

A microscopic view of cancer cells, showing a network of red, fibrous structures and several large, spherical, reddish-brown cells. The background is a mix of blue and purple hues.

BEYOND
CANCER™

Next Level ImmuNO-oncology

November 2021

Forward Looking Statements

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Ultra-High Concentration Nitric Oxide (UNO) Overview



Differentiated MOA utilizing ultra-high concentration NO (>10,000 ppm) which has been shown to have properties that lead to tumor suppression and plays an active role in immune surveillance



Targeting solid tumors with innovative gaseous NO-based treatment that may treat solid tumors locally and their distant metastases systemically via stimulation of an anti-tumor immune response



Partnership with Beyond Air (Nasdaq: XAIR), which has a robust platform dedicated to the development of nitric oxide for multiple respiratory indications



Intellectual portfolio: 2 patents pending and 6 provisional patents submitted for oncology, which if issued would expire in 2040 and 2042 respectively



First in human trial enrollment starts in early 2022

Beyond Cancer Leadership Expertise in Emerging Healthcare Companies and Clinical Oncology



Bailard

TIGERGLOBAL



Selena Chaisson, MD
Chief Executive Officer of Beyond Cancer

Selena Chaisson joined Beyond Cancer in 2021 as Chief Executive Officer. Selena was most recently the Director of Healthcare Investments at Bailard where she managed a specialized, emerging healthcare opportunities fund for over 16 years. Prior to Bailard, she held senior executive roles at RCM Capital Management and Tiger Management. RCM Capital Management was acquired and then merged with Allianz Global Investors U.S. in 2013.

Selena received a BS in Microbiology in 1987 from Louisiana State University in Baton Rouge, LA, where she graduated Summa Cum Laude. She earned her MBA and MD from Stanford University in 1992 and 1993, respectively.



Hila Confino, Ph.D.
Chief Scientific Officer of Beyond Cancer

Hila Confino joined Beyond Cancer as Chief Scientific Officer from Beyond Air in 2021, where she served as Head of Research in Israel. At Beyond Air, Hila led the oncology preclinical team and conducted *in vitro* and *in vivo* studies for ultra-high concentration nitric oxide in solid tumors. Hila has over 12 years of experience in cancer immunology research in both the academic and industry settings. Her work has been featured in numerous scientific conferences and published in peer-reviewed journals.

She holds a Ph.D. and Master of Science in Cancer Immunology from Tel Aviv University. Hila received a BS in Biotechnology from Bar-Ilan University in Israel, where she graduated Cum Laude.

Board of Directors with Proven Business Record and Clinical Experience with Nitric Oxide



Steve Lisi
Chairman of the Board



- 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)



Selena Chaisson
CEO & Director



- 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



Amir Avniel
Executive Director



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



Robert Carey
Director



- 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

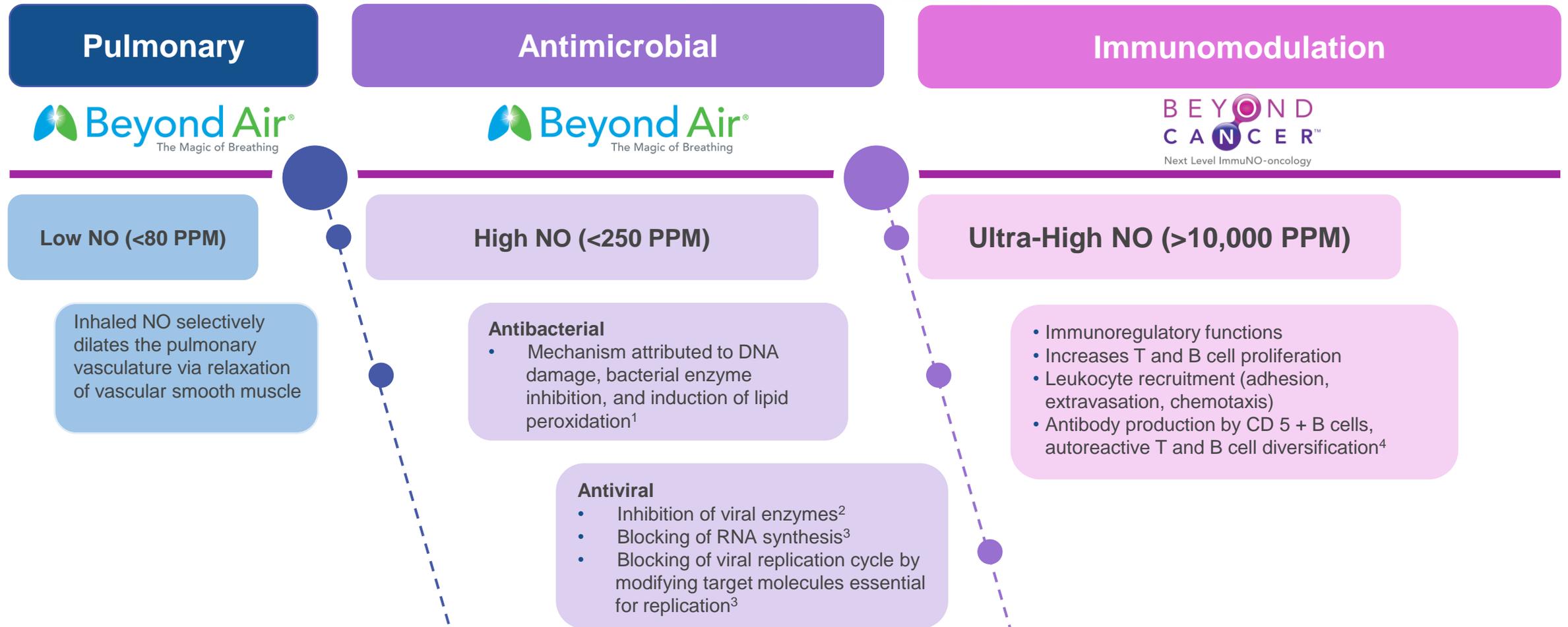
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The Role of Nitric Oxide (NO) in the Body

A microscopic view of cells and neurons, rendered in a purple and blue color scheme. The image shows a dense field of spherical cells, some with spiky protrusions, and a network of thin, branching structures resembling neurons or dendrites. The overall appearance is that of a complex biological tissue or a neural network.

Nitric Oxide Has Multiple Mechanisms of Action



1) 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.
 2) Saura, M., et al., An antiviral mechanism of nitric oxide: inhibition of a viral protease. Immunity, 1999. 10(1): p. 21-8
 3) Akerström S et al. Nitric oxide inhibits the replication cycle of severe acute respiratory syndrome coronavirus. J Virol. 2005; 79(3):1966-9
 4) Tripathi et al, FEMS Immunology and Medical Microbiology, December 2007

Low Concentration NO is the Established Standard of Care for PPHN and Some Cardiac Surgeries*

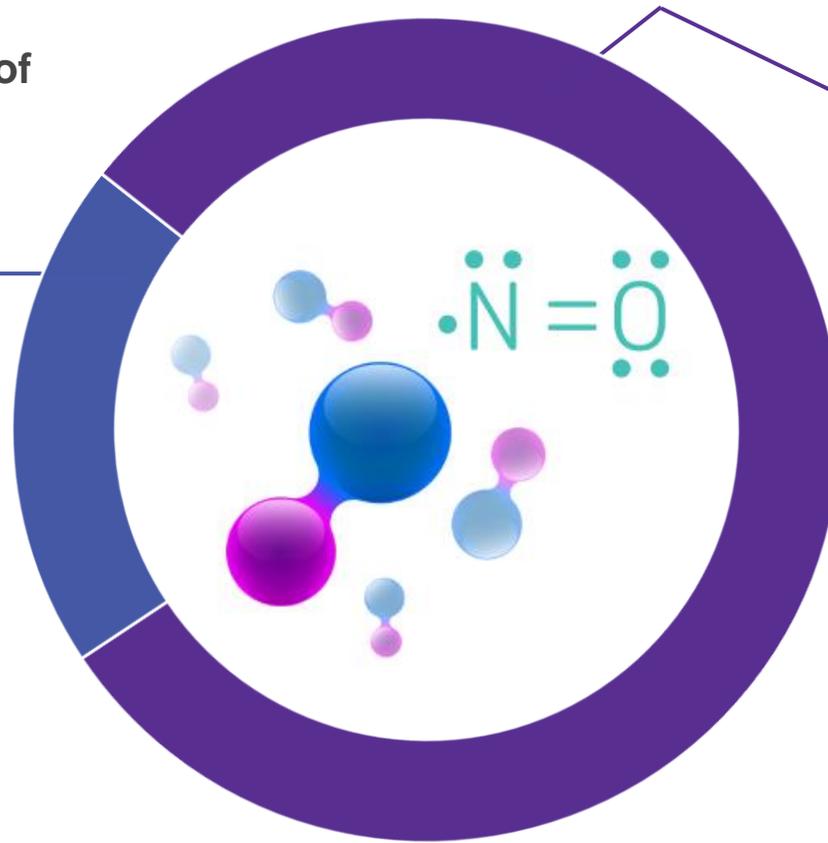
Low concentration inhaled NO causes smooth muscle relaxation, increasing blood flow to the lungs and decreasing right ventricular workload¹

PPHN – Persistent Pulmonary Hypertension of the Neonate²

- NO has been the approved standard of care for PPHN in the United States since 1999 and accounts for ~20% of sales
- In PPHN NO decreases right-to-left shunt through patent foramen ovale (PFO) and patent ductus arteriosus (PDA), dramatically improving oxygenation



†Caution - LungFit® is an Investigational Device, Limited by Federal (or United States) Law to Investigational Use.



