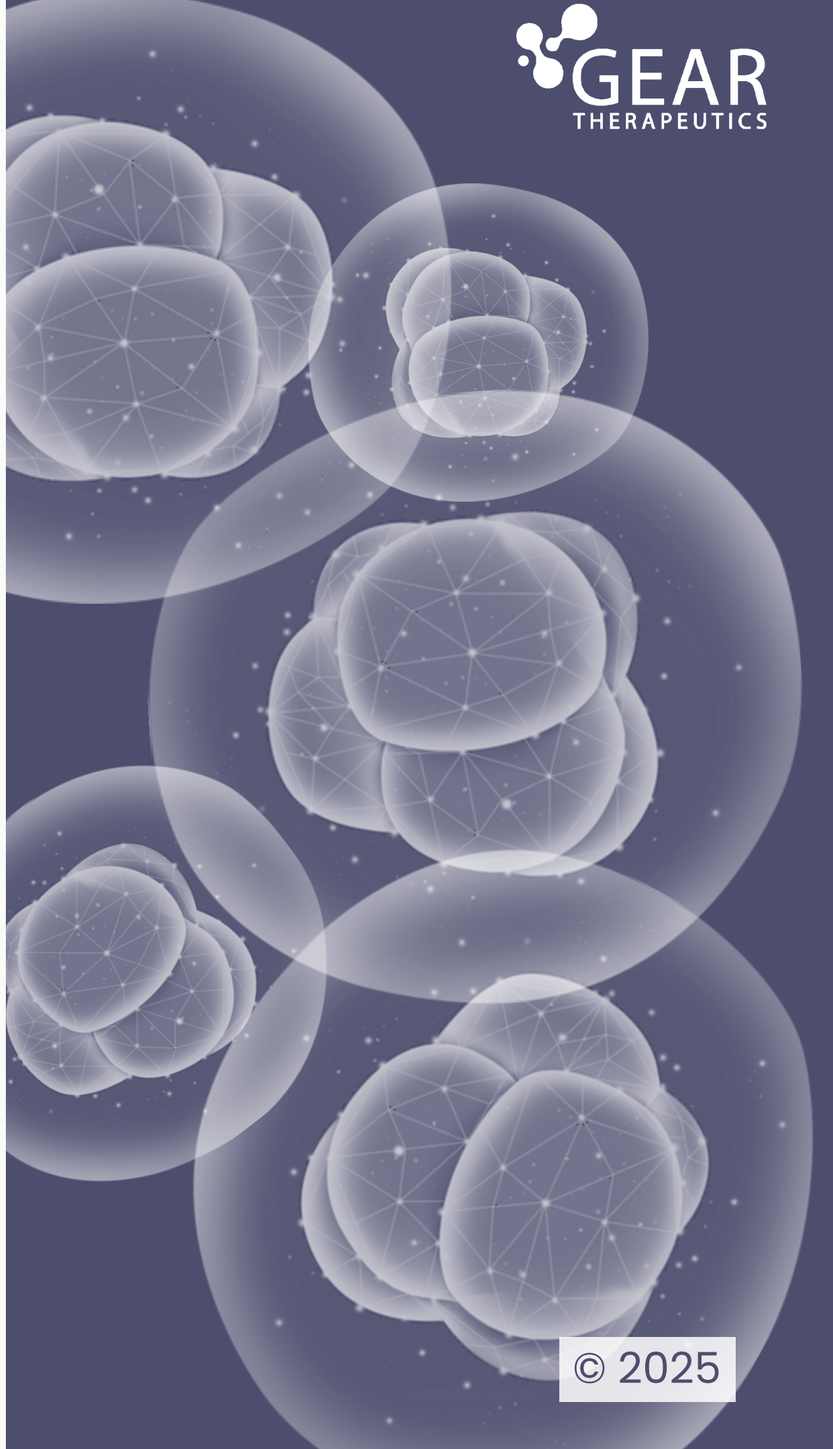
GEAR THERAPEUTICS

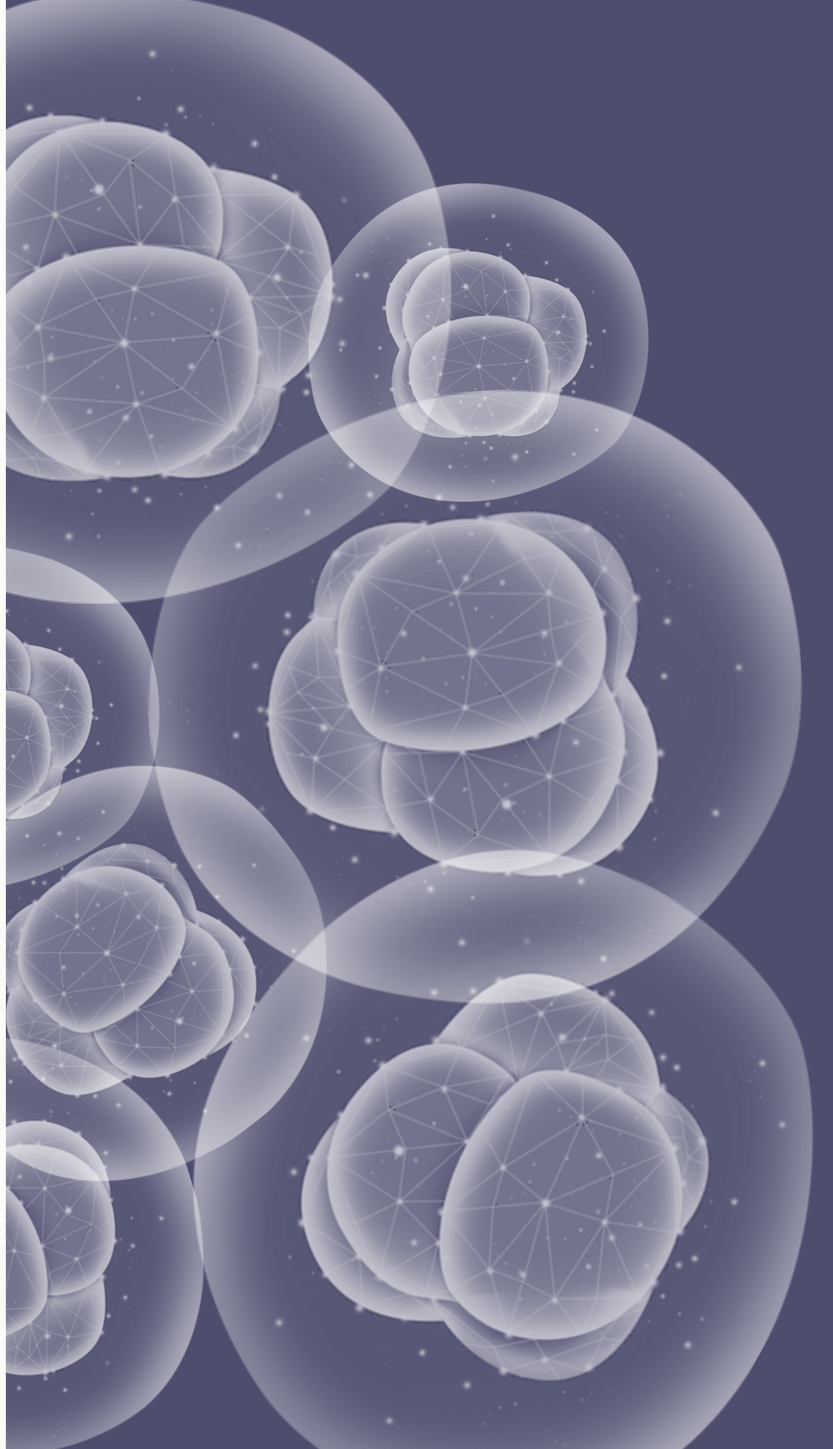
Redefining Combination Cancer Therapy w/ Precision Shielding

