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### Unleashing the Power of the Immune System to Fight Cancer

Investor Presentation December 2024



## 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 collectively referred to herein as "forward-looking statements"). Forward-looking statements contained in this presentation include are statements regarding our belief as to the potential, mechanism of action and benefits of pelareorep as a cancer therapeutic; our stated goals and objectives; our potential registration opportunities in breast and pancreatic cancer and the milestones and next steps associated therewith and the anticipated timing thereof; our anticipated cash runway; our key milestones in 2024 and beyond; our development strategy; 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 forwardlooking 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. We may incur expenses or delays relating to such events outside of our control, including public health crises such as pandemics and epidemics, 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.

## Pelareorep in Breast & Pancreatic Cancer: Overview & Highlights



#### Non-pathogenic, unmodified immunotherapy

- Targets cancer cells, but not normal cells
- Administered IV, delivers dsRNA into tumors
- Strong safety profile has been given to >1,100 patients
- 147 patents provide extensive IP protection

#### Pela activates the immune system

- Induces anti-tumor innate and adaptive immune responses
- Makes tumors visible to the immune system
- Synergizes with chemotherapy and immuno-therapeutics including checkpoint inhibitors
- Clinical evidence showing changes to TME

#### **Clear registration path in two indications**

- Strong efficacy signal in breast and pancreatic cancer
- Fast Track designation for both indications
- Efficient registration path identified for both indications with potential for accelerated approval for breast cancer

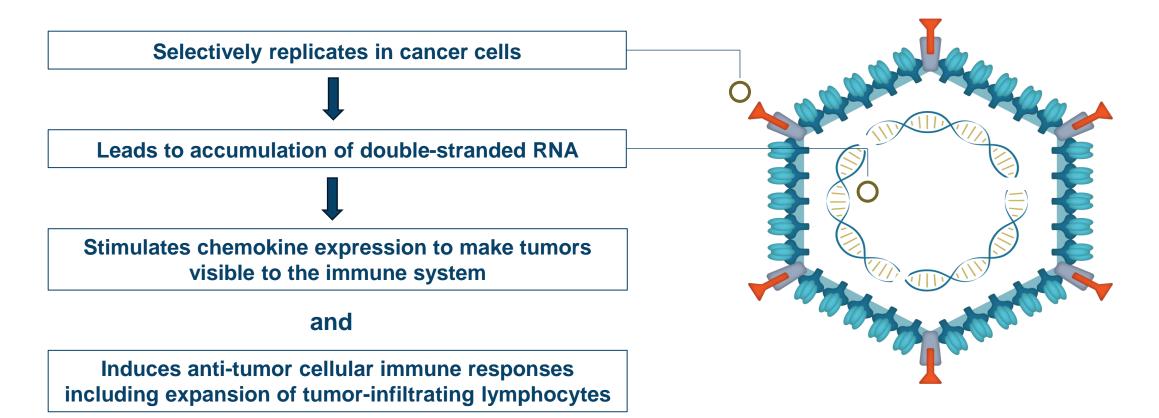
#### **Experienced** team

- Extensive oncology drug development experience
- Track record of success in bringing new drugs to the market
- Decades of experience in manufacturing and product development
- Distinguished Scientific Advisory Board

## Pelareorep is a First in Class Immunotherapeutic Agent



- > Non-genetically modified, non-pathogenic reovirus
- > IV administration allows direct targeting of both primary and metastatic tumors
- > Manufactured at commercial scale; requires no special handling





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## Pelareorep in HR+ / HER2- Breast Cancer



## Pelareorep Offers New Options in the Evolving HR+/HER2-Advanced/Metastatic Breast Cancer Treatment Pathway



Hormonal and targe	eted treatment lines	Post-hormonal treatment lines	
First-line treatment	Second-line treatment	Third-line treatments	Fourth-line treatments
Endocrine therapy	Endocrine therapy	Antibody-drug conjugate therapy, e.g., T-DXd (Enhertu)* Or	Chemotherapy
CDK4/6 inhibitors	CDK4/6 inhibitors	Traditional chemotherapy (if T-DXd ineligible)	
	Targeted therapy	Pelareorep + paclitaxel 3 <sup>rd</sup> -line option for pts ineligible for T-DXd	Pelareorep + paclitaxel 4 <sup>th</sup> -line option for pts who fail T-DXd <sup>‡</sup>

\* Anticipated based on Destiny-Breast06 results (ASCO 2024)

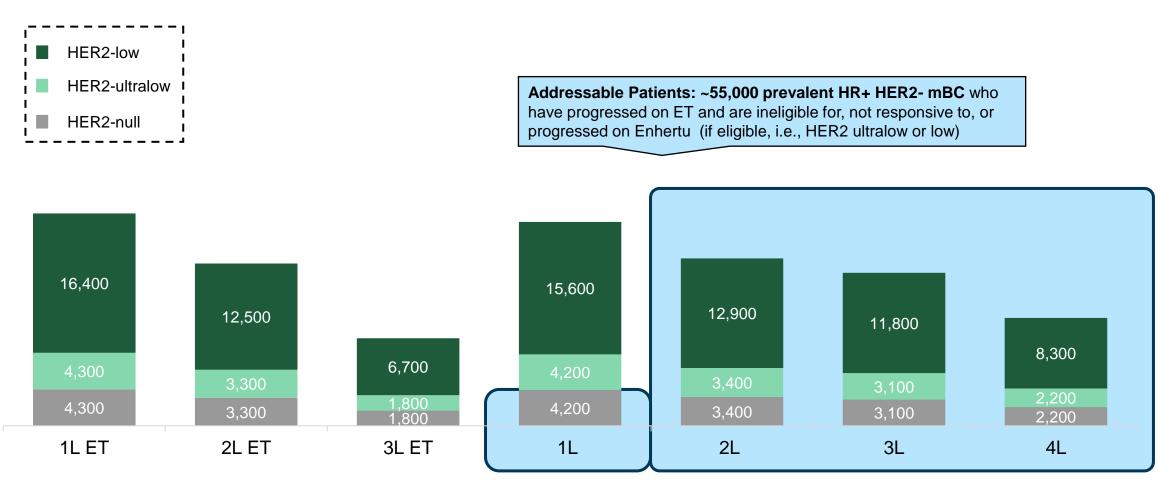
<sup>‡</sup>Due to progression on or inability to tolerate T-DXd