Cardiac Surgery³

NO reversal of pulmonary hypertension reduces RV workload and improves cardiac output pre-, intra- and post-cardiac surgery

**not on label in the US, but off-label usage accounts for ~80% sales*



1) Inhaled Medical Gases: More to Breathe Than Oxygen, Michael A Gentile, Respiratory Care September 2011, 56 (9) 1341-1359

2) Persistent Pulmonary Hypertension of the Newborn, Satyan Lakshminrusimha and Martin Keszler, NeoReviews December 2015, 16 (12) e680-e692;

3) Left ventricular heart failure and pulmonary hypertension, October 2015, European Heart Journal 37(12)

High Concentration NO has Antimicrobial Properties*



PEDIATRIC PULMONOLOGY

ORIGINAL ARTICLE: RESPIRATORY INFECTIONS

Nitric oxide inhalations in bronchiolitis: A pilot, randomized, double-blinded, controlled trial

Asher Tal, David Greenberg, Yossef Av-Gay, Inbal Golan-Tripot, Yael Feinstein, Shalom Ben-Shimol, Ron Dagan, Aviv D. Goldbart

First published 27 November 2017 | <https://doi.org/10.1002/ppul.23905> | Citations: 1

SCIENTIFIC REPORTS

nature research

Inhaled nitric oxide therapy in acute bronchiolitis: A multicenter randomized clinical trial

Aviv Goldbart^{1,2}, Inbal Golan-Tripot¹, Giora Pillar¹, Galit Livnat-Levanon¹, Ori Efrati¹, Ronen Spiegel¹, Ronit Lubetzky¹, Moran Lavie¹, Lior Carmon¹ & Amit Nahum¹

JOURNAL OF VIROLOGY, Feb. 2005, p. 1966-1969
0022-538X/05/081966-04 doi:10.1128/JVI.79.3.1966-1969.2005
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Nitric Oxide Inhibits the Replication Cycle of Severe Acute Respiratory Syndrome Coronavirus

Sara Åkerström,¹ Mehrdad Mousavi-Jazi,² Jonas Klingström,^{1,3} Mikael Leijon,² Åke Lundkvist,^{1,3} and Ali Mirzazimi^{1,3}

Center for Microbiological Preparations, Swedish Institute for Infectious Disease Control, Solna,¹ LightUp Technologies, Huddinge,² and MTC/Karolinska Institute, Stockholm,³ Sweden

Received 13 May 2004/Accepted 16 September 2004

Nitric oxide (NO) is an important signaling molecule between cells which has been shown to have an inhibitory effect on some virus infections. The purpose of this study was to examine whether NO inhibits the replication cycle of the severe acute respiratory syndrome coronavirus (SARS-CoV) in vitro. We found that an organic NO donor, S-nitroso-N-acetylpenicillamine, significantly inhibited the replication cycle of SARS-CoV in a concentration-dependent manner. We also show here that NO inhibits viral protein and RNA synthesis. Furthermore, we demonstrate that NO generated by inducible nitric oxide synthase, an enzyme that produces NO, inhibits the SARS-CoV replication cycle.

Antiviral – multiple publications show that high concentration NO has antiviral activity, demonstrating a reduction in length of hospital stay in bronchiolitis, and inhibiting the SARS coronavirus replication cycle

Antibacterial – high concentration NO (up to 250 ppm) has bactericidal effects *in vitro*

NO activity against multi-drug resistant *M. abscessus*¹ with continuous or intermittent exposure

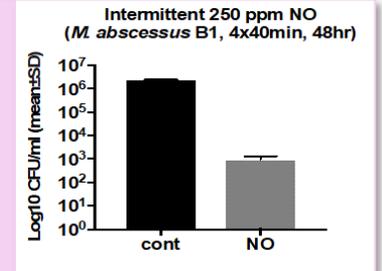
NO has broad-spectrum activity against multiple bacteria at 200 ppm² including *Pseudomonas*, *Staphylococcus*, *E. coli*, and MRSA, and others

EUROPEAN RESPIRATORY journal
FLAGSHIP SCIENTIFIC JOURNAL OF ERS

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A phase-III multicenter, randomized, double-blind, controlled trial of high-dose inhaled nitric oxide in infants with acute bronchiolitis.

Aviv Goldbart, Inbal Golan-Tripot, Giora Pillar, Galit Livnat-Levanon, Ori Efrati, Ronen Spiegel, Ronit Lubetzky, Moran Lavie, Lior Carmon, Mark Mizel, Amit Nahum
European Respiratory Journal 2018; 52: P4642. DOI: 10.1183/13993003.congr-2018.P4642



High-Dose Inhaled Nitric Oxide as a Potential Therapy Against Mycobacterium Abscessus Lung Infection in Cystic Fibrosis

Authors: Kristijan Bogdanovski¹; Abdi A. Ghaffari, PhD²; Kenneth N. Olivier, MD, MPH³; Joas L. da Silva, PhD¹; Adrian M. Zelazny, PhD¹

¹National Heart, Lung and Blood Institute, NIH, Bethesda, MD; ²AIT Therapeutics Harrison, NY; ³NIH Clinical Center, Bethesda, MD

Background:

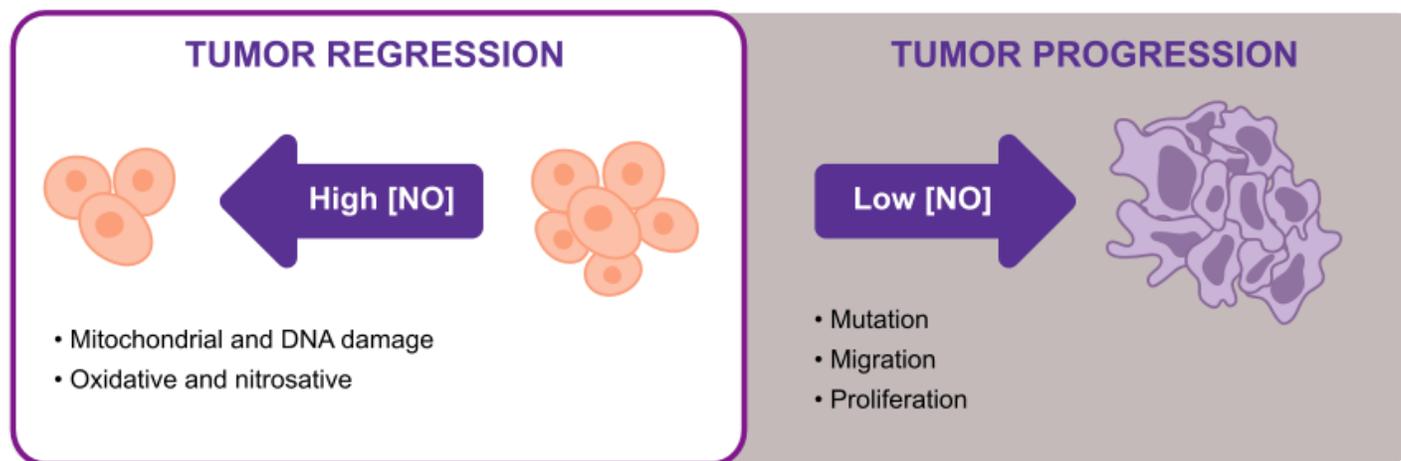
Mycobacterium abscessus (MAB) is an emerging, multidrug-resistant (MDR) nontuberculous mycobacterium (NTM) with limited treatment options. Exogenous high-dose nitric oxide (NO) has anti-bacterial activity against a broad-spectrum of bacterial species, including Mycobacterium smegmatis. In this study, we investigate whether high-dose NO exhibits antibacterial activity against MDR MAB strains in vitro.

