# Pelareorep

**A Novel Cancer Immunotherapeutic** 

## July 2025



NCOLYTICS BIOTECH INC.



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 our belief as to the potential, mechanism of action and benefits of pelareorep as a cancer therapeutic: our stated goals and objectives; our anticipated patent protection; our belief in the commercial opportunities for pelareorep; pelareorep's safety profile; 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 (PELA)

# Characteristics & Mechanism of Action

Website oncolyticsbiotech.com Nasdaq ONCY TSX ONC

## **PELA** is an Oncolytic Virus Cancer Immunotherapy

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



## **IV PELA is Shielded from Neutralization in the Blood**



# IV PELA is delivered to tumors by peripheral blood mononuclear cells (PBMCs), where it selectively infects cancer cells

Antibody-bound reovirus remains infectious when associated with mononuclear cells



A. Ab-bound reovirus

Free reovirus is neutralized by antibodies, so melanoma cells are not lysed



B. Ab-bound reovirus loaded onto monocytes

When loaded onto monocytes, Ab-bound reovirus is shielded from neutralization; consequently, it remains infectious and lyses melanoma cells

#### IV PELA is transported by PBMCs and handed-off to tumor cells





"In untransformed, reovirus-resistant cells, double-stranded RNA structures in reovirus transcripts activate PKR, which subsequently phosphorylates eIF-2a, inhibiting translation initiation of viral genes. In cells with an activated Ras signaling pathway (i.e., transformed cells), however, PKR phosphorylation in response to viral transcripts is inhibited and viral translation proceeds unimpeded." (emphasis and parentheses added)

Reovirus as a Novel Oncolytic Agent Journal of Clinical Investigation 2000;<u>105(8)</u>:1035-1038. <u>https://doi.org/10.1172/JCI9871</u>



# PELA Translational Research & Intellectual Property

NCOLYTICS

## Upon IV Administration, PELA is Found in Almost all Tumors Regardless of Type Including PDAC



#### PELA is found in almost all on-treatment tumor biopsies

Indication treated with IV PELA	# of biopsied tumors	# PELA-positive biopsies
Pancreatic ductal adenocarcinoma	12	12
Metastatic colorectal cancer	12	11
Head and neck cancer	3	3
Gliomas/metastatic brain tumors	9	8
Relapsed multiple myeloma	20	20
Primary breast cancer	23	23
Other	4	4

# PELA RNA is found in tumor but not stromal cells



 Berkeley, et al. Can Immunol Res. 2018
 4.
 Ilett, et al. \_ Ther 2009
 4.
 Phillips, et al. Oncolytic Virother. 2018

 Adair, et al. Sci Transl Med. 2012
 5.
 Ilett, et al. Clin Cancer Res. 2011
 6.
 Berkeley, et al. Cancer Imm. Res. 2018

3. Mahalingam. et al. British J Can. 2023

## REO 029 mPDAC Study Translational Data: TIL Expansion by Cycle 4 Correlates with Change in Tumor Size



NA = tumor response data not available for patient C1-017

#### Conclusions

- TIL expansion in the blood continued at least through Cycle 3 of therapy
- TIL clonal expansion in the blood correlates with a reduction in tumor volume

## AWARE-1 Neoadjuvant Study in HR+/HER2- Breast Cancer: PELA Modified the TME and Stimulated Anti-tumor Immunity



#### **PELA increased T cell infiltration into tumors**



#### • All tumors (N=20) were infected by PELA

- Intratumoral CD8+ T cells increased in all patients by day 21
- CD8+ T cells increased an average of 11-fold from baseline

#### PELA increased PD-L1 expression in tumors



#### In addition, PELA:

- Enhances tumor expression of IFN-α and IFN-γ regulated genes including CXCL9, CXCL10 and CXCL11
- Upregulates genes of the Tumor Inflammation Signature (TIS) pathway, which potentiate responses to CPIs
- Enhances T cell activation and expansion of TIL clones
- PELA induces an inflamed tumor phenotype, stimulates innate and adaptive immune responses, and primes the tumor to respond to PD-L1 therapy
- Consistent results demonstrate PELA's inflammatory and anti-tumor effects across indications

