ACR Convergence 2025

Abstract: 2132100

October 27, 2025

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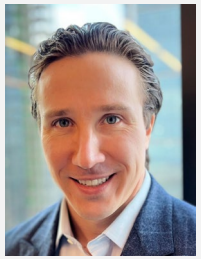
Deep Experience Across Cell Therapy and Oncology

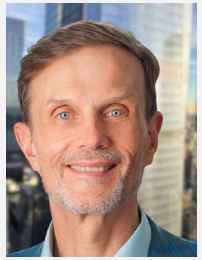
William Ho
Co-Founder, President and Chief Executive Officer

Lawrence Lamb, PhD
Co-Founder and Chief Scientific Officer



Patrick McCall, CPA
Chief Financial Officer

Kate Rochlin, PhD
Chief Operating Officer



Lou Vaickus, MD, FACP
Interim Consulting Chief Medical Officer

IN8bio's team has deep experience in gamma-delta T cells, cell therapy & oncology expertise:

- Our leadership team brings decades of extensive background in oncology discovery, business insights, franchise creation, product development, regulatory affairs, and commercialization
- Business development and licensing expertise across biopharmaceutical and biotechnology companies
- Founding of a private healthcare investment fund and management of public investments and cross-over portfolio at leading healthcare venture capital firm, New Leaf Venture Partners
- Specialization in transplantation immunology and recognized innovation in the field of γδ T cells
- Leadership of Curadigm's spin-out from Nanobiotix and platform collaborations and partnerships

AlephPoint Capital · Bank of America · BIOTAGENICS · CATALYST BIOSCIENCES · CHUBB · COWEN · CURADIGM EXPANDING LIFE · CuraGen Corporation · Deloitte. · filament BIOSOLUTIONS INC. · IMMUNOVENT · NEW LEAF VENTURE PARTNERS · O'NEAL COMPREHENSIVE CANCER CENTER UAB THE UNIVERSITY OF ALABAMA AT BIRMINGHAM · Palmetto Health USC MEDICAL GROUP · PiperJaffray · UNIVERSITY OF SOUTH CAROLINA · TURNSTONE BIOLOGICS

Revolutionizing γδ T cell Therapies

- **IN8bio is a leader in the development of gamma-delta (γδ) T cell therapies and T cell engagers (TCEs) in oncology and autoimmune diseases**
  - **Harnessing the Power of Immune Cells:** γδ T cells are “Nature’s CAR-T” cells that act as direct killers while orchestrating a comprehensive immune response to eliminate cancers and other targeted dysfunctional cells
  - **Durable Cancer Remissions:** IN8bio is targeting significant unmet needs by pioneering novel approaches to keep patients' progression-free longer with multiple remissions exceeding 3+ years in patients with difficult to treat cancers
  - **Precision and Safety:** γδ T cells have demonstrated in patients a better safety profile to date, with lower rates of adverse events and toxicities including cytokine release syndrome (CRS) and neurotoxicity (ICANs)
  - **Strong Capabilities:** We are translating over 30 years of expertise in γδ T cell research, our DeltEx™ platform has solved certain key biological, clinical and manufacturing issues that historically plagued the field across cell therapy and TCEs
  - **Powerful Platform Approaches**: We have developed a γδ TCE that can efficiently drive depletion of target cells, while inducing expansion of γδ T cells. This construct has unique differentiated properties to drive deeper cell depletion in cancer and autoimmune indications
- Our Mission: **Cancer Zero**™ - Driven by our goal to safely eradicate residual cancer cells. Join us in transforming cancer care

γδ T Cell Engagers (TCE)

Enhancing the cancer killing function of γδ T cells

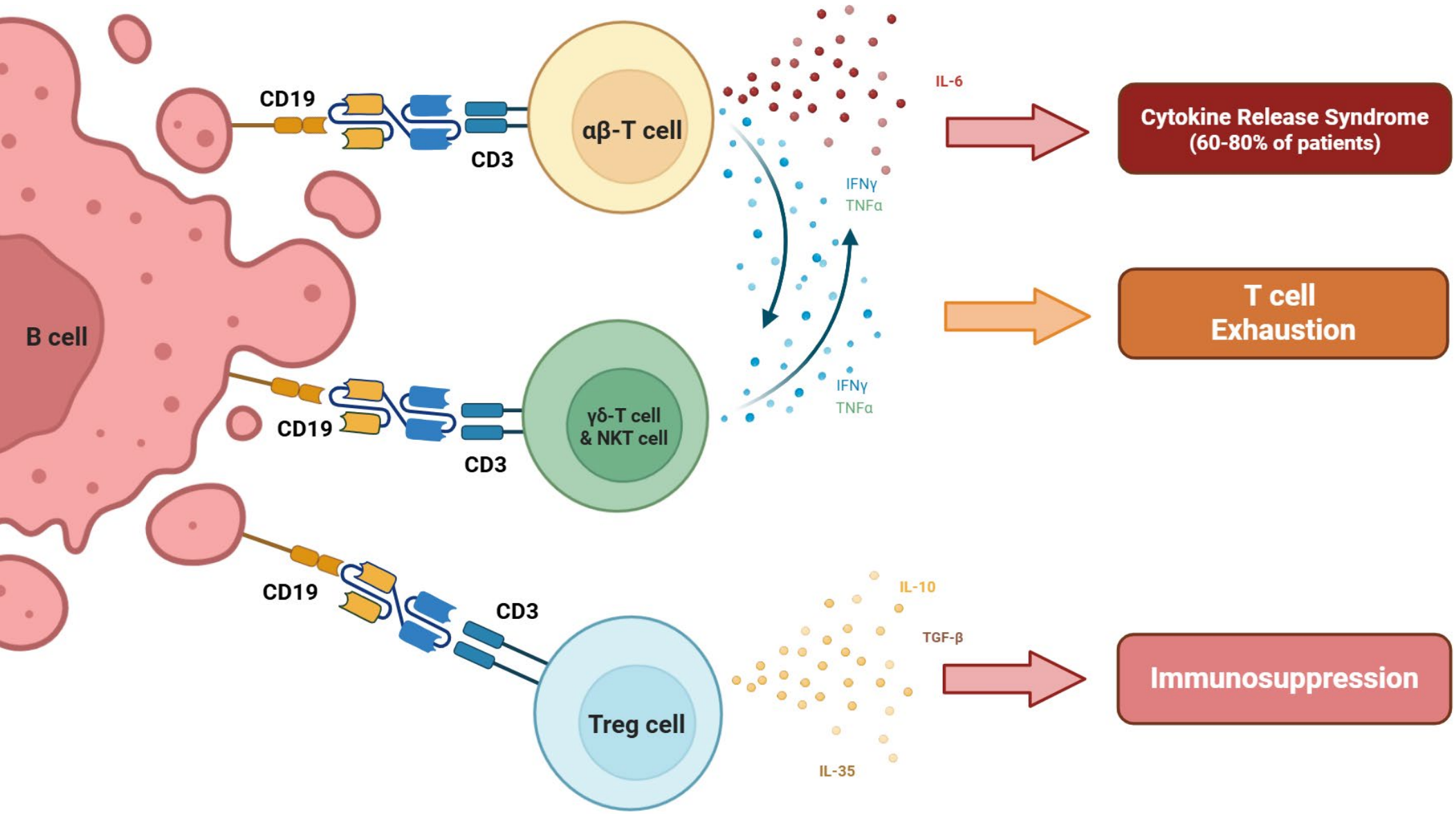
IN8bio's γδ TCE Depletes B cells with Major Advantages

- These data highlight the powerful ability of our pan-γδ TCE to drive target cell depletion, independent of initial γδ T cell levels
- γδ T cells have a lower the risk CRS and widen the therapeutic window allowing for higher doses and deeper B cell depletion from a protein-based engager
- The updated data generated for ACR highlights and demonstrates the following key findings:

1. IN8bio's TCE drives efficient target killing across the full physiological range of γδ T cell levels
2. Target cell depletion is driven by the TCE's ability to expand and activate γδ T cells independent of initial γδ T cell levels
3. B cell elimination is equivalent or better than commercially available drugs with a significantly improved cytokine profile lowering the risk of CRS
4. The pan-γδ T activation and expansion is critical to driving complete depletion of B cells in complex autoimmune backgrounds

IN8bio's TCE Platform Leverages the Power of γδ T cells for Autoimmune Diseases

Conventional CD3 TCEs Have a Narrow Therapeutic Window



…Resulting in Failure to Achieve Immune Reset to Date

- X Many TCE's in development do not offer the broad B cell coverage of CD19
- X 60-80% of patients experience CRS and ~10% >Gr. 3 CRS
- X Broadly targeting CD3 pushes T cells to exhaustion limiting their killing abilities
- X This narrow therapeutic window prevents higher dosing with current TCEs
- X Affinity de-tuning of the binding domains also causes the TCE to fall off the T cell
- X As a result, CD3 based TCE's may be ineffective at targeting tissue resident B cells

These factors drive the low depth of B cell depletion from protein engagers in Schett's data

IN8bio Has a Strategy to Overcome These TCE Limitations

Our three-pronged approach to TCE development:

Targeting and Tissue Penetration

Deep B cell depletion can be achieved through specific activation of immune subsets that can drive circulatory, lymphoid and tissue-specific targeting

T cell Expansion

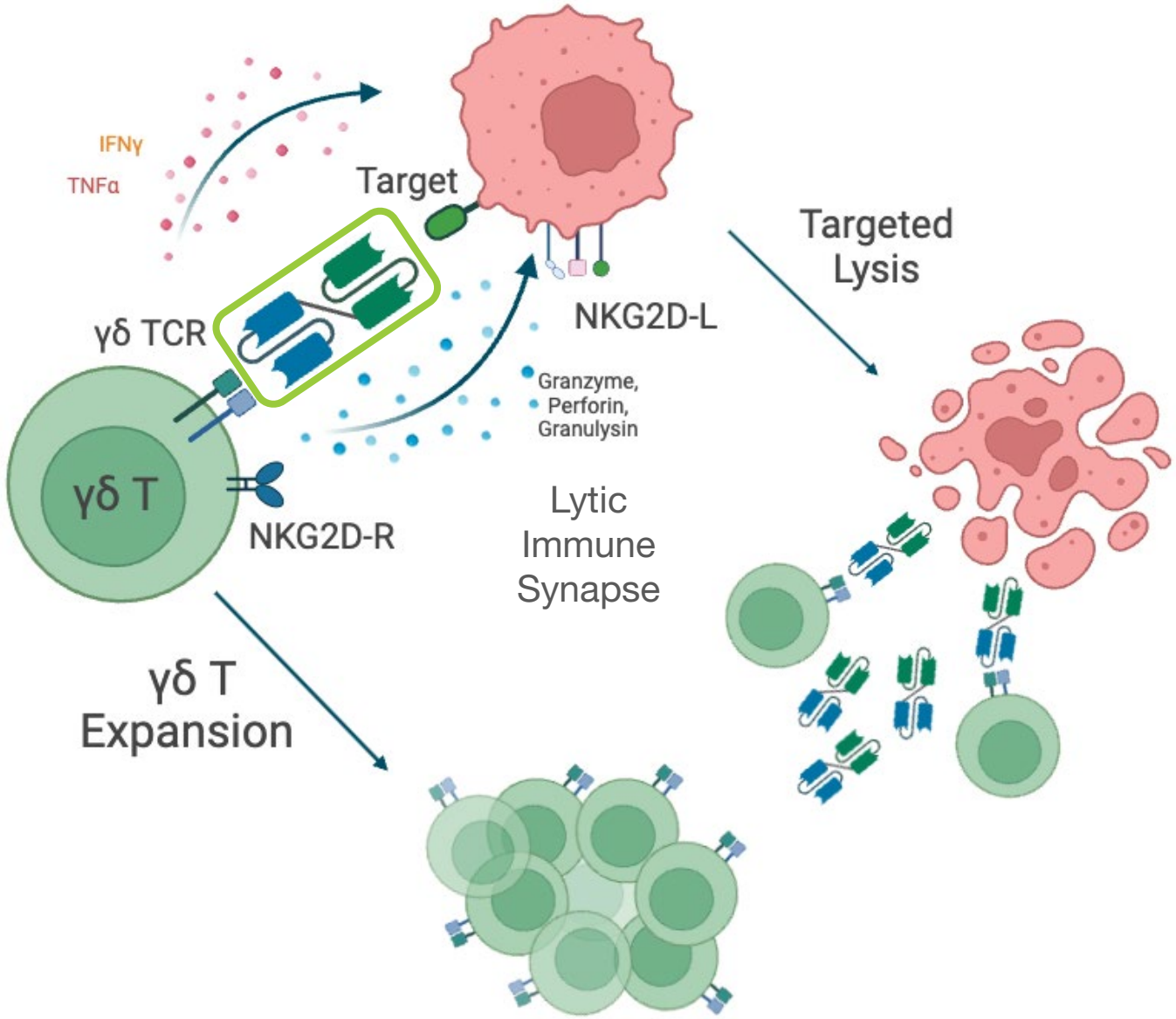
Meaningful responses require sufficient numbers of effector T cells, which can be achieved by targeted cell expansion through both the TCR and an expansion domain

