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Unleashing the Power of the Immune System to Fight Cancer

Investor Presentation January 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 are collectively referred to herein as "forwardlooking 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 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 advancement towards key near-term milestones; 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 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.



Robust Clinical Data in Breast and Pancreatic Cancer

Differentiated Approach to Immunotherapy

Favorable Safety, Positive Translational Data

Poised to Begin Registrational Studies

Strong Team, Collaborations, Cash Randomized and Open-Label Phase 1/2 studies demonstrate meaningful improvements in overall response rate, progression-free survival, and overall survival

Systemically dosed immunotherapeutic agent that delivers dsRNA to stimulate the immune system
 Can be dosed in combination with targeted agents, chemotherapy or checkpoint inhibitors

Favorable safety profile

Translational data (CeITIL scores, TIL counts) show immunotherapy MOA in the tumor/bloodstream

Guidance on breast cancer registration plan expected in H1 2024
 Pancreatic Cancer Adaptive Phase 3 intended to begin in mid-2024

Experienced team, supported by collaborations with Roche, Merck and others, Fast Track
 Designations, and cash of \$40 million¹, providing a runway of over 12 months

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	HR+ / HER2- Breast Cancer	First-line Advanced / Metastatic Pancreatic Cancer
Status	Positive data reported from two randomized phase 2 trials (IND-213 & BRACELET-1)	Phase 1/2 updated data reported October 2023
Key Data	Statistically significant near doubling of median overall survival observed in IND-213 (n=57) Robust improvement in PFS (HR=0.29) & 2.8-fold increase in confirmed ORR in BRACELET-1 (n=48*)	62% Objective response rate 7.2 months Median PFS 10.6 months interim Median OS 46% 12-month survival rate
Next Steps	Advancing to a licensure-enabling study	Advancing to a licensure-enabling study

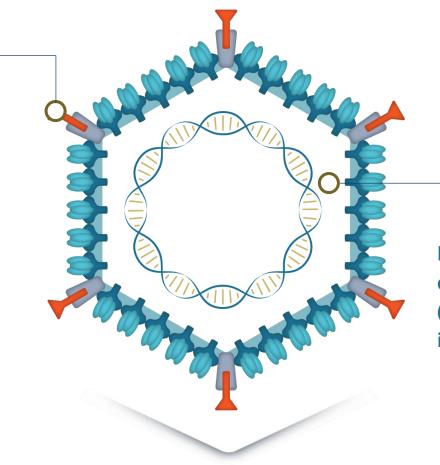
Both programs have U.S. FDA Fast Track Designation

*Trial included 48 patients across 3 cohorts with improvement in PFS and ORR seen between paclitaxel + pelareorep cohort (n=16) vs. paclitaxel monotherapy cohort (n=15). Third cohort evaluated paclitaxel + pelareorep + avelumab (n=17); PFS: Progression-free survival; ORR: Overall response rate; HR: Hazard Ratio; OS: Overall survival

Pelareorep is a 1st in Class, Immunotherapeutic Agent

An unmodified, non-pathogenic reovirus

Selectively replicates in cancerous cells



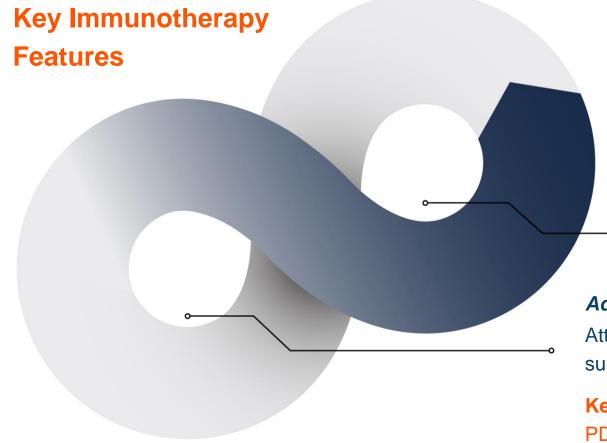
Enables the accumulation of double-stranded RNA (dsRNA) that stimulates the immune system

Leads to the activation of the Innate and Adaptive Immune System NCOLYTICS

Pelareorep is a Differentiated Immunotherapy



Key differentiators: Activation of the Innate and Adaptive Immune System, tumor microenvironment remodeling



Innate Immune System Activation

Promotes expression of interferons and inflammatory cytokines to promote recruitment and activation of immune cells such as dendritic cells to drive innate and adaptive immune response

