



NASDAQ: IBRX

# Overview Presentation

October 2022



# Forward-Looking Statements

This presentation and the accompanying verbal remarks contain forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Statements that are not statements of historical fact are considered forward-looking statements, which are usually identified by the use of words such as “anticipates,” “believes,” “continues,” “goal,” “could,” “estimates,” “expects,” “intends,” “may,” “plans,” “potential,” “predicts,” “indicate,” “projects,” “seeks,” “should,” “will,” and variations of such words or similar expressions. Statements of past performance, efforts, or results of our preclinical and clinical trials, about which inferences or assumptions may be made, can also be forward-looking statements and are not indicative of future performance or results. Forward-looking statements are neither forecasts, promises nor guarantees, and are based on the current beliefs of ImmunityBio’s management as well as assumptions made by and information currently available to ImmunityBio. Such information may be limited or incomplete, and ImmunityBio’s statements should not be read to indicate that it has conducted a thorough inquiry into, or review of, all potentially available relevant information. Such statements reflect the current views of ImmunityBio with respect to future events and are subject to known and unknown risks, including business, regulatory, economic and competitive risks, uncertainties, contingencies and assumptions about ImmunityBio, including, without limitation, (i) whether the FDA will file and/or approve ImmunityBio’s recently submitted BLA and the risks and uncertainties associated with the regulatory approval process, (ii) the ability of ImmunityBio to continue its planned preclinical and clinical development of its development programs, and the timing and success of any such continued preclinical and clinical development and planned regulatory submissions, (iii) ImmunityBio’s ability to retain and hire key personnel, (iv) ImmunityBio’s ability to obtain additional financing to fund its operations and complete the development and commercialization of its various product candidates, (v) ImmunityBio’s ability to successfully commercialize its product candidates and uncertainties around regulatory reviews and approvals, (vi) ImmunityBio’s ability to scale its manufacturing and commercial supply operations for its product candidates and future approved products, (vii) ImmunityBio’s ability to obtain, maintain, protect and enforce patent protection and other proprietary rights for its product candidates and technologies, and (viii) the unknown future impact of the COVID-19 pandemic on certain clinical trials or their milestones and/or ImmunityBio’s business operations or operating expenses. More details about these and other risks that may impact ImmunityBio’s business are described under the heading “Risk Factors” in the Company’s Form 10-K filed with the U.S. Securities and Exchange Commission (“SEC”) on March 1, 2022 and the Company’s Form 10-Q filed with the SEC on May 10, 2022, and in subsequent filings made by ImmunityBio with the SEC, which are available on the SEC’s website at [www.sec.gov](http://www.sec.gov). ImmunityBio cautions you not to place undue reliance on any forward-looking statements, which speak only as of the date hereof. ImmunityBio does not undertake any duty to update any forward-looking statement or other information.

**MISSION:**  
**Innate and Adaptive Immune Memory**

**Goal: Durable Complete Remission & Prevention of Cancer and Infectious Diseases**  
**Induce Memory NK, T & B Cells**

**PLATFORMS:**  
**NK, T and B Cells Activators**

DAMP Inducers	DNA Vaccine	RNA Vaccine	Recombinant & Cytokines	Toll Receptor Activators	NK Cell Therapy
<ul style="list-style-type: none"> <li>Albumin Bound Chemo Modulators</li> <li>Tumor Associated Antigen Regulators</li> </ul>	<ul style="list-style-type: none"> <li>hAd5 Adenovirus</li> </ul>	<ul style="list-style-type: none"> <li>Self Amplifying RNA (saRNA)</li> </ul>	<ul style="list-style-type: none"> <li>NK &amp; T Cell Activators</li> <li>Subunit Protein Antigens</li> </ul>	<ul style="list-style-type: none"> <li>TLR 4, 7, 8, 9</li> </ul>	<ul style="list-style-type: none"> <li>NK-92</li> <li>Memory Cytokine NK</li> <li>MSC</li> </ul>

**PRODUCT CANDIDATES:**  
**Clinical Development From Each Platform**

DAMP Inducers	DNA Vaccine	RNA Vaccine	Recombinant & Cytokine	Toll Receptor Activators	NK Cell Therapy
<ul style="list-style-type: none"> <li>Aldoxorubicin</li> <li>Nanatinostat</li> </ul>	<ul style="list-style-type: none"> <li>hAd5 MUC1 / Brachyury / CEA</li> <li>hAd5 PSA</li> <li>hAd5 E6 / E7 (HPV)</li> <li>hAd5 Spike + Nucleocapsid</li> </ul>	<ul style="list-style-type: none"> <li>saRNA S</li> <li>saRNA S+N</li> </ul>	<ul style="list-style-type: none"> <li>N-803 (Anktiva), IL-15 Fusion Protein</li> <li>Yeast Produced Recombinant RBD</li> </ul>	<ul style="list-style-type: none"> <li>3M-052</li> <li>GLA</li> <li>SLA</li> <li>Squalene</li> </ul>	<ul style="list-style-type: none"> <li>haNK</li> <li>PD-L1 t-haNK</li> <li>CD19 t-haNK</li> <li>HER2 t-haNK</li> <li>m-ceNK</li> </ul>

**CLINICAL INDICATIONS:**  
**Selected Clinical Trials Under Development Per Product**

Bladder Cancer (NMIBC)	<b>N-803 + BCG</b>	BLA Accepted on July 28. PDUFA Date May 23, 2023
Pancreatic Cancer	<b>N-803 + PD-L1 t-haNK + Aldoxorubicin</b>	
Lung Cancer	<b>N-803</b>	
Glioblastoma	<b>N-803 + PD-L1 t-haNK + Aldoxorubicin</b>	
COVID-19 Vaccine	<b>hAd5 S+N, saRNA S, saRNA S+N</b>	
HIV Therapy	<b>N-803</b>	

Solid Tumors	Phase	Target Indication	Preclinical	Phase I	Phase II	Phase III	
Bladder	2	BCG Unresponsive NMIBC CIS (Cohort A) QUILT 3.032	PDUFA Date May 23, 2023			Single Arm, NMIBC - <i>Breakthrough &amp; Fast Track</i>	NCT03022825
	2	BCG Unresponsive NMIBC Papillary (Cohort B) QUILT 3.032				Single Arm, NMIBC - <i>Fast Track</i>	NCT03022825
	3	BCG Naïve – QUILT 2.005				Randomized, Phase 3, NMIBC	NCT02138734
Lung	3	2L Non-Small Cell Lung Cancer (NSCLC) Checkpoint Relapsed and Refractory, LungMAP – S1800D (SWOG)				Randomized Phase 3, 2L Lung	NCT05096663
	3	1L Squamous & Non-Squamous Non-Small Cell Lung Cancer Checkpoint Alone QUILT-2.023				Randomized Phase 3, 1L Lung Chemo / Chemo Free	NCT03520686
	2	2L / 3L Non Small Cell Lung Cancer (NSCLC) Basket Trial Checkpoint Relapsed and Refractory QUILT-3.055				Multi-Arm, Phase 2, 2L & 3L	NCT03228667
Pancreatic	2	3L Metastatic Pancreatic Cancer QUILT-88 (Cohort C)				Single Arm, Phase 2 Pancreas	NCT04390399
	2	2L Metastatic Pancreatic Cancer QUILT-88 (Cohort B)				Randomized, Phase 2, 2L Pancreas	NCT04390399
	2 / 3	1L Metastatic Pancreatic Cancer QUILT-88 (Cohort A)				Randomized, Phase 2 / 3, 1L Pancreas	NCT04390399
Glioblastoma	1 / 2	Recurrent Glioblastoma				Randomized, Planned Phase 1/2, Glioblastoma	Pending
HPV	1	Human Papilloma Virus (HPV) – Anal, Cervical, Head & Neck				Single Arm, Planned Phase 1/2	Pending
Solid Tumors	1	Advanced Solid Tumors, M-ceNK – QUILT-3.076				Single Arm, Phase 1	NCT04898543

NMIBC – Non-Muscle Invasive Bladder Cancer, NCI – National Cancer Institute, QUILT – QUantitative Integrated Lifelong Trial, SWOG - Southwest Oncology Group, M-ceNK – Memory-Like Cytokine Enhanced Natural Killer

Infectious	Phase	Target Indication	Preclinical	Phase I	Phase II	Phase III	
HIV	1	ACTG / NIAID: HIV Broadly Neutralizing Antibodies		Single Arm, Phase 1, HIV			NCT04340596
	2	Thai Red Cross & Walter Reed Army Institute of Research Reducing HIV Persistence by IL-15		Randomized, Phase 2, HIV			NCT04505501
	1	National Institute of Allergy and Infectious Diseases (NIAID) / University of Minnesota Effect of N-803 on B Cell Follicles in Antiretroviral Treated HIV Disease		Single Arm, Phase 1, HIV			NCT04808908
COVID-19	1	<b>Homologous:</b> hAd5 S + N Platform, Prime & Boost in USA COVID-4.001 Cohort 1 & 2 (Subcutaneous: SC)		Single Arm, Phase 1			NCT04591717
	1	<b>Homologous:</b> hAd5 S + N Platform, Prime & Boost in USA COVID-4.005 Cohort 1 & 2 (SC + Oral)		Single Arm, Phase 1			NCT04732468
	1	<b>Homologous:</b> 'The ProVIVA-SA1' Trial in South Africa COVID-4.007 hAd5 S + N Platform, Prime & Boost (Cohort 1, 2, 3 & 6)		Single Arm, Phase 1			NCT04710303
	1 / 2 / 3	<b>Heterologous Mix &amp; Match:</b> 'SISONKE Universal Boost T Cell Trial' in South Africa COVID-4.010 South Africa Ad26 (Prime) + hAd5 S+N (Boost)		Multi-Arm Randomized Study, Phase 1, 2, 3			
	1 / 2	<b>Boost:</b> Self Amplifying RNA (saRNA) Nanostructured Lipid Carrier (NLC) COVID-4.015 THEMBA 2 South Africa, saRNA Alone (Enrolling) COVID-4.016 THEMBA 3 United States (Hoag), saRNA Alone (Pending)		Single Arm, Phase 1			
	1 / 2 / 3	<b>Boost:</b> PULA Trial in Botswana (Pending) COVID-4.014 RBD Subunit Protein + 3M-052-Alum		Single Arm, Phase 1			

