NASDAQ: NK

Jefferies Virtual Cellular Therapy Summit

October 6, 2020

General Disclaimer

Not all product candidates and/or services referenced in these slides are proprietary to NantKwest and may be owned or controlled by our affiliates or third parties.

FORWARD-LOOKING STATEMENTS

These slides and the accompanying oral presentation contain forward-looking statements within the meaning of the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, that are based on managements' beliefs and assumptions and on information currently available to our management. Forward-looking statements include, but are not limited to:

- our ability to pioneer immunotherapy, harness the power of the innate immune system, implement precision cancer medicine and change the current paradigm of cancer care;
- our ability to implement and support the Joint COVID-19 collaboration;
- any impact of the COVID-19 pandemic, or responses to the pandemic, on our business, clinical trials or personnel;
- our expectations regarding the potential benefits of our strategy and technology;
- our expectations regarding the operation of our product candidates and related benefits;
- our ability to utilize multiple modes to induce cell death;
- our beliefs regarding the benefits and perceived limitations of competing approaches, and the future of competing technologies and our industry;
- details regarding our strategic vision and planned product candidate pipeline, including that we eventually plan to advance therapies for virally induced infectious diseases;
- our beliefs regarding the success, cost and timing of our product candidate development activities and current and future clinical trials and studies, including study design;
- our expectations regarding our ability to utilize the phase I and II aNK and haNK clinical trials data to support the development of all of our product candidates, including our haNK, taNK and t-haNK product candidates;
- the timing or likelihood of regulatory filings or other actions and related regulatory authority responses, including any planned investigational new drug, or IND, filings or pursuit of accelerated regulatory approval pathways or orphan drug status and breakthrough therapy designations;
- our ability to implement an integrated discovery ecosystem and the operation of that planned ecosystem, including being able to regularly add neoepitopes and subsequently formulate new product candidates;
- the ability and willingness of strategic collaborators, including certain affiliates of NantWorks, LLC, or NantWorks, to share our vision and effectively work with us to achieve our goals;
- the ability and willingness of various third parties to engage in research and development activities involving our product candidates, and our ability to leverage those activities;
- our ability to attract additional third party collaborators;
- our expectations regarding the ease of administration associated with our product candidates;
- our expectations regarding the patient compatibility associated with our product candidates;
- our beliefs regarding the potential markets for our product candidates and our ability to serve those markets;
- our ability to produce an "off-the-shelf" therapy;
- our beliefs regarding the potential manufacturing and distribution benefits associated with our product candidates, and our ability to scale up the production of our product candidates;
- our plans regarding our manufacturing facility and our belief that our manufacturing is capable of being conducted in-house;
- our belief in the potential of our aNK cells as a technology platform, and the fact that our business is based upon the success of our aNK cells as a technology platform;
- our aNK platform and other product candidate families, including genetically modified taNK, haNK and t-haNK product candidates, will require significant additional clinical testing;
- even if we successfully develop and commercialize our aNK product candidate, we may not be successful in developing and commercializing our other product candidates either alone or in combination with other therapeutic agents;
- the ability to obtain and maintain regulatory approval of any of our product candidates, and any related restrictions, limitations and/or warnings in the label of any approved product candidate;
- our ability to commercialize any approved products;
- the rate and degree of market acceptance of any approved products;
- our ability to attract and retain key personnel;
- the accuracy of our estimates regarding our future revenue, as well as our future operating expenses, capital requirements and needs for additional financing;
- our ability to obtain funding for our operations, including funding necessary to complete further development and any commercialization of our product candidates;
- our ability to obtain and maintain intellectual property protection for our product candidates and not infringe upon the intellectual property of others;
- our expected use of the net proceeds to us from this offering;
- regulatory developments in the United States, or U.S., and foreign countries; and
- our expectations regarding the period during which we qualify as an "emerging growth company" under the JOBS Act, and a "smaller reporting company," as defined in Rule 12b-2 of the Exchange Act.

Forward-looking statements include statements that are not historical facts and can be identified by terms such as "anticipates," "believes," "could," "seeks," "estimates," "expects," "intends," "may," "plans," "potential," "predicts," "projects," "should," "will," "would," or similar expressions and the negatives of those terms.

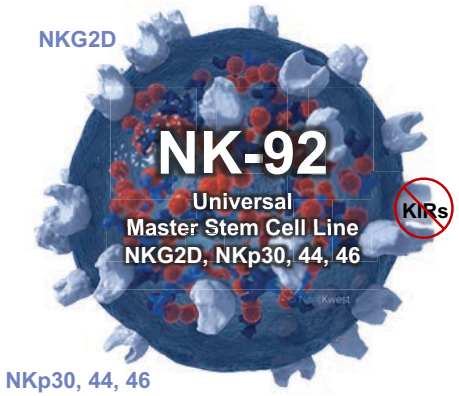
Forward-looking statements involve known and unknown risks, uncertainties, and other factors that may cause our actual results, performance, or achievements to be materially different from any future results, performance, or achievements expressed or implied by the forward-looking statements. These and other risks regarding our business are described in detail in NantKwest's Securities and Exchange Commission filings, including in NantKwest's Quarterly Report on Form 10-Q for the quarter ended June 30, 2020. We encourage you to review NantKwest's SEC filings in order to understand these risks. These forward-looking statements speak only as of the date thereof, and we disclaim any obligation to update these statements except as may be required by law. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Also, forward-looking statements represent our management's beliefs and assumptions only as of the date of this presentation.

Except as required by law, we assume no obligation to update these forward-looking statements, or to update the reasons actual results could differ materially from those anticipated in these forward-looking statements, even if new information becomes available in the future. No representation or warranty, express or implied, is given as to the completeness or accuracy of the information or opinions contained in this document and we do not accept any liability for any direct, indirect or consequential loss or damage arising from reliance on such information or opinions. Past performance should not be taken as an indication or guarantee of future performance. You should read this presentation completely and with the understanding that our actual future results may be materially different from what we expect.

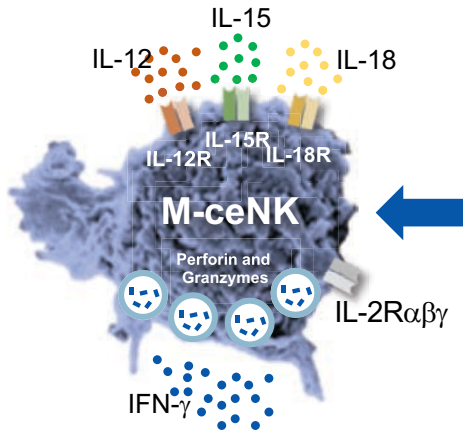
NantKwest Natural Killer Cell Clinical Stage Platform

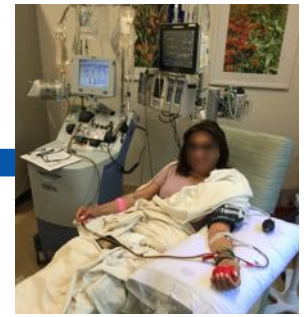
Comprehensive Leader in Natural Killer Cells

aNK (NK-92)
Universal Off-the-Shelf
Natural Killer (NK) Cell Line



M-ceNK
Memory Cytokine Enriched
Natural Killer





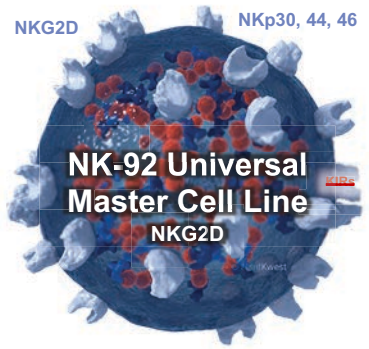
Autologous
Allogeneic Donor

CD16 haNK	PD-L1 t-haNK	HER2 t-haNK	CD19 t-haNK	M-ceNK
Merkel Cell Ca Phase II	Metastatic Pancreatic Ca Phase II TNBC	Breast Glioblastoma Phase I	DBLCL IND Authorized, FIH	AML, Multiple Myeloma IND Q4 2020
	Solid Tumors			Hematologic Tumors

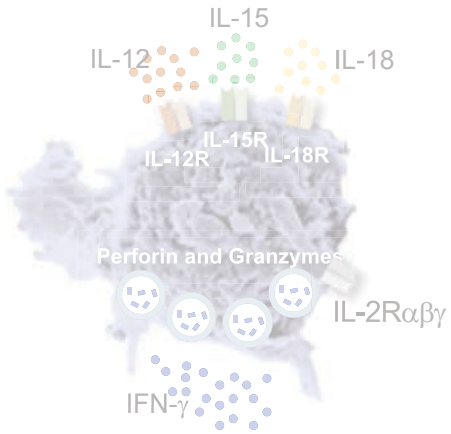
NantKwest Natural Killer Cell Clinical Stage Platform

Comprehensive Leader in Natural Killer Cells

aNK (NK-92)
Universal Off-the-Shelf
Natural Killer (NK) Cell Line



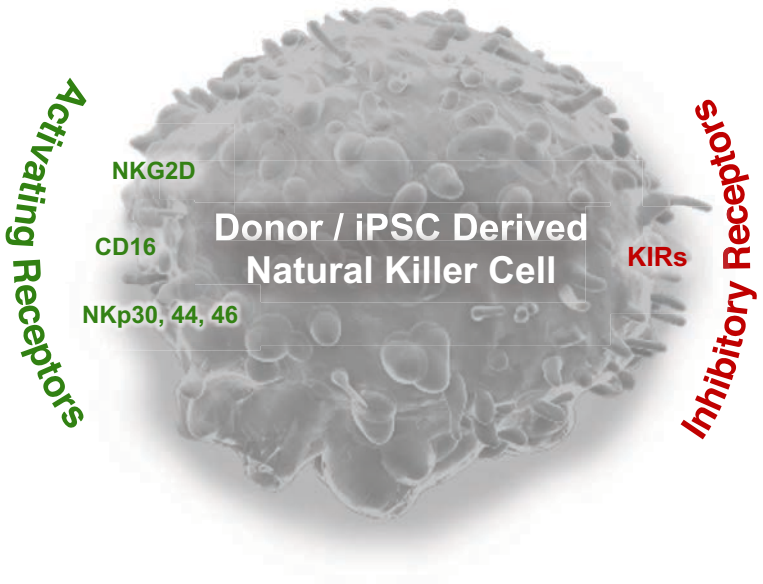
M-ceNK
Memory Cytokine Enriched
Natural Killer



CD16 haNK	PD-L1 t-haNK	HER2 t-haNK	CD19 t-haNK	M-ceNK
Merkel Cell Ca Phase II	Metastatic Pancreatic Ca Phase II TNBC	Breast Glioblastoma Phase I	DBLCL IND Authorized, FIH	AML, Multiple Myeloma IND Q4 2020
	Solid Tumors			Hematologic Tumors

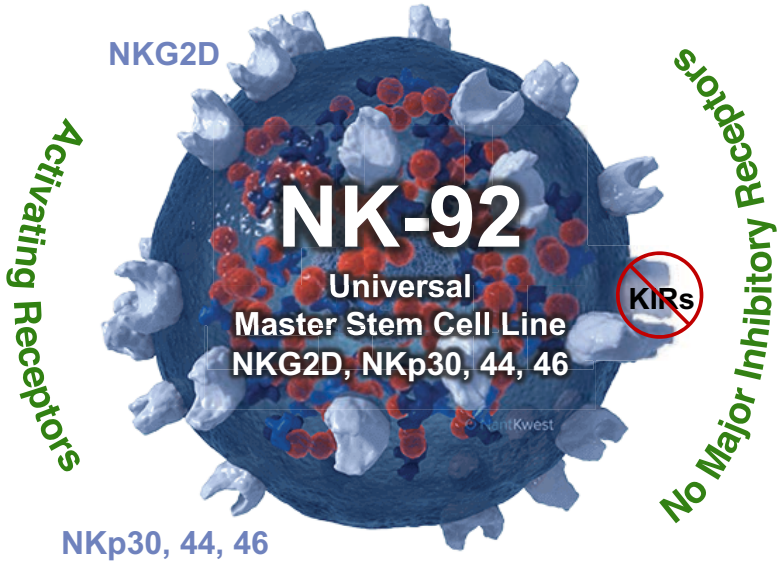
NantKwest Universal NK-92 Master Stem Cell Line

Donor / iPSC Derived
Natural Killer Cell (NK Cell)