*data generated by Beyond Air

1) Data presented at 3rd World Bronchiectasis Conference (2018)

2) Ghaffari et al., Potential application of gaseous nitric oxide as a topical antimicrobial agent. Nitric Oxide 14: 21-9, 2006.

Ultra-High Concentration Nitric Oxide (UNO) is Necessary for Solid Tumor Regression



The use of NO for cancer treatment can only be achieved by the delivery of **ultra-high concentrations (>10,000 ppm)** directly to the tumor. At these concentrations NO has demonstrated anticancer and immunogenic properties. Based on this, Beyond Air had been developing treatment protocols using **ultra-high nitric oxide to ablate primary tumors and treat metastatic disease**. A substantial amount of therapeutic focus in oncology has been dedicated to halting cancer growth. However, metastatic disease is responsible for 90% of deaths from solid tumors, hence there is a large **unmet medical need for the prevention and suppression of it**, which ultra high concentration NO could address.

Beyond Cancer Pipeline

Program	Initial Indication	Discovery	IND-Enabling	Clinical Development	Next Milestone
Monotherapy					
UNO	Surface level tumors				Begin Phase Ia Enrollment 1H22
UNO	Multiple solid tumors				Ongoing development
Combination Therapy					
UNO _{PLUS}	PD-1 sensitive tumors				Ongoing development
UNO _{PLUS}	Multiple solid tumors				Ongoing discovery

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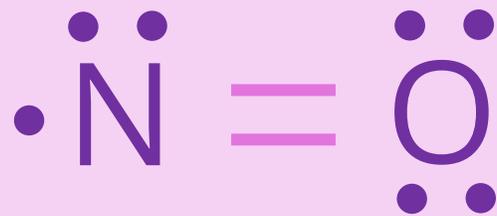
Preclinical Data for Nitric Oxide in Solid
Tumors

Nitric Oxide is a Powerful Anti-Cancer Agent

NO has shown anticancer properties at ultra-high concentrations by activating the immune system

Our data suggest that our innovative gaseous NO-based treatment may treat solid tumors locally and their distant metastases systemically via stimulation of an anti-tumor immune response

Hypothesis: Exogenous ultra-high concentration NO (UNO; >10,000 ppm) administered directly to a solid tumor may cause local cell death resulting in systemic exposure to tumor antigens. Tumor antigens may trigger a systemic immune response, thereby creating a memory immune bank that will recognize and attack subsequent primary tumor regrowth as well as distal metastases.



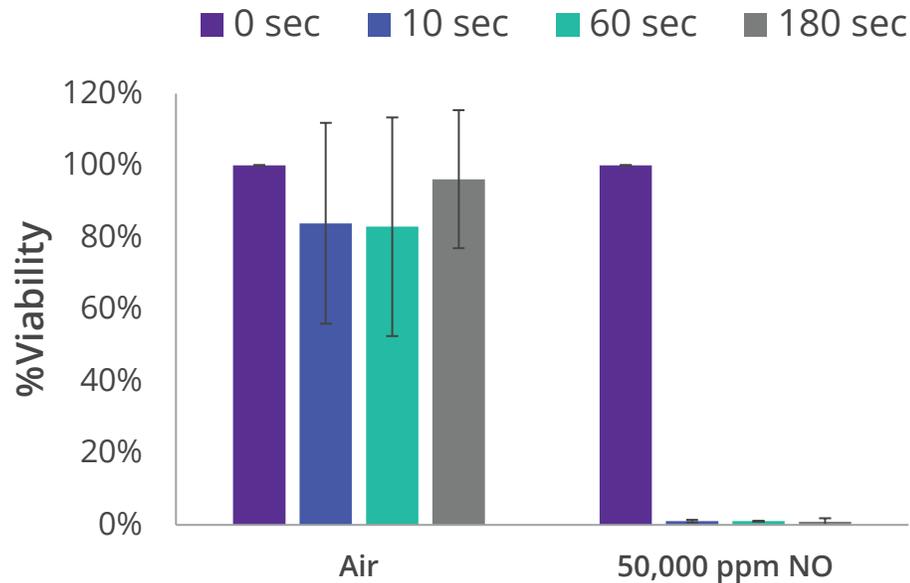
Nitric Oxide



- Tumor regression
- Oxidative and nitrosative stress
- Mitochondrial and DNA damage

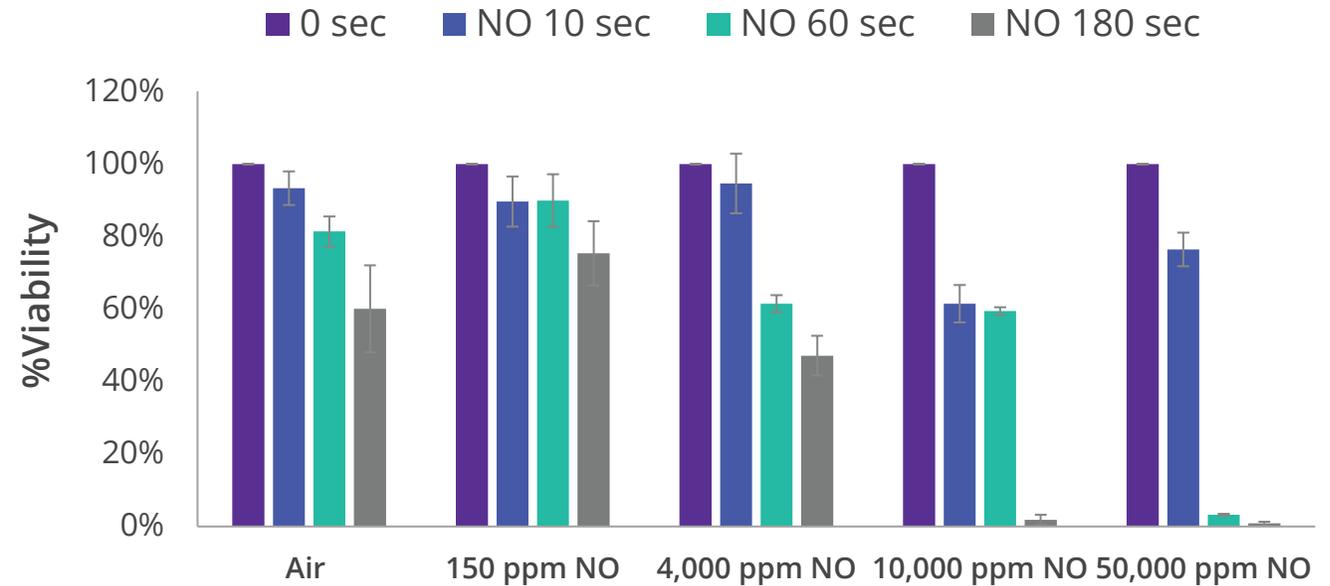
NO Shows a Cytotoxic Effect on Colon and Breast Cancer Cells *In Vitro*

Colon Cancer Cells



Significant reduction in the viability of mouse colon cancer cells after exposure to 50,000 ppm NO vs. air for 10-180 seconds.

Breast Cancer Cells

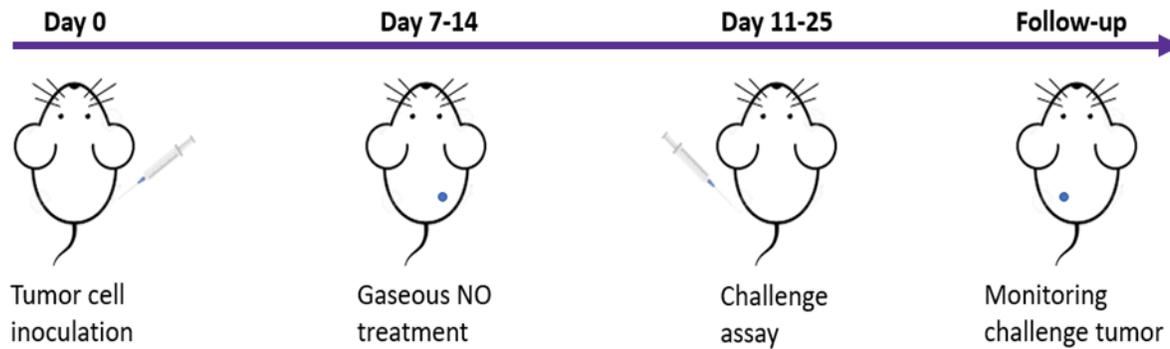


Significant time-dependent reductions in viability of mouse breast cancer cells after exposure to 150- 50,000 ppm NO vs. air for 10-180 seconds.