## The HR+/HER2- mBC Segment Post Enhertu Represents ~55,000 Addressable Patients



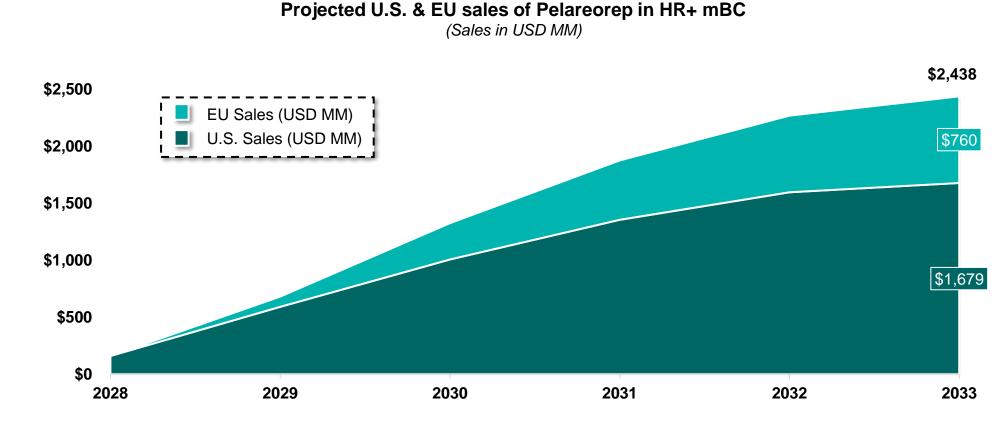


(# of patients in 1,000s, Not Mutually Exclusive)



Addressable Patients Methodology in Appendix. Sources: Gampenrieder, Simon Peter et al. "Landscape of HER2-low metastatic breast cancer (MBC): results from the Austrian AGMT\_MBC-Registry." Breast cancer research : BCR vol. 23,1 112. 14 Dec. 2021, doi:10.1186/s13058-021-01492-x; Schettini, Francesco et al. "Clinical, pathological, and PAM50 gene expression features of HER2-low breast cancer." NPJ breast cancer vol. 7,1 1. 4 Jan. 2021, doi:10.1038/s41523-020-00208-2 Mehta, Sandhya et al. "Prevalent of 'HER2 ultra-low' among patients with advanced breast cancer with historical IHC0 status." Journal of Clinical Oncology vol. 42, 16. 29 May 2024, doi.org/10.1200/JCO.2024.42.16\_suppl.e1315; Tarantino, Paolo et al. "HER2-Low Breast Cancer: Pathological and Clinical Andscape." Journal of clinical oncology : official journal of the American Society of Clinical Oncology vol. 38,17 (2020): 1951-1962. doi:10.1020/JCO.19.02488; DESTINY-BREAST04; D





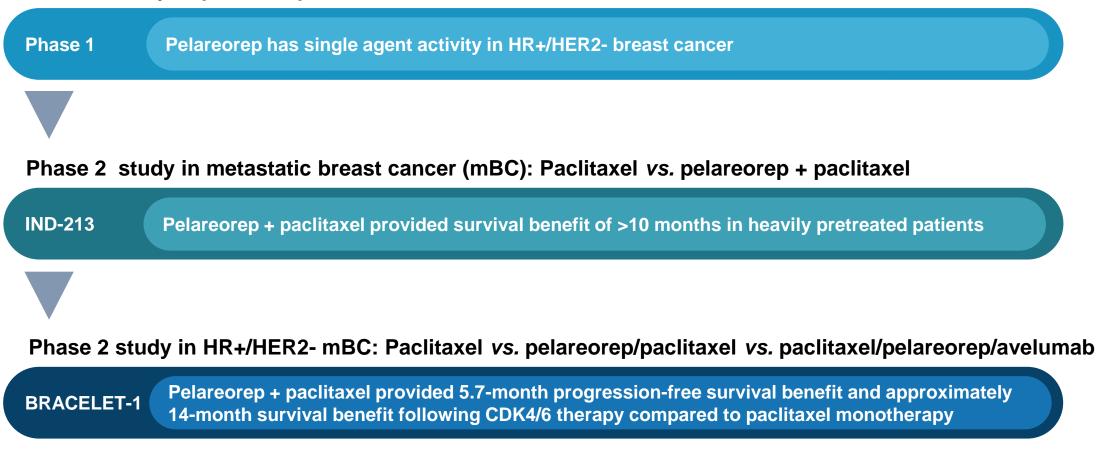
#### Treated patients

Total U.S Pela Patients	966	3,414	5,577	7,200	8,132	8,197
Total EU5 Pela Patients	-	995	3,517	5,745	7,416	8,376
Total US and EU5 Pela Patients	966	4,409	9,094	12,945	15,548	16,572

Sources: GlobalData HER2 negative BC Global Drug Forecast & Market Analysis to 2030; GlobalData Price Intelligence Database; Redbook; ICER



#### Phase 1 study of pelareorep in advanced breast cancer



## Pelareorep Treatment Led to a Statistically Significant Improvement in mOS in Phase 2 Breast Cancer Trial IND-213



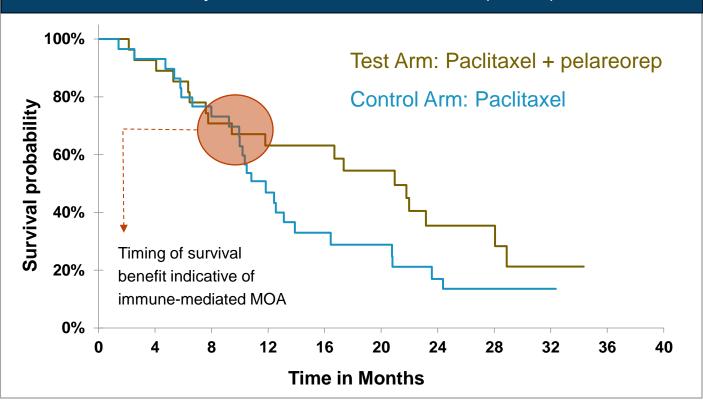
#### Phase 2 All Subtypes (n = 74)

HR	0.65
р	0.1 (powered to 90%)
mOS	17.4 months vs. 10.4 months
Test	n = 36
Control	n = 38

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

HR	0.60
р	0.1 (powered to 90%)
mOS	21.0 months vs 10.8 months
Test	n = 28
Control	n = 29