Key Translational Metrics

Interferon levels, other immunologically relevant chemokines and cytokines

Adaptive Immune System Activation

Attract NK cells, leading to the engagement of key T cell populations such as TILs that drive tumor microenvironment remodeling

Key Translational Metrics

PD-L1 expression, detectable pathological changes including cell death and inflammation (TILs)



H1 2024	Mid 2024	2024	2025 - 2026
Breast Cancer Provide guidance on the registration path	 Pancreatic Cancer Initiate Adaptive Phase 3 trial 	Pancreatic Cancer Expanded data from the GOBLET study cohorts 1 & 5	Pancreatic Cancer Interim analysis from the Adaptive Phase 3 trial
Pancreatic Cancer Initiation of Phase 1/2 PanCAN/mFOLFIRINOX GOBLET cohort 5 study		 Breast Cancer BRACELET-1 Phase 2 Overall survival data 	 Anal Cancer Expanded follow-up data from the GOBLET Phase 2 study



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Pelareorep in HR+ / HER2- Breast Cancer



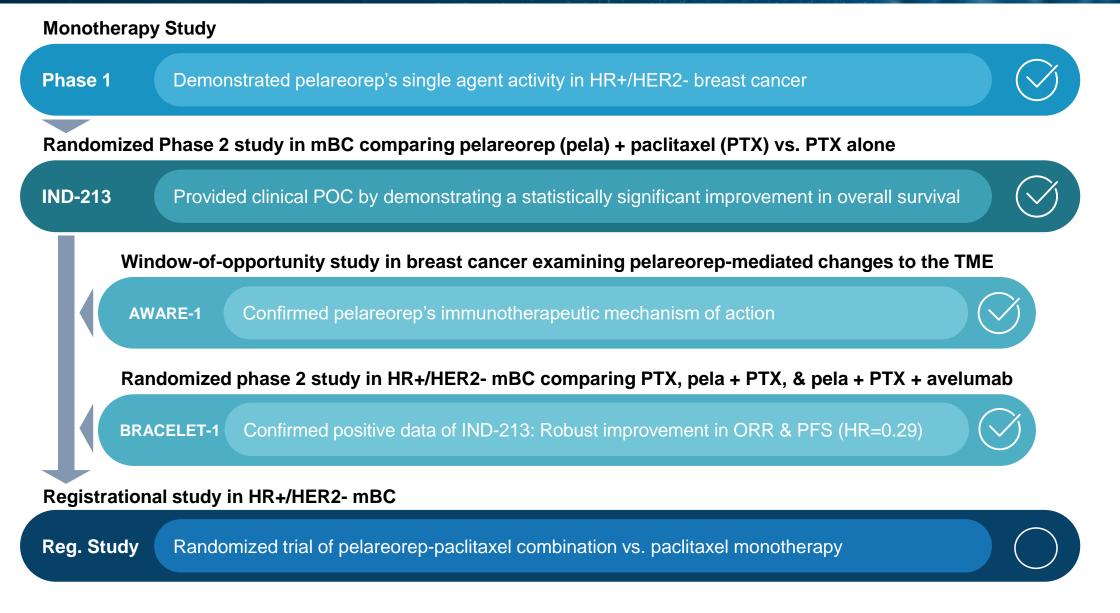
Breast Cancer Registrational Strategy Supported by Data from Two Randomized Trials and a Translational Study



Phase 2 Studies Highlight Benefit with Paclitaxel	»	Positive data from BRACELET-1 and IND-213 randomized trials showed meaningful improvements in response rates and survival for patients in the pelareorep/paclitaxel combination arms
Favorable Overall Safety	»>	Manageable safety profile, consistent with prior reported results for paclitaxel, with \leq 20% grade 3 (or greater) adverse events
Consistent Translational Data	>>	Data from BRACELET-1 and AWARE-1 studies consistently show that pelareorep produces an expansion of T cell clones and/or increase in CeITIL scores and peripheral TIL counts
BRACELET-1 Survival Data Next Milestone	»	Multiple patients in the pelareorep/paclitaxel arm continue to be followed for survival Overall survival will be reported once all "events" have been recorded, expected in 2024
Registrational Trial Plan	»»	Guidance on the registration path expected to be provided in H1 2024 Design expected to reflect positive PFS data from BRACELET-1's pelareorep/paclitaxel arm