Higher Tolerability

Most TCEs are limited by toxicity, such as CRS and ICANs that prevent higher dosing and deeper target elimination

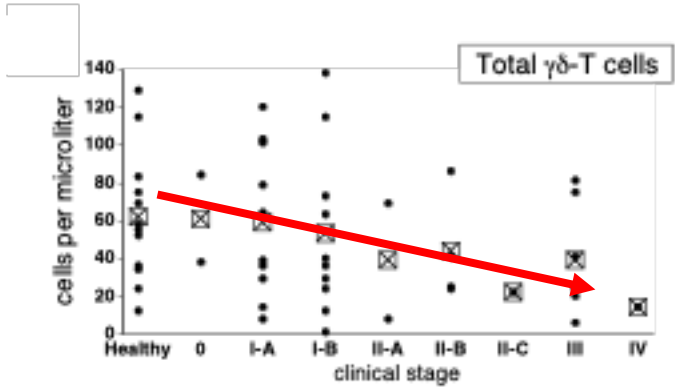
Our Novel γδ TCE Targets and Expands γδ T cells

- Engagers can be used to recruit, activate and expand γδ T cells in vivo at the site of the target cells
- Precision recruitment allows for targeted eradication of diseased cells through the engager in addition to endogenous receptor repertoire
- Proprietary and uniquely targeted TCE that functions through the γδ TCR with lower risk of CRS and a wider therapeutic index
- This technology is broadly applicable to **oncology and autoimmune disease**
    - New program INB-619 against **CD19** target to generate deep B cell depletion for use against cancer and Immunology & Inflammation (I&I) indications

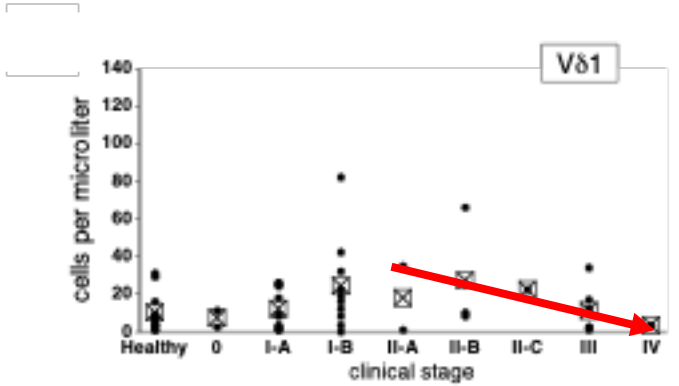


Which Overcomes the γδ T cell Decline with Disease Severity

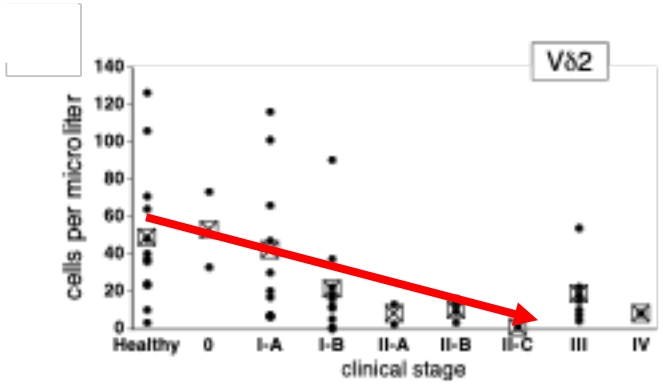
Cell expansion is important and has been a significant impediment to early generation of γδ TCEs in the clinic for oncology



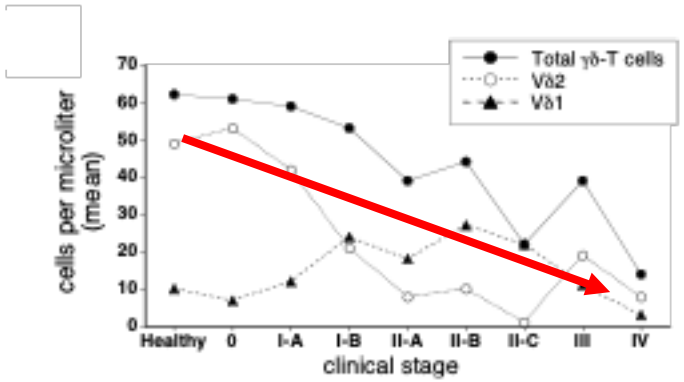
	Healthy	0	I-A	I-B	II-A	II-B	II-C	III	IV
n	12	2	10	10	2	4	1	7	1
mean	62	61	59	53	39	44	22	39	1
STD	35	33	40	45	43	29	na	29	na



	Healthy	0	I-A	I-B	II-A	II-B	II-C	III	IV
n	12	2	10	10	2	4	1	7	1
mean	10	7	12	24	18	27	22	11	3
STD	10	6	10	24	24	27	na	12	na



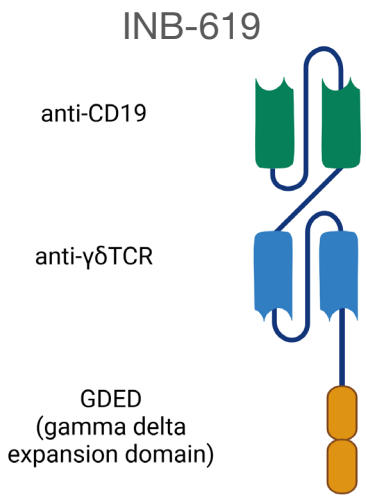
	Healthy	0	I-A	I-B	II-A	II-B	II-C	III	IV
n	12	2	10	10	2	4	1	7	1
mean	49	53	42	21	8	10	1	19	8
STD	37	28	40	27	8	6	na	17	na



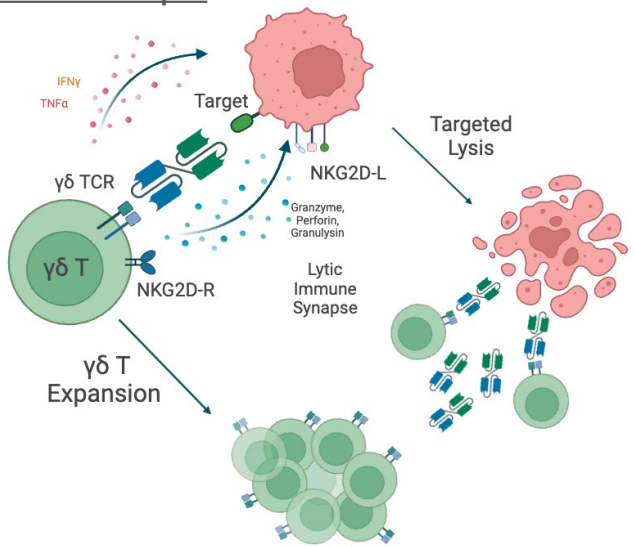
IN8bio's γδ TCE Platform: Differentiated and Broadly Applicable

- The first γδ TCE to show pan-γδ T cell expansion and activation
- Engages γδ T cells through a unique mechanism, binding of the γδ TCR
- Precision activation and expansion of γδ T cells drives efficient target cell elimination without the cytokine activation associated with CD3-directed TCEs
- The platform's design is versatile, allowing for the development of multiple products targeting different antigens, providing broad potential for treatment
- The ability to expand powerful γδ effector cells, together with the potentially enhanced safety profile, positions this approach for broad applicability across the autoimmune and oncology landscape

Novel Expansion Domain Technology



Novel pan-γδ TCR binding & activation for powerful effector function



IN8bio Leverages Biology & Engineering for a Powerful γδ TCE

The Key Features and Advantage of IN8bio's γδ TCE Platform

- Increasing γδ T cell levels can drive effective and deep target elimination
- Reduced cytokine levels are needed for higher TCE doses and broad application in autoimmune diseases
- Pan-γδ T cell expansion and activation of both Vd1+ and Vd2+ drives complete target cell elimination
- Pan-γδ TCE activity directs complete target elimination in healthy & dysregulated immune background
- This novel TCE approach is designed to work across healthy & disease associated immune variation

This approach was developed based on IN8bio's deep understanding of γδ T cell biology & effector function

INB-619: The Only Pan-γδ T cell Engager to Direct Expansion

The first pan-γδ T cell engager, utilizes TCR and GDED domain structure to expand both Vd1+ and Vd2+ cells

IN8bio's TCE Platform Comprised of 3 Primary Components

Targeting domain cassette:

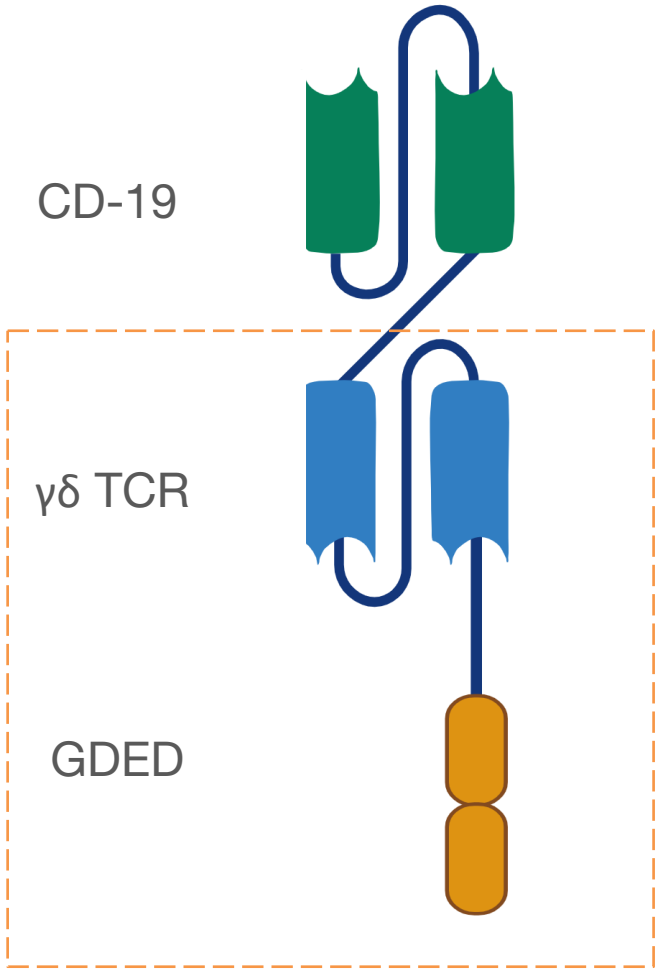
- Cassette structure which can be swapped for target of interest
- Demonstrated TCE properties across multiple targets (CD19, CD33)

TCR binding domain:

- Engages γδ T cells without the need to bind CD3
- Does not lead to cytokine release associated with CD3-based TCE