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

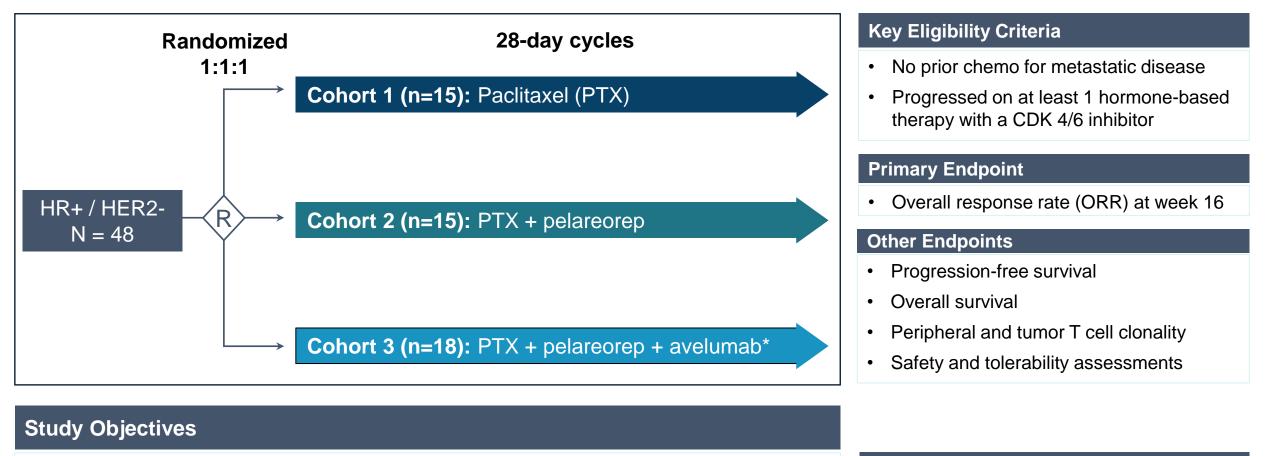


#### Near doubling of mOS in HR+/HER2- patients with pelareorep treatment

mOS: Median Overall Survival; HR: hazard ratio

## **BRACELET-1** Study Design





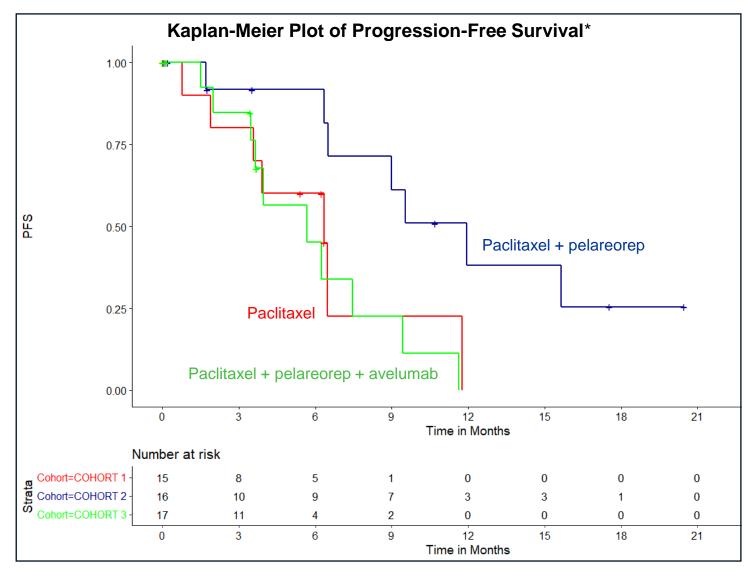
- To assess the clinical benefit of pelareorep combination therapy in patients who had received CDK4/6 therapy
- To assess whether avelumab added any additional benefit

Collaborators



## BRACELET-1 Study Showed Robust Improvement in Progression-free Survival (PFS) for the Pelareorep + Paclitaxel Arm



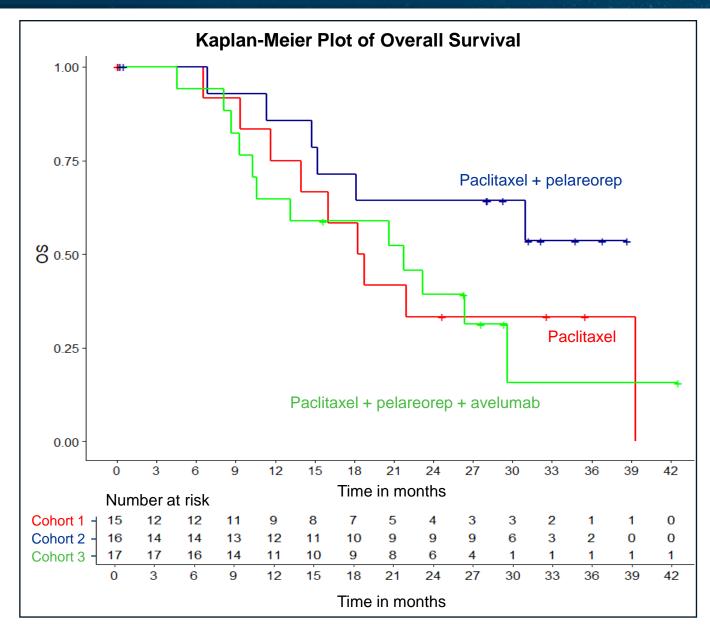


	Paclitaxel (PTX)	PTX + pelareorep	PTX + pelareorep + avelumab
<b>Median PFS</b> (months)	6.4	12.1	6.4
Hazard ratio vs. PTX	-	0.39	1.43

\*Progression-free survival is defined as the time from randomization to the first documented disease progression per RECIST v1.1 or death from any cause, whichever occurs first.

# BRACELET-1 Study Showed Meaningful Improvement in Overall Survival (OS) for the Pelareorep + Paclitaxel Arm





	Paclitaxel (PTX) Cohort 1	<b>PTX + pela</b> Cohort 2	PTX + pela + avelumab Cohort 3
<b>Median OS</b> (months)	18.2	Not reached Estimate: 32.1*	21.7
<b>Hazard ratio</b> vs. PTX alone	-	0.48	1.08

\*This estimate assumes patients survived only until the next per protocol follow-up in 4 months. Had the patients survived only one day past their final follow-up visits, the estimated median OS would be 28.7 months.



Response Measures <sup>1</sup>	PTX Monotherapy (n=15)	PTX + Pelareorep (n=16)	PTX + Pelareorep + Avelumab (n=17)	
Confirmed ORR	13.3%	37.5%	17.6%	
Median PFS (months)	6.4	12.1	6.4	
	Not Reached			
Median OS (months)	18.2	Estimate: 32.1*	21.7	
Hazard Ratio for OS	_	0.48	1.08	
24-Month OS Rate (%)	33%	64%	39%	

<sup>1</sup> Tumor responses based on RECIST version 1.1 ORR: Overall response rate; PTX: paclitaxel PFS: progression-free survival; OS: overall survival \*This estimate assumes patients survived only until the next per protocol follow-up in 4 months. Had the patients survived only one day past their final follow-up visits, the estimated median OS would be 28.7 months.

