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Unleashing the Power of the Immune System to Fight Cancer

Investor Presentation April 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 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.

Investment Opportunity Driven by Robust Pelareorep Results



Robust Clinical Data in Breast and Pancreatic Cancer

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

Differentiated Approach to Immunotherapy

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, Positive Translational Data

Favorable safety profile

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

Poised to Begin Registrational Studies

Suidance on breast cancer registration plan expected in H1 2024

Pancreatic Cancer Adaptive registration-enabling study intended to begin in 2024

Strong Team, Collaborations, <u>Cash</u> Experienced team, supported by collaborations with Pfizer, Roche, Merck and others, Fast Track Designations, and cash of \$34.9 million¹, providing a runway into 2025

Pipeline Includes Two Registration Opportunities



	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

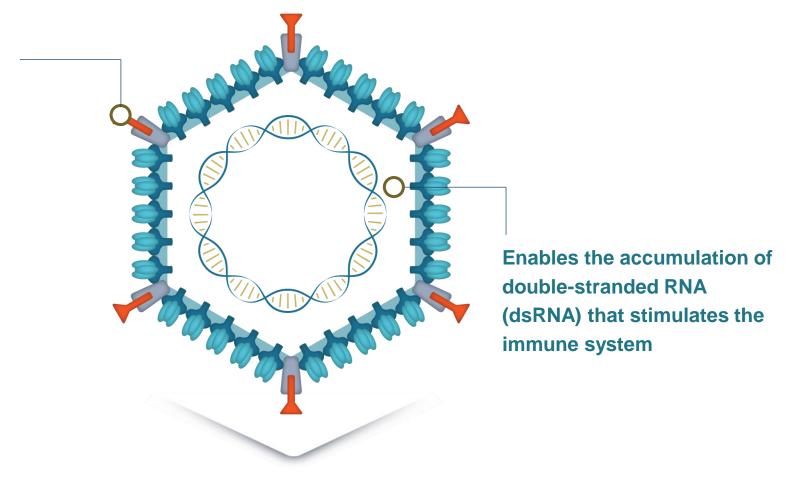
Both programs have U.S. FDA Fast Track Designation

Pelareorep is a 1st in Class, Immunotherapeutic Agent



An unmodified, non-pathogenic reovirus

Selectively replicates in cancerous cells

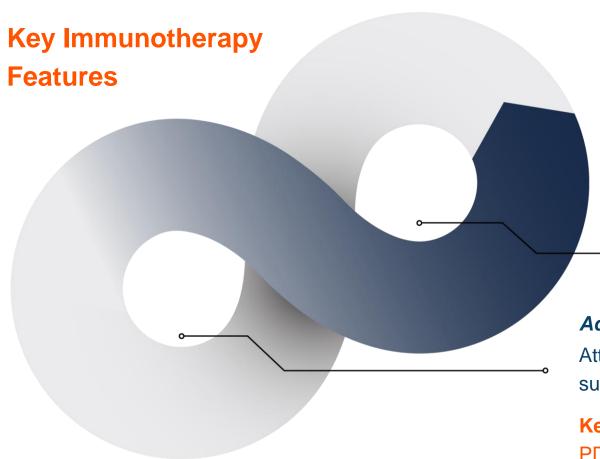


Leads to the activation of the Innate and Adaptive Immune System

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)



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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 ≤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 CelTIL 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 expected be reported 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



Monotherapy Study

Phase 1

Demonstrated pelareorep's single agent activity 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 mechanism of action



Randomized phase 2 study in HR+/HER2- mBC comparing PTX, pela + PTX, & pela + PTX + avelumab

BRACELET-1 Confirmed positive data of IND-213: Robust improvement in ORR & PFS (HR=0.29)



