Harnessing the Power of Naturally INDAPTA
THERAPEUTICS Occurring NK Cells to Fight Cancer



# Forward Looking Statement

This presentation contains forward-looking statements that are based on the company 's current expectations, assumptions, estimates and projections about the company and the pharmaceutical industry. The company makes no representations about the accuracy of such statements estimates or projections. Forward-looking statements are indicated by words such as: may, will, should, predict, continue, plan, expect, anticipate, estimate, intend, believe, could, goal objectives and similar expressions. Forward-looking statements may include, but are not limited to, statements concerning the company 's anticipated performance, including revenue and profit expectations; development and implementation of collaborations; benefits provided to collaboration partners by our technology; business mix; revenues and growth in our partner base; market opportunities; competing technologies, industry conditions and trends; and regulatory developments. Actual results may differ materially from the anticipated results due to substantial risks and uncertainties related to the company and the biopharmaceutical industry in which the company operates.





# INDAPTA THERAPEUTICS

Off-the-shelf, Best-in-Class NK Cells

#### NK cell platform technology with clear differentiation

- Off-the-shelf, allogeneic cells "engineered by nature"
- ADCC activity markedly superior to conventional NK cells
- In vivo activity superior to published preclinical myeloma model NK cell benchmarks

### Robust proprietary manufacturing process and cryopreservation method

- Expansion from select healthy donors with increased frequency of g-NK cells
- Low batch to batch variability

# G-NK cells are ideal for augmenting efficacy of mAbs, ADCs & innate immune engager molecules

### Phase 1 trial enrolling

- R/R multiple myeloma & lymphoma
- In combination with daratumumab & rituximab
- First patient treated Nov 2023

Future programs will incorporate genetic engineering



## Management



Mark Frohlich, MD CEO Xcyte Therapies, Dendreon, Juno, PACT, Neuvogen



Robert Sikorski, MD PhD **Chief Medical Officer** Amgen, AstraZeneca, MedImmune, Five Prime



Austin Bigley, PhD VP, Research Univ. Houston

## **Our Team**



**Guy DiPierro** Founder | COO AMGI Capital, **Chrono Therapeutics** 



Stefanie Mandl, PhD **Chief Scientific Officer** Exelexis, Bavarian Nordic, Cidara Therapeutics, PACT Pharma



Linda Barnes, DrPH **Head of Regulatory & Quality** AABB, Adicet, Janssen, Bloodworks NW, Dendreon, Univ WA

#### **Board of Directors**

Ronald Martell, Exec Chairman, Co-Founder Mark Frohlich, CEO Lori Hu, Vertex Ventures Ran Nussbaum, Pontifax Fabio Pucci, Leaps by Bayer Laura Stoppel, RA Capital Jim Weiss, Real Chemistry

Advisors

Scientific Founders Sungjin Kim, PhD | Associate Professor, UC Davis John Sunwoo, MD | Professor, Stanford Univ. School of Medicine

> Todd Fehniger | Professor, Dept of Medicine, Washington Univ., St. Louis Nina Shah, MD | Professor of Clinical Medicine, UCSF Catherine Polizzi | Chief IP Lawyer, Morrison Foerster, Palo Alto Vaughn Smider, MD, PhD | Associate Professor, Scripps Research Institute



# Allogeneic NK Cells

# Safe & Effective in Clinical Trials

#### Well-tolerated

- >800 Patients safely treated across ~30 human trials
- No GvHD (non-transplant)
- No cytokine storm
- No neurotoxicity

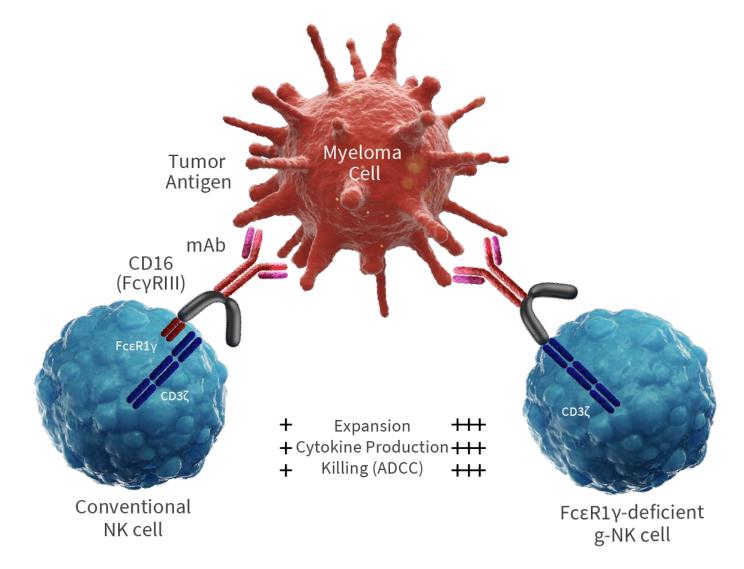
NK cells with targeting agent provide encouraging evidence of efficacy