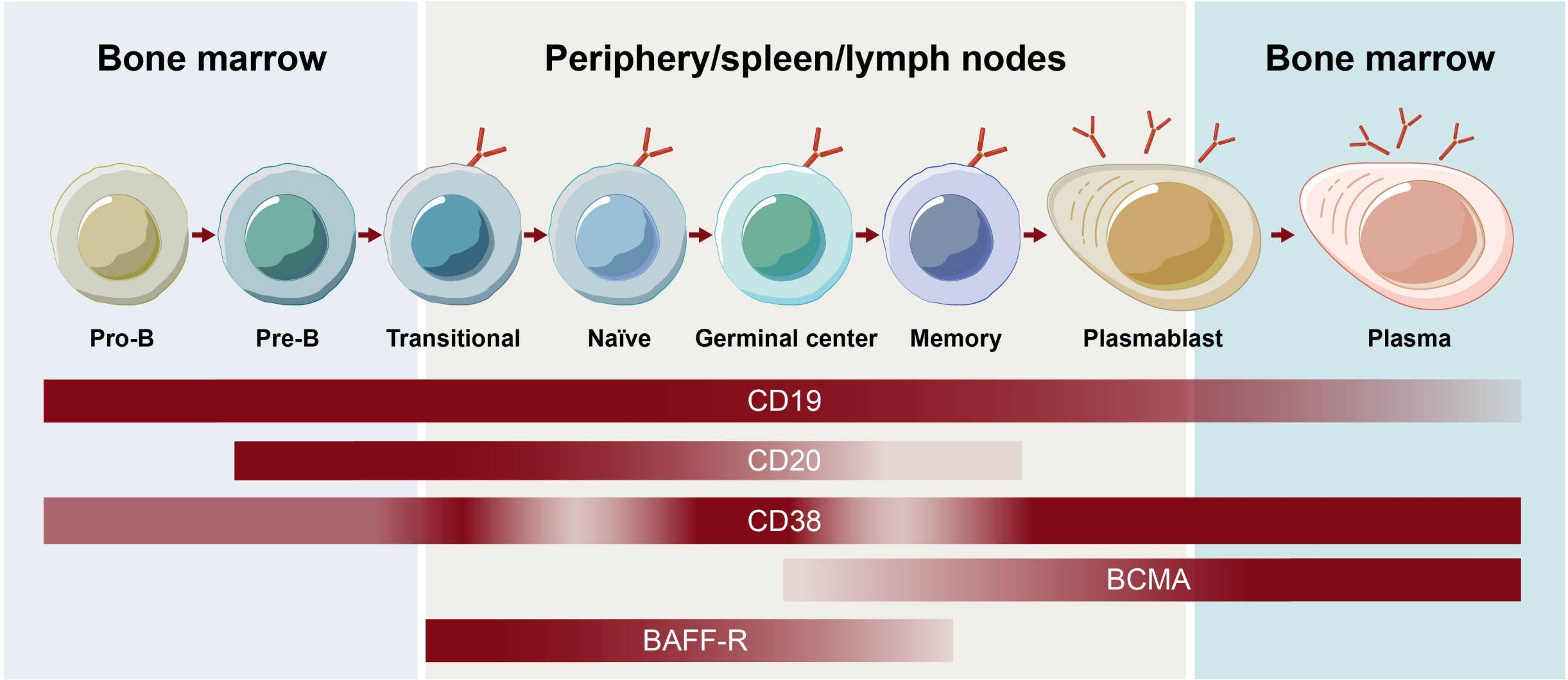
Gamma-delta Expansion Domain (GDED)

- γδ T cell expansion domain (GDED) induces pan-γδ T cell expansion
- Functions cooperatively with the γδ TCR binding to drive expansion



INB-619: A Unique B cell Depleting γδ TCE

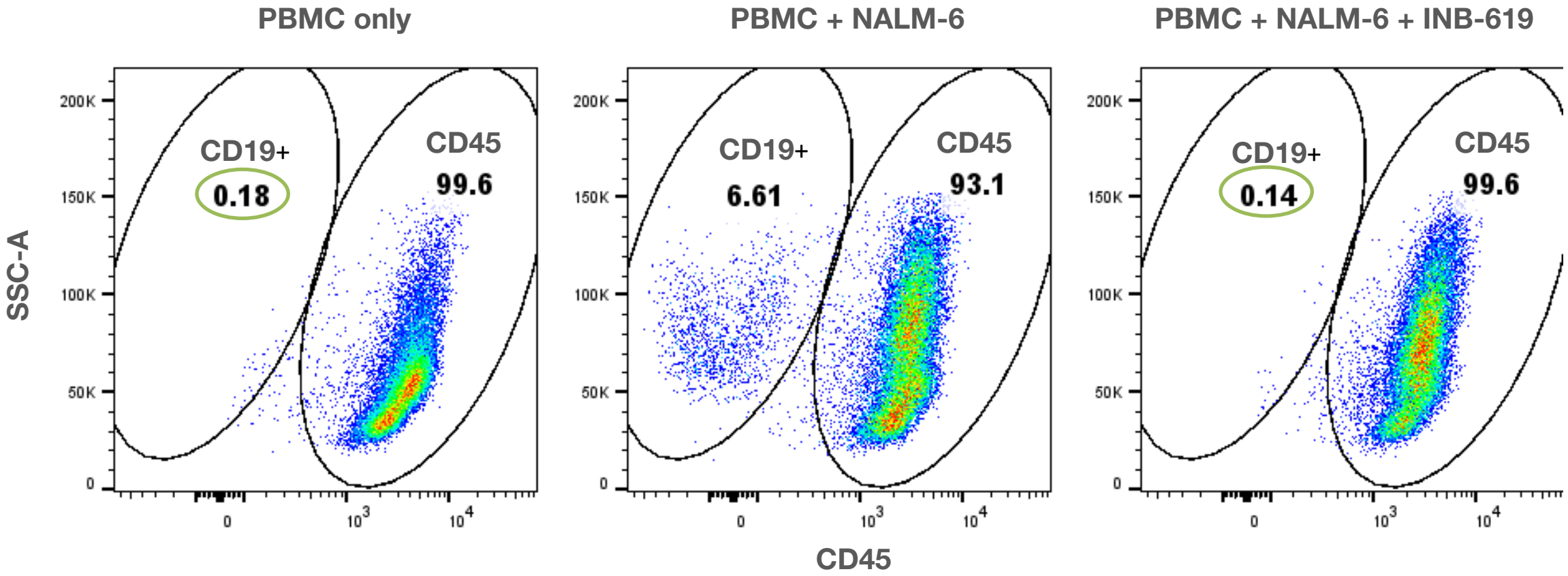
Targeting CD19 for the Broadest B cell Coverage



Source: Robinson et al., Front. Immunol. 15:1454747. doi: 10.3389/fimmu.2024.1454747

INB-619 Drives Target Elimination with γδ T cells from PBMC

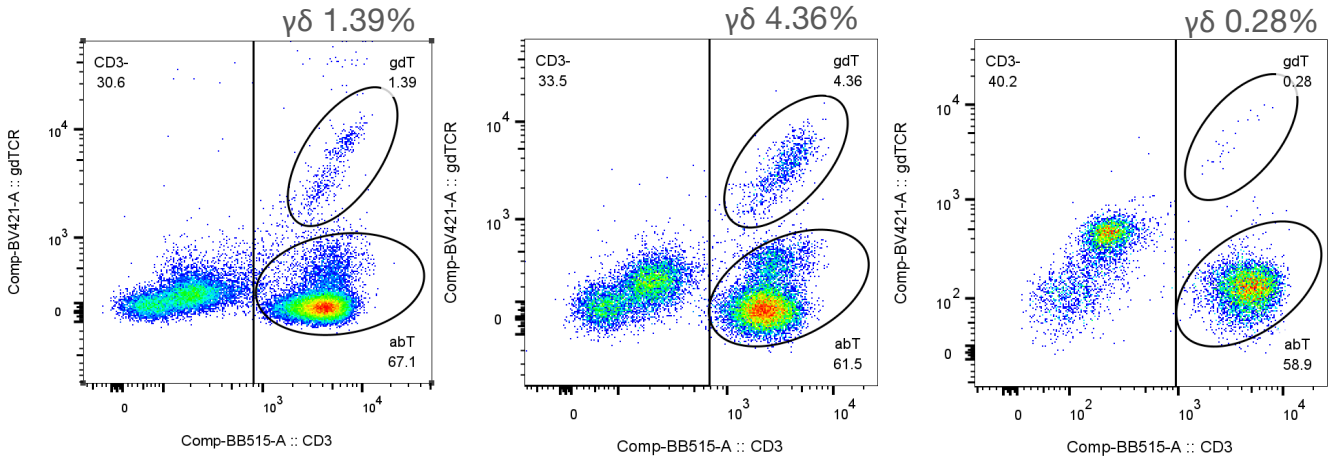
NALM-6 (CD19+) ALL cells were spiked into PBMC and cultured +/- CD19TCE over 6 days - Note complete eradication of CD19+ cells after 6 days culture with the CD19 TCE (INB-619)



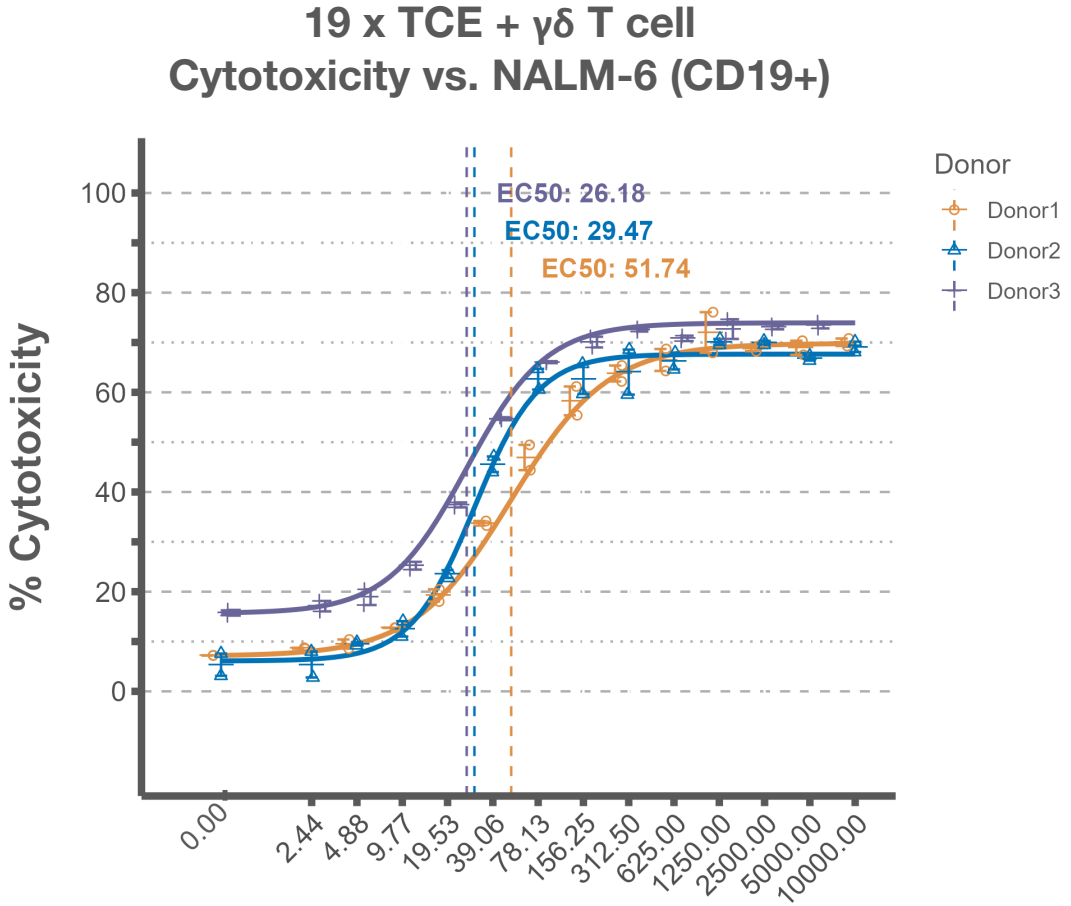
INB-619 Demonstrates Clustered EC50 across Donors

γδ T cell levels range from 1-5% in healthy donors and can be as low as 0.2% in cancer & autoimmune patients