Registrational study in HR+/HER2- mBC

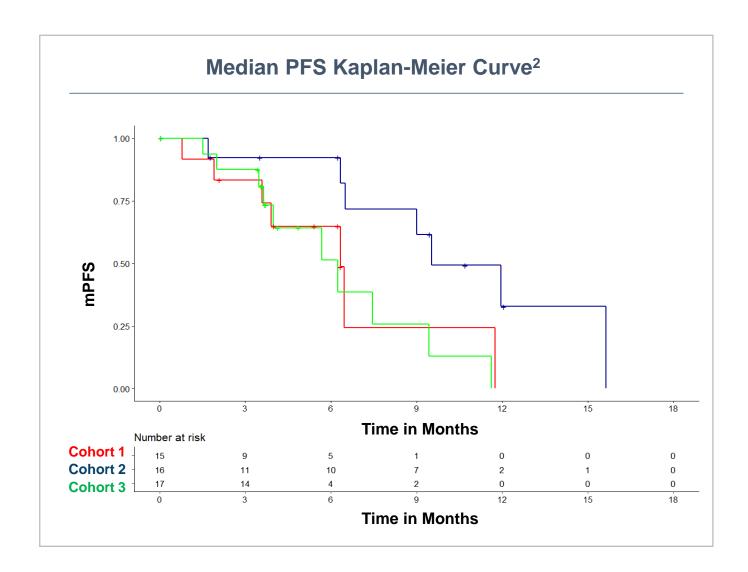
Reg. Study

Randomized trial of pelareorep-paclitaxel combination vs. paclitaxel monotherapy



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 Mono-therapy	-	0.29 (95% CI: 0.09, 0.98)	1.31 (95% CI: 0.47, 3.65)
12-Month PFS	0	32.8 (95% CI: 11.7, 92.4)	0
Rate (%)	(95% CI: -, -)		(95% CI: -, -)

BRACELET-1 Data Show Benefits in Pelareorep + Paclitaxel Arm¹



(95% CI: -, -)

Response Measures/ Study arms ²	PTX Monotherapy (n=15)	PTX + Pelareorep (n=16)	PTX + Pelareorep + Avelumab (n=17)³
Confirmed ORR Over Course of Trial	13.3%	37.5%	17.6%
mPFS (months)	6.3 (95% CI: 3.9, NR)	9.5 (95% CI: 6.5, NR)	6.2 (95% CI: 4.0, NR)
PFS Hazard Ratio vs. PTX Monotherapy	-	0.29 (95% CI: 0.09, 0.98)	1.31 (95% CI: 0.47, 3.65)
12 Month DEC Data (9/)	0	32.8%	0

(95% CI: 11.7, 92.4)

(95% CI: -, -)

12-Month PFS Rate (%)

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

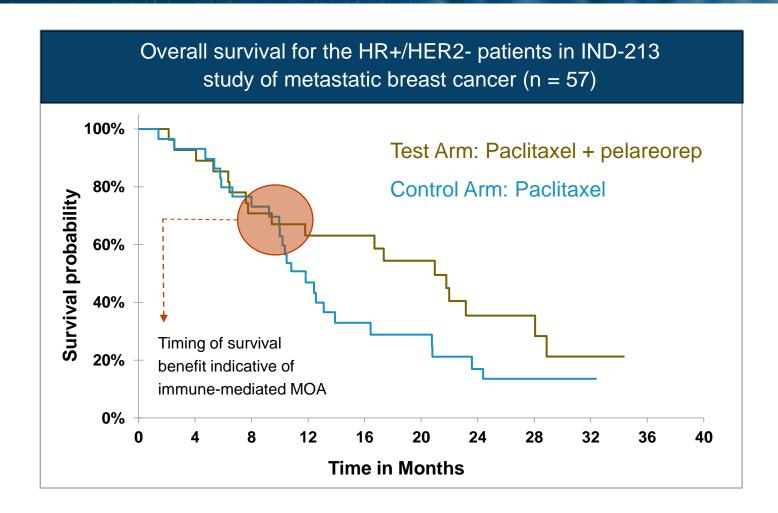


Phase 2 All Subtypes (n = 74)

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)

