gamida cell

Pioneering Next-Generation NK Cell Therapies

NK Pipeline Deep Dive

Julian Adams, Ph.D.
CEO

Disclaimer

This presentation contains forward-looking statements as that term is defined in the Private Securities Litigation Reform Act of 1995, including with respect to timing of initiation and progress of, and data reported from, the clinical trials of Gamida Cell's product candidates (including GDA-201), anticipated regulatory filings (including the submission of the BLA for omidubicel to the FDA), and the potentially life-saving or curative therapeutic and commercial potential of its product candidates. Any statement describing Gamida Cell's goals, expectations, financial or other projections, intentions or beliefs is a forward-looking statement and should be considered an at-risk statement. Such statements are subject to a number of risks, uncertainties and assumptions, including those related to the impact that the COVID-19 pandemic could have on our business, and including the scope, progress and expansion of Gamida Cell's clinical trials and ramifications for the cost thereof; clinical, scientific, regulatory and technical developments; and those inherent in the process of developing and commercializing product candidates that are safe and effective for use as human therapeutics, and in the endeavor of building a business around such product candidates. In light of these risks and uncertainties, and other risks and uncertainties that are described in the Risk Factors section and other sections of Gamida Cell's Annual Report on Form 20-F, filed with the Securities and Exchange Commission (SEC) on March 9, 2021, as amended, and other filings that Gamida Cell makes with the SEC from time to time (which are available at http://www.sec.gov), the events and circumstances discussed in such forward-looking statements may not occur, and Gamida Cell's actual results could differ materially and adversely from those anticipated or implied thereby. Although Gamida Cell's forward-looking statements reflect the good faith judgment of its management, these statements are based only on facts and factors currently known by Gamida Cell. As a result, you are cautioned not to rely on these forward-looking statements.

Agenda

1. **Gamida Cell introduction**
   Julian Adams, Ph.D.
   Chief Executive Officer, Gamida Cell
2. **NAM-enabled NK cell therapy mechanism of action**
   Julian Adams, Ph.D.
   Chief Executive Officer, Gamida Cell
3. **Potential of NK cell therapy**
   Jeff Miller, M.D.
   Deputy Director of the University of Minnesota Masonic Comprehensive Cancer Center
4. **GDA-201 Phase 1/2 trial**
   Ronit Simantov, M.D.
   Chief Medical Officer, Gamida Cell
5. **Unmet need in lymphoma**
   Michele Korfin, R.Ph.
   Chief Operating and Chief Commercial Officer, Gamida Cell
6. **A GDA-201 patient's perspective**
   Wayne Altenbernd
   GDA-201 recipient
   Veronika Bachanova, M.D., Ph.D.
   Hematologist/Oncologist at University of Minnesota Health
7. **Genetically-modified NK cell pipeline**
   Yona Geffen, Ph.D.
   Vice President, Research and Development, Gamida Cell
8. **Q&A**

Committed to Cures: Near-term Promise and Long-term Potential

Proprietary nicotinamide (NAM) cell expansion platform enables a continuing series of advanced cell therapy programs

Readying for commercialization

Omidubicel

- Preparing for BLA submission in 4Q21*
- Potential to be first FDA-approved cell therapy for bone marrow transplantation
- Breakthrough Therapy and Orphan Drug status

Progressing clinical program in NK cells

GDA-201

- Innate NK cell product with positive Phase 1 data
- Submitted IND for a Phase 1/2 trial in NHL
- IND on clinical hold prior to patient dosing pending ongoing discussions with FDA

Opening new frontiers in cancer immunotherapy

GDA-301/401/501/601

- Proof-of-concept for CAR and CRISPR editing
- Evidence of increased cytotoxicity in preclinical studies
- Potential in blood cancers and solid tumors

*Subject to pre-BLA meeting with the FDA in 4Q21

Gamida Cell NK Points of Differentiation

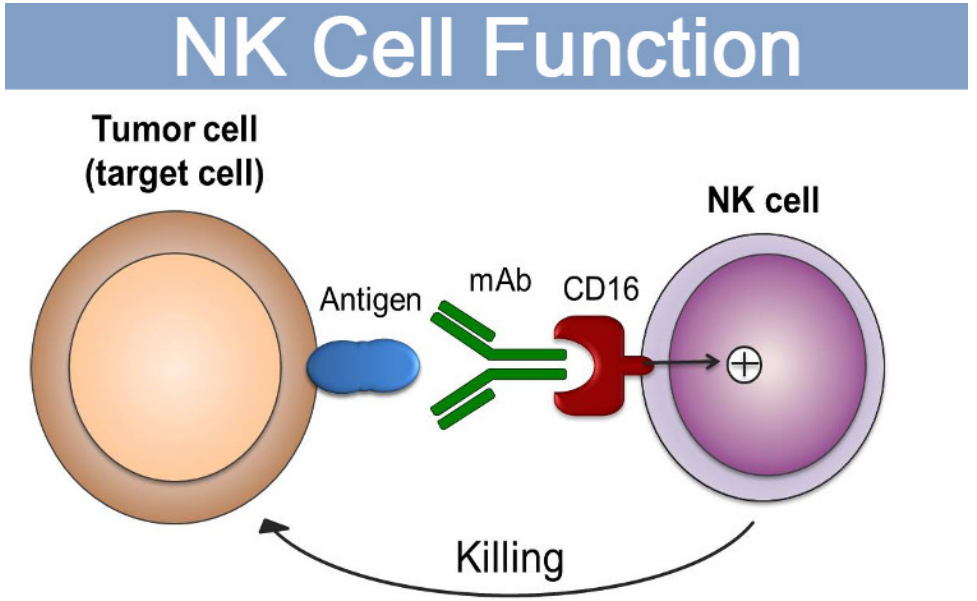
NAM-enabled cell expansion technology	• Enhances potency, function and persistence • Improves homing and retention to lymphoid tissues
Compelling NK product with positive clinical data (GDA-201)	• Positive Phase 1 clinical study completed • Phase 1/2 study planned with cryopreservation*
R&D engine of unique genetically-modified NK cell constructs	• Customized modifications using CAR and CRISPR • Potential indications include solid tumors and hematologic malignancies
Cell therapy manufacturing capabilities and experience	• Established manufacturing facility in Israel with experienced scientific and operations team • Commercial scale-up capabilities

*IND on clinical hold pending ongoing discussions with FDA

Putting NK Cells to Work Using Our NAM Technology Platform

Benefits of NK Cells

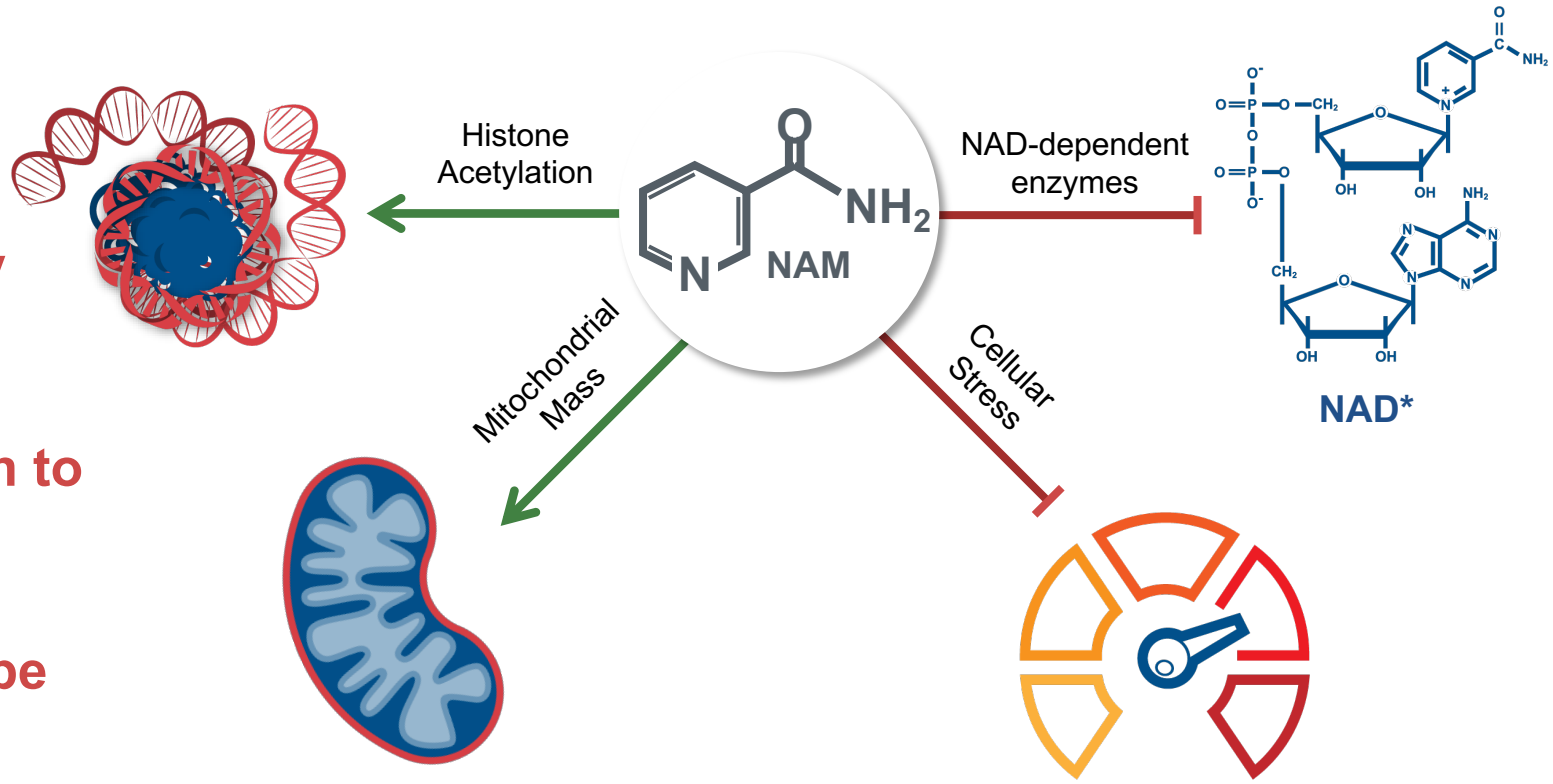
- **Natural killer (NK) cells infusion is a promising immune therapy for cancer**
  - No HLA matching required
  - Synergy with antibodies
  - Potential for off-the-shelf therapy
- **Expansion is necessary to obtain clinically meaningful doses with retained cell function**



Pipeline Built on Proprietary NAM Platform Technology

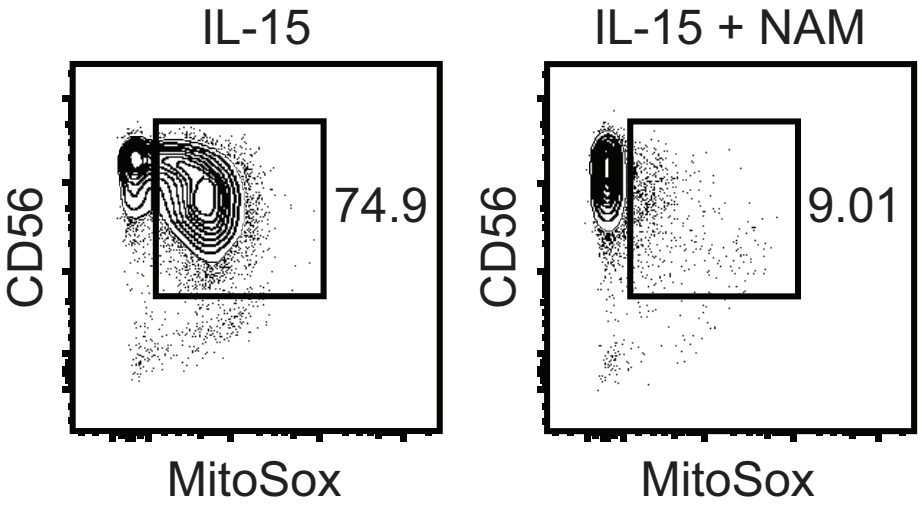
NAM Platform Technology

- Enhances the number of allogeneic donor cells
- Enhances cellular functionality and phenotype
- Improves homing and retention to lymphoid tissues
- Potential to expand any cell type

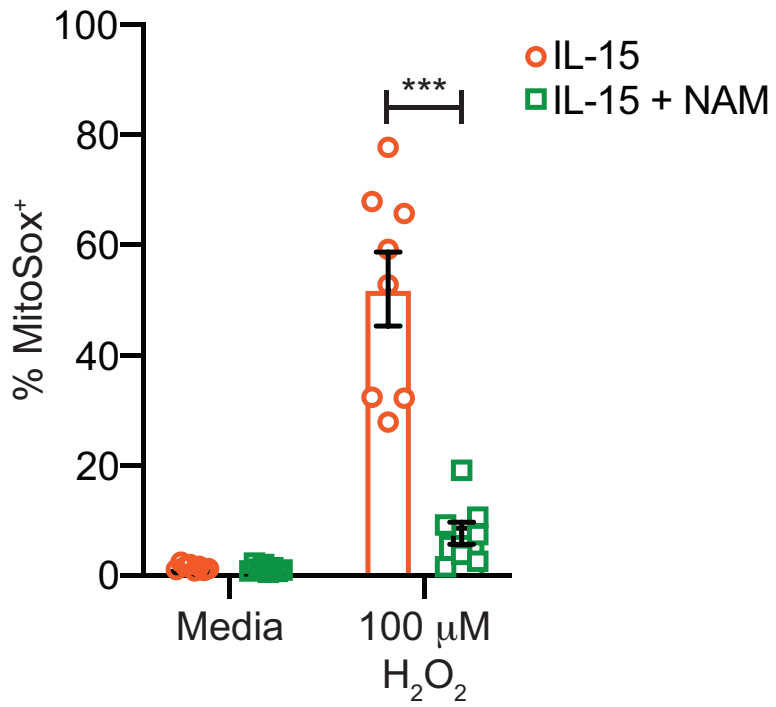


Strongly Protective Effect Against Oxidative Stress Favors Survivability in the Tumor Microenvironment

NK cells were expanded with IL-15 and with or without NAM



NAM-expanded NK cell mitochondria produce decreased levels of lethal **superoxide** (labeled with fluorescent marker) when the cells are challenged with hydrogen peroxide, reducing oxidative stress.



- F. Cichocki, presented at the American Association of Immunologists (AAI) conference, May 2021

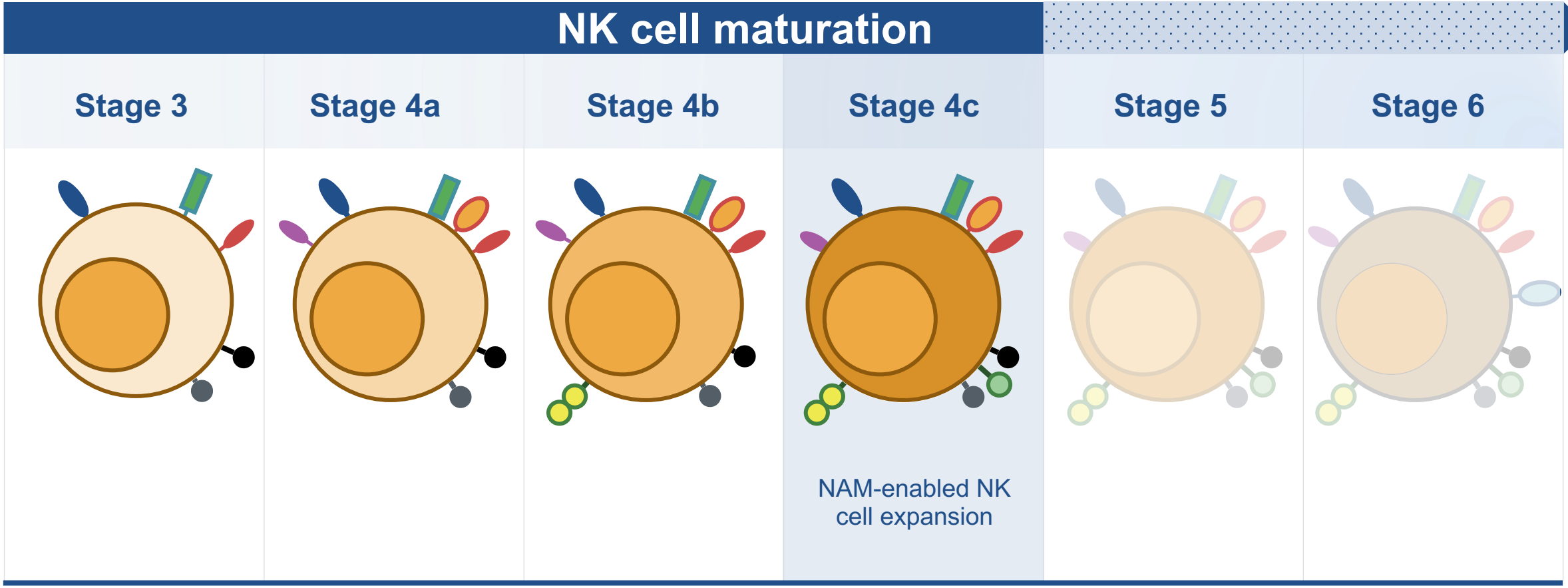
GDA-201: NAM-Expanded NK Cells Display “Memory-Like” Phenotype