**IP** Profile



Issued Patents	<ul> <li>146 patents issued worldwide</li> <li>11 in the U.S.</li> <li>7 in Canada</li> </ul>
Patent Life	<ul> <li>Composition of matter protection through 2028</li> <li>Method of use and manufacturing protection through 2031</li> </ul>
Extension Strategy	<ul> <li>Pending filings regarding proprietary manufacturing methods for virus harvest and extraction</li> <li>New patents expected to extend protection to 2044</li> </ul>

# **PELA Clinical Development**

NCOLYTICS BIOTECH INC.



#### **PELA** evaluated in:

- >20 Oncolytics-sponsored studies and several externally sponsored studies (NCI, CCTG, etc.)
- Multiple cancer indications (breast, pancreatic, colorectal, myeloma, brain, etc.)
- >1,100 patients treated; >900 intravenously
- No maximum tolerated dose (MTD) identified
- Most common PELA-adverse reactions
  - "Flu-like" symptoms: Fever, chills, headache, fatigue, myalgia, cough, anorexia
  - GI symptoms also common: Nausea, diarrhea, vomiting
  - Lymphopenia, neutropenia, thrombocytopenia also common, but rarely clinically significant
- Adverse events usually last <6 hours and can be managed with OTC meds</p>
- Serious PELA-related adverse events or severe symptoms are <u>uncommon</u>

ABSTRACTS | IMMUNOTHERAPY OF CANCER · Volume 28, Supplement 5, V422, September 2017 · Open Archive

1193P - Pooled data analysis of the safety and tolerability of intravenous pelareorep in combination with chemotherapy in 500 + cancer patients <u>A.A. Gutierrez · C. Reid · M. Crawford · … · D. Galindez · R. O'Flynn · M. Coffey …</u> Show more Affiliations & Notes ✓ Article Info ✓

📜 Download PDF 🍠 Cite 🛯 Share 📮 Set Alert 🔘 Get Rights 🕞 Reprints

Background: Oncolytic viruses are promising cancer immunotherapies but questions have been raised regarding their safety. Pelareorep (REOLYSIN, R), an unmodified Reovirus Dearing strain, selectively replicates and lyses cancer cells and induces antitumor immunity. To date, goo+ patients (pts) have been treated with intravenous (IV) pelareorep. In a phase 2 trial, its combination with paclitaxel improved overall survival (17,4m) vs paclitaxel (10.4m) in metastatic breast cancer (MBC) pts (HR 0.65, 80% CI 0.46-0.91, p=0.1; Berstein et.al. AACR2017). A pooled analysis was thus conducted to better characterize pelareorep's safety profile in combinations with paclitaxel.

Methods: 1417 pts have been enrolled in 36 trials: 934 pts received IV pelareorep and 359 were in control arms. Data from 8 trials with paclitaxel (P), paclitaxel + pelareorep (PR), carboplatin + paclitaxel (CP) or carboplatin + paclitaxel + pelareorep (CPR) were pooled. Standard doses of P (weekly) and CP were administered. Pelareorep IV dose was 31000 TCID50 (5-6 doses q21-28 d). Various advanced solid tumors were evaluated, including the 8 pts with MBC.

**Results:** A total of 563 pts were included in P (86), PR (95), CP (118) or CPR (264) groups. Median age (59-62 y) and ECOG o-1 status (90-96%) were similar across the groups. All pts in P or PR had received prior chemo but only 26% in CP and 38% in CPR. Fatigue was the most common grade  $\ge 3$  treatment related adverse event (TRAE) in PR (9,5%) and CPR (8,3%) vs P (8,1%) and CP (2,5%). Grade  $\ge 3$  neutrophil count decreased and/or WBC decreased were more frequent in PR (15,5%)/27,9%) than in P (5,8%)(3,5%), but addition of pelareorep did not increase the frequency or severity of other grade  $\ge 3$  TRAEs with P or CP. Serious TRAEs (%) of interest in P vs PR and CP vs. CPR, included: fever (o vs 3,2 & o vs 3,8), febrile neutropenia (o vs 1,1 & 3,4 vs 3,4), sepsis (1,2 vs 0 & o vs 1,5) and flu-like syndrome (o vs 1,1 & o vs 0,8).