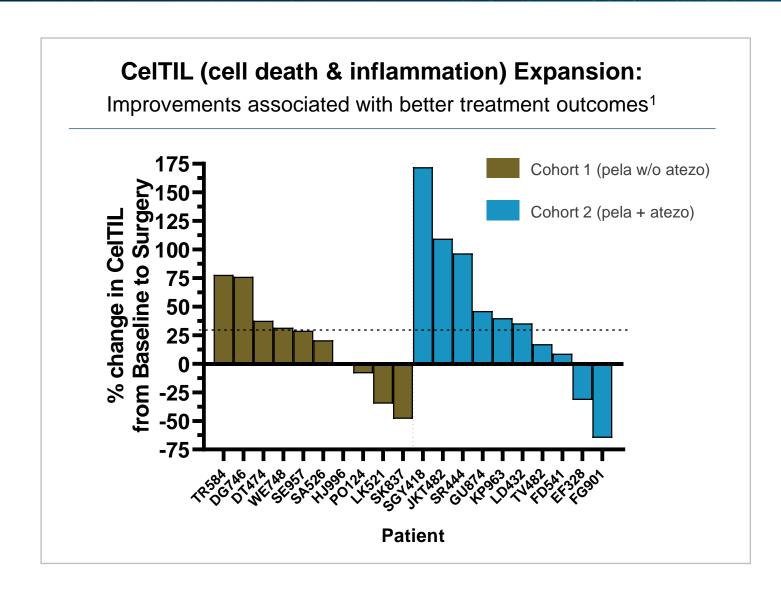
	,
HR	0.60
р	0.1 (powered to 90%)
mOS	21.0 months vs 10.8 months
Test	n = 28
Control	n = 29



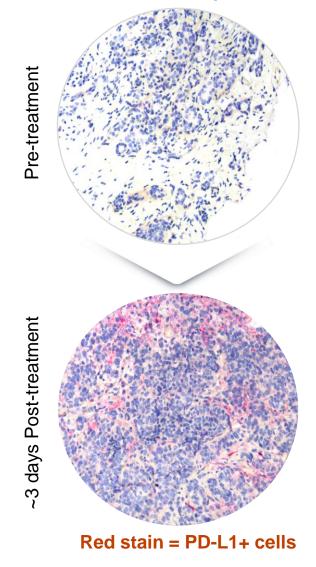
Near doubling of mOS in HR+/HER2- patients with pelareorep treatment

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





Tumor PD-L1 expression



Breast Cancer Registrational Trial Update Planned for H1 2024



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:

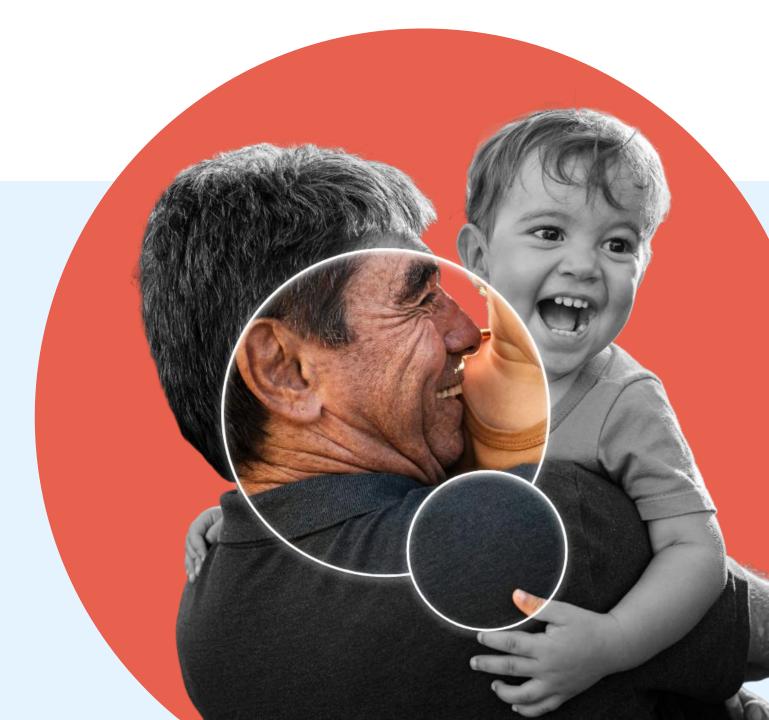
- Primary and Key Secondary: To potentially include Progression-Free Survival and Overall Survival
- Other Endpoints: Overall Response Rate and Translational Assessments





