



# Investor Presentation

February 2022

# Forward-Looking Statements

This presentation contains forward-looking statements, within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended and forward-looking information under applicable Canadian securities laws (such forward-looking statements and forward-looking information are collectively referred to herein as "forward-looking statements"). Forward-looking statements contained in this presentation include statements regarding Oncolytics' belief as to the potential and benefits of pelareorep as a cancer therapeutic; Oncolytics' expectations as to the purpose, design, outcomes and benefits of its current or pending clinical trials involving pelareorep; pelareorep's potential synergies with ICIs and beliefs regarding the size and growth of the ICI market; plans respecting the delivery of additional clinical data and the timing thereof; the potential commercial opportunity of pelareorep; Oncolytics' expectations for its various partnerships and collaborations; Oncolytics' anticipated milestones and catalysts; Oncolytics' objectives, including registration opportunities; and other statements related to anticipated developments in Oncolytics' business and technologies. In any forward-looking statement in which Oncolytics expresses an expectation or belief as to future results, such expectations or beliefs are expressed in good faith and are believed to have a reasonable basis, but there can be no assurance that the statement or expectation or belief will be achieved. Such forward-looking statements involve known and unknown risks and uncertainties, which could cause Oncolytics' actual results to differ materially from those in the forward-looking statements. Such risks and uncertainties include, among others, the availability of funds and resources to pursue research and development projects, the efficacy of pelareorep as a cancer treatment, the success and timely completion of clinical studies and trials, Oncolytics' ability to successfully commercialize pelareorep, uncertainties related to the research and development of pharmaceuticals, uncertainties related to the regulatory process and general changes to the economic environment. In particular, we may be impacted by business interruptions resulting from COVID-19 coronavirus, including operating, manufacturing supply chain, clinical trial and project development delays and disruptions, labour shortages, travel and shipping disruption, and shutdowns (including as a result of government regulation and prevention measures). It is unknown whether and how Oncolytics may be affected if the COVID-19 pandemic persists for an extended period of time. We may incur expenses or delays relating to such events outside of our control, which could have a material adverse impact on our business, operating results and financial condition. Investors should consult Oncolytics' quarterly and annual filings with the Canadian and U.S. securities commissions for additional information on risks and uncertainties relating to the forward-looking statements. Investors are cautioned against placing undue reliance on forward-looking statements. The Company does not undertake to update these forward-looking statements, except as required by applicable laws.

Our goal is to improve patient survival by developing **pelareorep**, an intravenously-delivered immunotherapy that makes tumors more susceptible to a broad range of oncology treatments

Exchanges	Nasdaq: ONCY / TSX: ONC
Market Cap.	\$108M
Cash & Equivalents	CDN \$48M (USD \$38M) <i>Based on FX as of Nov. 22, 2021</i>
Shares Outstanding	55,027,123
Fully Diluted	61,672,906
Cash Runway	Q1 2023
HQ	San Diego, CA, US Calgary, AB, Canada

**First-in-class Asset. Strong Clinical Data. Large Market Opportunity. World-class Collaborators.**



**Pelareorep: Immunotherapeutic agent that generates an anti-tumor immune response**

Generates and trains anti-cancer immune cells and reverses immunosuppressive TMEs



**Randomized Phase 2 data show stat. sig. near doubling of OS in HR+/HER2- breast cancer**

Data support lead breast cancer program and de-risk trials in gastrointestinal and hematological cancers



**Clinically demonstrated ability to synergize with immune checkpoint inhibitors (ICIs)**

ICI market expected to exceed \$55B by 2025 despite as few as 1 in 5 patients responding to ICI therapy



**Data from randomized Phase 2 pelareorep-ICI combo trial in HR+/HER2- breast cancer expected in 2022**

Upcoming catalyst is expected to facilitate pelareorep's advancement to a registrational study



**Established collaborations with industry leaders evaluate pelareorep-ICI combinations**

Clinical collaborators include Pfizer, Merck Serono, Roche, Incyte, and Bristol-Myers Squibb

# Pelareorep Treatment Led to a Statistically Significant Improvement in OS in a Phase 2 Breast Cancer Trial

## Phase 2 All Subtypes (n = 74)

HR 0.65

p 0.1 (powered to 90%)

mOS 10.4 months vs. 17.4 months

Test n = 36

Control n = 38

## HR+/HER2- Patients (n = 57)

HR 0.60

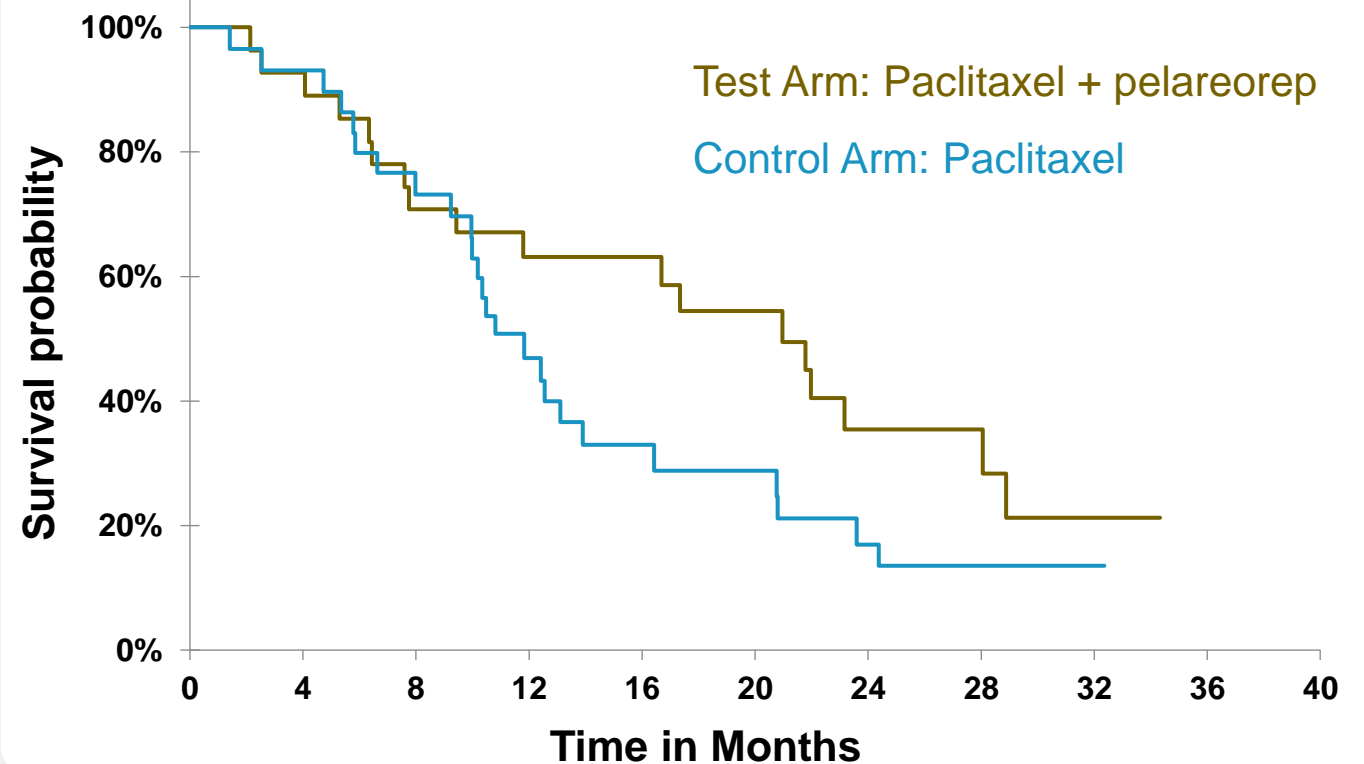
p 0.1 (powered to 90%)

mOS 10.8 mos vs 21.0 mos

Test n = 28

Control n = 29

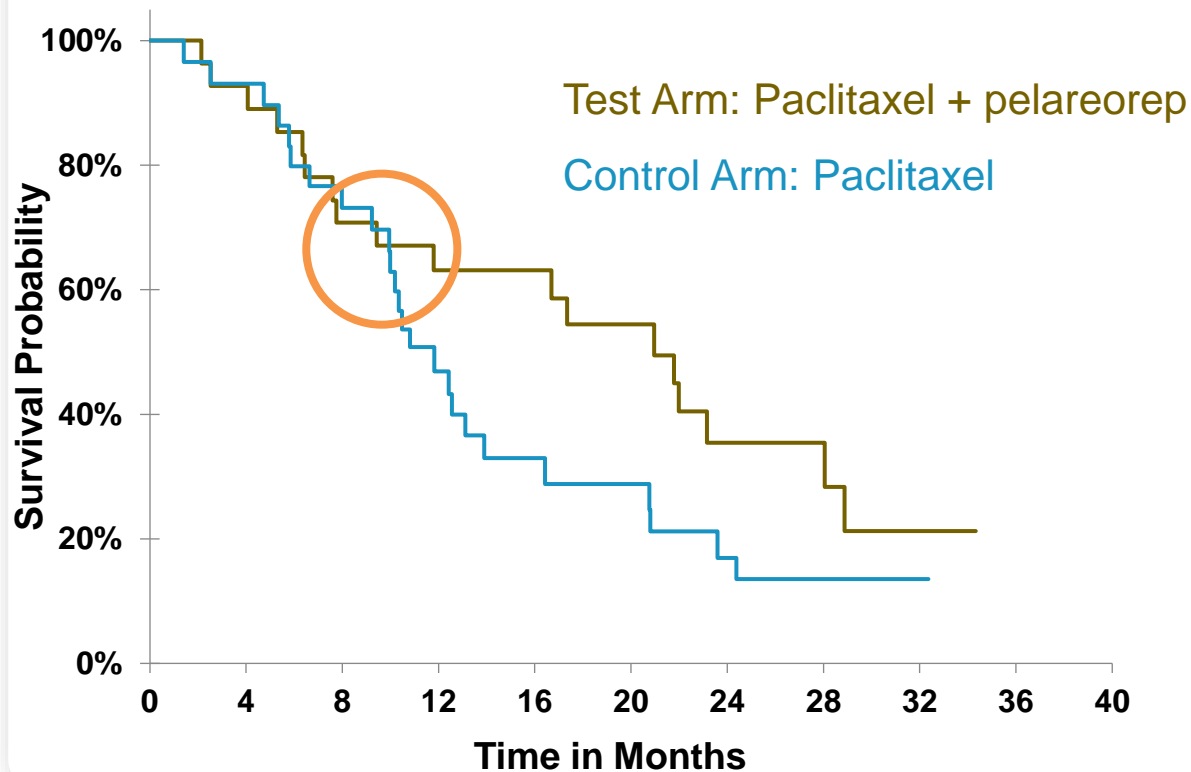
## Overall survival for the HR+/HER2- patients in IND-213 study of metastatic breast cancer (n = 57)



Near doubling of OS in HR+/HER2- patients with pelareorep treatment

# Phase 2 Data Provided POC and Posed Two Key Questions For Regulators and Partners

## Survival Benefit Becomes Apparent After Approximately 10 Months



## Questions on the Path to Registration

### What is pelareorep's mechanism of action?

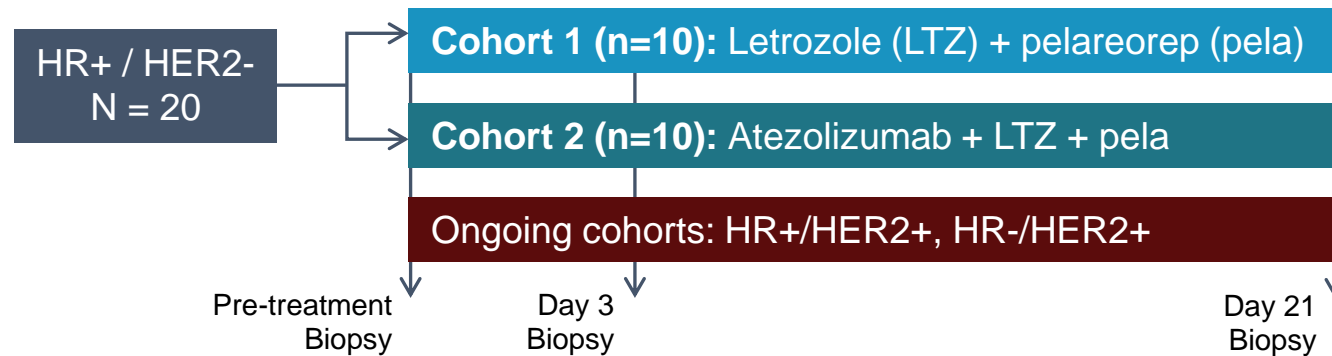
Delayed survival benefit suggested pelareorep's anti-cancer activity was derived from an immunotherapeutic MOA rather than from virus-mediated tumor lysis

