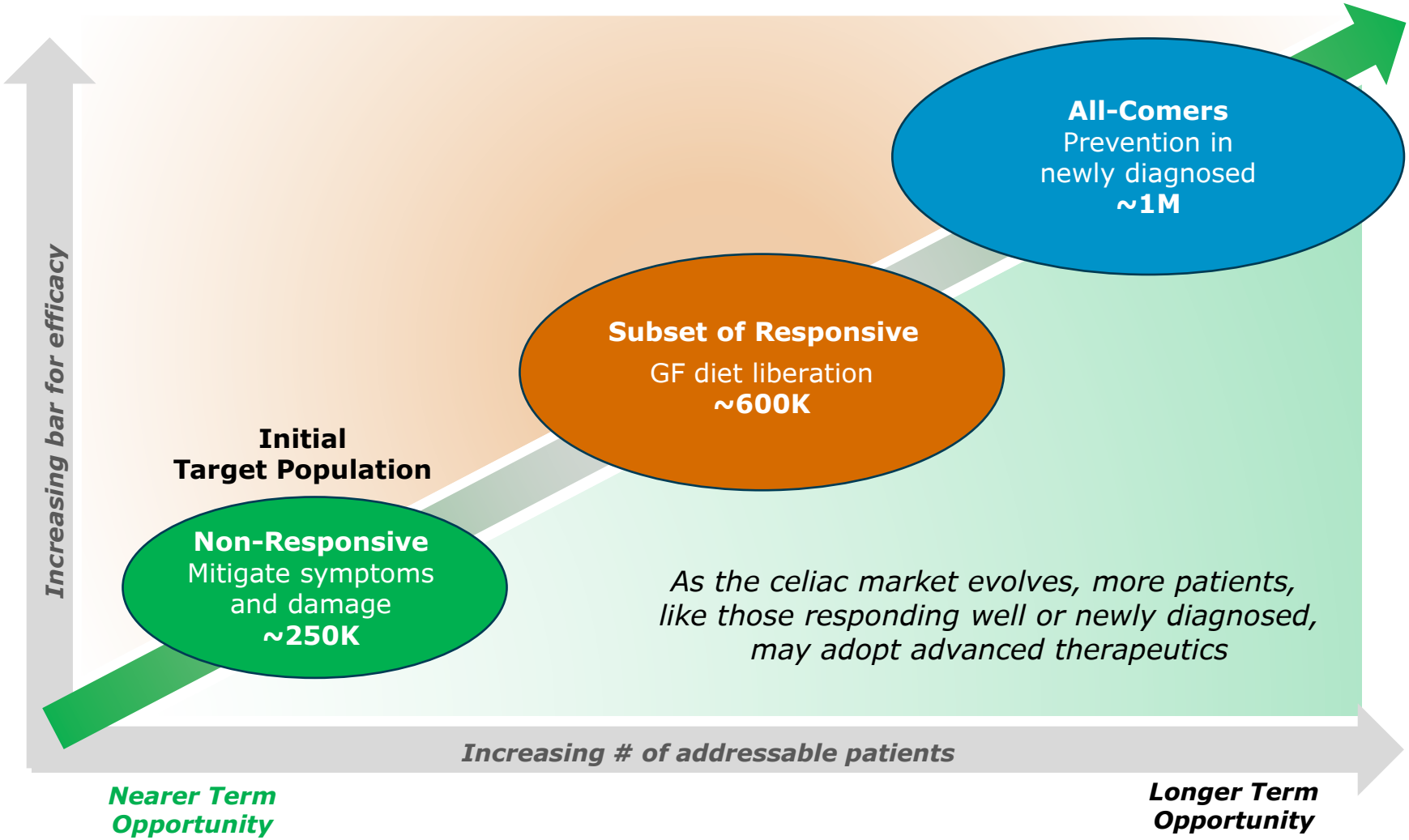
- HCPs favor MOA that targets both symptoms and histology

$4-5B U.S. market in patients non-responsive to gluten-free diet

- Potential to reach IBD diagnosis and biologic penetration analogs given substantial unmet need
- Expect reimbursement with limited utilization management

1. Singh et al. (2018), Choung et al. (2016), Katz et al. (2011), Trinity Life Sciences Commercial Assessment HCP Primary Market Research (2025). CeD sizing reflects future US market in 2030 assuming growth in diagnosis rate based on historic trends and projected growth with entrance of novel therapies
i2. Leffler et al. (2007), Abhijeet et al. (2016), Aggarwal et al. (2025) Mahadev et al. (2017, Trinity Life Sciences Commercial Assessment HCP Primary Market Research (2025) Percent of CeD non-responders to Gluten Free Diet with or without villous atrophy.