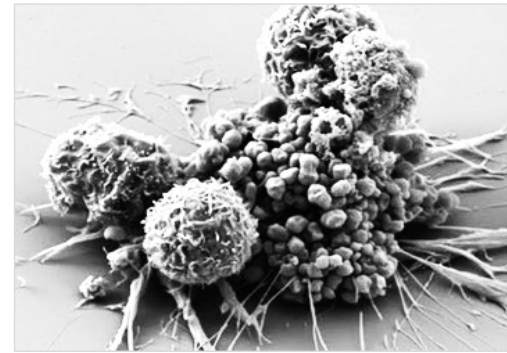
**hAd5** – Human Adenovirus 5, **saRNA** – Self Amplifying RNA, **SC** – Subcutaneous, **RBD** – Receptor Binding Domain

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**> 5 Trillion**

Over 5 Trillion Natural Killer (NK) Cells Manufactured to Date



**6**

Immune Enhancing Platforms

<p><b>DAMP Inducers</b></p> <ul style="list-style-type: none"> <li>• Aldoxorubicin</li> </ul>	<p><b>DNA Vaccine</b></p> <ul style="list-style-type: none"> <li>• hAd5 Adenovirus</li> </ul>	<p><b>RNA Vaccine</b></p> <ul style="list-style-type: none"> <li>• Self-Amplifying RNA (saRNA)</li> </ul>	<p><b>Recombinant &amp; Cytokines</b></p> <ul style="list-style-type: none"> <li>• NK &amp; T Cell Activators</li> <li>• Subunit Protein Antigens</li> </ul>	<p><b>Toll Receptor Activators</b></p> <ul style="list-style-type: none"> <li>• TLR 4, 7, 8, 9</li> </ul>	<p><b>NK Cell Therapy</b></p> <ul style="list-style-type: none"> <li>• NK-92</li> <li>• Memory-Like Cytokine NK</li> </ul>
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**2038+**

Worldwide Patents Extending to 2035 and Beyond



**> 700,000**

Square Feet of Manufacturing R&D, Office and Corporate Facilities



**1,800+**

Patients Studied



# Orchestrating the Immune System

First-in-Class Comprehensive Platforms



## NK + T Cells

- IL-15 Fusion Proteins  
Anktiva



## Natural Killer Cells

- NK-92 Off-the-Shelf
- Autologous m-ceNK
- iNKT Cells



## Memory B & T Cells

- Adenovirus
- Subunit Proteins
- Toll Receptor Activators
- saRNA

## Late-Stage U.S. Clinical Trial Updates:

- Bladder Cancer
- Pancreatic Cancer
- Head & Neck Cancer
- Lung Cancer
- HIV
- COVID Vaccine

# Orchestrating the Immune System

First-in-Class Comprehensive Platforms



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## Late-Stage U.S. Clinical Trial Updates:



### Bladder Cancer

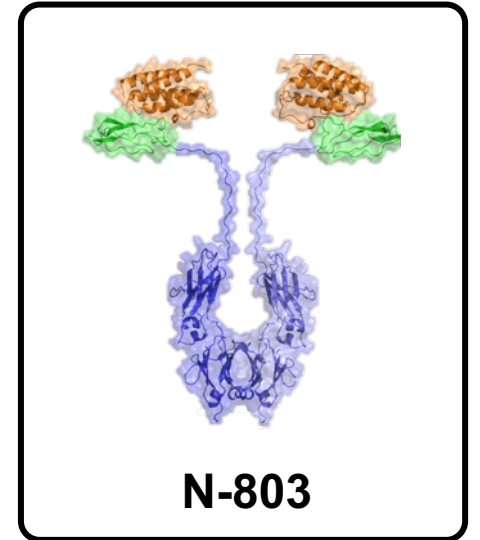
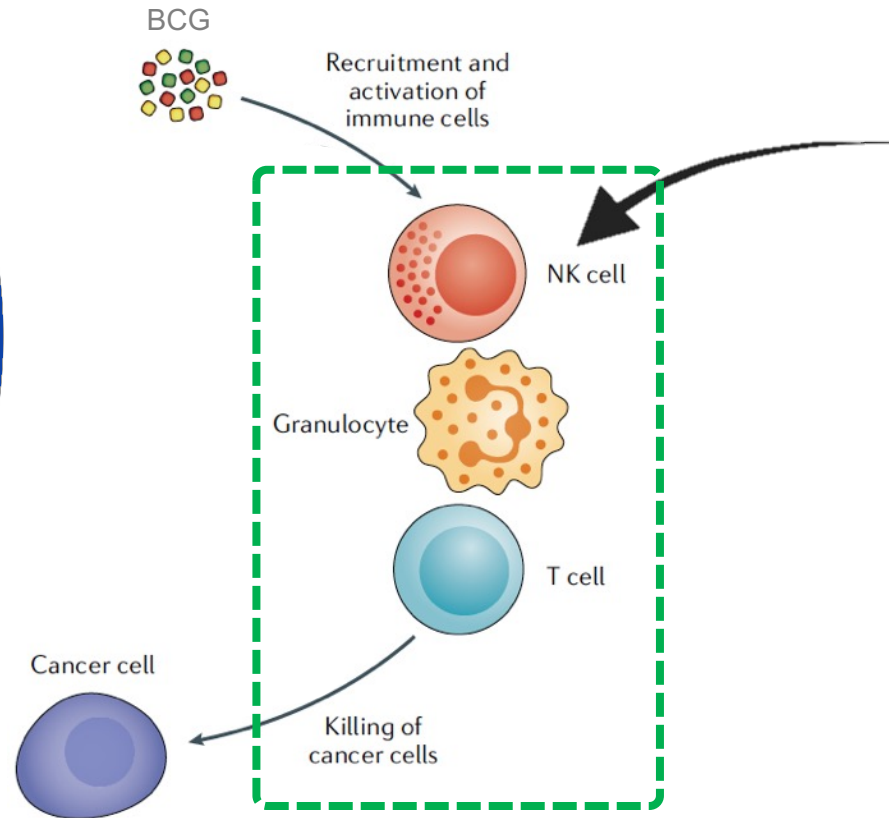
- Pancreatic Cancer
- Head & Neck Cancer
- Lung Cancer
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- COVID Vaccine



# N-803, an IL-15 Superagonist, Proliferates and Activates NK & T Cells, Providing the Secondary Stimulus (The Boost) to Trained Innate Immune Memory of BCG (The Prime)

*“Trained immunity or innate immune memory enables innate immune cells to mount a more robust response to secondary non-related stimuli [N-803, the boost] after being initially primed (or trained) by a challenge such as BCG.”*

Jelmer H. van Puffelen et al. Nature Reviews 2020

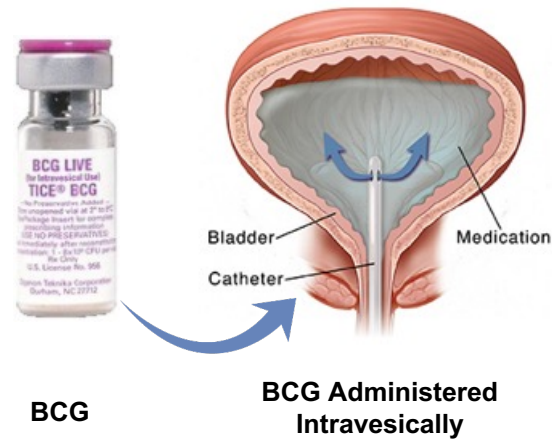


N-803 Proliferates NK & T Cells thereby boosting Immune Memory

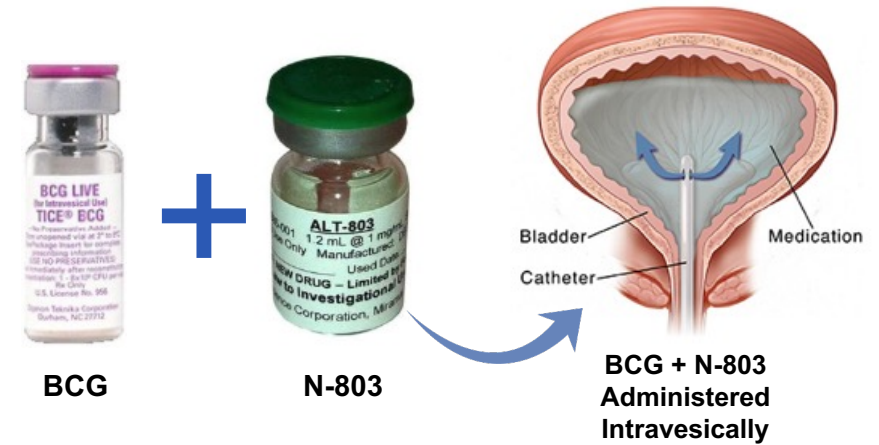
# QUILT-3.032: NMIBC Trial Rationale

N-803 Synergistic with BCG: Enhances Proliferation of NK and T Cells

**Prime: BCG Activates Natural Killer Cells**



**Boost: N-803 IL-15 Proliferates Natural Killer Cells & T Cells**



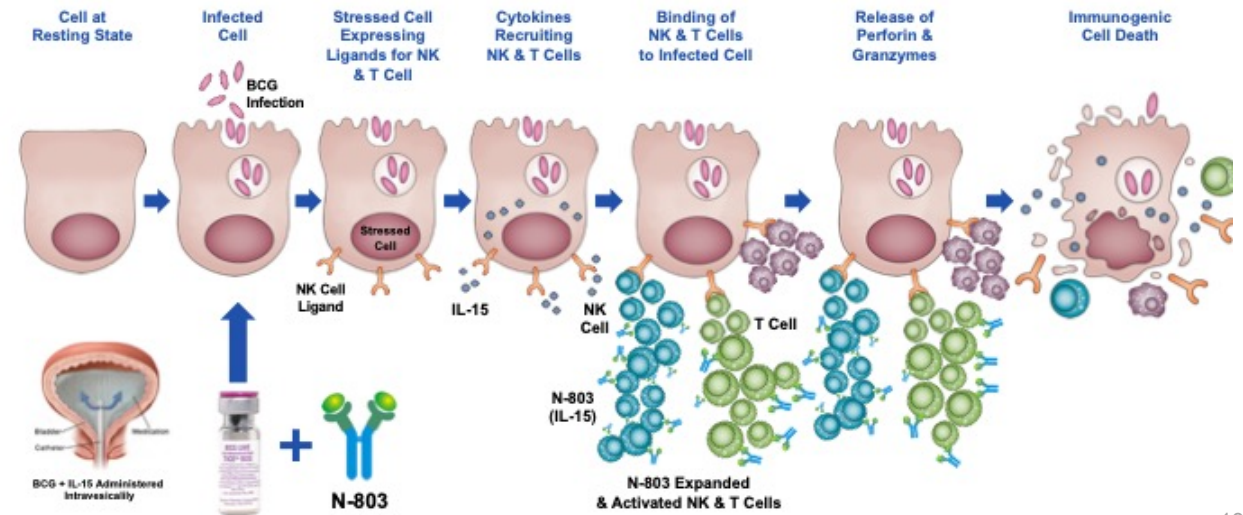
European Urology 2001

Eur Urol 2001;39:518-524 Accepted after revision: August 18, 2000

## Activation of Natural Killer Cells by Bacillus Calmette-Guérin

Sven Brandau<sup>a</sup>, Andreas Böhle<sup>a, b</sup>

<sup>a</sup>Division of Immunotherapy, Research Center Borstel, and <sup>b</sup>Department of Urology, Medical University of Lübeck, Germany