Targeting	Specifics	Patients	Efficacy	Reference	Sponsor
Monoclonal Ab	Rituximab	NHL	ORR 74%, CR 68%	Cichocki, Sci Transl Med 2023	Gamida Cell
	Rituximab	NHL	ORR 73%, CR 55% (9x10 <sup>7</sup> cells)	Patel, ASH 2021	Fate
	Rituximab	NHL	ORR 57.1%, CR 43%	Graef, ASCO 2023	Artiva
Innate engager	CD30 NK engager	CD30+	ORR of 93%, CR 67%	Nieto, ASH 2023	Affimed/MDA
CAR	CD19 CAR	NHL, CLL	ORR 48.6%, 1 yr CR 27.8%, 1 yr PFS 32%	Marin, Nature Med 2024	Takeda/MDA
	NKG2D CAR	R/R AML	4/6 CR/CRi with flu/AraC conditioning, 3 x 1.5 x 10e9 cells	Sauter, ASH 2023	NKarta



# G-NK Cell Mechanism

Powerful ADCC Through CD3ζ



G-NK cells have markedly higher antibody-dependent cytotoxicity (ADCC) than conventional NK-cells





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## **G-NK Cells**

## **Epigenetically Modified by CMV Permanently**

### Engineered by nature to be the ideal cancer-killing NK cell

Property	Mechanism	G-NK	cNK
ADCC	Exclusive signaling thru CD3ζ	++	-
Cytokine production, antibody dependent	SYK-deficiency	++	-
Target killing capacity	↑granzyme B	++	-
Memory-like persistence in vivo	<b>↓CD38</b> , <b>↑Bcl-2</b>	++	-
Low daratumumab-mediated fratricide	↓CD38 expression	++	-
Cytotoxicity against HLA-deficient tumors	√NKp30 & NKp46 expression	+*	++
Cytotoxicity against HLA-E+ tumors	↑% NKG2C+/NKG2A- NK-cells	++	-

<sup>\*</sup> Can be partially overcome by expansion method.