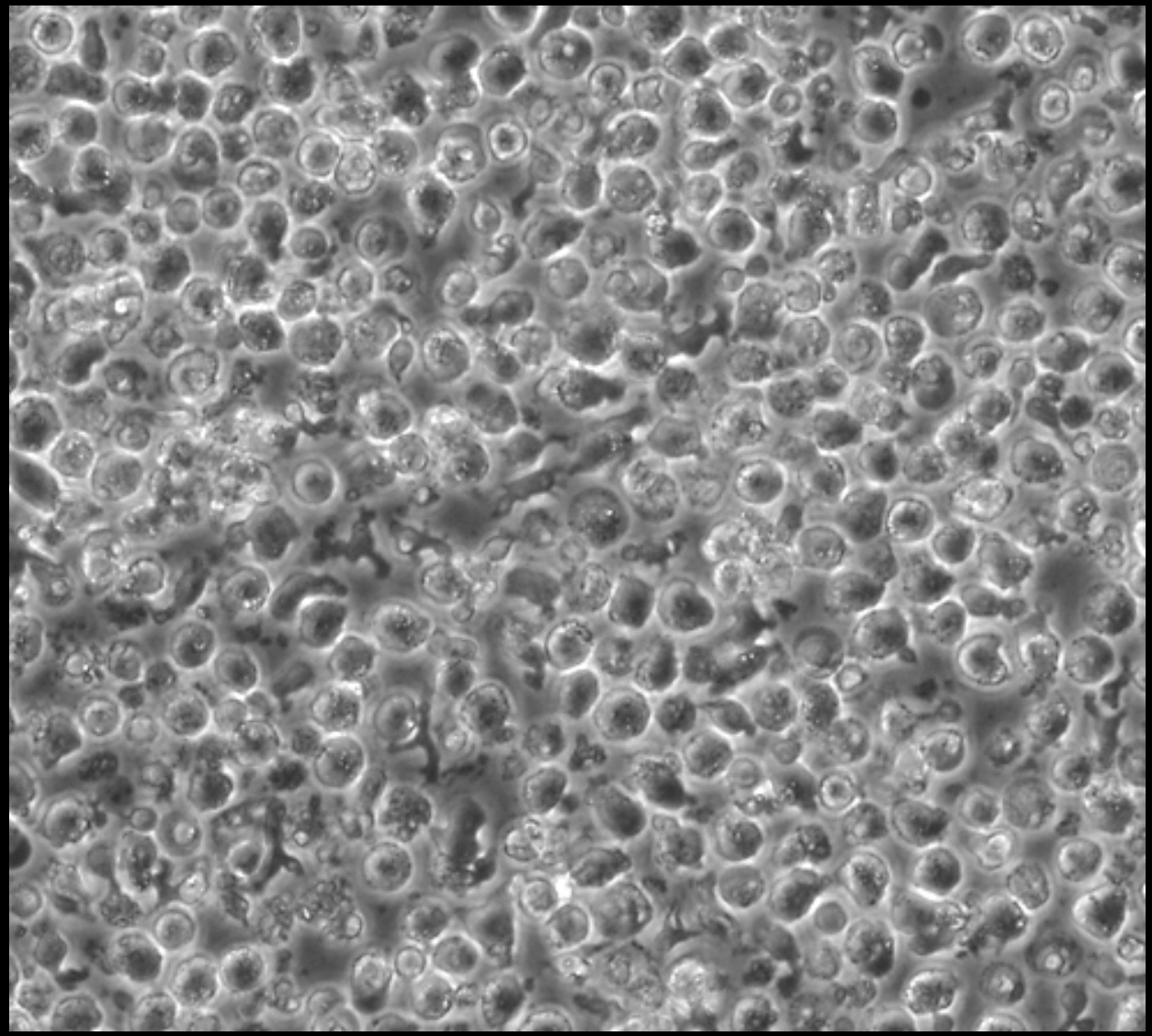
- INB-619 shows tight clustering of EC50 in donors ranging from 0.2-5% initial γδ T cell levels
- This suggests that target cell elimination and tight EC50 clustering is due to the ability to induce γδ expansion and activation and not initial γδ levels



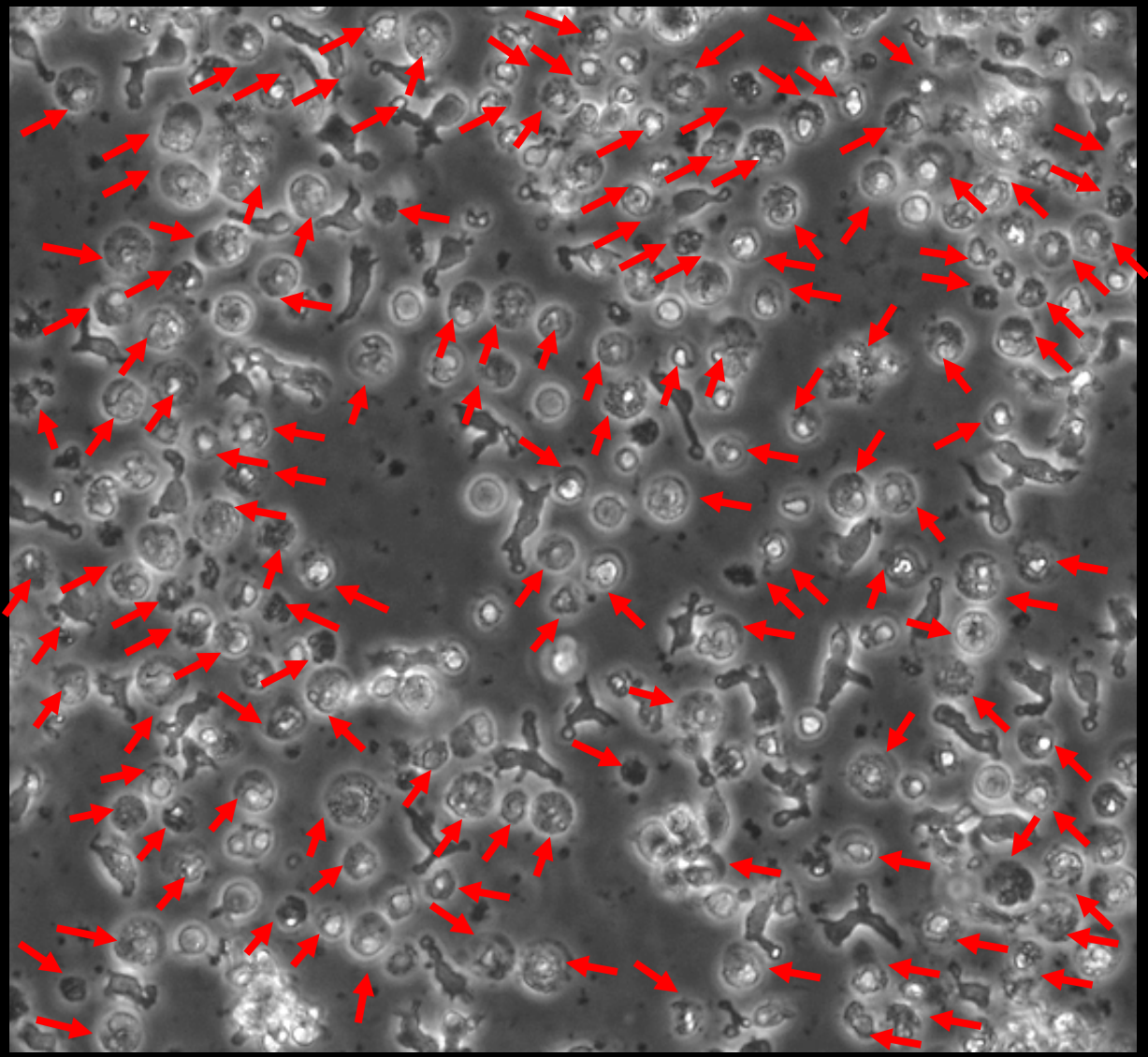
Donor 1, Day 0 | Donor 2, Day 0 | Donor 3, Day 0



CD19-γδ TCE Induced Killing is Clearly Visible



γδ T vs. Nalm6 without 19xTCE

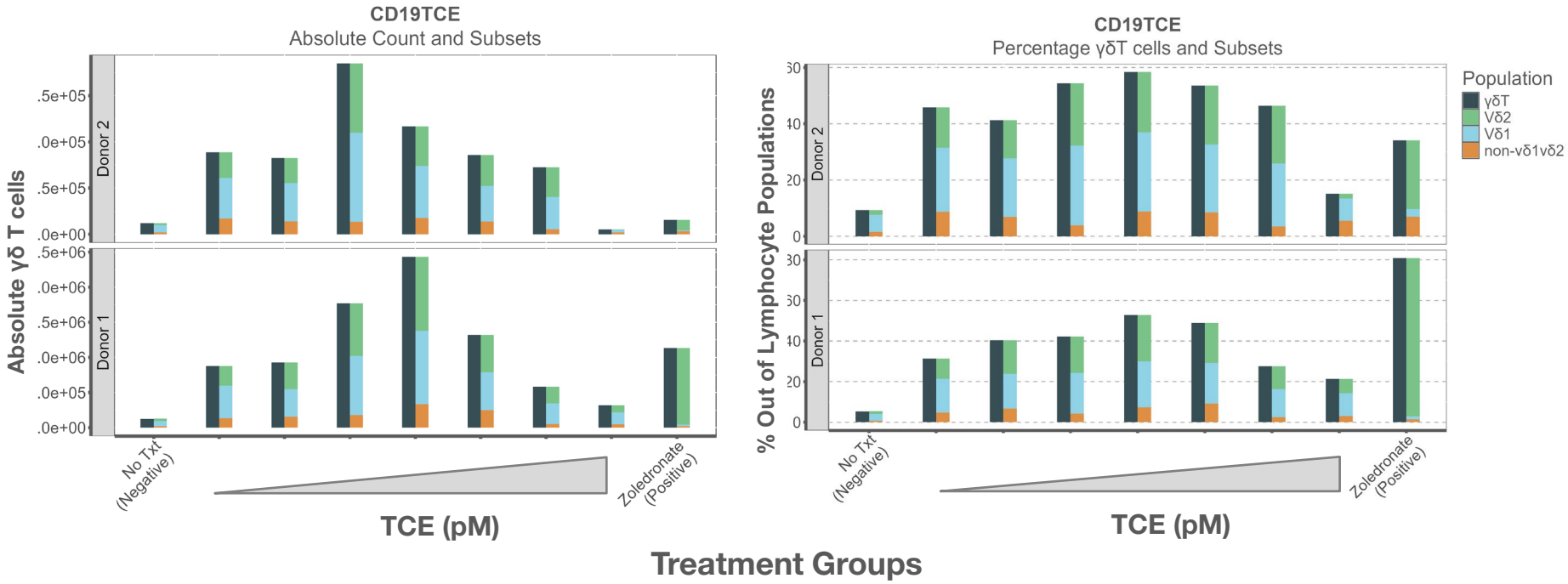


γδ T vs. Nalm6 with 19xTCE

E:T = 1:1 @ 24 hours

IN8bio's γδ TCE's function as a Pan-γδ T cell Expander

CD19-γδ TCE significantly expanded both Vδ1+ and Vδ2+ T Cells

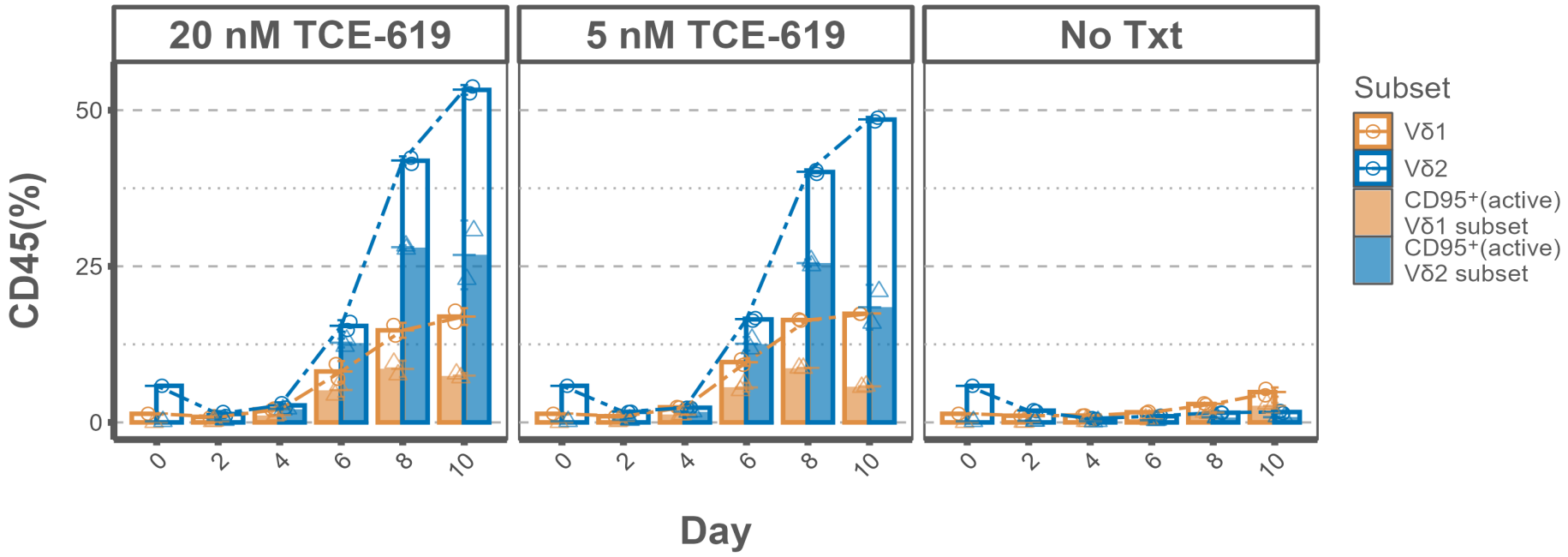


Frequency of Expanded γδ T cell Numbers (Day 10)