# Phase 1: NMIBC – Complete Response in 9 of 9 Subjects

## With Durable 24 Month Response When N-803 is Combined with BCG (Trained Innate Immune Memory)

**Phase I**  
NCT02138734  
QUILT 2.005

Phase I (N=9)  
**A Study of Intravesical BCG in Combination With N-803 in Patients With Non-Muscle Invasive Bladder Cancer**

### N-803 + BCG Inducing 24-Month Durable Response

Durable Complete Responses (CR) or No Recurrence (NR) in 9 out of 9 Patients

Dose (intravesicular instillation)	Patient	Stage	Response Assessments								
			W12	6M	9M	12M	15M	18M	21M	24M	
100 µg	1	Pap T1	CR*	CR	CR	CR	CR	CR	CR	CR	CR
	2	Pap Ta	CR*	CR	CR	CR	CR	CR	CR	CR	CR
	3	Pap T1	CR*	CR	CR	CR	CR	CR	CR	CR	CR
200 µg	4	Pap T1	IC	CR*	CR	CR	CR	CR	CR	CR	CR
	5	CIS	IC	IC	IC	CR	CR	CR	CR	CR	CR
	6	Pap T1	CR*	CR	CR	CR	CR	CR	CR	CR	CR
400 µg	7	Pap T1	CR*	CR	CR	CR	CR	CR	CR	CR	CR
	8	CIS	CR*	CR	CR	CR	CR	CR	CR	CR	CR**
	9	Pap Ta	CR*	CR	CR	CR	CR	CR	CR	CR	CR

### 9 of 9 (100%) Patients Disease-Free at 24 Months

BCG naïve alone (SoC): Historical response rate is 55-75% at 3-6 months post BCG alone

**Based on this data, FDA granted Fast Track Designation to the Pivotal Trial**

\*CR termed as No Recurrence (NR) in Papillary Disease \*\*Negative Cystoscopy Inconclusive Cytology

IC: Inconclusive Cystoscopy

ONCOIMMUNOLOGY  
2021, VOL. 10, NO. 1, e1912885 (7 pages)  
<https://doi.org/10.1080/2162402X.2021.1912885>

Taylor & Francis Group

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ORIGINAL RESEARCH OPEN ACCESS

### Safety, Tolerability, and Long-Term Clinical Outcomes of an IL-15 analogue (N-803) Admixed with Bacillus Calmette-Guérin (BCG) for the Treatment of Bladder Cancer

Charles J. Rosser<sup>a</sup>, Sergei Tikhonenkov<sup>a</sup>, Jeffrey W. Nix<sup>b</sup>, Owen T.M. Chan<sup>a</sup>, Irina Ianculescu<sup>c</sup>, Sandeep Reddy<sup>a,c</sup>, and Patrick Soon-Shiong<sup>d</sup>

<sup>a</sup>Clinical & Translational Research Program, University of Hawaii Cancer Center, Honolulu, Hawaii; <sup>b</sup>Department of Urology, University of Alabama, Birmingham, Alabama; <sup>c</sup>ImmunityBio, Inc., Culver City, California; <sup>d</sup>NantHealth Inc, Culver City, California

**ABSTRACT**  
Intravesical BCG is active against non-muscle invasive bladder cancer (NMIBC), but bladder cancer will recur and even progress in a significant number of patients. To improve the response rate, N-803, an IL-15 superagonist was administered in combination with BCG. To evaluate the safety and efficacy associated with the use of intravesical N-803 and BCG in patients with BCG-naïve NMIBC. This phase 1b clinical trial used a 3 + 3 dose-escalation design. Participants were enrolled from July 2014 and July 2015, with follow-up and analyses through January 15, 2021. Eligibility criteria included histologically confirmed non-muscle invasive urothelial carcinoma of intermediate or high risk who had not received prior treatment with intravesical BCG (ie, BCG-naïve). All 9 participants met the eligibility criteria, received treatment according to the protocol, and were included in all analyses. Treatment was done once weekly for 6 consecutive weeks with bladder infusion of the standard dose of BCG, 50 mg/instillation, in combination with increasing doses of N-803 (100, 200, or 400 µg N-803 per instillation). No DLTs were noted in any of the dose cohorts. All adverse events (AEs) were manageable and less than grade 3. During the 2-year follow-up, all 9 participants were disease free. Furthermore, 6 y after treatment, all 9 participants (100%) were disease free with no evidence of disease progression and an intact bladder. This phase 1b trial found the combination of intravesical N-803 and BCG to be associated with modest toxic effects, low immunogenicity, and substantial prolonged antitumoral activity; phase 2 trials are in progress.

**ARTICLE HISTORY**  
Received 3 March 2021  
Revised 31 March 2021  
Accepted 31 March 2021

**KEYWORDS**  
Non-muscle Invasive bladder cancer; IL15; BCG

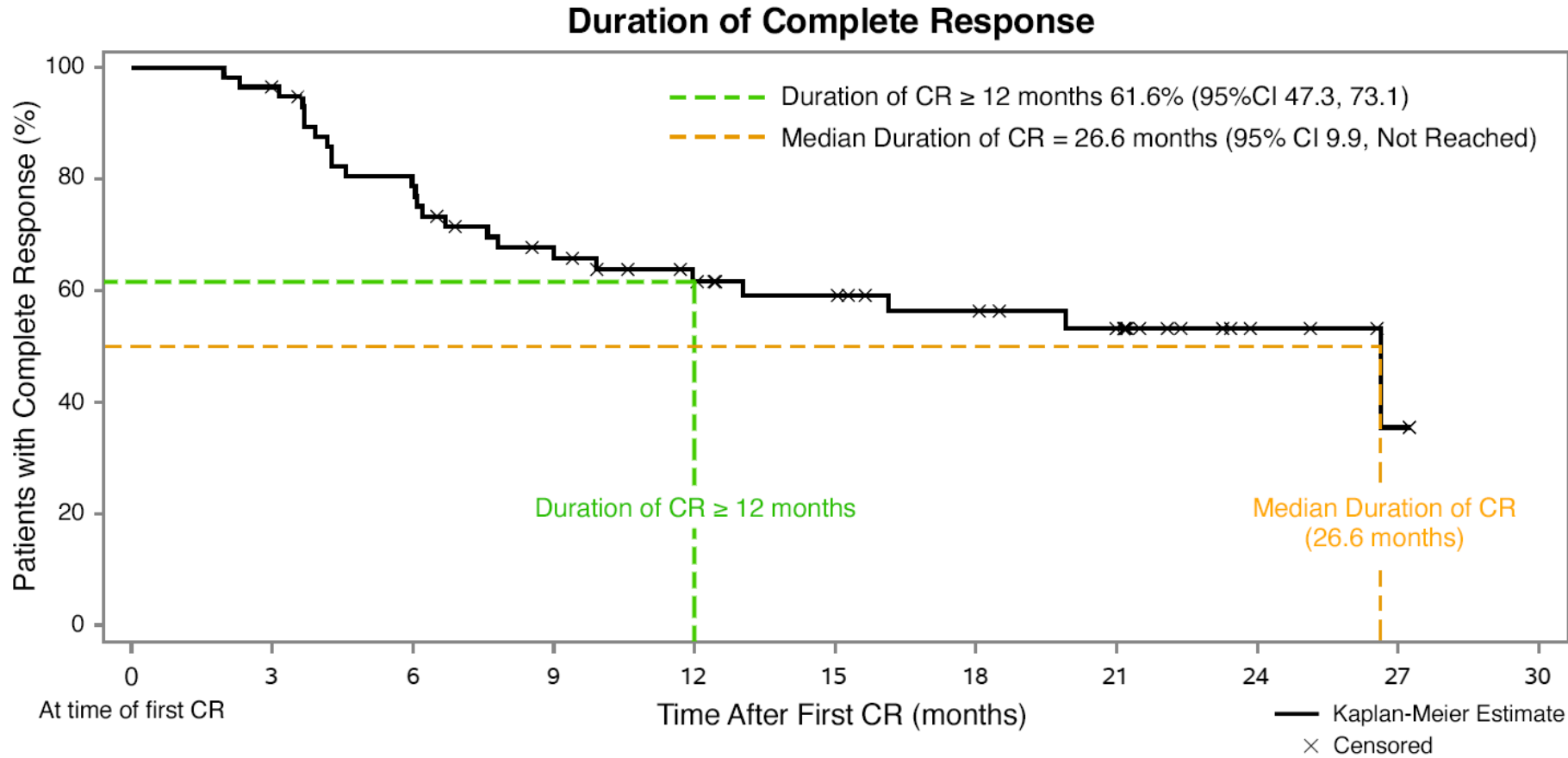
<https://doi.org/10.1080/2162402X.2021.1912885>