Conclusions: This is the largest database reported to date examining the safety of an IV viral agent. Pelareorep's administration, in combination with paclitaxel or carboplatin-paclitaxel, is safe and well tolerated. Continued evaluation in a registration trial is planned.

Gutierrez, A.A., et al., Pooled data analysis of the safety and tolerability of intravenous pelareorep in combination with chemotherapy in 500 + cancer patients, Annals of Oncology, Volume 28, V422, September 2017

## **Pancreatic Cancer Program**







## 66,440

Estimated PDAC cases in the US in 2024<sup>1</sup>, with 5-year survival rate of  $\sim 8\%^2$ 

51%

Percentage of PDAC that has metastasized at diagnosis<sup>1</sup>

20%

Percentage of PDAC patients with resectable disease at diagnosis<sup>3</sup>

Common Types of Cancer	Estimated New Cases 2024	Estimated Deaths 2024	Pancreatic cancer represen new cancer cases in t
1. Breast Cancer (Female)	310,720	42,250	
2. Prostate Cancer	299,010	35,250	
3. Lung and Bronchus Cancer	234,580	125,070	
4. Colorectal Cancer	152,810	53,010	
5. Melanoma of the Skin	100,640	8,290	
6. Bladder Cancer	83,190	16,840	3.3%
7. Kidney and Renal Pelvis Cancer	81,610	14,390	3.370
8. Non-Hodgkin Lymphoma	80,620	20,140	
9. Uterine Cancer	67,880	13,250	
10. Pancreatic Cancer	66,440	51,750	

Pancreatic cancer is the third deadliest cancer the US in 2024<sup>1</sup> (14% of annual deaths)

Year	Revenue Projections Range for RMC-6236 in PDAC*
2027	\$51 - \$522 million
2028	\$217 - \$978 million
2029	\$555 - \$1,308 million
2030	\$885 - \$1,679 million

\*Sources include TD Securities (USA) LLC, Needham & Company, LLC, Piper Sandler & Co., Jefferies LLC; 2L: second-line; 1. National Cancer Institute. (2024). Cancer Stat Facts: Pancreatic Cancer. SEER Program, Surveillance, Epidemiology, and End Results. Retrieved April 7, 2025, from <a href="https://seer.cancer.gov/statfacts/html/pancreas.html">https://seer.cancer.gov/statfacts/html/pancreas.html</a>, 2. American Cancer Society Cancer Facts & Figures 2025.; 3. Janssen QP, et al Neoadjuvant Treatment in Patients With Resectable and Borderline Resectable Pancreatic Cancer. Front Oncol. 2020 Jan 31;10:41. doi: 10.3389/fonc.2020.00041. PMID: 32083002; PMCID: PMC7005204.



Study	Ν	CPI	Treatment regimen	
REO 017	34	-	PELA + gemcitabine	
NCI 8601 (randomized trial)	73	-	PELA + carboplatin + paclitaxel vs. carboplatin + paclitaxel	
<b>REO 029</b> (Cohort 1)	19	+	PELA + gemcitabine/nab-paclitaxel + atezolizumab	
<b>REO 029</b> <sup>*</sup>	Ongoing	-	PELA + modified FOLFIRINOX	
(Cohort 5)	Ongoing	+	PELA + modified FOLFIRINOX + atezolizumab	



Design	Single-arm, mPDAC cohort
Population	mPDAC (1L)
Treatment	<ul> <li>PELA + gemcitabine/nab-paclitaxel + atezolizumab</li> <li>PELA dose: 4.5 x 10<sup>10</sup> TCID<sub>50</sub></li> </ul>
Primary	Objective response rate (ORR)
Secondary	Progression-free survival (PFS), overall survival (OS), disease control rate (DCR), safety



#### **Study population**

- Median age: 61 years
- Sex: 85% male; 15% female
- All patients had metastatic disease;
   69% had liver metastases