NK Marker	Function	+ NAM		P value
CD56*	Lineage and cytotoxicity	▲	+	P=0.09
CD57*	Lineage and terminal differentiation receptor/exhaustion	▼	-	P=6.37x10^-8
NKp80*	Lineage and activation receptor	▼	-	P=0.52
CD62L*	Lymph node homing receptor	▲	+	P=0.02
CD49a*	Integrin/adhesion receptor	▲	+	P=0.03
CD200R**	Checkpoint inhibitor	▼	-	P=0.04
LAG**	Checkpoint inhibitor	▼	-	P= 3.2x10^-5

*Correlates with cytokine-induced memory-like cell

**Correlates with decreased exhaustion and downregulation of checkpoint inhibition

NAM Enhances NK Cells Functionality During Cell Expansion by Preventing the Exhausted Phenotype



Natural Killer Cells: Development, Maturation, and Clinical Utilization. Frontiers in Immunology, 2018

Upcoming NAM-Enabled NK Cell Presentations at SITC

Friday, November 12, 2021

7:00 a.m. – 8:30 p.m. EST

Cytotoxicity of nicotinamide enhanced natural killer cells GDA-201 is based on metabolic modulation as demonstrated by AI assisted analysis of NK cell transcriptome and metabolome

Abstract number: 217
Location: Hall E

Saturday, November 13, 2021

7:00 a.m. – 8:30 p.m. EST

Nicotinamide rejuvenates ex-vivo expanded NK cells and enhances their tumor killing capacity

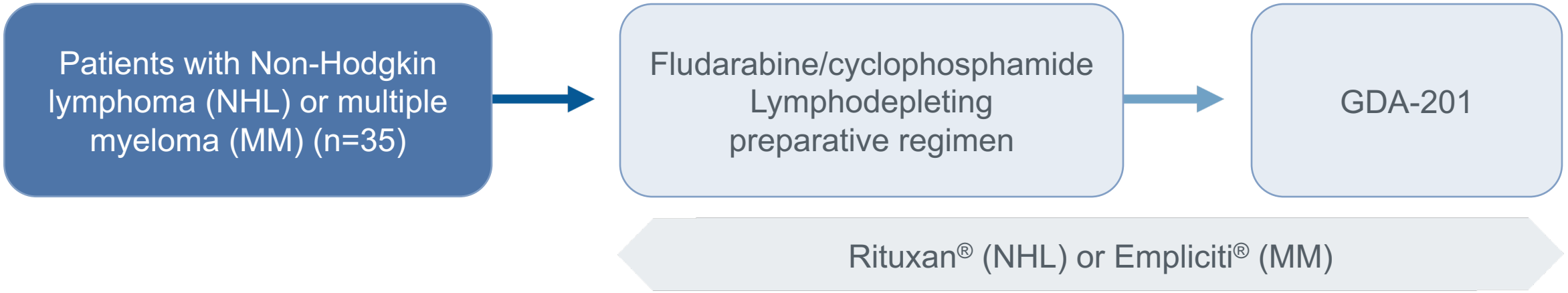
Abstract Number: 162
Location: Hall E

GDA-201 Phase 1 Trial

Proof of concept

gamida cell

Phase 1 Study of GDA-201 in Patients with Non-Hodgkin Lymphoma and Multiple Myeloma



- **Primary endpoint:** Maximum tolerated dose of GDA-201 (3 doses evaluated)
- **Secondary endpoints:** Overall response, toxicity

Bachanova et al., ASH 2020

Safety Summary

- 35 patients treated (19 NHL, 16 MM)
- No dose limiting toxicities
- One patient died of E. coli sepsis, initially reported as CRS
- Most common grade 3/4 adverse events:
  - Thrombocytopenia (n=9)
  - Hypertension (n=5)
  - Neutropenia (n=4)
  - Febrile neutropenia (n=4)
  - Anemia (n=3)
- No neurotoxic events, graft versus host disease, or confirmed CRS

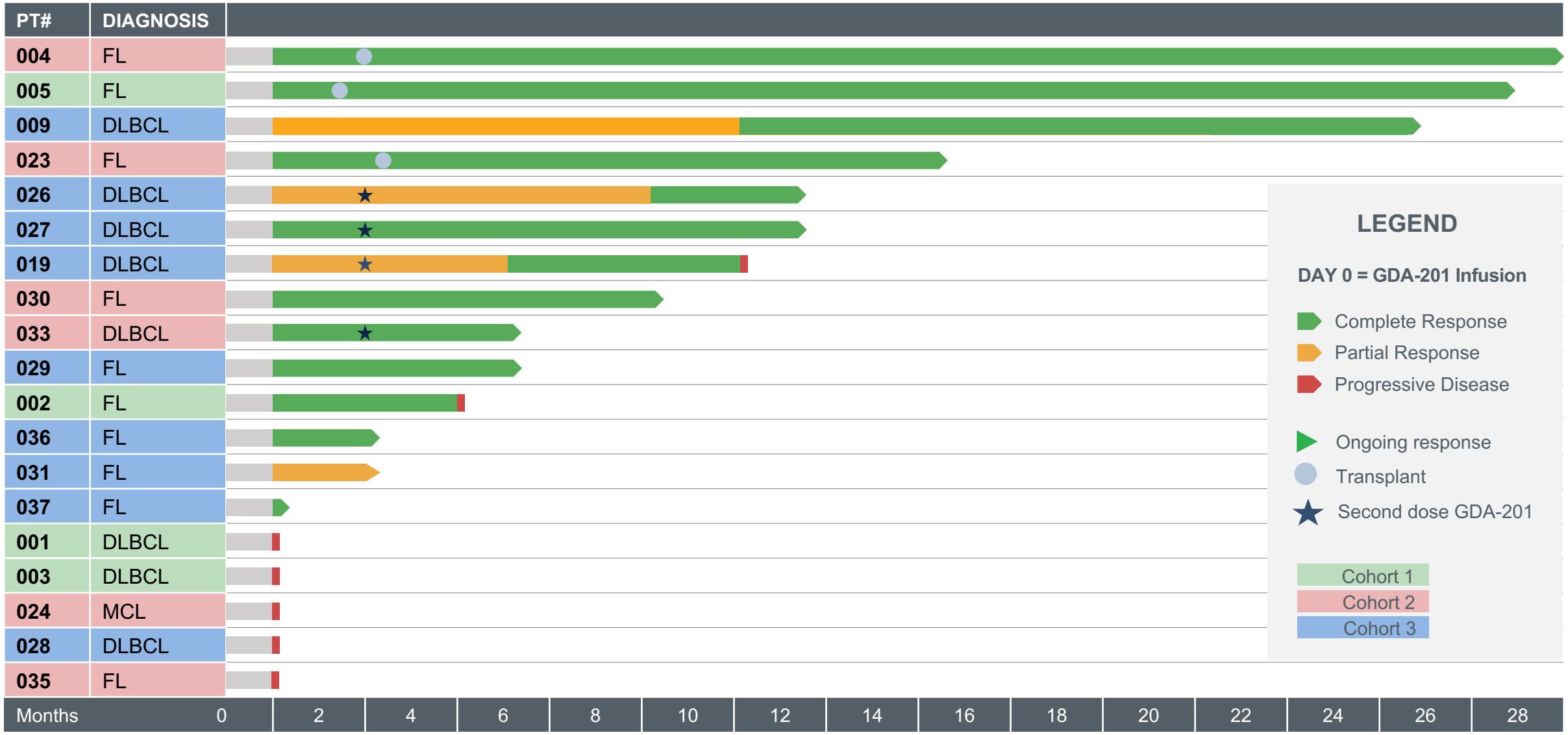
- NHL: non-Hodgkin lymphoma; MM: multiple myeloma; CRS: cytokine release syndrome
- Bachanova et al., ASH 2020

Encouraging Clinical Outcomes: Complete Remissions 68% and Overall Response Rate of 74%

19 PATIENTS WITH NHL	Follicular Lymphoma (FL) (n=10)	Diffuse Large B-Cell Lymphoma (DLBCL) (n=8)
13 CR	8 CR	5 CR
1 PR	1 PR	
5 PD		
ORR: 74%		
CR rate: 68%		

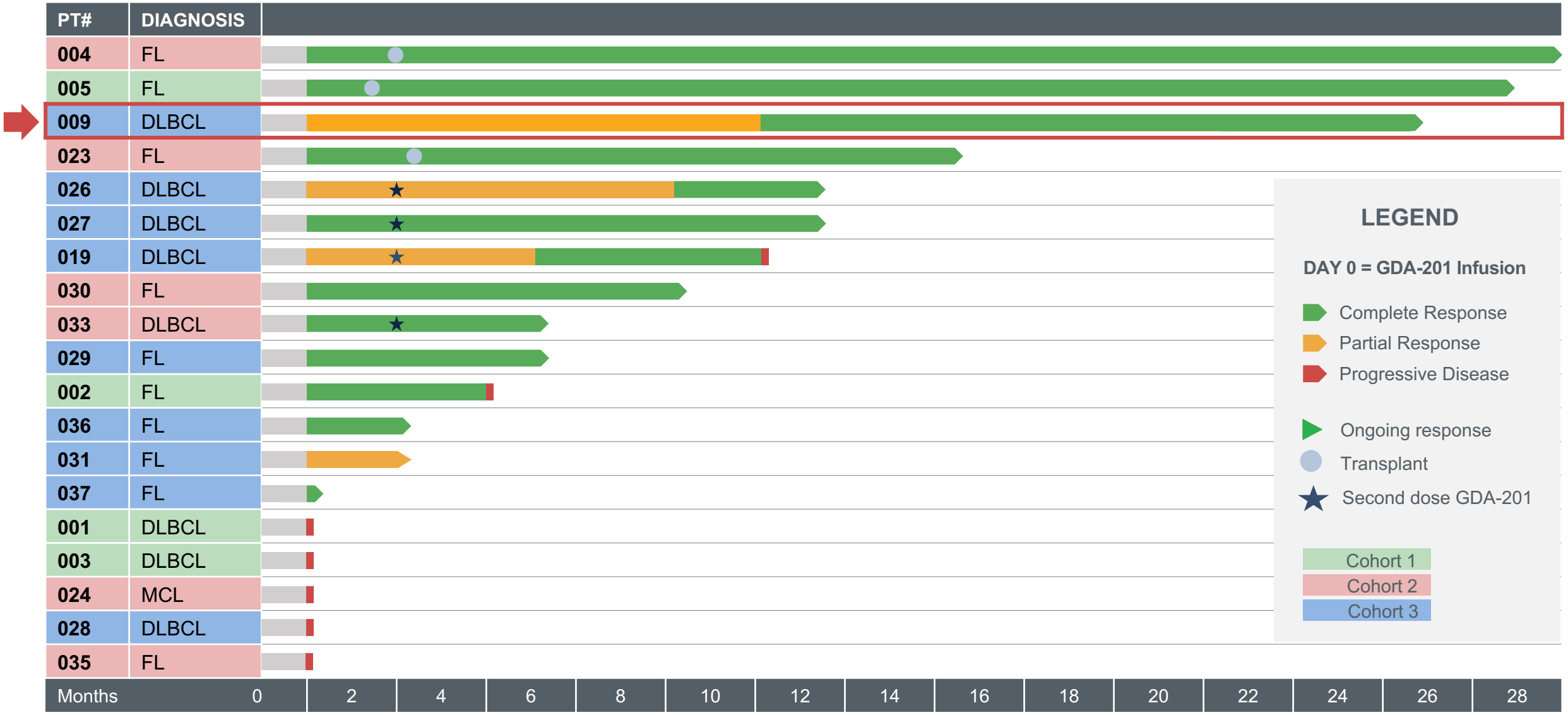
Bachanova et al., ASH 2020

GDA-201 Is Highly Active in Non-Hodgkin Lymphoma



- Note: Cohort 1 dose = 2.0 x 10^7 cells / kg; Cohort 2 dose = 1.0 x 10^8 cells / kg; Cohort 3 dose = 2.0 x 10^8 cells / kg
- Bachanova et al., ASH 2020

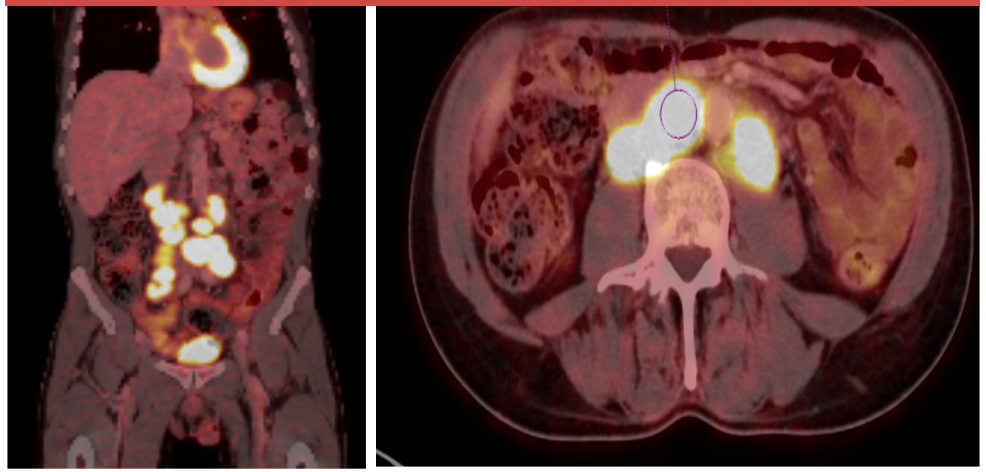
GDA-201 Is Highly Active in Non-Hodgkin Lymphoma



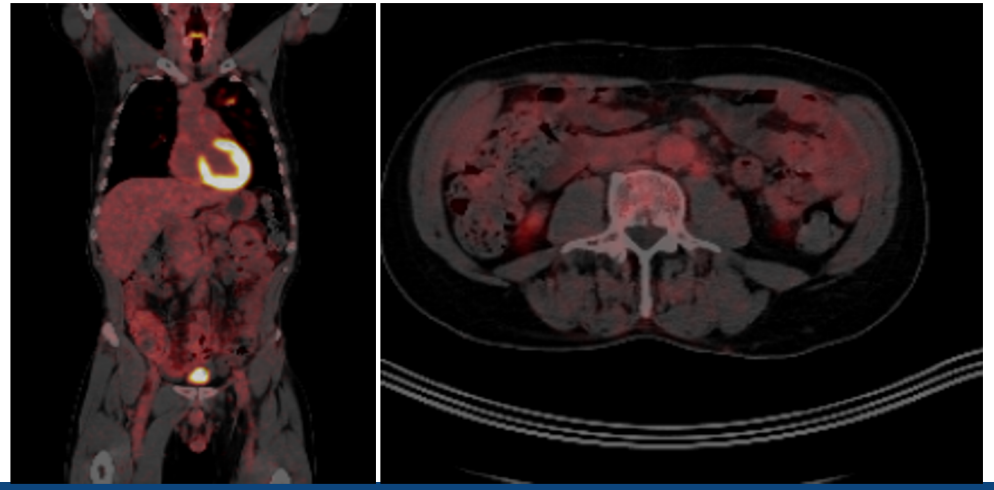
- Note: Cohort 1 dose = 2.0 x 10^7 cells / kg; Cohort 2 dose = 1.0 x 10^8 cells / kg; Cohort 3 dose = 2.0 x 10^8 cells / kg
- Bachanova et al., ASH 2020

Complete Response in Heavily Pretreated Lymphoma Patient

Pt 009: Baseline



Pt 009: 6-month post GDA-201



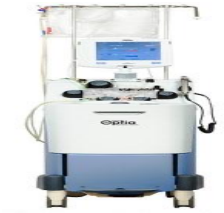
- 57-year-old man with history of CLL and Richter's transformation-large cell lymphoma, measurable retroperitoneal lymph nodes at baseline
- Prior therapy: FCR-light, Rituximab/Bendamustine Ibrutinib/Revlimid, R-CHOP, Venetoclax/Rituximab
- Allogeneic HSCT (matched sibling)
- Relapse at 6 months
- Treated with GDA-201
- 28-day response: Tumor shrinkage
- 6 months: PR with continued tumor shrinkage
- 12 months: Complete response

Bachanova et al. ASH 2019.