# Clinically Meaningful Efficacy Results in Responders Cohort A (CIS)

	<b>Responder Population (N = 58)</b>	<b>QUILT-3.032</b>
Complete Response	Complete Response (n)	58 / 82
	CR Rate (95% CI)	71% (59.6, 80.3)
Duration of Response	Median Duration of Response in Months (95% CI)	26.6 (9.9, NR)
	Duration of Response $\geq$ 24 Months per KM	53% (38.0, 66.2)
Progression Free Survival	Bladder Cancer Specific Progression Free Survival $\geq$ 24 Months per KM	96% (86.2, 99.1)
Cystectomy Avoidance	Cystectomy Avoidance Rate in Responders	91% (53 / 58)
	Cystectomy Rate in Responders	9% (5 / 58)
Safety Profile	Cystectomy Rate in All Patients	16% (13/82)
	Treatment Related SAEs	1%
	Immune Related SAEs	0%
	Treatment Related Grade 4 or 5 AEs	0%

# QUILT 3032

## 26.6 Month Durable Complete Remission in CIS (Cohort A)



Median Duration of CR  
**26.6 Months**

Ongoing Response,  
Still on Study  
**21 / 58 (36%)**



Data Presented ASCO June 2022 by Dr. Karim Chamie



# QUILT 3032 Compared to KEYNOTE-057 in NMIBC BCG Unresponsive CIS Disease

## Primary Endpoint: Efficacy

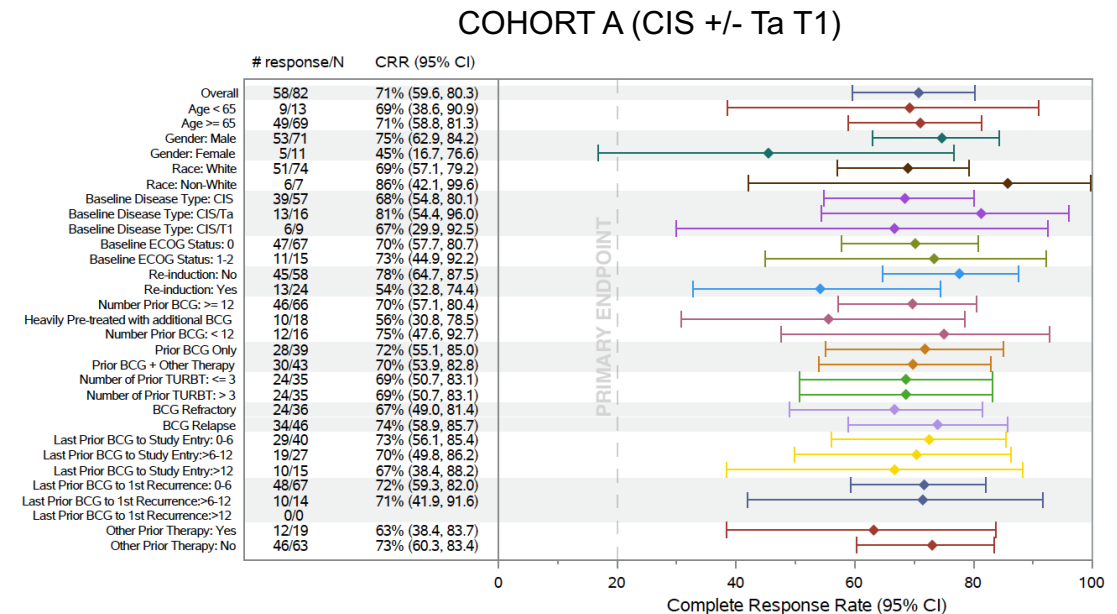
Study	N-803 + BCG QUILT-3.032	Pembrolizumab (Balar 2021, ODAC)
<b>STUDY DESIGN</b>	<b>Pivotal phase 2/3 open-label</b>	<b>Phase 2 open-label (KEYNOTE-057)</b>
<b>Overall Efficacy Population</b>	82	96
<b>Median Duration of Follow-up (months)</b>	23.9	24.1
<b>COMPLETE RESPONSE (CR)</b>		
<b>CR Rate at Anytime</b>		
CR Rate	71%	41%
CR Rate 95% CI	(59.6, 80.3)	(31, 52)
<b>CR Rate in US Population % (n)</b>		
CR Rate, United States Population	71% (58/82) (95% CI: 59.6, 80.3)	29% (10/34) (95% CI: 15.1, 47.5)
CR Rate, International	No Internationally Enrolled Subjects	47% (29/62) (95% CI: 34.0, 59.9)
<b>CR Rate in High Risk Disease State % (n)</b>		
CIS/HG Ta at baseline	81% (13/16) (95% CI: 54.4, 96.0)	29% (7/24) (95% CI: 12.6, 51.1)
CIS/T1 at baseline	67% (6/9) (95% CI: 29.9, 92.5)	42% (5/12) (95% CI: 15.2, 72.3)

**Primary Endpoint:** 30% CR rate with the lower bound 95% confidence interval at  $\geq 20\%$

Lower bound 95% CI of QUILT 3032  $\gt$  Upper bound 95% CI of KEYNOTE-057

CR Rate of US Population Differs

*Further evidence of a clinically meaningful difference in efficacy across multiple subgroups favoring N-803 plus BCG*





# QUILT 3032 Compared to KEYNOTE-057 in NMIBC BCG Unresponsive CIS Disease

## Cystectomy Avoidance

Oral  
Presentation

Study	N-803 + BCG QUILT-3.032	Pembrolizumab (Balzar 2021, ODAC)
<b>STUDY DESIGN</b>	<b>Pivotal phase 2/3 open-label</b>	<b>Phase 2 open-label (KEYNOTE-057)</b>
<b>Overall Efficacy Population</b>	82	96
<b>CYSTECTOMY AVOIDANCE</b>		
<b>Number of Cystectomy, n (%)</b>		
Cystectomy Rate	13 (15.8%)	40 (41.6%)
Cystectomy Avoidance, No Cystectomy	69 (84%)	56 (58%)
Cystectomy in Non-Responders	8 / 24 (33%)	29 / 57 (51%)
Cystectomy After Initial CR	5 / 58 (9%)	11 / 39 (28%)

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ANNUAL MEETING  
ADVANCING EQUITABLE CANCER CARE THROUGH INNOVATION

### Higher cystectomy rate in KEYNOTE-057

**KEYNOTE-057:** 42% subjects overall population and 28% subjects in responders  
**VS**  
**QUILT 3032:** 16% subjects overall population and 9% subjects in the responders

Data Presented ASCO June 2022 by Dr. Karim Chamie

# QUILT 3032 Compared to KEYNOTE-057 in NMIBC BCG Unresponsive CIS Disease

## Safety: Immune Related AEs

Study	N-803 + BCG QUILT-3.032	Pembrolizumab (Balar 2021)
Study design	Pivotal phase 2/3 open-label	Phase 2 open-label (KEYNOTE-057)
Safety population	171	101
Any adverse immune-mediated events	4.1% <sup>a</sup>	22%
Treatment-related grade 3-5 immune-related AEs	0%	2.9%
Treatment-related serious immune-related AEs	0%	4.9%
Steroid Treatment for Immune Mediated Adverse Events (n)	0	7

- N-803 + BCG Well Tolerated with AEs Comparable to BCG Alone
- Pembrolizumab with Systemic Immune-Related AEs Requiring Steroid Therapy

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Data Presented ASCO June 2022 by Dr. Karim Chamie

# Orchestrating the Immune System

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## NK + T Cells

- IL-15 Fusion Proteins



## Natural Killer Cells

- NK-92 Off-the-Shelf
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## Memory B & T Cells

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- Toll Receptor Activators
- saRNA