Company Overview – 2025



About Us

We are a Pittsburgh, PA-based biotechnology company developing **NK cell therapies that incorporate a "precision shielding" genetic editing strategy designed to augment the immunological activity of therapeutic antibodies.**



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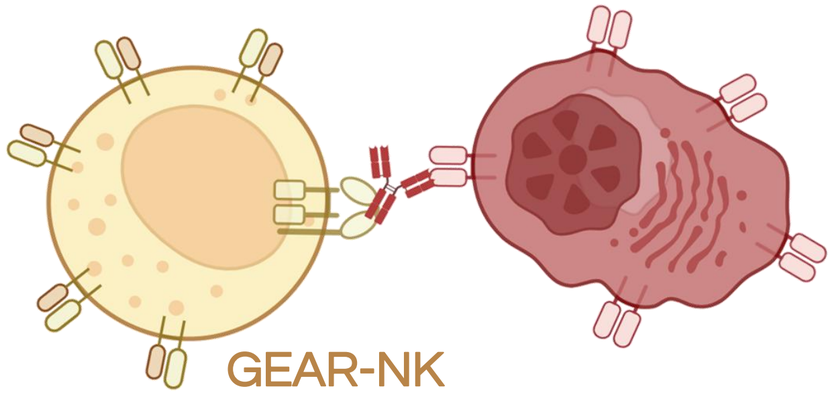
GEAR-NK Cells

GEAR-NK Cells



Precision shielded NK cells are administered in combination with therapeutic antibodies

✓ Effective & Safe ✓ Adaptable

Overview of GEAR-NK

- Genetically engineered to avoid antibody-mediated “fratricide”
- Designed to boost anti-cancer activity of therapeutic monoclonal antibodies (**mAbs**)
- Primary focus initially is CD38-associated Multiple Myeloma

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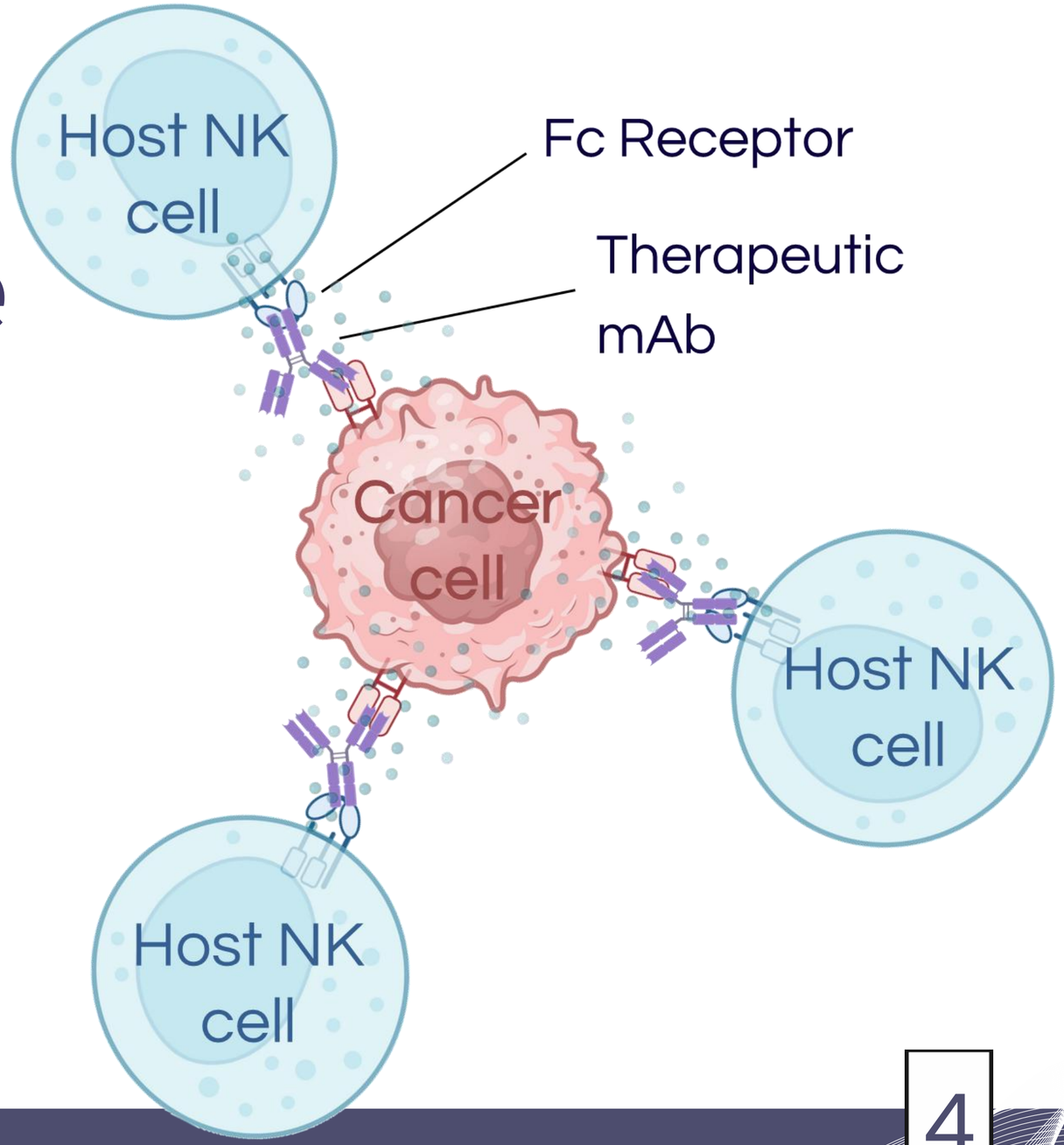
NK Cells Engage Therapeutic Antibodies

Endogenous NK cells cooperate with therapeutic antibodies to eliminate targets through **antibody-dependent cellular cytotoxicity** (ADCC).