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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 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 trials¹-⁴

Generally Favorable Overall Safety

>> GOBLET 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

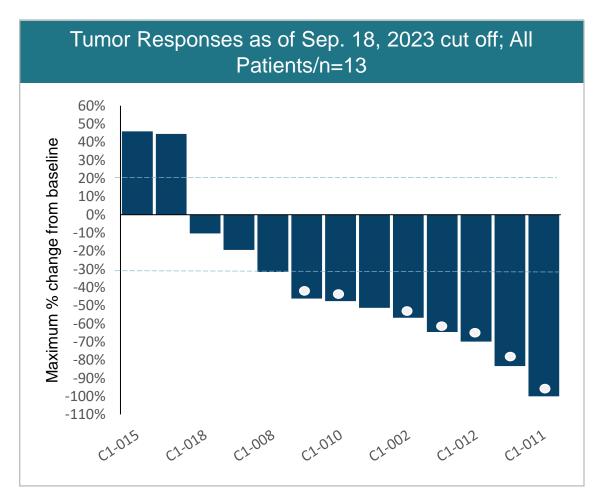
Registrational Trial Plan and Beyond

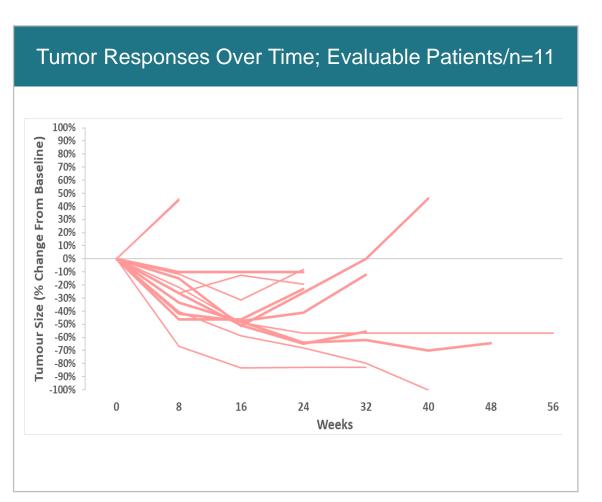
Plans to define a registration-enabled adaptive-design protocol in H1 2024, initiate the study in 2024;

\$5M PanCAN grant to explore pelareorep/mFOLFIRINOX regimen, expecting H1 2024 start

PDAC GOBLET Results Showing 62% ORR





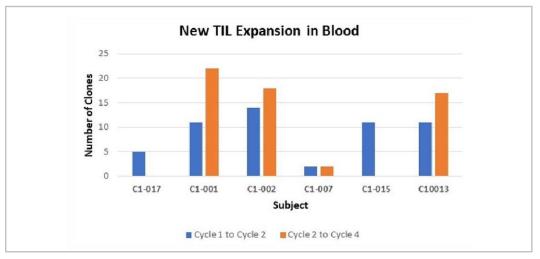


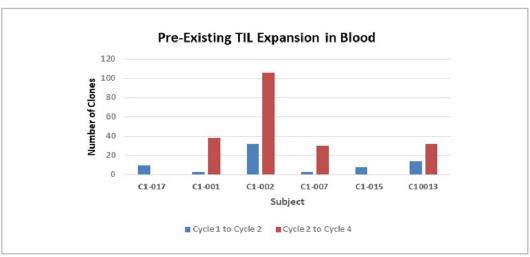
Dotted lines represent cut-offs for PD (+20%) and PR (-30%)