Off-The-Shelf Manufacturing with NAM Expansion

NAM rejuvenates NK cell preservation during expansion and cryopreservation

Allogenic NK cells collected by apheresis



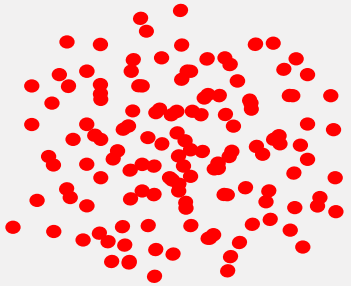
HEALTHY DONOR

Seed CD3- cells from apheresis material

DAY 0

Proprietary expansion with NAM +IL-15 + autologous irradiated CD3+ feeder cells

Highly functional NK cells: ~50-100 billion NK cells with purity >99%



DAY 14

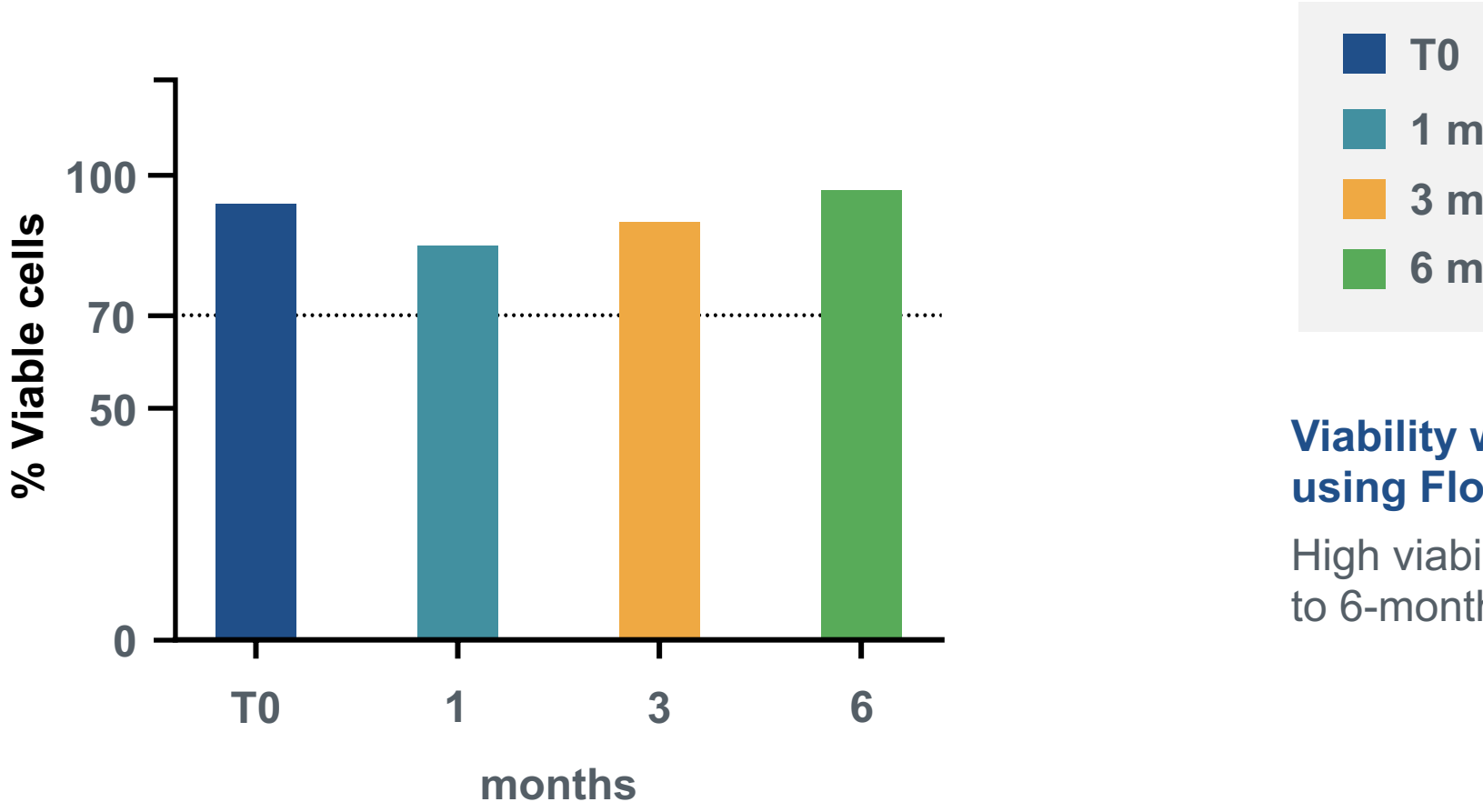
Proprietary cryopreservation and infusion ready

One apheresis procedure can provide several clinical doses

Stability of GDA-201 Cryopreserved Formulation Exhibits High Viability and Maintains Profile Six Months Post-Thaw

- GDA-201 cryopreserved formulation exhibits high viability up to six months post-thaw
- GDA-201 cryopreserved formulation maintained:
  - Phenotype expression of CD56 NK cells; increased CD62L homing and retention marker and expression of CD16; NK cell activity marker
  - Cytotoxicity function: Killing and ADCC
  - Enhanced potency: Intracellular secretion of INF-γ, TNF-α and extracellular degranulation marker CD107a

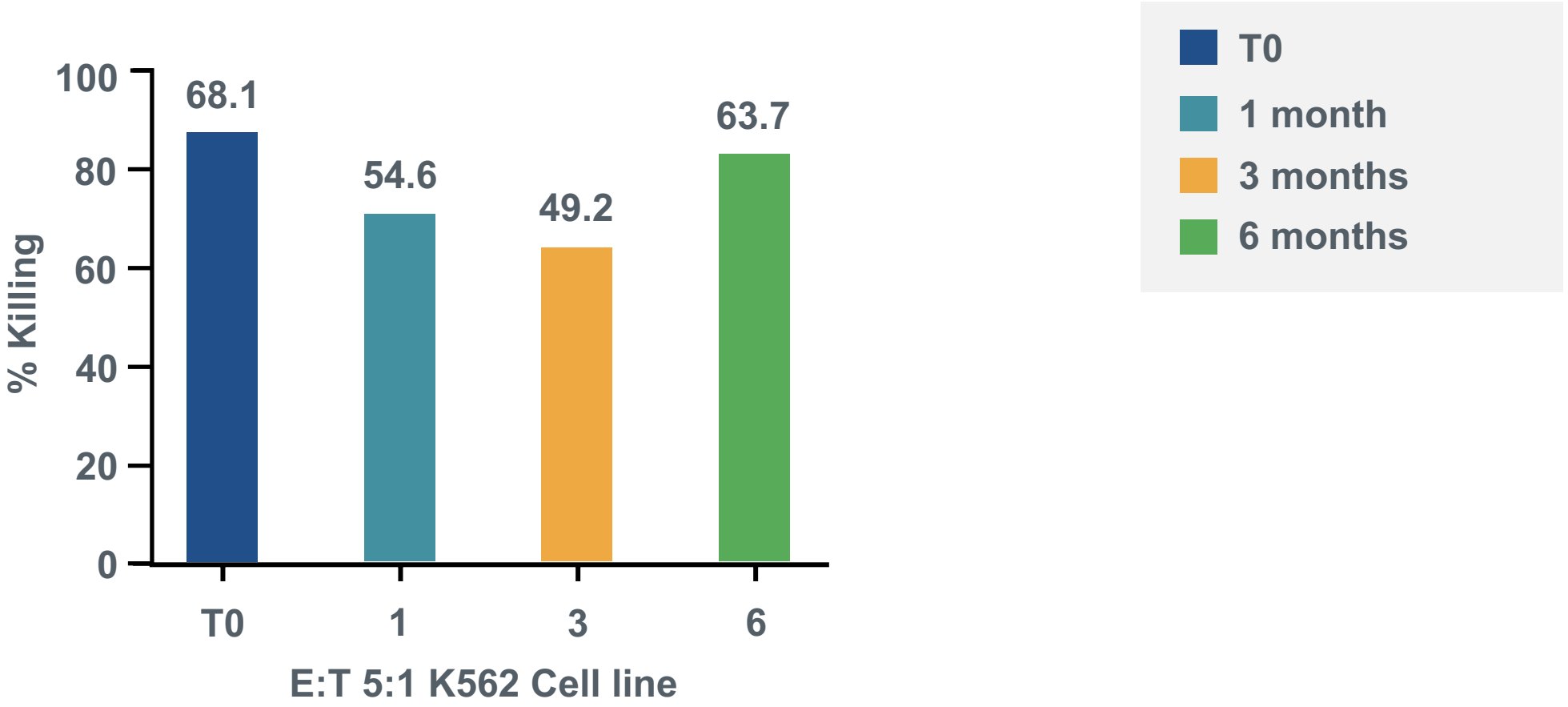
GDA-201 Cryopreserved Formulation Exhibits High Viability Six Months Post-Thaw



Viability was measured using Flow cytometry:

High viability is maintained up to 6-month post thaw

GDA-201 Cryopreserved Formulation Maintained High Cytotoxicity Function (measured at 4-6 hours)



ER#1 data

FACS Killing

gamida cell

GDA-201: Encouraging Clinical Activity and Safety Profile Supports Continued Development

Key Accomplishments

- Preclinical proof of principle
- Clinical proof of concept
- Maximum target dose achieved
- Cryopreserved formulation

Next Step

Phase 1/2 multi-center study in lymphoma for cryo-preserved GDA-201

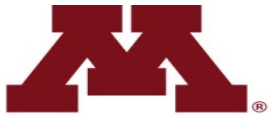
Potential of NK Cell Therapy

Jeff Miller, M.D.

gamida cell

WHAT HAVE WE LEARNED AFTER HUNDREDS OF NK CELL INFUSIONS FOR CANCER THERAPY

Jeffrey S. Miller, MD
Deputy Director, Masonic Cancer Center
Director, NK Cell Program
Minneapolis, MN



Masonic Cancer Center
UNIVERSITY OF MINNESOTA

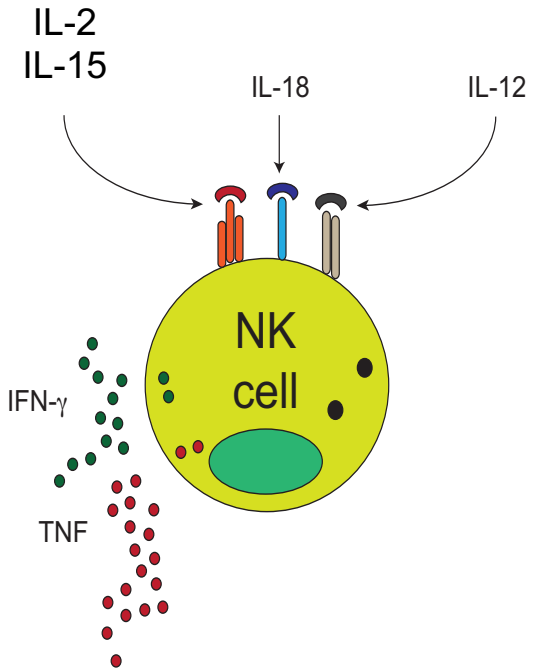
Comprehensive Cancer Center designated by the National Cancer Institute

Disclosures Jeffrey S. Miller, MD

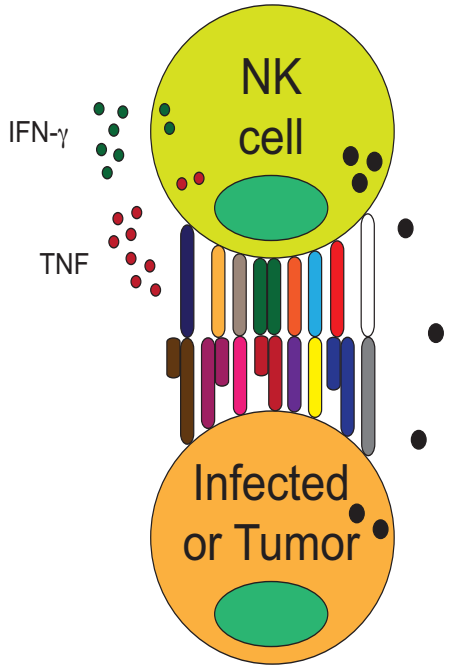
- Fate Therapeutics
  - Research Support, Consulting, Stock options
- Gamida Cell
  - Consulting
- GT BioPharma
  - SAB, Research Support, Consulting, Stock options
- OnkImmune, Nektar
  - SAB
- Vycellix
  - Consulting, Stock options

NK Cell Functions in Health and Disease

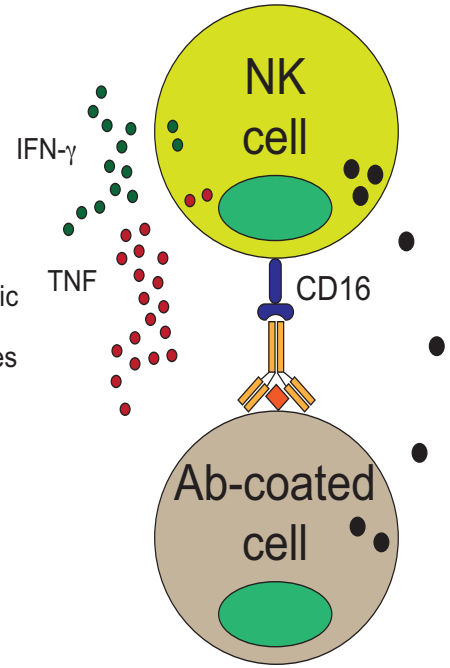
Cytokine Stimulation



Natural Cytotoxicity

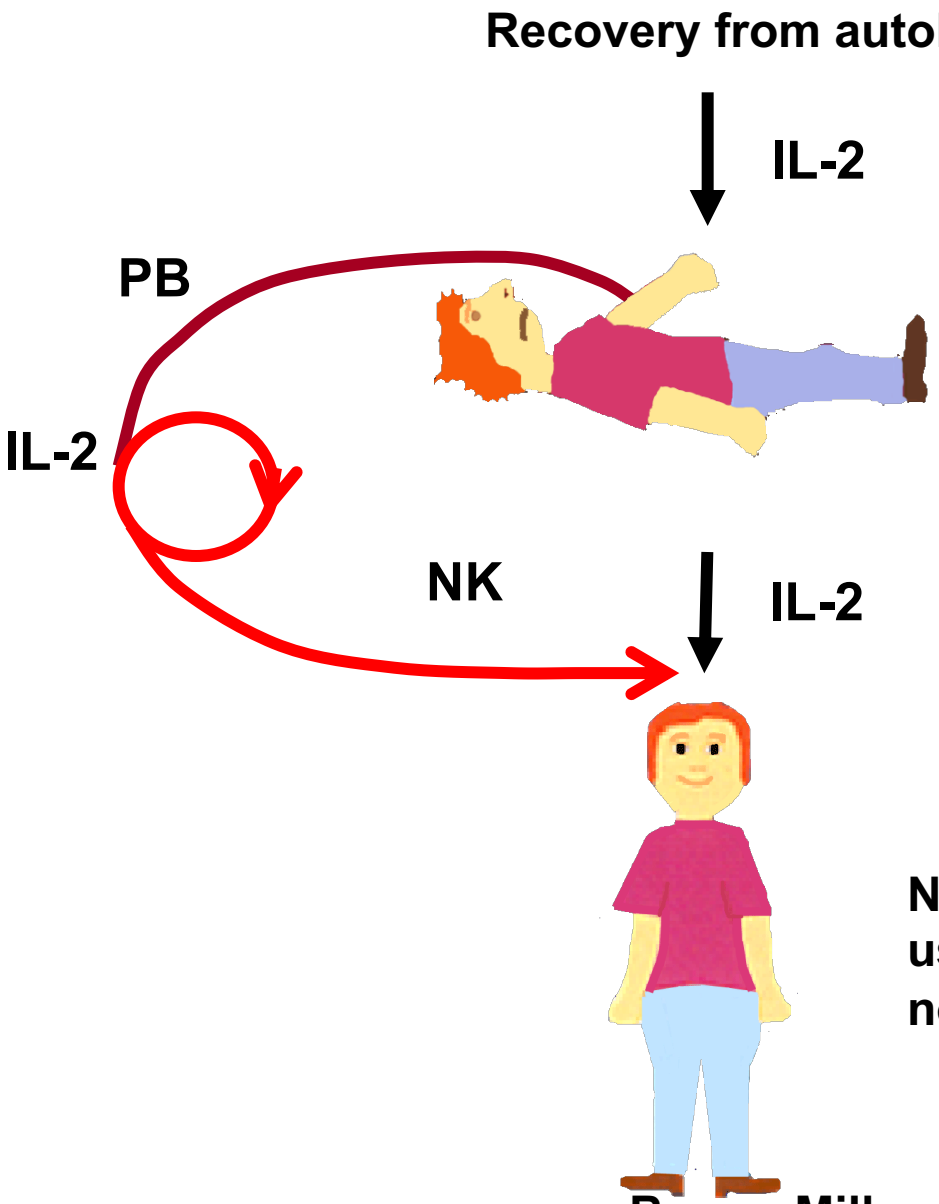


Antibody-Dependent Cellular Cytotoxicity (ADCC)