## Pelareorep's Favorable Overall Safety Highlighted by BRACELET-1 Safety Summary



	Paclitaxel (PT	X) (n=12)	PTX + Pelareorep (n=16)		PTX + Pelareorep +	PTX + Pelareorep + Avelumab (n=17)	
Grade	Any	≥ 3	Any	≥ 3	Any	≥ 3	
Alopecia	6 (50%)	-	9 (56%)	-	8 (47%)	-	
Anemia	7 (58%)	-	5 (31%)	-	10 (59%)	1 (6%)	
Anorexia	4 (33%)	-	5 (31%)	-	5 (29%)	-	
Chills	-	-	7 (44%)	-	5 (29%)	-	
Diarrhea	1 (8%)	-	6 (38%)	1 (6%)	8 (47%)	2 (12%)	
Fatigue	5 (42%)	-	12 (75%)	2 (12%)	8 (47%)	1 (6%)	
Infusion related reaction	1 (8%)	-	3 (19%)	-	9 (53%)	1 (6%)	
Leucopenia	2 (17%)	-	3 (19%)	1 (6%)	11 (65%)	5 (29%)	
LFT <sup>3</sup> Abnormality	3 (25%)	-	6 (38%)	2 (12%)	9 (53%)	2 (12%)	
Lymphopenia	3 (25%)	-	3 (19%)	1 (6%)	4 (24%)	2 (12%)	
Nausea	4 (33%)	-	7 (44%)	-	8 (47%)	-	
Neuropathy	3 (25%)	-	8 (50%)	1 (6%)	10 (59%)	1 (6%)	
Neutropenia	3 (25%)	1 (8%)	5 (31%)	3 (19%)	10 (59%)	6 (35%)	
Proteinuria	2 (17%)	-	6 (38%)	-	4 (24%)	1 (6%)	
Pyrexia	-	-	8 (50%)	-	11 (65%)	-	

Fifteen Most Common Adverse Events<sup>1,2</sup> as Attributed to Study Drug(s)

Safety data presented by Clark et al. at ASCO 2023, <sup>1</sup>Adverse Events collected using CTCAE V5.0, <sup>2</sup>Only the 45 randomized patients who received any study therapy included in this analysis, <sup>3</sup> Liver function test abnormality



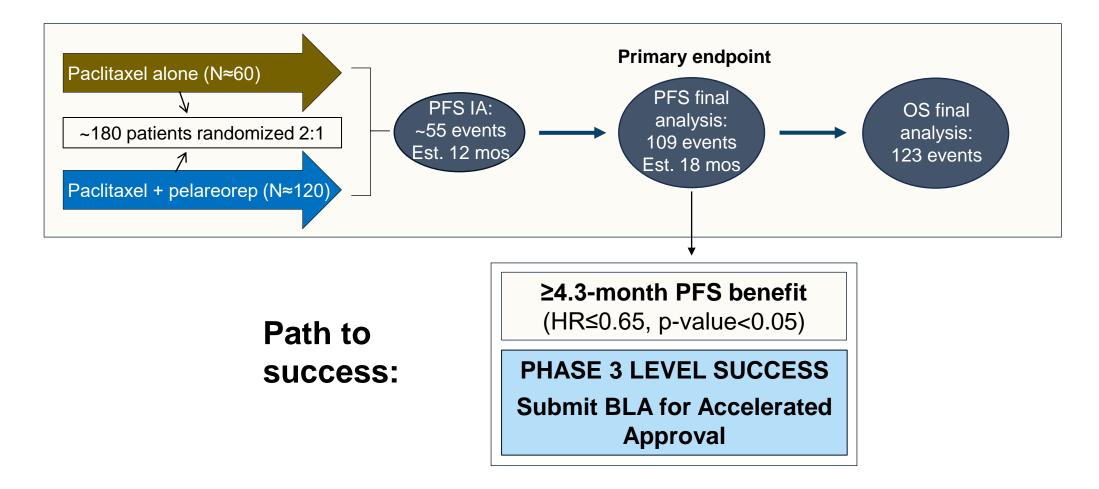
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## Licensure Pathway Plan & FDA Type C Meeting Feedback



## Registration-Enabling Phase 2 Study in HR+/HER2- mBC Patients





> 4.3-month PFS benefit target achievable based on BRACELET-1 results (5.7-month PFS benefit)

Licensure path based on the approach used by Ibrance (PALOMA-2) and Enhertu (DESTINY-01)

mBC: metastatic breast cancer; PFS: progression-free survival; OS: overall survival; IA: interim analysis





### Summary of key outcomes

- FDA agreed that the proposed study population is appropriate (i.e., patients who failed hormonal therapy and received either 0 or 1 line of ADC therapy)
- FDA agreed that PFS is acceptable primary endpoint. They noted that OS should also be formally tested.
- FDA provided guidance on what constitutes a clinically meaningful benefit

### **General comments:**

 The tone of the discussion was very collegial with a thoughtful dialogue between Oncolytics and the FDA medical reviewers



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## Pelareorep in Gastrointestinal Cancer





### Phase 1/2 multiple indication biomarker, safety & efficacy study

Success Criteria ≥ 3 responses

Success Criteria  $\geq$  6 responses



Primary Endpoints: Safety ORR

Secondary Endpoints: PFS, OS

Exploratory Endpoints: Biomarker and MOA assessments

Unresectable Anal Cancer ≥2L n=10

**Advanced / Metastatic** 

**Pancreatic Cancer** 

1L n=12

**Newly Diagnosed** 

**Pancreatic Cancer** 

1L n=15



Success Criteria ≥ 2 responses

Pelareorep + mFOLFIRINOX +/- Atezolizumab

Pelareorep + Atezolizumab + Gemcitabine + Nab-paclitaxel

## Efficacy Signals Shown in Two Gastrointestinal Cancers



	First-line Advanced / Metastatic Pancreatic Cancer	Second-line or Later Anal Cancer
Status	Phase 1/2 updated data reported October 2023	Phase 1/2 initial data reported November 2023
Key Data	62% Objective response rate 7.2 months Median PFS 10.6 months Median OS 46% 12-month survival rate	37.5% Objective response rate Including a complete response
Next Steps	Advancing to a licensure-enabling study	Expansion of enrollment to confirm efficacy signal