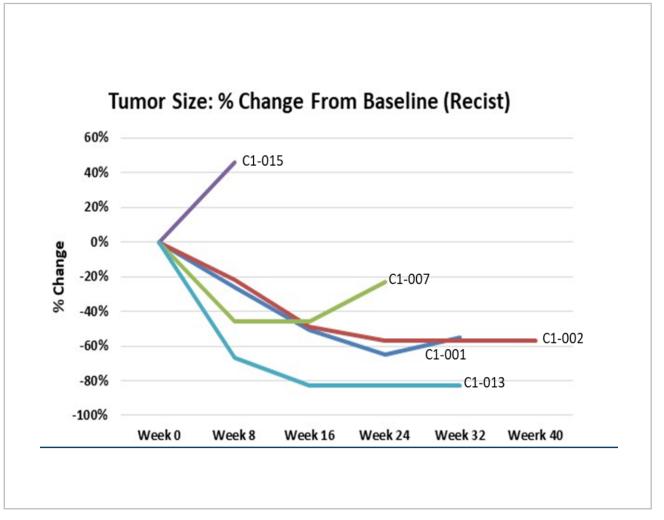
Patients with a white dot have confirmed responses (2 or more consecutive scans with PR or CR)

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









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:

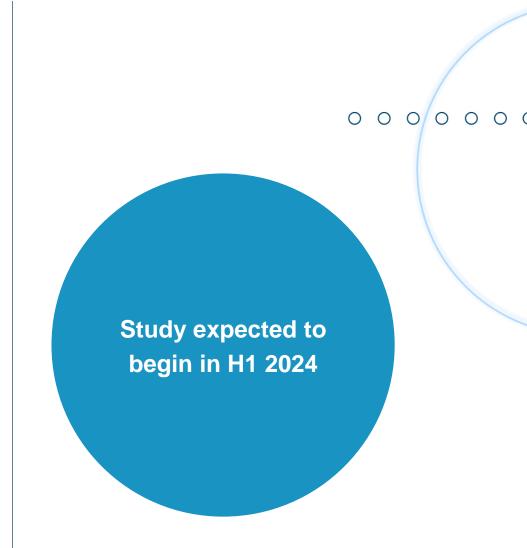
- Newly diagnosed metastatic PDAC patients (as defined by RECIST 1.1)
- To be supported by PanCAN Therapeutic Accelerator Grant

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



Next Steps: Define PDAC Registrational Trial Plan 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 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, Expanding Enrollment, Highlights Synergy with CPI



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

Enrollment Expansion:

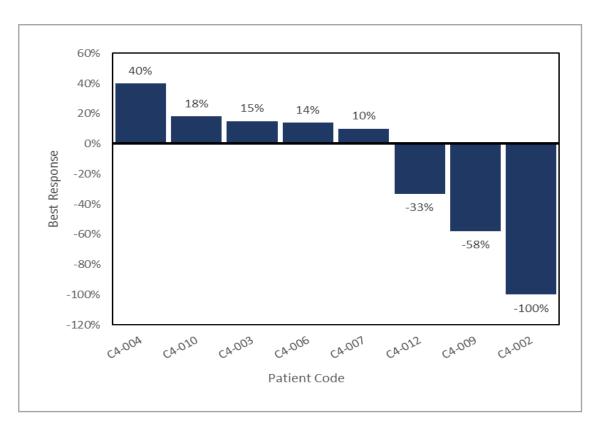
 Estimated ≤20 additional patients will be sufficient to confirm the efficacy signal and move to a registrational study ORR of 37.5%, with 1
CR ongoing at 12
months and 2 PRs
Data satisfied the prespecified success
criteria for the study
Follow-up is
ongoing

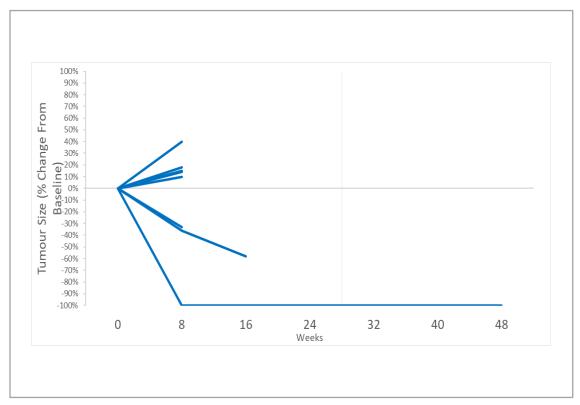
Pelareorep-Atezolizumab Combination in Anal Cancer, ORR Exceeds Historical Efficacy Rates of Like Studies



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





Pelareorep Has Expansive Potential, Starting with Breast and Gastrointestinal Cancers