- Innate
- Rapid killing
- Activating & Inhibitory Receptors

NantKwest Universal NK-92 Cell Line
Off The Shelf, Cryopreserved



- Discovered 1992 human NK stem cell
- Loss of major inhibitory receptors
- Preserved activating receptors: NKG2D, NKp30, NKp44, NKp46
- Abundant perforin / granzyme
- Always switched on
- Rapid killing
- Rapid doubling*

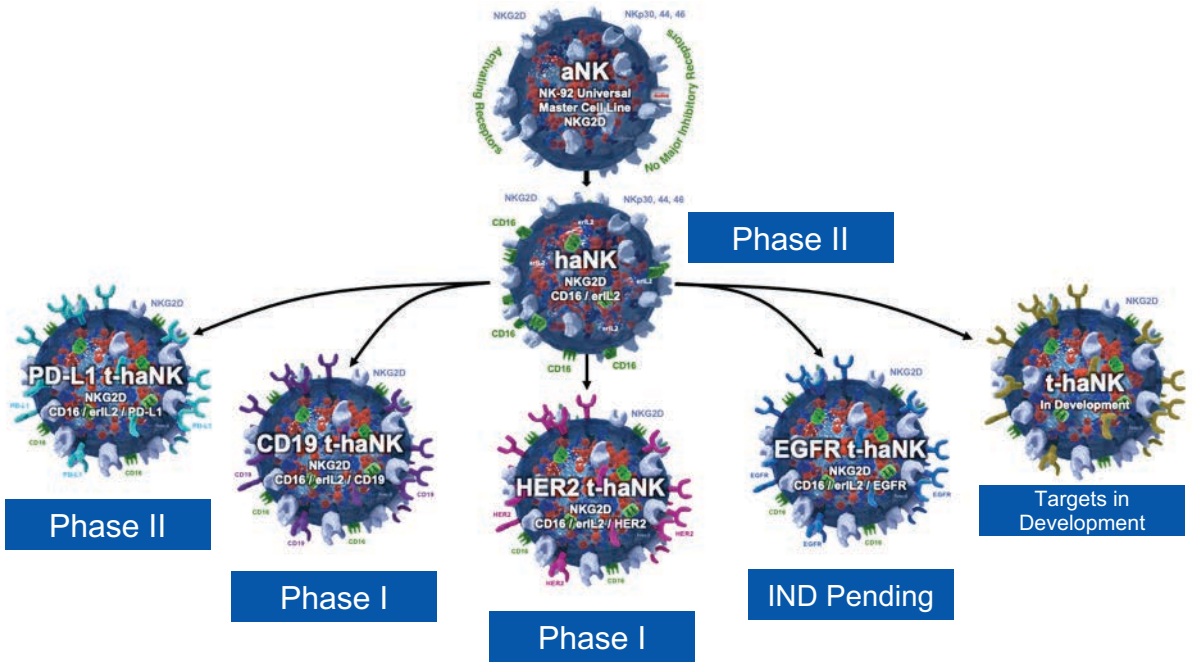
* Per internal manufacturing process

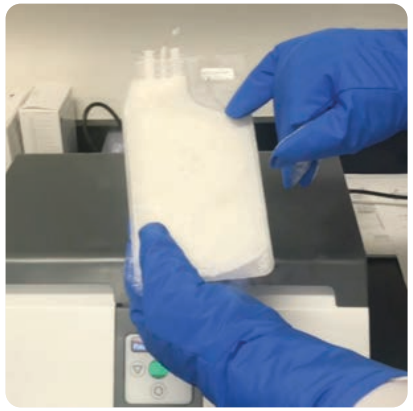
NantKwest Leading Clinical Stage Platform for Off-The-Shelf Natural Killer Cells

	aNK (NK-92)	haNK	PD-L1 t-haNK	CD-19 t-haNK	HER2 t-haNK	EGFR t-haNK
Clinical Indication	**Core Universal Cell Line**	**Merkel Cell**	**1L, 2L, 3L Pancreatic, TNBC, & NSCLC**	**Lymphoma**	**Breast Glioblastoma**	**Head & Neck**
Current Status	Universal NK Cell Line	**Phase II**	**Phase II**	**Phase I**	Breast: **IND, Q4 2020** Glioblastoma: **Phase I**	**IND Pending**
Innate Immunity Without Major Inhibitory Receptors (e.g. NKG2D)	✓	✓	✓	✓	✓	✓
High-Affinity CD16	X	✓	✓	✓	✓	✓
erIL2	X	✓	✓	✓	✓	✓
CAR Insertion(s)	X	-	**PD-L1**	**CD19**	**HER2**	**EGFR**

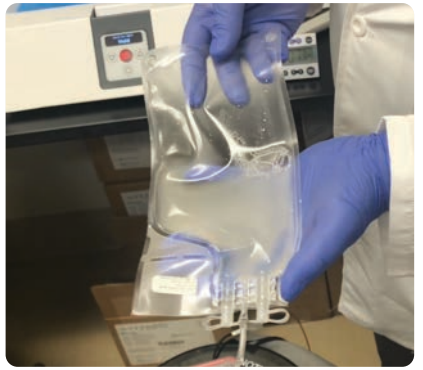
NantKwest Leading Clinical Stage Platform for Off-The-Shelf Natural Killer Cells with Commercial Scale GMP Manufacturing

aNK (NK-92)
Universal Off-the-Shelf
Natural Killer (NK) Cell Line



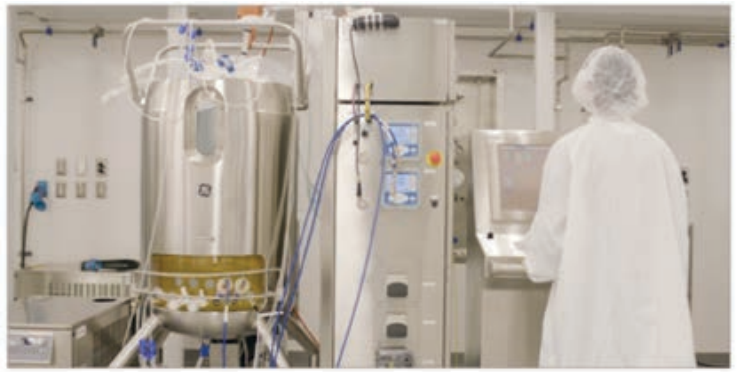


Cryopreserved / Ready-to-Use



Natural Killer Cell Administration
Thaw and Transfuse

Commercial Scale GMP Manufacturing Facility



haNK / PD-L1 t-haNK / HER2.taNK	2017 - 2020
Number of Cells Manufactured in GMP Facility to Date	>3 Trillion Cells*
Number of Patients Dosed as Outpatient	>60
Number of Doses Administered	>800
Number of Cells Administered to Over 60 Patients Since 2017	>1 Trillion Cells*
Number of Cells in Storage	>1 Trillion Cells*
NK Treatment Related Cytokine Storm	Zero**

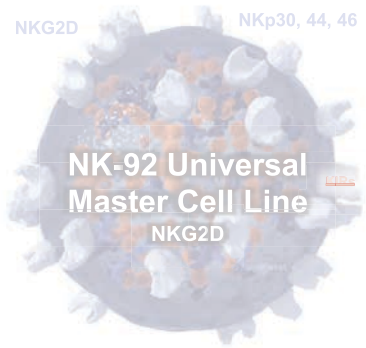
*Based on Internal Production Numbers and Patients Dosed to Date
**Based on clinical trial safety data to date

Phase I / II Clinical Development

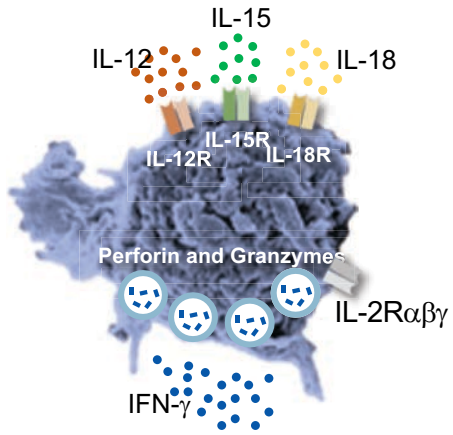
NantKwest Natural Killer Cell Clinical Stage Platform

Comprehensive Leader in Natural Killer Cells

aNK (NK-92)
Universal Off-the-Shelf
Natural Killer (NK) Cell Line



M-ceNK
Memory Cytokine Enriched
Natural Killer

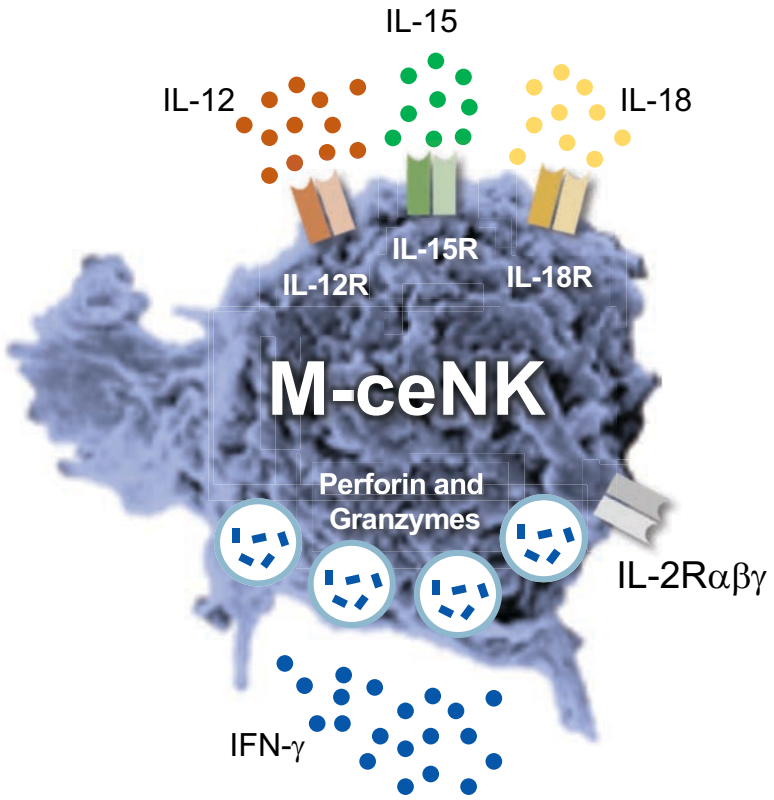


CD16 haNK	PD-L1 t-haNK	HER2 t-haNK	CD19 t-haNK	M-ceNK
Merkel Cell Ca Phase II	Metastatic Pancreatic Ca Phase II TNBC	Breast Glioblastoma Phase I	DBLCL IND Authorized, FIH	AML, Multiple Myeloma IND Q4 2020
	Solid Tumors			Hematologic Tumors

NantKwest Proprietary – IND Ready
Memory Cytokine Enhanced Natural Killer cells (M-ceNK)

Stem Cell Memory NK

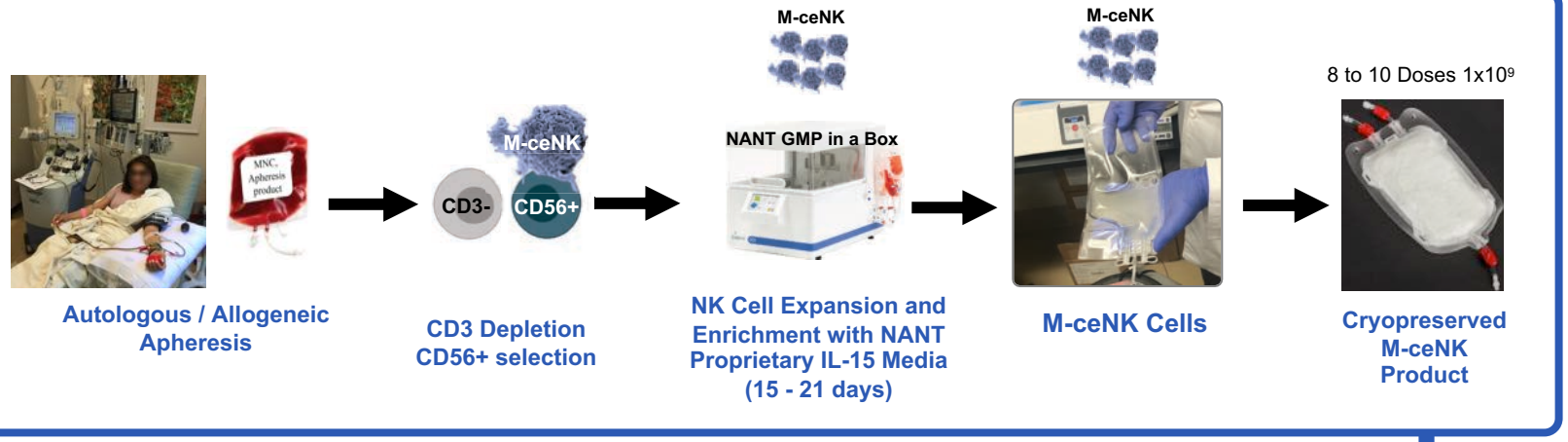
Cytokine Induced



Cytokines and Activating Receptors

Enhanced IFN-γ Production

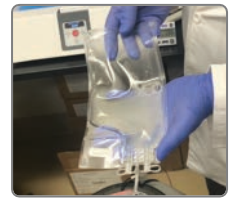
A Single Apheresis Collection Provides 8-10 Doses of $1x10^9$ M-ceNK