### Can efficacy be enhanced by adding an ICI?

This question was top-of-mind for large pharma collaborators and is a driving force behind our business development efforts

# Clinical Data Confirm Pelareorep's Immunotherapeutic Mechanism of Action in HR+/HER2- Breast Cancer

## AWARE-1 Window-of-opportunity Study Design

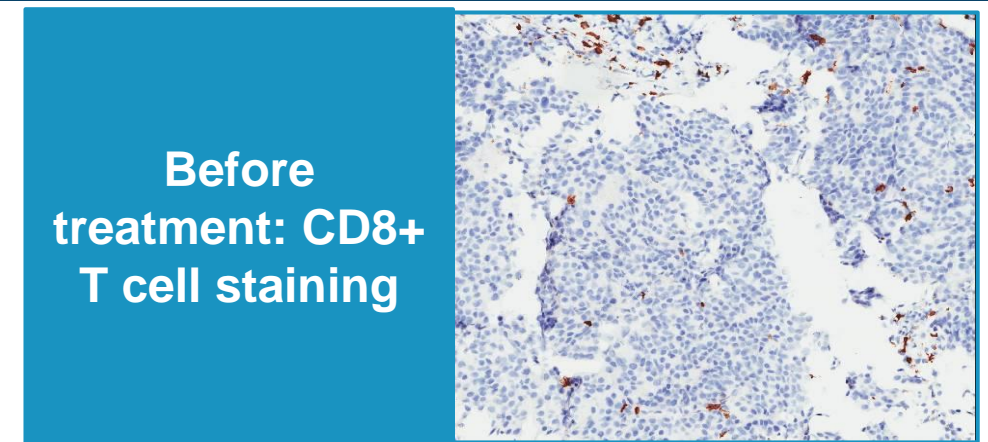


**Objective:** Confirm pela's MOA and potential to synergize with ICIs via biomarker measurements such as CelTIL score, T cell infiltration and PD-L1 expression

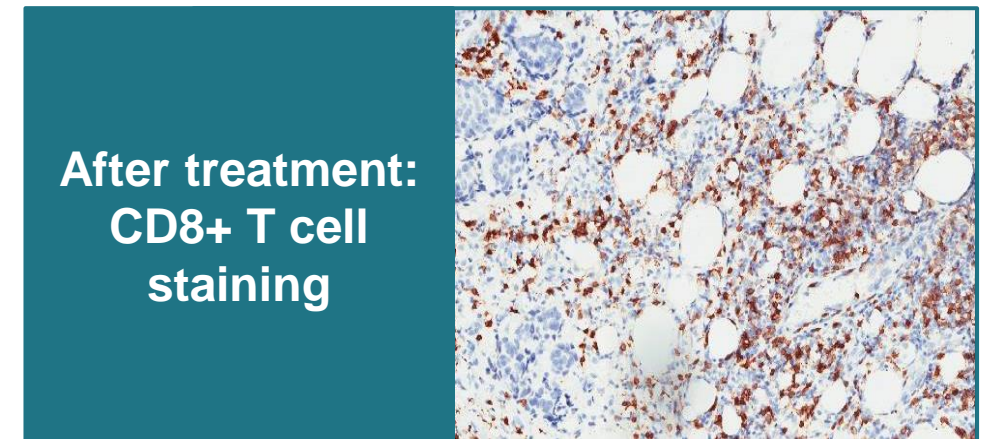
## Key Takeaways From Cohorts 1 and 2

- Pelareorep remodels TMEs by enabling the influx of CD8+ and memory T cells into the tumor and training them to fight cancer
- Changes in the peripheral blood T cell population may be a predictive biomarker of pelareorep therapy

## Pre vs. Post Treatment CD8+ T Cell Infiltration



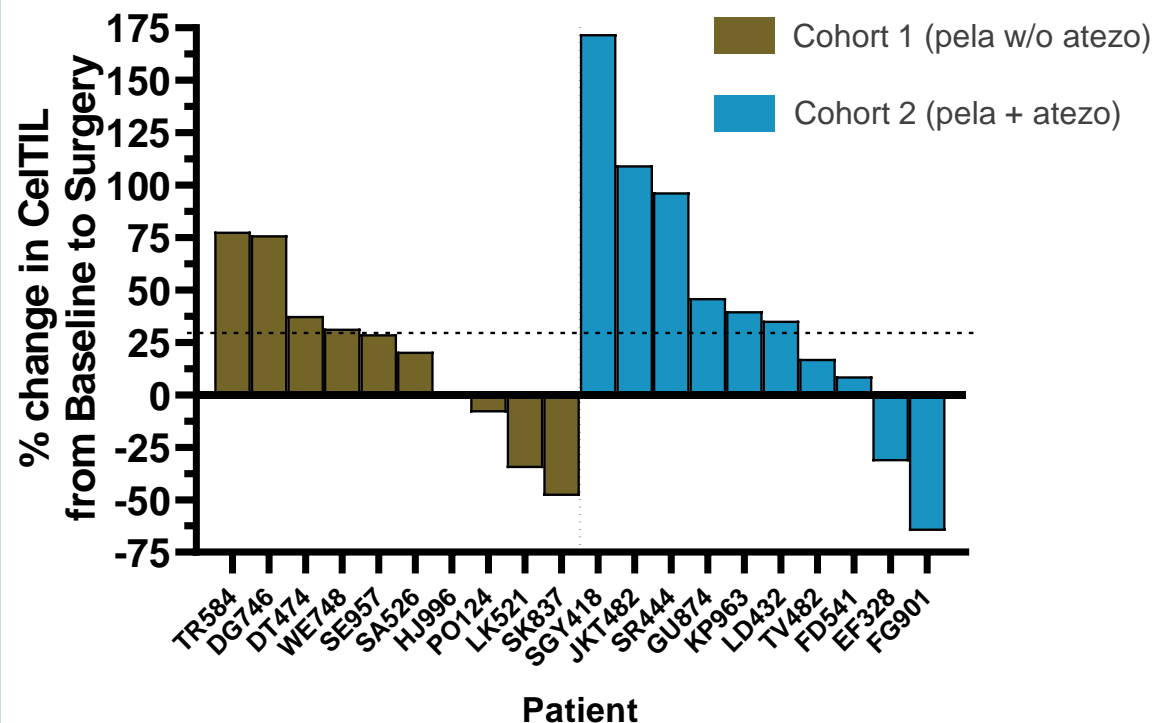
~3 weeks post-treatment



Brown staining shows CD8+ T cells

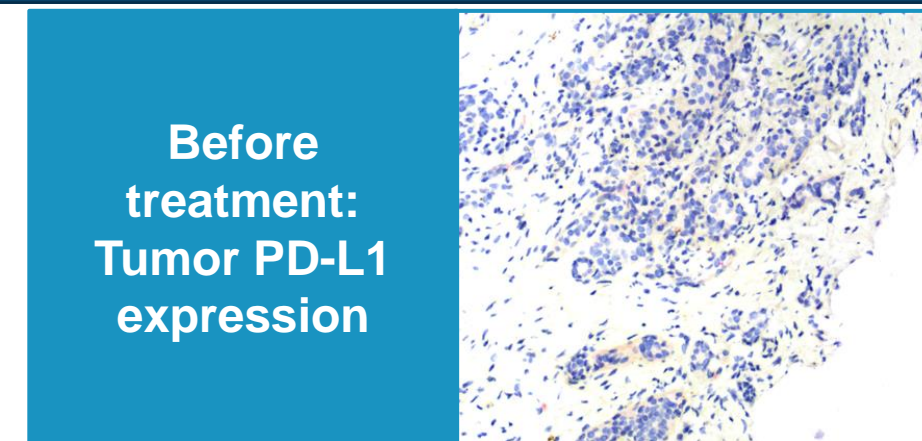
# Clinical Data Demonstrate Synergy Between Pelareorep and Checkpoint Blockade Therapy

CelTIL (Primary Endpoint): A composite measure of tumor cellularity and immune cell infiltration

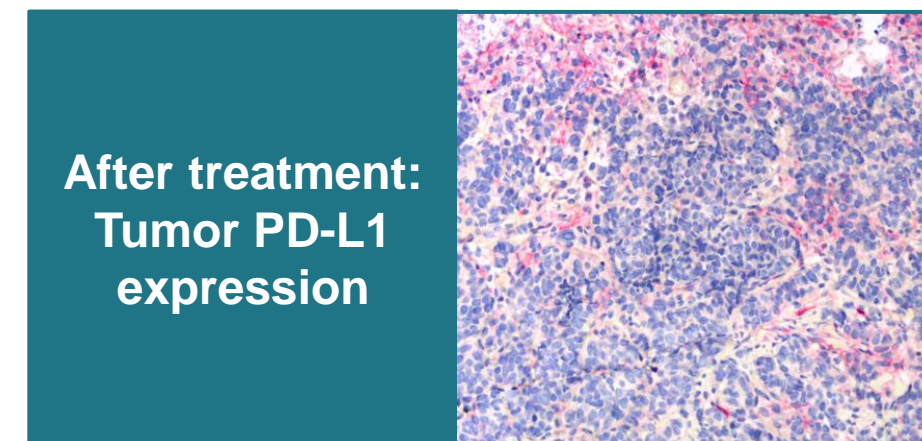


- Increases in CelTIL are associated with better treatment outcomes<sup>1</sup>
- Cohort 1: 40% of patients showed CelTIL increase  $\geq 30\%$
- Cohort 2: 60% of patients showed CelTIL increase  $\geq 30\%$
- **Cohort 2 met the trial's prespecified criteria for success**