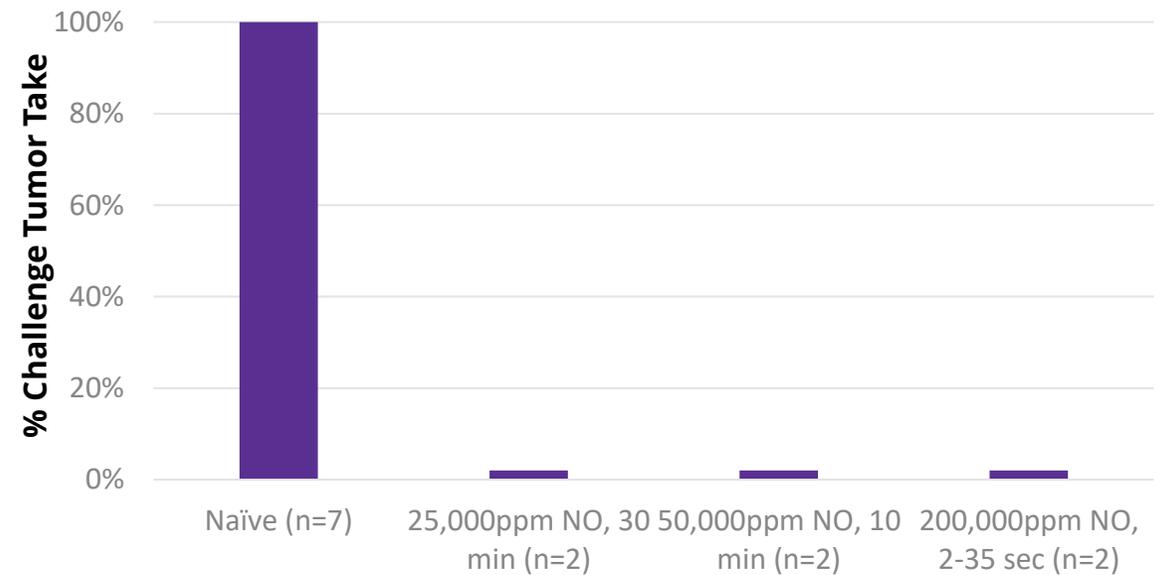
Data presented at the American Association for Cancer Research (AACR) June 22, 2020 via virtual AACR

Findings from In Vivo Murine Colon Cancer Model Are Consistent with Previous Data

In vivo results showed that all treated colon tumor-bearing mice were resistant to a second CT26 cancer cell inoculation in a contralateral tumor challenge model

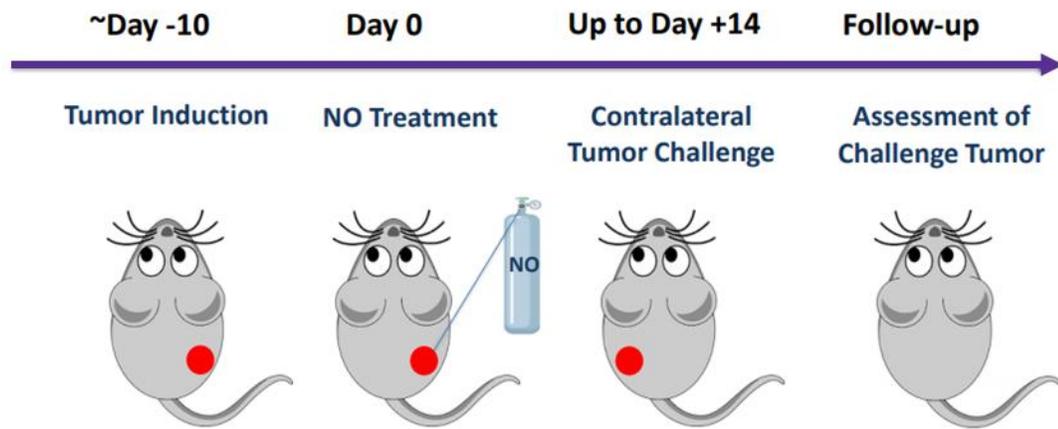


Challenge assay: The tumors of colon cancer tumor-bearing mice were treated with NO. Up to 14 days post NO treatment, mice were re-inoculated with second ("challenge") colon cancer cells (CT26 cells) and the percentage of tumor take was monitored.

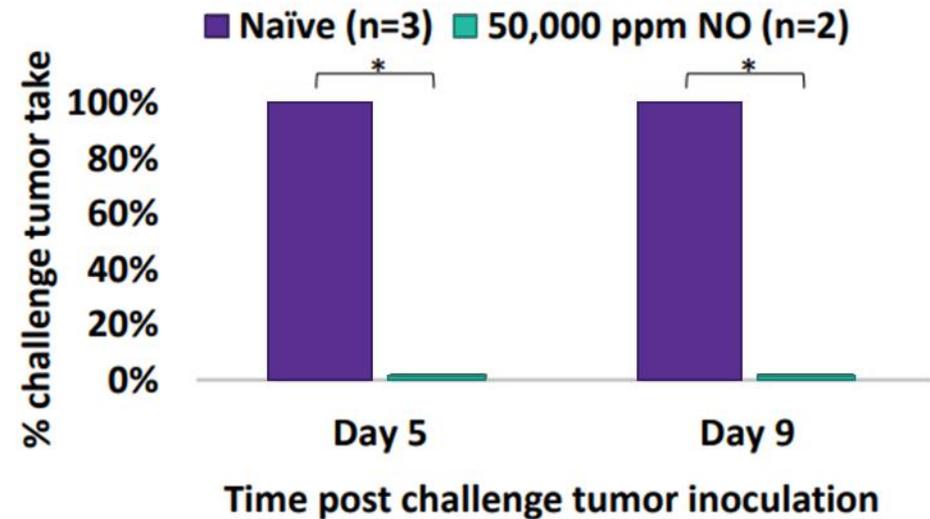


Exogenous UNO Stimulates an Anti-Tumor Immune Response in Murine Lung Cancer Model

In vivo results showed that lung tumor-bearing mice treated with 50,000 ppm NO for 10 minutes were resistant to a second LLC1 cancer cell inoculation



Challenge assay: The tumors of lung cancer tumor-bearing mice were treated with NO. Up to 14 days post NO treatment, mice were re-inoculated with lung cancer cells (LLC1 cells) and the percentage of tumor take was monitored.

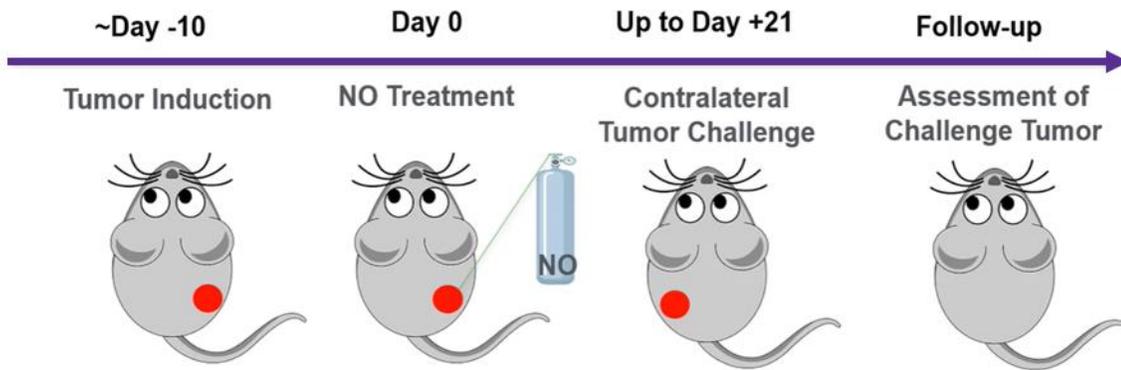


* P-value (chi-square) <0.05

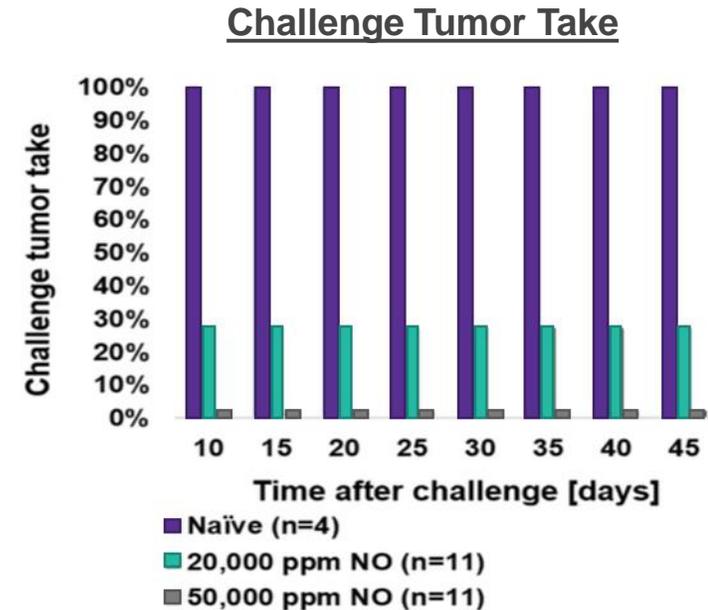
Treatment: 50,000 ppm NO for 10 minutes

Effects of UNO on CT26 Cells In Vivo Showed Evidence of Dose-Dependent Effects on Challenge Tumor Take

Dose-dependent effects of primary tumor treatment on challenge tumor growth and tumor take were observed in CT26 tumor-bearing mice treated with 20,000 or 50,000 ppm NO



Challenge assay: CT26 study mice were treated with either 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 the percentage of tumor take was monitored.