Ideal to combine with monoclonal antibodies, ADCs & innate immune engagers





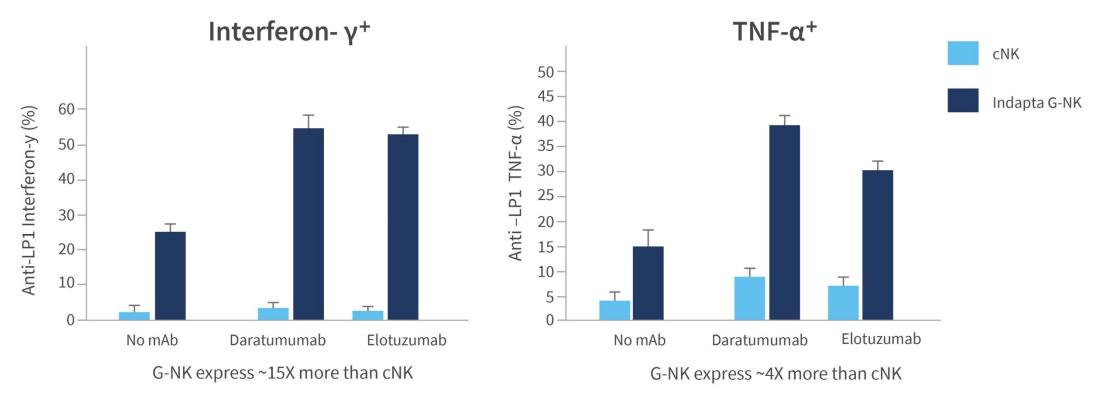








# G-NK Cells (IDP-023) Produce Higher Amounts of Interferon- $\gamma$ & TNF- $\alpha$ upon Encounter with Tumor



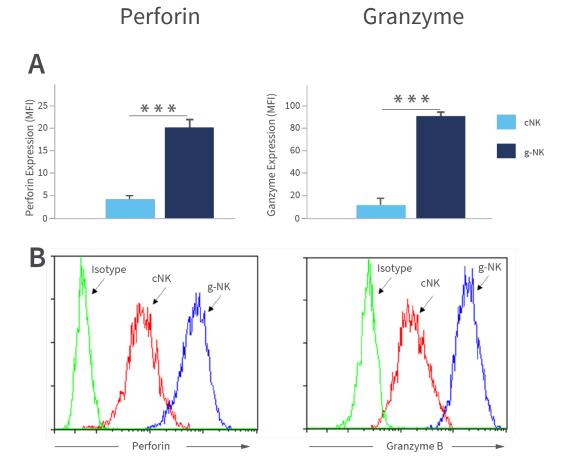
Tumor-Specific Release: Little TNF/IFN is released if no cancer present

Expression of expanded IDP-023 vs cNK against the anti-LP1 myeloma cell line. N=6 per arm. Values are mean  $\pm$  SE. Statistically significant differences between G-NK and cNK are reached (p<0.001).



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# Expanded g-NK Cell Express Increased Levels of Cytotoxic Enzymes

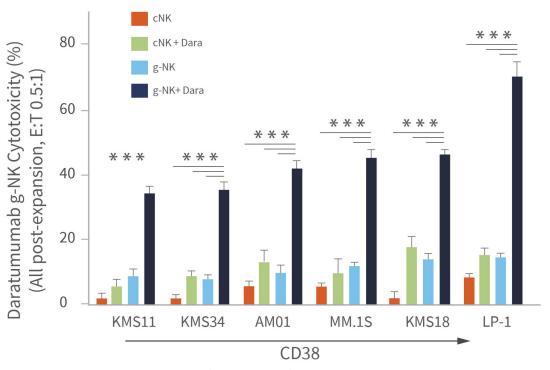




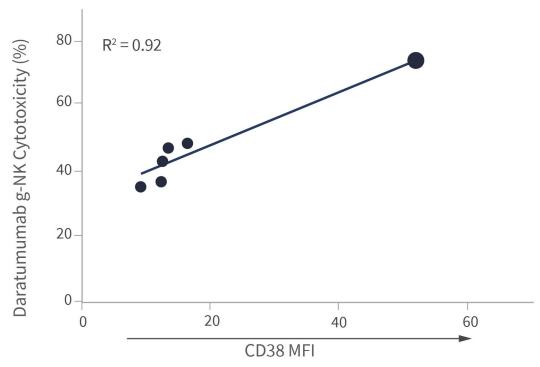


## **Expanded G-NK Cells Have Greater ADCC Than cNK**

## Potential to Rescue Daratumumab When Target Expression Low



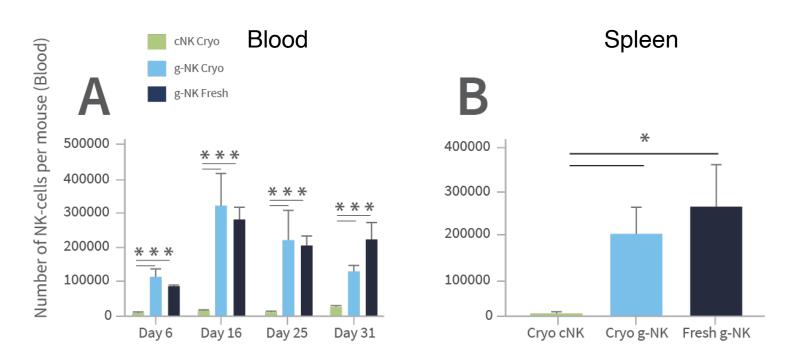
- ADCC of G-NK (0.5:1 E:T) against 6 myeloma cell lines with increasing CD38 expression
- Values are mean ± SE. \*p<0.05, \*\*p<0.01, and \*\*\*p<0.001 (one-way ANOVA with Bonferroni adjustment)