## Late-Stage U.S. Clinical Trial Updates:

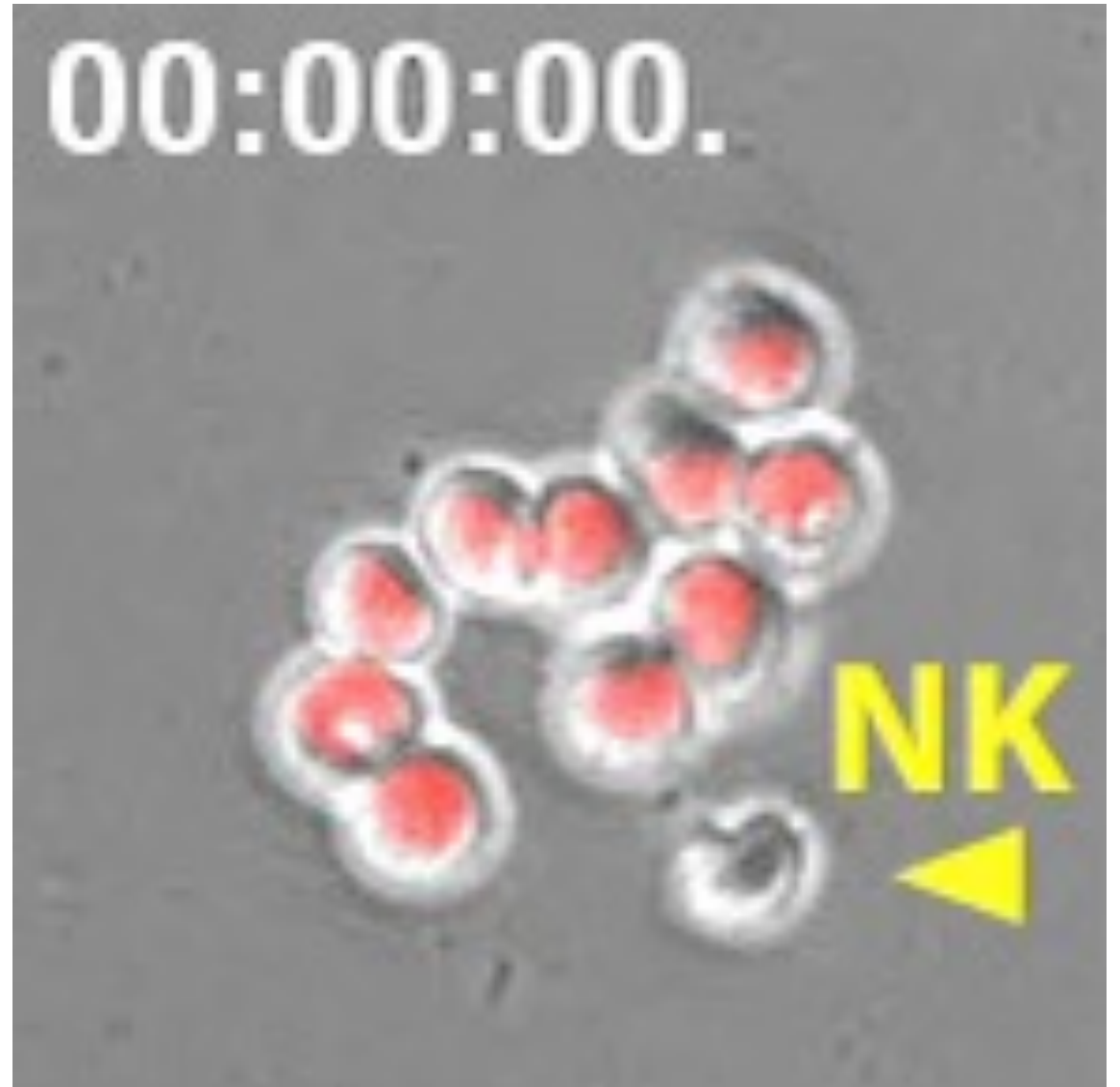
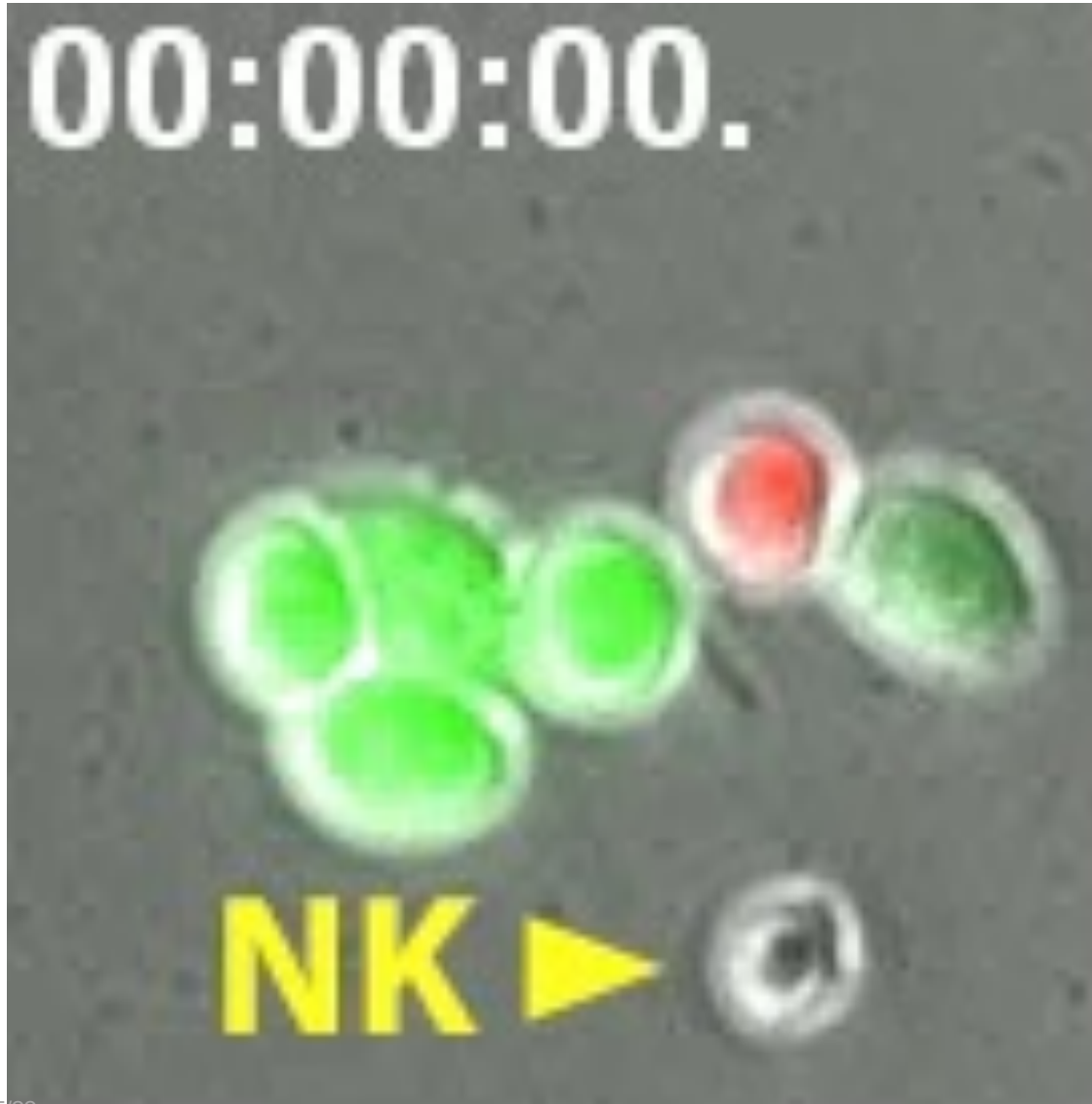
- Bladder Cancer



## Pancreatic Cancer

- Head & Neck Cancer
- Lung Cancer
- HIV
- COVID Vaccine

# Natural Killer Cells



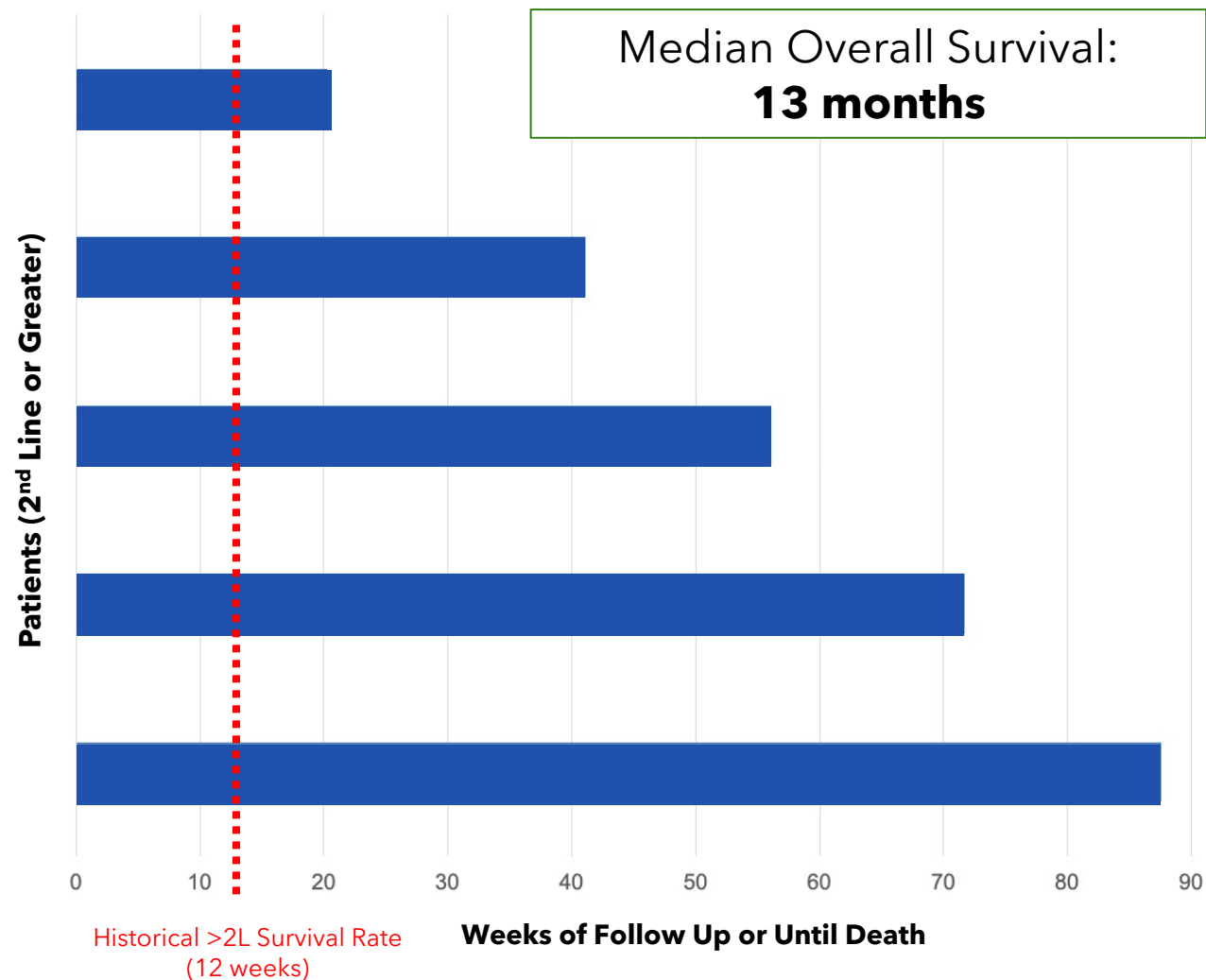
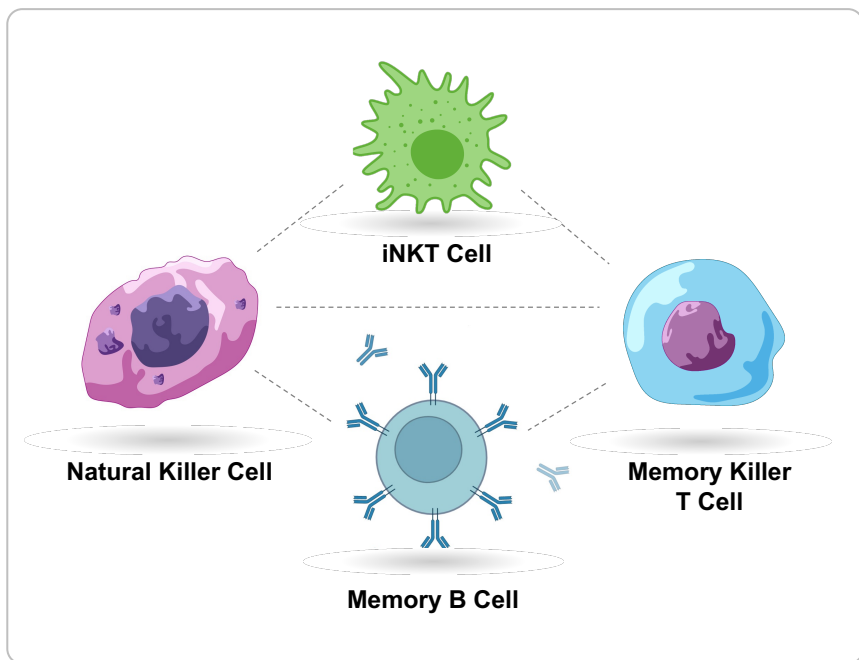
# Exploratory Trial of PD-L1 t-haNK and Anktiva in Combination with Chemo Modulation in Metastatic Pancreatic Cancer