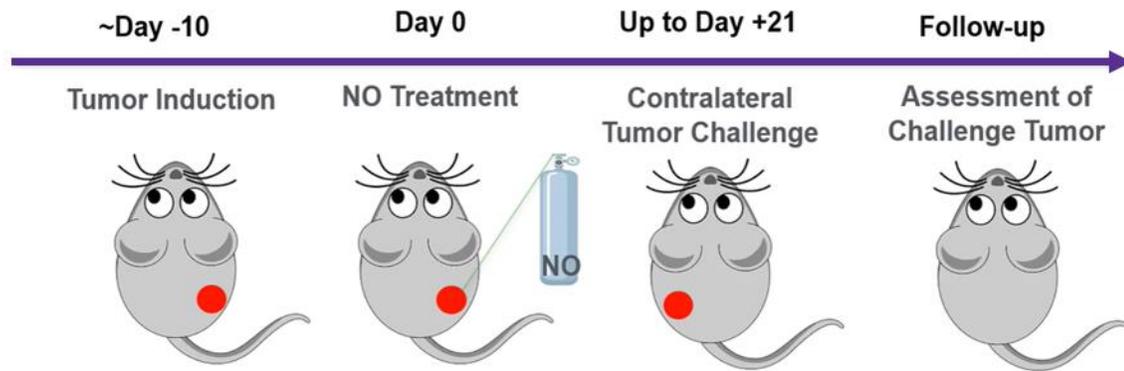
Results:

- At day 45, challenge tumor uptake was observed in 100% of naïve mice, 27% of 20,000 ppm NO mice, and 0% of 50,000 ppm NO mice, suggesting dose-dependence

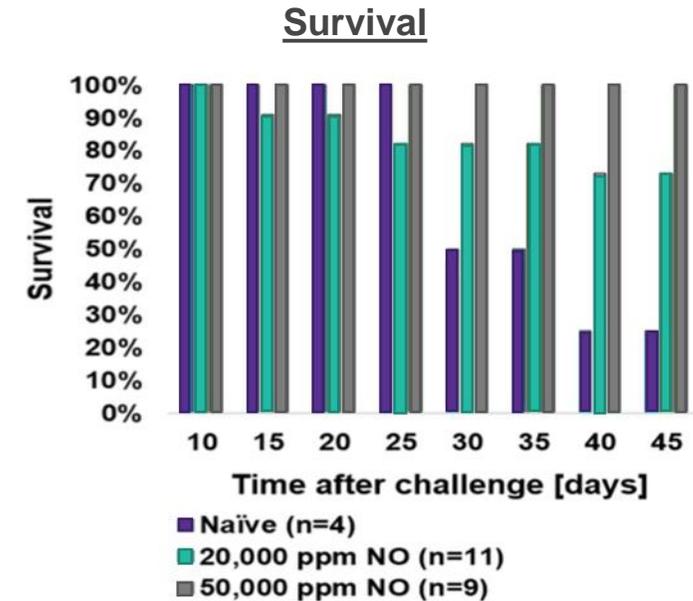
Effects of UNO on CT26 Challenge Tumors In Vivo

Showed Evidence of Dose-Dependent Effects on Survival

Dose-dependent effects of primary tumor treatment on survival was observed in CT26 tumor-bearing mice treated with 20,000 or 50,000 ppm NO



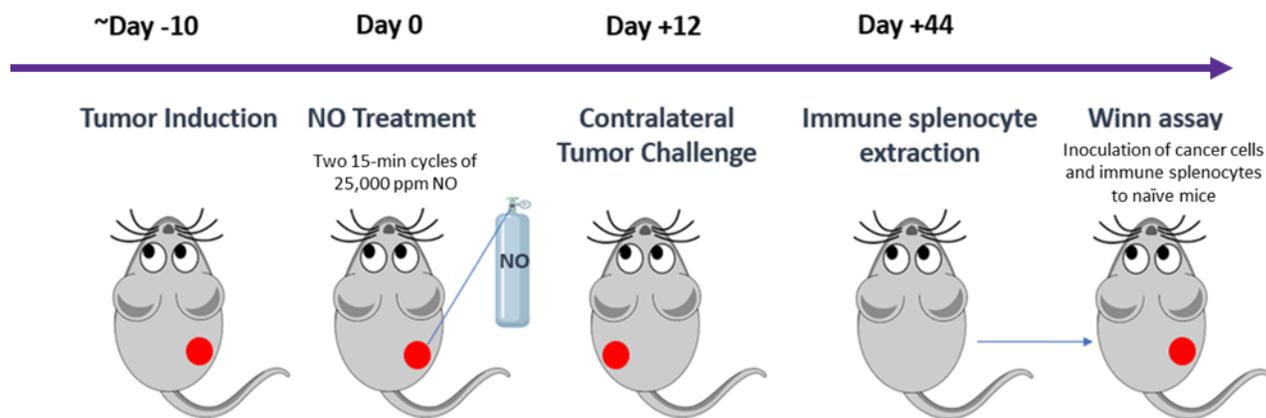
Challenge assay: CT26 study mice were treated with either 20,000 or 50,000 ppm NO for 5 minutes. Naïve mice inoculated with the same cancer cells served as an internal control. Up to 21 days post NO treatment, all mice were re-inoculated with colon cancer cells (CT26 cells) as a challenge tumor and survival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



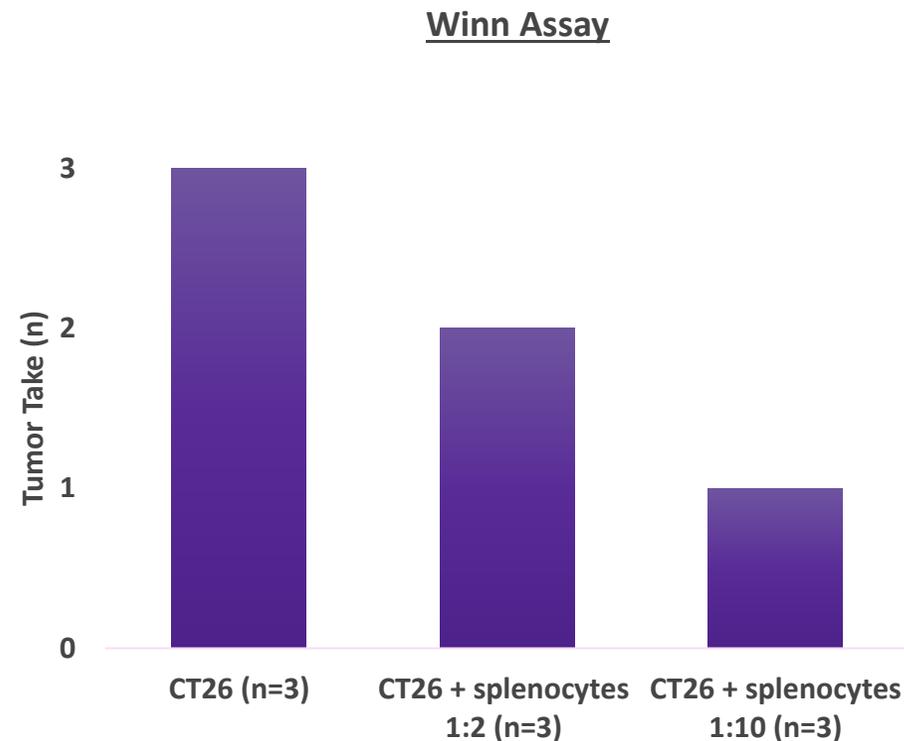
Results:

- At day 45, 25% of naïve mice, 73% of 20,000 ppm NO mice and 100% of 50,000 ppm NO mice were alive

Effects of UNO on Mouse CT26 Tumors with the Winn Assay (Splenocyte Inoculation)