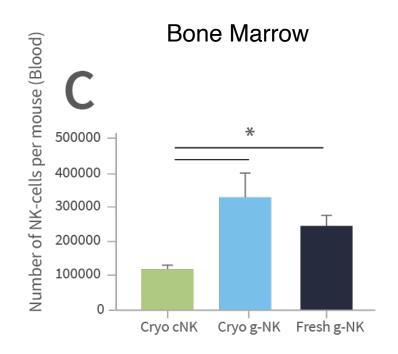


- ADCC is proportionate to target antigen expression
- G-NK ADCC is still markedly elevated against MM cell lines with dim expression of target antigen



## **G-NK Cells Show Improved Persistence in NSG Mice**

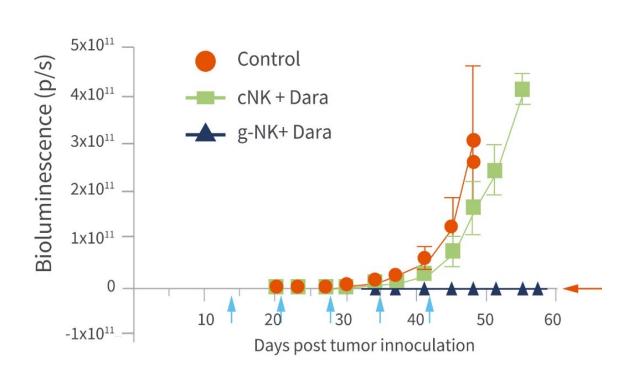




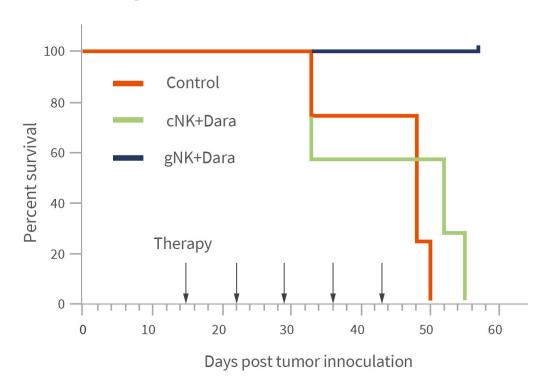
Comparison of the number of human NK-cells present in (A) whole blood at days 6, 16, 26, and 31 post-infusion, (B) spleen at day 31, and (C) bone marrow at day 31 between NSG mice infused with 1x10<sup>7</sup> g-NK or cNK cells (n=3 for each arm) as measured by flow cytometry. To compare *in vivo* persistence between g-NK and cNK cells, a one-way ANOVA was performed with Bonferroni post-hoc testing to determine differences between fresh or cryopreserved g-NK and cNK cells. Values are mean ± SE. \*p<0.05, \*\*p<0.01, and \*\*\*p<0.001.



# IDP-023 Produces Potent Tumor Regression and Extends Survival in Aggressive Myeloma Model



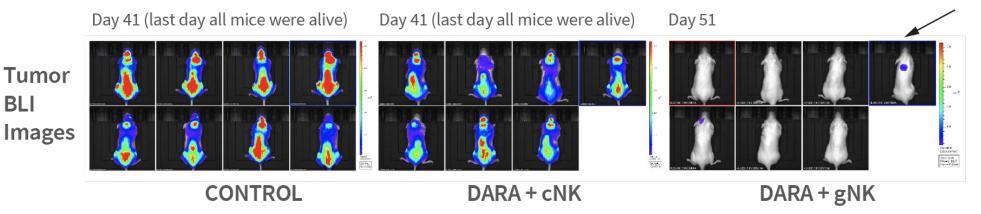
**TUMOR REGRESSION:** NSG mice were inoculated with luc-MM.1S and either untreated (N=8) or treated with daratumumab and either g-NK (N=7) or cNK (N=7). g-NK cells were injected starting 14 days post tumor inoculation (q1wk x 5). Mice treated with g-NK were sacrificed at 56 days post-inoculation. Untreated mice or mice treated with cNK were sacrificed at terminal end-point.



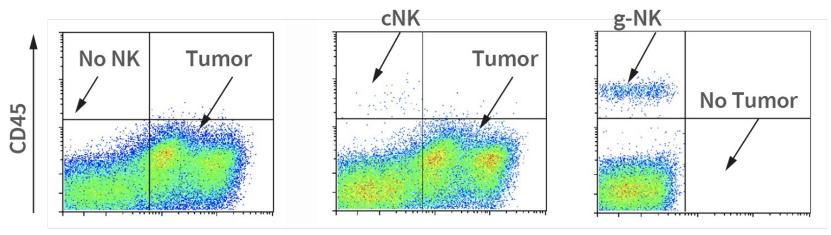
**SURVIVAL MM1.S myeloma model:** Log rank test: P<0.0001, survival curves are significantly different. Gehan-Breslow-Wilcoxon test: P=0.0007, survival curves are significantly different.