Pre vs. Post Treatment Tumor PD-L1 Expression



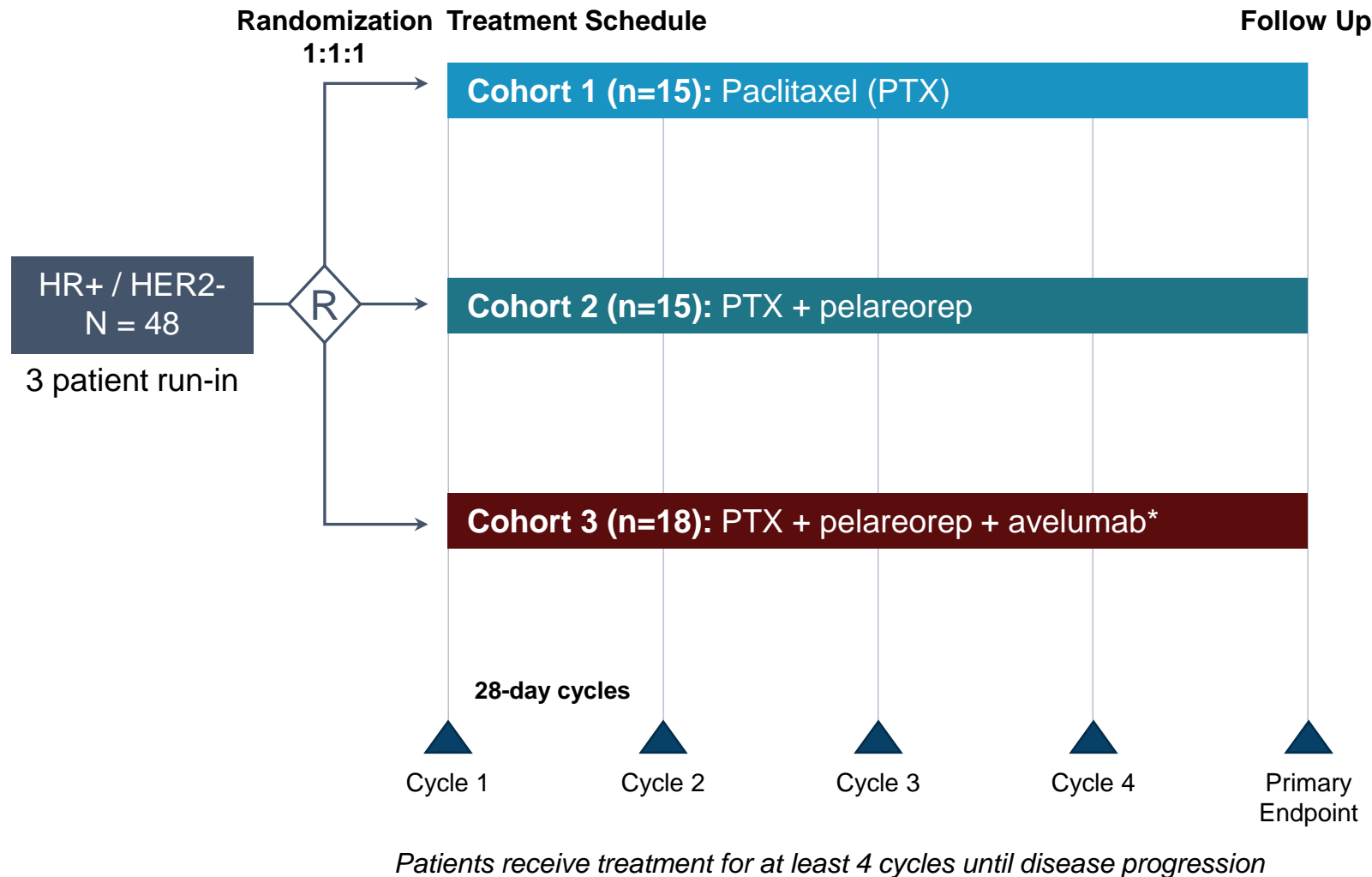
3 days post-treatment



Red staining indicates PD-L1 expression



# Phase 2 BRACELET-1 Study Seeks to Support IND-213 and Leverage Pelareorep-Checkpoint Inhibitor Synergy



## Primary Endpoints

- Overall response rate (ORR) at week 16

## Exploratory Endpoints

- Peripheral and tumor T cell clonality
- Inflammatory markers
- Safety and tolerability assessments
- Overall survival at end of study

## Timeline

- Full enrollment expected Q1 2022

## Collaborators



# Path to Registration in HR+/HER2- Breast Cancer

## Randomized phase 2 study in mBC comparing pelareorep (pela) + paclitaxel (PTX) vs. PTX alone

**IND-213**

Provided clinical POC by demonstrating a statistically significant improvement in overall survival



## Window-of-opportunity study in breast cancer examining pelareorep mediated changes to the TME

**AWARE-1**

Confirmed pelareorep's immunotherapeutic MOA and demonstrated synergy between pelareorep and checkpoint blockade therapy



## Randomized phase 2 study in HR+/HER2- mBC comparing PTX, pela + PTX, & pela + PTX + anti-PD-L1

**BRACELET-1**

Ongoing trial designed to confirm the survival benefit seen in IND-213 and evaluate the effect of adding a checkpoint inhibitor to pelareorep + paclitaxel therapy. Full enrollment expected in Q1 2022



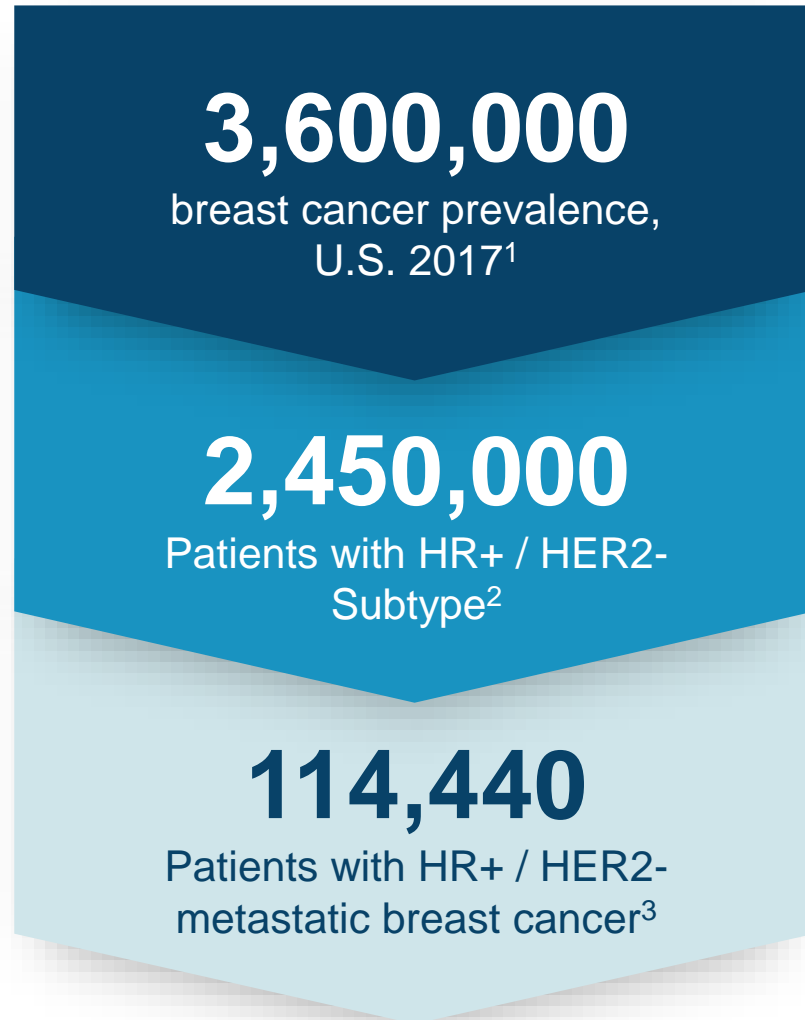
## Registrational study in lead HR+/HER2- mBC program

**Reg. Study**

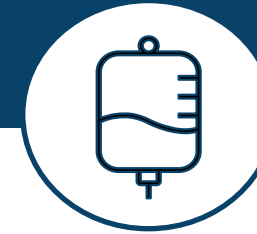
Design to be informed by AWARE-1 and BRACELET-1 data including the potential use of T cell clonality as a predictive biomarker



## HR+ / HER2- mBC Unmet Need & Market Opportunity



### HR+ / HER2- Collaborators



### Significant SOC limitations

Currently approved therapies are unable to produce a meaningful survival advantage

# Pelareorep's MOA Opens Up Market Opportunities Beyond Lead HR+/HER2- mBC Program

The ICI market is expected to reach \$55B by 2025, yet less than 1 in 5 patients respond to these therapies  
**Clinical data suggest that pelareorep treatment can reverse ICI resistance mechanisms**

## Resistance Mechanisms of Immune Checkpoint Inhibitors

Low tumor PD-L1 expression

Lack of pre-existing T cells

Lack of T cell expansion and mobilization



## Immune Activating Effects of Pelareorep

Upregulates tumor PD-L1 expression

Generates new reactive T cell clones

Induces T cell expansion and tumor infiltration



# Clinical Studies Leverage Pelareorep's Synergy with Checkpoint Inhibitors and Collaborations With Industry Leaders

Program	Collaborator	Combination	Preclinical	Phase 1	Phase 2	Phase 3	Milestone
<b>BREAST CANCER</b>							
BRACELET-1		BAVENCIO <sup>®</sup> avelumab 20 mg/mL					Fully Enrolled Q1 2022
AWARE-1		TECENTRIQ <sup>®</sup> atezolizumab		Window-of-opportunity study			Biomarker Data Reported H2 2021
IRENE		Retifanlimab*					Phase 2 Safety Data Q4 2021
<b>GASTRO-INTESTINAL CANCER</b>							
GOBLET		TECENTRIQ <sup>®</sup> atezolizumab					Enrolled Safety Run-ins Q1 2022
NU 18101		KEYTRUDA <sup>®</sup> (pembrolizumab) 100 mg					Phase 2 Data Achieved Q2 2021
<b>MULTIPLE MYELOMA</b>							
NCI-9603	NATIONAL CANCER INSTITUTE	Kyprolis. <sup>®</sup> (carfilzomib) 20 mg					Safety Data Achieved Q2 2020
WINSHIP 4398-18		Kyprolis. <sup>®</sup> (carfilzomib) 20 mg  OPDIVO <sup>®</sup> (nivolumab)					Phase 1 Safety Data H1 2022

\*Anti-PD-1 checkpoint inhibitor in development by Incyte (also known as INCMGA00012)

## Objective: Pelareorep As An Enabling Technology Across Immunotherapeutic Classes

1

Preserve primary focus and resources on advancing lead breast cancer program towards a registrational study

2

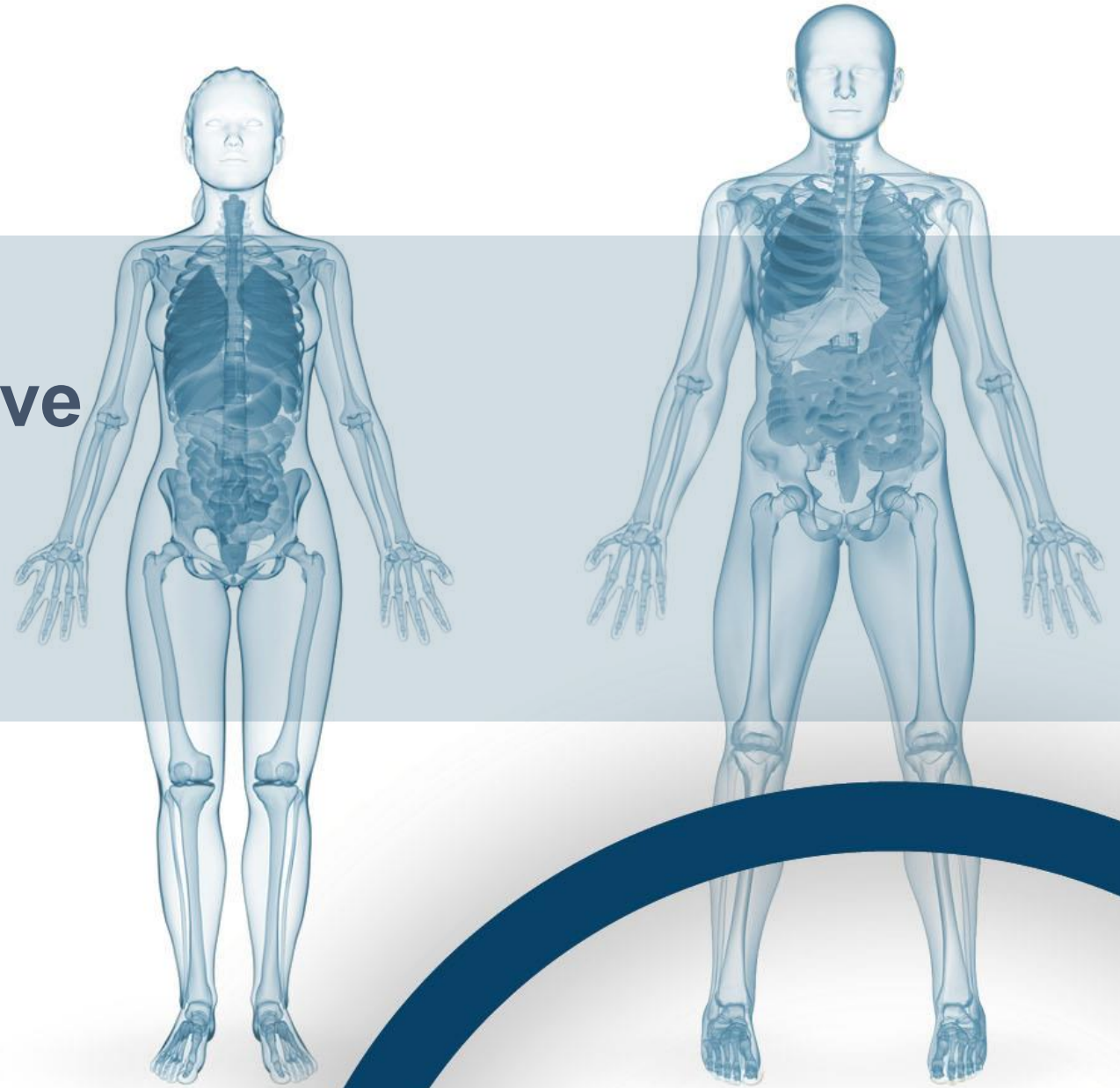
Leverage collaborations with industry leaders and academia to execute on stated clinical milestones outside of lead breast cancer program