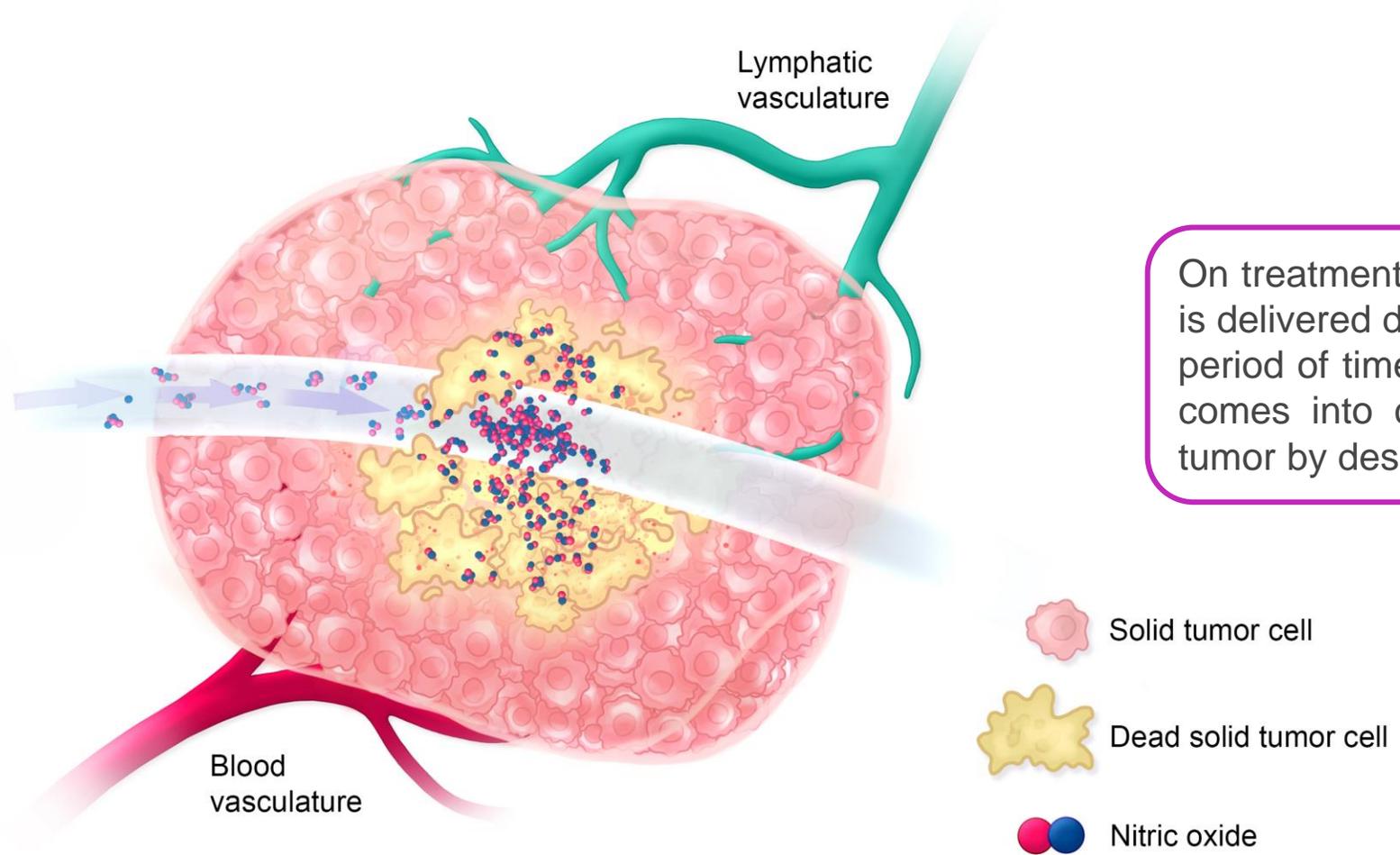


- Immune splenocytes extracted from an NO-treated CT26 tumor-bearing mouse were inoculated along with CT26 cells to naïve mice, resulting in a trend toward “splenocyte dose-dependent” reduction in tumor take.



Data presented at the AACR Annual Meeting, June 2020
Data were included in the background slides presented at the AACR meeting on Tumor Immunology and Immunotherapy, October 2020

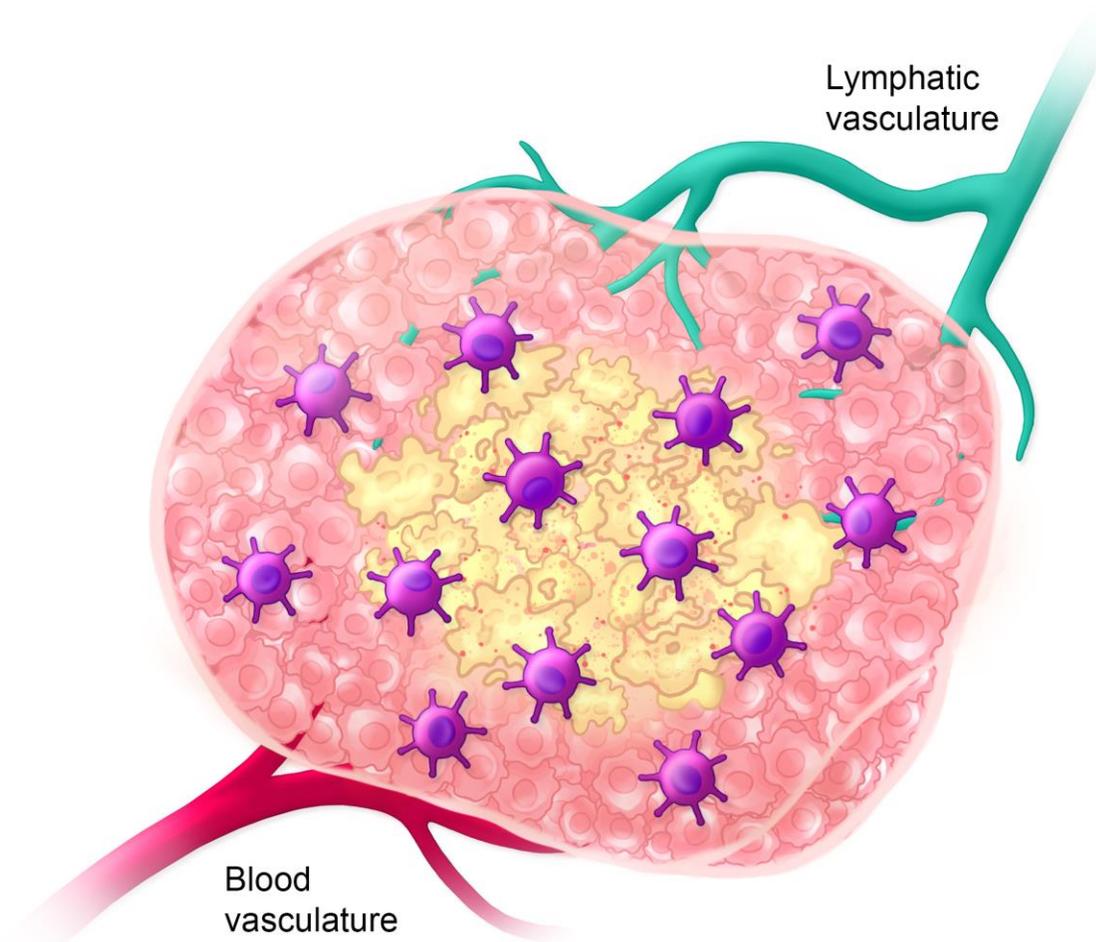
Mechanism of Action: Treatment Received Day 0



On treatment day ultra-high concentration nitric oxide is delivered directly into a large solid tumor for a short period of time to allow for the killing of all cells that it comes into contact with, only partially ablating the tumor by design.