# G-NK Persist & Eliminate Myeloma Cells When Combined with Daratumumab



Replacement mouse\* where cancer was allowed to grow for 3 weeks before therapy was started



Representative Flow Plots (taken at day of sacrifice). One of the g-NK mice was not dosed until 3 weeks after tumor engraftment. For all other mice treated with g-NK or cNK, dosing began after 2 weeks.





## Indapta Phase 1 Trial in Lymphoma & Myeloma

### **G-NK Cells in Combination with Rituximab or Daratumumab**

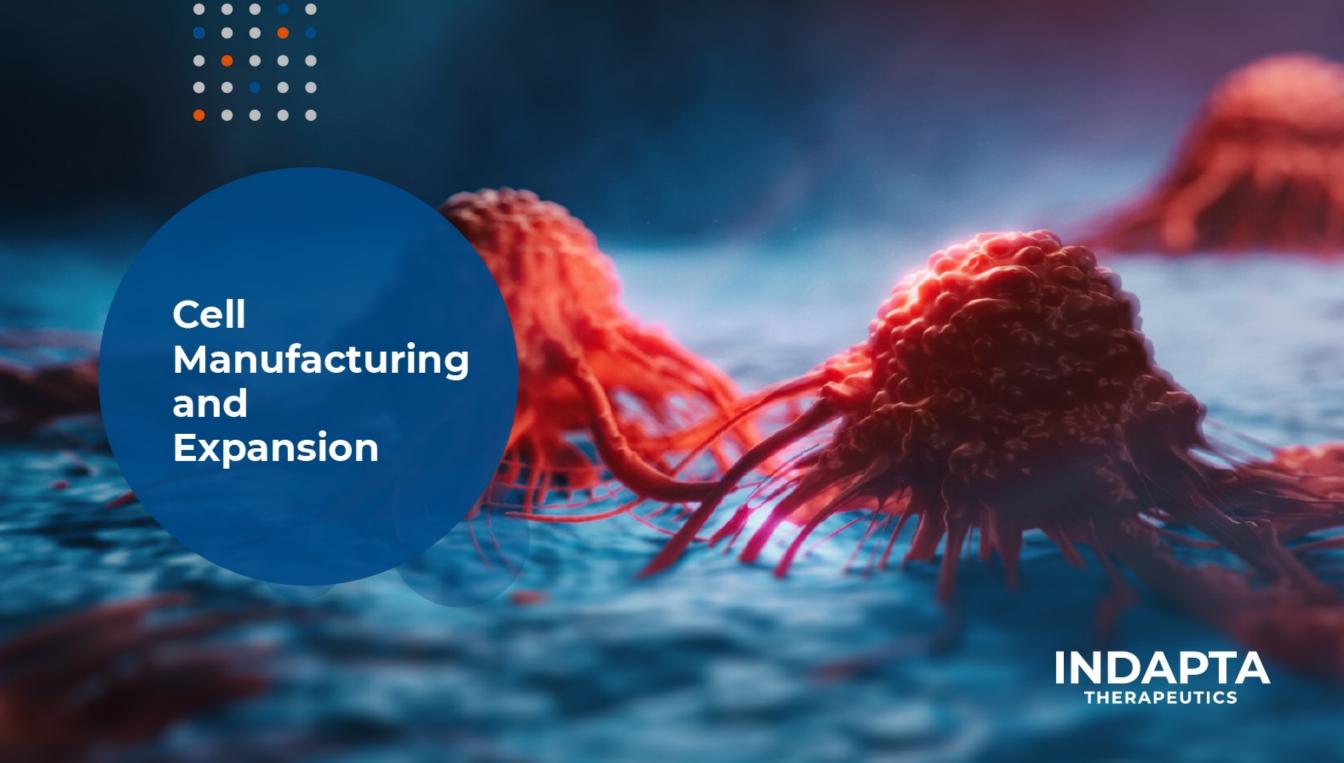
## **Primary Objectives**

- To define the safety and tolerability of IDP-023 with or without IL-2 & with or without daratumumab or rituximab therapy.
- To determine the MTD, RP2D, or MPD of IDP-023 with or without IL-2 & with or without daratumumab or rituximab therapy.