Program	Collaborator	Combination	Phase 1	Phase 2	Registration-Enabling Study	Milestone	
BREAST CANCER	BREAST CANCER						
BRACELET-1 HR+/HER2- mBC	Pfizer Merck	pela + PTX				OS data expected in 2024	
HR+/HER2- mBC	TBD	pela + PTX				Registrational Study Plan H1 2024	
GASTROINTESTINAL O	CANCERS						
GOBLET cohort 1 1L Adv/Metastatic PDAC	Roche	pela + gem + nab-PTX + atezo				OS data pending	
Adaptive Study 1L Adv/Metastatic PDAC	Roche	pela + gem + nab-PTX + atezo				Study initiation 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 Expansion H1 2024	

Key Value-Driving Clinical Milestones Ahead in 2024+



H1 2024

Mid 2024

2024

2025 - 2026

Breast Cancer

Provide guidance on the registration path

Pancreatic Cancer

Initiation of Phase 1/2
PanCAN/mFOLFIRINOX
GOBLET cohort 5

Pancreatic Cancer

Initiate Adaptive registration-enabling study

Pancreatic Cancer

Expanded data from the GOBLET study cohorts 1 & 5

Breast Cancer

BRACELET-1 Phase 2
Overall survival data

Pancreatic Cancer

Interim analysis from the Adaptive registration-enabling study

Anal Cancer

Expanded follow-up data from GOBLET cohort 4

Cash Balance Supports Planned Operations Through Key Milestones Oncolytics



Financial Overview		Research Coverage		
Ticker	ONCY: NASDAQ ONC: TSX	Patrick Trucchio	H.C. Wainwright & Co.	
Avg. Daily Volume (1 mo*)	519,553	John Newman	Canaccord Genuity	
Shares Outstanding	75,419,768	Jason McCarthy	Maxim Group	
Market cap¹	~\$79 M	Douglas Miehm	RBC Capital Markets	
Cash ²	\$34.9 M	Louise Chen	Cantor Fitzgerald	
HQ	San Diego, CA / Calgary, AB, Canada	Douglas Loe	Leede Jones Gable	
		Soumit Roy	JonesTrading	
ing days from Feb. 12, 2024 – Mar. 8, 2024; 1. Ma	ırket Cap as of March 8, 2024;	Rahul Sarugaser	Raymond James	

^{2.} Cash as of December 31, 2023

Innovative Leadership Team with Strong Immuno-oncology, 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



Amy Levin, RN, BSN VP, Clinical Operations



















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Appendix



Robust Intellectual Property Portfolio



150 patents issued worldwide, including 15 US and 7 Canadian

16 pending applications worldwide

Reovirus issued patent claims cover:

Compositions of matter comprising reovirus

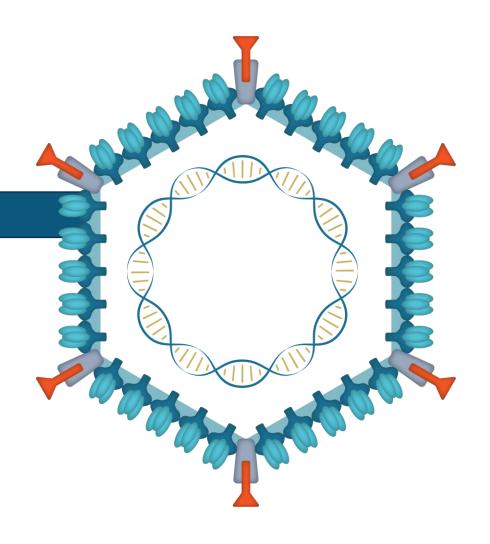
Patent rights extend to at least the end of 2031