Mechanism of Action: Estimated Timeline Day 0-5

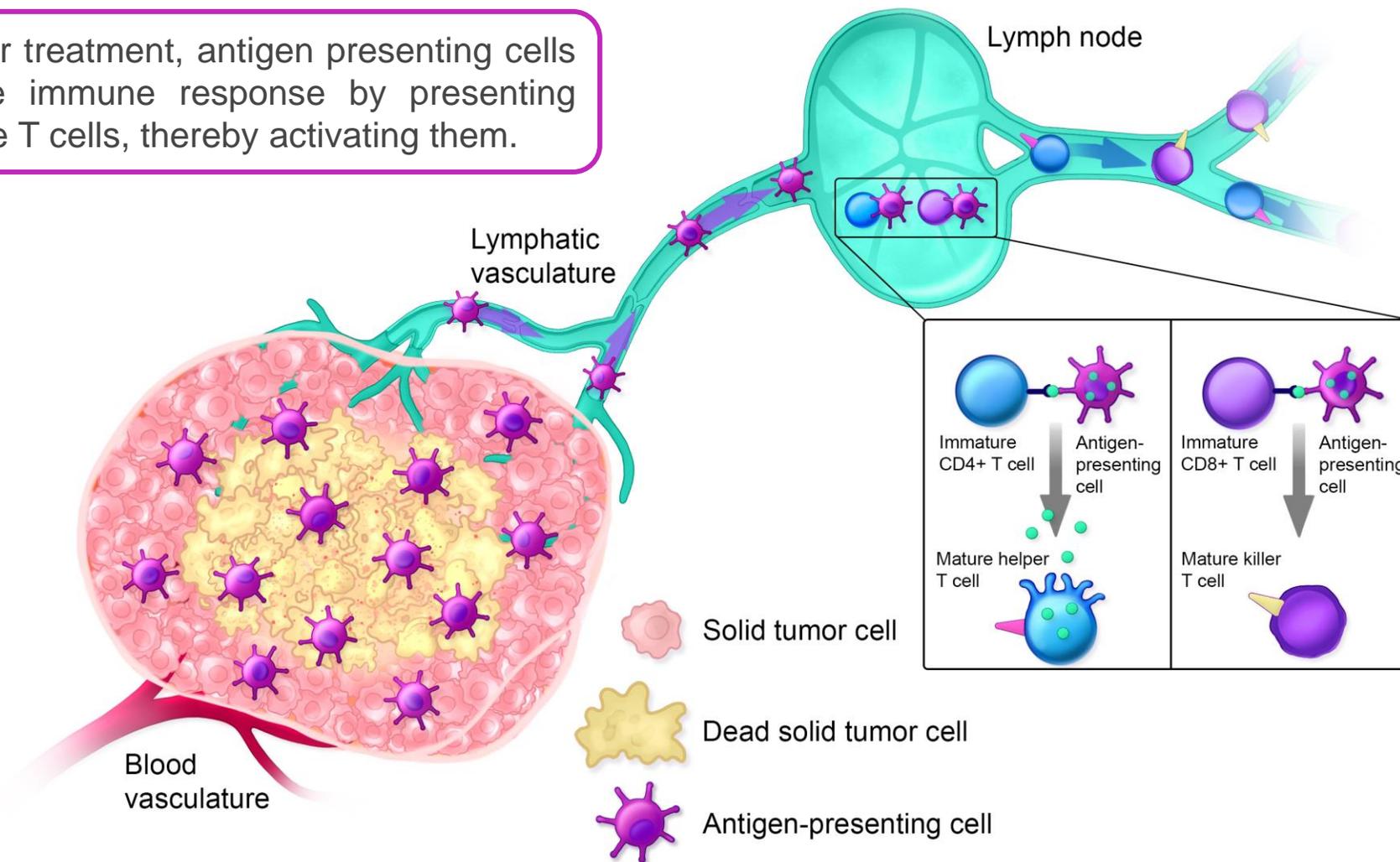
Within 5 days after treatment with ultra-high concentration nitric oxide, antigen presenting immune cells invade the tumor environment, detecting and engulfing dead solid tumor cells.



-  Solid tumor cell
-  Dead solid tumor cell
-  Antigen-presenting cell

Mechanism of Action: Estimated Timeline Day 5-14

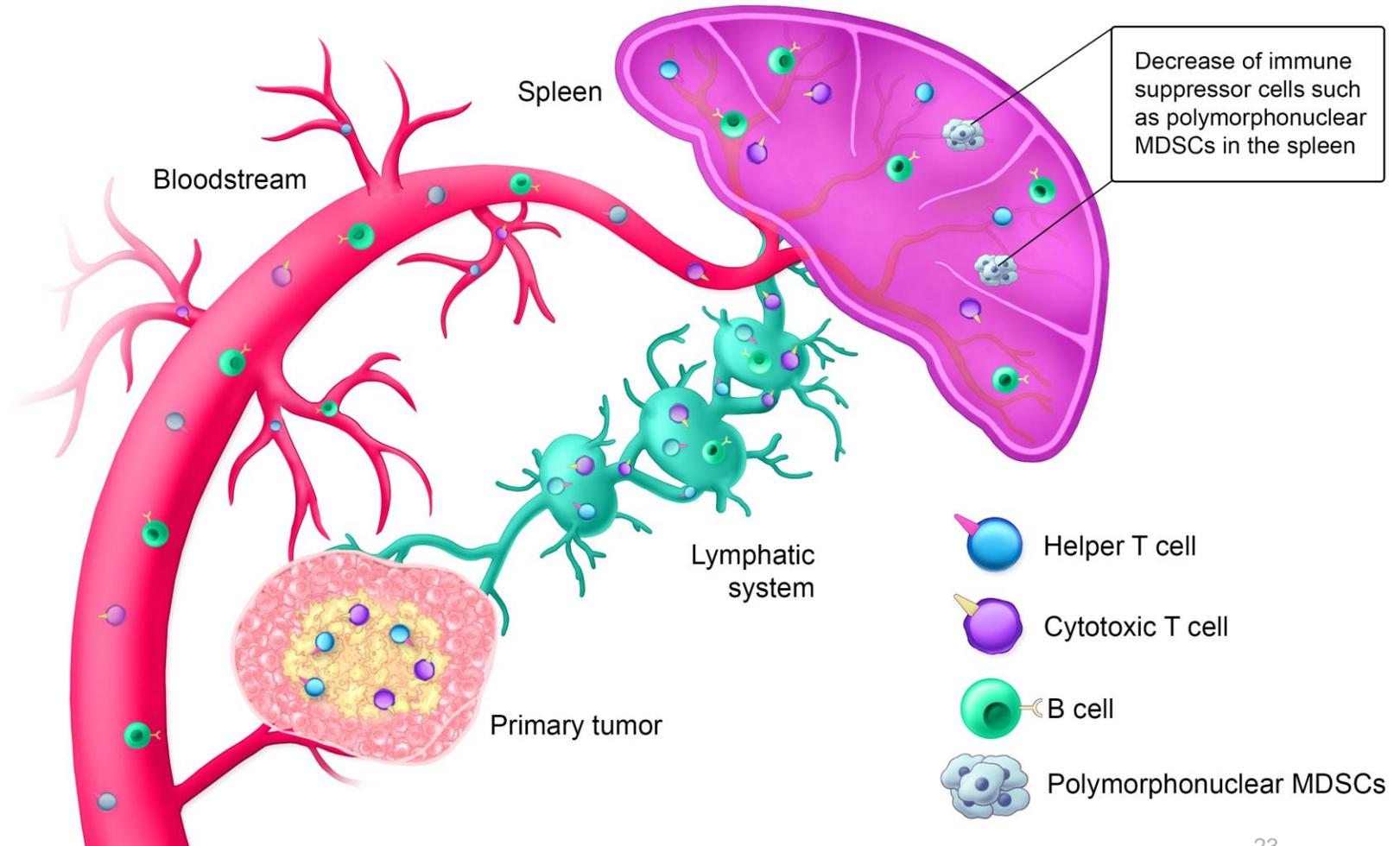
On days 5 – 14 after treatment, antigen presenting cells inform the adaptive immune response by presenting antigens to immature T cells, thereby activating them.



Mechanism of Action: Estimated Timeline Day 14+

Approximately 14+ days after treatment the innate immune system is activated with helper T cells, cytotoxic T cells and B cells circulating in the blood stream and lymphatic system armed against the specific solid tumor type.

