## BEYOND CANCER<sup>™</sup>

Next level immuNO-oncology

Corporate Presentation

**April 2024** 

## Ultra-High Concentration Nitric Oxide (UNO) as a Potent Immunotherapy



## Upregulates Immune Activity

Utilizing Ultra-high concentration Nitric Oxide (UNO) to upregulate immune activity to treat solid tumors and distant metastases

## Promising Early Phase 1a Results

First in human, Phase 1 clinical trial ongoing in unresectable, relapsed or refractory solid tumors

## Combination Therapy

Combination therapy with immune checkpoint inhibitors (ICIs) to improve patient outcomes

### Patented Delivery Approach

Differentiated MOA with 2 U.S. issued patents (expiry 2040) involving a novel delivery system

### **Beyond Cancer Leadership Expertise in Emerging Healthcare Companies and Clinical Oncology**





Selena Chaisson, MD Chief Executive Officer

**Bailard** 

**TIGERGLOBAL RCM** 



- · 16 years as Head of Healthcare Investments at Bailard managing the **Emerging Life Science strategy**
- Over 25 years of experience as a healthcare investor
- Stanford MD/MBA



Jedd Monson, MD Chief Medical Officer









- Founding partner of cCARE
- Practiced at City of Hope, Valley Radiotherapy Associates, and 21st Century Oncology
- Stanford MD, a member of American College of Radiology and American Society of Therapeutic Radiology & Oncology



Gavin Choy, PharmD Chief Operating Officer







- 20+ years of biopharmaceutical operating experience
- Integral member of four New Drug Applications (NDA) and seven Investigational New Drug (IND) filings
- PharmD from University of Southern California and MBA from University of California, Irvine

## **Board of Directors with Proven Business Record**





#### Gregory Berk, MD

and Development Experience

- Independent oncology drug development consultant
- Over 30 years of experience. Served as interim CEO, CMO at GT Biopharma, Inc.
- Weill Medical College of Cornell University, New York Presbyterian Hospital, Case Abraxis Western Reserve University





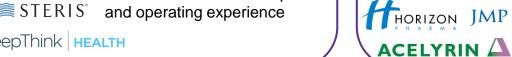








- Served as President & CEO of Zimmer Biomet Holdings, Inc.
- Over 20 years of global executive-level leadership and operating experience





### **Robert Carey**

- Board member at Beyond Air (XAIR) since February 2019
- Co-Founder, President & COO of ACELYRIN
- Served as Executive VP and **CBO** at Horizon
- **Previously Managing Director** & Head of Healthcare Investment Banking at JMP Securities



intellikine

#### Steve Lisi Chairman

- · CEO & Chairman of Beyond Air (XAIR) since 2017
- 18 years experience as a healthcare investor 3 years as SVP Head of Strategy and BD at Avadel (AVDL)



#### **Amir Avniel Executive Director**

- · CBO and Co-Founder of Beyond Air (XAIR)
  - Over 20 years of executivelevel experience in finance, business development and operations, including M&A







**TIGERGLOBAL** 

#### Selena Chaisson, M.D. **CEO**

- 16 years as Head of Healthcare Investments at Bailard managing the **Emerging Life Science** strategy
- Over 25 years of experience as a healthcare investor
- Stanford MD/MBA





## Therapeutic Concentrations of Nitric Oxide (NO)



#### **Pulmonary**

#### **Antimicrobial**

#### BEYOND CANCER\*

### **Immuno-Oncology**

Low NO (<80 PPM)

#### **Neonatal Hypertension:**

Currently approved in term and near-term (>34 weeks gestation) neonates with hypoxic respiratory failure High NO (>80 PPM <400 PPM)

#### **Antiviral**

- Inhibition of viral enzymes<sup>2</sup>
- Blocking of RNA synthesis<sup>3</sup>
- Blocking of viral replication cycle by modifying target molecules essential for replication<sup>3</sup>

#### **Antibacterial**

 Mechanism attributed to DNA damage, bacterial enzyme inhibition, and induction of lipid peroxidation<sup>1</sup>

## Ultra-High NO (UNO) (>10,000 PPM)

#### Immunoregulatory Functions<sup>4</sup>

- Increase
  - T/B cells
    - Dendrocytes
    - T memory cells
- Decrease
  - Regulatory T cells
  - MDSCs

<sup>1)</sup> Wink DA et al., Chemical biology of nitric oxide: Insights into regulatory, cytotoxic, and cytoprotective mechanisms of nitric oxide. Free Rad Biol Med 1998: (4-5): 434-56.