IND Ready Q1 2021

Barrier Addressed	Property
Persistence	Proliferate, Long lived
Enhanced Function	Enhanced Cytokine / Chemokine, Enhanced Killing
Recognition	Non-functional Inhibitory KIR, Fully Activated NK Cell

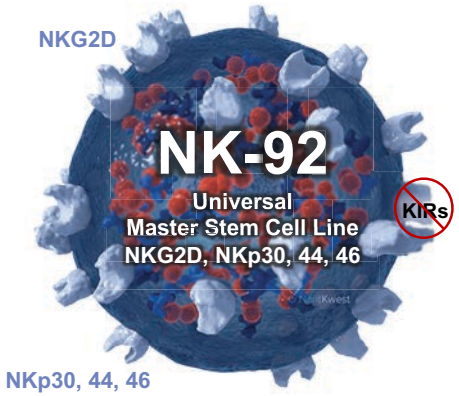
M-ceNK



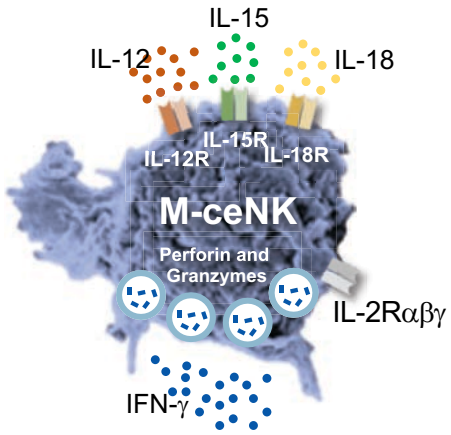
NantKwest Natural Killer Cell Clinical Stage Platform

Comprehensive Leader in Natural Killer Cells

aNK (NK-92)
Universal Off-the-Shelf
Natural Killer (NK) Cell Line



M-ceNK
Memory Cytokine Enriched
Natural Killer

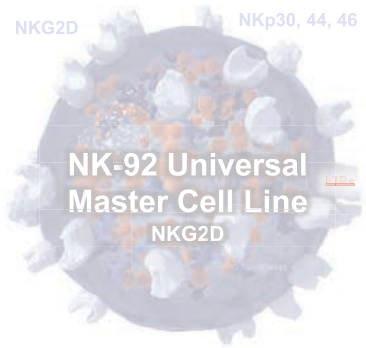


CD16 haNK	PD-L1 t-haNK	HER2 t-haNK	CD19 t-haNK	M-ceNK
Merkel Cell Ca Phase II	Metastatic Pancreatic Ca Phase II TNBC & NSCLC	Breast Glioblastoma Phase I	DBLCL IND Authorized, FIH	AML, Multiple Myeloma IND Q4 2020
	Solid Tumors		Hematologic Tumors	

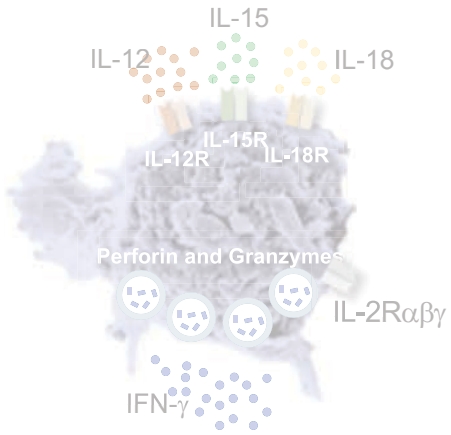
NantKwest Natural Killer Cell Clinical Stage Platform

Comprehensive Leader in Natural Killer Cells

aNK (NK-92)
Universal Off-the-Shelf
Natural Killer (NK) Cell Line



M-ceNK
Memory Cytokine Enriched
Natural Killer

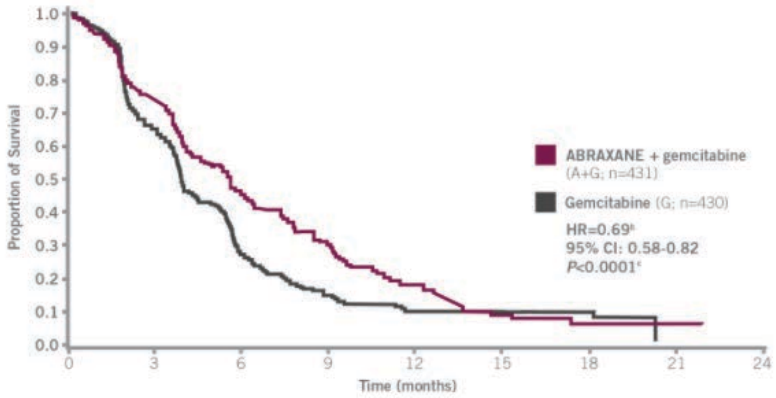


CD16 haNK	PD-L1 t-haNK	HER2 t-haNK	CD19 t-haNK	M-ceNK
Merkel Cell Ca Phase II	Metastatic Pancreatic Ca Phase II	Breast	DBLCL IND Authorized, FIH	AML, Multiple Myeloma IND Q4 2020
	TNBC & NSCLC	Glioblastoma Phase I		
	Solid Tumors		Hematologic Tumors	

Phase I / Ib Study Completed
2nd Line or Greater Metastatic Pancreatic Cancer

ABRAXANE + GEMCITABINE SIGNIFICANTLY IMPROVED PFS[a]

49% increase in median PFS with ABRAXANE (125 mg/m² QW3/4) + gemcitabine compared with gemcitabine alone[1]



First Line

ABRAXANE + gemcitabine

5.5 MONTHS
(95% CI: 4.5-5.9)

— VS —

Gemcitabine

3.7 MONTHS
(95% CI: 3.6-4.0)

[a] Based on independent radiological reviewer assessment.
[b] Stratified using Cox proportional hazard model.
[c] Based on a stratified log-rank test (stratified by geographic region, KPS, and presence of liver metastasis).

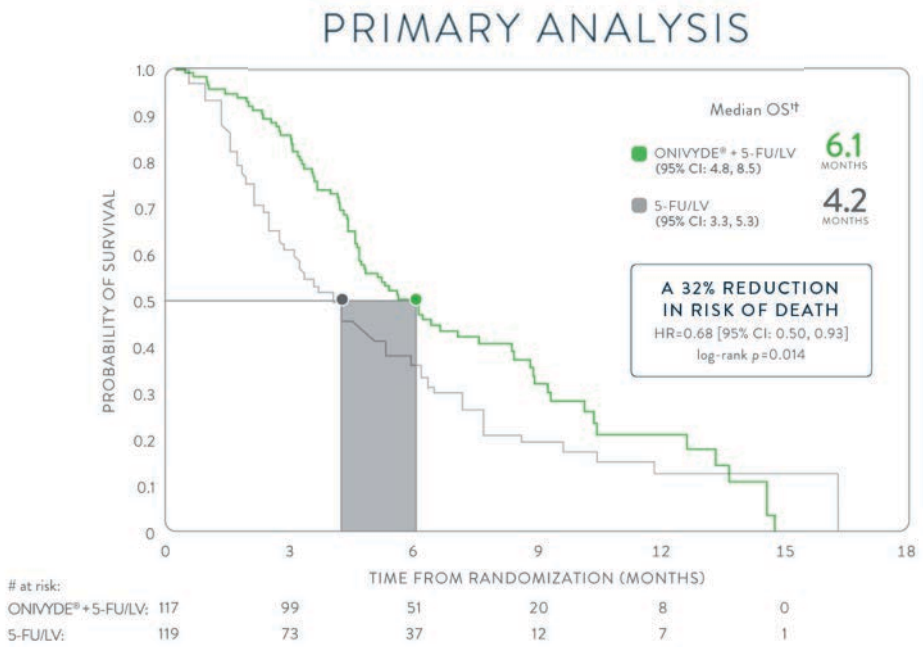
Second Line or Greater

Progression Free Survival using RECIST by Local Independent Radiologist Assessment

Variable	All Subjects (N=17)
Number of Subjects with Disease Progression or Death	11 (65%)
Median Progression-Free Survival (months)	7.1
95% CI for the Median PFS	4.4, 8.8

Caution should be exercised when comparing two different clinical trials as cross trial comparisons may potentially suggest misleading similarities and differences.

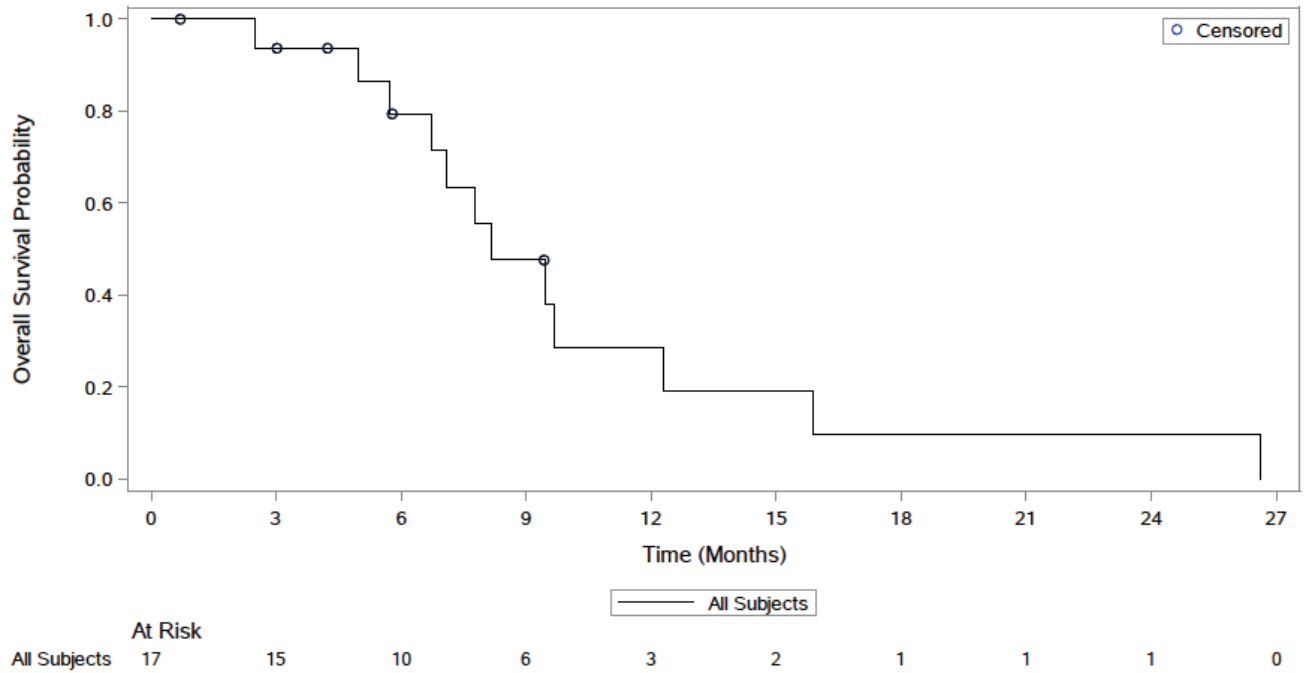
Phase I / Ib Study Completed
2nd Line or Greater Metastatic Pancreatic Cancer



Overall Survival

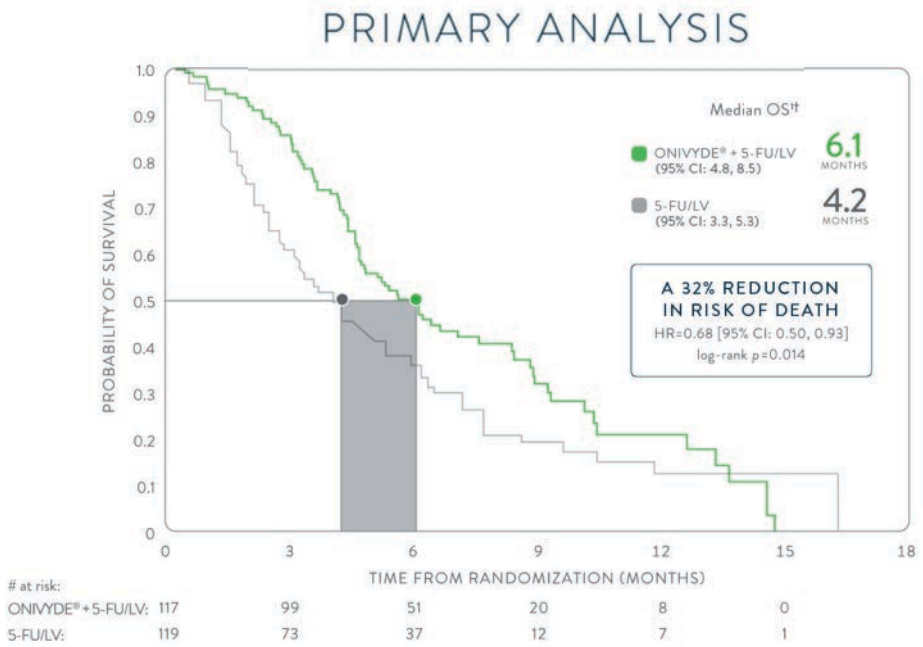
Variable	All Subjects (N=17)
Number of Deaths	12 (71%)
Median Survival (months)	8.2
95% CI for the Median Survival	5.7, 12.3

Second Line or Greater
Overall Survival



Caution should be exercised when comparing two different clinical trials as cross trial comparisons may potentially suggest misleading similarities and differences.