#### **Results Summary**

- Treatment well-tolerated with no safety concerns
- Strong tumor responses: 62% ORR; 85% DCR
- Encouraging survival outcomes: **45% 1-year survival rate**
- Treatment well-tolerated with no safety concerns
- Expansion of TIL clones correlates with tumor response

## REO 029 Best Published ORR and Strong 12-month Survival Rate



ORR	DCR	12-month survival rate
62% (54% confirmed)	85%	45%

NCOLYTICS

## REO 029 Patient Characteristics and Treatment Response



Age (years)	Sex	ECOG score	Metastases (location)	Baseline target lesion size (mm)	Best Response
72	F	1	Liver	65	PR
54	М	1	Peritoneum	37	PR
63	F	1	Lung	13	PR
71	М	0	Liver	79.5	SD
54	М	0	Liver	63	PD
53	М	0	Liver	187	PR
67	М	0	Liver	39.1	PR
69	М	0	Liver	15.7	PR
49	М	0	Liver	52.1	PR
65	М	1	Lymphangitis carcinomatosis	30	PR
71	М	0	Liver	24	PD
54	М	0	Peritoneum	29	SD
54	М	0	Liver	39	SD

# Characteristics of REO 029 evaluable patients:

- Mean age: 61.2 years
- Male: 85%
- Liver metastases: 69%
- ECOG 0/1: 69%/31%
- Average size of target lesions at baseline: 52 mm

Strong tumor responses in patients with liver metastases, a poor prognostic indicator in PDAC

- ORR = 56%
- DCR = 78%

Patients with liver metastases shown in blue (liver metastasis is a poor prognostic factor in PDAC)

## REO 029 Safety Results



#### Most frequent treatment emergent adverse events

Adverse Event (MedDRA Preferred Term)	All TEAEs N=19, n (%)	Grade 3/4 TEAEs N=19, n (%)
Pyrexia	15 (78.9%)	1 (5.3%)
Anaemia	12 (63.2%)	4 (21.1%)
Chills	10 (52.6%)	0 (0.0%)
Fatigue	10 (52.6%)	2 (10.5%)
Thrombocytopenia	8 (42.1%)	1 (5.3%)
Nausea	7 (36.8%)	0 (0.0%)
Platelet count decreased	6 (31.6%)	1 (5.3%)
Neutrophil count decreased	6 (31.6%)	5 (26.3%)
Urinary tract infection	6 (31.6%)	2 (10.5%)
Alanine aminotransferase increased	5 (26.3%)	0 (0.0%)
Diarrhoea	5 (26.3%)	1 (5.3%)
Dyspnoea	5 (26.3%)	1 (5.3%)
Hypertension	5 (26.3%)	2 (10.5%)
Leukopenia	5 (26.3%)	2 (10.5%)
Neutropenia	5 (26.3%)	3 (15.8%)
Oedema peripheral	5 (26.3%)	1 (5.3%)
Alopecia	4 (21.1%)	0 (0.0%)
Aspartate aminotransferase increased	4 (21.1%)	0 (0.0%)
Hypotension	4 (21.1%)	0 (0.0%)

#### **REO 029 mPDAC Safety Results Summary**

- **REO 029** study adverse events in line with well-established PELA safety profile
- Most common AEs are "flu-like" symptoms, GI symptoms, cytopenias
- Most reactions Grade 1 or 2 and transient

## **REO 017: PELA + Gemcitabine in 1L PDAC**



Design	Single-arm
Population	Metastatic or advanced PDAC; No previous chemotherapy (1L)
Treatment	Gemcitabine (Days 1, 8) + PELA (Days 1, 2 & Days 8, 9); PELA dose: 1 x 10 <sup>10</sup> TCID <sub>50</sub>
Primary Endpoint	Clinical benefit rate (CBR) at ≥12 weeks
Secondary Endpoints	PFS, OS, safety

34 patients enrolled; 29 evaluable for response

- Median age: 66 years
- Sex: 53% male; 47% female
- Metastatic disease: 91%; Liver metastases: 65%