<sup>2)</sup> Saura, M., et al., An antiviral mechanism of nitric oxide: inhibition of a viral protease. Immunity, 1999. 10(1): p. 21-8

<sup>3)</sup> Akerström S et al. Nitric oxide inhibits the replication cycle of severe acute respiratory syndrome coronavirus. J Virol. 2005; 79(3):1966-9

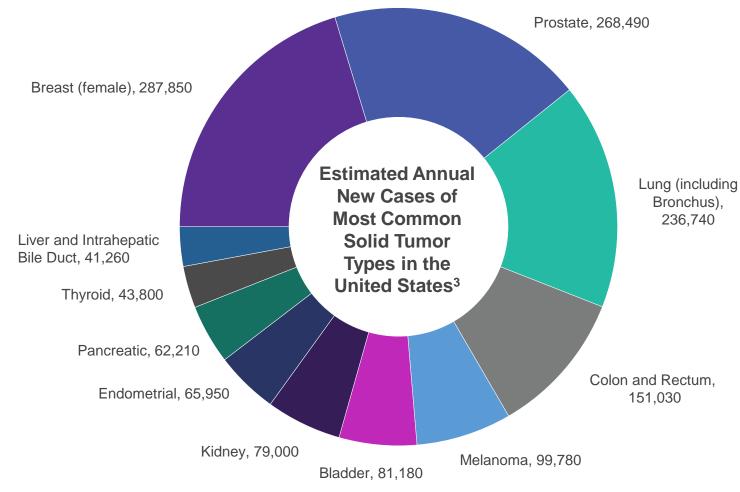
<sup>4) 2023-10-30-</sup>SITC Poster Final.pdf (beyondcancer.com)

## Immunotherapy has Emerged as a Cornerstone Treatment for Solid Tumors



Solid Tumors represent approximately 90% of adult human cancers<sup>1</sup>, accounting for approximately 1.4 million annual new cases of most common cancer types in the United States<sup>3</sup>

**Metastatic Disease** is responsible for 90% of solid tumor deaths<sup>2</sup>



<sup>1)</sup> Cooper GM. The Cell: A Molecular Approach. 2nd edition. Sunderland (MA): Sinauer Associates; 2000. The Development and Causes of Cancer. Available from: https://www.ncbi.nlm.nih.gov/books/NBK9963/

Fontebasso Y, Dubinett SM. Drug Development for Metastasis Prevention. Crit Rev Oncog. 2015;20(5-6):449-473. doi:10.1615/CritRevOncog.v20.i5-6.150

According to the National Cancer Institute: https://www.cancer.gov/types/common-cancers. Accessed: August 8, 2022. Data as of May 10, 2022.

## The Majority of Immunotherapies are Checkpoint Inhibitors



Company	Drug Name	First FDA Approval	2023 Revenue
Bristol-Myers Squibb	Yervoy	March 2011	\$2.2 Billion
Merck	Keytruda	Sept 2014	\$25.0 Billion
Bristol-Myers Squibb	Opdivo	Dec 2014	\$9.0 Billion
Roche	Tecentriq	May 2016	\$3.4 Billion
AstraZeneca	Imfinzi	May 2017	\$4.2 Billion

Despite a >\$40B Market, Most Cancer Patients are Either Ineligible, Do Not Respond, or Develop Resistance

# Proprietary UNO Delivery System Directly Targets the Tumor



### Novel system to deliver Ultra-high concentration Nitric Oxide (UNO)

- Advantages
  - Ability to obtain significantly higher intra-tumoral NO concentrations than endogenous or NO donor systems
  - Quick and simple procedure
- Optimizing delivery to meaningfully improve ease of use
  - Current high-volume system has produced promising results both preclinically and in Phase 1a
  - Low volume system expected for use in Phase 1b trial
- Encouraging toxicity profile allows for potential combination with approved therapies to enhance clinical outcomes