Autologous NK Administration in Cancer Patients

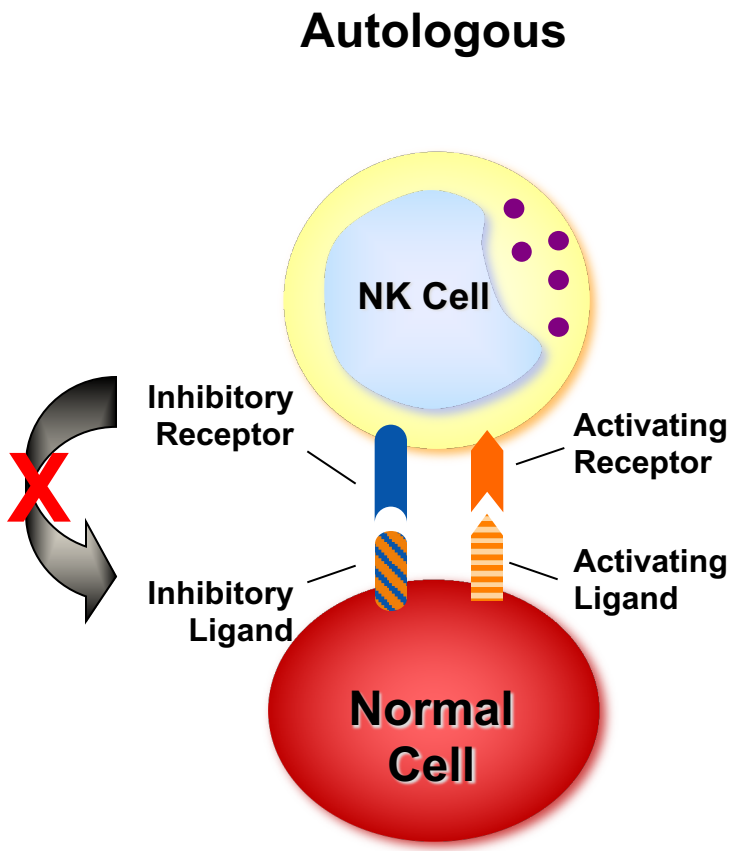
1997



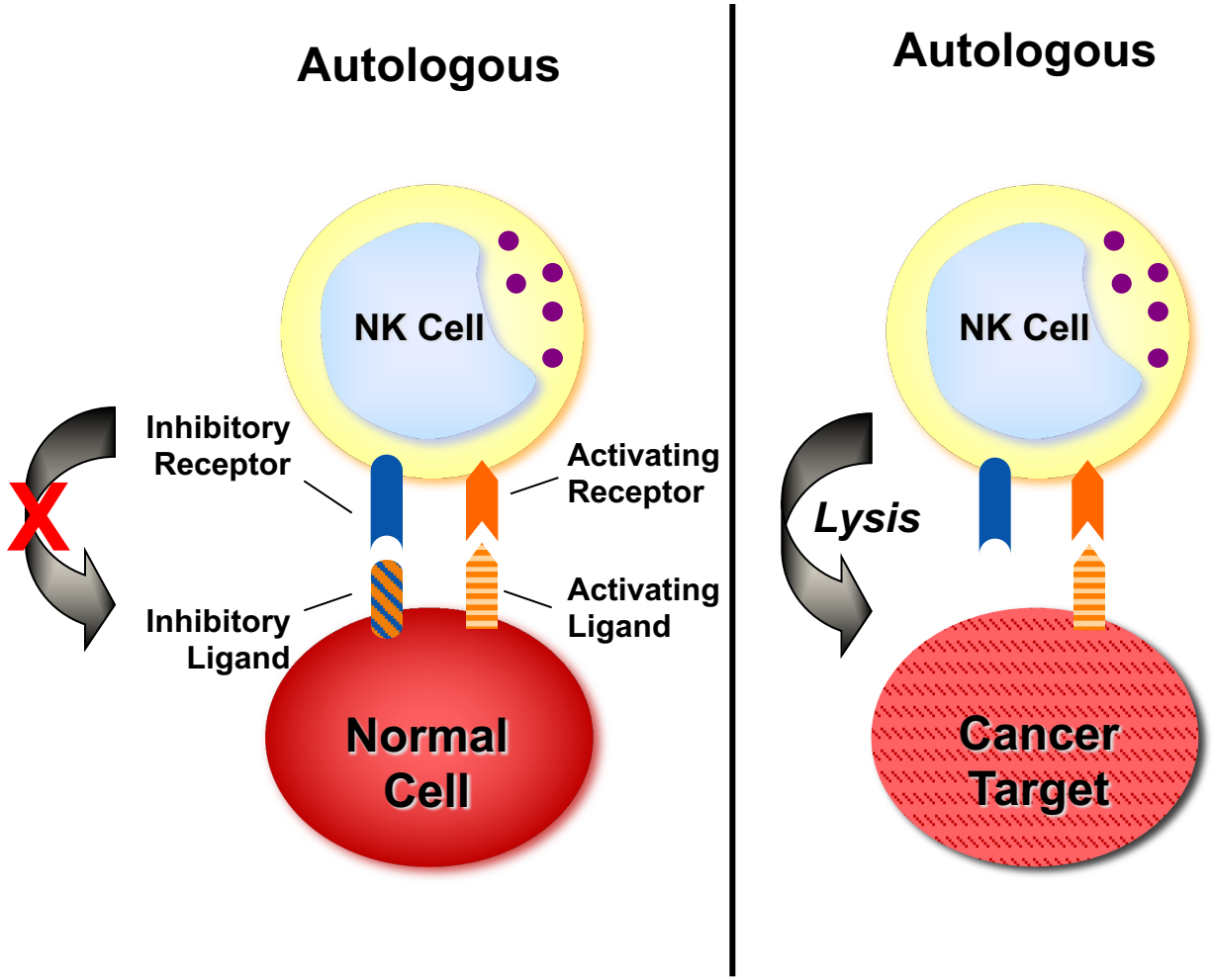
NK cells are activated using this approach…. no apparent efficacy

Burns. Miller et al, BBMT 32:177-186, 2003

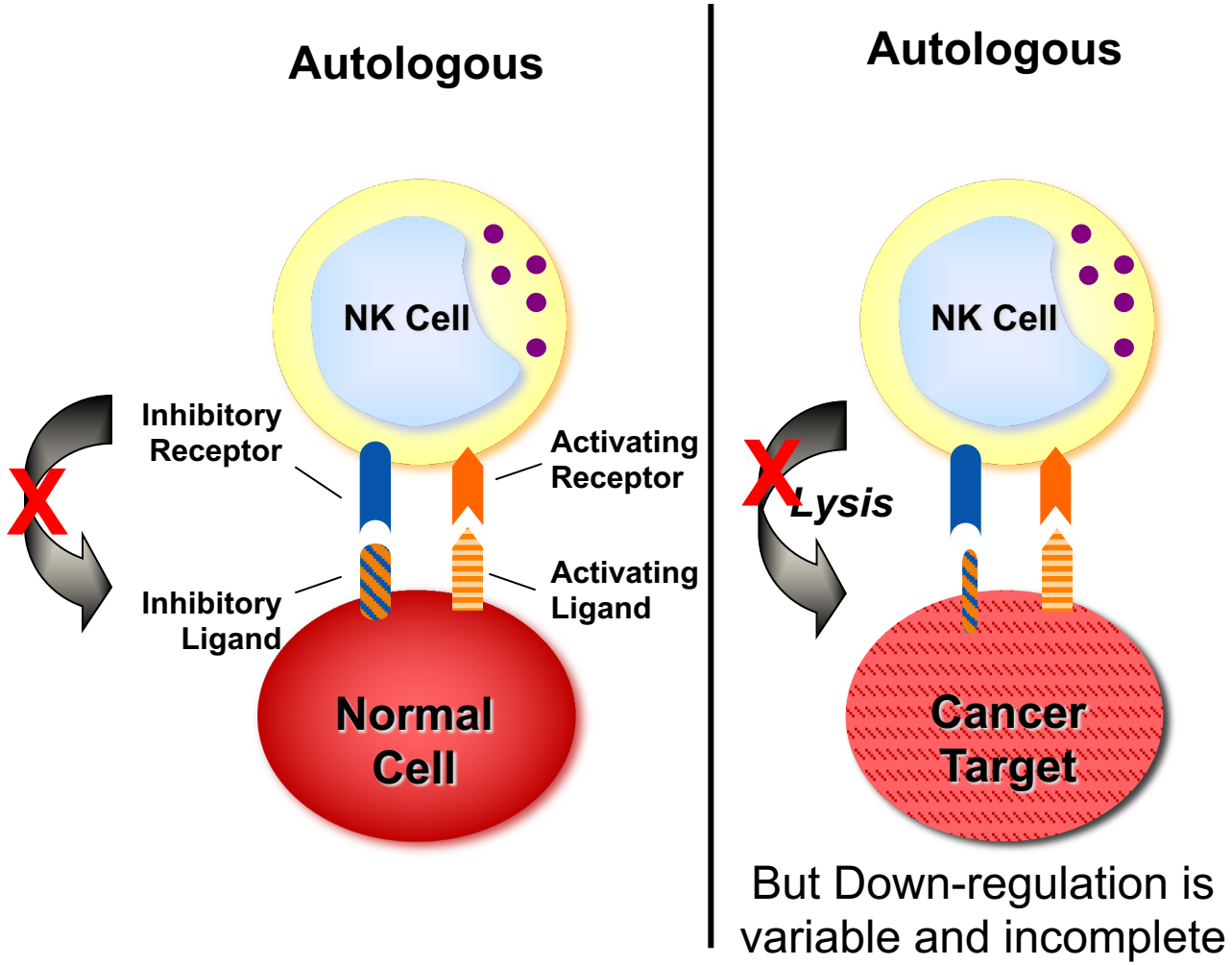
The Problem With Autologous NK Cells Is“Missing Self”



The Problem With Autologous NK Cells Is"Missing Self"

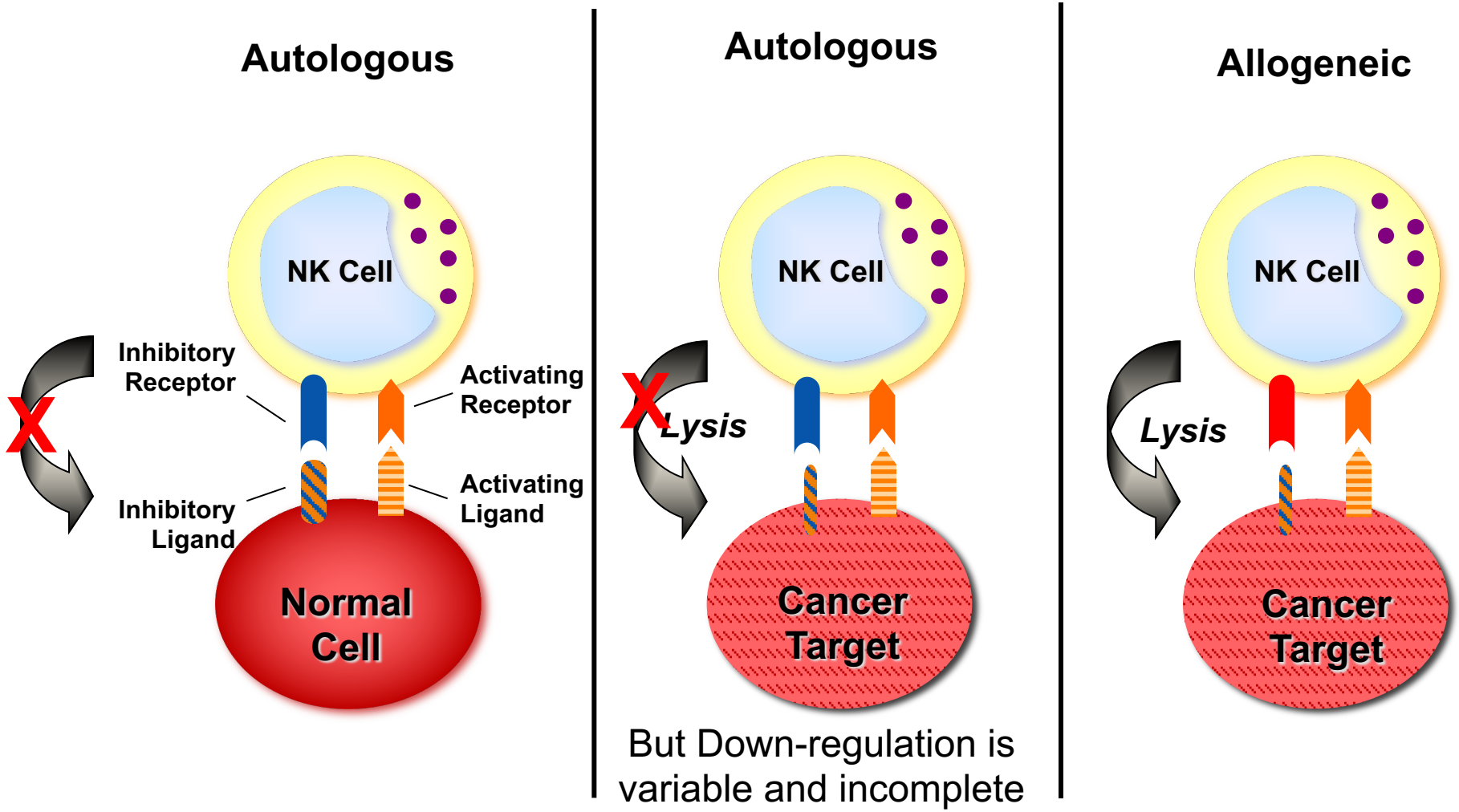


The Problem With Autologous NK Cells Is"Missing Self"

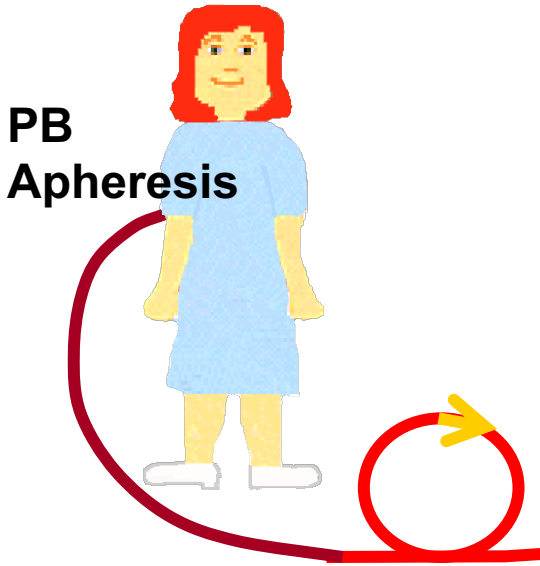


But Down-regulation is variable and incomplete

The Problem With Autologous NK Cells Is"Missing Self"



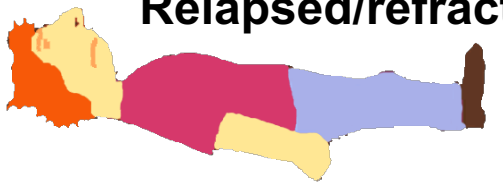
Allogenic NK Cell Adoptive Transfer: Two Decades and Hundreds of Patients



PB
Apheresis

CD3/CD19-depletion
Overnight IL-2 or IL-15

NK-enriched
product



Relapsed/refractory AML

Cy 60 mg/kg x 2
Flu 25 mg/m^2 x 5
} Surge IL-15

NK cells 2-8 x 10^7 MNC/kg

IL-2 10 MU SQ QOD x 6
IL-15 0.3-1.0 µg/kg IV x 12 or
2.0 µg/kg SC x 10

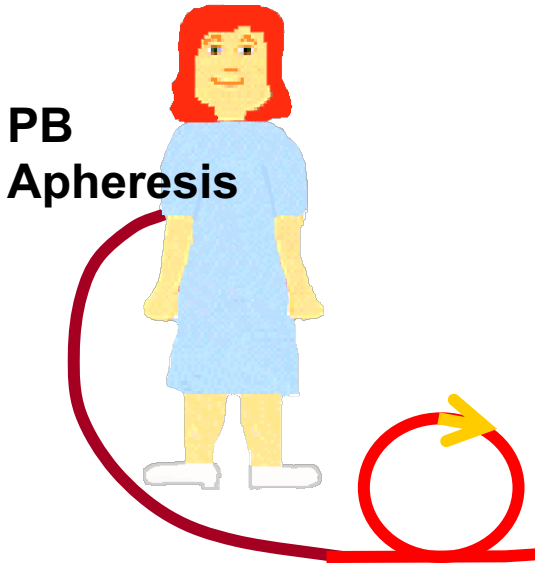
Clinical Data:

Donor NK cell persistence (up to 1 month)
- 10% >100 cells/µL d14 with IL-2[1,2]
- 35% >100 cells/µL d14 with IL-15[3]

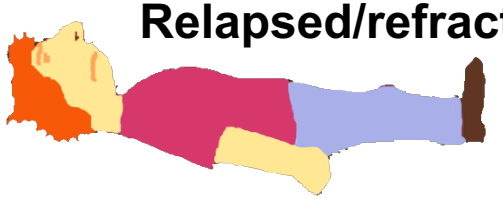
CR: 26[1]-53[2]% IL-2 or ~35[3]% IL-15

[1]Miller et al, Blood, 2005; [2]Bachanova et al, Blood 2014; [3]Cooley et al, Blood Advances 2019