Advancing to Registrational Study in HR+/HER2- mBC

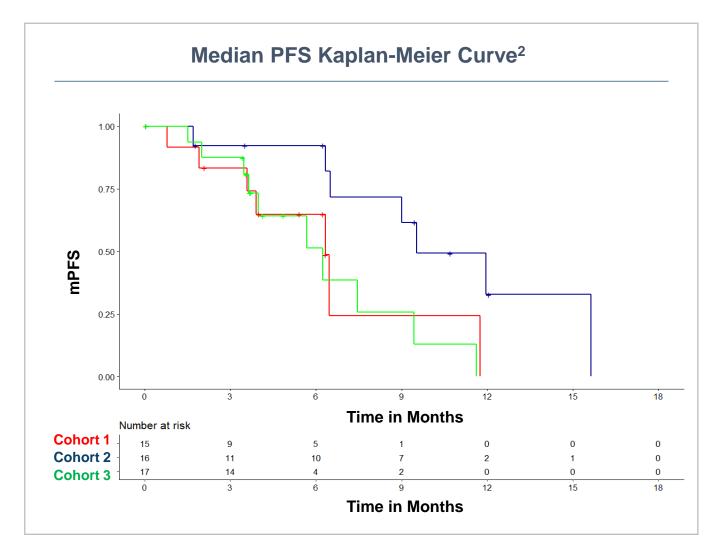




mBC: Metastatic breast cancer; POC: Proof-of-concept; ORR: Overall Response Rate; PFS: Progression-Free Survival, HR: Hazard ratio

BRACELET-1 Study Showed Robust Improvement in mPFS for the Pelareorep + Paclitaxel Arm¹





	Paclitaxel (PTX) Monotherapy	PTX + Pelareorep	PTX + Pelareorep + Avelumab
Median PFS	6.3	9.5	6.2
(months)	(95% CI: 3.9, NR)	(95% CI: 6.5, NR)	(95% CI: 4.0, NR)
HR vs. PTX	-	0.29	1.31
Mono-therapy		(95% Cl: 0.09, 0.98)	(95% CI: 0.47, 3.65)
12-Month PFS	0	32.8	0
Rate (%)	(95% Cl: -, -)	(95% Cl: 11.7, 92.4)	(95% CI: -, -)

¹Data from a March 3, 2023 cut-off date. Numbers presented may change as they are derived from an unlocked database

²Data include all patients enrolled in trial. Response data presented by Clark et al. at ASCO 2023 included the 45 randomized patients and excluded participants in the three-patient safety run-in.

mPFS: median progression-free survival; PFS: Progression-free survival; CI: Confidence interval; NR: Not reached; HR: Hazard ratio



Response Measures/	PTX Monotherapy	PTX + Pelareorep	PTX + Pelareorep +
Study arms ²	(n=15)	(n=16)	Avelumab (n=17) ³
Confirmed ORR Over Course of Trial	13.3%	37.5%	17.6%
mPFS (months)	6.3	9.5	6.2
	(95% CI: 3.9, NR)	(95% CI: 6.5, NR)	(95% CI: 4.0, NR)
PFS Hazard Ratio vs.	-	0.29	1.31
PTX Monotherapy		(95% CI: 0.09, 0.98)	(95% CI: 0.47, 3.65)
12-Month PFS Rate (%)	0	32.8%	0
	(95% CI: -, -)	(95% CI: 11.7, 92.4)	(95% CI: -, -)

ORR: Objective response rate; mPFS: median Progression-Free Survival; PFS: Progression-Free Survival; PTX: paclitaxel; OS: Overall Survival; mOS: median Overall Survival;

¹Data from a March 3, 2023 cut-off date. Numbers presented may change as they are derived from an unlocked database.

²Response based on RECIST V1.1 investigator assessment.

³Data include all patients enrolled in trial. Response data presented by Clark et al. at ASCO 2023 included the 45 randomized patients and excluded participants in the three-patient safety run-in in cohort CI: Confidence interval; NR: Not reached.

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



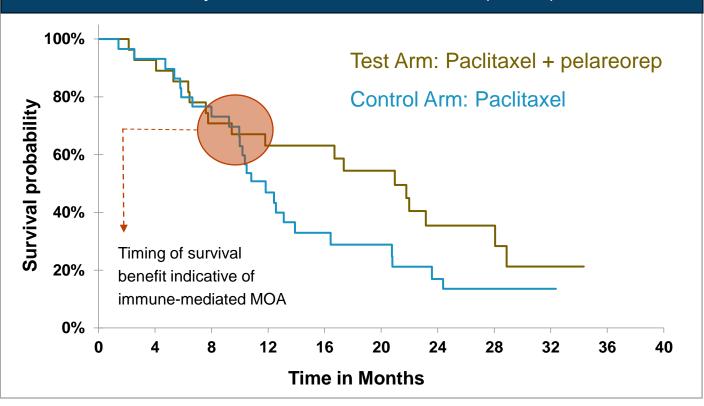
Phase 2 All Subtypes (n = 74)