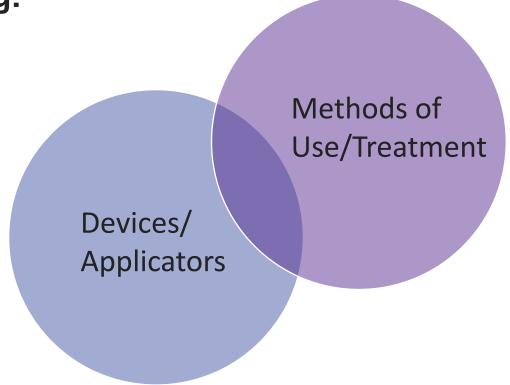
### **Intellectual Property Portfolio**





Two issued U.S. patents (expiry 2040), with more pending from patent families including:

- UNO monotherapy for the treatment of solid tumors
- UNO in combination with checkpoint therapies and other anti-cancer agents
- Delivery systems
- Delivery applicators



# Platform Technology Targeting Multiple Solid Tumors



Program	Initial Indication	Discovery	Pre-Clinical	Phase 1a	Phase 1b
Monotherapy					
UNO101	Cutaneous / near cutaneous tumors				
Combination Therapy	1				
UNO201 + anti-PD-1	PD-1 Resistant or Refractory Patients with Cutaneous / near cutaneous tumors				
UNO201 + other agents	Multiple solid tumors				

UNO101: High Volume

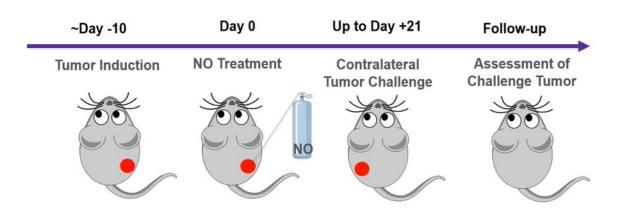
**UNO201: Low Volume** 



# UNO Preclinical Data Demonstrates Immune Response

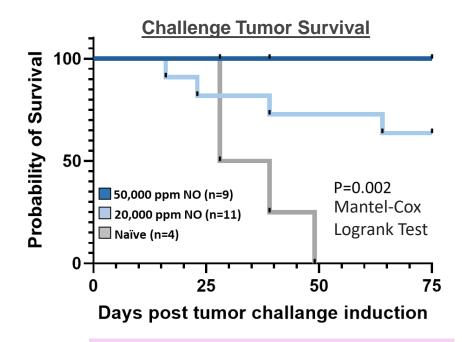
# UNO in CT26 Challenge Tumors In Vivo Showed Evidence of Dose-Dependent Effects on Survival





#### Challenge assay:

- CT26 study mice treated with 20,000 or 50,000 ppm NO for 5 minutes.
- Naïve mice inoculated with the same cancer cells served as an internal control.
- Up to 21 days post NO treatment, all mice were re-inoculated with colon cancer cells (CT26 cells) as a challenge tumor and survival was monitored.



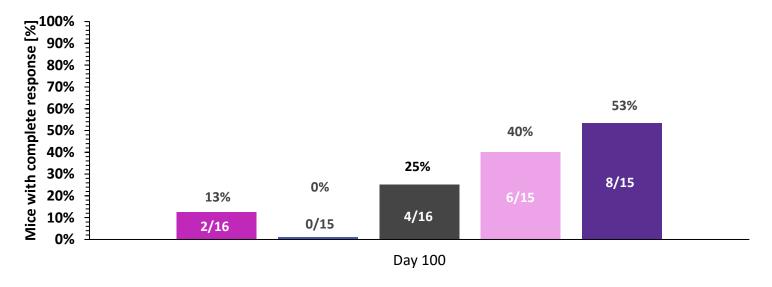
#### **Survival Results at Day 75:**

- 100% of 50,000 ppm NO mice alive
- 64% of 20,000 ppm NO mice alive
- 0% of naïve mice alive

## UNO in Combination with Anti-mPD-1 Showed a Doubling of Tumor-Free Mice



#### **CT26 Primary and Secondary Tumor-free Mice**



Time post NO treatments [NO]

- NO 50,000 ppm 5min' (n=16)
- Anti-mPD1 (n=16)
- NO 50,000 ppm 10min' + Anti-mPD1 (n=15)
- NO 50,000 ppm 10min' (n=15)
- NO 50,000 ppm 5min' + Anti-mPD1 (n=15)

Statistical analysis: Fisher's Exact Test: P-value = 0.1489,
Pairwise Treatment Group Comparison - 50,000 10 min + Anti-mPD1 vs Anti-mPD1