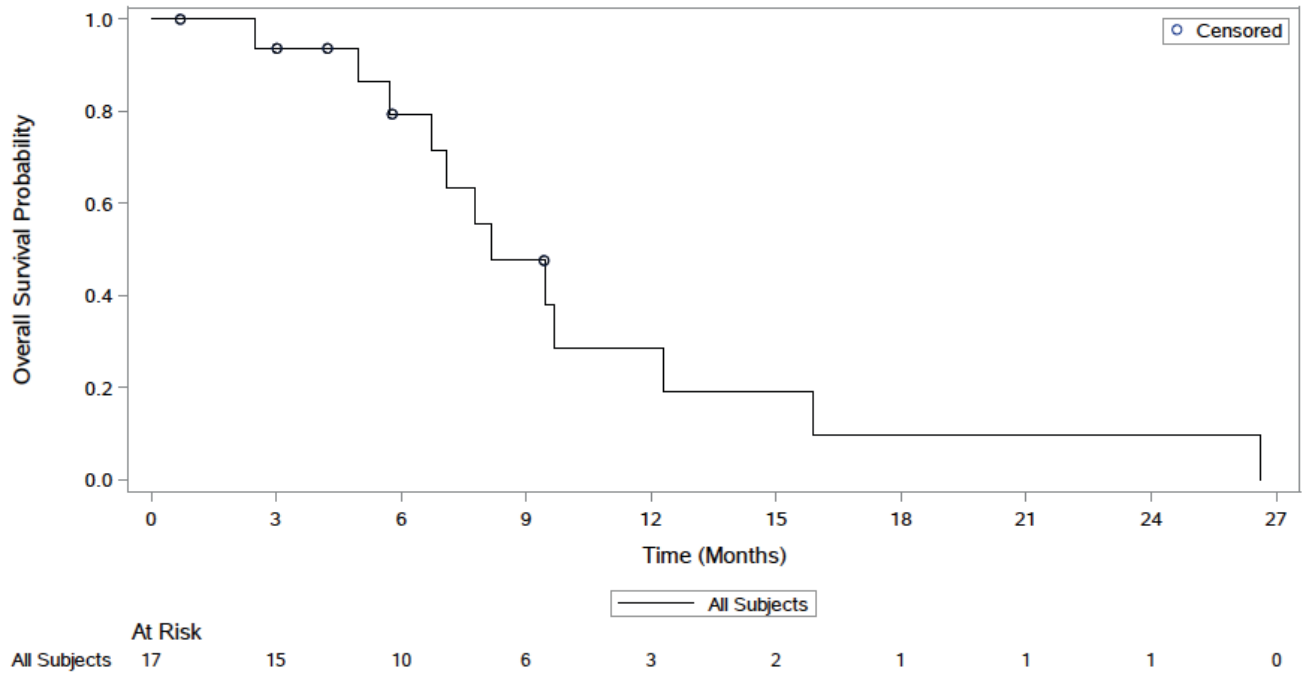
Phase I / Ib Study Completed
2nd Line or Greater Metastatic Pancreatic Cancer



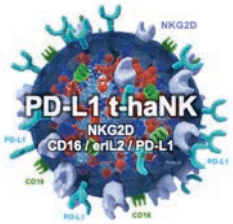
Overall Survival

Variable	All Subjects (N=17)
Number of Deaths	12 (71%)
Median Survival (months)	8.2
95% CI for the Median Survival	5.7, 12.3

Second Line or Greater
Overall Survival



Caution should be exercised when comparing two different clinical trials as cross trial comparisons may potentially suggest misleading similarities and differences.



PD-L1 t-haNK is Superior to haNK + PD-L1 Checkpoint Inhibitor

Open access Original research

Journal for ImmunoTherapy of Cancer

PD-L1 targeting high-affinity NK (t-haNK) cells induce direct antitumor effects and target suppressive MDSC populations

Kellsye P Fabian,[1] Michelle R Padget,[1] Renee N. Donahue,[1] Kristen Solocinski,[1] Yvette Robbins,[1] Clint T. Allen,[2] John H. Lee,[3] Shahrooz Rabizadeh,[4,5] Patrick Soon-Shiong,[4,5] Jeffrey Schlom ,[1] James W Hodge [1]

To cite: Fabian KP, Padget MR, Donahue RN, *et al*. PD-L1 targeting high-affinity NK (t-haNK) cells induce direct antitumor effects and target suppressive MDSC populations. *Journal for ImmunoTherapy of Cancer* 2020;**8**:e000450. doi:10.1136/jitc-2019-000450

► Additional material is published online only. To view, please visit the journal online (http://dx.doi.org/10.1136/jitc-2019-000450).

Accepted 29 April 2020

ABSTRACT

Background Although immune checkpoint inhibitors have revolutionized cancer treatment, clinical benefit with this class of agents has been limited to a subset of patients. Hence, more effective means to target tumor cells that express immune checkpoint molecules should be developed. For the first time, we report a novel natural killer (NK) cell line, programmed death-ligand 1 (PD-L1) targeting high-affinity natural killer (t-haNK), which was derived from NK-92 and was engineered to express high-affinity CD16, endoplasmic reticulum-retained interleukin (IL)-2, and a PD-L1-specific chimeric antigen receptor (CAR). We show that PD-L1 t-haNK cells also retained the expression of native NK receptors and carried a high content of granzyme and perforin granules.

Methods NanoString, flow cytometry, and immunofluorescence analyses were performed to preferentially lysed the myeloid-derived suppressor cell population but not other immune cell types.

Conclusion These studies demonstrate the antitumor efficacy of PD-L1 t-haNK cells and provide a rationale for the potential use of these cells in clinical studies.

BACKGROUND

The discovery and establishment of continuously expanding natural killer (NK) cell lines provide a potential source of allogeneic 'off-the-shelf' cellular therapy due to its low risk of causing graft-versus-host disease or other alloimmune toxicities.[1] NK-92, which was derived from a non-Hodgkin's lymphoma patient, is a highly cytotoxic NK shown to have activity

April 2020

eLife RESEARCH ARTICLE

Tumor control via targeting PD-L1 with chimeric antigen receptor modified NK cells

Yvette Robbins[1], Sarah Greene[1], Jay Friedman[1], Paul E Clavijo[1], Carter Van Waes[2], Kellsye P Fabian[3], Michelle R Padget[3], Houssein Abdul Sater[4], John H Lee[5], Patrick Soon-Shiong[5], James Gulley[4], Jeffrey Schlom[3], James W Hodge[3], Clint T Allen[1,6]*

[1]Translational Tumor Immunology Program, National Institute on Deafness and Other Communication Disorders, National Institutes of Health, Bethesda, United States; [2]Tumor Biology Section, National Institute on Deafness and Other Communication Disorders, National Institutes of Health, Bethesda, United States; [3]Laboratory of Tumor Immunology and Biology, National Cancer Institute, National Institutes of Health, Bethesda, United States; [4]Genitourinary Malignancies Branch, National Cancer Institute, National Institutes of Health, Bethesda, United States; [5]NantKWest, Culver City, United States; [6]Department of Otolaryngology-Head and Neck Surgery, Johns Hopkins School of Medicine, Baltimore, United States

***For correspondence:** clint.allen@nih.gov

Competing interest: See page 14

Funding: See page 14

Received: 02 January 2020
Accepted: 24 June 2020
Published: 07 July 2020

Abstract Failed T cell-based immunotherapies in the presence of genomic alterations in antigen presentations pathways may be overcome by NK cell-based immunotherapy. This approach may still be limited by the presence of immunosuppressive myeloid populations. Here, we demonstrate that NK cells (haNKs) engineered to express a PD-L1 chimeric antigen receptor (CAR) haNKs killed a panel of human and murine head and neck cancer cells at low effector-to-target ratios in a PD-L1-dependent fashion. Treatment of syngeneic tumors resulted in CD8 and PD-L1-dependent tumor rejection or growth inhibition and a reduction in myeloid cells endogenously expressing high levels of PD-L1. Treatment of xenograft tumors resulted in PD-L1-dependent tumor growth inhibition. PD-L1 CAR haNKs reduced levels of macrophages and other myeloid cells endogenously expressing high PD-L1 in peripheral blood from patients with head and neck cancer. The clinical study of PD-L1 CAR haNKs is warranted.

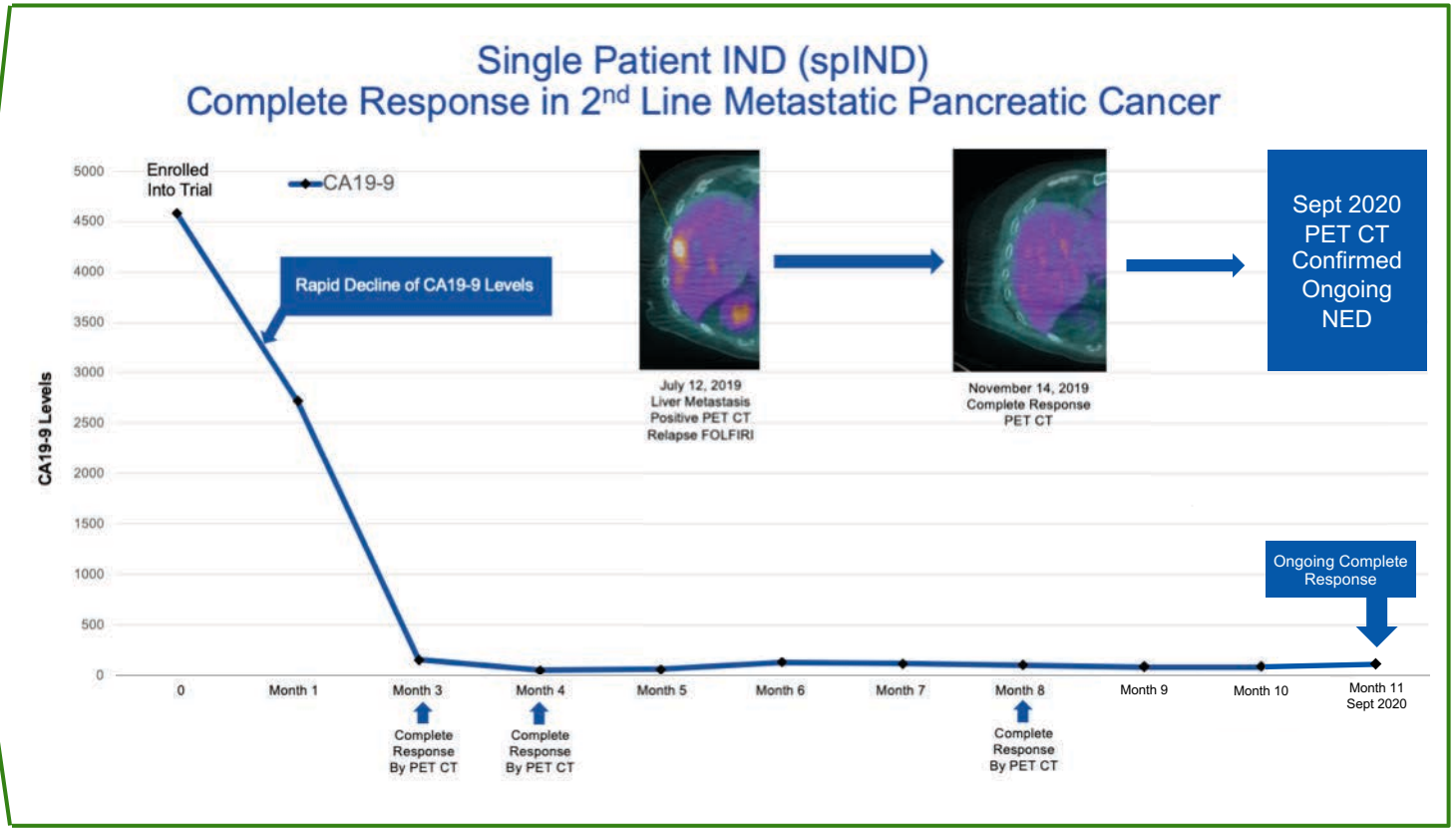
Introduction

July 2020

Metastatic Pancreatic Cancer

Promising Complete Remission in Patients with 2nd Line Metastatic Pancreatic Disease