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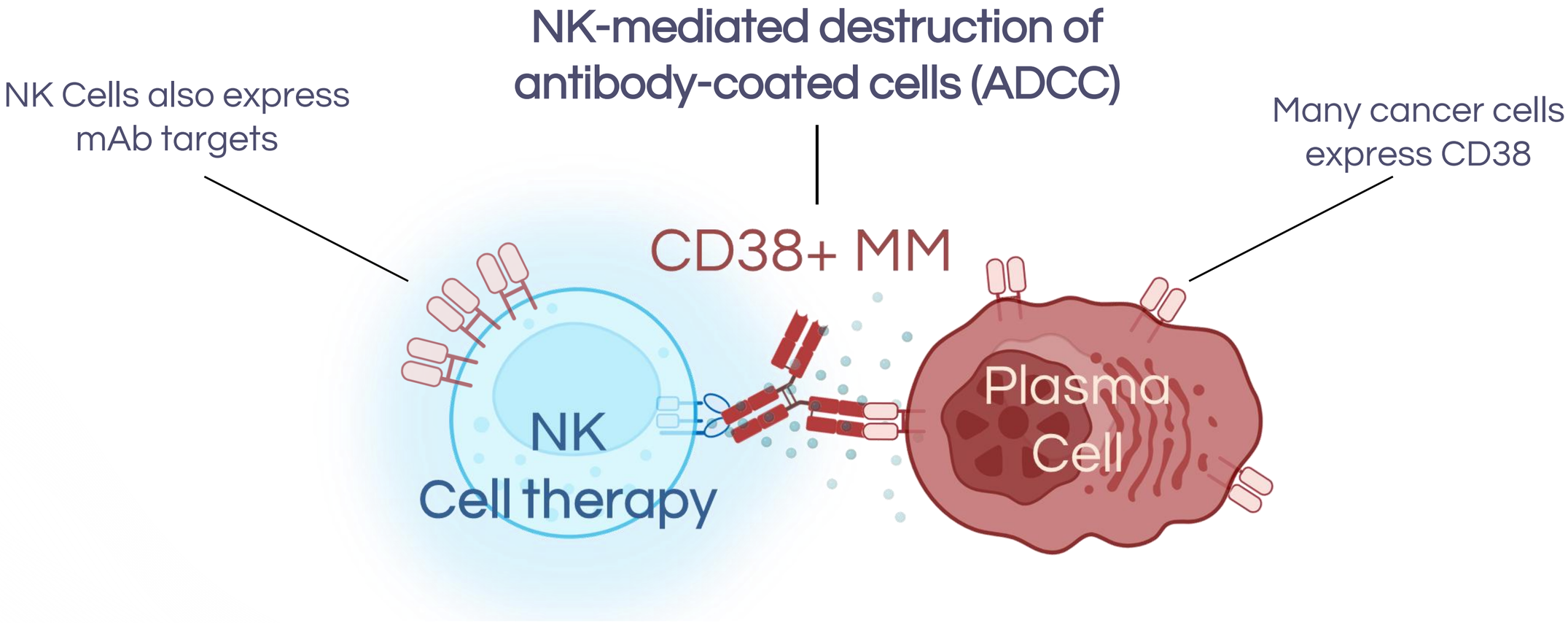
NK Cells Augment mAbs[1], but there is a problem…



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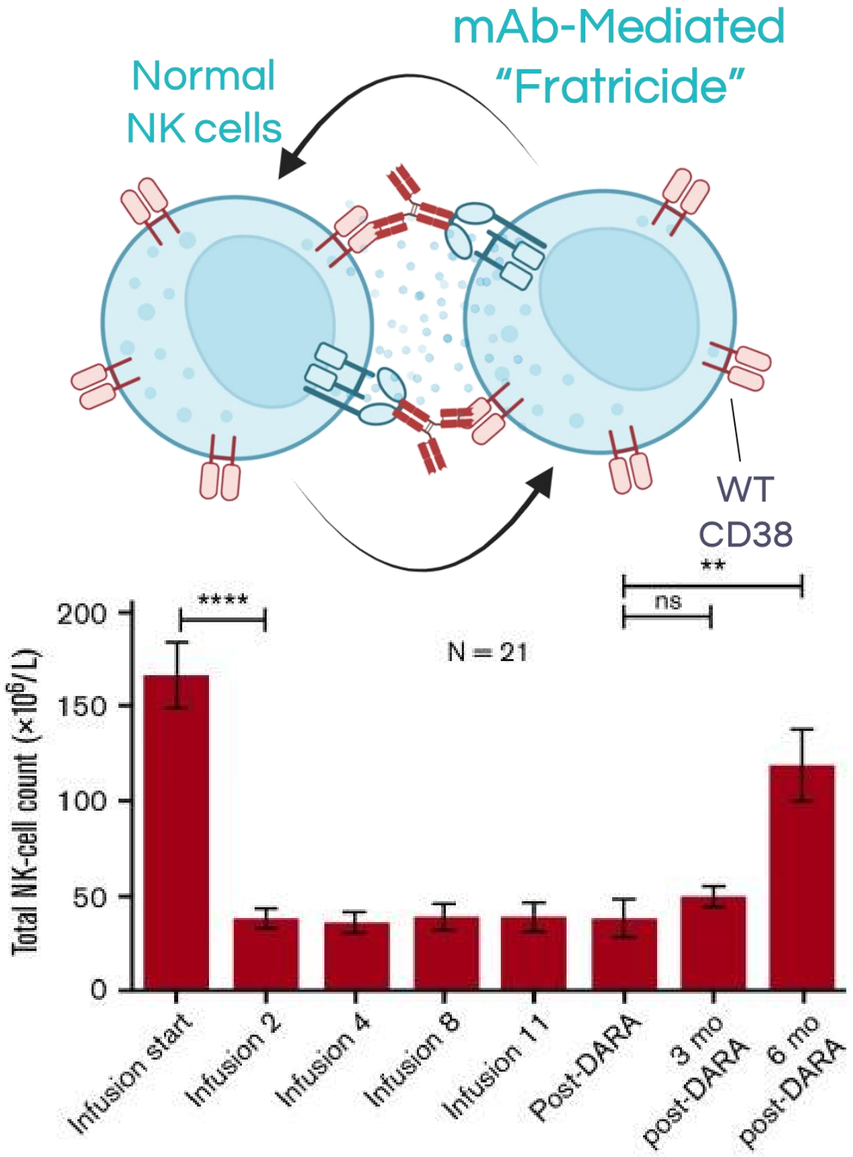
Fratricide Reduces NK Cell Numbers in Patients

- CD38 is expressed on healthy NK cells, so a CD38 antibody makes them target and kill each other, a phenomenon known as “**fratricide**”.

- This results in a dramatic and prolonged reduction of NK cells in patients[2].



Casneuf, et al., Blood Adv. 2017 Oct

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The Problem

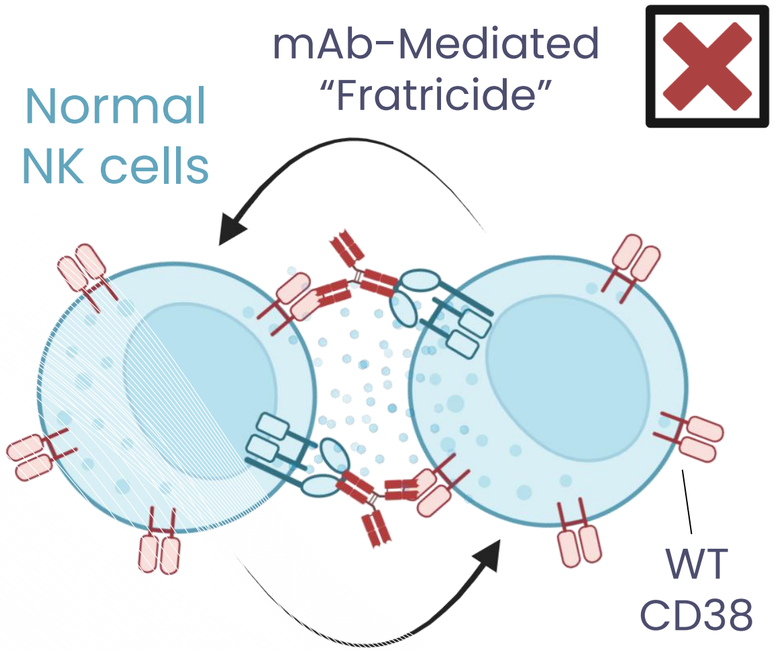
- CD38 is expressed on healthy NK cells, so a CD38 antibody makes them target and kill each other[2].
- This is called “fratricide”, and it is known to severely hinder mAb activity[3].