UNO+anti-PD-1
Complete Response



Control
Primary &
Secondary tumors

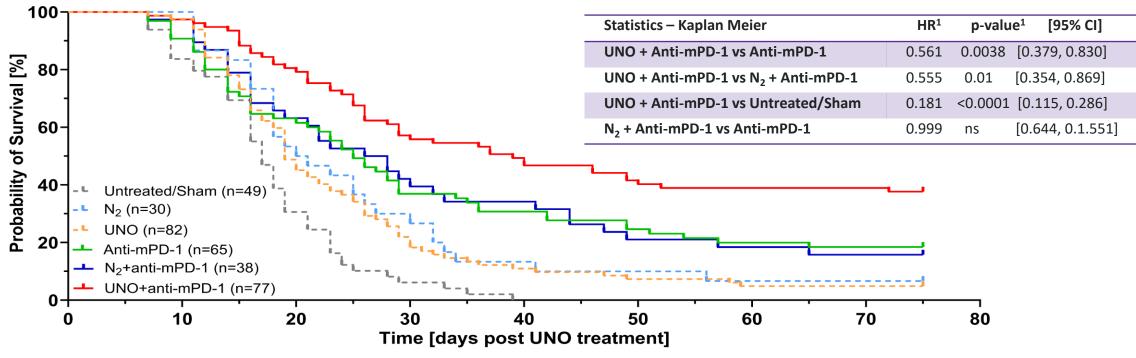
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Source: SITC Annual Meeting, November 2022

## Effect of a Single UNO Treatment and Anti-mPD-1



The combination of Ultra-high concentration NO with anti-mPD-1 improved outcomes and mice survival compared to UNO or anti-mPD-1 alone, as UNO assists the immune system in overcoming anti-mPD-1 resistance.



Pooled data across studies of 5 or 10-min UNO and anti-mPD-1 (5 or 10 mg/kg) treatment - survival data.

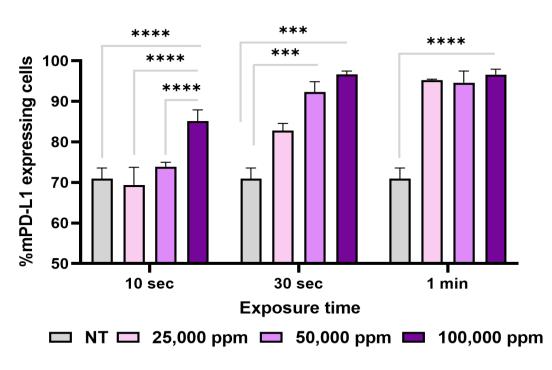
on Mice Survival

<sup>&</sup>lt;sup>1</sup>Hazard ratio and p-value derived from Cox proportional hazard model.

## **UNO Upregulates mPD-L1 Expression at Day 5**



#### mPD-L1 expression in PI-negative CT26 tumor cells



- mPD-L1 expression 5 days after exposure to UNO
- Two-way ANOVA, multiple comparison test, \*\*\*P<0.001, \*\*\*\*P<0.0001.

Source: AACR Annual Meeting, April 2023

### **Dose-Dependent Effects of NO in Cancer**



		Tumor Response/Survival	Intra-tumoral Effects	Systemic Effects	Source
ONO	1,000,000's	Prevents challenge tumors <sup>2</sup> +ICI: Complete tumor regression/ survival in >50% (Day 100) <sup>3</sup>	↑ Central Memory T cells ↑ T cells	<ul> <li>↑ Central Memory T cells</li> <li>↓ T regs¹</li> <li>↑ Dendritic cells</li> </ul>	Mouse colon, CT26 + Clinical data
ırs	1,000's	Tumor growth inhibition⁵	↓ Antigen presentation by Dendritic cells (in vitro) <sup>4</sup>		Mouse melanoma B16.F10 & squamous cell carcinoma scc7
NO Donors	10's	Tumor growth inhibition <sup>6</sup> ± Chemo: ↓ tumor volume/ 20% survival (Day 60)	<ul><li>✓ Central memory T cells</li><li>↑ T regs</li></ul>		Mouse lung cancer, LLC1, B16 & CT26
	1X*	Insignificant prolongation in survival <sup>7</sup> + ICI: ↓ Primary & secondary tumor volume		± ICI: Unchanged / ↑ T regs	Mouse breast cancer 4T1 & B16