- In aggregate, **82% of patients (14 / 17)** with advanced pancreatic cancer achieved disease control
- A single patient demonstrated an ongoing complete response, over 10 months and ongoing

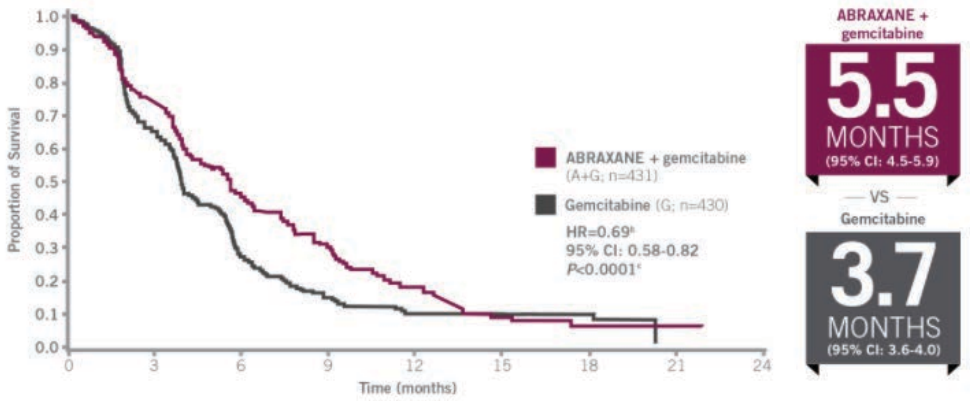


NED: No Evidence of Disease

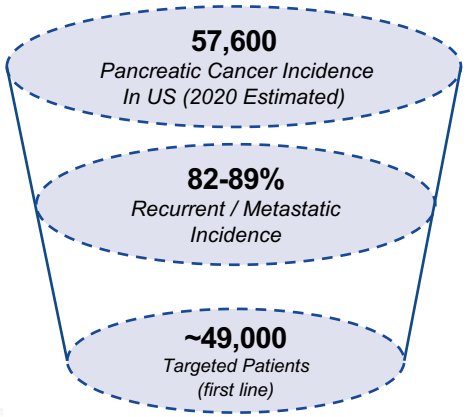
Randomized Phase II Trial with Registrational Intent Trials First Line Metastatic Pancreatic Cancer (QUILT-88)

ABRAXANE + GEMCITABINE SIGNIFICANTLY IMPROVED PFS[a]

49% increase in median PFS with ABRAXANE (125 mg/m² QW3/4) + gemcitabine compared with gemcitabine alone[1]



[a] Based on independent radiological reviewer assessment.
[b] Stratified using Cox proportional hazard model.
[c] Based on a stratified log-rank test (stratified by geographic region, KPS, and presence of liver metastasis).



First Line Pancreatic

Locally Advanced or Metastatic Pancreatic Cancer treated with Gemcitabine + Nab-Paclitaxel

Randomize 1:1 — N=138

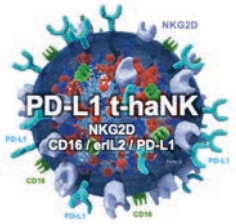
Control Arm
Nab-paclitaxel +
Gemcitabine +

Experimental Arm
Nab-paclitaxel +
Gemcitabine +
Cyclophosphamide
Anktiva™
Aldoxorubicin™

Experimental Arm
Nab-paclitaxel +
Gemcitabine +
Cyclophosphamide
Anktiva™
Aldoxorubicin™
PD-L1 t-haNK

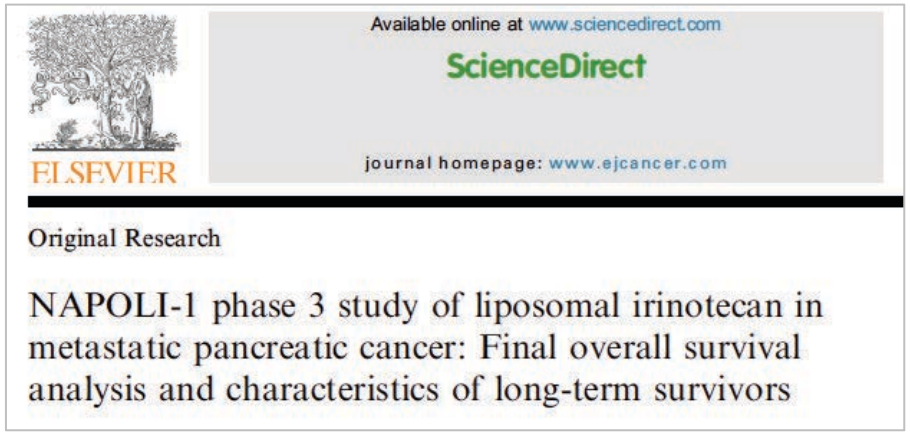
Status as of Oct 2020:

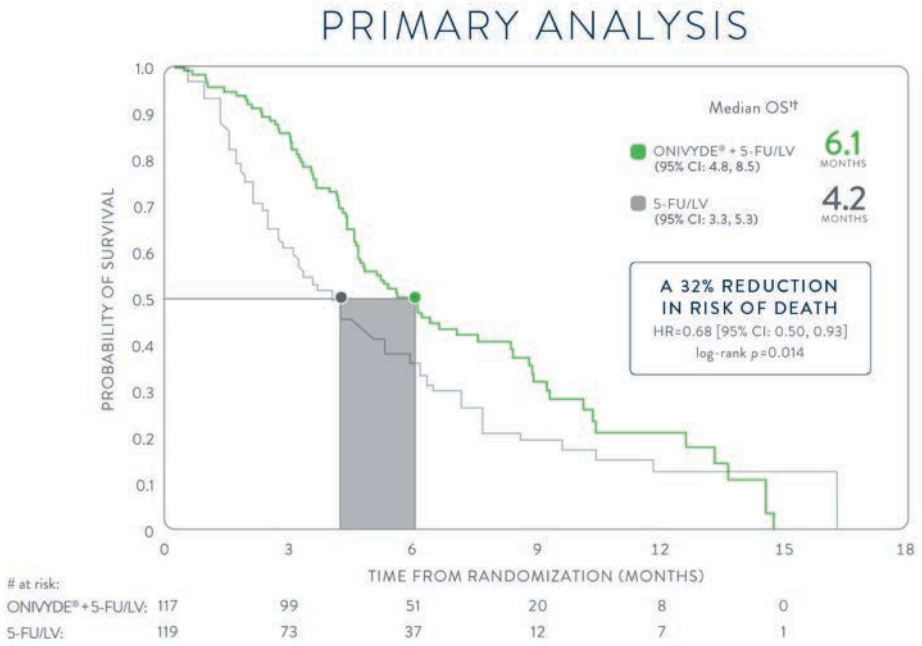
- Study opened, actively recruiting
- Number of sites opened to date: **3**

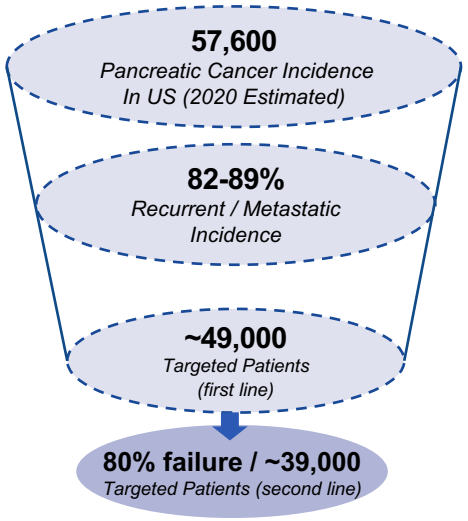


Caution should be exercised when comparing two different clinical trials as cross trial comparisons may potentially suggest misleading similarities and differences.

Randomized Phase II Trial with Registrational Intent Trials Second Line Metastatic Pancreatic Cancer (QUILT-88)







Second Line Pancreatic

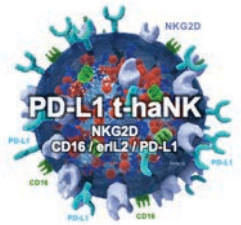
Locally Advanced or Metastatic Pancreatic Cancer treated with Gemcitabine or paclitaxel-based therapy or FOLFOX or FOLFIRINOX

Randomize 1:1 — N=110

Control Arm
Irinotecan Liposome
Leucovorin
5-FU

Experimental Arm
Nab-paclitaxel +
Gemcitabine +
Cyclophosphamide
Anktiva
Aldoxorubicin
PD-L1 t-haNK*

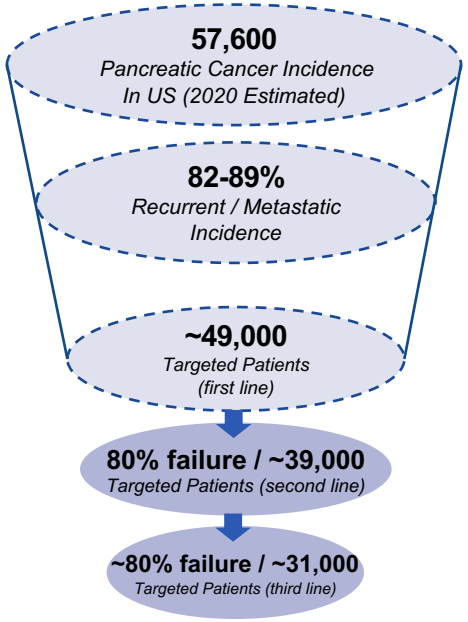
Status as of Oct 2020:
- Study opened, actively recruiting
- Number of sites opened to date: **3**
- Number of patients enrolled to date: **14** (in 9 weeks since opening)



Caution should be exercised when comparing two different clinical trials as cross trial comparisons may potentially suggest misleading similarities and differences.