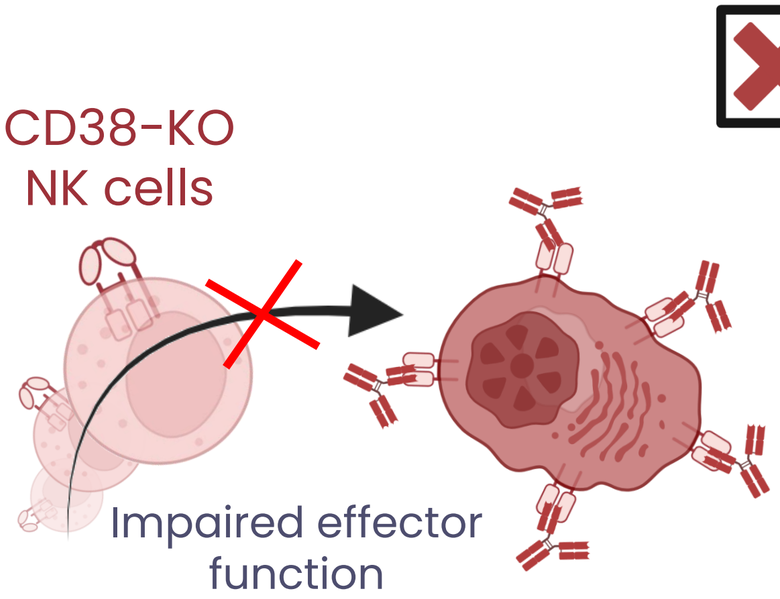
Gen. I Approach

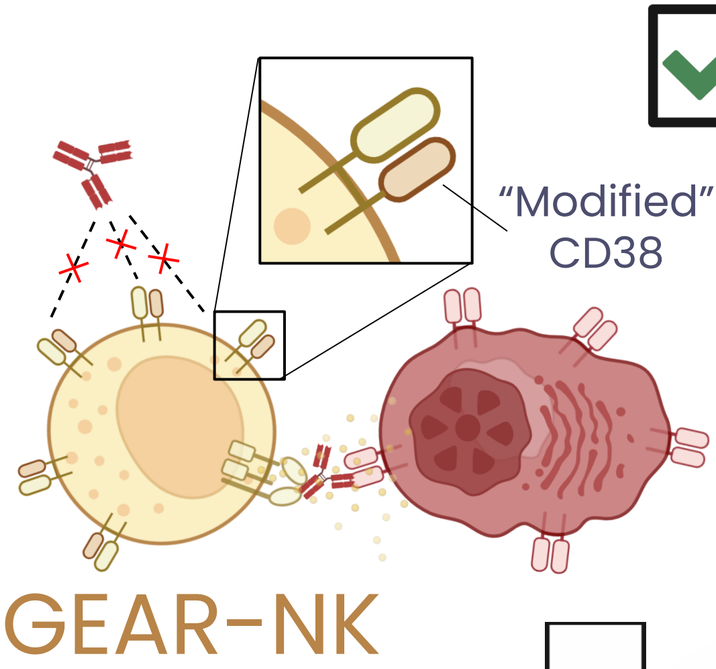
- Some have attempted to simply KO CD38 from NK cells to avoid fratricide.
- This limits fratricide but CD38 deletion significantly impairs NK cell function *in vivo*[4,5].

Our Novel Solution

- At GEAR we precisely modify CD38 so the function is not disrupted, but the mAb can’t bind.
- This allows our GEAR-NK cells to avoid fratricide while maintaining full effector function.







GEAR-NK

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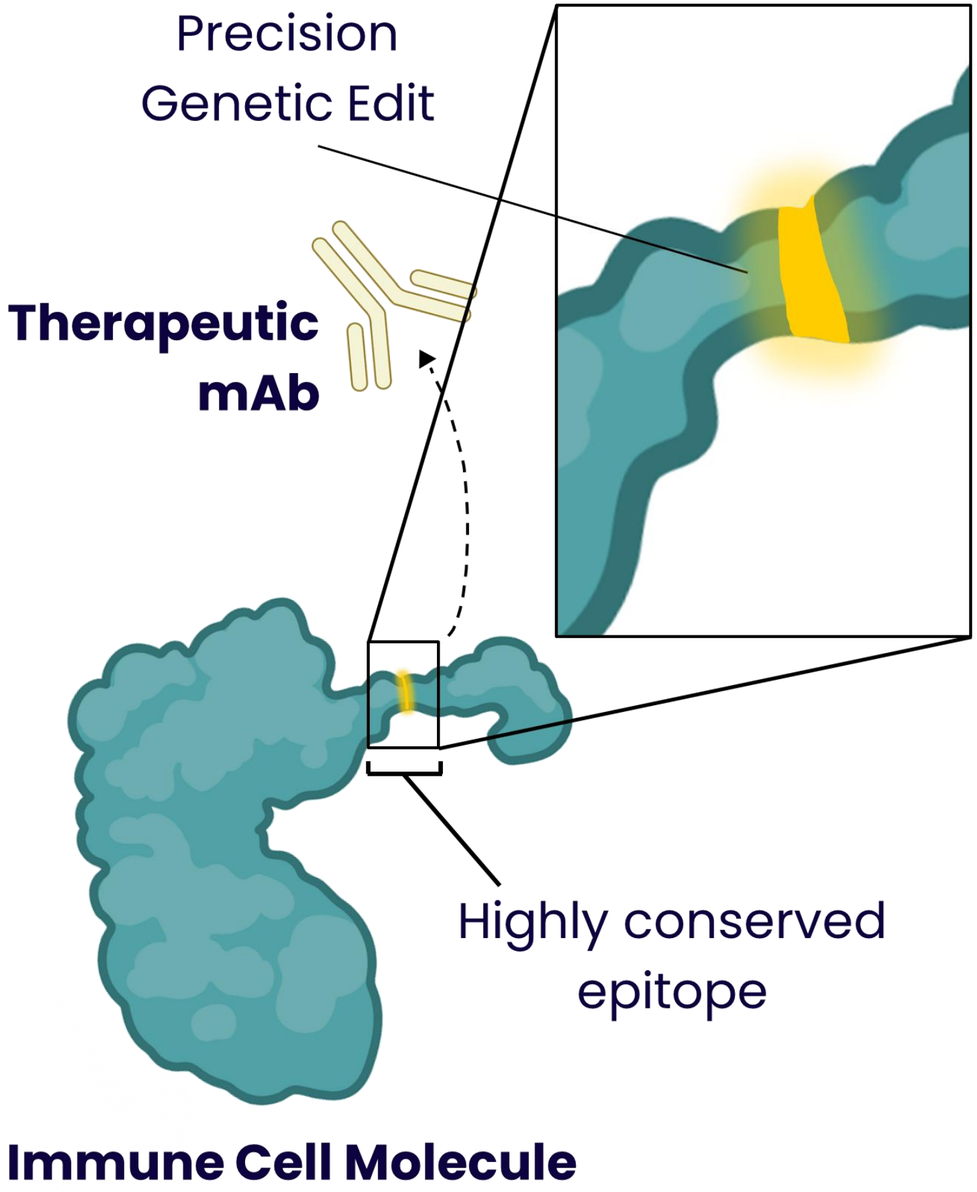