Allogenic NK Cell Adoptive Transfer: Two Decades and Hundreds of Patients



PB
Apheresis



Relapsed/refractory AML

NK-enriched
product

CD3/CD19-depletion
Overnight IL-2 or IL-15

Cy 60 mg/kg x 2
Flu 25 mg/m^2 x 5
} Surge IL-15

NK cells 2-8 x 10^7 MNC/kg

IL-2 10 MU SQ QOD x 6
IL-15 0.3-1.0 µg/kg IV x 12 or
2.0 µg/kg SC x 10

Limitations:

1) No Ag-specificity
2) Donor heterogeneity
3) Manufacturing hard to export
4) Only 1 dose/donor

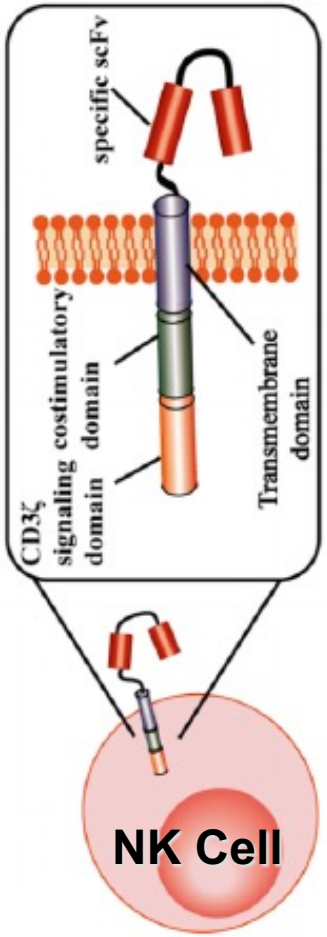
[1]Miller et al, Blood, 2005; [2]Bachanova et al, Blood 2014; [3]Cooley et al, Blood Advances 2019

The Future Of NK Cell Therapy Is Targeting:

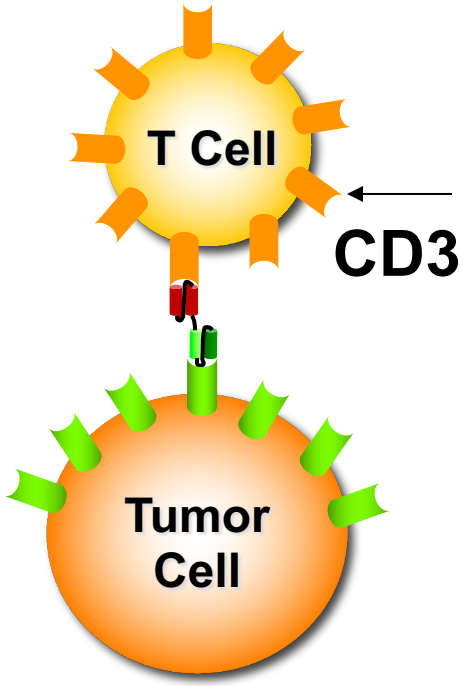
NK-CAR vs NK Cell Engagers

Immune engagement

NK-CARs

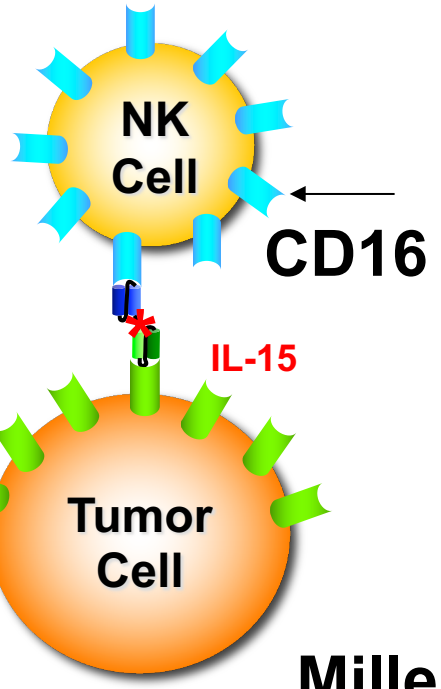


BiTE-Killing



Blinatumomab (Amgen)
CD3 x CD19

TriKE-Killing



Miller
Felices
Vallera

Gene Therapy vs Off-The-Shelf Proteins

Example Schema of NK cells + IL-15 after LD Chemotherapy in r/r AML

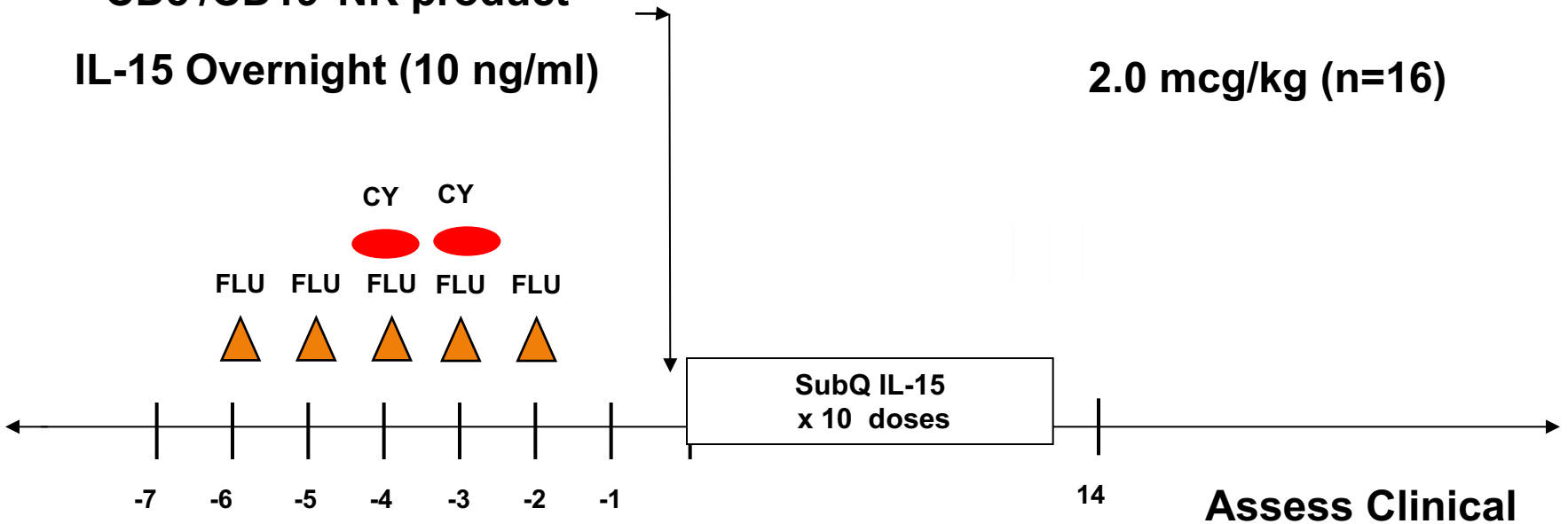
Haplo Donor Apheresis

$CD3^-/CD19^-$ NK product

IL-15 Overnight (10 ng/ml)

SubQ IL-15 Dosing
5 Days on, 2 days off, 5 days on

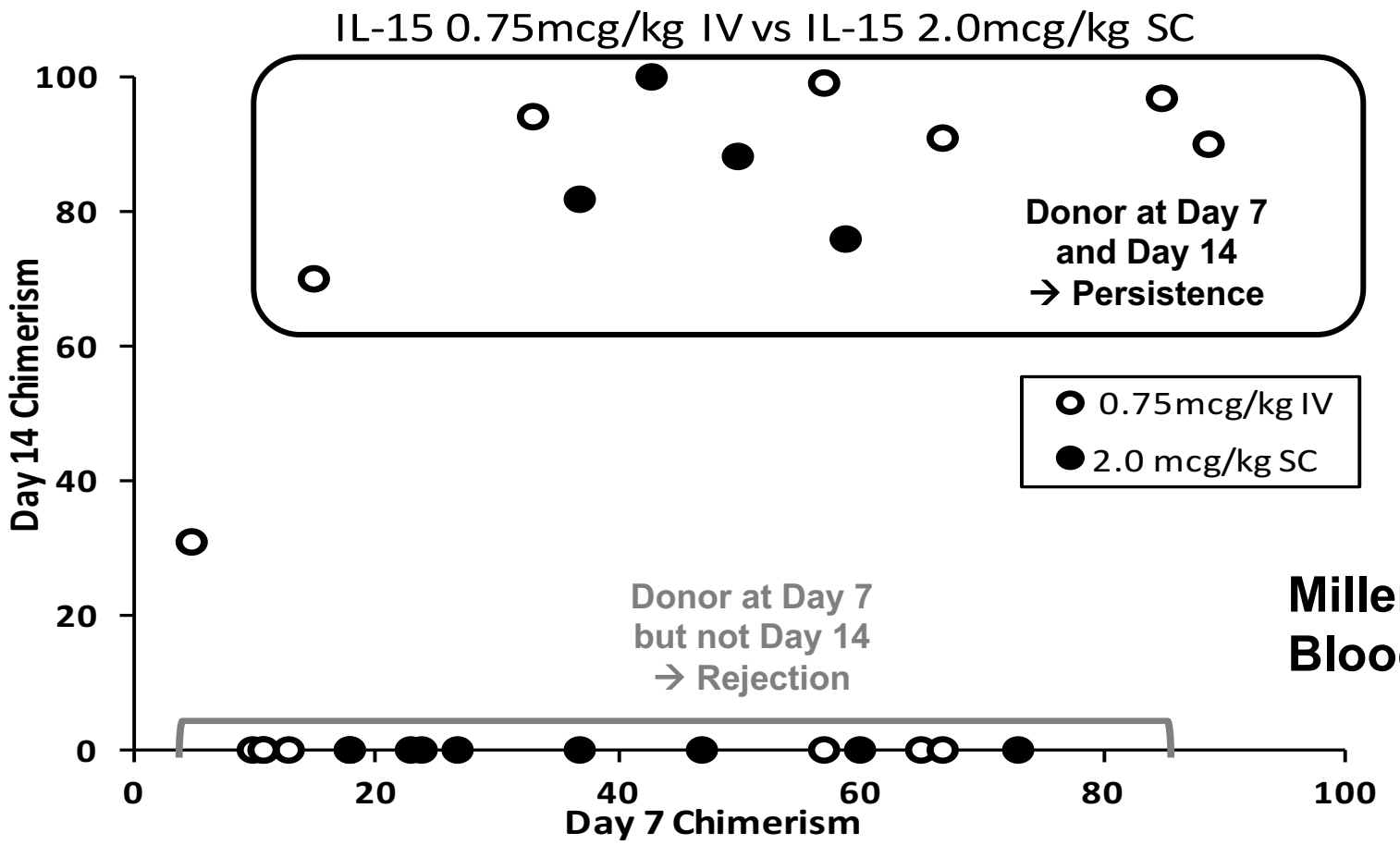
2.0 mcg/kg (n=16)



Assess Clinical Outcomes and NK Expansion

Miller and colleagues Blood Advances 2019

Allo NK Cells + IL-15 Can Persist For Weeks At A Macrochimerism Level In Some Patients



Miller and colleagues
Blood Advances 2019

Summary

- The field is moving rapidly
- Off-the-shelf NK cell therapy has started with multiple products
- The Future: Optimizing NK cells for better persistence, better homing, and avoiding allo-rejection will drive clinical efficacy

GDA-201 Phase 1/2 Trial

Ronit Simantov, M.D.

gamida cell

GDA-201 Study: Objectives*

- Evaluate the safety and efficacy of GDA-201
- Phase 1: Dose limiting toxicities and recommended phase 2 dose
- Phase 2: Safety and efficacy in two patient cohorts:
  - Follicular lymphoma (FL)
  - Diffuse large B cell lymphoma (DLBCL)

*Subject to ongoing IND review by the FDA

Proposed Key Inclusion Criteria*

- Age ≥ 18
- Relapsed/refractory B Cell FL or DLBCL
  - Received at least 2 prior lines of therapy (including anti-CD20 antibody)
  - Prior autologous or allogeneic hematopoietic stem cell transplant permitted
  - Prior chimeric antigen receptor modified T-cells (CAR-T) cell therapy permitted
- Measurable disease as defined by Lugano response criteria
- ECOG Performance Status ≥1
- Adequate organ function, no active infection

*Subject to ongoing IND review by the FDA

Proposed Study Design*

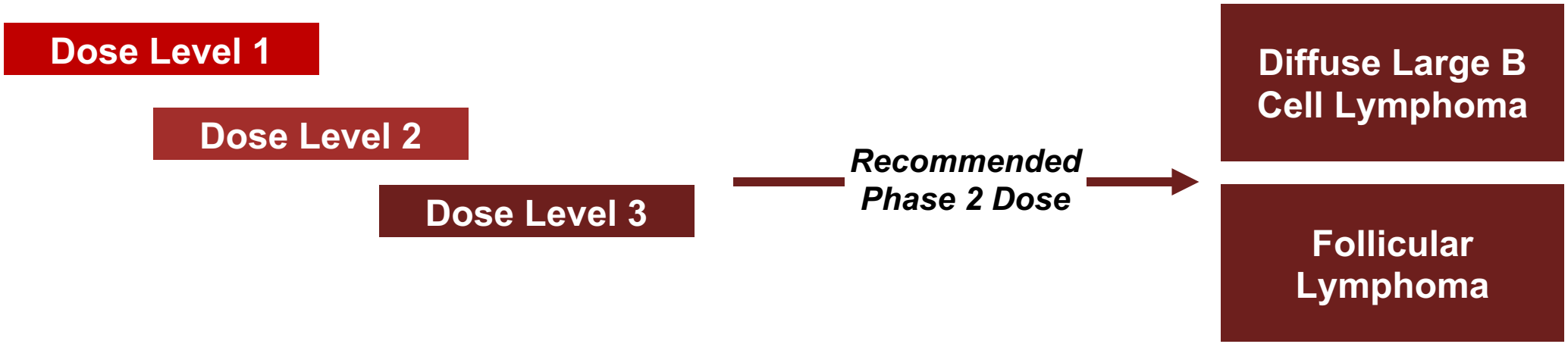
Sample size: N=80-100

Phase 1: Dose Escalation

Standard 3x3 design
Primary endpoint: Safety

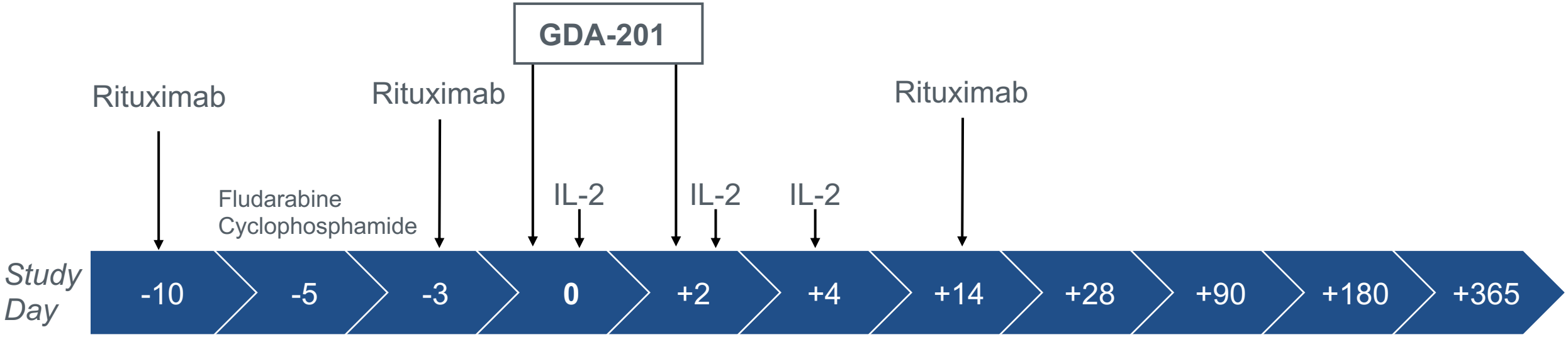
Phase 2: Expansion

Simon two stage design
Primary endpoint: Overall Response Rate



*Subject to ongoing IND review by the FDA

Proposed Treatment Plan*



Doses

Rituximab: 375 mg/m^2
Fludarabine: 30 mg/m2 IV x 3 days
Cyclophosphamide: 400 mg/m2 IV x 3 days
Interleukin-2 (IL-2): 6 million units SC

*Subject to ongoing IND review by the FDA

Summary*

Overall Goals of the Phase 1–2 Trial:

- Confirm safety of cryopreserved, allogeneic GDA-201
- Conduct dose escalation to confirm dose
- Assess activity of GDA-201 in patients with indolent and aggressive B cell lymphomas
- Two-stage analyses to provide early response data for each cohort