Randomized Phase II Trial with Registrational Intent Trials
Third Line or Greater Metastatic Pancreatic Cancer (QUILT-88)

No standard of care to date for patients in third line or greater metastatic pancreatic cancer



Third-Line or Greater Pancreatic

Locally Advanced or Metastatic Pancreatic Cancer Treated with at Least 2 Lines of Therapy

Experimental Arm
Nab-paclitaxel +
Gemcitabine +
Cyclophosphamide
Anktiva
Aldoxorubicin
PD-L1 t-haNK*

N=50

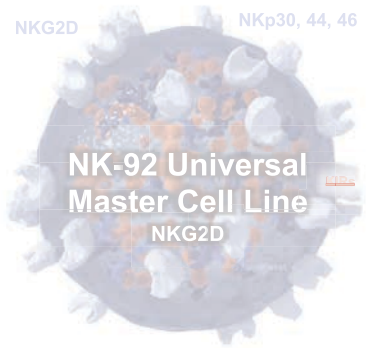
Status as of Oct 2020:

- Study opened, actively recruiting
- Number of sites opened to date: 3
- Number of patients enrolled to date: 2 (Open less than 1 week)
- Number of patients being evaluated >25

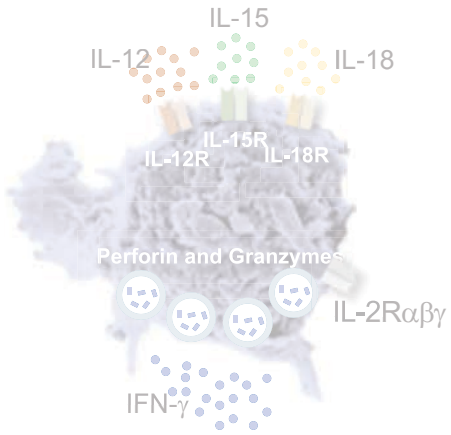
NantKwest Natural Killer Cell Clinical Stage Platform

Comprehensive Leader in Natural Killer Cells

aNK (NK-92)
Universal Off-the-Shelf
Natural Killer (NK) Cell Line



M-ceNK
Memory Cytokine Enriched
Natural Killer

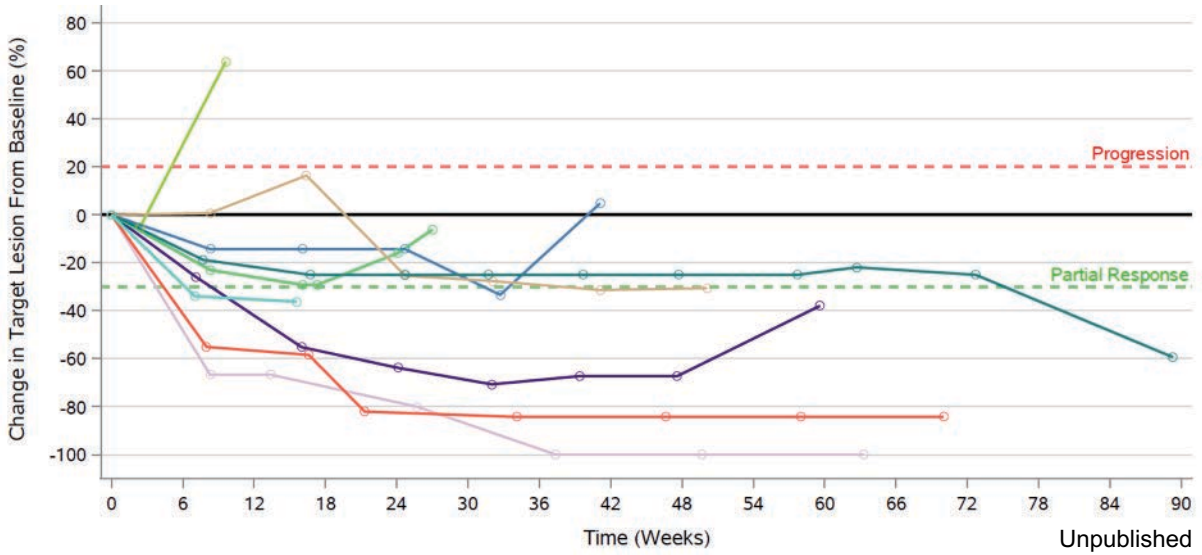


CD16 haNK	PD-L1 t-haNK	HER2 t-haNK	CD19 t-haNK	M-ceNK
Merkel Cell Ca Phase II	Metastatic Pancreatic Ca Phase II TNBC & NSCLC	Breast Glioblastoma Phase I	DBLCL IND Authorized, FIH	AML, Multiple Myeloma IND Q4 2020
	Solid Tumors		Hematologic Tumors	

Completed Phase Ib Trial (N=9) in Triple Negative Breast Cancer with haNK + Avelumab: Data Locked Promising Disease Control (89%) and Complete Response (22%) in Advanced Metastatic Disease

Phase Ib Exploratory Trial in Advanced Triple Negative Breast Cancer	
Subjects with Complete or Partial Overall Response (irRC)	6 / 9 (67%)
Subjects with Complete Response (irRC)	2 / 9 (22%)
Subjects with Disease Control (irRC)	8 / 9 (89%)
Median Duration of Response (irRC)	12.7 months
Median Progression-Free survival (irRC)	13.7 months
Median Overall Survival	19.2 months

- **Median progression free survival was 13.7 months** with **median overall survival of 19.2 months to date**



Unpublished

Triple Negative Breast Cancer

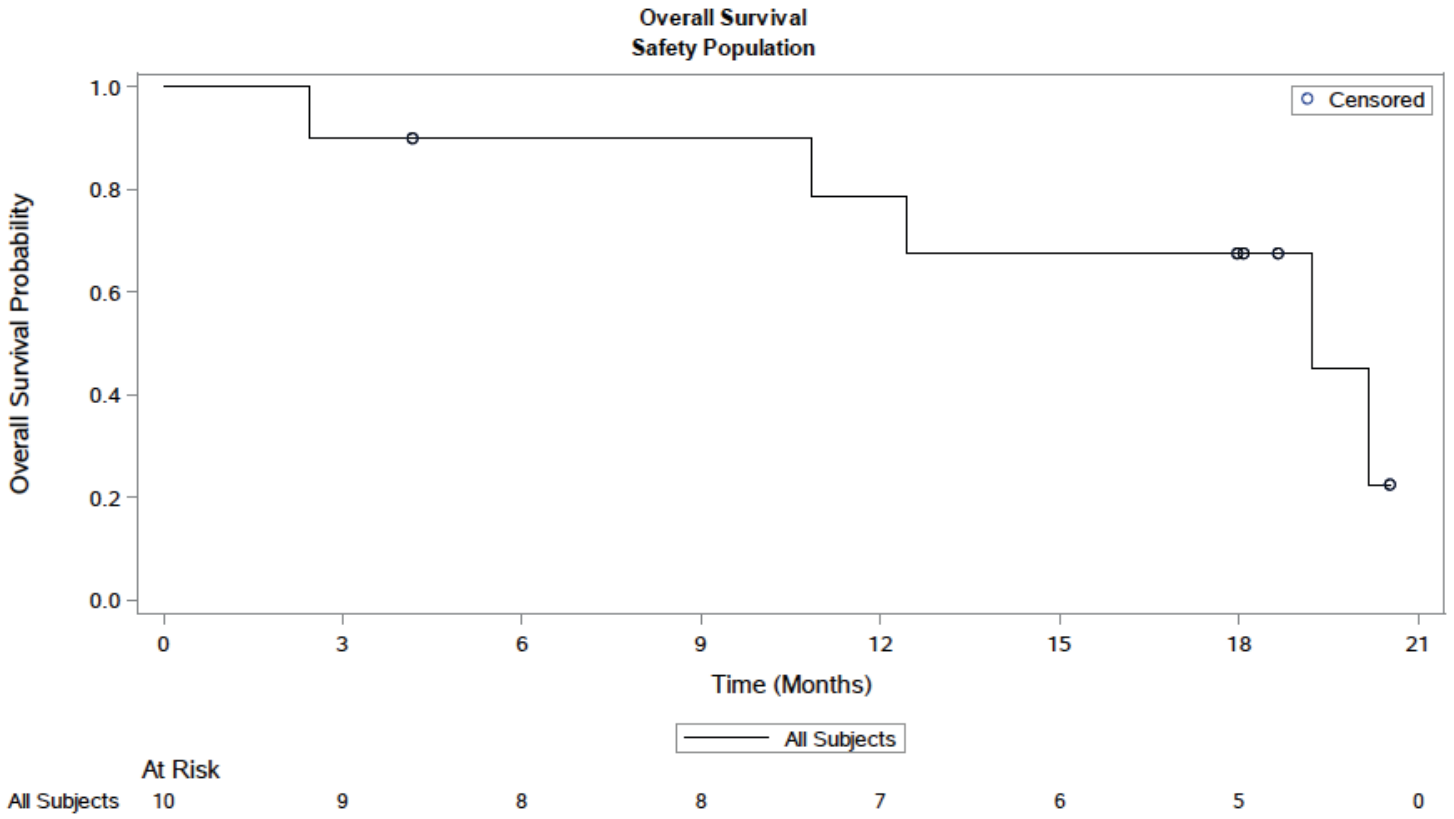
Progression Free Survival using irRC

Variable	All Subjects (N=9)
Number of Subjects with Disease Progression or Death	5 (56%)
Median Progression-Free Survival (months)	13.7
95% CI for the Median PFS	2.2, -

Competitive Analysis in TNBC 2nd Line or Greater

Trodelvy (Immunomedics/Gilead)

- **OS with a median of 12.1 months** (95% confidence interval (CI), 10.7-14.0) versus 6.7 months (95% CI, 5.8-7.7) for chemotherapy
- **4% complete responses**

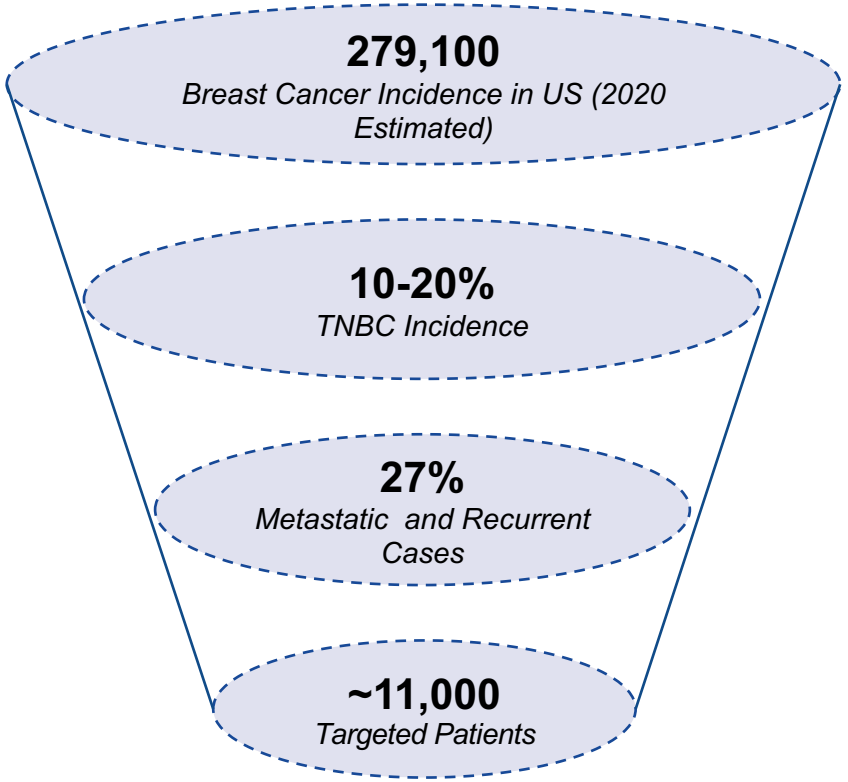


2nd Line or Greater: Triple Negative Breast Cancer
Overall Survival

Variable	All Subjects (N=10)
Number of Deaths	5 (50%)
Median Survival (months)	19.2
95% CI for the Median Survival	2.4, -

Phase II / III Randomized Clinical Trial in 2nd Line or Greater TNBC with PD-L1 t-haNK

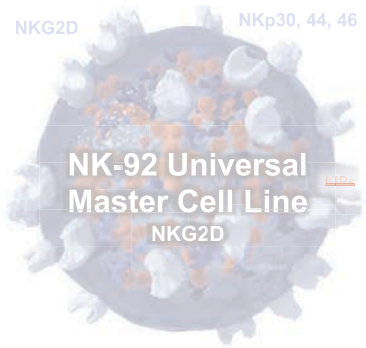
- **Median progression free survival of 13.7 months** with **median overall survival of 19.2 months to date compares favorably to Sacituzumab (Trodelvy)**
- Based on promising results of durable complete responses in the exploratory Phase I clinical trials on metastatic triple negative breast, **a third line metastatic triple negative breast cancer trial is currently being designed as a randomized trial using PD-L1 t-haNK in combination therapy in patients with 2nd line or greater TNBC.**



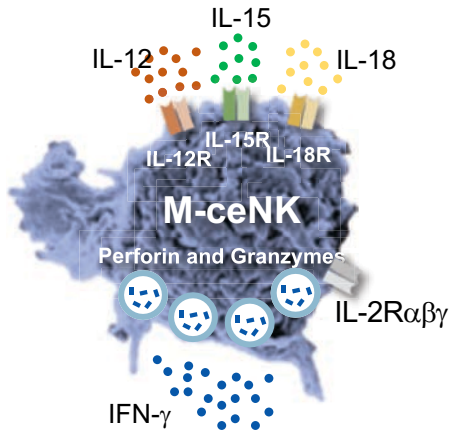
NantKwest Natural Killer Cell Clinical Stage Platform