## **Secondary Objectives**

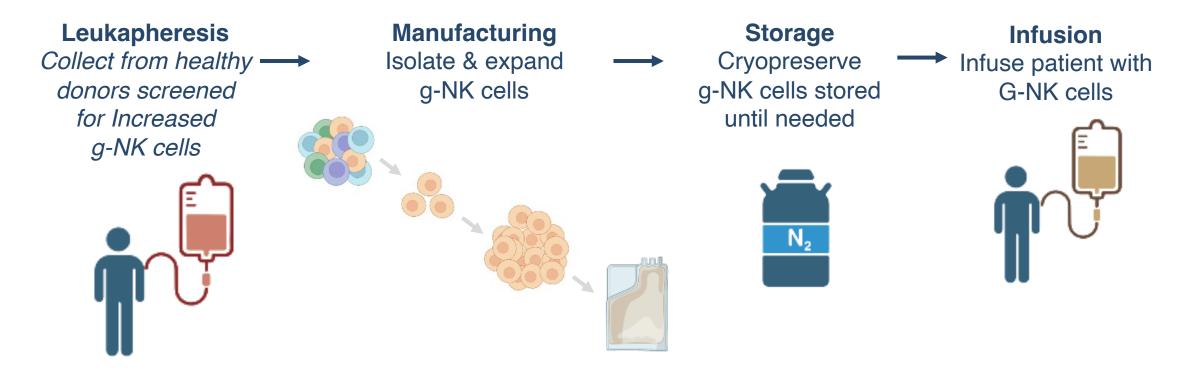
- To assess the PK of IDP-023 with or without IL-2 & with or without daratumumab or rituximab therapy.
- To evaluate preliminary antitumor activity of IDP-023 with or without IL-2 & with or without daratumumab or rituximab therapy.





## **Manufacturing Process**

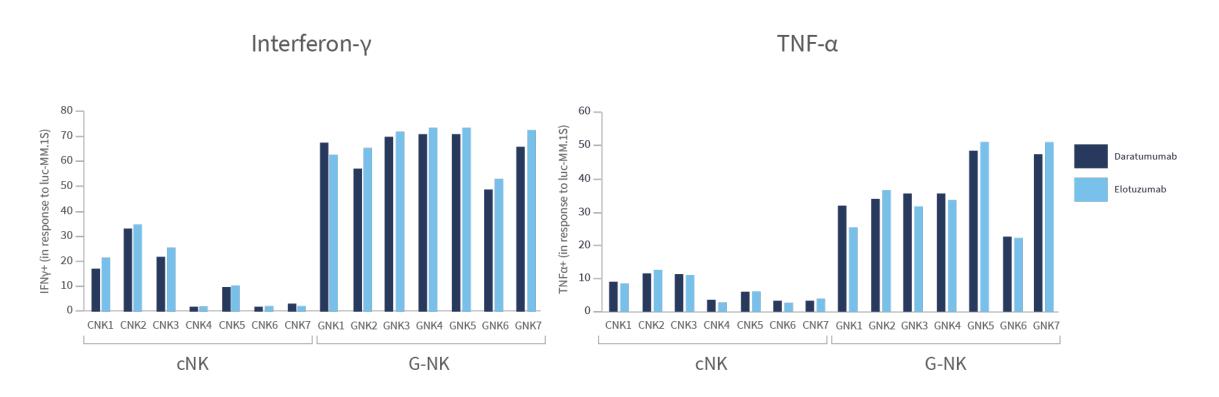
## Allogenic 'Off-the-Shelf' Donor Derived Product



The Indapta manufacturing process is robust and reproducible, with minimal donor to donor variability. Donors with an increased frequency of g-NK cells are selected to undergo large volume apheresis. Following an isolation step to enrich for NK cells, g-NK cells are preferentially expanded for approximately 2 weeks using a proprietary process involving feeder cells and cytokines. Release testing includes product potency, identity and sterility.