Pancreatic cancer program has U.S. FDA Fast Track Designation

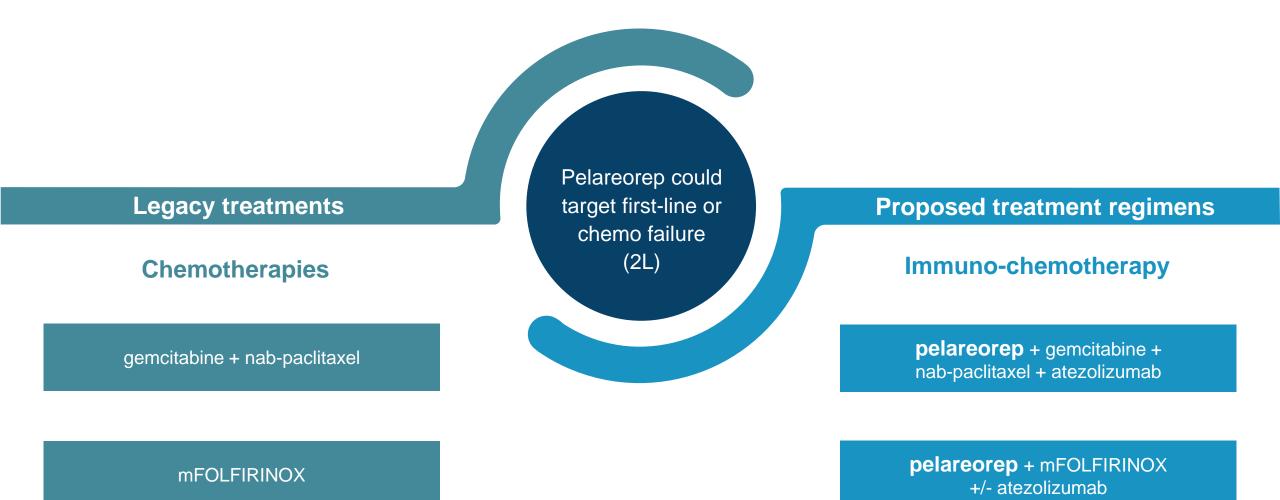


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## Pelareorep in Metastatic Pancreatic Cancer

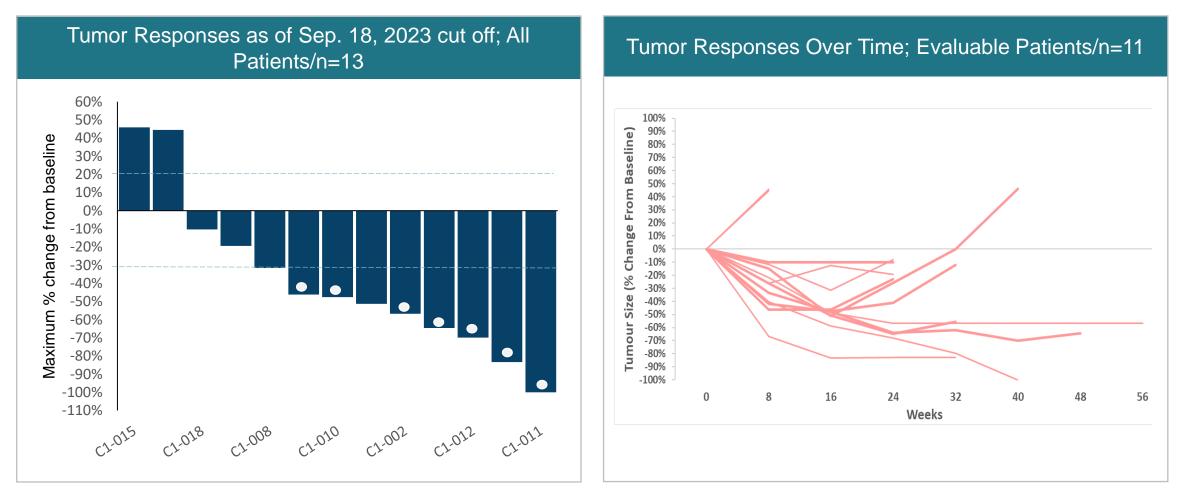






## PDAC GOBLET Results Showing 62% ORR, Nearly Triple The Rate Seen in Prior Studies





Dotted lines represent cut-offs for PD (+20%) and PR (-30%)

Patients with a white dot have confirmed responses (2 or more consecutive scans with PR or CR)

# Next Steps: Finalize GCAR PDAC Registrational Trial Protocol and Initiate Study



#### **Patient Population:**

- Patients receiving 1L treatment for PDAC
- Prior Treatments: None
- Adaptive trial design to be based on positive GOBLET cohort 1 results

#### **Treatment Regimen:**

 Randomized trial of pelareorep + atezolizumab + gemcitabine + nab-paclitaxel vs. gemcitabine + nab-paclitaxel

#### **Registrational Endpoints:**

- Primary Endpoint: Overall Survival
- Secondary Endpoints: Progression-Free Survival, Overall Response Rate, and Translational Data



Fast Track Designation

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Trial plan to include study size, timing for the first interim analysis, and definition of clinical and translational endpoints

## mFOLFIRINOX Cohort Design



Strategic rationale: to investigate the use of pelareorep with another commonly used treatment regimen

#### **Patient Population:**

- Newly diagnosed metastatic PDAC patients (as defined by RECIST 1.1)
- To be supported by PanCAN Therapeutic Accelerator Grant

#### **Treatment Regimen:**

Phase 1/2 randomized trial of pelareorep + mFOLFIRINOX vs.
 mFOLFIRINOX + pelareorep + atezolizumab (n=15/arm in Stage 1)

#### Endpoints: Based on Simon two-stage screened selection design:

- **Stage 1**: success criteria of  $\geq$  6 responses in the first 30 subjects
- **Stage 2**: success of  $\geq$  13 responses (41%):
- Study to include Translational Data

Safety run-in enrollment completed, safety run-in data expected H1 2025 Pancreatic Cancer Opportunity Driven by Promising GOBLET Phase 1/2 Data & Supported by FDA Fast Track Designation



GOBLET Study Shows Increased ORR

Studies Show Survival Benefit

Favorable Overall Safety

Consistent Translational Data

Registrational Trial Plan and Beyond

- An ORR of 62% was observed, more than double the response rates recorded in historical control trials<sup>1-4</sup>
- >> Prior studies also showed clinically meaningful improvements in survival

» GOBLET data indicate the treatment has been well tolerated with no safety concerns

Translational data from GOBLET show that patients with increases in blood TILs showed a decrease in tumor volumes

- » Registration-enabled study protocol being finalized after pelareorep selected for inclusion by GCAR
- \$5M PanCAN grant to explore pelareorep/mFOLFIRINOX regimen, H1 2025 safety run-in data

ORR: objective response rate; mPFS: median progression-free survival; mOS: median overall survival; TILs: tumor-infiltrating lymphocytes; GCAR: Global Coalition for Adaptive Research; mFOLFIRINOX: modified FOLFIRINOX; PanCAN: Pancreatic Cancer Action Network; Sources: 1. Von Hoff D et al. N Engl J Med 2013; 369:1691-1703 DOI: 10.1056/NEJMoa1304369; 2. O'Reilly et al. Eur J Cancer. 2020 June ; 132: 112–121. DOI:10.1016/j.ejca.2020.03.005; 3. Karasic et al. JAMA Oncol. 2019 Jul 1;5(7):993-998. DOI: 10.1001/jamaoncol.2019.0684; 4. Tempero et al. Ann Oncol. 2021 May;32(5):600-608. DOI: 10.1016/j.annonc.2021.01.070.