GEAR Therapeutics' Novel Solution

Precision Shielding

- Highly rational, CRISPR-mediated epitope editing platform
- **Disrupts mAb binding epitope while retaining enzymatic function**
- Versatile technology that can be used in many different disease settings

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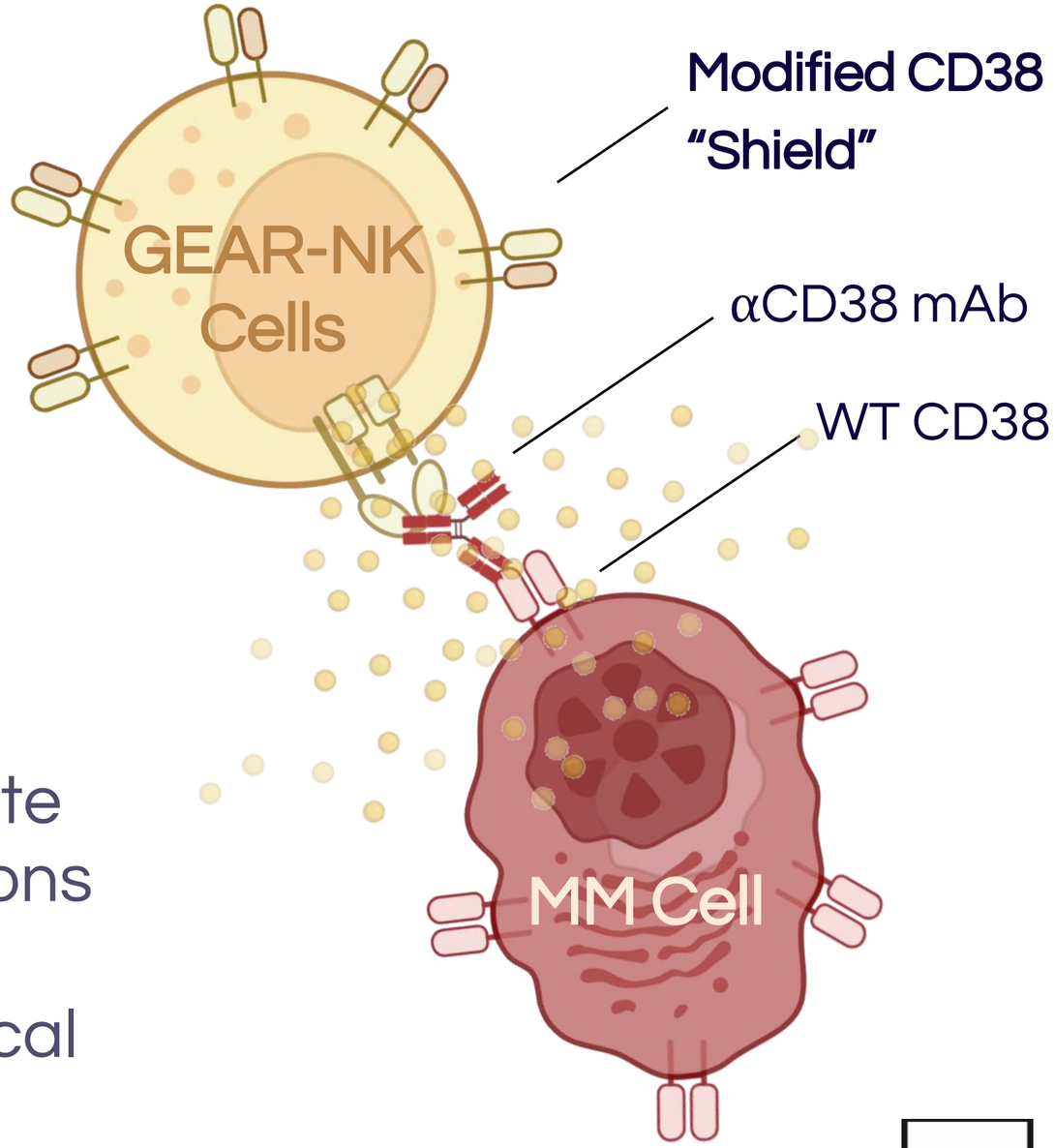
CD38-Positive Multiple Myeloma

- Multiple myeloma is the first cancer indication
- GEAR platform can be used to generate other GEAR-NK cells for other indications
- Great potential in multiple hematological indications including autoimmunity



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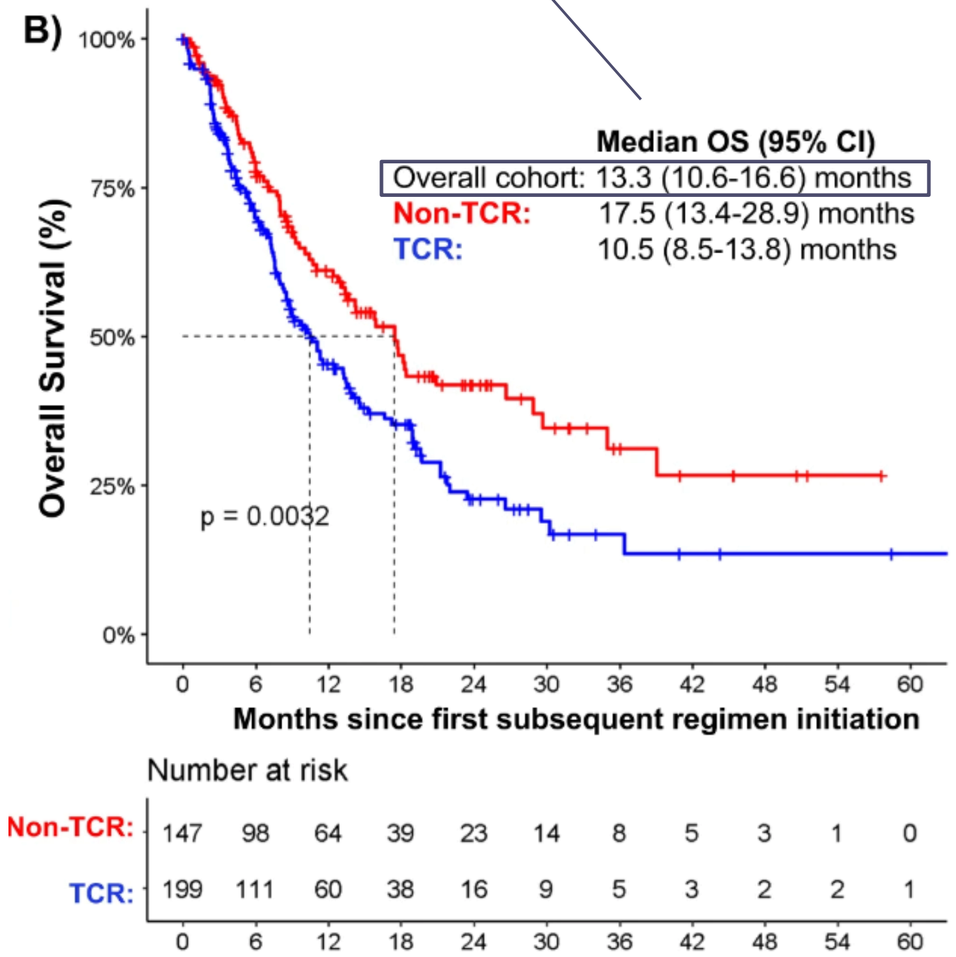
Unmet Medical Need in r/r MM