- CD19-γδ TCE expanded γδ T cells from PBMC during the cytotoxic lysis of normal B cells or malignant B cell lines
- Zoledronate (positive control) expanded Vδ2+ cells from PBMC as expected
- γδ T cells + PBMC without added CD19-γδ TCE (NoTxt) did not expand any γδ T cells (negative control)
- Both Vδ1+ and Vδ2+ T cells are activated and proliferate
- Vδ1+ γδ T cells are known to be **tissue resident** potentially allowing for **deeper B cell depletion**
- **To our knowledge, no other TCE has been shown to drive expansion and proliferation at this magnitude**

IN8bio's γδ TCE Expands and Activates both Vδ1+ and Vδ2+

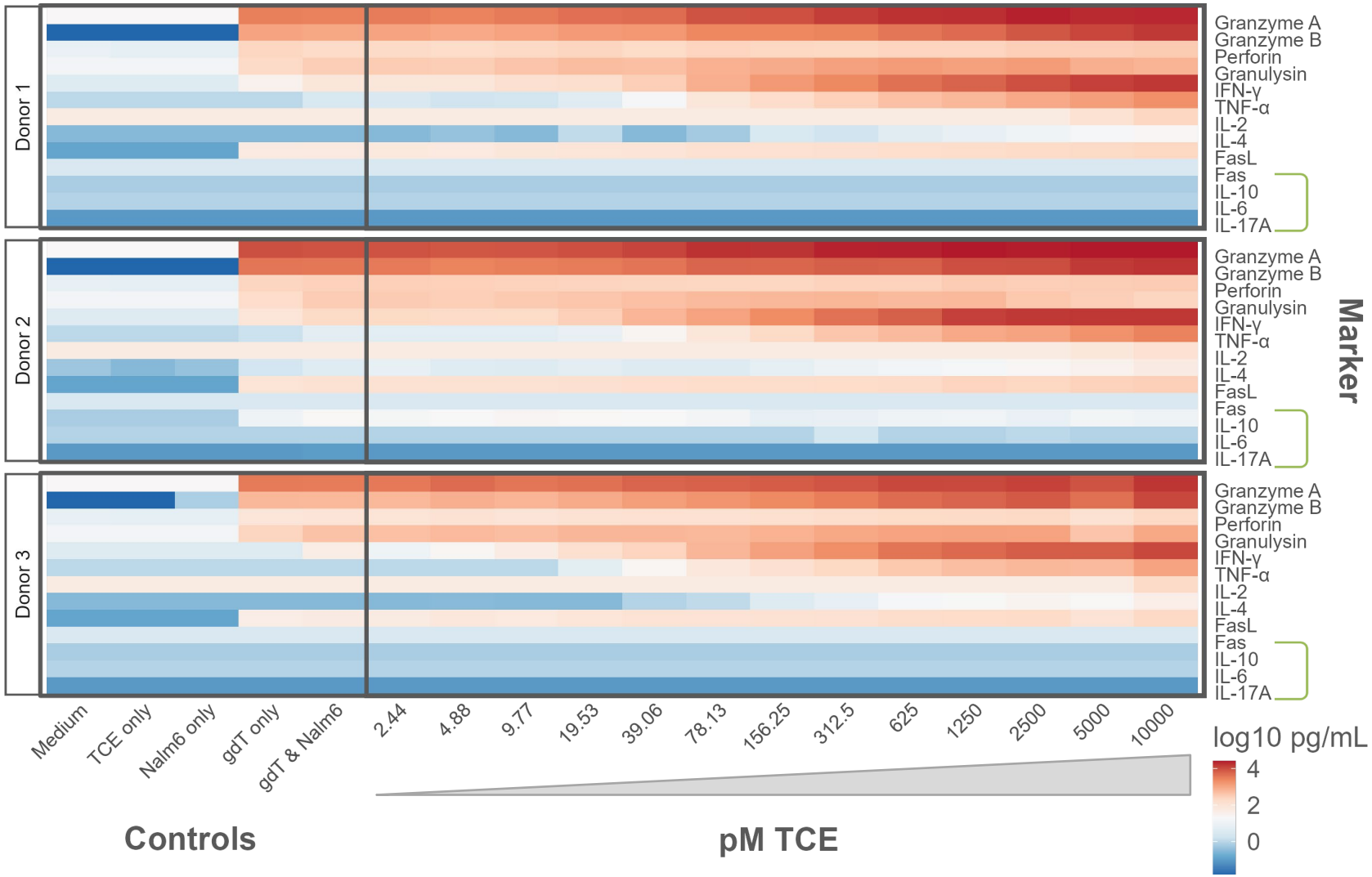
Expansion and activation (CD95+) of γδ T cell subsets from PBMCs



- CD19-γδ **expands both Vδ1+ and Vδ2+** T Cell subsets from PBMC's
- CD19-γδ **activates both Vδ1+ and Vδ2+** T Cells, shown by the expression of **CD95 (FAS)** from PBMCs
- **No significant expansion or activation is seen without CD19-γδ** (No Txt) over 10-day culture of PBMC's

Adverse Cytokines Not Observed with IN8bio's CD19-γδ TCE

IL-6, IL10 or IL-17 cytokine secretion remain flat across the dose curve, in-line with controls



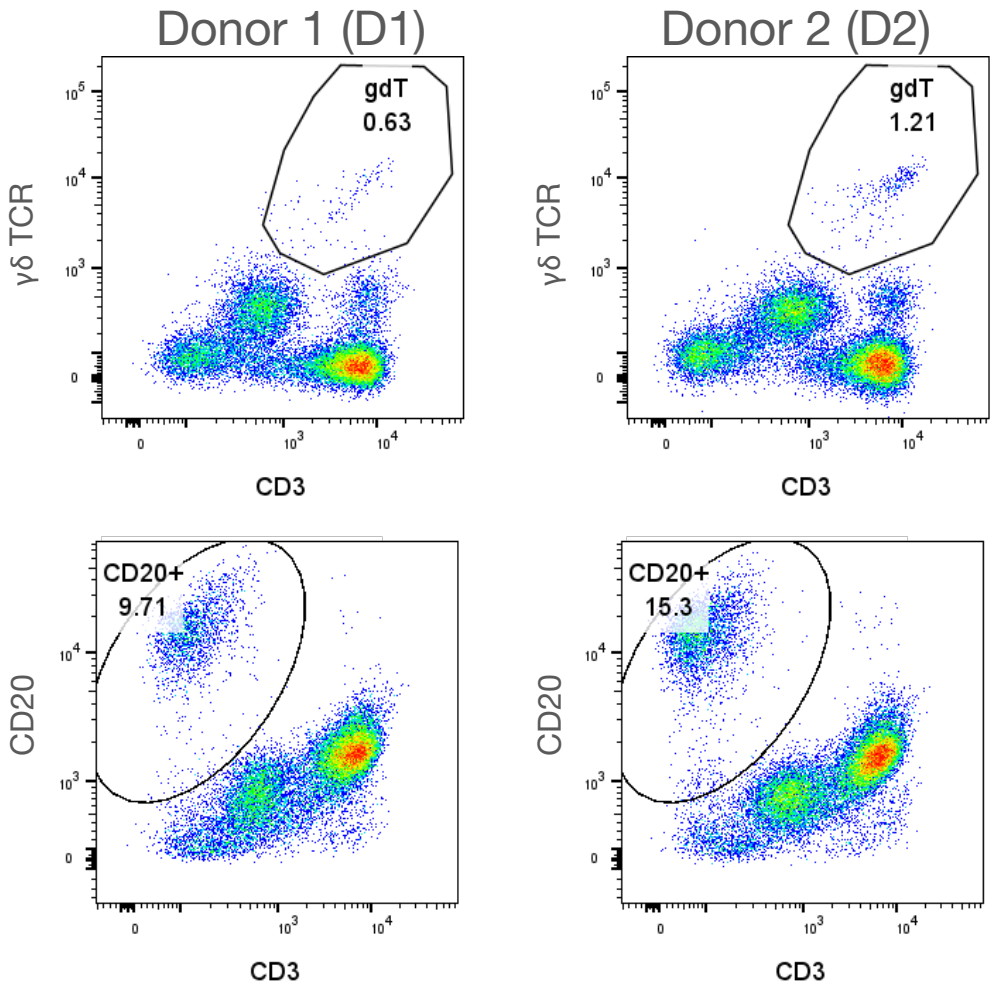
INB-619 for Autoimmune Disease

Lupus (SLE) Patients Have Low & Variable Levels of γδ T cells

Donors with active SLE disease were selected for this study

γδ T cells are low & variable

B cells are expanded & high

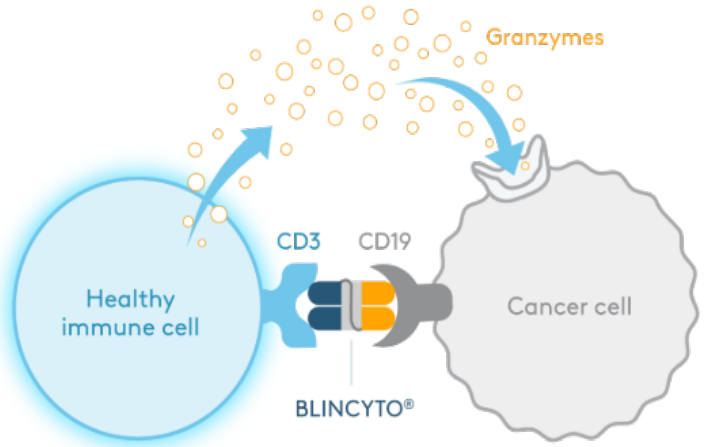


INB-619 vs Blinatumomab and Mosunetuzumab: A Comparative Analysis of B cell Killing

Commercial B cell Targeting Agents vs. IN8bio's CD19-TCE

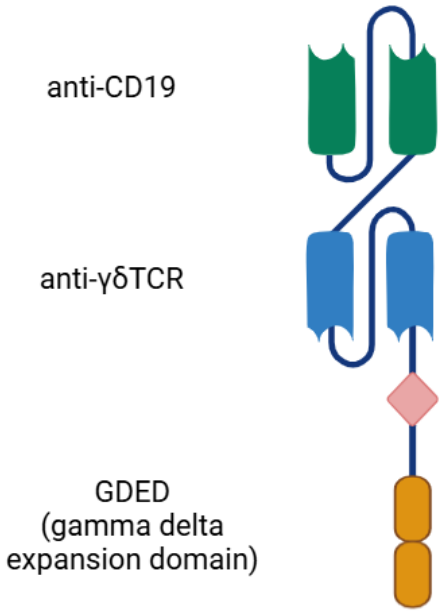
Structure of IN8bio's γδ TCE compared to commercially available CD19 or CD20 B cell targeting therapies