Final study design will be posted on ClinicalTrials.gov

*Subject to ongoing IND review by the FDA

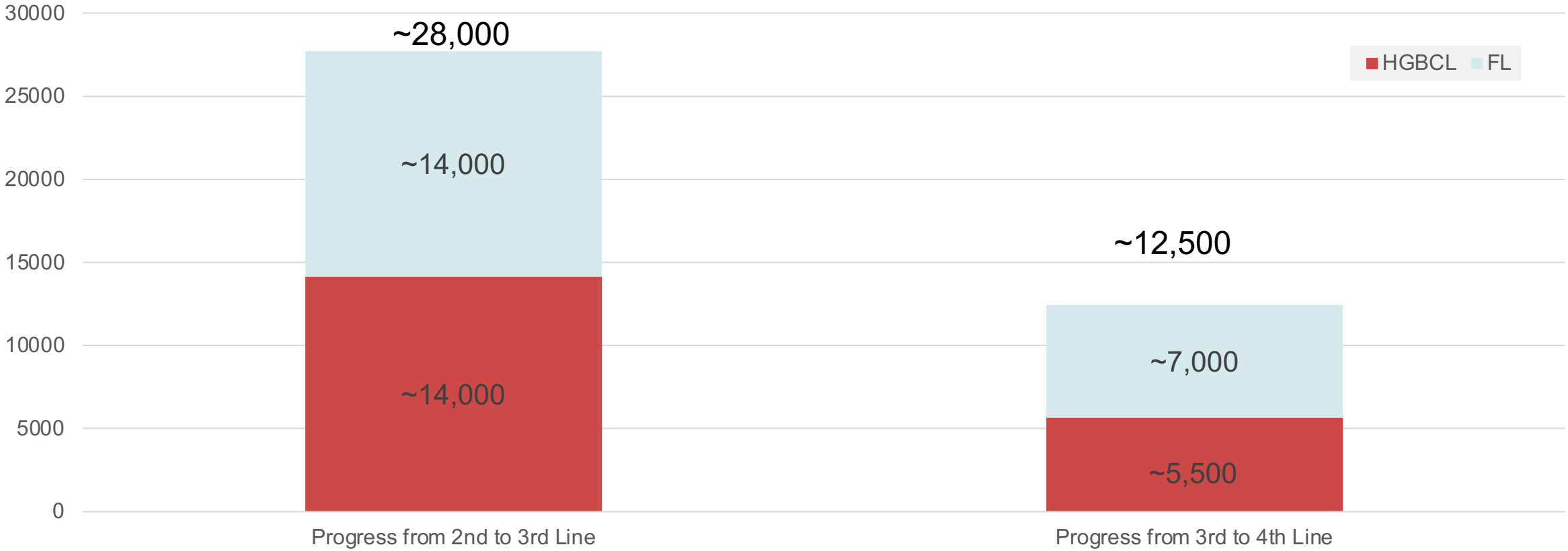
Unmet Need in Lymphoma

Michele Korfin, RPh

gamida cell

Relapsed/Refractory Lymphoma Opportunity Can Reach ~40,000 Patients in US and EU5

Patients reaching 3L+ currently have limited opportunities for therapies which can provide durable responses



Source: Health Advances market research and analysis

Current Challenges Associated with Therapies for Patients with Relapsed/Refractory Lymphoma

U.S. and EU physicians were consistent with the challenges they see with their current treatment options in relapsed/refractory lymphoma

Unmet need for patients with relapsed/refractory DLBCL

- Need a rapidly available therapy due to the aggressive nature of this histology
- Patients need a therapy that balances efficacy, especially CRs, with a tolerable safety profile
- Improved duration of response

Unmet need for Follicular Lymphoma

- Quality of life is a focus: patients usually see multiple lines of therapy so need to assure there are not irreversible side effects
- Therapies with limited “drug burden” (ie one or two doses) to enable more time off therapy
- Efficacy is still key, especially CRs
- Improved duration of response

Source: Health Advances market research and analysis

Current Challenges Associated with Therapies for Patients with Relapsed/Refractory Lymphoma

Non-curative treatment options

"The majority of patients, who go down this path will ultimately relapse and die from lymphoma."
— US physician

Safety

"We need a safer alternative of CAR-Ts so we can safely move the age of eligible patients up and avoid ICU costs."
— US physician

Delays to treatment

"Unfortunately, there are a number of R/R patients who have highly aggressive disease. They can't wait four weeks for production, so current CAR-Ts are not an option." — US physician

Bed capacity challenges

"We have limited beds to house CAR-T patients post-infusion. If there's a similar product that doesn't require an inpatient stay, it would allow me to reserve auto-CAR-T for those who need it most." — UK physician

Source: Health Advances market research and analysis

Feedback on the GDA-201 Target Product Profile was Encouraging

- Market insight study conducted with physicians and payers in both the U.S. and EU-5
  - Community and academic physicians were included
- GDA-201 efficacy, safety and availability were noted as all encouraging attributes

"The absence of CRS and neurotoxicity is key for NK cell therapies and will make them suitable for those older and more fragile patients."
– U.S. physician

"Allogeneic cells hold the potential to treat those patients that can't wait for autologous CAR-T manufacturing."
– U.S. physician

"The results look exceptional in 3L. I think the efficacy is very similar to that of CAR-T today."
– FR physician

Source: Health Advances market research and analysis

GDA-201's Response Rates in Late Line NHL in Line with Other Allogeneic NK Cell Therapies

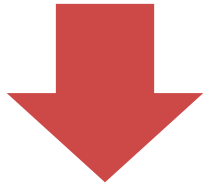
					Clinical Data			
Modality	**Generic Name**	**Originator/ Licensee**	**Phase**	**Dose**	**Efficacy**		**Patient Population**	**Safety[2]**
					CR	**ORR**		
Allogeneic NK	**GDA-201**	gamida cell	I		68%	74%	N = 19, R/R FL, DLBCL	No confirmed CRS[3] No ICANS, No GVHD Infection Gr 3+: 9%
	FT-516	Fate THERAPEUTICS	I	DC2 + DC3	57%[1]	86%[1]	N = 7, R/R BCL, auto CAR-T naive	No CRS, No ICANS, No GVHD Infection Gr 1-2: 7%, 3+: 8%
Allogeneic CAR-NK	**KUR-502/ CMD-502**	kuur THERAPEUTICS	I		100%[1]	100%[1]	**N = 1**, R/R Lymphoma, auto CAR-T naïve	No CRS, No ICANS, No GVHD
	TAK-007	Takeda	I/II		67%	67%	N = 6, R/R FL, DLBCL, auto CAR-T naive	No CRS, No ICANS, No GVHD Infection Gr 1-2: 18%, 3+: 9% B-cell aplasia post-CAR NK: 1 patient
	FT-596	Fate THERAPEUTICS	I	DC2 + DC3 Monotherapy	50%[1]	100%[1]	N= 6, R/R BCL, auto CAR-T naive	No ICANS, No GVHD, CRS: Gr 1-2: 10%, Gr 3+: 0%
				DC2 + DC3 Combination	50%[1]	50%[1]	N= 4, R/R BCL, auto CAR-T naive	

[1] Only includes results from auto-CAR-T naïve patients.
[2] Infection rate included where available. Safety data reported for efficacy cohort where available. Where not available, safety data reported for full study population.
[3] One case of unconfirmed CRS occurred in a patient with multiple myeloma.
Note: ICANS: Immune effector cell-associated neurotoxicity syndrome. CRS: cytokine release syndrome. GVHD: Graft vs. Host Disease.
Source: Health Advances analysis, Pharmaprojects, ClinicalTrials.gov, NEJM 2020 Liu et al, ASH presentation 2020 Bachanova et al, company press releases: FT-516 June 2021, FT-596 Aug 2021, KUR-502/CMD-502 Jan 2021.

Source: Health Advances analysis

Encouraging Global GDA-201 Commercial Opportunity

- GDA-201 clinical data received positive feedback from physicians and payers in a global assessment
  - Efficacy feedback: ORR and CR rates were viewed positively
  - Safety feedback: No CRS and/or neurotoxicity as seen with other cell therapies
- Although there have been advances for patients with lymphoma, there are significant unmet needs in relapsed/refractory patients that GDA-201 could address



~40,000 Line 3+ patients in the U.S. and EU-5 could potentially benefit from a new therapy that addresses the unmet needs for efficacy and safety

Source: Health Advances market research and analysis

gamida cell

GDA-201 Patient Perspective

Wayne Altenbernd

Veronika Bachanova, M.D., Ph.D.

Disclosures, Veronika Bachanova, M.D., Ph.D.

- BMS (research funding)
- Citius Therapeutics (research funding)
- Fate Therapeutics (research funding)
- Gamida Cell (advisory board, research funding)
- Incyte (research funding)
- Karyopharm (advisory board)
- Kite / Gilead (advisory board)

Engineered NK Cell Programs

Yona Geffen, Ph.D.

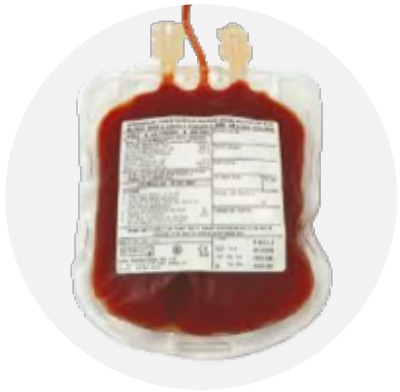
gamida cell

A Leading Genetically Engineered NK Cell Pipeline

PROGRAM	STRATEGY	GENETIC MODIFICATION	INDICATION(S)
GDA-301	Increased potency and persistence	*CISH* KO + membIL-15	Hematologic + solid tumors
GDA-401	Undisclosed		
GDA-501	HER2 Targeting	HER2 CAR	HER2+ solid tumors
GDA-601	CD38 Targeting	CD38 KO + CD38 CAR	Multiple myeloma

- memb-IL15 = Membrane-bound IL-15
- KO = Knockout
- CAR = Chimeric antigen receptor
- HER2 = Human epidermal growth factor receptor 2

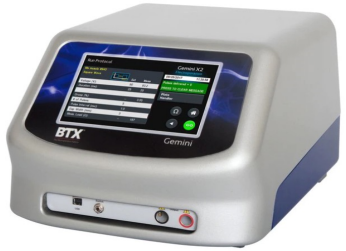
Genome Editing in NK Primary Cells Using the CRISPR/Cas9 System



Human peripheral blood

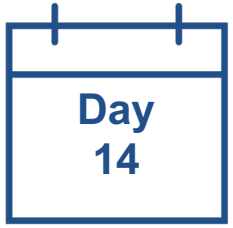
CD56+ magnetic separation

IL-2 (50ug/mL)- media recovery 24h-72h



CRISPR/Cas9-RNP electroporation

4 × 10^6 NK cells + Irradiated PBMCs /2mL in G-Rex flask MEMα media + NAM+ IL-15 + 10% human AB+ serum



gamida cell

GDA-301

CISH Knockout and Membrane-bound IL-15 for Solid Tumors

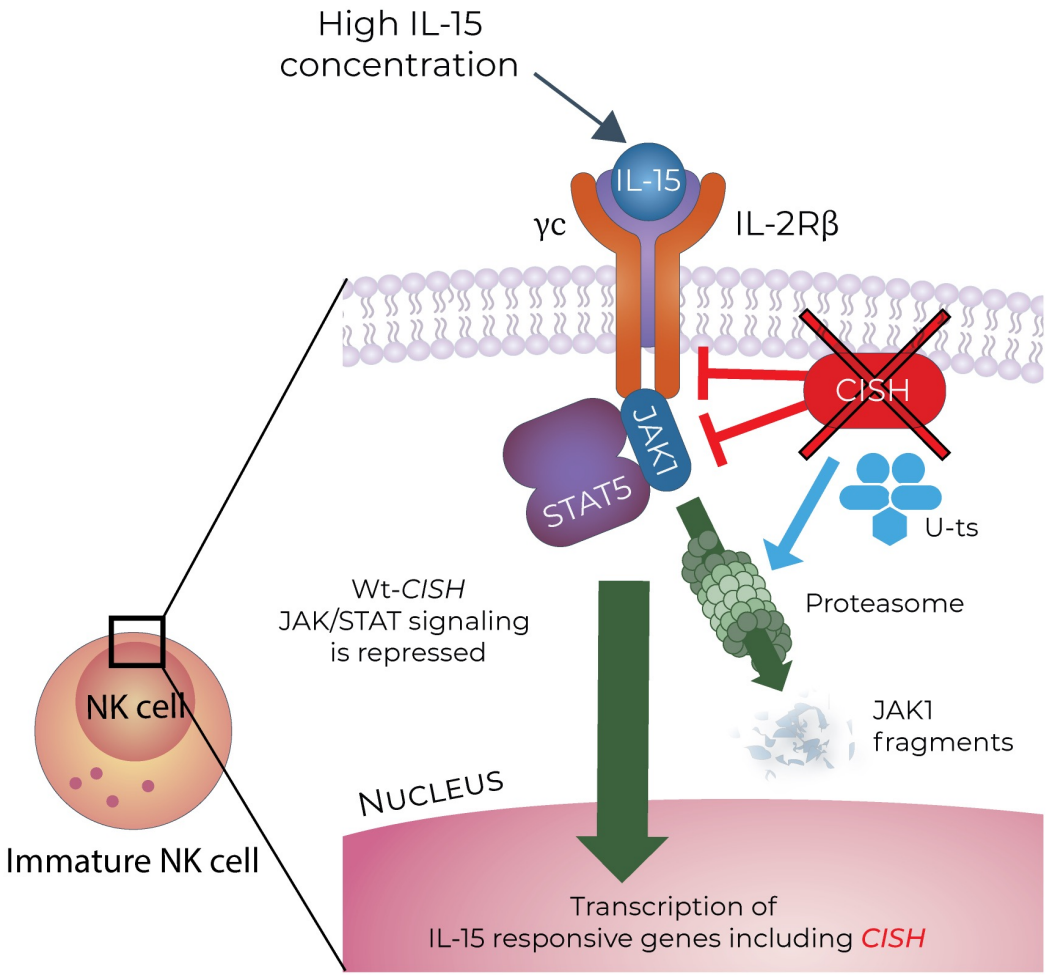
gamida cell

Combined Genetic Engineering: CRISPR Cas9 Gene Knockout of *CISH* and Expression of Membrane-bound IL-15

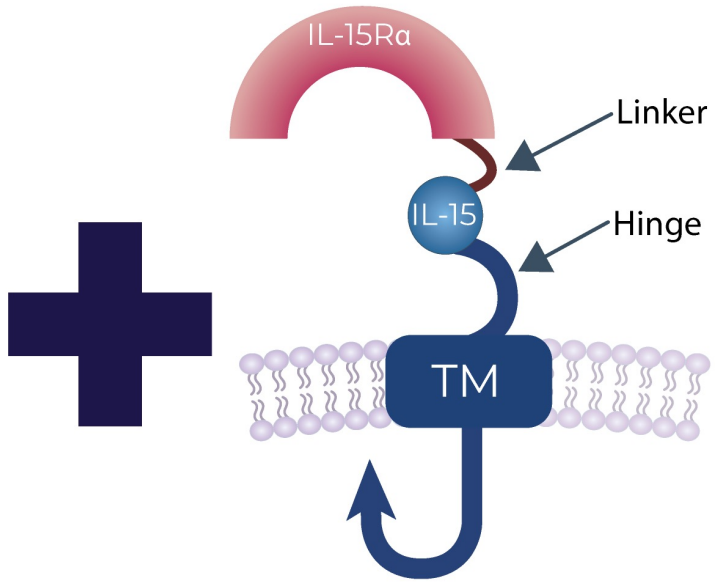
1. **CISH *regulates IL-15 signaling***
   - *CISH* deletion increases sensitivity to IL-15 by lowering the NK activation threshold
2. ***Membrane-bound IL-15***
   - The lack of persistence of infused NK cells is a principal limitation of adaptive immunotherapy
   - NKs equipped with memIL-15 will be fully autonomous and will obviate the need for patient IL-2 administration regimen

Combining *CISH* KO with membrane-bound IL-15 will improve *in vivo* persistence and killing capacity

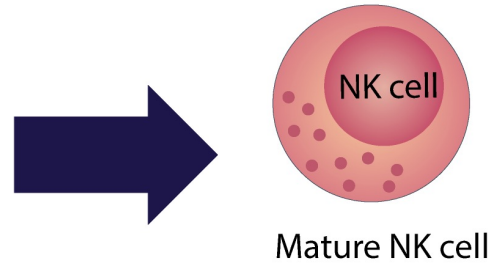
GDA-301: Increasing NK Potency and Persistence