<sup>\*</sup> Estimated ratio of maximum NO delivered intratumorally

- 1. 2023-10-30-SITC Poster Final.pdf (beyondcancer.com)
- 2. Confino, H., Cancer Cell International: Gaseous nitric oxide tumor ablation. BMC; (2022) 22:405
- 3. Confino, H., Cells: Intratumoral Administration of High-Concentration Nitric Oxide. MDPI; 2023,12,2439
- 4. Markowitz, J., Scientific Reports: Nitric oxide mediated inhibition of antigen presentation from DCs to CD4+ T cells in cancer. Nature; (2017) 7: 15424
- 5. Ning S., Dinitroazetidines Are a Novel Class of Anticancer Agents and Hypoxia-Activated Radiation Sensitizers Developed from Highly Energetic Materials Volume 72, Issue 10
- 6. Li et al. J Exp Clin Cancer Res: Repurposing nitric oxide donating drugs in cancer therapy through immune modulation. BMC; (2023) 42-22
- 7. Kim, J, NATURECOMMUNICATIONS: Thermosensitive hydrogel releasing nitric oxide donor and anti-CTLA-4 micelles for anti-tumor immuno-therapy. Nature; (2022) 13:1479,

### Improved Immunogenic Profile with UNO



Intra-Tumoral Effects	UNO Preclinical* (50k ppm NO, 5 minutes)	Nitric Oxide Donors <sup>1</sup> ^ SNAP: Nine doses (12 days)
T cells	<b>↑</b> 50%	SNAP: <b>↓</b> 21%
Cytotoxic T cells		SNAP/ISMN: ↓ 15%
Ag Specific T cells	<b>↑</b> 45%	
T Central Memory	<b>↑</b> 29%	<b>SNAP: ↓</b> 35%
T regs		SNAP: ↑ 38%

1. Li et al. J Exp Clin Cancer Res: Repurposing nitric oxide donating drugs in cancer therapy through immune modulation. BMC; (2023) 42-22

Notes: isosorbide mononitrate (ISMN), N-acetylpenicill-amine (SNAP)

<sup>\* 4</sup>T1, Day 7

<sup>^</sup> LL2, Day 9



# UNO Clinical Data Corroborates Preclinical Observations

### Scientific Advisory Board





Frederick M. Dirbas, MD

Assoc. Prof. of Surgery, Div. of Surgical Oncology, Stanford University School of Medicine

- Internationally acclaimed surgeon and pioneer in the field of breast cancer
- Published nearly 50 articles in peerreviewed journals



Mark D. Pegram, MD

Assoc. Dean for Clinical Research Quality, Stanford University School of Medicine

- Suzy Yuan-Huey Hung Endowed
   Professor of Medical Oncology at the
   Stanford University School of Medicine
- Medical Director of the Stanford Clinical Translational Research Unit



Sunil J. Panchal, MD

President of the National Institute of Spine and Pain

- Minimally invasive spine and interventional pain specialist
- Editorial reviewer for Clinical Researcher, Anesthesia and Analgesia, Pain, Pain Medicine, and the Clinical Journal of Pain
- Former Chair of National Comprehensive Cancer Network Pain Panel

### Phase 1a Designed to Establish 3 Key Objectives



#### **Primary Objectives:**

- 1. Determine safety profile
- Determine maximum tolerated dose (MTD) and/or optimal biologically effective dose (OBD)
- 3. Recommend Phase 2 dose (RP2D)

**Secondary Objective:** Anti-tumor activity of single intra-tumoral escalating UNO101 dose per RECIST v1.1, iRECIST

**Exploratory Objectives:** Biomarkers predictive of response via itRECIST

#### **Major Eligibility Criteria**

- ≥ 18 years of age
- ECOG PS 0 − 3
- Unresectable, cutaneous or SQ primary or metastatic tumor
- Measurable disease
- Tumor 4.5 mm 30 mm

Part A: Dose Escalation 3 + 3 Scheme Follow-up to Day 21 (Max N = 18)

Cohort 1: 25,000 ppm gNO over 5 minutes (expansion to 6 patients)