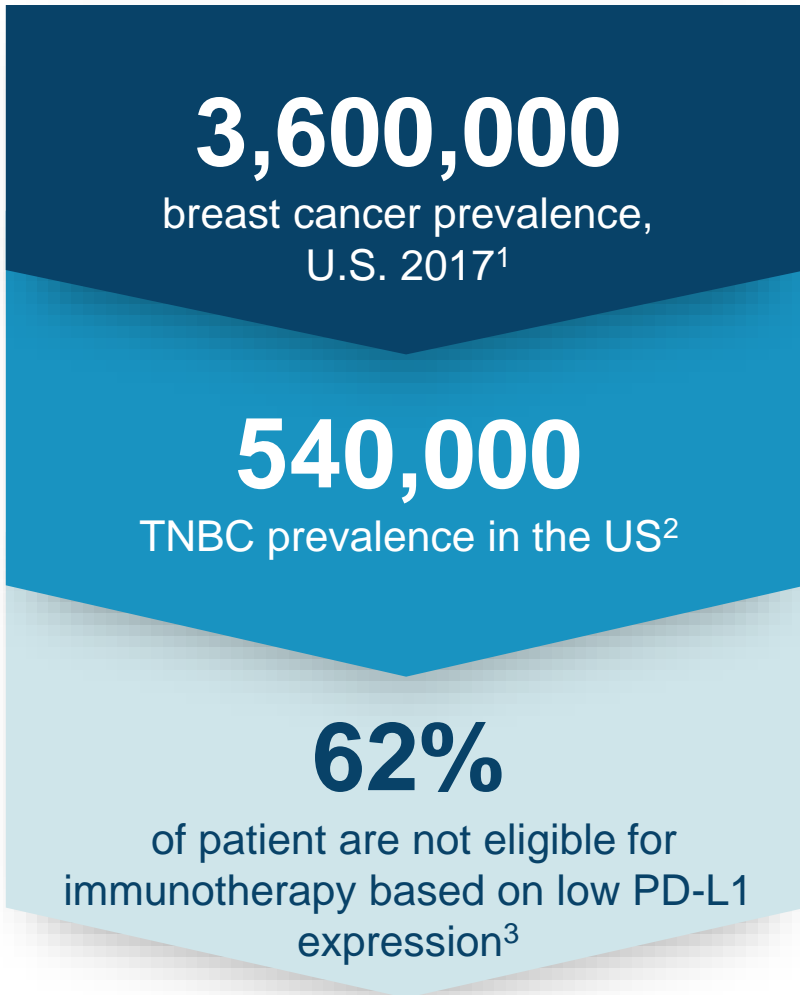
3

Selectively pursue partnership opportunities to further pelareorep's development as an immunotherapy backbone beyond checkpoint inhibitors



# Pelareorep in Triple-Negative Breast Cancer

Combination with anti-PD-1





TNBC Collaborator



Nearly all patients saw increased  
PD-L1 expression in the  
AWARE-1 study following  
pelareorep treatment<sup>4</sup>

TNBC: Triple-negative breast cancer

Sources:

<sup>1</sup>NIH SEER. *Cancer Stat Facts: Female Breast Cancer*. January 18, 2021.

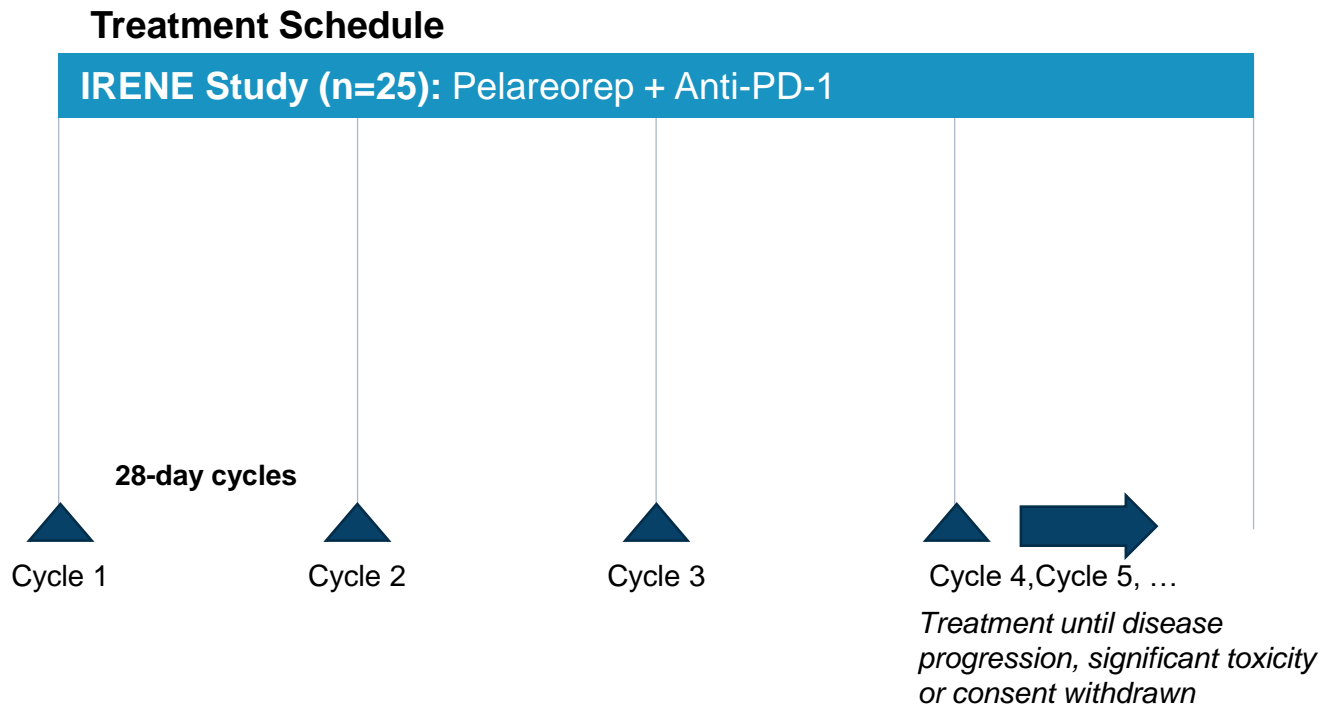
<sup>2</sup>BreastCancer.org. *Triple-Negative Breast Cancer: Overview, Treatment, and More*. September 21, 2020.

<sup>3</sup>Cortes et al. *The Lancet*. Vol 396, issue 10265, p1817-1828. December 2020.

<sup>4</sup>Manso L et al. A window-of-opportunity study with atezolizumab and the oncolytic virus pelareorep in early breast cancer (AWARE-1). In: AACR Virtual Annual Meeting 2021; 2021 Apr 10-15; Virtual. AACR; 2021. Abstract CT191