- 160,000 diagnoses globally with a 66% mortality rate[6].
- Median OS for αCD38 mAb-refractory patients is ~13 months[6]
- Combination with CD38-GEAR-NK will greatly improve patient outcomes

Median OS for αCD38 mAb-refractory patients is 13.3 months



Visram et al., Blood Cancer J. 2023[6]

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CD38-Targeting Monoclonals

janssen

DARZALEX®
(daratumumab)

$9.7B USD in 2023†

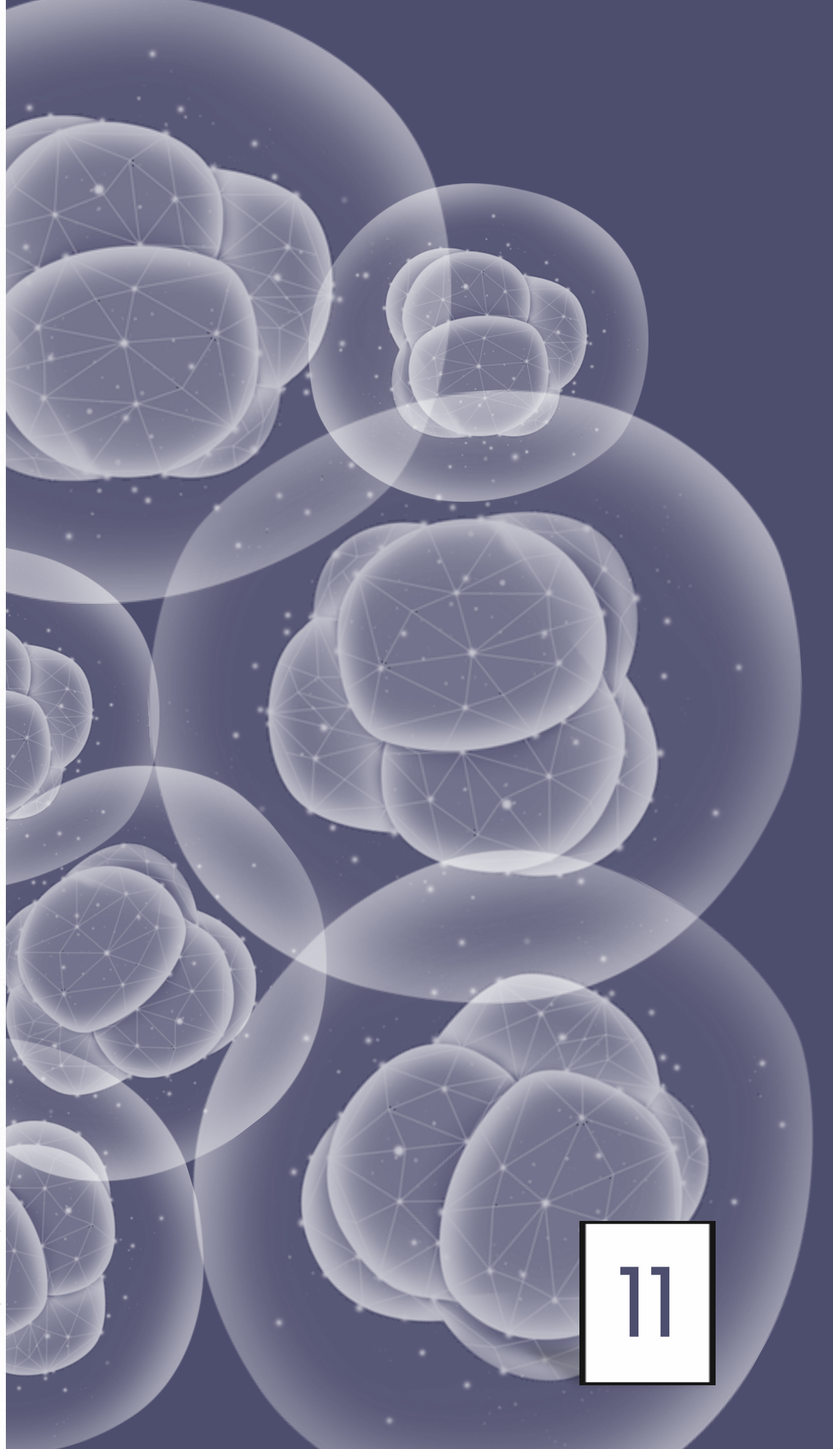
- 22% increase from 2022†
- Projected to hit $14.7B by 2030

sanofi

SARCLISA®
(isatuximab-irfc)

$412M USD in 2023†

- 37% increase from 2022



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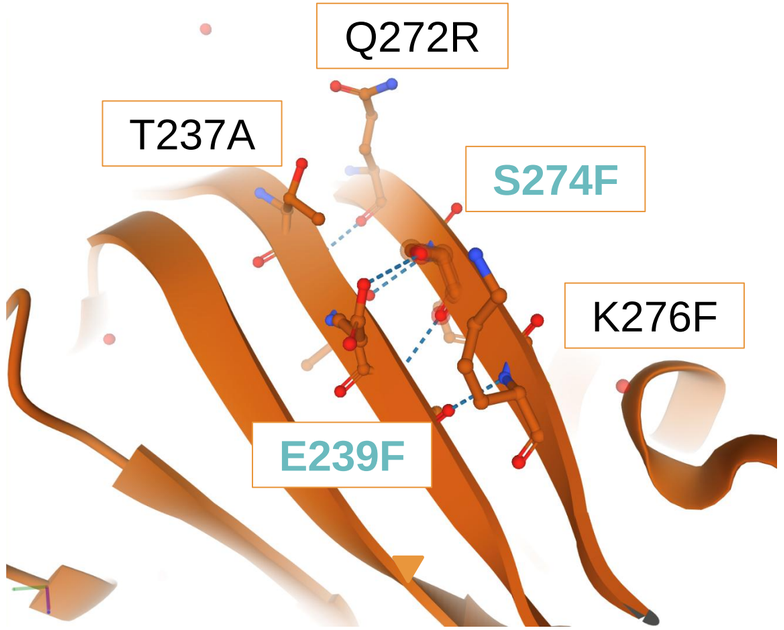
*According to Bloomberg Intelligence
†According to Fierce Pharma