CISH Knockout



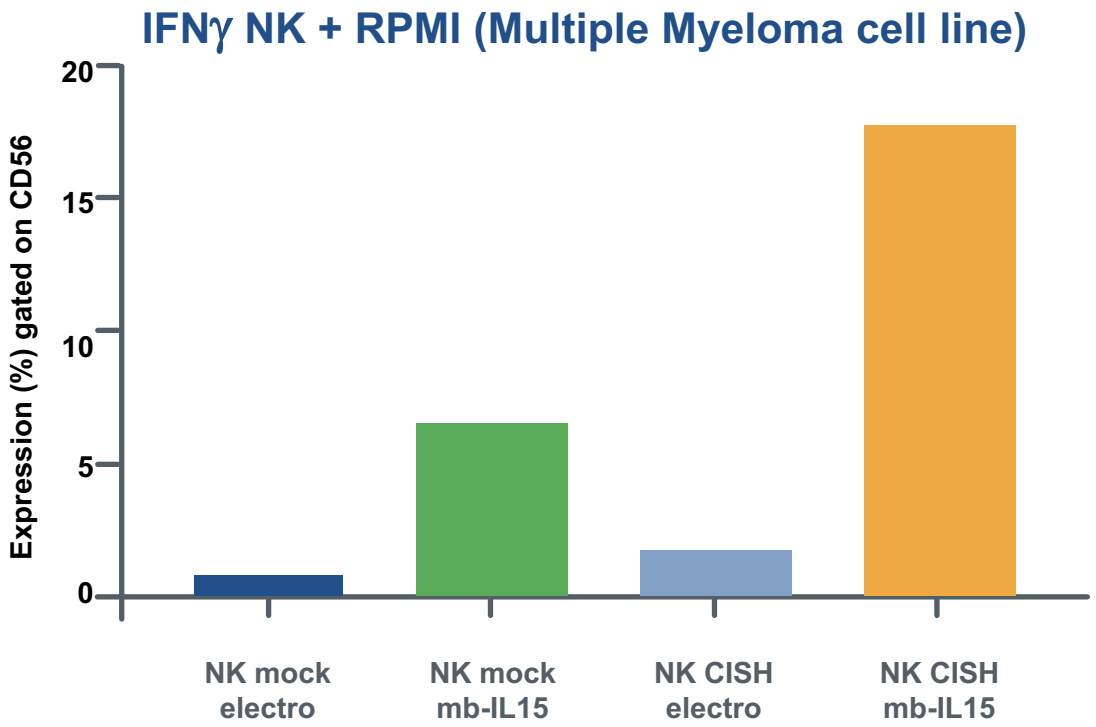
Membrane-bound IL-15

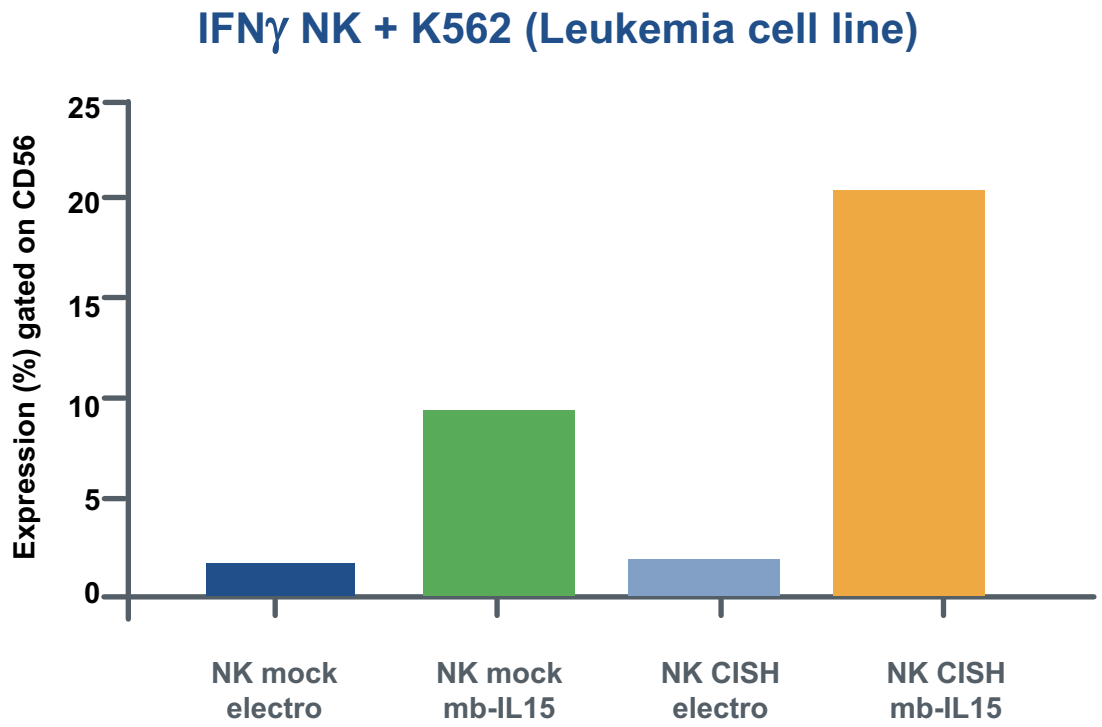


Increased NK cell potency and persistence

gamida cell

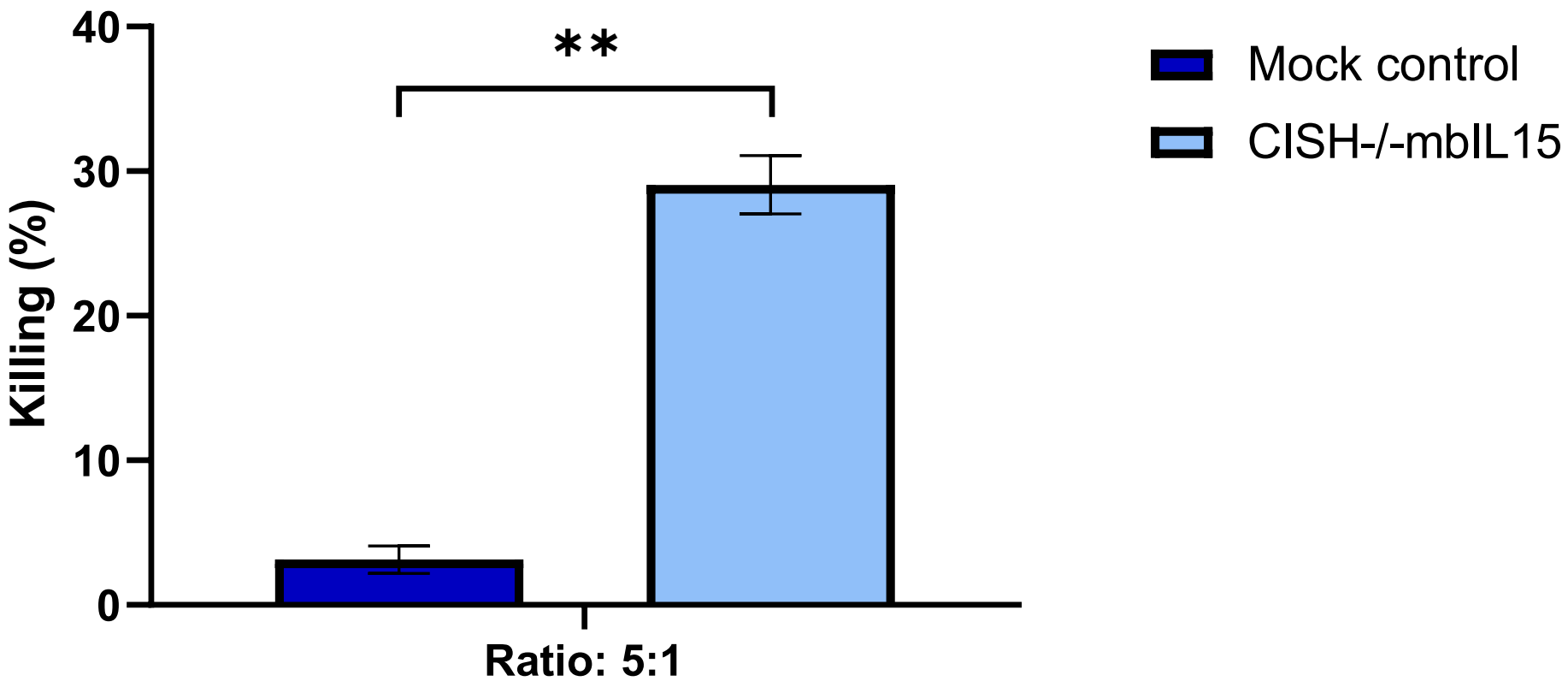
GDA-301: Combination of *CISH* CRISPR KO and Membrane-Bound IL15 Increases Potency Against Multiple Myeloma and Leukemia Cell Lines





Deletion of *CISH* gene in NK cells with subsequent mb-IL-15.1B mRNA electroporation reveals upregulation of cytokine production associated with NK cell activation, 3-4h post co-culture

GDA-301: CISH Knockout NK Cells that co-express mbIL-15 Increase Cytotoxicity Function Against Multiple Myeloma Cell Line (RPMI)



Deletion of CISH and co-expression of mb-IL15 on NK cells enhances their cytotoxicity activity. Killing assay was performed on CISH knocked cells ,24h after the electroporation of mRNA-mbIL-15 that followed a 6hr co-culture of NK cells with RPMI cell line

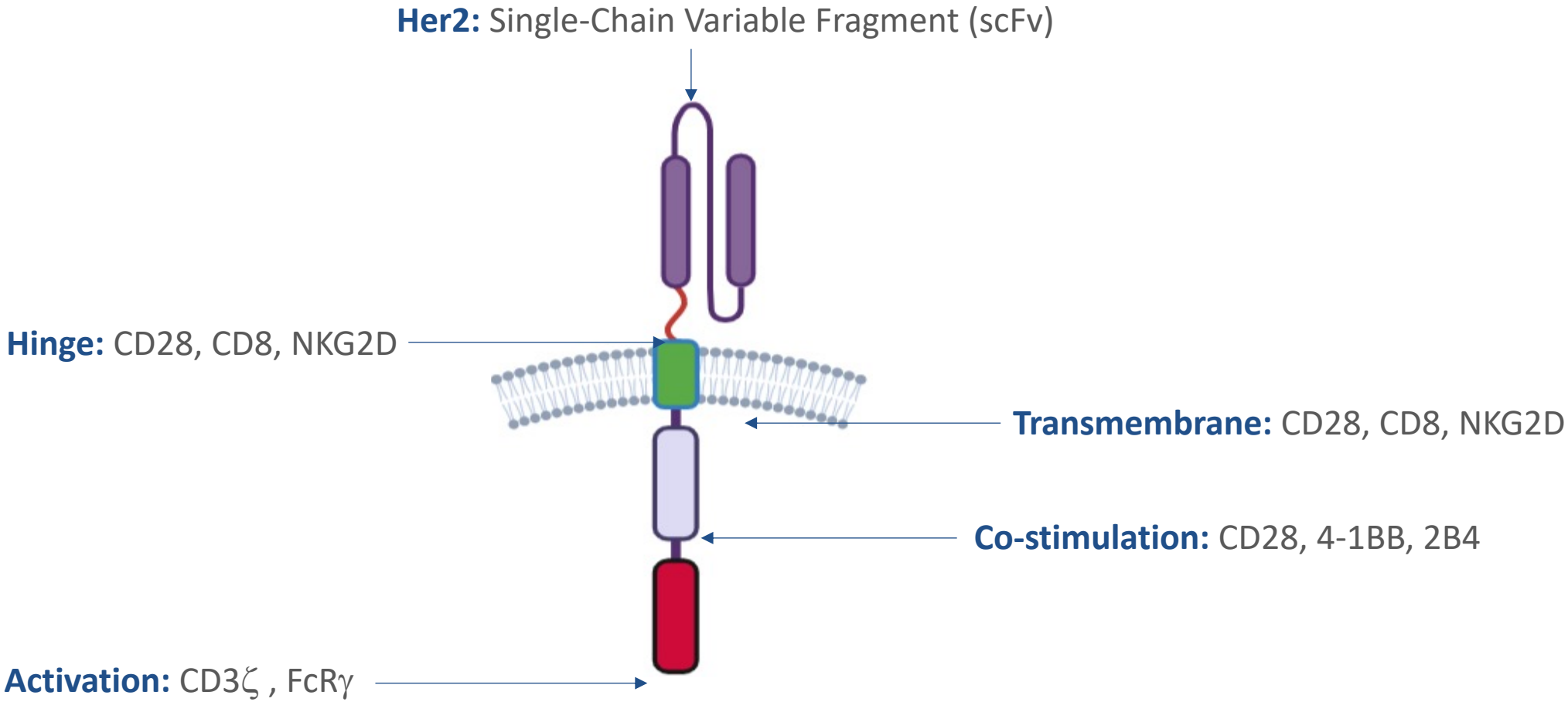
GDA-501

HER2 CAR for Solid Tumors

gamida cell

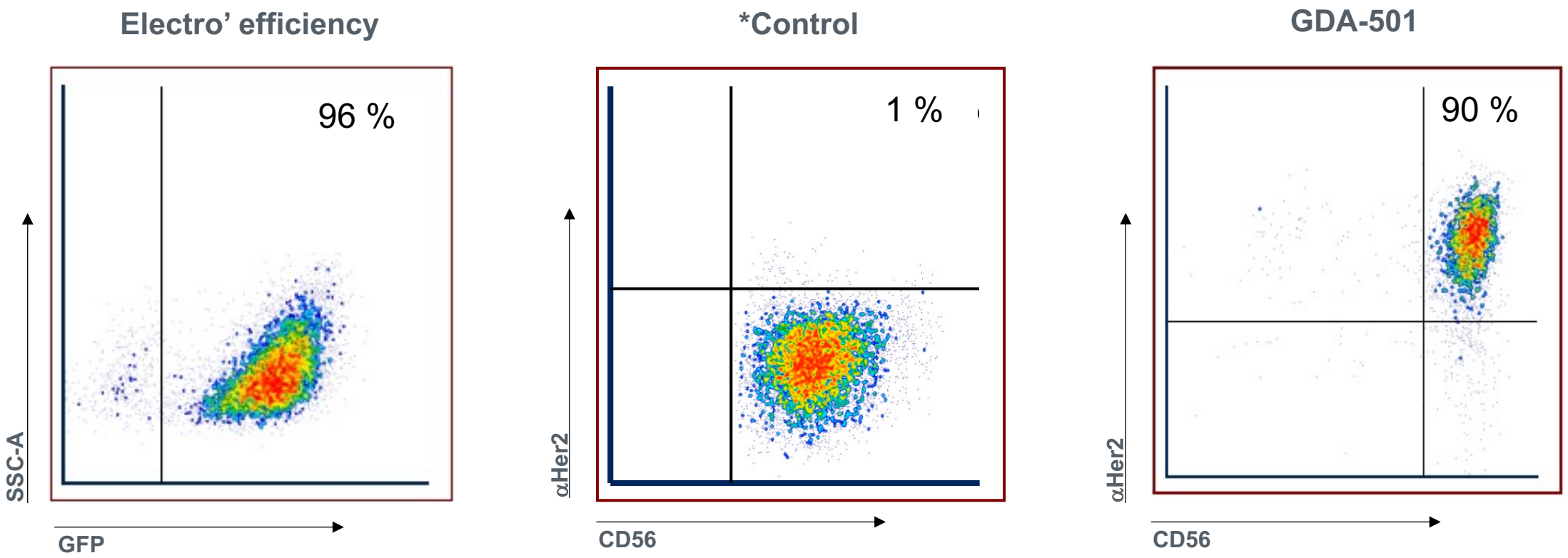
GDA-501: Targeting Solid Tumors Expressing HER2

Multiple tailor-made NK CARs were developed to target and activate NKs against HER2+ tumors



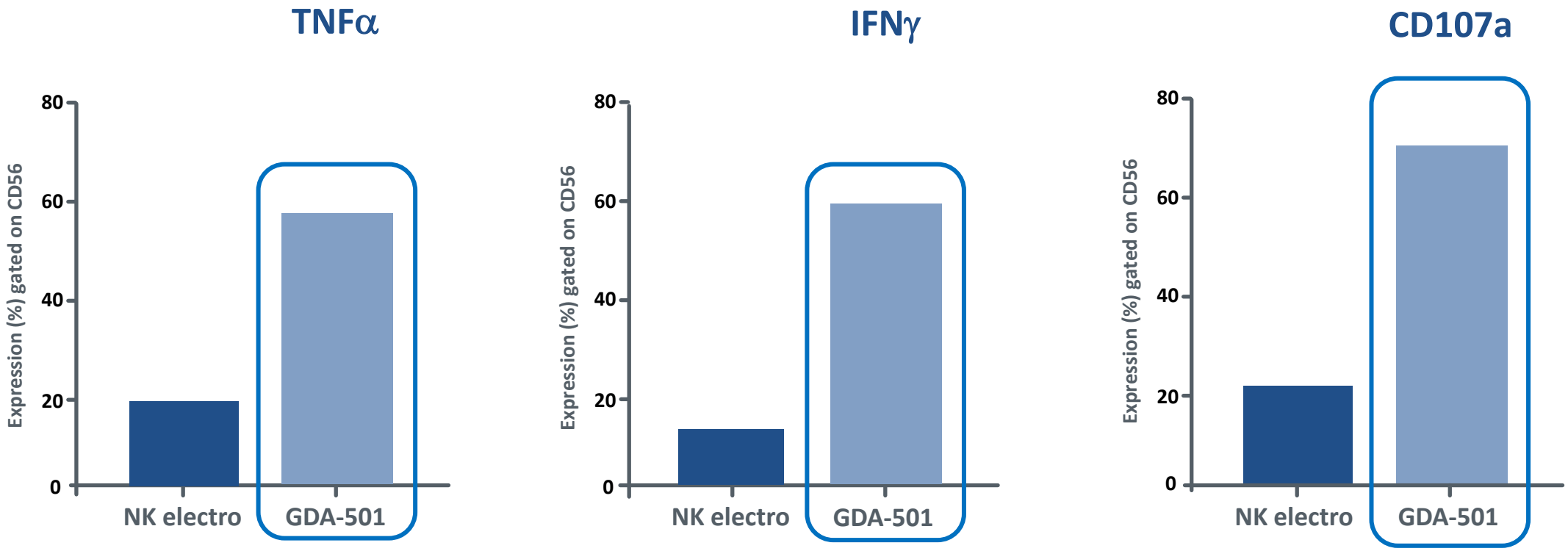
GDA-501: αHER2 CAR Constructs Proof of Concept