Blinatumomab
CD-19 TCE



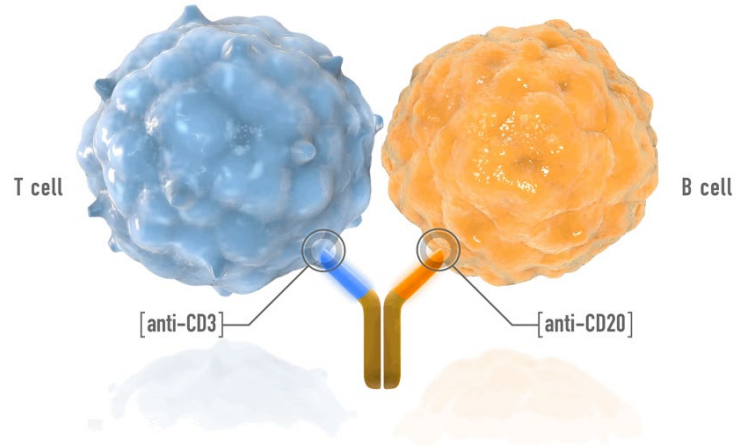
~54 kDa

INB-619
CD-19 TCE



~100 kDa

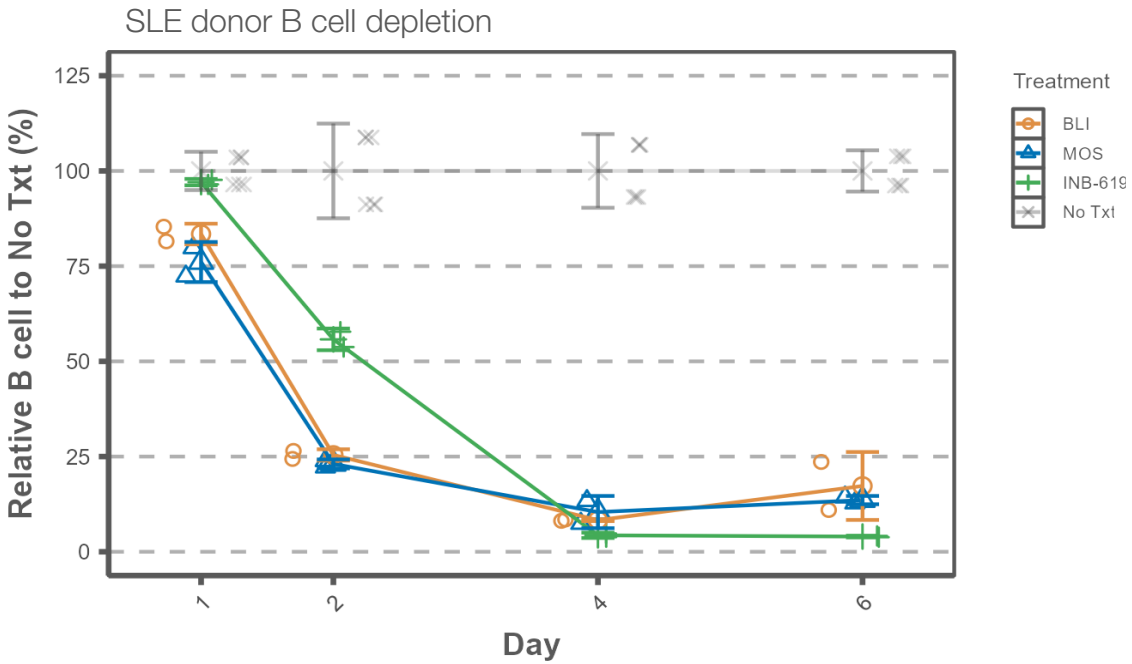
Mosunetuzumab
CD-20 TCE

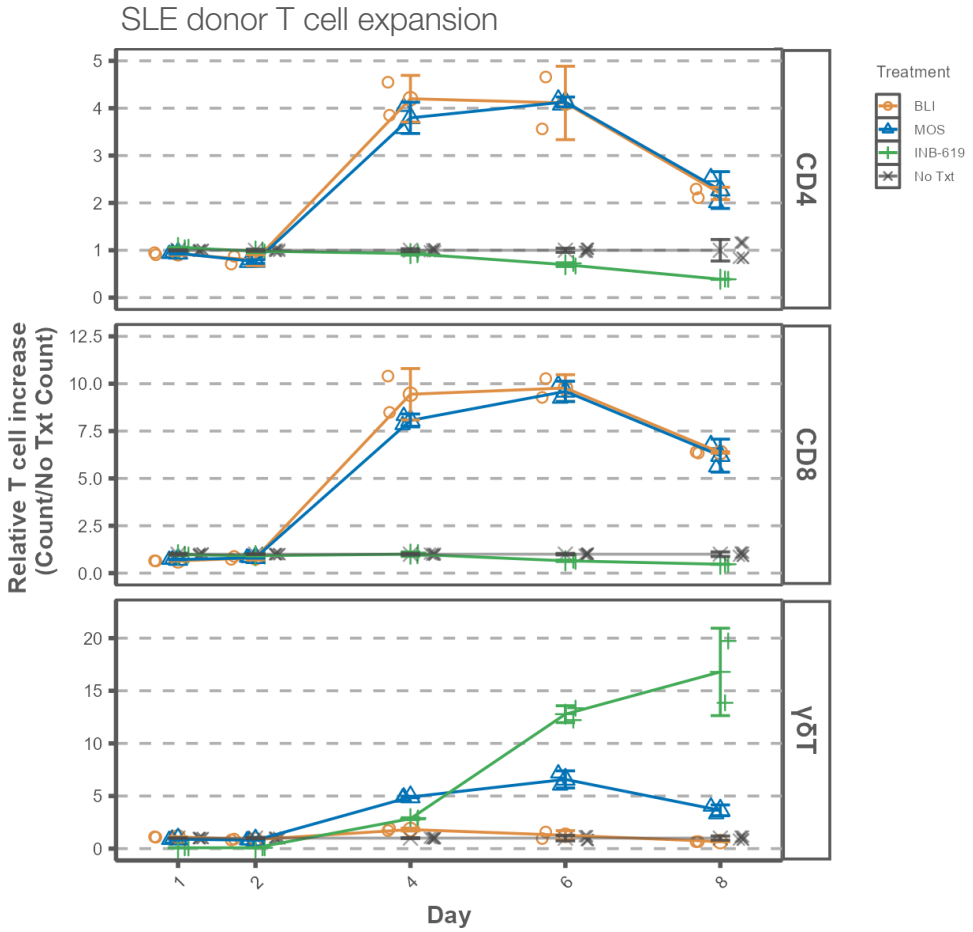


~146 kDa

INB-619 T cell Expansion and B cell Depletion in SLE D1

IN8bio's novel TCE compared to commercially available *Blinatumomab* (BLI) and *Mosunetuzumab* (MOS)



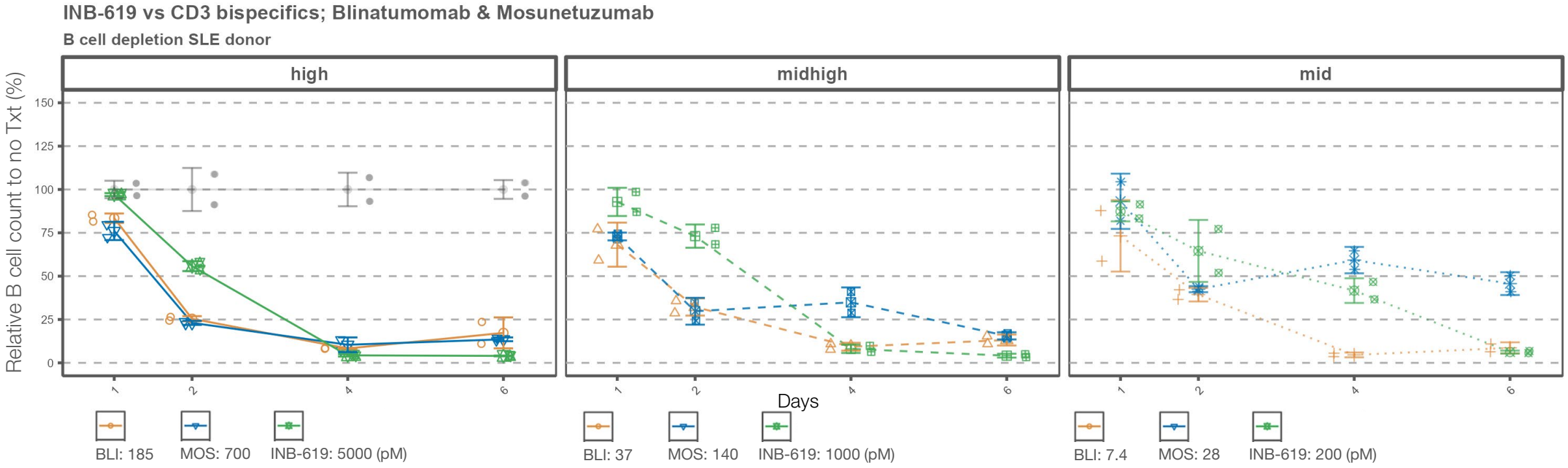


INB-619 does not show CD4 or CD8 cell expansion but shows **significant γδ T cell expansion in SLE donors** which tracks with complete B cell elimination

Both **BLI and MOS show significant CD4 and CD8 expansion** in SLE donors, which could drive clinical CRS and toxicities

INB-619 Depletes B cells Across a Range of Concentrations

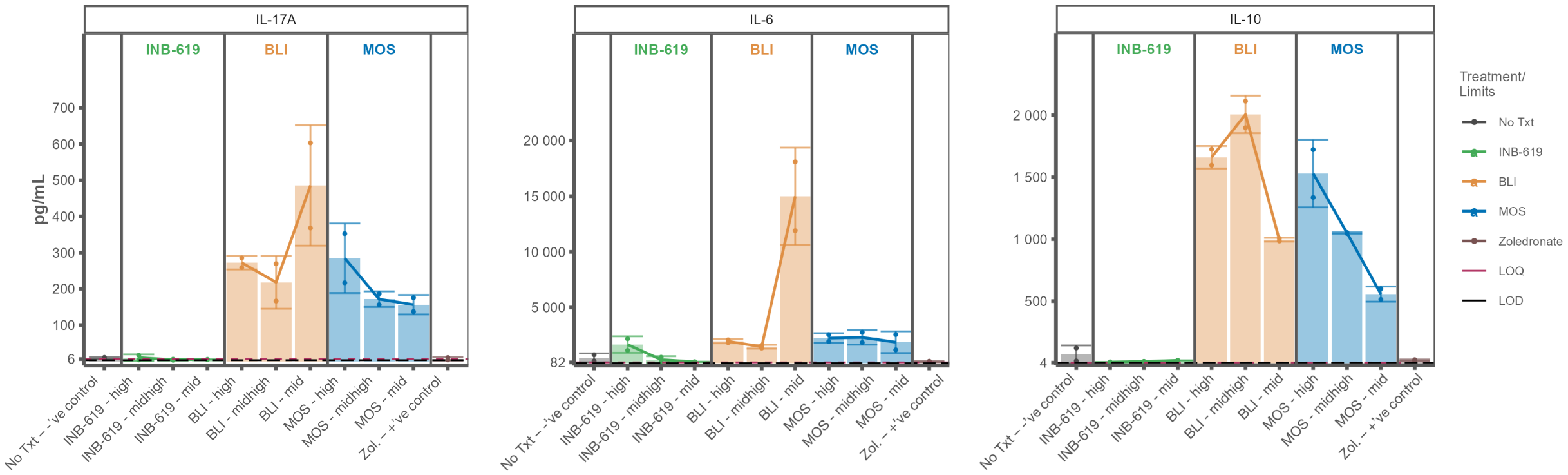
SLE donor B cell depletion comparing INB-619, BLI and MOS