GEAR Therapeutics' Novel Solution

GEAR-NK Precision Genetic Editing Approach for CD38

We identified **5 amino acid residues** likely responsible for Daratumumab binding and generated subsequent mutants.




```
P28907 CD38_HUMAN   1   MANCEFSPVSGDKPCCRLSRRAQLCLGVSILVL-ILVVVLAVVVPRWRQQWSGPGTTKRF  59
                        MANCEFSPVSGDKPCCRLSRRAQ+CLGV +LVL ILVVV+AVV+PRWRQQWSG GTT RF
Q5VAN0 CD38_MACFA   1   MANCEFSPVSGDKPCCRLSRRAQVCLGVCLLVLLILVVVVAVVLPRWRQQWSGSGTTSRF  60

P28907 CD38_HUMAN   60  PETVLARCVKYTEIHPEMRHVDCQSVWDAFKGAFISKHPCNITEEDYQPLMKLGTQTVPC 119
                        PETVLARCVKYTE+HPEMRHVDCQSVWDAFKGAFISK+PCNITEEDYQPL+KLGTQTVPC
Q5VAN0 CD38_MACFA   61  PETVLARCVKYTEVHPEMRHVDCQSVWDAFKGAFISKYPCNITEEDYQPLVKLGTQTVPC 120

P28907 CD38_HUMAN   120 NKILLWSRIKDLAHQFTQVQRDMFTLEDTLLGYLADDLTWCGEFNTSKINYQSCPDWRKD 179
                        NK LLWSRIKDLAHQFTQVQRDMFTLED LLGYLADDLTWCGEFNT +INYQSCPDWRKD
Q5VAN0 CD38_MACFA   121 NKTLLWSRIKDLAHQFTQVQRDMFTLEDMLLGYLADDLTWCGEFNTFFINYQSCPDWRKD 180

P28907 CD38_HUMAN   180 CSNNPVSVFWKTVSRRFAEAACDVVHVMLNGSRSKIFDKNSTFGSVEVHNLQPEKVQTLE 239
                        CSNNPVSVFWKTVSRRFAE AC VVHVMLNGSRSKIFDKNSTFGSVEVHNLQPEKVQ LE
Q5VAN0 CD38_MACFA   181 CSNNPVSVFWKTVSRRFAETACGVVHVMLNGSRSKIFDKNSTFGSVEVHNLQPEKVQALE 240

P28907 CD38_HUMAN   240 AWVIHGGREDSRDLCQDPTIKELESIISKRNIQFSCKNIYRPDKFLQCVKNPEDSSCTSE 299
                        AWVIHGGREDSRDLCQDPTIKELESIISKRNI+F CKNIYRPDKFLQCVKNPEDSSC S
Q5VAN0 CD38_MACFA   241 AWVIHGGREDSRDLCQDPTIKELESIISKRNIRFFCKNIYRPDKFLQCVKNPEDSSCLSG 300
```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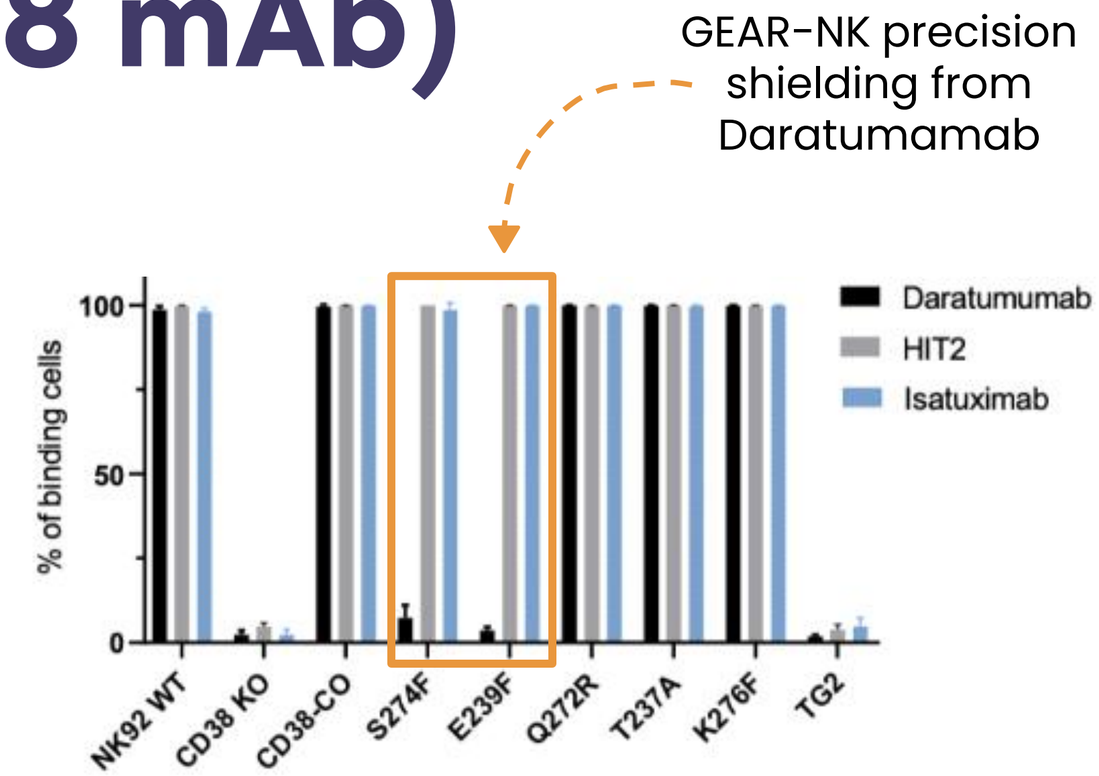
CD38 Variants are Shielded from Daratumamab (aCD38 mAb)

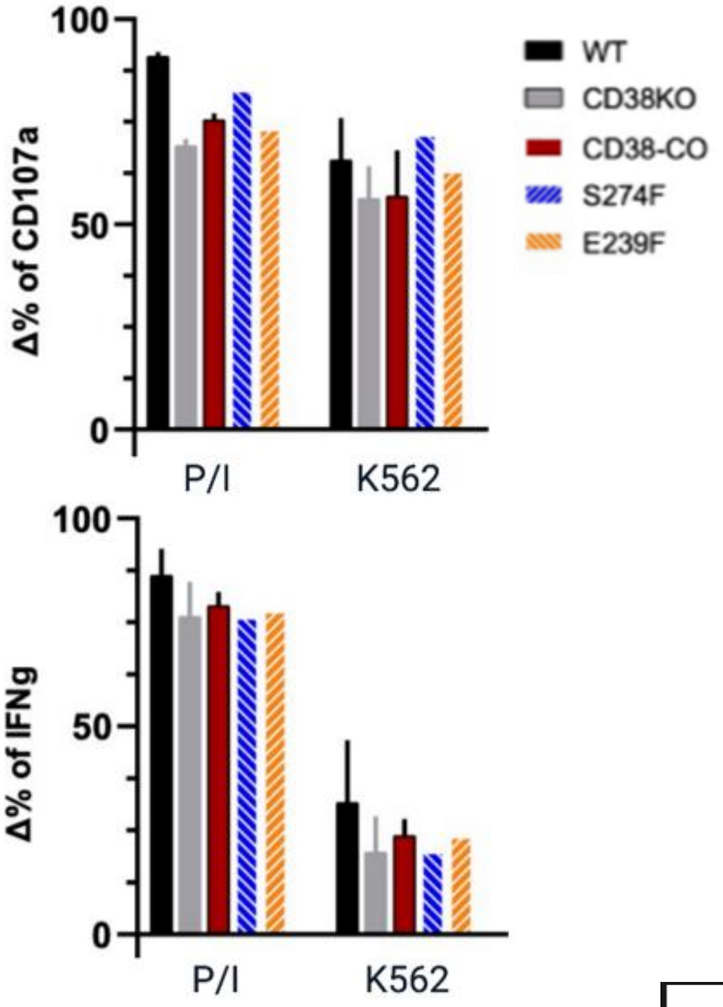
- CD38 mAb Daratumamab (black bars) does not recognize 2 CD38 variants:
  - S274F
  - E239F
- Other CD38 mAbs (HIT2 and Isatuximab) can bind…
  - Modified CD38 is present on the surface but not bound by Dara.