## REO 017 83% of Evaluable Patients Demonstrated Clinical Benefit





## REO 017 6-Fold Increase in 2-year OS vs. Historical Benchmarks





PELA + gemcitabine resulted in substantially higher mOS and 12- and 24-month survival rates than historical results for gemcitabine alone

## NCI 8601: PELA + Paclitaxel/Carboplatin in 1L mPDAC



Design	Open-label, randomized	Treatment overview for 21-day cycle
Population	Metastatic PDAC; No previous chemotherapy (1L)	D1 D2 D3 D4 D5
Treatment	Arm A: Paclitaxel/carboplatin (Day 1) + PELA (Days 1-5) Arm B: Paclitaxel/carboplatin (Day 1) PELA dose: 3 x 10 <sup>10</sup> TCID <sub>50</sub>	Chemotherapy in both arms
Primary Endpoint	PFS	PELA in Arm A only
Secondary Endpoints	ORR, DCR, OS, safety	Paclitaxel/ Carboplatin PELA

73 evaluable patients enrolled: Arm A = 36; Arm B = 37

- Median age: 64 years
- Sex: 56% male; 44% female No significant differences between groups
- Liver metastases: 78%
- 17 patients crossed over from Arm B to Arm A upon progression

## NCI 8601 Nearly 4-Fold Increase in 2-year OS vs. Control





#### Discussion (Mahalingham, et. al., Cancers 2018)

*"the mature data showed a possible delayed effect on OS, with a divergence of survival curves occurring around year 1, <u>and the strongest efficacy signal for improvement in OS occurring around year 2 in the pelareorep-containing arm in comparison to the control arm (20% vs. 9%, respectively)."*</u>

#### No difference between arms for:

- Median PFS (4.9 vs. 5.2 months)
- Median OS (7.3 vs. 8.8 months)
- ORR (19% in both arms)

However, 2-year survival rate favored the PELA arm:

- ITT: 20% vs. 9%
- Excluding crossover: 20% vs. 6%

<section-header><section-header><section-header><text><text><text><text><text><text><text><text>

#### Randomized Phase 2 Trial of the Oncolytic Virus PELA (Reolysin) in Upfront Treatment of Metastatic Pancreatic Adenocarcinoma Noonan, et al., Mol Ther. 2016

Jun;24(6):1150-1158

#### Provides immunologic rationale for combining PELA with a CPI

## Pelareorep Enhances 2-year Survival Rates in 1L Metastatic PDAC: Comparison to Landmark Studies





Gem = gemcitabine; GnP = gemcitabine + nab-paclitaxel; S1 = oral fluoropyrimidine; FOLFOX = folinic acid, fluorouracil and oxaliplatin; FOLFIRINOX = = FOLFOX + irinotecan; Dotted lines: weighted means

Conroy, et al., NEJM, 2011



# *3 completed studies of PELA in 1L PDAC* have demonstrated promising efficacy

**REO 017:** PELA + gemcitabine

- 6x 2-year survival over benchmark
- 24% vs 4% for 2-year survival / 45% vs 22% for 1-year survival

NCI 8601: PELA + paclitaxel/carboplatin vs. carboplatin + paclitaxel

- ~4x 2-year survival rate vs. chemo control (excluding crossover)
- 20% vs 6% for 2-year survival (excluding crossover)

**REO 029:** PELA + gemcitabine/nab-paclitaxel (GnP) + atezolizumab – 62% ORR; 85% DCR

- 45% vs 35% for 1-year survival

Safety profile in PDAC comparable to that in other indications

Most common PELA-associated AEs are "flu-like" symptoms, GI symptoms, neutropenia

Most reactions Grade 1 or 2 and transient

PELA *received FDA Fast Track designation* in 2022 for the treatment of metastatic pancreatic cancer in combination with chemotherapy and atezolizumab

## **Breast Cancer Program**





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





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 Landscape." Journal of clinical oncology : official journal of the American Society of Clinical Oncology vol. 38,17 (2020): 1951-1962. doi:10.1200/JCO.19.02488; DESTINY-BREAST06