Comprehensive Leader in Natural Killer Cells

aNK (NK-92)
Universal Off-the-Shelf
Natural Killer (NK) Cell Line



M-ceNK
Memory Cytokine Enriched
Natural Killer



CD16 haNK	PD-L1 t-haNK	HER2 t-haNK	CD19 t-haNK	M-ceNK
Merkel Cell Ca Phase II	Metastatic Pancreatic Ca Phase II TNBC	Breast Glioblastoma Phase I	DBLCL IND Authorized, FIH	AML, Multiple Myeloma IND Q4 2020
	Solid Tumors			Hematologic Tumors

The Untapped Potential of Memory-Like Natural Killer Cells

PNAS

Cytokine-induced memory-like natural killer cells

Megan A. Cooper[a,b], Julie M. Elliott[a], Peter A. Keyel[a], Liping Yang[a], Javier A. Carrero[c], and Wayne M. Yokoyama[a,1]

[a]Rheumatology Division, Department of Medicine, and Howard Hughes Medical Institute and Departments of [b]Pediatrics and [c]Pathology and Immunology, Washington University School of Medicine, St. Louis, MO 63110

Contributed by Wayne M. Yokoyama, December 23, 2008 (sent for review December 11, 2008)

The mammalian immune response to infection is mediated by 2 broad arms, the innate and adaptive immune systems. Innate immune cells are a first-line defense against pathogens and are thought to respond consistently to infection, regardless of previous exposure, i.e., they do not exhibit memory of prior activation. By contrast, adaptive immune cells display immunologic memory that has 2 basic characteristics, antigen specificity and an amplified response upon subsequent exposure. Whereas adaptive immune cells have rearranged receptor genes to recognize the universe of antigens, natural killer (NK) cells are innate immune lymphocytes

properties, because they were shown to mediate a hapten-specific contact hypersensitivity-like reaction in mice lacking T and B lymphocytes (14). The mechanism of NK cell activation is unclear in this model and whether the observed memory-like property is intrinsic to the NK cell is unknown. When considering the possibility of a memory-phenotype among innate immune cells, such as NK cells, it is important to note that current concepts of memory are built upon studies of adaptive immune lymphocytes, which
antigens. However, does this

NIH Public Access

Author Manuscript

Immunol Rev. Author manuscript; available in PMC 2011 May 1.

Published in final edited form as:
Immunol Rev. 2010 May ; 235(1): 297–305. doi:10.1111/j.0105-2896.2010.00891.x.

Memory-like Responses of Natural Killer Cells

Megan A. Cooper[1] and **Wayne M. Yokoyama**[2]

[1]Division of Rheumatology, Department of Pediatrics, Washington University School of Medicine, St. Louis, MO, USA.

[2]Division of Rheumatology, Department of Internal Medicine and Howard Hughes Medical Institute, Washington University School of Medicine, St. Louis, MO, USA.

HHS Public Access

Author manuscript

Sci Transl Med. Author manuscript; available in PMC 2017 May 18.

Published in final edited form as:
Sci Transl Med. 2016 September 21; 8(357): 357ra123. doi:10.1126/scitranslmed.aaf2341.

Cytokine-induced memory-like natural killer cells exhibit enhanced responses against myeloid leukemia

Rizwan Romee[1,*], **Maximillian Rosario**[1,2,*], **Melissa M. Berrien-Elliott**[1,*], **Julia A. Wagner**[1], **Brea A. Jewell**[1], **Timothy Schappe**[1], **Jeffrey W. Leong**[1], **Sara Abdel-Latif**[1], **Stephanie E. Schneider**[1], **Sarah Willey**[1], **Carly C. Neal**[1], **Liyang Yu**[3], **Stephen T. Oh**[3], **Yi-Shan Lee**[2], **Arend Mulder**[4], **Frans Claas**[4], **Megan A. Cooper**[5], and **Todd A. Fehniger**[1,†]

Journal of Innate Immunity

Review

J Innate Immun 2015;7:563–571
DOI: 10.1159/000382019

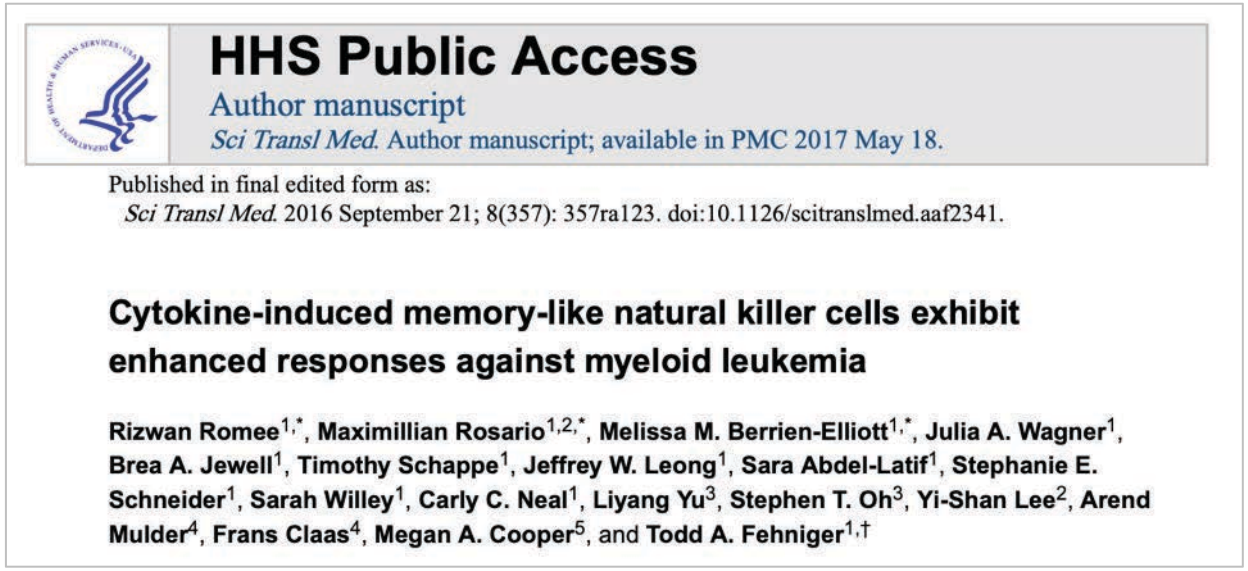
Received: January 17, 2015
Accepted after revision: April 1, 2015
Published online: April 30, 2015

Human Cytokine-Induced Memory-Like Natural Killer Cells

Melissa M. Berrien-Elliott Julia A. Wagner Todd A. Fehniger

Department of Medicine, Division of Oncology, Washington University School of Medicine, St. Louis, Mo., USA

Rationale for Cytokine Enriched Natural Killer Cell (ceNK): Cytokine-Induced Memory-like Natural Killer Cells Exhibit Enhanced Responses Against Myeloid Leukemia in Pre-Clinical Models



Published in final edited form as:
Sci Transl Med. 2016 September 21; 8(357): 357ra123. doi:10.1126/scitranslmed.aaf2341.

Cytokine-induced memory-like natural killer cells exhibit enhanced responses against myeloid leukemia

Rizwan Romee[1,*], Maximillian Rosario[1,2,*], Melissa M. Berrien-Elliott[1,*], Julia A. Wagner[1], Brea A. Jewell[1], Timothy Schappe[1], Jeffrey W. Leong[1], Sara Abdel-Latif[1], Stephanie E. Schneider[1], Sarah Willey[1], Carly C. Neal[1], Liyang Yu[3], Stephen T. Oh[3], Yi-Shan Lee[2], Arend Mulder[4], Frans Claas[4], Megan A. Cooper[5], and Todd A. Fehniger[1,†]

Abstract: Natural killer (NK) cells are an emerging cellular immunotherapy for patients with acute myeloid leukemia (AML); however, the best approach to maximize NK cell antileukemia potential is unclear. Cytokine-induced memory-like NK cells differentiate after a brief pre-activation with interleukin-12 (IL-12), IL-15, and IL-18 and exhibit enhanced responses to cytokine or activating receptor re-stimulation for weeks to months after pre-activation. We hypothesized that memory-like NK cells exhibit enhanced antileukemia functionality. We demonstrated that human memory-like NK cells have enhanced interferon-γ production and cytotoxicity against leukemia cell lines or primary human AML blasts in vitro. Using mass cytometry, we found that memory-like NK cell functional responses were triggered against primary AML blasts, regardless of killer cell immunoglobulin-like receptor (KIR) to KIR-ligand interactions. In addition, multidimensional analyses identified distinct phenotypes of control and memory-like NK cells from the same individuals. Human memory-like NK cells xenografted into mice substantially reduced AML burden in vivo and improved overall survival. In the context of a first-in-human phase 1 clinical

Ovarian Cancer

Published in final edited form as:
Gynecol Oncol. 2019 April ; 153(1): 149–157. doi:10.1016/j.ygyno.2019.01.006.

Cytokine-induced memory-like natural killer cells have enhanced function, proliferation, and *in vivo* expansion against ovarian cancer cells

Locke D. Uppendahl[a,+], **Martin Felices**[b,+], **Laura Bendzick**[a], **Caitlin Ryan**[a], **Behiye Kodal**[b], **Peter Hinderlie**[b], **Kristin L.M. Boylan**[c], **Amy P.N. Skubitz**[c], **Jeffrey S. Miller**[b,^], and **Melissa A. Geller**[a,^,*]

[a]Department of Obstetrics, Gynecology and Women's Health, Division of Gynecologic Oncology, University of Minnesota, Minneapolis, MN, United States

[b]Department of Medicine, Division of Hematology, Oncology, and Transplantation, University of Minnesota, Minneapolis, MN, United States

[c]Department of Laboratory Medicine and Pathology, University of Minnesota, Minneapolis, MN, United States

Abstract

Objective: Natural killer (NK) cells are lymphocytes well suited for adoptive immunotherapy. Attempts with adoptive NK cell immunotherapy against ovarian cancer have proven unsuccessful, with the main limitations including failure to expand and diminished effector function. We investigated if incubation of NK cells with interleukin (IL)-12, IL-15, and IL-18 for 16 hours could produce cytokine-induced memory-like (CIML) NK cells capable of enhanced function against ovarian cancer.

Methods: NK cells were preactivated briefly with IL-12, IL-15, and IL-18, rested, then placed against ovarian cancer targets to assess phenotype and function via flow cytometry. Real-time NK-cell-mediated tumor-killing was evaluated. Using ascites cells and cell-free ascites fluid, NK cell proliferation and function within the immunosuppressive microenvironment was evaluated *in vitro*. Finally, CIML NK cells were injected intraperitoneal (IP) into an *in vivo* xenogeneic mouse model of ovarian cancer.

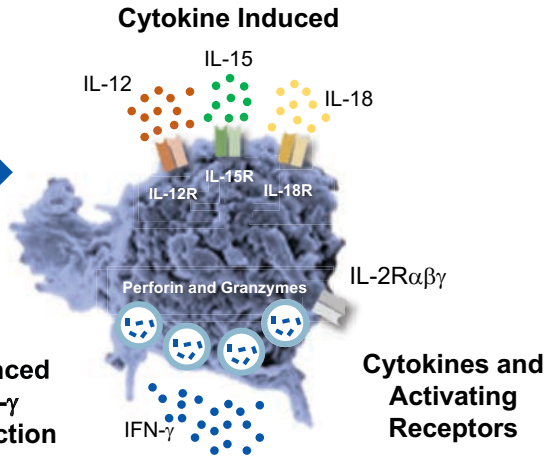
Results: CIML NK cells demonstrate enhanced cytokine (IFN-γ) production and NK-cell-mediated killing of ovarian cancer. NK cells treated overnight with cytokines led to robust

*Corresponding author: Melissa Geller, MD, Division of Gynecologic Oncology, MMC 395, 420 Delaware St. S.E., Minneapolis, MN 55455, gelle005@umn.edu, *Telephone:* 612-626-3111, *Fax Number:* 612-626-0665.
+Authors contributed equally to this work
^Authors contributed equally to this work

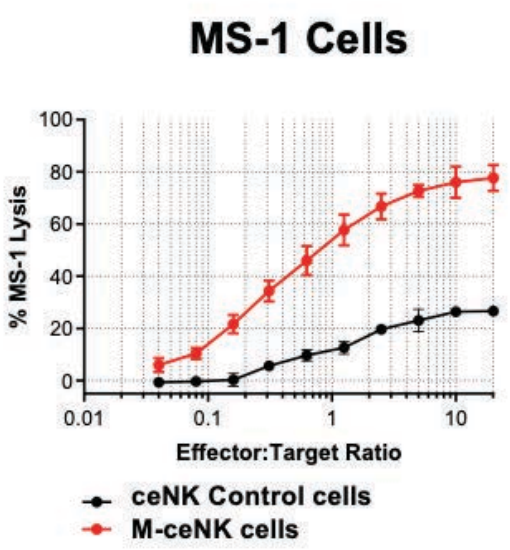
Author contribution: LDU, MF, and MAG were involved with study conception and design. LDU, BK, LB, CR, PH, KLB, and APS were involved with the acquisition of data. LDU, MF, LB, and PH analyzed and interpreted the data. LDU, MF, MAG, and JM drafted the manuscript and critically revised it.