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Pelareorep in ≥ Second-Line Unresectable Anal Cancer



## Positive GOBLET Anal Cancer Data Meets Success Criteria, Expanding Enrollment, Highlights Synergy with CPI



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Presented November 9, 2023 at the 2<sup>nd</sup> International Multidisciplinary Anal Cancer Conference (IMACC)

#### **Patient Population:**

- Patients with 2L, unresectable squamous cell carcinoma of the anal canal (SCCA)
- Prior treatments included chemotherapy and radiation therapy

#### **Study Design & Treatment Regimen:**

 Open-label, single arm, Simon Two-stage study of pelareorep + atezolizumab (n=10)

#### **Enrollment Expanded:**

 Stage 1 success criteria met; Stage 2 enrollment (18 patients) ongoing

#### Combined results could lead to a single-arm registration study

ORR of 37.5%, with 1 CR ongoing at 12 months and 2 PRs Data satisfied the prespecified success criteria for the study Follow-up is ongoing

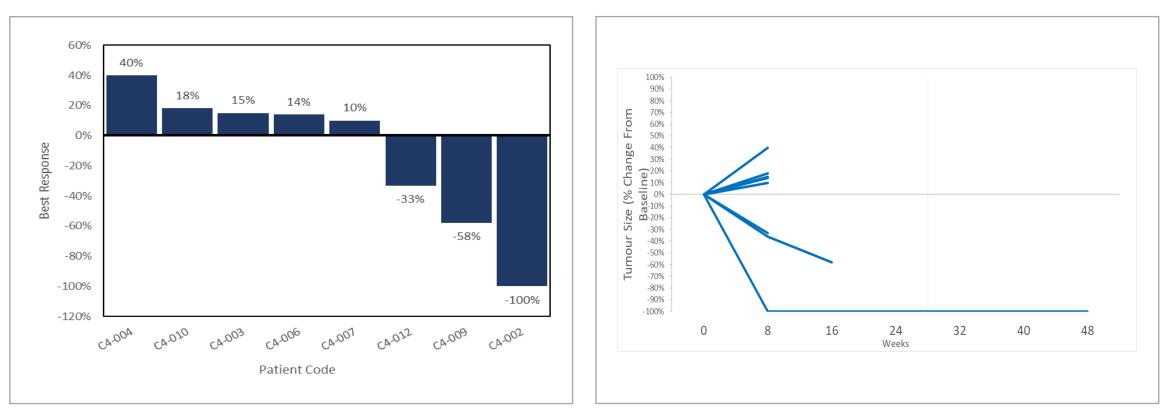
#### CPI: Checkpoint Inhibitor; 2L: Second-Line; ORR: objective response rate; CR: complete response; PR: partial response

## Pelareorep-Atezolizumab Combination in Anal Cancer, ORR Exceeds Historical Efficacy Rates of Like Studies



### ORR of 37.5% meets the pre-specified efficacy success criteria. Of 8 evaluable patients:

- 1 CR (ongoing at 12 months)
- 2 PR (one at week 8 and one ongoing at week 16)
- ~11% Average ORR reported in historical control trials of checkpoint inhibitor therapies<sup>1-3</sup>



ORR: objective response rate; CR: Complete Response; PR: Partial Response; Sources: 1. <u>Sheela Rao</u> (Frontier Oncol) 2022; 2. Marabelle et al Lancet Oncology (2022)/NCT02628067; 3. Sara Lonardi (2021) J. Immu Cancer/<u>NCT03944252</u>;



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Intellectual Property, Management Team, Financials, Pipeline, Additional Information



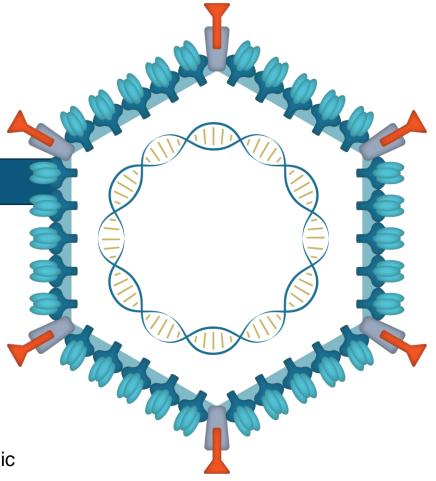


148 patents issued worldwide, including 13 US and 7 Canadian

14 pending applications worldwide

#### Pelareorep issued patent claims cover:

- Compositions of matter comprising pelareorep
- Patent rights extend to at least the end of 2031
- Pharmaceutical use of pelareorep to treat neoplasia and cellular proliferative diseases
- Combination therapy with radiation, chemotherapy and/or immunosuppressants
- Methods for manufacturing pelareorep and screening for susceptibility to pelareorep
- Upon approval, eligible for minimum 12 years of U.S. market exclusivity for new biologic



Innovative Leadership Team with Strong Immuno-oncology, Business Development, Clinical Trial and Finance Expertise





Matt Coffey, Ph.D., MBA President and CEO



Kirk Look, CA, MSJ Chief Financial Officer



Thomas Heineman, M.D., Ph.D. Chief Medical Officer



Allison Hagerman, PEng, PMP, MBT VP, Product Development



**Christophe Degois** VP, Business Development



**Amy Levin, RN, BSN** VP, Clinical Operations

Genentech

















## Financials Overview



Financial Overview		Research Coverage	
Ticker	ONCY: NASDAQ ONC: TSX	Patrick Trucchio	H.C. Wainwright & Co.
Avg. Daily Volume (1 mo*)	740,798	John Newman	Canaccord Genuity
Shares Outstanding	77,074,089	Jason McCarthy	Maxim Group
Market cap <sup>1</sup>	~\$86 M	Douglas Miehm	RBC Capital Markets
Cash <sup>2</sup>	\$19.6 M	Louise Chen	Cantor Fitzgerald
HQ	San Diego, CA / Calgary, AB, Canada	Douglas Loe	Leede Jones Gable
		Soumit Roy	JonesTrading
g days from Oct. 4, 2024 – Nov. 12, 2024	1 Market Cap as of Nov 12 2024	Michael Freeman	Raymond James

2. Cash as of September 30, 2024

# Pelareorep Has Expansive Potential, Starting with Breast and Gastrointestinal Cancers



Program	Collaborator	Combination	Phase 1	Phase 2	Registration-Enabling Study	Milestone
BREAST CANCER						
Planned Study	TBD	pela + PTX	Preparing protocol f	or FDA submission		Registrational Study Plan H1 2024