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)

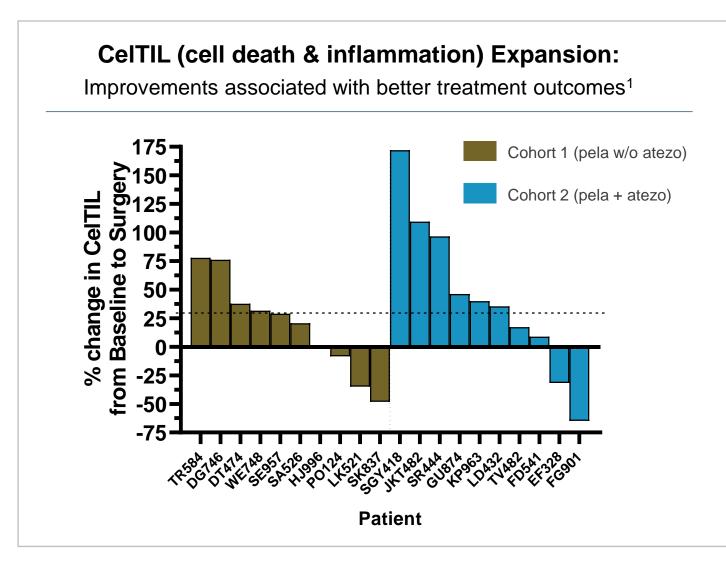


Near doubling of mOS in HR+/HER2- patients with pelareorep treatment

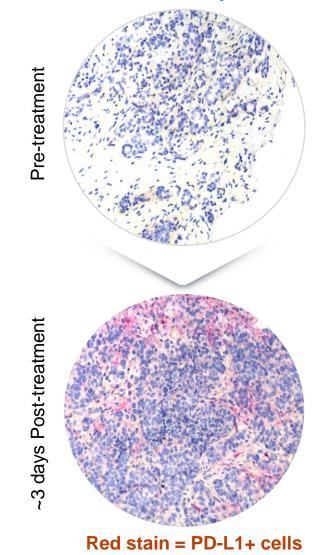
mOS: Median Overall Survival; HR: hazard ratio

AWARE-1 Translational Data Shows Consistent Impact on CeITIL Score, PD-L1 Expression





Tumor PD-L1 expression



Pela: Pelareorep; Atezo: Atezolizumab

¹Nuciforo 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



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Patient Population HR+/HER2- mBC:

- Prior Treatments: hormonal therapy including CDK4/6 inhibitors, and patients who failed or were ineligible for ADC therapy
- Design to be based on positive BRACELET-1 Phase 2 results

Treatment Regimen:

 Randomized trial of pelareorep + paclitaxel combination vs. paclitaxel monotherapy

Registrational Endpoints:

- **Primary and Key Secondary:** To potentially include Progression-Free Survival and Overall Survival
- Other Endpoints: Overall Response Rate and Translational Assessments

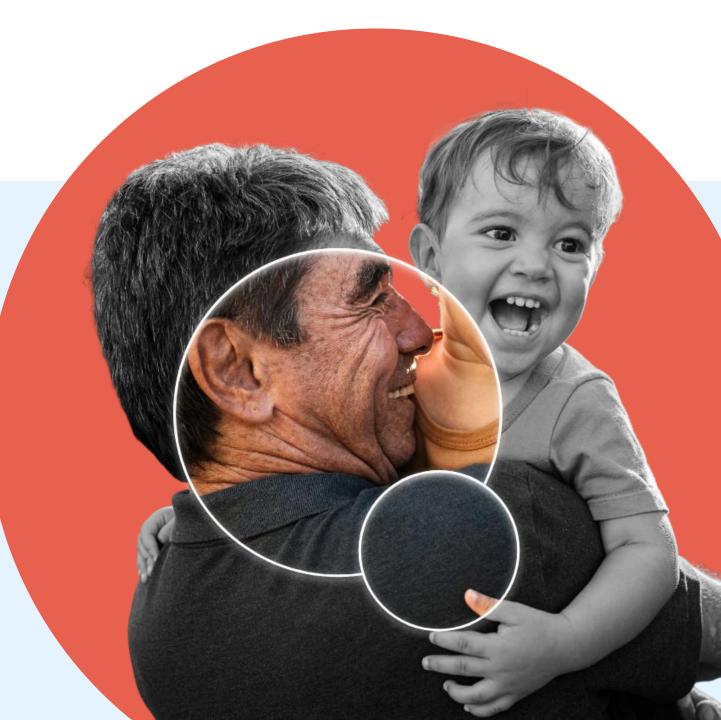
Update to include definition of study size, endpoints and estimated start timing

mBC: metastatic breast cancer; ADC: antibody drug conjugate



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Pelareorep in First-Line Advanced / Metastatic Pancreatic Cancer