# Phase 2 IRENE Study Evaluates the Efficacy of Pelareorep-anti-PD-1 Combination Therapy in Metastatic TNBC



## Primary Endpoints

- Safety
- Objective response rate

## Secondary Endpoints

- PFS
- OS
- Duration of response

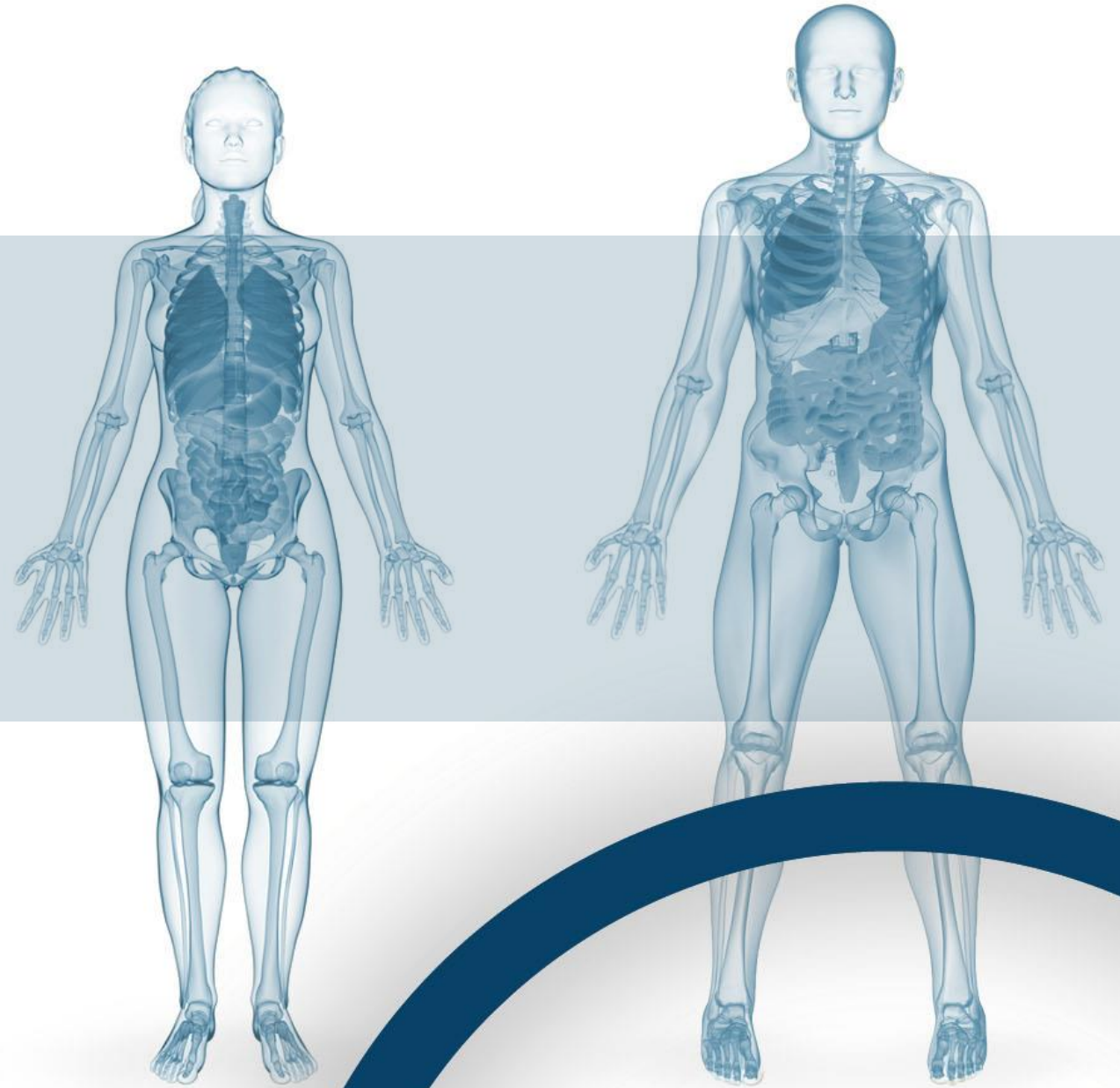
## Exploratory Endpoints

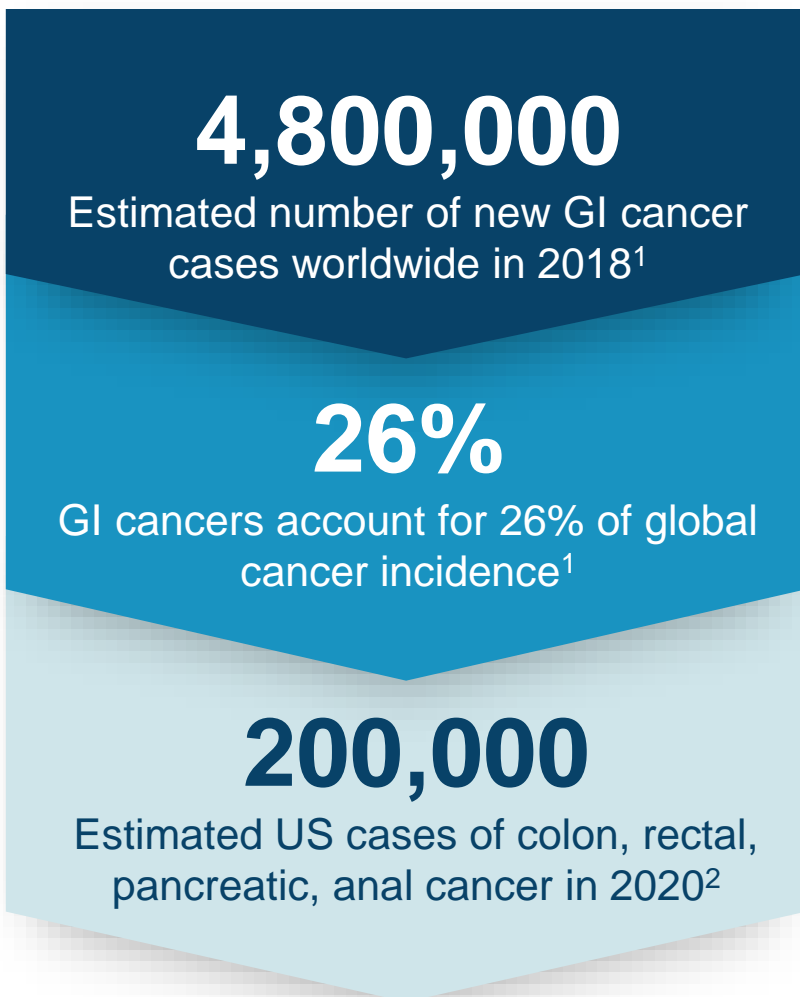
- Peripheral T cell clonality
- Pre- vs. post-treatment change in tumor PD-L1 expression

## Collaborator





# Expanding the Frontiers of Immunotherapy Gastrointestinal Cancers & Hematologic Malignancies





GI Collaborator



**Pela combo therapies have shown:**

- >**90%** clinical benefit rate in KRAS-mutated colorectal cancer patients<sup>3</sup>
- >**80%** increase in PFS in pancreatic cancer patients with low levels of CEACAM6 expression<sup>4</sup>

SOC: Standard of care; GI: Gastrointestinal; ICI: Immune checkpoint inhibitor; Sources: 1: *Gastroenterology*. 2020 Apr 2; S0016-5085 (20) 30452-2. 2: "Key Statistics for Colorectal Cancer." The American Cancer Society, American Cancer Society, Inc., <https://www.cancer.org/cancer/colon-rectal-cancer/about/key-statistics.html>, "Key Statistics for Pancreatic Cancer." The American Cancer Society, American Cancer Society, Inc., <https://www.cancer.org/cancer/pancreatic-cancer/about/key-statistics.html>, "Key Statistics for Anal Cancer." The American Cancer Society, American Cancer Society, Inc., <https://www.cancer.org/cancer/anal-cancer/about/what-is-key-statistics.html>; 3. <https://ir.oncolyticsbiotech.com/press-releases/detail/498/oncolytics-biotech-announces-publication-of-pelareoreps>; 4. <https://ir.oncolyticsbiotech.com/press-releases/detail/494/oncolytics-biotech-announces-statistically-significant>

# Clinical Data Highlight the Potential of Pelareorep-Checkpoint Inhibitor Combination Therapy in GI Cancer



## Clinical studies evaluating pelareorep-based combination treatments in GI cancer have shown:

- A >90% clinical benefit rate in KRAS-mutated colorectal cancer patients<sup>1</sup>
- A >80% increase in PFS in pancreatic cancer patients with low levels of CEACAM6 expression<sup>2</sup>



## Clinical data from colorectal and pancreatic cancer studies suggest pelareorep has significant potential to synergistically increase the effectiveness of immune checkpoint inhibitors in GI cancers

- Rapid maturation of dendritic cells after pelareorep treatment
- Increase in activation of CD8+ cells after pelareorep treatment
- Upregulation of PD-L1 in tumor cells following pelareorep treatment



## Predictive and prognostic biomarker candidates have been identified in a pancreatic cancer study

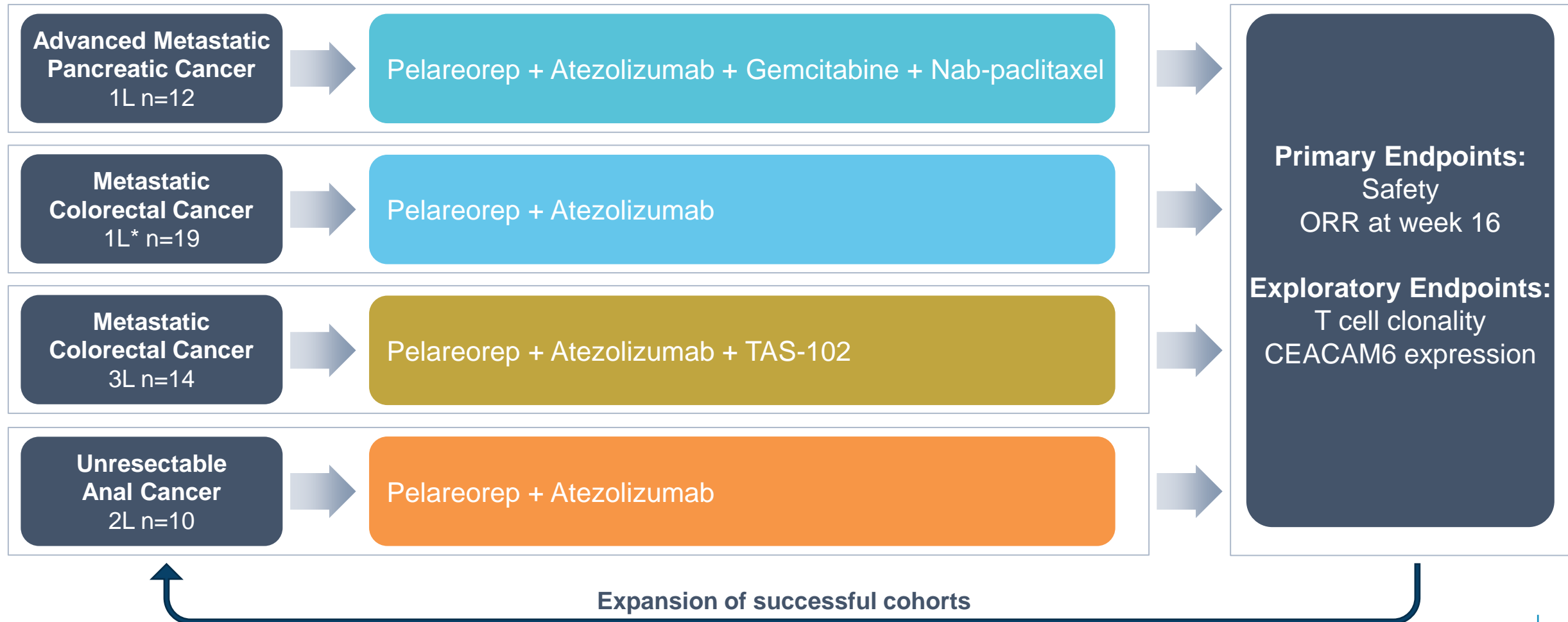
- T cell clonality - candidate biomarker of response
- CEACAM6 - candidate biomarker of resistance

# GOBLET Study Design



AIO-Studien-gGmbH

Phase 1/2 multiple indication biomarker, safety and efficacy study



\*1L MSI-high focused; ORR: Objective response rate; BM: Biomarker; L: Line; Atezolizumab (Tecentriq®)

**Clinical data demonstrate pelareorep's potential to synergistically combine with proteasome and/or immune checkpoint inhibitors in the treatment of hematologic malignancies**

## Proof-of-Concept Clinical Data

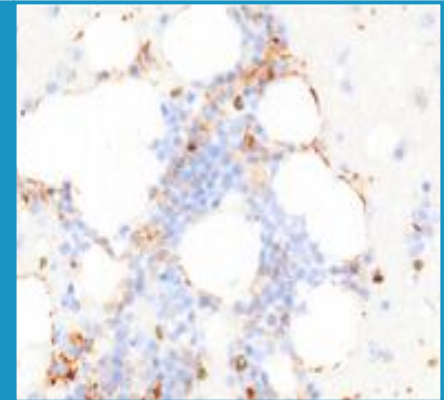
Pelareorep targets and selectively replicates in MM tumor cells

Achieved a **50% ORR** and **83% CBR** in patients who have failed carfilzomib<sup>1</sup>

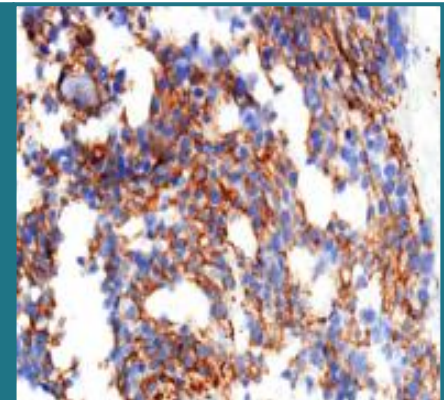
Observed T cell activation and the first report of cytokine storm associated with tumor response in MM