INB-619 can eradicate target B-cells as efficiently or more efficiently than commercial BLI and MOS therapies at multiple concentrations, all compounds are less effective at low concentration overtime likely due to degradation

INB-619 Demonstrates Lower Secretion of CRS Cytokines

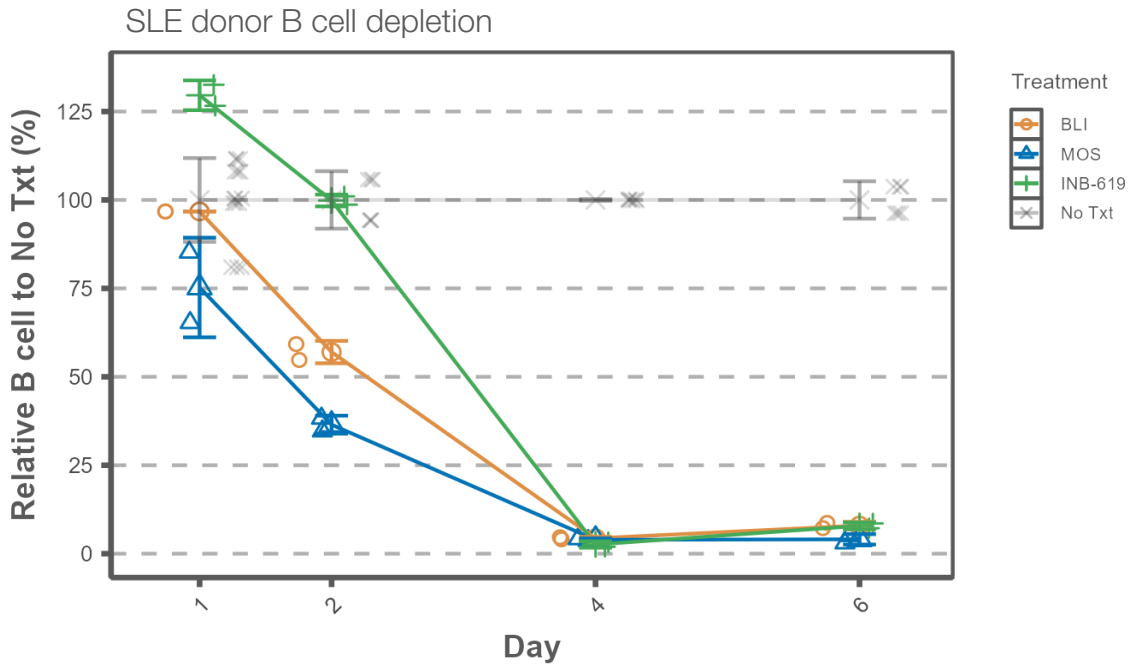
SLE donor cytokine secretion at Day 4

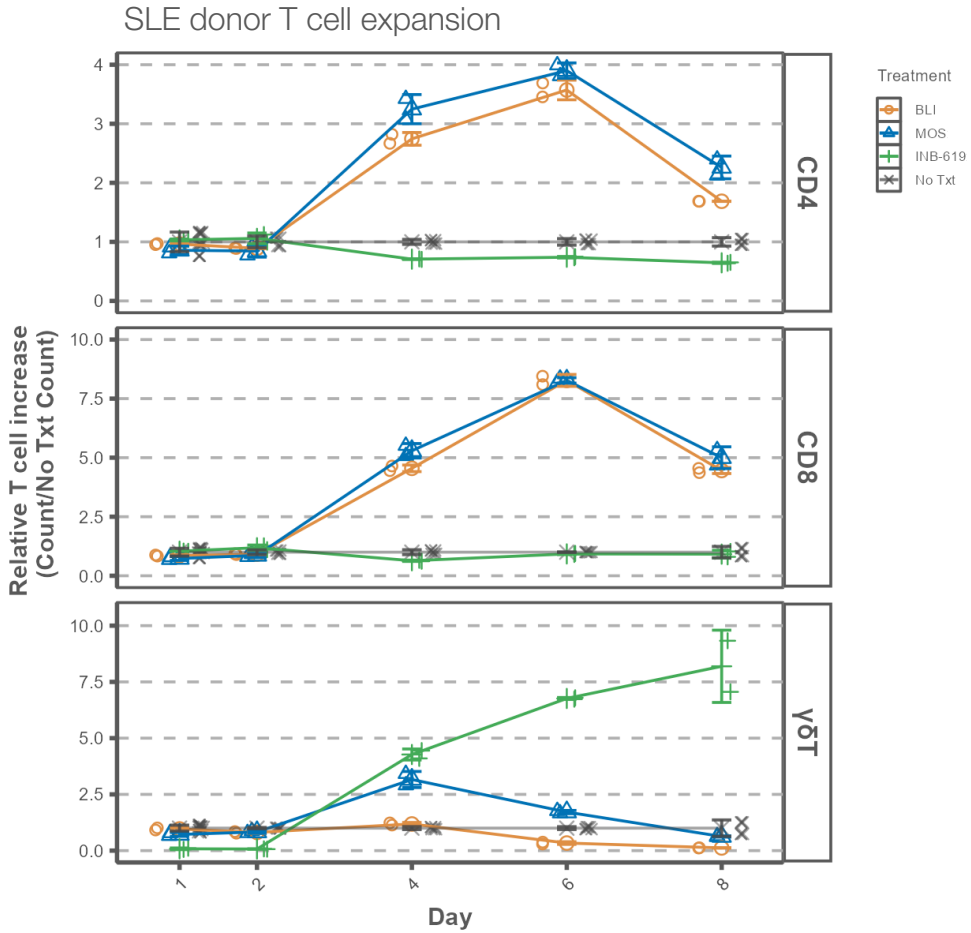


INB-619 demonstrated significantly lower secretion of cytokines associated with CRS at doses that completely deplete B cells. This widens the therapeutic index related to commercial BLI and MOS therapies at multiple concentrations

INB-619 T cell Expansion and B cell Depletion in SLE D2

IN8bio's novel TCE compared to commercially available BLI and MOS





INB-619 does not show CD4 or CD8 cell expansion but shows **significant γδ T cell expansion in SLE donors** which tracks with complete B cell elimination

Both **BLI and MOS show significant CD4 and CD8 expansion** in SLE donors, which could drive clinical CRS and toxicities

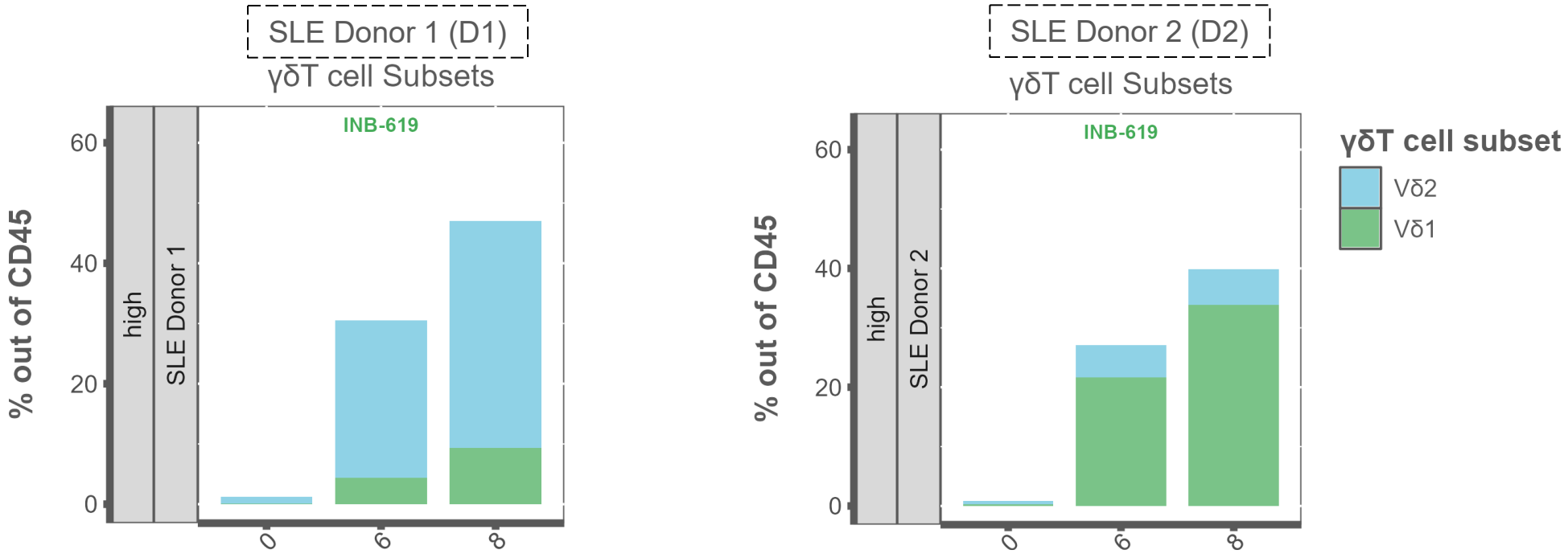
INB-619: Designed to Overcome Autoimmune Challenges

IN8bio's γδ TCE significantly expands both Vδ1+ and Vδ2+ T cells

- Autoimmune disease often exhibits immune dysregulation with both overactive and exhausted immune cell subsets, which can change overtime
- Different immune subsets may respond differently in different patients, which can be difficult to predict at the time of treatment
- To effectively drive B cell elimination, the IN8bio TCE was designed to function as a pan-γδ T cell engager, expanding and activating both primary γδ T cell subtypes, the Vd1+ and Vd2+
- This can induce B cell depletion through activation of either or both γδ T cell subtypes, driving target elimination in patients and tissues with variable immune response to stimulation
- This cannot be achieved by the other γδ TCE's that only target a single γδ T cell subtype, which leads to inefficient target elimination in some patients

INB-619 Drives B cell Elimination with both γδ T cell Subtypes

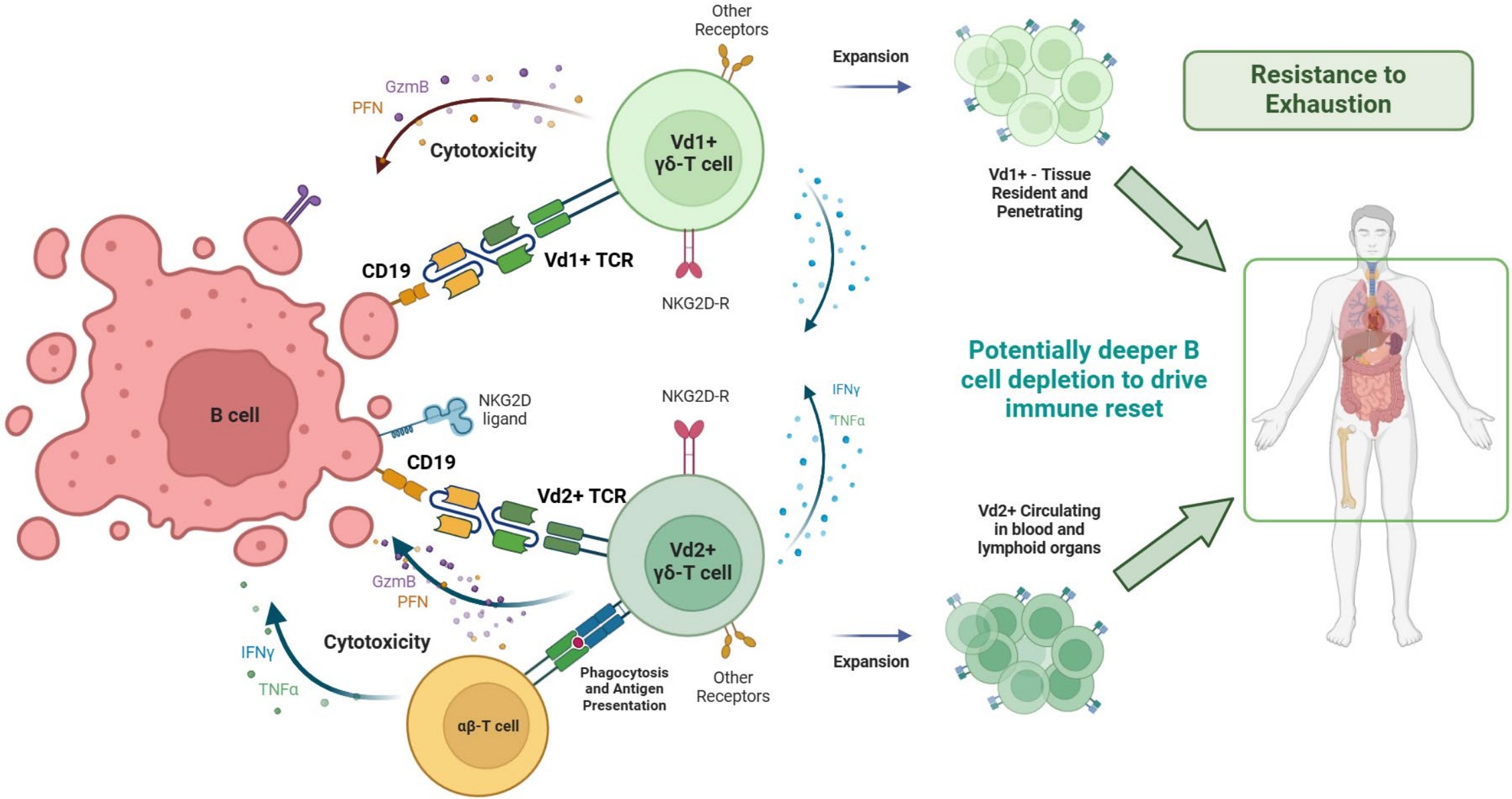
Complete B cell elimination is achieved despite differential patient subtype response in SLE