CD38-GEAR-NK Cells Are Functional

- Compared to WT (black bars), CD38-edited GEAR NK cells (blue and yellow bars) displayed no significant reduction in:
  - cytotoxicity (**top**)
  - release of IFN-g (**bottom**).

Activation of **primary NK** cells w/ various GEAR-NK edits



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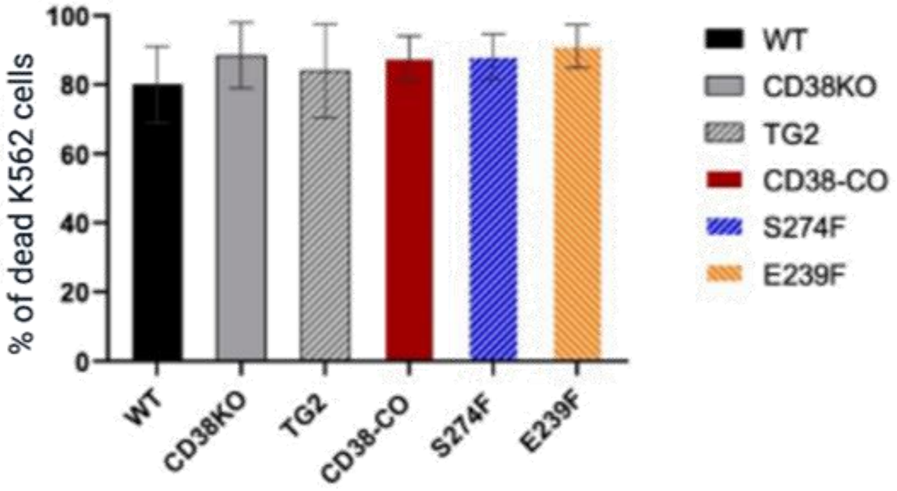
CD38-GEAR-NK Cells Are Functional

- CD38-edited GEAR NK cells (blue and yellow bars) displayed >80% killing of K562 cells (CML) cells – even outperforming WT NK cells (black bars)

In vitro cell killing assay against K562 cells



GEAR THERAPEUTICS

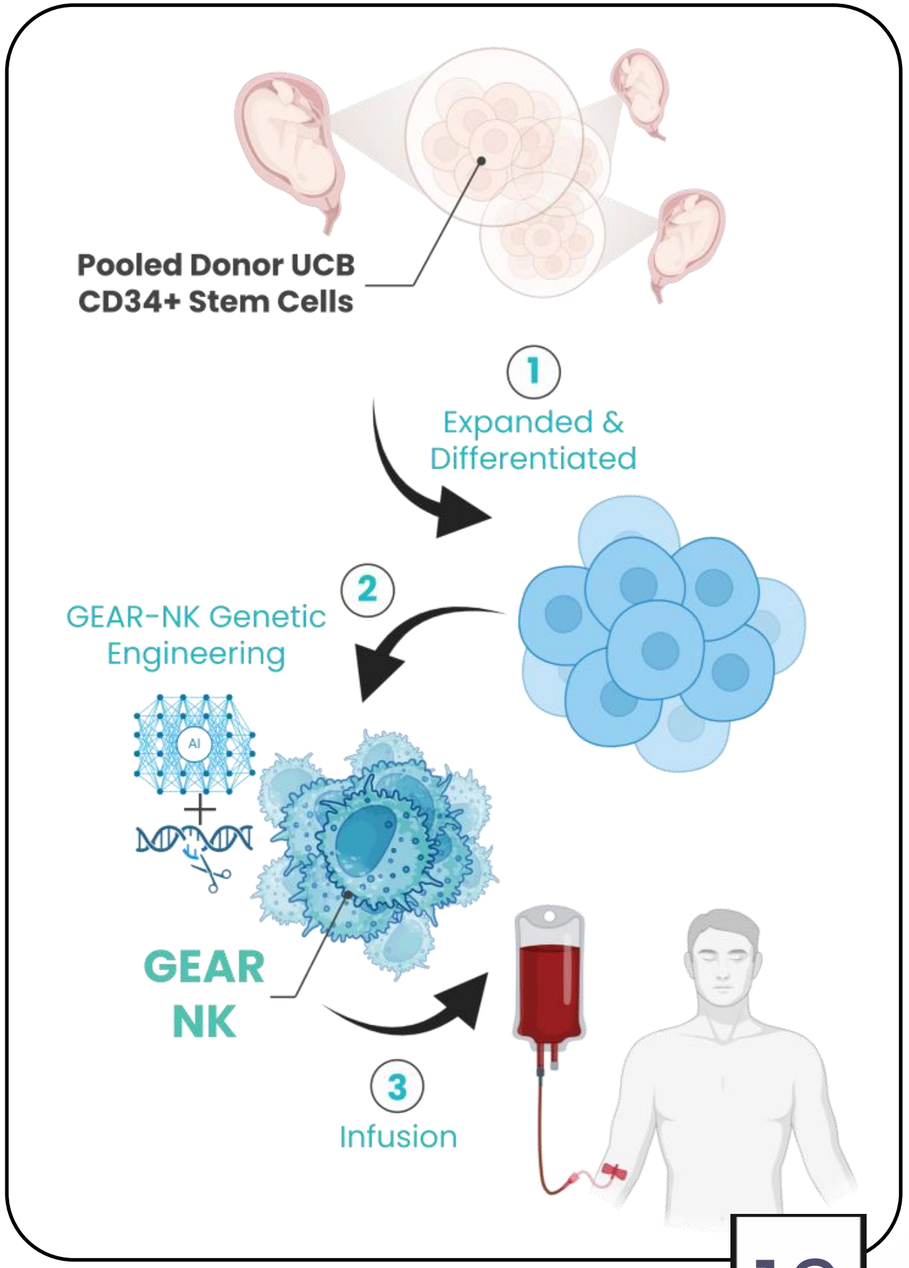
Our Superior Cell Source

Pooled-Donor UCB-Derived CD34+ Stem Cells

- Proven Safety in Multiple Clinical Trials

- **Umbilical Cord blood is:**

  - ☑ Young & Healthy
  - ☑ Plentiful & Cost-Effective
  - ☑ Safe & Powerful
  - ☑ No Need for HLA Matching
  - ☑ Truly Universal



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Scientists Behind GEAR

Evren Alici MD, PhD

Head of the Gene and Cell Therapy Group, Division of Hematology, Department of Medicine, **Karolinska Institutet**, Karolinska University Hospital, Stockholm

Hans-Gustaf Ljunggren, MD, PhD

Former Dean of Research, Karolinska Institutet and founder of the Center for Infectious Medicine, Department of Medicine, **Karolinska Institutet**, Karolinska University Hospital, Stockholm

Arnika K. Wagner, PhD

Assistant Professor, Department of Medicine, **Karolinska Institutet**, Karolinska University Hospital, Stockholm

GEAR THERAPEUTICS

Management Team

Dave Mehalick
Chief Executive Officer

30 years of diverse business experience in healthcare, information technology and finance including consulting, capital markets, private equity, and investments

Brian Cogley
Chief Financial Officer

15 + years of corporate financial experience in life sciences, pharmaceuticals, and financial services, expertise in asset management, and investments

**Through a Management Services Agreement with Coeptis Therapeutics, we will have access to their management team at a significantly reduced cost

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