New therapies in CeD could grow market in responsive and newly diagnosed patients



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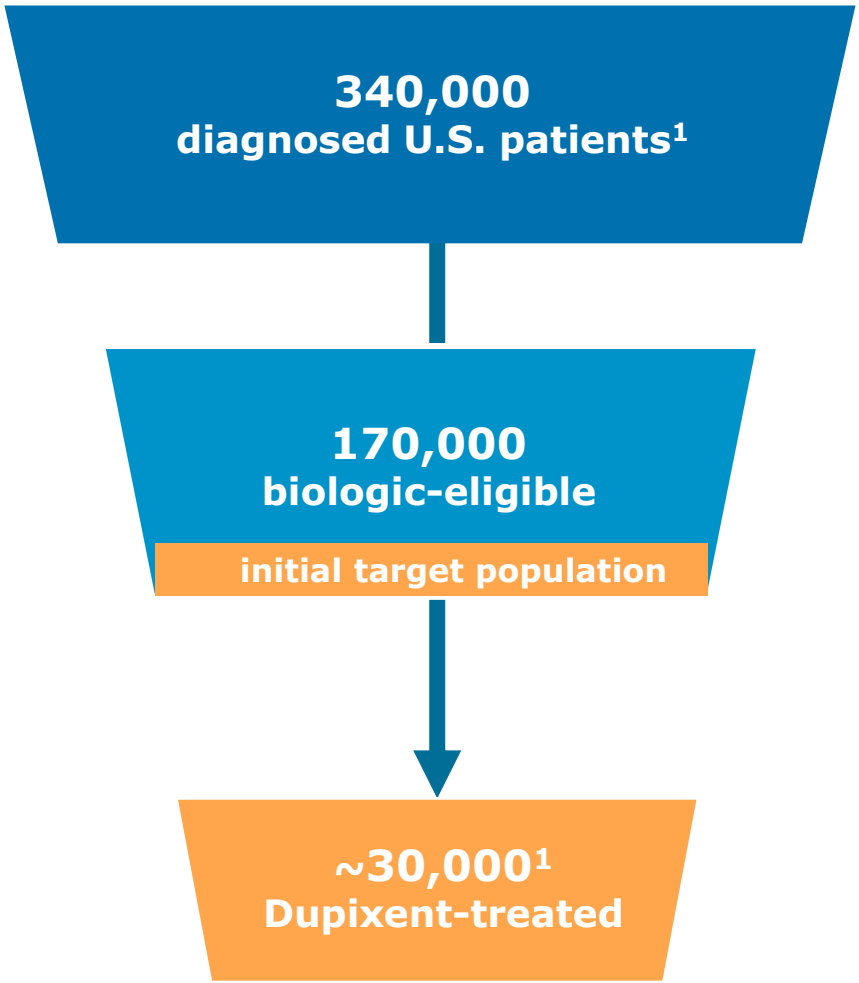
Assessing potential to treat EoE: significant market with increasing prevalence and unmet need



Significant unmet need with limited approved therapies

- ~50% PPI or steroid non-responsive or intolerant
- Dupixent QW approved in 2022
- 20-30% Dupixent non-responsive

Increasing disease recognition with >8% CAGR[1,2]

- Heightened rates of endoscopic procedures and biopsies

~$5B+ U.S. sales anticipated by 2030

- Potential to reach IBD diagnosis and biologic penetration analogs given substantial unmet need

1. ZS Claims analysis and KOL interviews August 2025; 2. "Prevalence and costs of eosinophilic esophagitis in the United States" (Thel 2024, Clinical Gastroenterology and Hepatology). 8% CAGR from 2019-2024; expected to continue through 2030.

ANB033, a potential best-in-class CD122 antagonist, has pipeline-in-a-product potential

Development Stage and Anticipated Milestones

	Antibody Program	Therapeutic Indication	IND Enabling	Phase 1	Phase 2	Phase 3
Immune Cell Modulators	**Rosnilimab** (Pathogenic T cell depleter)	**Rheumatoid Arthritis**			**P2b trial complete** **ACR late-breaker on Oct. 29th**	
		Ulcerative Colitis			**P2 data through Week 12 anticipated Nov. / Dec. 2025**	
	ANB033 (CD122 antagonist)	**Celiac Disease**		**Top-line P1b data anticipated by YE 2026**		
		Inflammatory Disease		**P1b to initiate in 2026**		
	ANB101 (BDCA2 modulator)	**Inflammatory Disease**		**P1 in healthy volunteers ongoing**		