#### **GASTROINTESTINAL CANCERS** Planned Study initiation pela + gem + Preparing arm-specific protocol Roche **Adaptive Study** GCAR nab-PTX + atezo 2025 1L Adv/Metastatic PDAC PANCREATIC Safety run-in data **GOBLET** cohort 5 pela + mFOL CANCER (Roche) ACTION +/- atezo Newly Diagnosed PDAC expected H1 2025 NETWORK **GOBLET** cohort 4 Updated efficacy data Roche ≥2L Unresectable Anal pela + atezo expected H1 2025 Cancer

PDAC: pancreatic ductal adenocarcinoma; GCAR: Global Coalition for Adaptive Research; pela: pelareorep; PTX: paclitaxel; gem: gemcitabine; atezo: atezolizumab; mFOL: modified FOLFIRINOX; Adv: Advanced; 1L: First-Line; 2L: Second-Line



Q4 2024	H1 2025	H2 2025	2026 - 2027
GOBLET study mFOLFIRINOX PDAC cohort safety run-in enrollment update	<ul> <li>Breast Cancer</li> <li>First patient enrolled in registration-enabling mBC study</li> <li>GI Cancer</li> <li>GOBLET study mFOLFIRINOX PDAC cohort safety update</li> <li>GOBLET study anal cancer cohort efficacy data update</li> </ul>	<ul> <li>Breast Cancer</li> <li>Translational data</li> <li>GI Cancer</li> <li>GOBLET study mFOLFIRINOX PDAC cohort stage 1 data</li> </ul>	<ul> <li>Breast Cancer</li> <li>H1 2026: PFS interim analysis, approx.</li> <li>55 events</li> <li>H2 2026: last patient enrolled</li> <li>H1 2027: PFS readout</li> </ul>

## Why Did Avelumab Eliminate the Benefit of Pelareorep?



Avelumab is the only licensed anti-PD-L1 Ab with a native Fc region that retains FcγR binding

### Hypothesis:

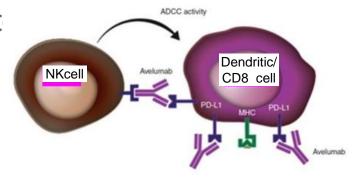
Binding of avelumab to Fc receptors impairs the expansion of T cell clones thereby diminishing the generation of potentially beneficial pelareorep-induced immune responses

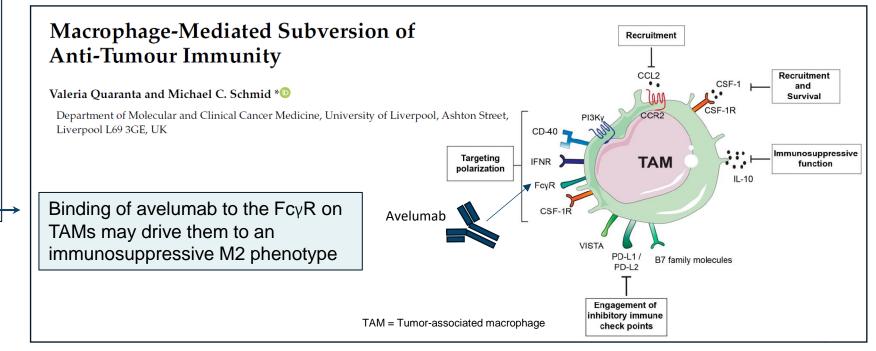
Possible mechanisms are shown

Evaluation of immune cell subsets of cancer patients treated with Avelumab, a fully human IgG1 anti-PD-L1 MAb capable of mediating ADC of human tumor cells

Lauren Lepone<sup>1</sup>, Renee Donahue<sup>1\*</sup>, Italia Grenga<sup>1</sup>, Caroline Jochems<sup>2</sup>, Kwong-Yok Tsang<sup>1</sup>, Simon Metenou<sup>1</sup>, Jacob Richards<sup>1</sup>, Christopher R Heery<sup>1</sup>, Ravi Madan<sup>3</sup>, James L Gulley<sup>4</sup>, Jeffrey Schlom<sup>1</sup>

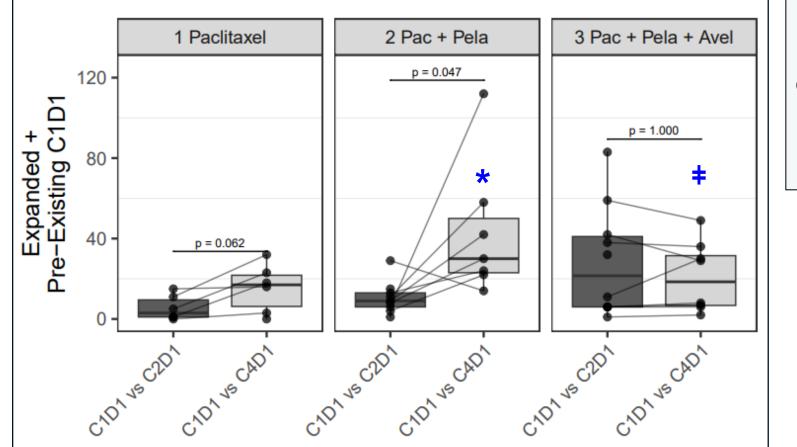
Avelumab binding to the  $Fc\gamma R$  on NK cells may induce ADCC-mediated killing of T cells





## T Cell Expansion in BRACELET Patients Blocked by Avelumab





#### **Pelareorep + paclitaxel:**

Statistically significant expansion of T cell clones at Cycle 4 Day 1 (\*)

**Pelareorep + paclitaxel + avelumab :** 

No T cell expansion at Cycle 4 Day 1 (**‡**)

Pac = paclitaxel; Pela = pelareorep; Avel = avelumab

C = cycle; D = day

# Pelareorep Expected to be Efficacious Following Progression on Enhertu (T-DXd)



- Pelareorep is efficacious in heavily pre-treated breast cancer patients
- T-DXd failure results from reduced HER2 expression or deruxtecan resistance neither should affect pelareorep's efficacy<sup>1</sup>
- T-DXd has no known immunosuppressive effects that would impair pelareorep's MOA
  - T-DXd does not directly target immune cells, which are key to pelareorep's activity<sup>2</sup>
  - T-DXd is associated with leukopenia or neutropenia; however, these are transient are not expected to affect pelareorep's efficacy based on prior studies
- T-DXd may stimulate anti-cancer immunity and enhance the effects of immune therapies
  - o Deruxtecan stimulates innate and adaptive immune responses through DNA damage-mediated effects<sup>1</sup>
  - o T-DXd enhances tumor-infiltrating CD8+ T cells and MHC class I expression on tumor cells in mice<sup>1</sup>
  - o T-DXd induces CXCL9/10/11 on HER2-positive gastric cells resulting enhanced anti-tumor immunity<sup>2</sup>