#### Phase 1: PELA in advanced breast cancer



## **IND.213 Study**



#### Overview

- Phase 2, randomized, open-label
- Conducted at 8 Canadian cancer centers



#### Key Eligibility Criteria

- ≥18 years
- Advanced or metastatic breast cancer (histologically/cytologically confirmed)
- Disease for which systemic paclitaxel is indicated
- Measurable disease per RECIST v1.1
- ≥1 prior chemotherapy regiment for adv/met breast cancer

#### Dose/schedule

- PELA : 3x10<sup>10</sup> TCID<sub>50</sub> on days 1,2; 8,9; 15,16
- Paclitaxel:  $80 \text{ mg/m}^2 \text{ on days } 1, 8, 15$

#### **Study Objectives**

- Primary: Progression-free survival
- Secondary: Overall survival, objective response rate, biomarker evaluation

## **IND.213: Strong Survival Benefit in PELA Combination Arm**





Overall survival in HR+/HER2- patients (n = 57)



PELA-based therapy led to near doubling of mOS in HR+/HER2- breast cancer patients

## **BRACELET-1 Study**





Avelumab (Bavencio®) \*Includes 3 patient safety run-in

# BRACELET-1: Robust Improvement in Progression-free Survival (PFS) in the PELA-combination Arm





	Paclitaxel (PTX)	PTX + PELA	PTX + PELA + 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: Robust Improvement in Overall Survival (OS) in the PELA-combination Arm



	Paclitaxel (PTX)	PTX + PELA	PTX + PELA + avelumab	
<b>Median OS</b> (months)	18.2	Not reached		
		Conservative estimate: 32.1*	21.7	
<b>Hazard ratio</b> vs. PTX alone	-	0.48	1.08	

\* Survival estimate assumes death of all patients at next follow-up visit in 4 months

NCOLYTICS

## **BRACELET-1:** Results Summary



Response Measures <sup>1</sup>	PTX Monotherapy (n=15)	PTX + PELA (n=16)	PTX + PELA + 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	Conservative 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 \* Survival estimate assumes death of all patients at next follow-up visit in 4 months

## **PELA's Favorable Safety Profile Observed in BRACELET-1**



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

	Paclitaxel (PT)	Paclitaxel (PTX) (n=12)		PTX + PELA (n=16)		PTX + PELA + Avelumab (n=17)	
Grade	e 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%)	-	

PELA was well-tolerated with a safety profile as expected based on prior studies

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

## **Anal Cancer Program**







#### Checkpoint Inhibitors Provide Limited Efficacy

Historical control trials evaluating checkpoint inhibitors for relapsed anal cancer show an <u>average ORR of</u> <u>approximately 10-24%<sup>1-3</sup></u> Case numbers have been rising over the past decade

10,930 estimated new cases of anal cancer are expected in 2025 age-adjusted rates for anal cancer have been rising 2.2% each year from 2013-2022 and death rates have been rising 4.1% each year from 2014-2023<sup>4</sup>

#### **Poor Prognosis**

The 71.3% 5-year survival rate for anal cancer drops to a **14% 5-year survival if it metastasizes** per the U.S. National Cancer Institute<sup>4</sup>

ORR: Objective response rate; 1. Sheela Rao (Frontier Oncol) 2022; 2. Marabelle et al Lancet Oncology (2022)/NCT02628067; 3. Sara Lonardi (2021) J. Immu Cancer/<u>NCT03944252</u>. 4. National Cancer Institute. (2025). Cancer Stat Facts: Anal Cancer. SER Program, Surveillance, Epidemiology, and End Results. Retrieved June 30, 2025, from https://seer.cancer.gov/statfacts/html/anus.html.

## ORR for PELA-Atezolizumab Combination in Anal Cancer Exceeds Historical Rates



#### ORR of 33%, expanding enrollment to confirm efficacy signal. Of 12 evaluable patients:

- 1 CR (ongoing at 15 months)
- 3 PR (one at week 8, week 16, and one ongoing at week 80)
- ~10-24% 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>;