**Cohort 2**: 50,000 ppm gNO over 5 minutes

Cohort 3: 100,000 ppm gNO over 5 minutes

MTD/OBD









# Patient Characteristics – SITC Data as of November 3, 2023



Baseline Characteristics	N (%)	Mean	Min	Max
Age (yrs.) (n=5)	5* (100%)	64.4	43	81
# of Prior Treatment Regimens	5 (100%)	5.8	2	12
Time from Diagnosis to First UNO Treatment (yrs.)	5 (100%)	4.7	1.4	9.5
Male/Female	2 (40%) / 3 (60%)			
ECOG PS 0/1/2/3 (Day 1)	0 = 2 (40%) / 1 = 3 (60%) / /			
Diagnosis •Squamous cell carcinoma •Melanoma •Breast	2 1 2			

<sup>\*</sup>all patients treated with 25,000 ppm NO

# BA-ONC-01 25,000 ppm Preliminary Safety



System Organ Class	Adverse Event (Preferred Term)	Grade 1	Grade 2	Grade 3	Grade 4
Respiratory, thoracic and Mediastinal disorders	Dyspnea <sup>1</sup> (Certainly related) Hypoxia <sup>2</sup> (Possibly related)	✓			✓
Skin and subcutaneous tissue disorders	Palmar-plantar erythrodysesthesia syndrome (Certainly related)	✓			
Gastrointestinal disorders	Nausea <sup>1</sup> (Possibly related)	$\checkmark$			

<sup>&</sup>lt;sup>1</sup> Dyspnea and Nausea were all experienced by the same patient

<sup>&</sup>lt;sup>2</sup> IMOH causality assessment.

## Case Report: Early Response Observed



#### Data presented at the SITC Annual Meeting, November 2023

- 82 y/o male with history of squamous cell carcinoma: 2017 metastases to neck and back
- Received:
  - 2 prior surgeries
  - 2 prior lines of immunotherapy
  - 2 prior lines of chemotherapy/targeted therapy, and
  - 5 prior cycles of XRT.
- Early response observed by Day 7 post UNO treatment

**Treatment Day** 



Treatment Day +1



Treatment Day +7



# Interim Phase 1a Biomarker Results Correlate with Preclinical Data



Systemic Effects	UNO Clinical <sup>1</sup>	UNO Preclinical <sup>2</sup>	Nitric Oxide Donors <sup>3</sup>
Cytotoxic T cells	<b>↑</b> 5%	<b>1</b> 4%	N/S
Helper T cells		<b>↑</b> 34%	N/S
Ag Specific T cells		<b>1</b> 400%	N/S
T Central Memory	↑84% ↑167% (day 21)	↑ 161% (100k ppm NO)	
Dendritic cells	↑ 59% ↑280% (day 21)	112% (day 5)	↓ Antigen presentation (in vitro) <sup>4</sup>
T regs	<ul><li></li></ul>	<ul><li></li></ul>	N/S

**UNO Clinical:** 25k ppm UNO101, 5 minutes , Day 7 data (unless otherwise noted) **UNO Preclinical;** 50k ppm UNO101, 5 minutes, CT26 model, Day 7 data (unless otherwise noted) **NO Donor:** GSNO, Three doses / 5 days, B16.F10-OVA, Day 6 data

<sup>1. 2023-10-30-</sup>SITC\_Poster\_Final.pdf (beyondcancer.com)

<sup>2.</sup> https://beyondcancer.com/wp-content/uploads/2023/10/MOA-poster-EORTC-vFinal-5.pdf

<sup>3.</sup> Kim, J, NATURE COMMUNICATIONS: Thermosensitive hydrogel releasing nitric oxide donor and anti-CTLA-4 micelles for anti-tumor immuno-therapy. Nature; (2022) 13:1479

<sup>4.</sup> Markowitz, J., Scientific Reports: Nitric oxide-mediated inhibition of antigen presentation from DCs to CD4+ T cells in cancer. Nature; (2017) 7: 15424

## UNO is Well Tolerated and Demonstrated Proof of Concept



- Local administration of UNO is well tolerated in the initial cohort
- Immune biomarkers compare favorably to previously published murine data
- Demonstrated proof of concept with early response observed on Day 7 in a heavily pretreated squamous cell carcinoma
- Next Steps:
  - Advance to subsequent trial cohort
  - Combine with Immune Checkpoint Inhibitors (ICIs)
  - Introduce repeat dosing