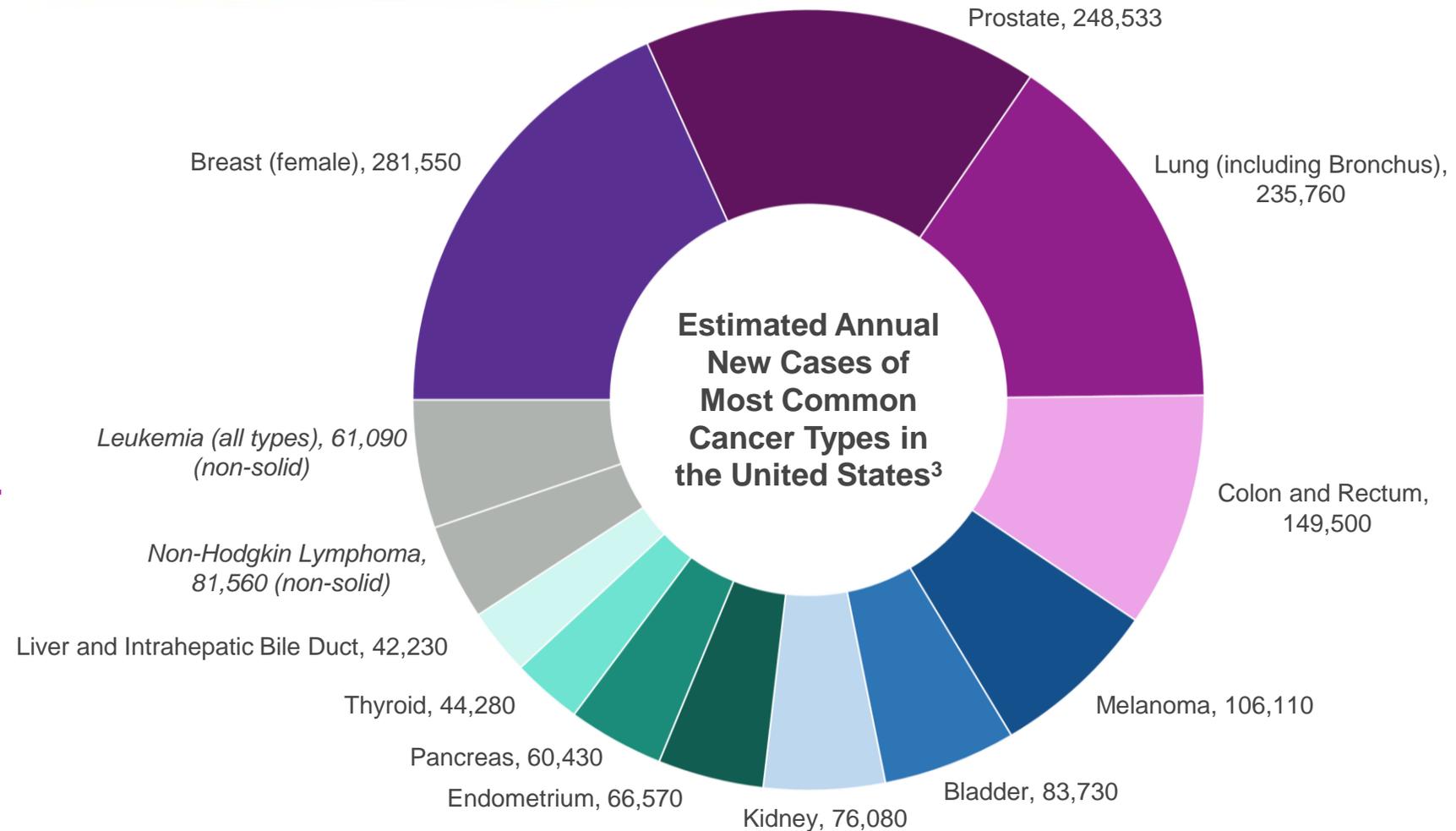
Additionally, polymorphonuclear MDSCs, which suppress the immune system when tumors are present, are decreased in the spleen.



Project UNO Will Target Patients with Solid Tumors

Solid Tumors represent approximately 90% of adult human cancers¹, accounting for approximately 1.4 million annual new cases of most common cancer types in the United States³

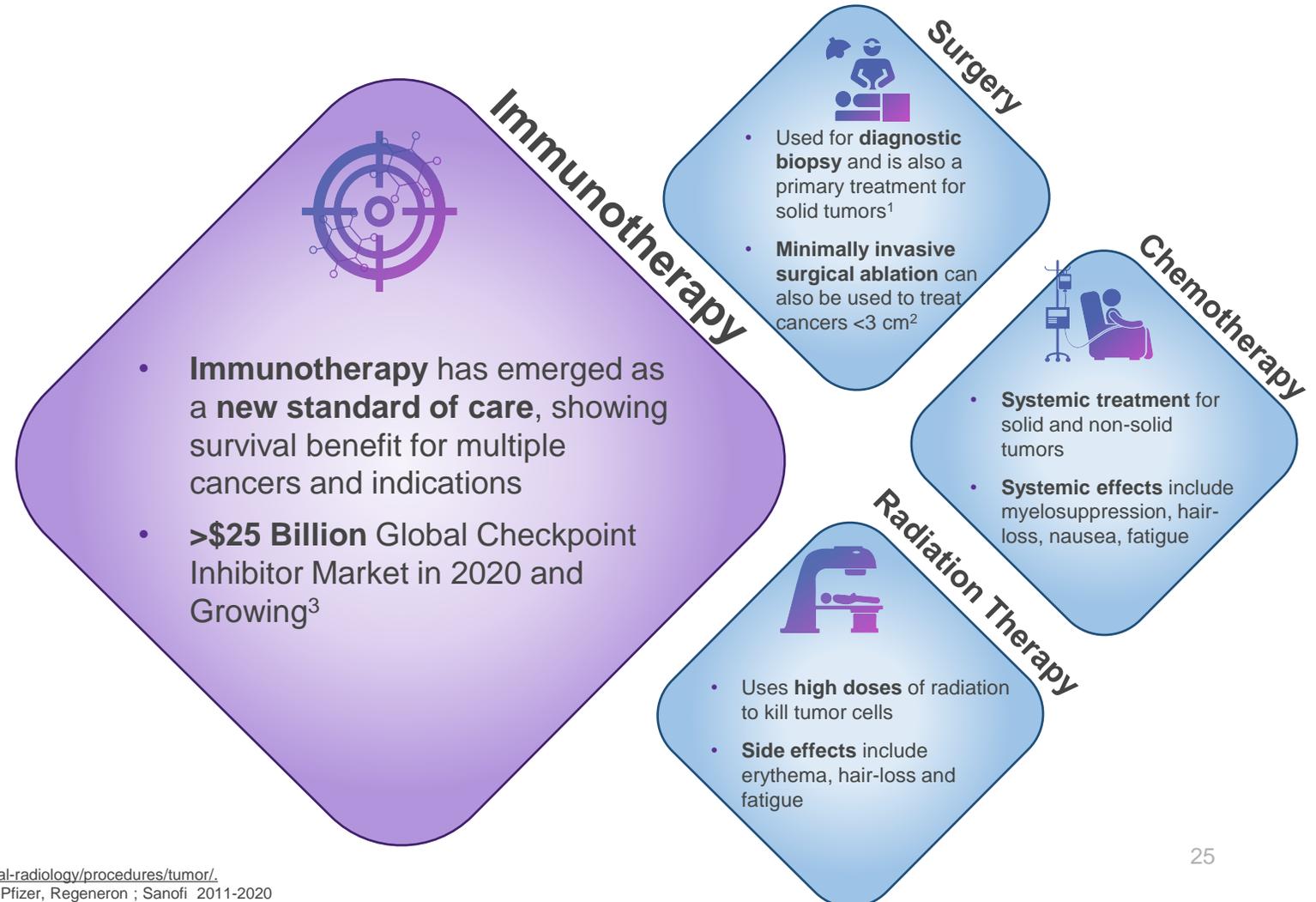
Metastatic Disease is responsible for 90% of solid tumor deaths²



1) 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/>
 2) 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
 3) According to the National Cancer Institute: <https://www.cancer.gov/types/common-cancers>

Current Standard of Care for Treatment of Solid Tumors

Treatment for solid tumors combines several types of treatment and is dependent on tumor type, size, and location



1) St. Jude Research Hospital Solid Tumor Treatment Process Overview
 2) Molnar, Heather. "Tumor Ablation." Tumor Ablation, 19 Aug. 2019, www.hopkinsmedicine.org/interventional-radiology/procedures/tumor/.
 3) Company Presentations and Regulatory Filings from Bristol-Myers Squibb, Merck, Roche, AstraZeneca, Pfizer, Regeneron; Sanofi 2011-2020

UNO has the Potential to be an Entirely New Modality in the Immuno-oncology Market

>\$25 Billion Checkpoint Inhibitor Market in 2020 and Growing

Company	Drug Name	First FDA Approval	2020 Revenue
Bristol-Myers Squibb	Yervoy	March 2011	\$1.7 Billion
Merck	Keytruda	Sept 2014	\$11.4 Billion
Bristol-Myers Squibb	Opdivo	Dec 2014	\$7.0 Billion
Roche	Tecentriq	May 2016	\$3.0 Billion
AstraZeneca	Imfinzi	May 2017	\$2.0 Billion

Next Steps for Beyond Cancer

Timing	Milestone
2021	<ul style="list-style-type: none">• Complete Mezzanine Financing of up to \$30 million – \$23.9 million committed as of 11/4/2021• Complete IND-enabling Studies• Build/Expand Beyond Cancer Team
2022	<ul style="list-style-type: none">• Initiate Enrollment in Phase Ia Study• Conduct Preclinical Combination Therapy Studies with Checkpoint Inhibitors• Present Additional Preclinical Data at Major Medical Meeting• Publication of Preclinical Manuscript in Major Scientific Journal• Build/Expand Beyond Cancer Team• Initiate Phase Ib Study• Present Initial Phase 1a Data• IPO

Contact



Investor Relations

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