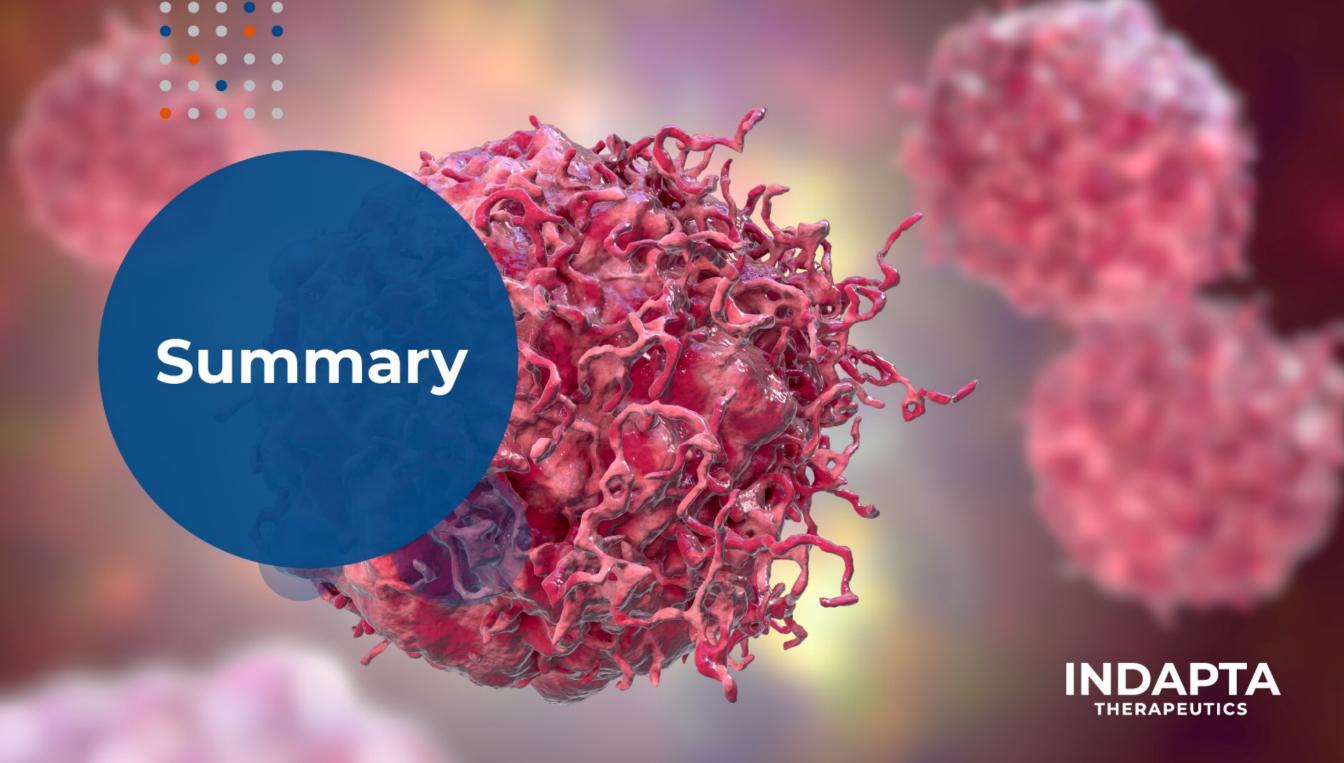


## **G-NK Cell Donor Variability is Low**



Daratumumab- and elotuzumab-induced IFN $\gamma$  and TNF $\alpha$  levels against luc-MM.1S cells from 7 individual cNK and g-NK donors. Donor variability amongst g-NK donors is very low: standard error is less than 5 for mAb-dependent IFN $\gamma$  and TNF $\alpha$  response.





## Indapta Value Proposition

**Universal G-NK Cell Platform** 

#### Off-the-Shelf

- "Engineered by nature": collected from CMV positive donors
- No need for genetic engineering or post expansion cell selection
- Cryopreserved final product

#### Superior to cNK

- Superior mediators of ADCC
- Greater
  - Cytokine secretion
  - Cytolytic activity
  - Persistence
- Lower CD38 expression

### De-Risked Manufacturing

- GMP Engineering Runs completed
- Multiple doses per donor

#### Rapid Timeline to FIH

- IND cleared April 2023
- Phase 1 initiated Q4 2023
  - NHL
  - Multiple myeloma

### · Characterized & Reproducible

- Donor screening optimized
- Low batch to batch variability
- Product well characterized & homogeneous

#### Strong IP

- Broad granted patent protection
- Portfolio of pending applications