Registrational Plan in Pancreatic Cancer Driven by Promising GOBLET Phase 1/2 Data & Supported by FDA Fast Track Designation

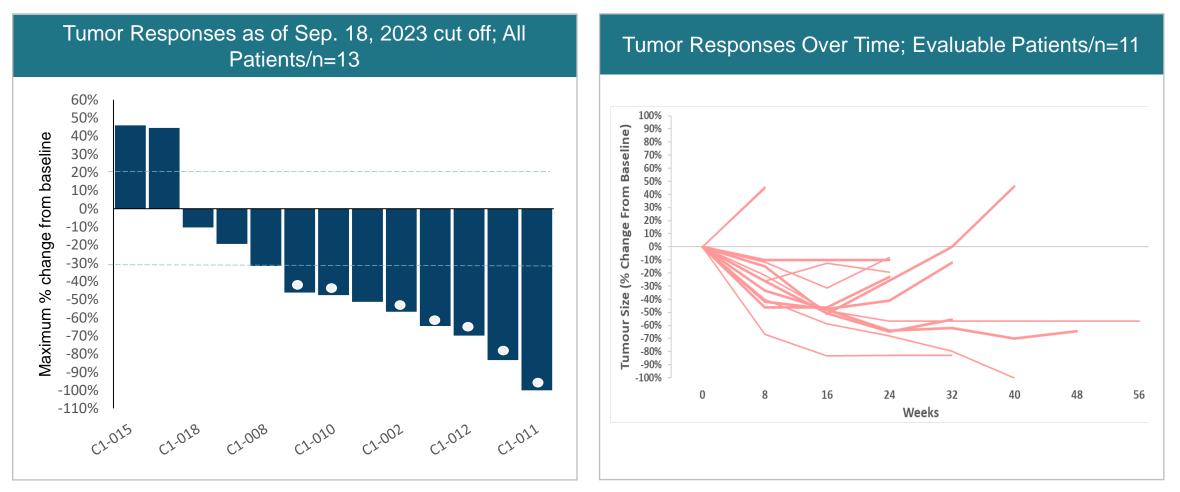


Studies Show Survival Benefit	Positive Data from over 120 pancreatic cancer patients in the GOBLET and REO-017 open- label trials showed meaningful improvements in survival
GOBLET Study Shows Increased ORR	An ORR of 62% was observed, representing a near tripling from historical controls; 7.2 mo mPFS, 10.6 mo interim mOS are ≥25% compared to historical control trials ¹⁻⁴
Generally Favorable Overall Safety	SOBLET data indicate the treatment has been well tolerated with no safety concerns
Consistent Translational Data	Translational data from GOBLET show that patients with increases in blood TILs showed a decrease in tumor volumes
Registrational Trial Plan and Beyond	 Plans to define the Phase 3, adaptive-design protocol in H1 2024; initiate the study in mid-2024 \$5M PanCAN grant to explore pelareorep/mFOLFIRINOX regimen, expecting H1 2024 start

ORR: overall response rate; mo: month; mPFS: median progression-free survival; mOS: median overall survival; TILs: tumor-infiltrating lymphocytes; 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.