CAR construct is expressed by NK cells and recognizes the HER2 protein



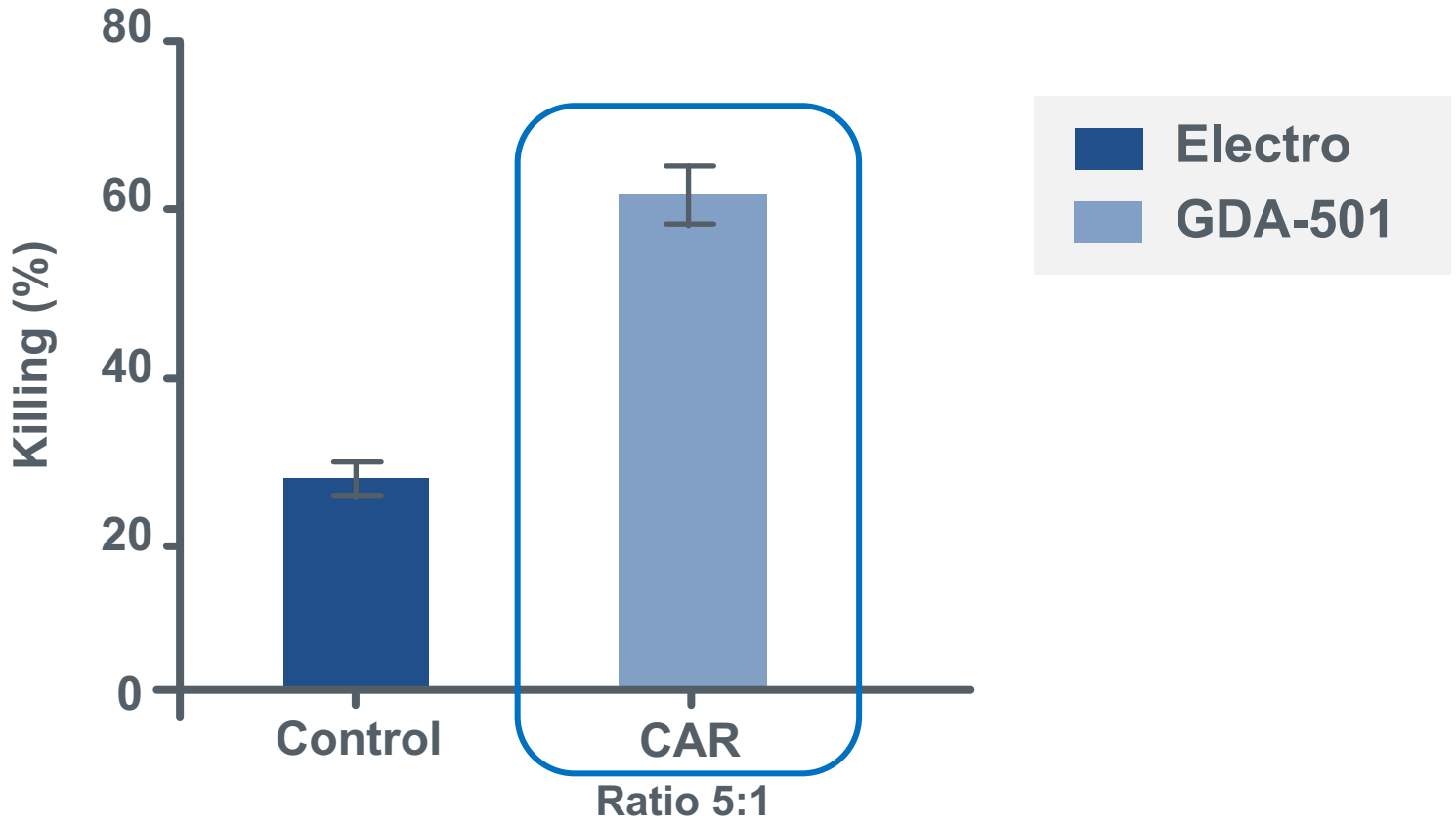
* GDA-501 cells were expanded using Gamida's NAM technology, gene editing was done on the NAM expanded cells

GDA-501: CAR-HER2 NK Cells Enhance Potency Activity Against Tumor Cell Lines



Expression of anti-HER2 CAR on NK cells reveals an upregulation of degranulation marker CD107a and inflammatory cytokine production associated with NK cell cytotoxicity. Potency assay was performed 24h after the electroporation.

GDA-501: CAR-HER2 NK Cells Increase Cytotoxicity Function Against Ovarian Tumor Cell Line (SKOV3)



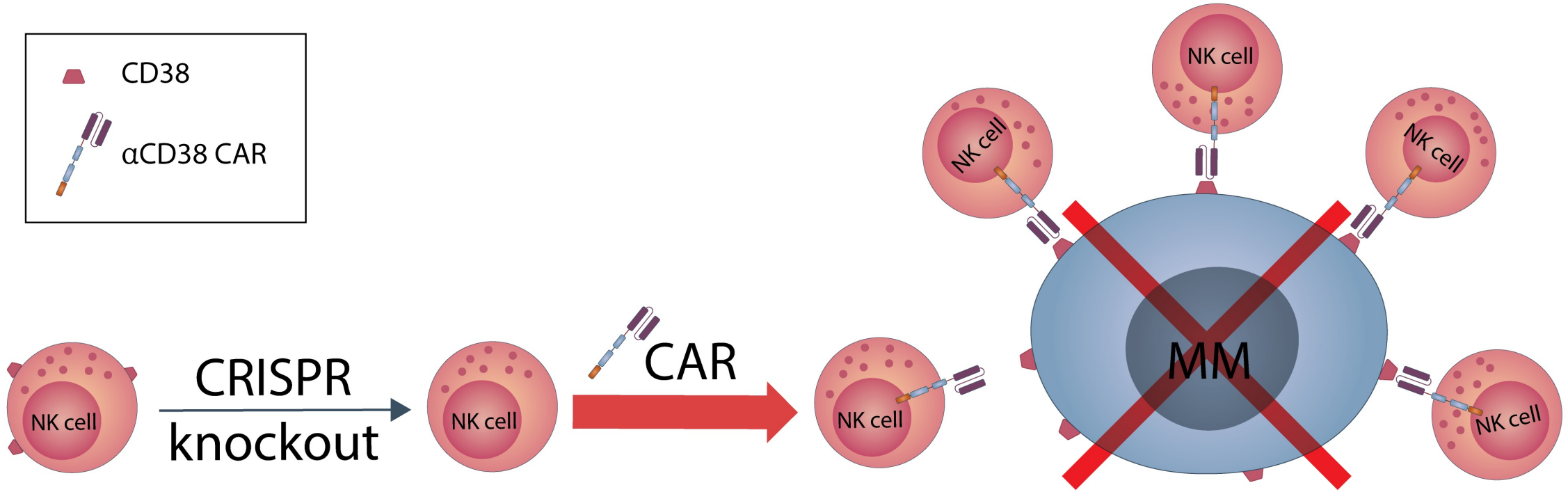
Expression of anti-Her2 CAR on NK cells enhances their killing activity. Killing assay was performed 24h after the electroporation that followed a 6hr co-culture of NK cells with SKOV-3 cell line

GDA-601

CD38 Knockout and CD38 CAR
for Multiple Myeloma

gamida cell

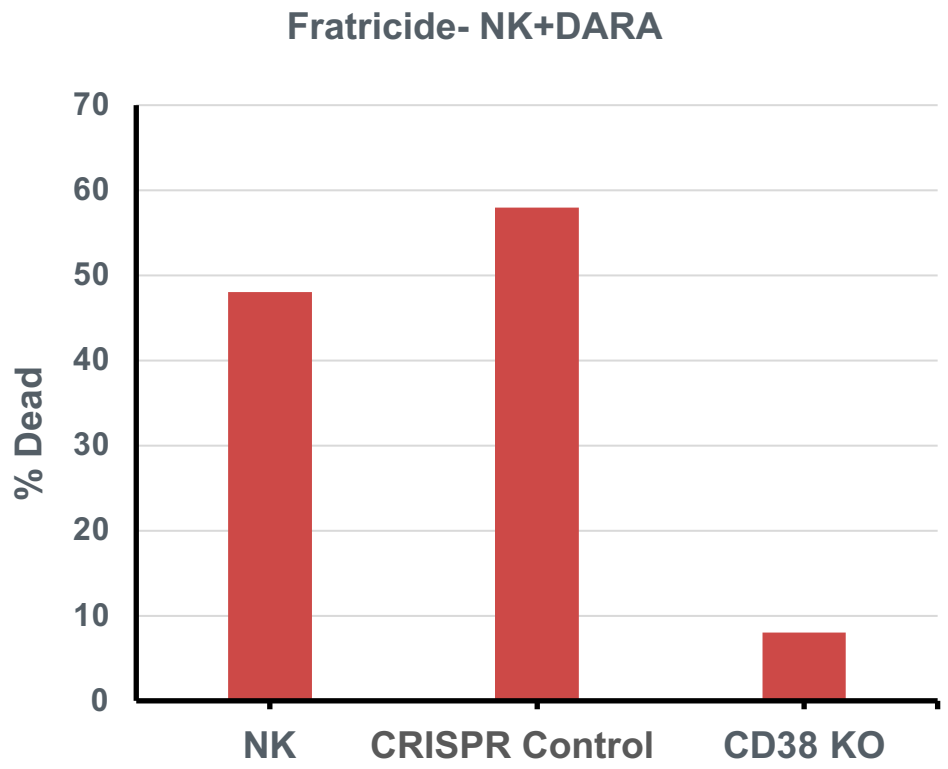
CD38 Knockout and CD38 CAR Targeting Multiple Myeloma

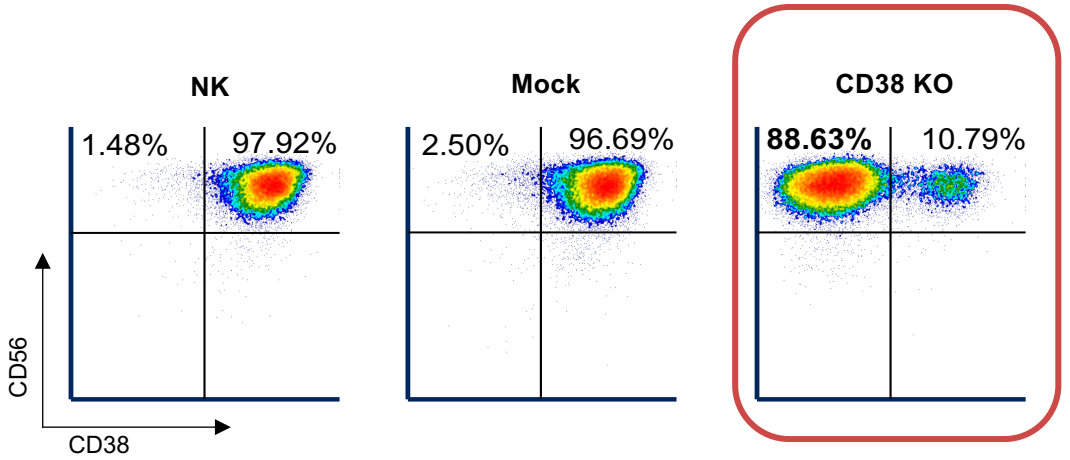


We used the CRISPR/Cas9 system to knockout CD38 in NKs

CD38 KO NKs are Resistant to Fratricide in the Presence of Daratumumab

The fratricide rescue and addition of αCD38 CAR improved cytotoxicity

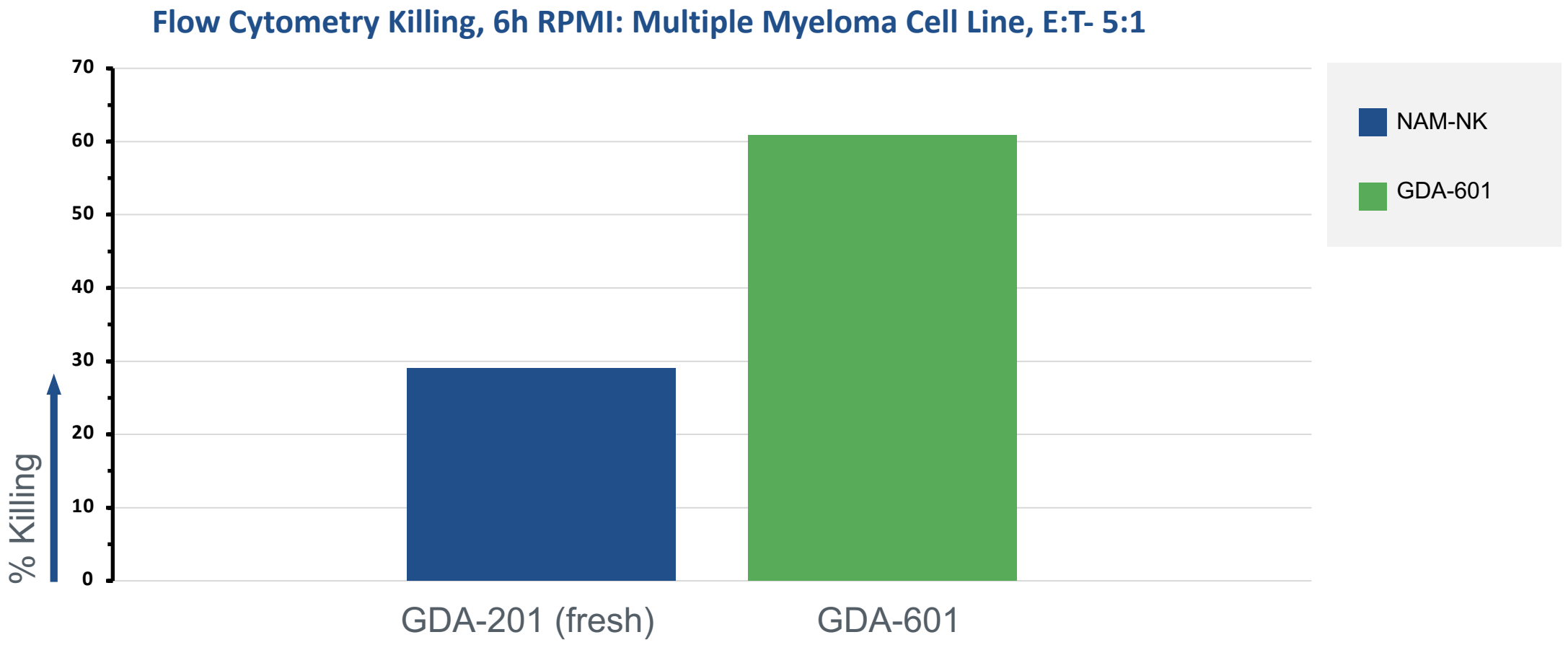




CD38 KO in NAM-NK cells expanded ex-vivo.Representative flow cytometry analysis of untreated NK cells (NK), Cas 9 control (Mock) and NK cells treated with CD38 CRISPR-Cas9 (CD38KO).Cells were expanded 14 days post electroporation and analyzed for CD56/CD38 expression and viability staining.

GDA-601: CD38 KO & αCD38 CAR — Increased Cytotoxicity Against Multiple Myeloma

The fratricide rescue and addition of αCD38 CAR improve cytotoxicity



Robust Genetic Modification Capability for to NAM-Enabled NK Cells

Multiple genetically modified NK constructs with demonstrated potency in preclinical studies

GDA-301

CISH knockout + membrane-bound IL-15 increased potency against leukemia and multiple myeloma cell lines

GDA-501

CAR-HER2 increased cytotoxicity against ovarian tumor cell line

GDA-601

CD38 knockout + CD38 CAR increased cytotoxicity against multiple myeloma cell line

- Research collaboration with Dana-Farber using fresh patient samples ongoing

R&D engine to continually introduce new NK constructs into the clinic

gamida cell

Committed to Cures