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,<sup>1</sup> Michelle R Padget,<sup>1</sup> Renee N. Donahue,<sup>1</sup> Kristen Solocinski,<sup>1</sup> Yvette Robbins,<sup>1</sup> Clint T. Allen,<sup>2</sup> John H. Lee,<sup>3</sup> Shahrooz Rabizadeh,<sup>4,5</sup> Patrick Soon-Shiong,<sup>4,5</sup> Jeffrey Schlom,<sup>1</sup> James W Hodge,<sup>1</sup>



# Phase 2 QUILT 88 trial of DAMP inducers combined with IL15 superagonist, N-803 and anti PDL1-t-haNK cell therapy more than doubles historical overall survival with 3rd to 6th line advanced Pancreatic Cancer

Tara Seery<sup>1</sup>, Chaitali Nangia<sup>1</sup>, Heide McKean<sup>2</sup>, Leonard Sender<sup>3</sup>, Sandeep Reddy<sup>3</sup>, Patrick Soon-Shiong<sup>3</sup>

NCT04390399

<sup>1</sup>Hoag Cancer Center, Newport Beach, CA; <sup>2</sup> Avera Cancer Institute, Sioux Falls, SD <sup>3</sup> ImmunityBio Inc. Culver City, CA.

## BACKGROUND

Pancreatic cancer will claim an estimated 47,050 lives in the USA in 2020. In patients with advanced disease (>3<sup>rd</sup> line) the median overall survival is 3 months. We hypothesize that effective response against pancreatic cancer requires a coordinated approach that orchestrates both the innate and adaptive immune system. We further hypothesize that by orchestrating the activation of the entire immune system, we could accomplish immunogenic cell death with durable responses in this previously immunotherapy unresponsive disease. We describe a novel combination immunotherapy protocol of low-dose chemo-radiation to enhance antigen cascade and reduce MDSC's, cytokine-induced NK and T cell activation and proliferation via N-803 (Anktiva, IL-15 cytokine fusion protein), and off-the-shelf PDL1-targeted high-affinity NK cell (PD-L1 t-haNK) infusion.

## STUDY EXPERIMENTAL TREATMENT

### Days 1 and 15, every 4 weeks:

- Nab-paclitaxel
- Gemcitabine

### Days 1–5 and 15–19, every 4 weeks:

- Cyclophosphamide

### Days 1, 8, 15, and 22; for first cycle only:

- SBRT (not to exceed 8 Gy, exact dose to be determined by the radiation oncologist)

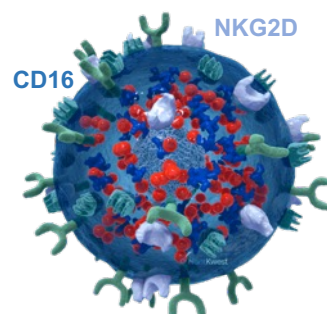
### Day 8, every 4 weeks:

- Aldoxorubicin HCl
- N-803 (15 µg/kg SC)

### Days 1, 8, and 15; every 4 weeks:

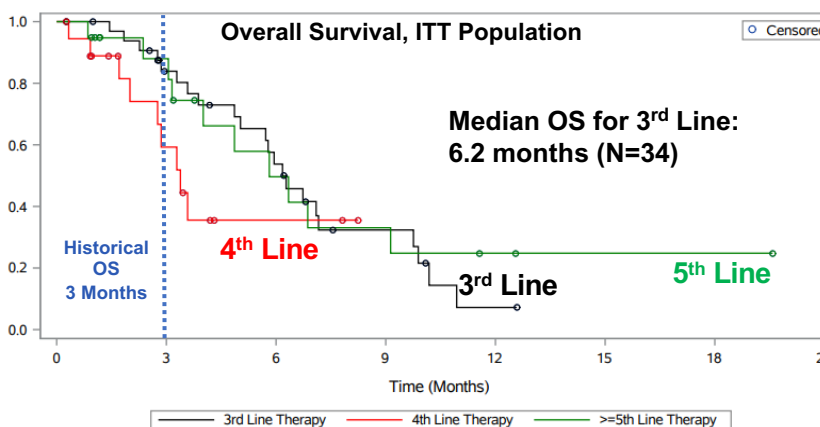
- PD-L1 t-haNK (~2 × 10<sup>9</sup> cells/dose IV)

## PD-L1 t-haNK



PD-L1 t-haNK  
NKG2D  
PD-L1/CD16/erIL2

## RESULTS



Median OS for ITT (≥ 3<sup>rd</sup>, 4<sup>th</sup> and 5<sup>th</sup> line): 5.8 months (N=78)

TABLE 1

Demographics	N / (%)
Age	62 (24, 78)
Age≥65	42%
M:F	58/42
ECOG 0-1	96%
Metastasis	93%

TABLE 2

Any grade TR-AE >10%	%
Chills	47
Pyrexia	46
injection site rxn	40
fatigue	36
anemia	50
neutropenia	19
thrombocytopenia	13
vomiting	28
nausea	26
stomatitis	13
decreased appetite	14
infusion rxn	13

TABLES 1,2,3: Demographics, Treatment related Adverse Events (AEs), TR G3+AEs: Median 3 cycles (1,18),

TABLE 3

Grade ≥3 TR AE ≥5%	%
anemia	41
neutropenia	29
thrombocytopenia	17
fatigue	5

## KEY FINDINGS

- Nant Cancer Vaccine (NCV) **more than doubled median OS** versus historical OS (Manax ASCO GI 2019) of 3 months after >2L
- In QUILT 88 median OS in 3<sup>rd</sup> line subjects (n=34) was **6.2 months** (95% CI: 4.9, 9.8)
- Overall survival for ITT population (N=78) of 3<sup>rd</sup>, 4<sup>th</sup> and 5<sup>th</sup> line is **5.8 months** (95% CI: 4.0, 6.9)
- Treatment related (TR) SAE's were uncommon (6%), no TR deaths were reported
- All treatments were performed as outpatient
- Treatment ongoing for 25 patients

## CONTACT

info@immunitybio.com 310-883-1300 Main

## REFERENCES

1. Fabian KP, Padgett MR, Donahue RN, Solocinski K, Robbins Y, Allen CT, Lee JH, Rabizadeh S, Soon-Shiong P, Schlom J, Hodge JW. PD-L1 targeting high-affinity NK (t-haNK) cells induce direct antitumor effects and target suppressive MDSC populations. *J Immunother Cancer*. 2020 May;8(1):e000450. doi: 10.1136/jitc-2019-000450. PMID: 32439799; PMCID: PMC7247398.
2. Lee MY, Robbins Y, Sievers C, et al. Chimeric antigen receptor engineered NK cellular immunotherapy overcomes the selection of T-cell escape variant cancer cells. *Journal for ImmunoTherapy of Cancer* 2021;9:e002128. doi: 10.1136/jitc-2020-002128
3. Wolfson B, Franks SE, Hodge JW. Stay on Target: Reengaging Cancer Vaccines in Combination Immunotherapy. *Vaccines (Basel)*. 2021 May 15;9(5):509. doi: 10.3390/vaccines9050509. PMID: 34063388; PMCID: PMC8156017
4. Chu Y, Nayyar G, Jiang S, Rosenblum JM, Soon-Shiong P, Saifrit JT, Lee DA, Cairo MS. Combinatorial immunotherapy of N-803 (IL-15 superagonist) and dinutuximab with ex vivo expanded natural killer cells significantly enhances in vitro cytotoxicity against GD2<sup>+</sup> pediatric solid tumors and in vivo survival of xenografted immunodeficient NSG mice. *J Immunother Cancer*. 2021 Jul;9(7):e002267. doi: 10.1136/jitc-2020-002267. PMID: 34244307; PMCID: PMC8268924.