PDAC GOBLET Results Showing 62% ORR

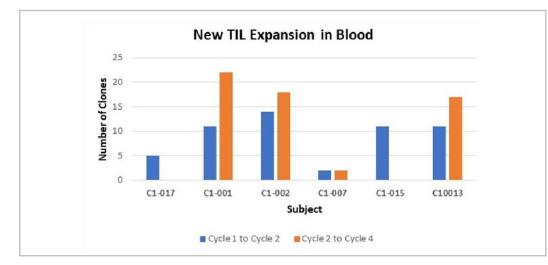


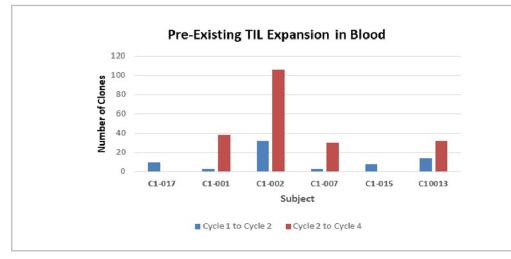


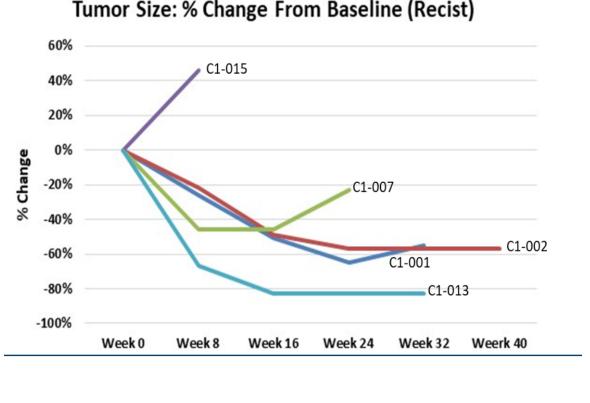
Dotted lines represent cut-offs for PD (+20%) and PR (-30%)

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

Expansion of New/Pre-Existing T cell Clones Correlate with Tumor Shrinkage Provides a Valuable Potential Biomarker







Tumor Size: % Change From Baseline (Recist)

NCOLYTICS

Next Steps: mFOLFIRINOX Study to Further Explore Combinations with the Most Common PDAC Treatment Regimens

Strategic rationale: to investigate the use of pelareorep with the most commonly used treatment regimens

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)

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

Study expected to begin in H1 2024





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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 and Secondary:** To include Overall Survival, Progression-Free Survival, and Overall Response Rate
- Additional Secondary: To include Translational Data

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



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Pelareorep in ≥ Second-Line Unresectable Anal Cancer



Positive GOBLET Anal Cancer Data Meets Success Criteria, Further Highlights Synergy with Checkpoint Inhibitors



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

Patient Population:

- Phase 2 Simon Two-Stage Cohort
- Patients with 2L, unresectable squamous cell carcinoma of the anal canal (SCCA)
- Prior Treatments: chemotherapy (100%) and radiation therapy (88%)

Treatment Regimen:

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

Registrational Endpoints:

- Simon Two-stage criteria to progress: 2 or more responses out of the first 10 enrolled
- Additional Secondary: To include translational data

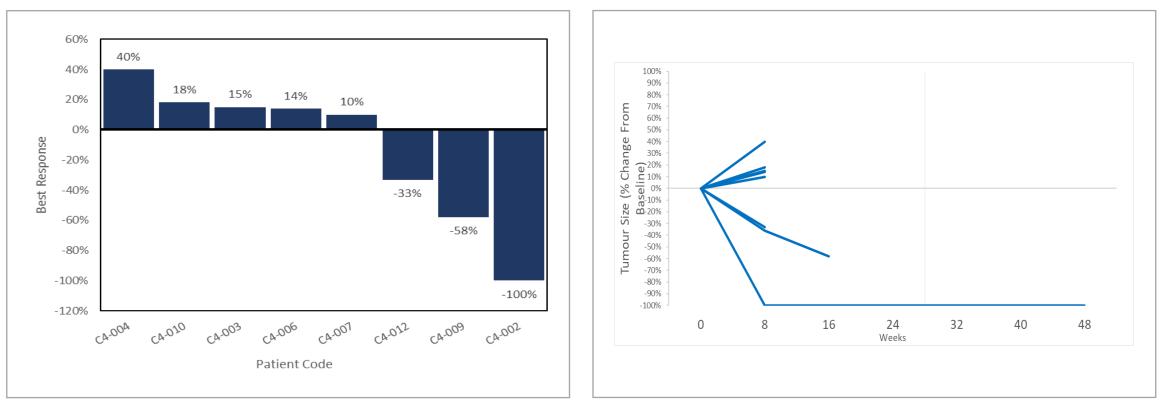
ORR of 37.5%, with 1 CR ongoing at 12 months and 2 PRs Data satisfied the prespecified success criteria for the study Follow-up is ongoing

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 therapies¹⁻⁷



ORR: objective response rate; CR: Complete Response; PR: Partial Response; Sources: 1. Ott et al Annal Oncology (2017)/NCT02054806; 2. Morris et al, The Lancet (2017)/NCT02314169; 3. Lao et al Annal Oncology (2020)/NCT02628067; 5. Sara Lonardi (2021) J. Immu Cancer/NCT03944252; 6. Kim et al, BMC Cancer.2020 Apr 25;20(1):352.; 7. Sheela Rao (Frontier Oncol) 2022