- Both SLE donors presented with low levels of γδ T cells at initial assessment (Day 0)
- In both, the addition of INB-619 led to complete elimination of B cells by Day 4 (slide 15, 16)
- While both donors expanded γδ to ~40%, SLE donor 1 expanded primarily Vd2+ (suggesting that the Vd1+ compartment may be less responsive), and SLE donor 2 expanded primarily Vd1+ (suggesting the converse)
- In these complex patients, complete B cell elimination could be achieved by INB-619 - a pan-γδ TCE

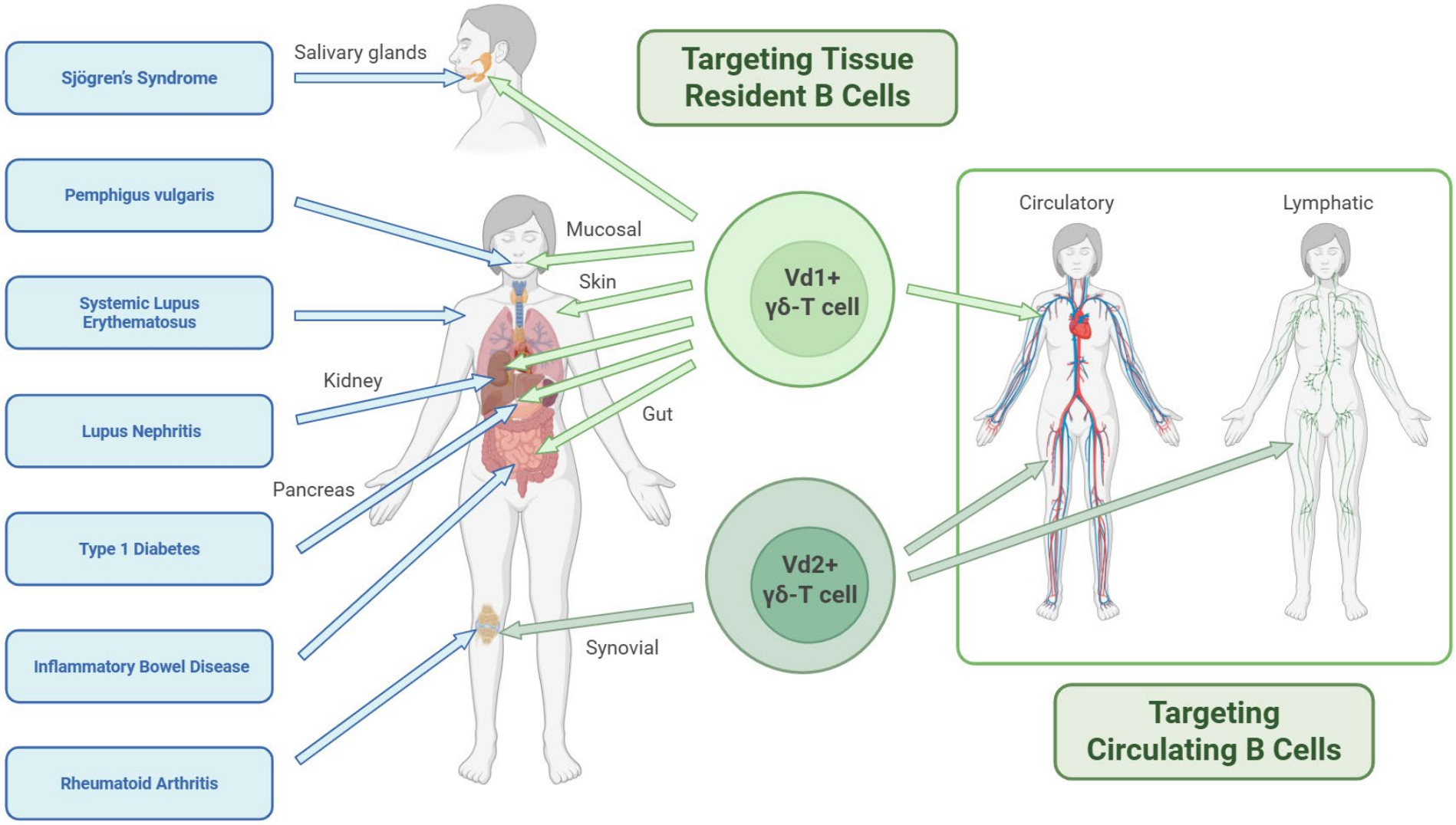
Our γδ TCE has Therapeutic Advantages

Driving to Deeper B cell Depletion with a Pan-γδ TCE



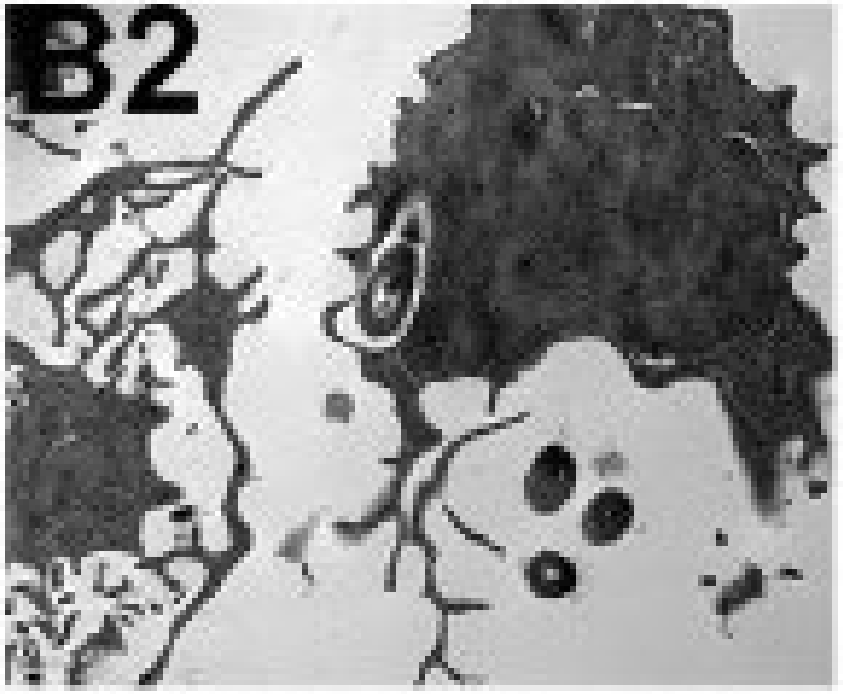
γδ T cell Residence in Tissues of Autoimmune Diseases

Tissue, circulatory and lymphoid residence of γδ T cells may result in deeper B cell depletion

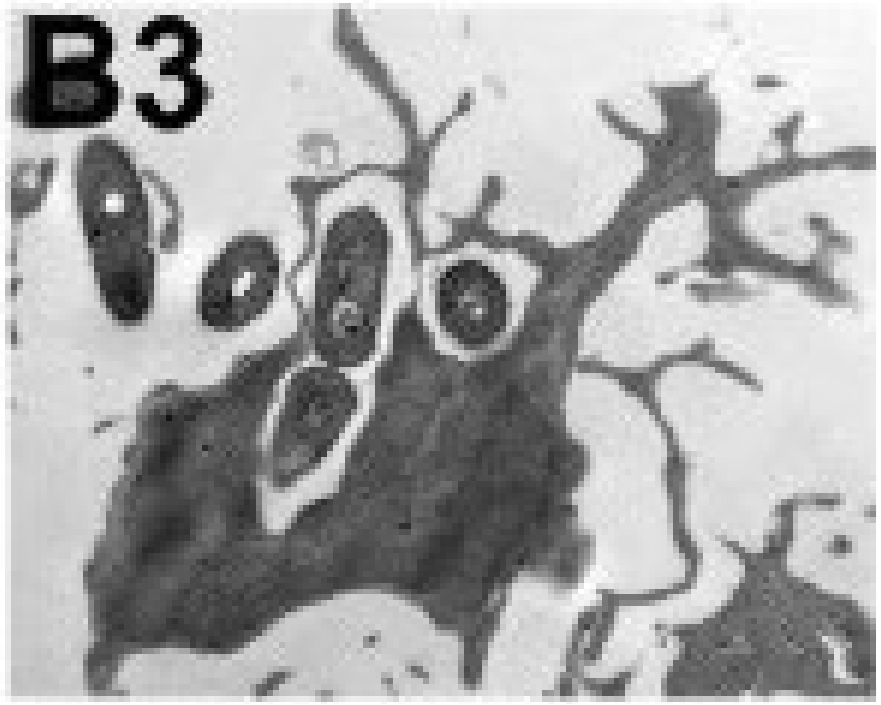


Vδ2+ cells are Phagocytes for Deeper B cell Depletion

Human γδ T cells phagocytose *Listeria Monocytogenes*



After 1 hour



After 5 hours

Source: Zhu, Y., Wang, H., Xu, Y. et al. Human γδ T Cells Augment Antigen Presentation in Listeria Monocytogenes Infection. Mol Med 22, 737–746 (2016). https://doi.org/10.2119/molmed.2015.00214

INB-619 - CD19-γδ TCE Provides Unique Advantages

- ✓ Pan γδ TCE demonstrates ability to eliminate specific target cells in a dose-dependent manner
- ✓ Significantly expands both Vδ1+ and Vδ2+ T cells
- ✓ CD19 broadly targets the B cell compartment
- ✓ Vδ1+ cells resist exhaustion and can target tissue resident B cells for deeper B cell depletion
- ✓ Vδ2+ cells are phagocytes that drive deeper B cell depletion as seen with Dren Bio's myeloid cells
- ✓ γδ T cells secrete less IL-6 and may reduce CRS and ICANs as is common with CAR-T & CD3 TCE's
- ✓ TCEs allow simpler manufacturing, lower costs, repeat dosing and avoids lymphodepletion

Harnessing the Power of γδ T cells

- **Differentiated Mechanism of Action –** The unique properties of IN8bio's TCE, which functions through the γδ-TCR drives efficient γδ T cell expansion and deep target depletion
- **Superior Safety Profile –** Our clinical data demonstrates no CRS nor ICANs to date. Current CD3-TCE's are significantly limited by a narrow therapeutic window, preventing higher doses to achieve complete B cell depletion
- **Unique Value in a Large Market –** INB-619 delivers potent B cell elimination with lower release of cytokines associated with CRS. Addresses a key unmet need for autoimmune diseases affecting 1 in 6 women
- **Proven Execution –** An experienced team with a track record of achieving milestones and delivering strong clinical data to advance a differentiated γδ T cell pipeline
- **Multiple Near-Term Value Catalysts –** Creating clear opportunities for additional funding and stock price appreciation

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