SCAN ME



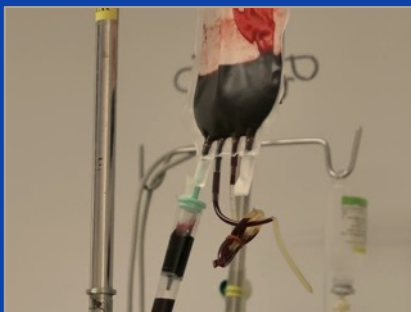
# Orchestrating the Immune System

First-in-Class Comprehensive Platforms



## NK + T Cells

- IL-15 Fusion Proteins



## Natural Killer Cells

- NK-92 Off-the-Shelf
- Autologous m-ceNK
- iNKT Cells



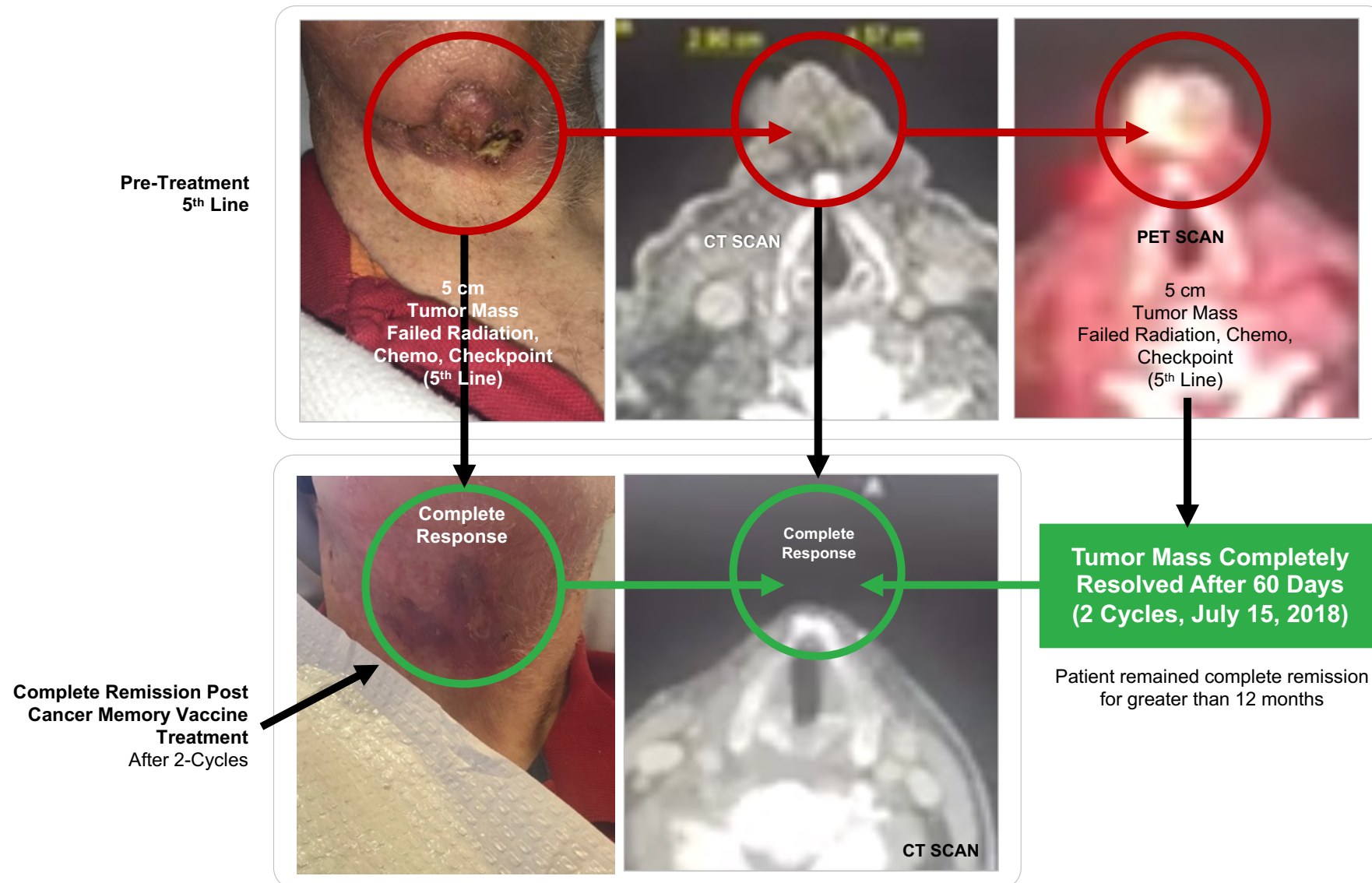
## Memory B & T Cells

- Adenovirus
- Subunit Proteins
- Toll Receptor Activators
- saRNA

## Late Stage USA Clinical Trial Updates:

- Bladder Cancer
- Pancreatic Cancer
- ▶ Head & Neck Cancer
- Lung Cancer
- HIV
- COVID Vaccine

# Complete Response: 5<sup>th</sup> Line Metastatic Head & Neck Cancer



## NANT Cancer Vaccine Therapies Used:

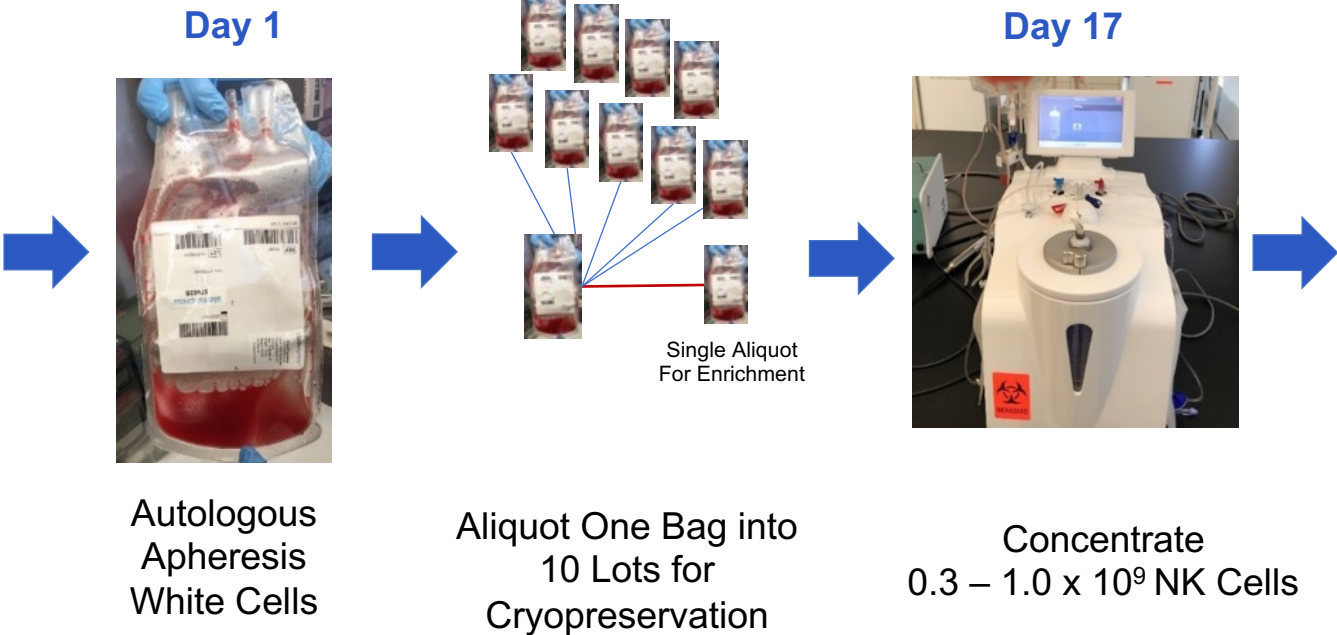
- haNK
- N-803
- Ad5 CEA
- Chemo

# Memory-Like Cytokine Enhanced Natural Killer (M-ceNK) Cells from Peripheral Blood First-in-Human Clinical Trials

Day 1



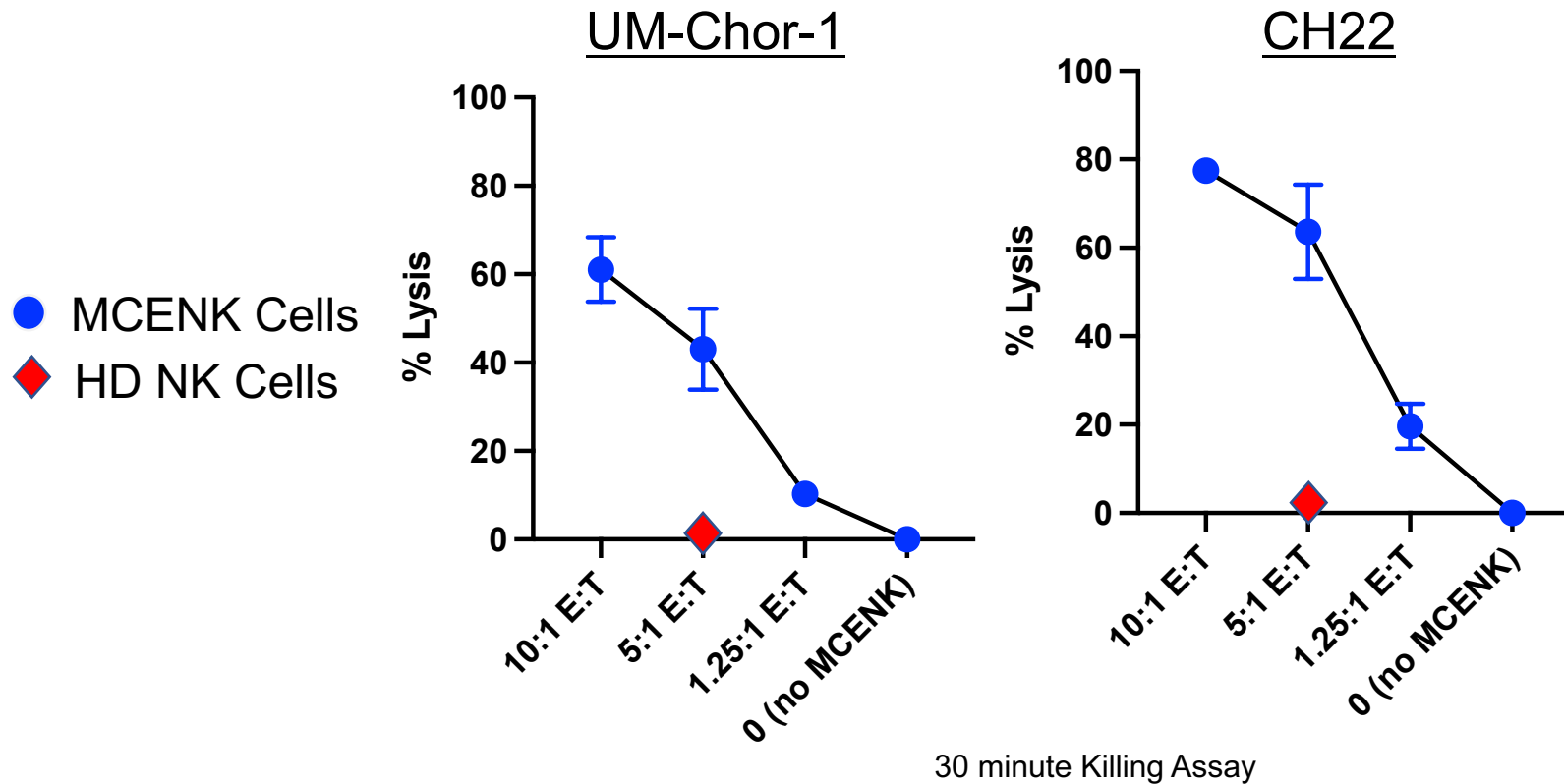
Autologous Apheresis  
Patient White Cell Collection



First-in-human subjects dosed with M-ceNK in 2022

NCT04898543

# Chordoma Cells Lines are Efficiently Killed by M-ceNK Cells



- Two chordoma tumor cell lines (UM-Chor-1, CH22) were incubated with M-ceNK cells.
- Tumor cell killing was assessed over 18h.
- Depicted is 30 minute killing.
- Timepoint after this showed 100% killing at all ratios containing M-ceNK cells.
- HD NK cells were assessed at a single 5:1 ratio.