Pelareorep Has Expansive Potential, Starting with Breast and Gastrointestinal Cancers



Program	Collaborator	Combination	Phase 1	Phase 2	Phase 3	Milestone
BREAST CANCER						
BRACELET-1 HR+/HER2- mBC	Pfizer Merck	pela + PTX				OS data expected in 2024
Registrational Study HR+/HER2- mBC	TBD	pela + PTX				Registrational Study Plan H1 2024
GASTROINTESTINAL C	ANCERS					
GOBLET cohort 1 1L Adv/Metastatic PDAC	Roche	pela + gem + nab-PTX + atezo				OS data pending
Adaptive Phase 3 1L Adv/Metastatic PDAC	Roche	pela + gem + nab-PTX + atezo				Study initiation Mid-2024
GOBLET cohort 5 Newly Diagnosed PDAC	Roche	pela + mFOL +/- atezo				Study initiation H1 2024
GOBLET cohort 4 ≥2L Unresectable Anal Cancer	Roche	pela + atezo				Enrollment Expansio H1 2024

mBC: Metastatic Breast Cancer; PDAC: pancreatic ductal adenocarcinoma; pela: pelareorep; PTX: paclitaxel; gem: gemcitabine; atezo: atezolizumab; mFOL: modified FOLFIRINOX; OS: Overall Survival; Adv: Advanced; 1L: First-Line; 2L: Second-Line



Financial Overview		Research Coverage	Research Coverage		
Ticker	ONCY: NASDAQ ONC: TSX	Patrick Trucchio	H.C. Wainwright & Co.		
Avg. Daily Volume (1 mo*)	408,766	John Newman	Canaccord Genuity		
Shares Outstanding	73,398,847	Jason McCarthy	Maxim Group		
Market cap ¹	~\$97 M	Douglas Miehm	RBC Capital Markets		
Cash ²	\$40 M	Louise Chen	Cantor Fitzgerald		
HQ	San Diego, CA / Calgary, AB, Canada	Douglas Loe	Leede Jones Gable		
		Soumit Roy	JonesTrading		

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





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



Kirk Look, CA **Chief Financial Officer**



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



Allison Hagerman, Peng, PMP VP, Product Development



Amy Levin, **VP, Clinical Operations**















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Appendix





153 patents issued worldwide, including 19 US and 7 Canadian

19 pending applications worldwide

Reovirus issued patent claims cover:

Compositions of matter comprising reovirus

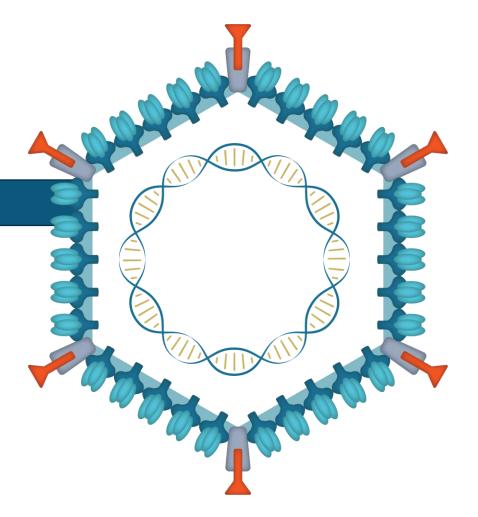
Patent rights extend to at least the end of 2031

Pharmaceutical use of reoviruses to treat neoplasia and cellular proliferative diseases