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

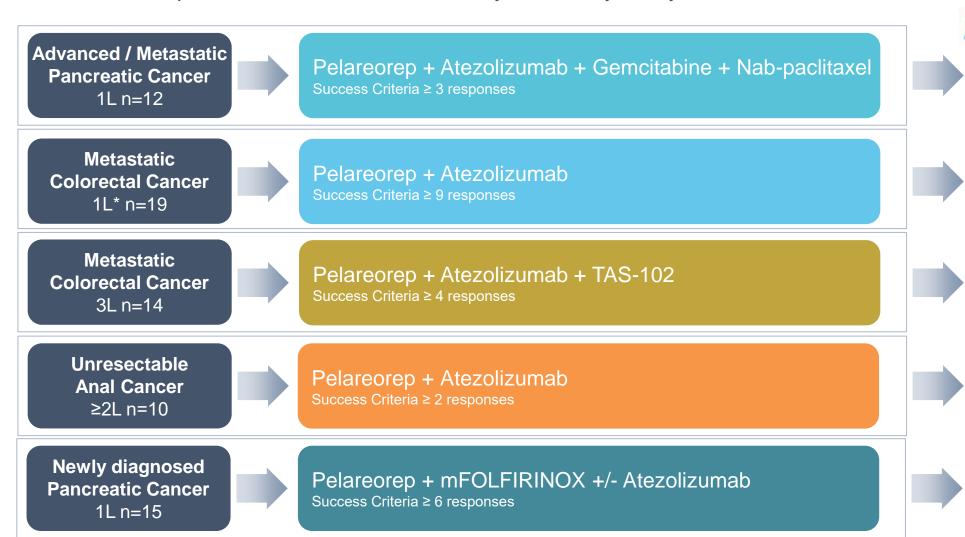
Eligible for 12 years of U.S. market exclusivity upon approval



GOBLET Study Design



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



AIO-Studien-gGmbH

Roche

Primary Endpoints:
Safety
ORR at week 16

Secondary Endpoints: PFS, OS

Exploratory Endpoints:

T cell clonality

CEACAM6 expression

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)

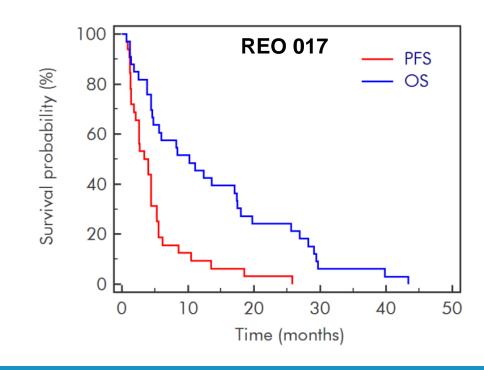
Treatment: Gemcitabine (Days 1, 8) + pelareorep (Days 1, 2 & Days 8, 9)

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 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

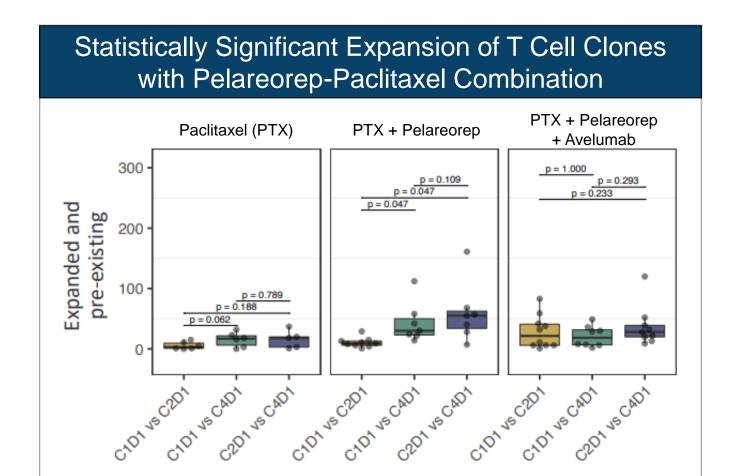


Key Takeaways*:

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

BRACELET-1 Translational Data Align with ORR and PFS Endpoints





Key Translational Findings

- Statistically significant expansion of T cell clones seen by Cycle 4 Day 1 with pelareorep + paclitaxel
- No significant expansion of T cell clones
 with pelareorep + paclitaxel + avelumab
- T cell expansion associated with measures of efficacy in BRACELET-1
- Data are consistent with pelareorep's mechanism of action

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



Fifteen Most Common Adverse Events^{1,2} as Attributed to Study Drug(s)

	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%)	-

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