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## Lung Cancer

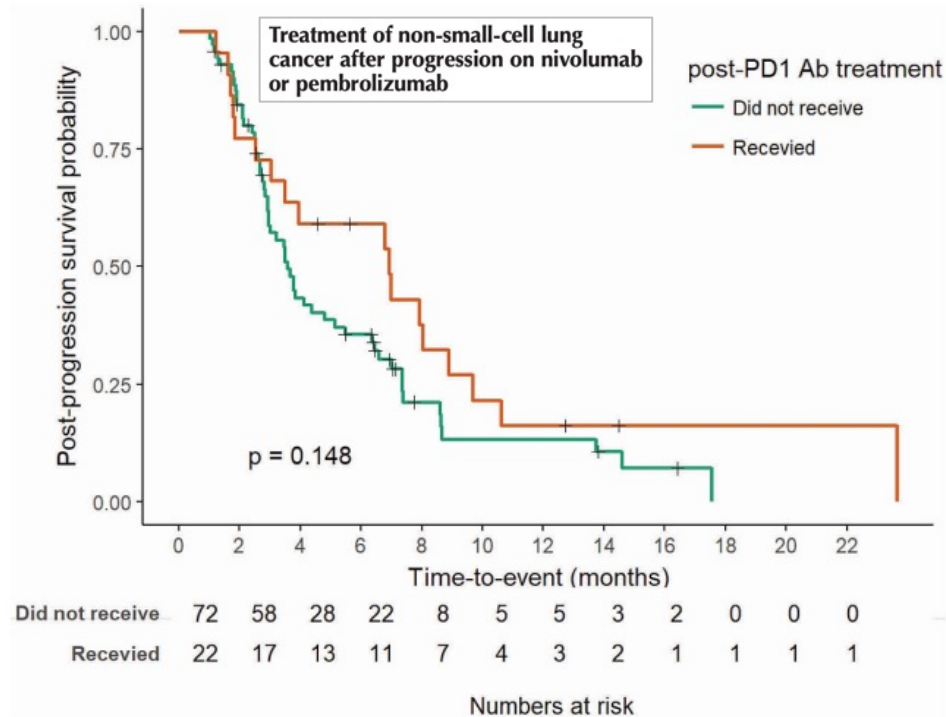
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# Median Overall Survival of Anktiva Compared to Any Therapy in Patients Who Progressed on Checkpoint Inhibitor

## Additional Therapy Following Checkpoint Inhibitor Progression

**Median OS: 6.1 Months**

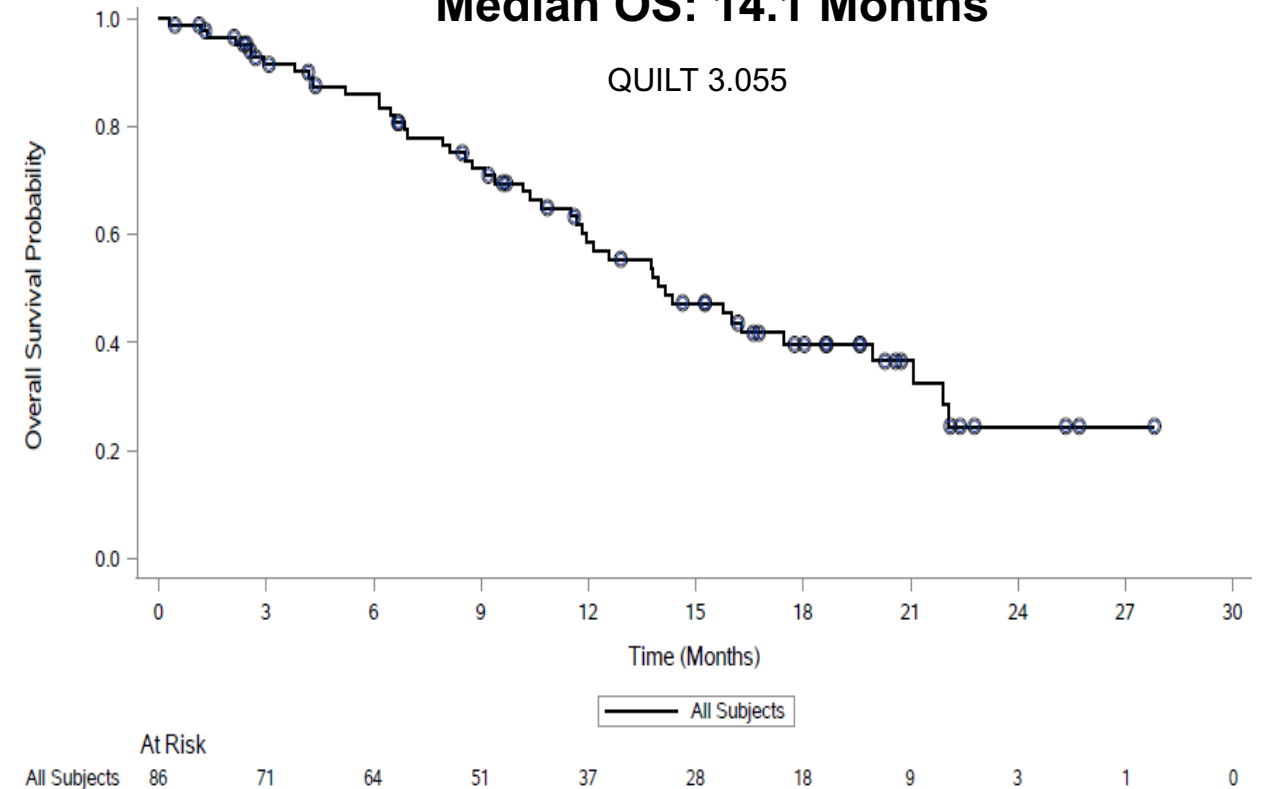


**FIGURE 3** Post-progression survival after cessation of PD-1 monoclonal antibody (Ab) in 22 patients who received post-progression therapy and 72 patients who did not within 30 days of PD-1 Ab cessation.

doi: 10.3747/co.27.5495

## Anktiva IL-15 Therapy Following Checkpoint Inhibitor Progression

**Median OS: 14.1 Months**



Note: Subjects alive were censored at the last contact date in database.



# Anktiva Selected by LUNG-MAP for 2<sup>nd</sup> Line Patients who Progressed on Checkpoint Therapy



## ImmunityBio Announces First Participants Have Been Enrolled in Lung-MAP Trial Studying Anktiva to Activate NK and T Cells in Non-Small Cell Lung Cancer

April 25, 2022

- Novel combination therapy of Anktiva, an IL-15 superagonist, and Keytruda targeted at patients with lung cancer who have failed checkpoint inhibitor therapy
- The study currently includes nearly 200 U.S. sites and will involve 478 patients when fully enrolled
- Nearly 237,000 new cases of lung cancer estimated to be diagnosed in the U.S. this year, making it the second most common cancer in the U.S.



NCT05096663

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HIV

- COVID Vaccine

# ImmunityBio HIV Clinical Programs: Active Phase 1/2 Clinical Trials in Progress



UNIVERSITY OF MINNESOTA



## Phase 1 B Cell Follicle Study

Principle Investigator: Tim Schacker, UMinn

NCT04808908

10 HIV+ (ART) patients treatment, ART + N-803

**Fully Enrolled**

## Phase 1 ACTG 5386: N-803 +/- 2 bNABs in HIV+ subjects

Principle Investigator: Tim Wilken, Weill Cornell Medicine

NCT04340596

46 HIV+ patients on ART randomized to Arm A or B

Arm A: N-803 alone

Arm B: 2 bNAbs + N-803

**Trial Active**



## Phase II Thailand Trial: N-803 in Acute HIV Infection

Study Chair: Denise C Hsu, MD PhD – Henry M. Jackson Foundation

NCT04505501

15 Acutely infected HIV patients on ART: N-803 Treatment Alone vs. Placebo

**11 Enrolled (May 2022)**

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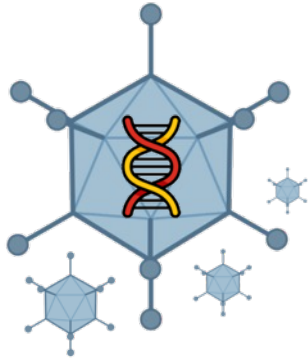
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 COVID Vaccine

# ImmunityBio Vaccine Platforms Against COVID

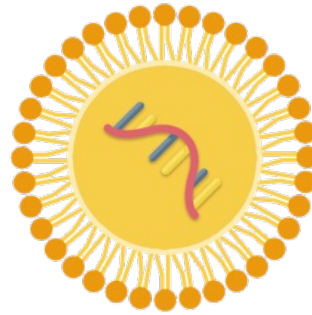


## Adeno hAd5

Human Adenovirus 5 DNA Based



- Spike & Nucleocapsid T Cells
- Memory B and Memory T Cells

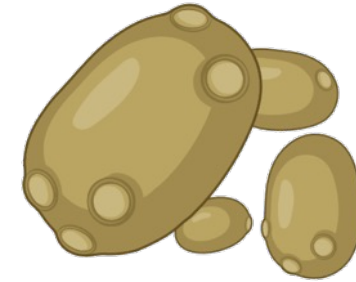


## mRNA saRNA

Self Amplifying RNA



- Potent Antibodies
- Spike & Nucleocapsid T Cells
- Memory B and Memory T Cells



## Yeast

RBD Subunit Protein

RBD + 3M-052 Adjuvant



- Potent Antibodies
- Spike & Nucleocapsid T Cells





**Thank You**