Saw PD-L1 upregulation with pelareorep treatment

PD-L1  
expression  
before  
pelareorep  
treatment



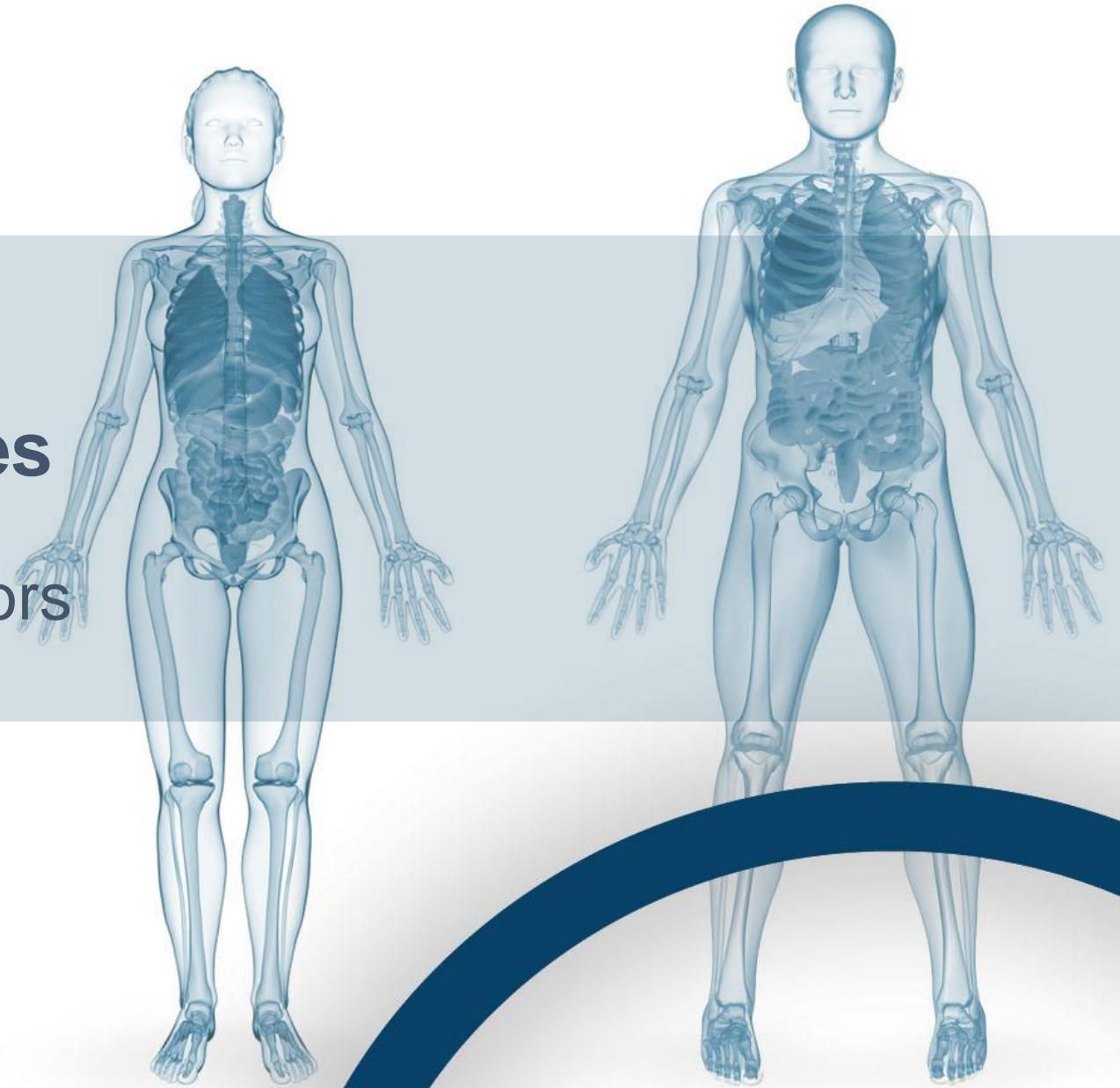
PD-L1  
expression one  
week after  
pelareorep +  
carfilzomib



Brown staining indicates PD-L1 expression

# Additional Immunotherapy Combinations & Opportunities

CAR T in Solid Tumors, Bispecific  
Antibodies, PARP & CDK4/6 inhibitors



## Current Challenges for CAR T Cells in Solid Tumors



- 1 Early CAR T cell exhaustion: CAR T cells are short lived with responses that are not durable
- 2 Antigen escape
- 3 Impaired CAR T cell trafficking to the tumor
- 4 Immunosuppressive tumor microenvironment

## How Pelareorep Enables CAR T Cells to Overcome Traditional Solid Tumor Challenges

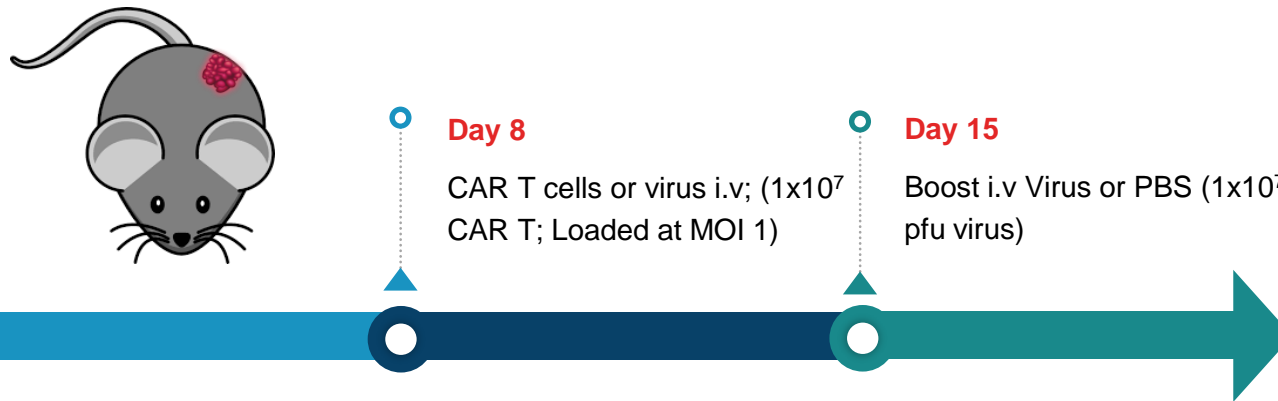


- 1 Pelareorep-loaded CAR T cells are long lasting, and can be reactivated with a pelareorep boost
- 2 Pelareorep can promote antigen cross presentation
- 3 Pelareorep can promote the expression of chemokines that recruit lymphocytes to the tumor
- 4 Pelareorep can preferentially activate chemokines that recruit CD8 T cells rather than Tregs



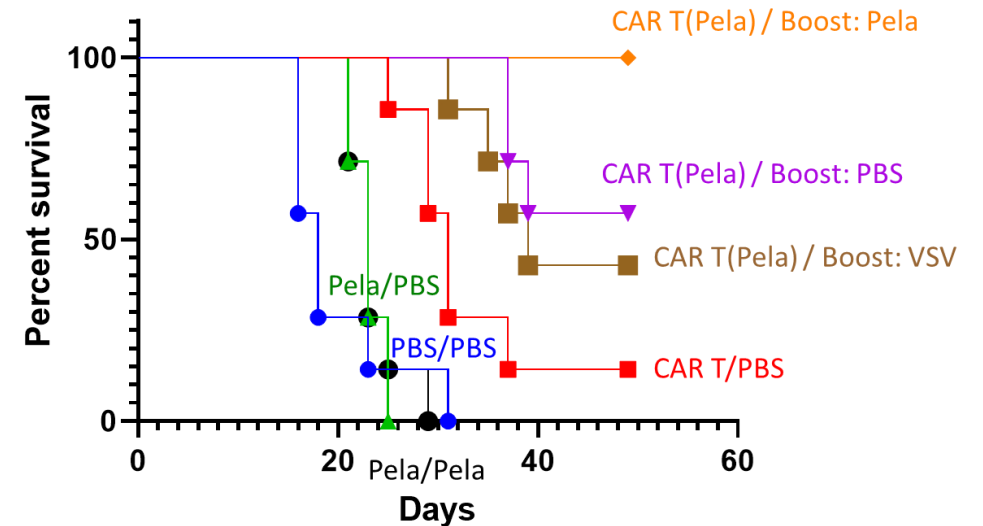
# Synergistic Anti-Cancer Activity of Pelareorep Combined With CAR T Therapy in Solid Tumors

B16-EGFRviii tumor s.c.



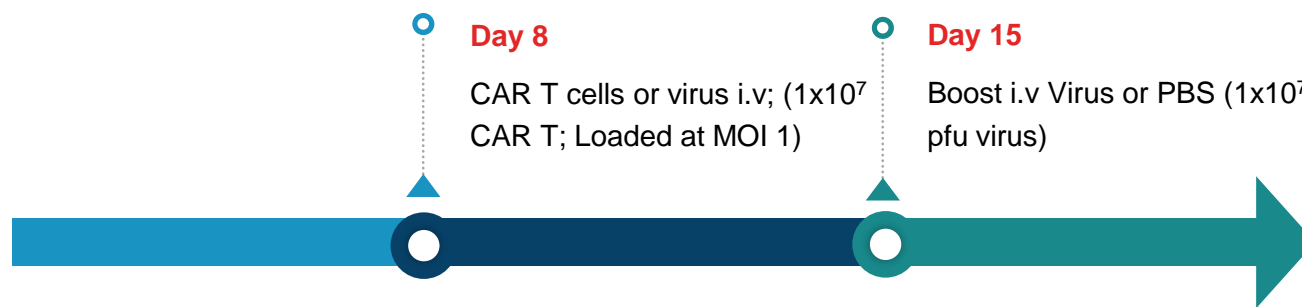
Collaboration between Oncolytics and researchers at the Mayo Clinic and Duke University evaluated pelareorep and CAR T cell combination therapy in a murine solid tumor model

Enhanced survival with pelareorep + CAR T combination therapy relative to either monotherapy

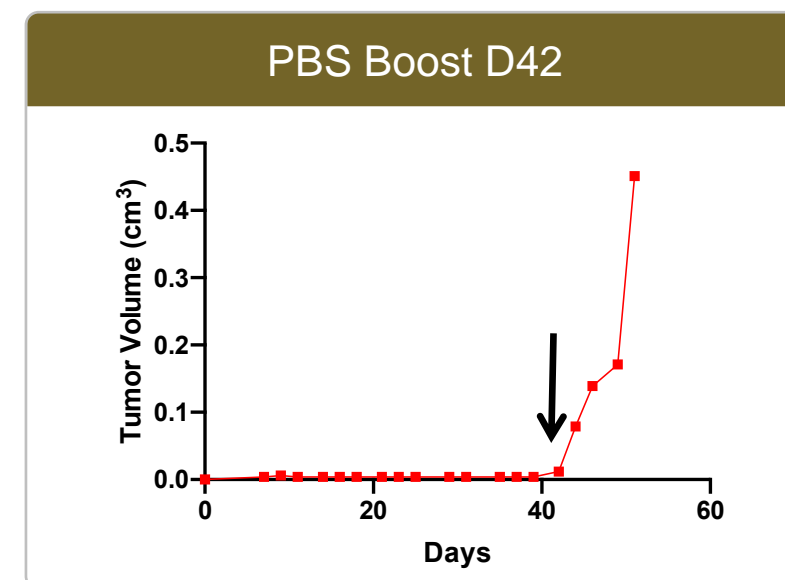
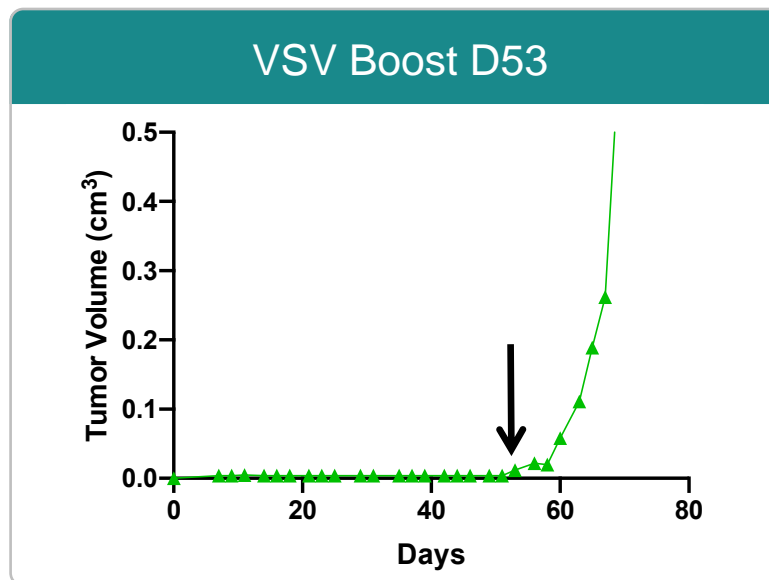
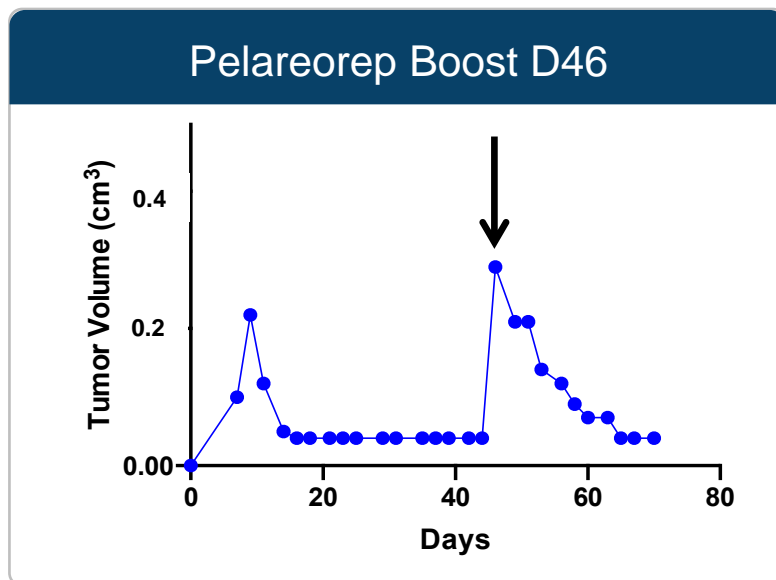


# Tumors Which Recur Can Be Treated With a Further Boost of Homologous Virus But Not Heterologous Virus

B16-EGFRviii tumor s.c.