### **Low Volume Study: Primary Tumor Results**



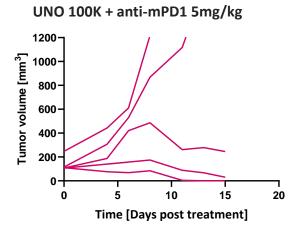
#### Tumor Shrinkage is seen in 3/5 tumors in UNO combo arm vs. 0/5 in N2 combo arm at Day 15

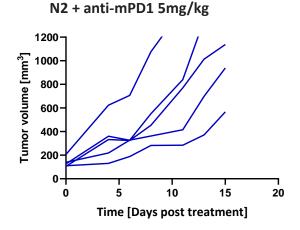
#### **Experimental Conditions**

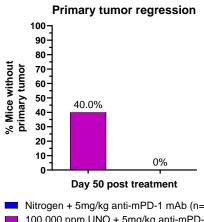
- 100,000 ppm NO + anti-mPD1 vs. N2 + anti-mPD-1 (5mg/kg)
- Treatment time: 2.5 min

#### Results

- 40% of UNO-treated tumors regressed through Day 50
- No safety events



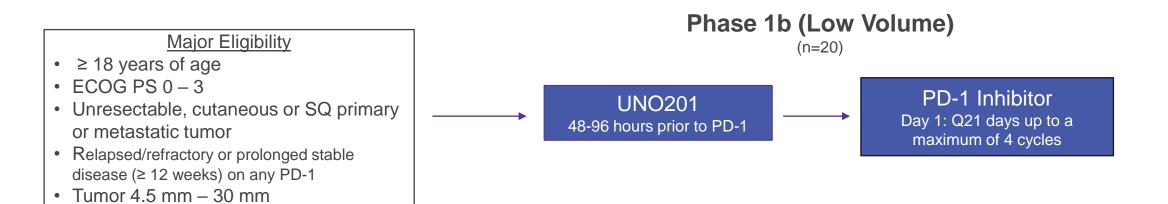




### Proposed Design: Phase 1b BC-ONC-01



**Hypothesis:** Can UNO therapy convert "cold tumor" → "hot tumor"



**Primary Objective:** To assess preliminary efficacy by objective response rate (ORR) and duration of response (DOR) per Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1, and secondarily immune-related RECIST (iRECIST).

**Secondary Objectives:** To assess progression free survival (PFS) and overall survival (OS), clinical benefit rate (CBR: CR+PR+SD ≥ 6 months), time to response (TTR) by RECIST and iRECIST, and incidence and severity of non-serious adverse events, including immune related adverse events (irAEs).

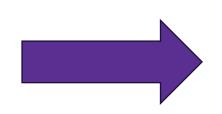
**Exploratory Objectives:** To assess biomarkers that may be predictive of the anti-tumor activity of a intratumoral UNO101 injection.

### **UNO Device Development**





UNO Delivery System



Future State (Alpha Prototype)



## **Upcoming Catalysts**



Timing	Milestone
2023	<ul> <li>✓ Present Initial Phase 1a Data</li> <li>✓ Additional Preclinical Data Presentations</li> <li>✓ Publication of Additional Manuscript in Major Scientific Journal</li> <li>✓ Additional Patent Issuance and Filings</li> </ul>
2024	<ul> <li>Series B Financing</li> <li>Present Final Phase 1a Data</li> <li>Initiate Phase 1b Study</li> <li>Present Interim Phase 1b Data</li> <li>Activate Clinical Sites Globally</li> <li>Pre-IND Filing</li> </ul>
2025	<ul> <li>Present Final Phase 1b Data</li> <li>IPO</li> <li>U.S. IND Approval</li> <li>Initiate Phase 2 Study</li> </ul>

### Forward Looking Statements



All statements and expressions are the sole opinion of Beyond Cancer (the "Company"), and not Beyond Air, the Company's majority shareholder. The statements and expression herein by the Company are subject to change without notice. The Company is not liable for any investment decisions by its readers or subscribers. It is strongly recommended that any purchase or sale decision be discussed with a financial advisor, or a member of any financial regulatory bodies. The information contained herein has been provided as an information service only. The accuracy or completeness of the information is not warranted and is only as reliable as the sources from which it was obtained. Investors are cautioned that they may lose all or a portion of their investment in this or any other company.

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