Combination therapy with radiation, chemotherapy and/or immunosuppressants

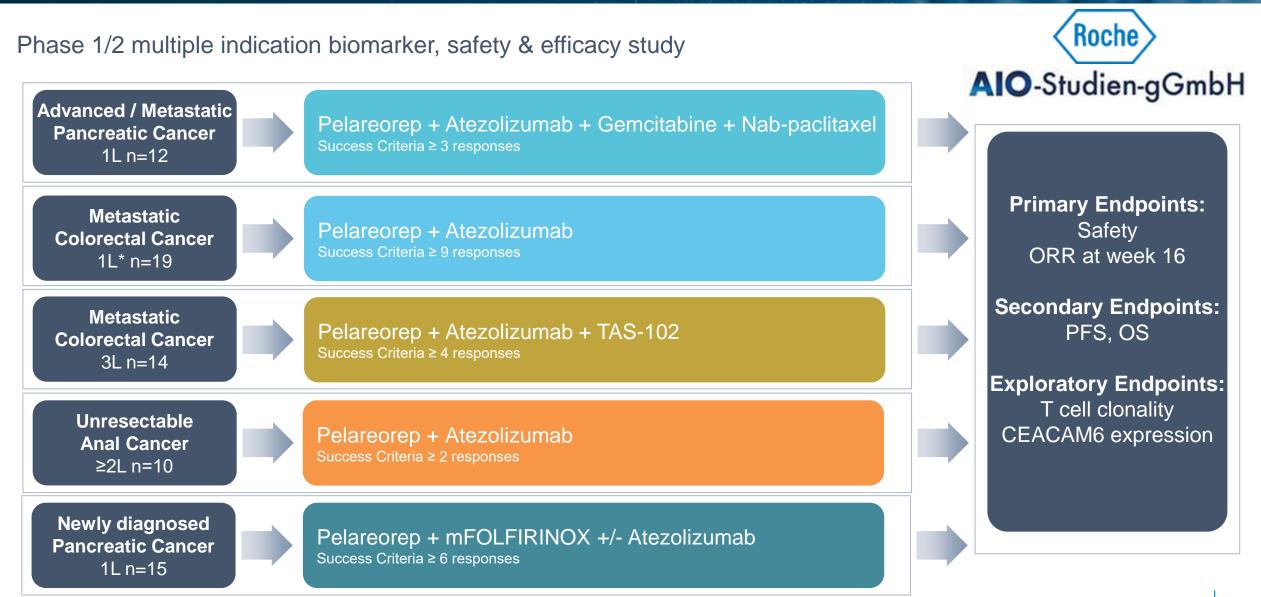
Methods for manufacturing reovirus and screening for susceptibility to reovirus

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



GOBLET Study Design





L: Line; *1L MSI-high focused; mFOLFIRINOX: modified FOLFIRINOX; ORR: Objective response rate; Atezolizumab (Tecentriq®); PFS: Progression-free survival; OS: Overall survival

REO 017: Pelareorep + Chemotherapy in PDAC Generated Median Overall and Landmark Survival Rates That Compare Favorably to 3rd – Party Historical Data



Design: Single-arm; 34 patients enrolled, 29 evaluable for response

Population: Metastatic or advanced PDAC; No previous chemotherapy (1L)

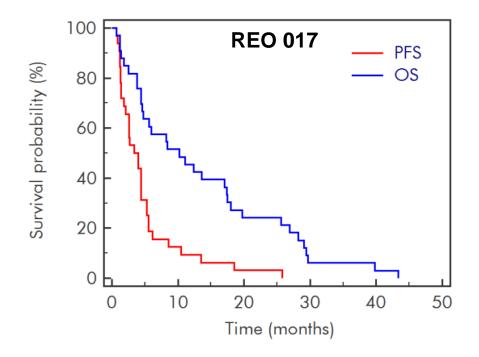
Treatment: Gemcitabine (Days 1, 8) + pelareorep (Days 1, 2 & Days 8, 9)

Primary Endpoint: Clinical benefit rate (CBR) at ≥12 weeks

Secondary Endpoints: PFS, OS, safety

Endpoint	REO 017	Benchmark data ¹				
Median PFS	3.4 months	3.4 months				
Median OS	10.2 months	6.8 months (range 4.9-8.8 mo)				
1-year survival rate	45%	23.4% (range 16-35%)				
2-year survival rate	24%	6.1% (range 4-9.4%)				
1 Von Hoff Diet al N Engl I Med 2013	1. Von Hoff Diet al, N Engl J Med 2013: 369:1691-1703 DOI: 10.1056/NE Moa1304369: Conroy et al, N Engl J Med 2011: 364:1817-1825					

1. Von Hoff D et al. N Engl J Med 2013; 369:1691-1703 DOI: 10.1056/NEJMoa1304369; Conroy et al. N Engl J Med 2011; 364:1817-1825. DOI: 10.1056/NEJMoa1011923; Poplin, et al., J Clin Oncol 2009. 27:3778; Ueno, et al., J Clin Oncol 2013. 31 :1640



Key Takeaways*:

Pelareorep + gemcitabine resulted in higher median OS, 12-month survival rates and 24-month survival rates than historical results for gemcitabine alone

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



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	Paclitaxel (PTX) (n=12)		PTX + Pelareorep (n=16)		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 ³ 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^{1,2} as Attributed to Study Drug(s)

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