In three mice, tumors recurred around **day 40-50**. When recurrent tumors started to grow ( $>0.2$ cm in diameter) they were administered a further i.v. injection of  $10^7$  pfu pelareorep, PBS or VSV-GFP (arrows).





Pelareorep vastly improved the persistence and efficacy of CAR T cell therapy, leading to cures in murine solid tumor models



Pelareorep's synergistic effects with CAR T therapy appear to be specific and are not observed with other oncolytic viruses



Pelareorep has the potential to broaden the applicability of CAR T cells for solid tumors



Pursuing a partnership strategy to further pelareorep's development as an enabling technology for CAR T cells and other immunotherapies beyond checkpoint inhibitors

## **Bispecific Antibodies<sup>1</sup>**

Pelareorep combined with CD3-bsAbs increased T cell numbers, induced tumor regression, and prolonged survival in solid tumor models

The combination strategy may be effective in the treatment of metastatic disease

## **PARP Inhibitors<sup>2</sup>**

Pelareorep and talazoparib synergistically interact to increase cancer cell apoptosis

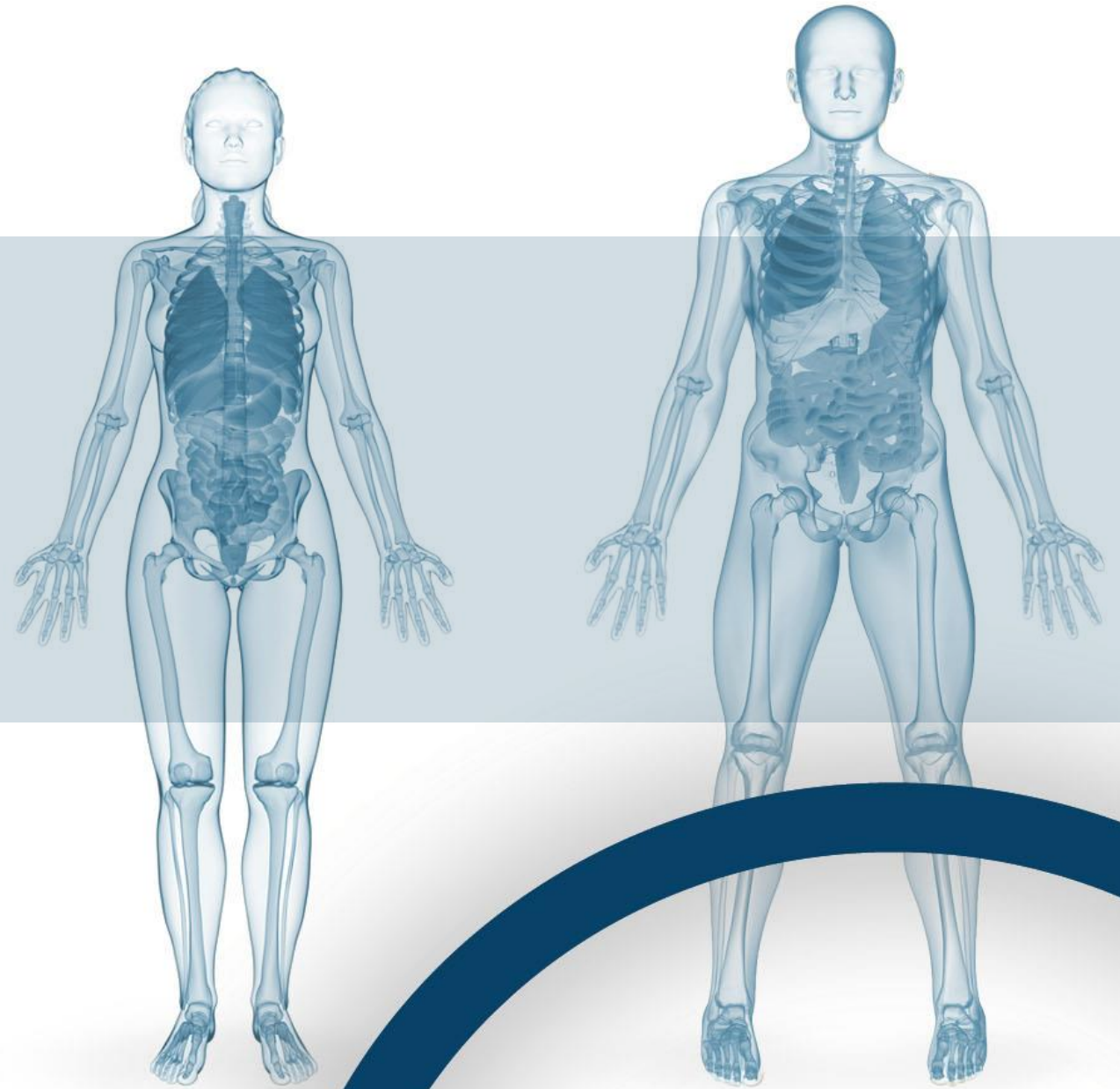
The synergistic anti-cancer effects of the combination correlated with an increased immune response

## **CDK4/6 Inhibitors<sup>3</sup>**





Combining pelareorep with palbociclib led to enhanced immunogenic cell death

The effects of the combination were mediated by increased immune activation and effector function

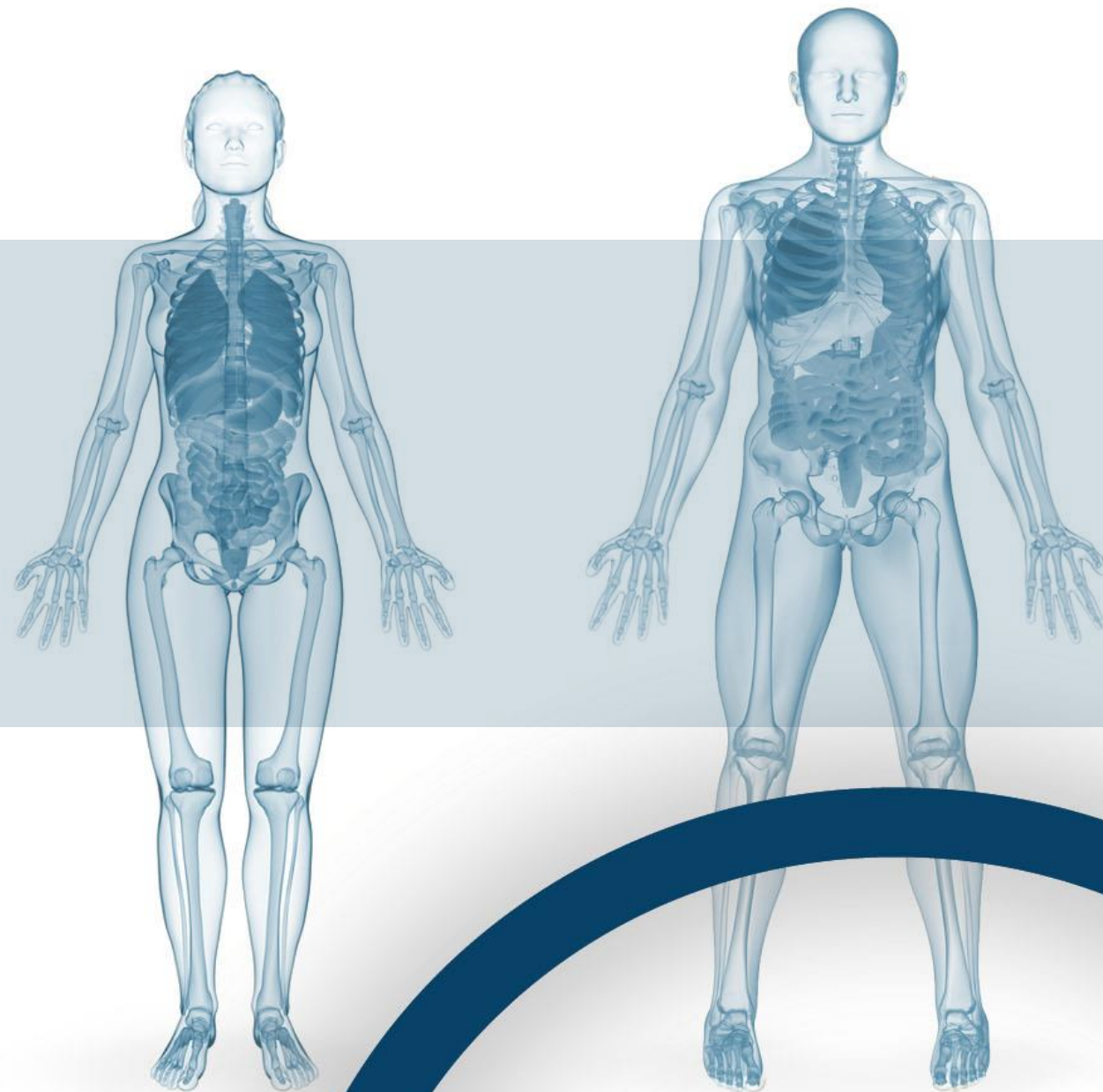
# Catalysts & Milestones



Upcoming Catalysts & Milestones	Combination With	Timing
Complete enrollment in <b>BRACELET-1</b> mBC study	 	Q1 2022
Glioblastoma study update		H1 2022
Multiple myeloma study data		H1 2022
<b>BRACELET-1</b> mBC study top-line data	 	Q4 2022

Anticipated Catalysts & Milestones	Combination With
Phase 2 <b>BRACELET-1</b> mBC study: interim safety update	 
Phase 2 <b>BRACELET-1</b> mBC study: final data	 

# Appendix





**313 patents** issued worldwide, including **31 US** and **14 Canadian**  
**19 pending applications** worldwide

## Reovirus issued patent claims cover:

Compositions of matter comprising reovirus

Through 2028 and extendable to 2033

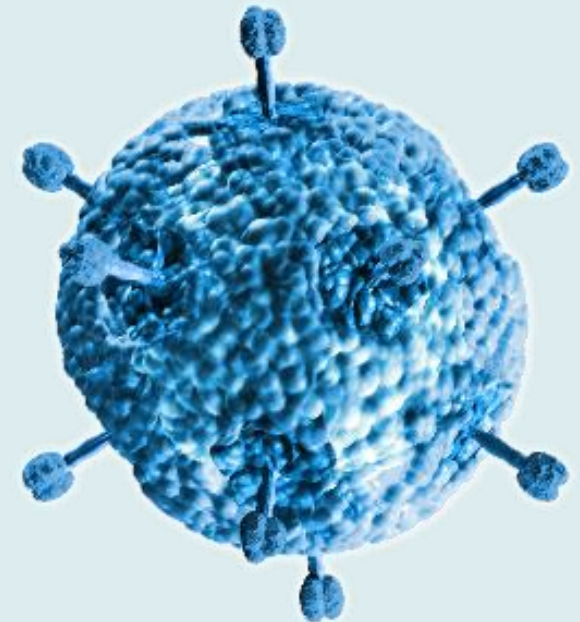
Pharmaceutical use of reoviruses to treat neoplasia and cellular proliferative diseases