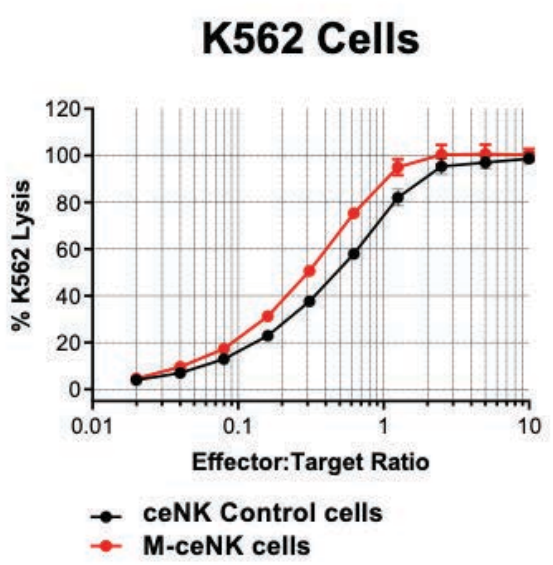
Conflict of interest statement: The authors have no conflicts of interest to report.

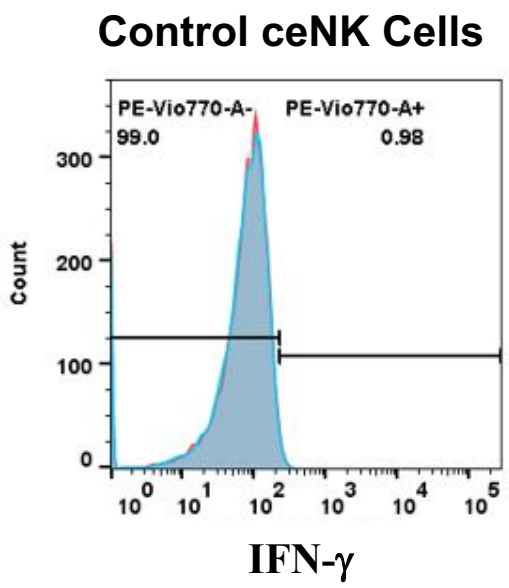
Significant Cytotoxicity of M-ceNK Cells From Allogeneic or Autologous Apheresis Source

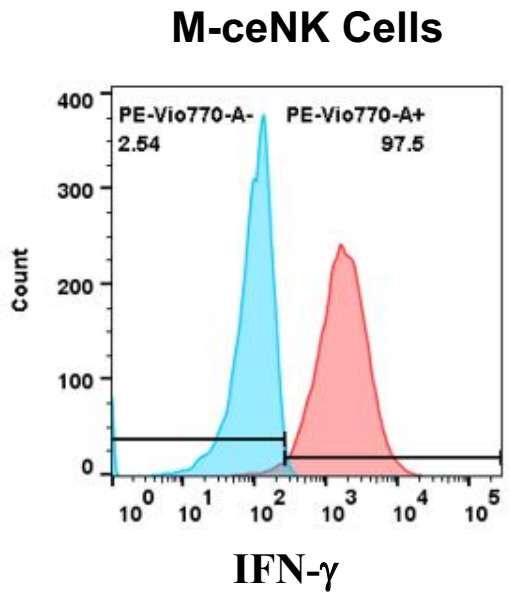


Barrier Addressed	Property
Persistence	Proliferate, Long lived
Enhanced Function	Enhanced Cytokine / Chemokine, Enhanced Killing
Recognition	Non-functional Inhibitory KIR, Fully Activated NK Cell

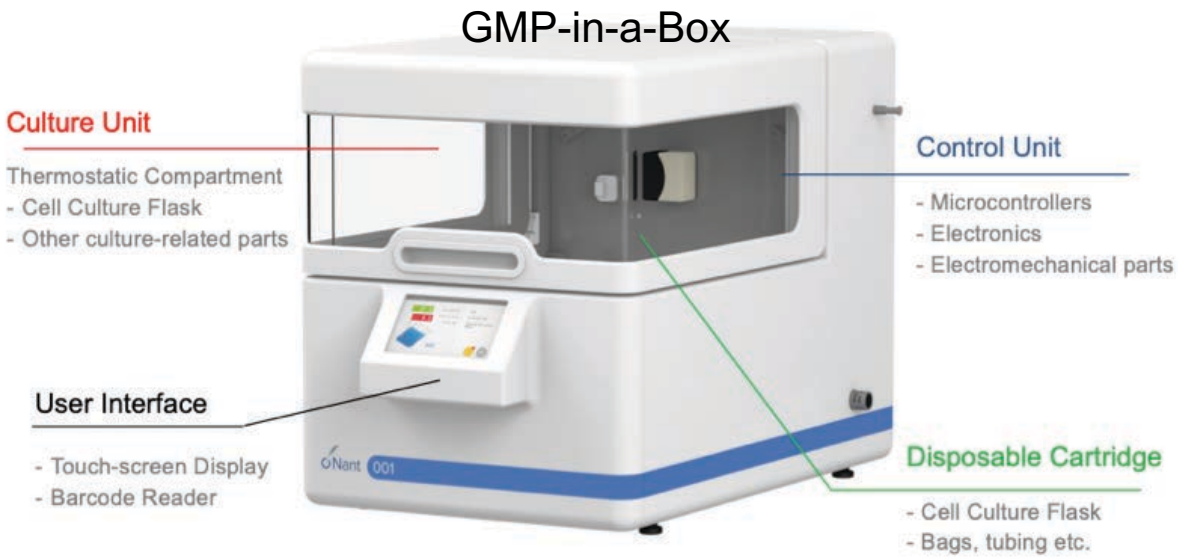




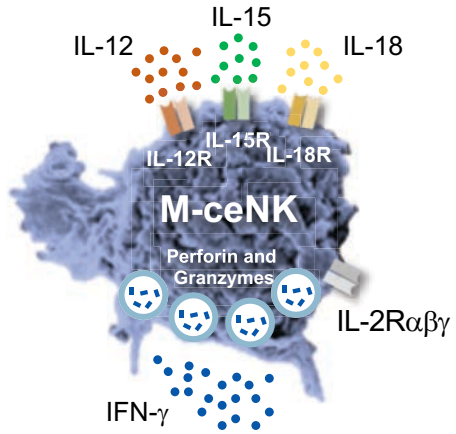




NantKwest Proprietary – IND Ready
Memory Cytokine Enhanced Natural Killer cells (M-ceNK)



M-ceNK
Memory Cytokine Enriched Natural Killer



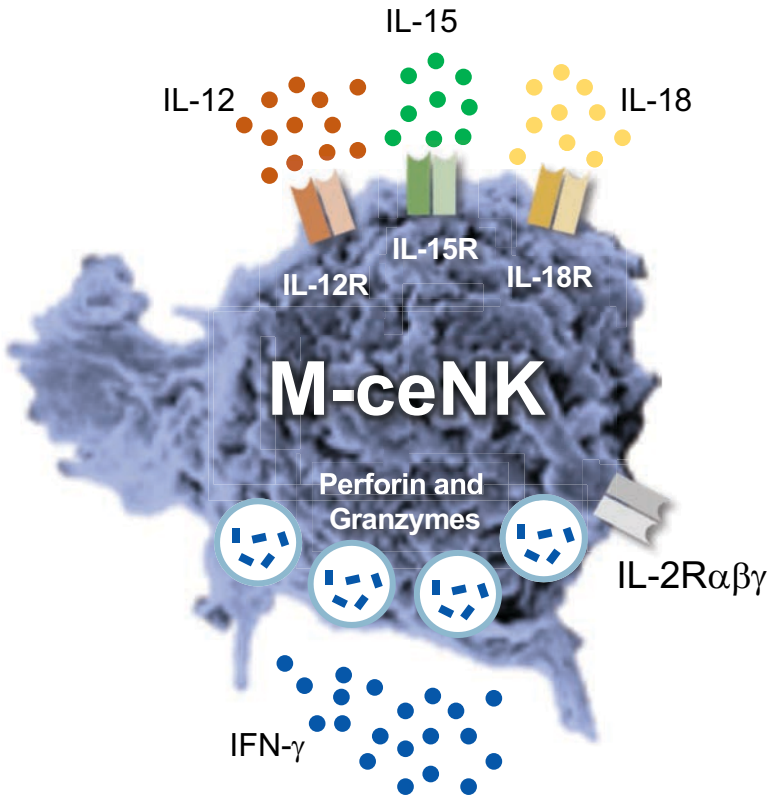
A Single Apheresis Collection Provides 8-10 Doses of $1x10^9$ M-ceNK

	M-ceNK
Autologous & Allogenic Cytokine Enriched Stem Cells	Peripheral Blood / Cord Blood
Cytokine Enriched Closed System GMP in a Box	✓
CAR Insertion Potential	✓
Current Status	IND Ready
Clinical Indication	• Ovarian, • Multiple Myeloma • AML

NantKwest Proprietary – IND Ready
Memory Cytokine Enhanced Natural Killer cells (M-ceNK)

Stem Cell Memory NK

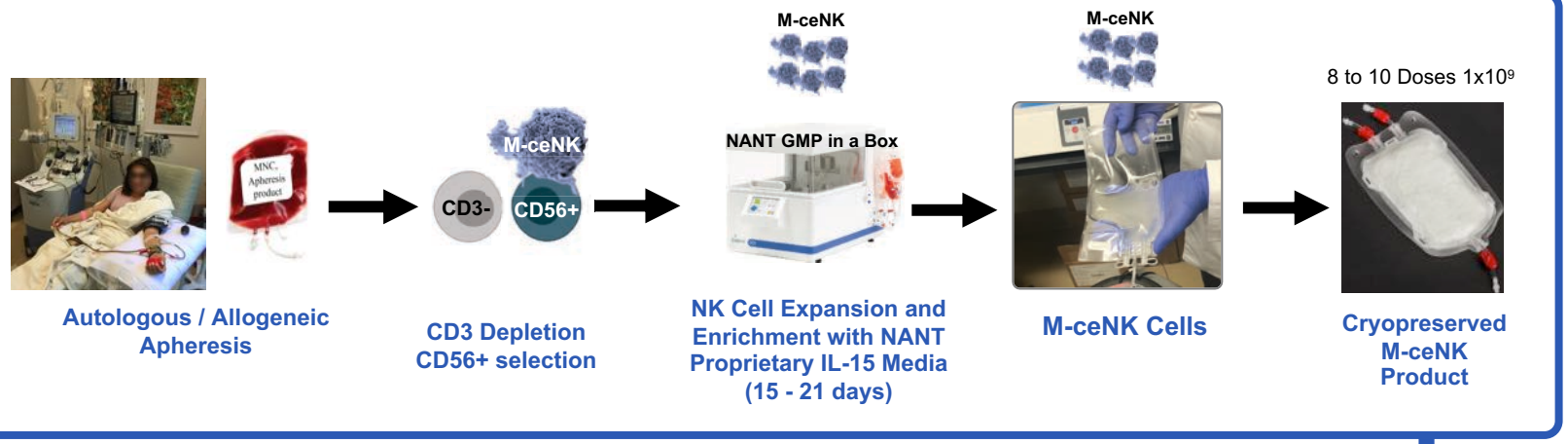
Cytokine Induced



Cytokines and Activating Receptors

Enhanced IFN-γ Production

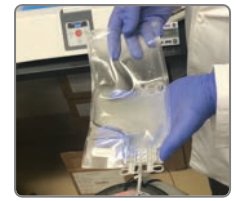
A Single Apheresis Collection Provides 8-10 Doses of $1x10^9$ M-ceNK



IND Ready

Indication	Clinical Status
Ovarian Cancer	IND Filing Q4 2020
Multiple Myeloma	IND Filing Q1 2021
AML	IND Filing Q2 2021

M-ceNK



NantKwest Natural Killer Cell Clinical Stage Platform

Investment Highlights:

- Most mature natural killer cell platform
- First in human and first in class clinical experience
- Established GMP manufacturing at commercial scale
- Broadest natural killer cell therapy platform from both universal cell line and allogeneic / autologous source
- Advanced clinical trials across multiple indications
- Addressing large unmet needs in solid and liquid tumors with promising safety and efficacy data to date