## BRACELET-1 Study Groups are Well-balanced for Key Attributes



	PTX Monotherapy N=15	<b>PTX + Pelareorep</b> N=16	PTX + Pelareorep + Avelumab N=17	
Age	60 (46-74)	52.5 (38-71)	59 (37-70)	
Performance status (ECOG score)				
0	10 (67%)	11 (69%) 10 (59%)		
1	5 (33%)	5 (31%)	7 (41%)	
White race	12 (80%)	12 (75%)	13 (76%)	
Stage at diagnosis				
1-111	8 (53%)	4 (25%)	7 (42%)	
IV	7 (47%)	12 (75%)	10 (59%)	
Visceral disease	12 (80%)	13 (81%)	15 (88%)	
Prior lines of therapy				
Neo/adjuvant taxane <sup>1</sup>	6 (40%)	4 (25%)	6) 5 (29%)	
Targeted therapy (alpelisib or everolimus)	2 (20%)	1 (12%)	3 (18%)	
Subsequent therapy <sup>2</sup>	Chemotherapy: 10 Radiation only: 1 No treatment: 1 ADC: 4	Chemotherapy: 10 Radiation only: 1 No treatment: 2 ADC: 2	Chemotherapy: 15 Radiation only: 0 No treatment: 2 ADC: 1	

<sup>1</sup> Patients receiving taxanes in the neoadjuvant or adjuvant setting must have had a disease-free interval of at least 12 months prior to enrollment.

<sup>2</sup> Subsequent therapy is defined as any breast cancer treatment received after discontinuation of study treatment, e.g., due to radiologic or clinical disease progression or to an adverse event.

### Benefit of Pelareorep-based Therapy Compare Favorably to T-DXd



Endpoint	<b>Destiny-Breast04</b> Chemotherapy vs. T-DXd 1-line prior chemotherapy		<b>Destiny-Breast06</b> Chemotherapy vs. T-DXd No prior chemotherapy		BRACELET-1 Pac vs. Pac + Pela No prior chemotherapy	
	TPC	T-DXd	TPC	T-DXd	Paclitaxel	Pac-Pela
Confirmed ORR	16.3%	52.6%	32.2%	56.5%	13.3%	37.5%
<b>PFS</b> (HR [95% CI])	5.4 mo	<b>mo</b> ) 10.1 mo	+5.1 8.1 mo	mo) 13.2 mo	6.4 mo	mo 12.1 mo
	(0.51 [0.40, 0.64])		(0.62 [0.51, 0.74])		(0.39 [0.12, 1.24])	
<b>OS</b> (HR [95% CI])	17.5 mo	23.9 mo	NR	NR	18.2 mo	32.1 mo*
	(0.64)		NA		(0.48 [0.17, 1.35])	

T-DXd: Trastuzumab deruxtecan

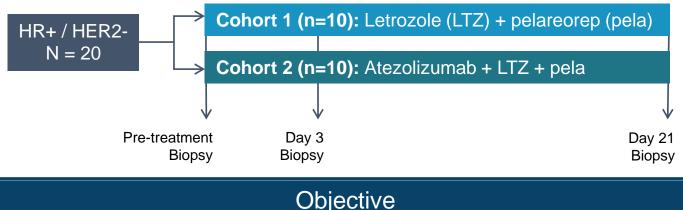
- TPC: Capecitabine, nab-paclitaxel, paclitaxel
- Pac: Paclitaxel
- Pela: Pelareorep
- NA/NR: Not available/Not reached

\*This estimate assumes patients survived only until the next per protocol follow-up in 4 months. Had the patients survived only one day past their final follow-up visits, the estimated median OS would be 28.7 months.

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



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



Objective

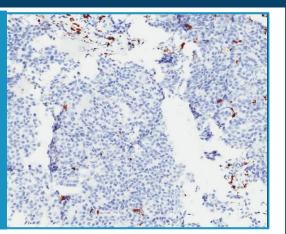
Confirm pelareorep's MOA and evaluate its potential to synergize with ICIs via biomarker measurements such as CeITIL score, T cell infiltration and PD-L1 expression

#### Key Takeaways

-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

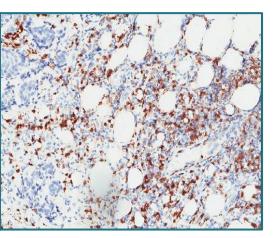
#### Pre vs. Post Treatment CD8+ T Cell Infiltration

**Before** treatment: CD8+ T cell staining



~3 weeks post-treatment

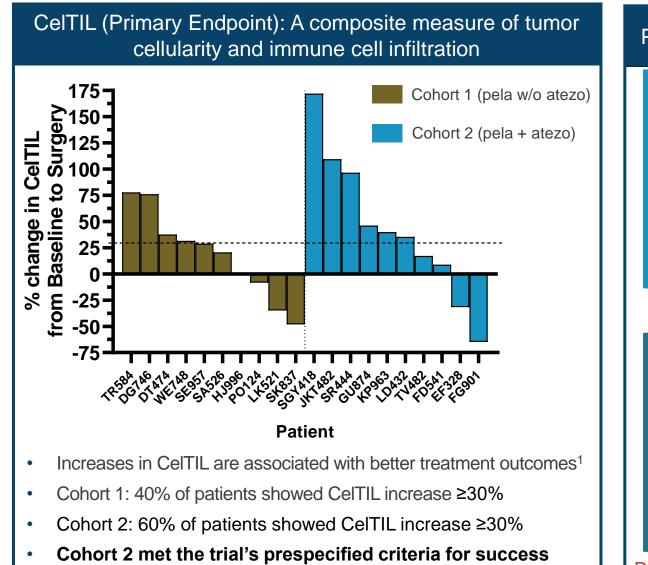
After treatment: CD8+ T cell staining



Brown staining shows CD8+ T cells

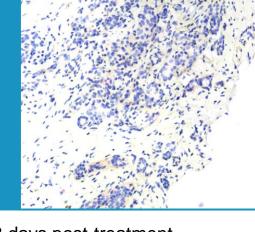
## **AWARE-1 Achieved Primary Objective**



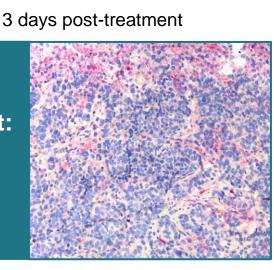


#### Pre vs. Post Treatment Tumor PD-L1 Expression





After treatment: Tumor PD-L1 expression



Red staining indicates PD-L1 expression

Pela: Pelareorep; Atezo: Atezolizumab

<sup>1</sup>Nuciforo P et al. A predictive model of pathological response based on tumor cellularity and tumor-infiltrating lymphocytes (CeITIL) in HER2-positive breast cancer treated with chemo-free dual HER2 blockade. Ann Oncol, 2017