Combination therapy with radiation, chemotherapy and/or immunosuppressants

Methods for manufacturing reovirus and screening for susceptibility to reovirus

Pharmaceutical use of reoviruses in transplantation procedures

Eligible for 12 years of U.S. market exclusivity upon approval





# Experienced Leadership and Advisory Board

Extensive knowledge of immuno-oncology | Public company experience | Strong business development and commercialization expertise

## MANAGEMENT

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Professor, Immunology, Mayo Clinic  
Director, Immuno-oncology and Gene and Virus  
Therapy, Mayo Clinic



## Delivered Intravenously

Accesses primary and metastatic disease

## BSL 2 classification

Administered via standard practices, does not require special handling for administration

## Potentiates multiple immunotherapies

Synergistic potential with both PD-L1 and PD-1 inhibitors, plus other immunotherapies, including CAR T, PARP-1, CDK4/6

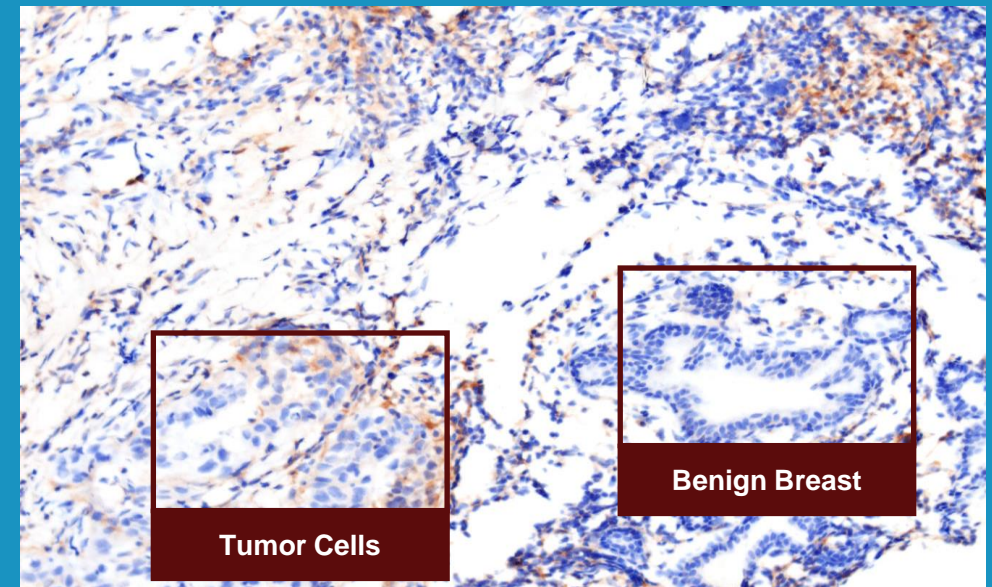
## Selectively replicates in tumor cells

As shown in multiple clinical studies

## Predictive and prognostic biomarkers identified

Peripheral T cell clonality (measure by TCR sequencing)  
CEACAM6 (measure by immunostaining)

## Selective PD-L1 Response in Tumor Cells



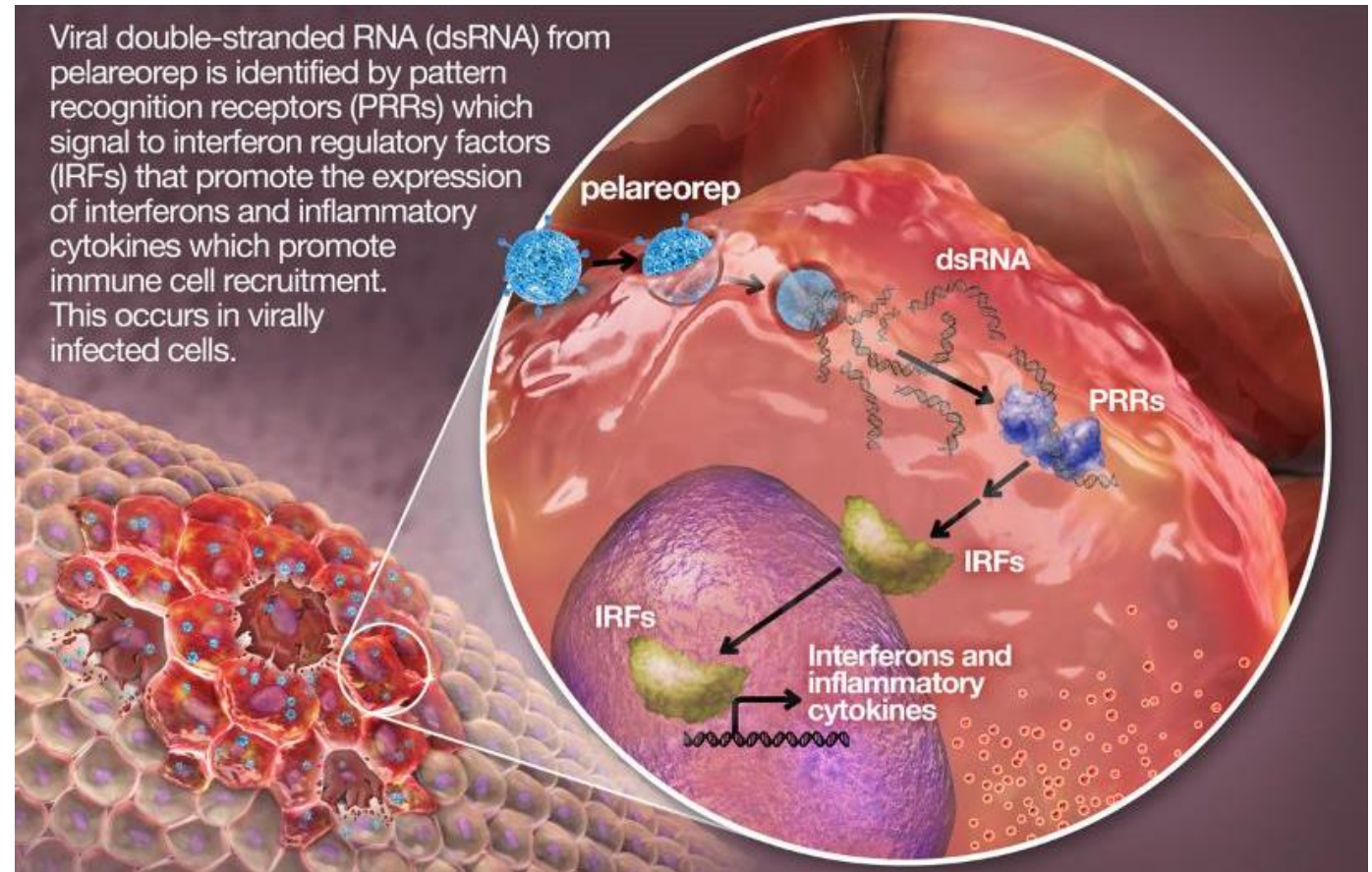
Brown indicates PD-L1 expression  
Blue is counterstain

# Underlying Biology of Pelareorep's Immunotherapeutic Mechanism of Action

## Intravenous administration of pelareorep leads to

- Selective replication in cancerous cells with accumulation of dsRNA
- Promotion type 1/2 interferon signaling via pattern recognition receptors such as RIG-I and TLR3
- Activation of natural killer (NK) cells, dendritic cells, and T cells

**MORE THAN 40**  
supporting publications



# Pelareorep is Safe and Well-Tolerated



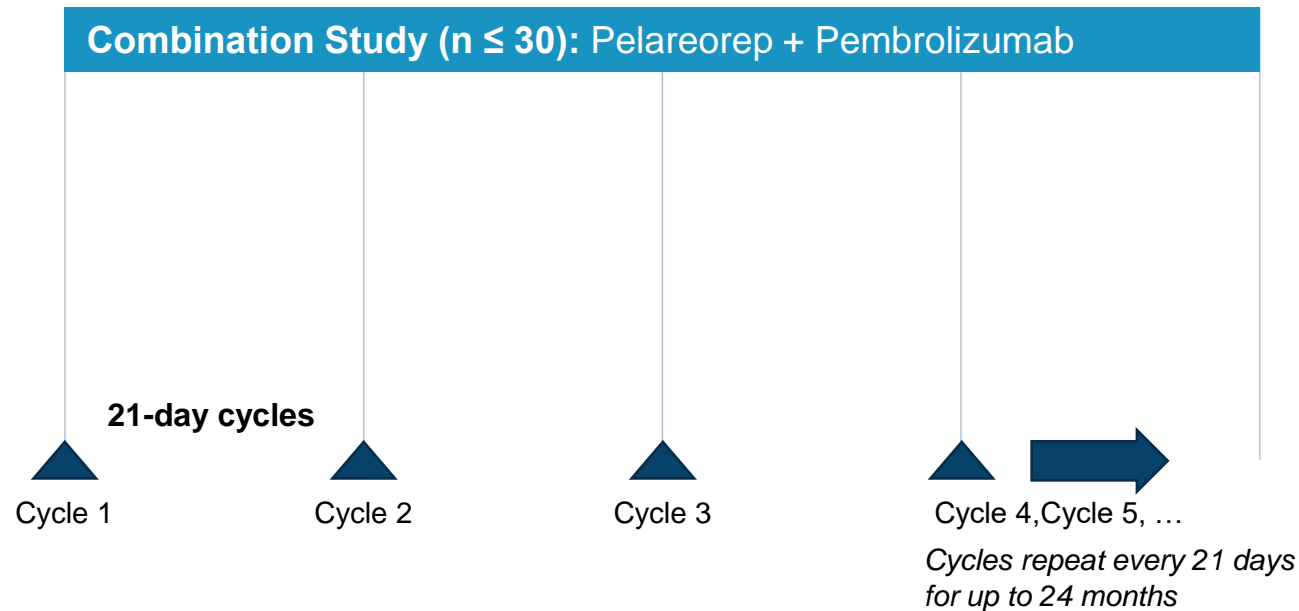
- 1,100 patients treated, 900+ intravenously

## Monotherapy Toxicity Symptoms

- Toxicities have generally been mild (grade 1 or 2) and included chills, fever, headache, cough, myalgia, runny nose, sore throat, fatigue, lymphopenia or neutropenia
- Transient toxicities (grade 3 or 4) also included lymphopenia or neutropenia
- Symptoms usually last < 6 hours

No maximum tolerated dose has been reached to date

## Treatment Schedule



## Primary Endpoints

- ORR by iRECIST

## Secondary Endpoints

- Confirmation of blood draw biomarkers
- PFS
- mOS

## Collaborators



# Business Development Strategy Anchored By Partnerships With Large Pharmaceutical Companies

## Objective: Joint Development and Commercialization Partnership

- Support of breast cancer registration study as well as other potential registration opportunities
- Financial and clinical support for other company-sponsored and/or investigator-sponsored studies
- Expansion of indications
- Improved ability to meet timelines while lowering development and manufacturing costs
- Maintain rights in North America in part or in whole
- Out-license ROW rights

## Co-Development Study

- Co-development agreement with **Pfizer/EMD Serono** to evaluate Bavencio® in 2L mBC

## Oncolytics or Investigator Sponsored Trials (IST's)

- 6 ongoing combination studies with **Merck, Roche, Bristol-Myers Squibb, & Incyte**

## Monetize Certain Geographies

### Successful partnership with Adlai Nortye

- China, Hong Kong, Macau, Singapore, South Korea and Taiwan
- Upfront and milestone payments of up to \$86.6M
  - \$21M in milestone payments largely under Oncolytics' control, with double-digit royalties
  - \$65M tied to potential development expansion

