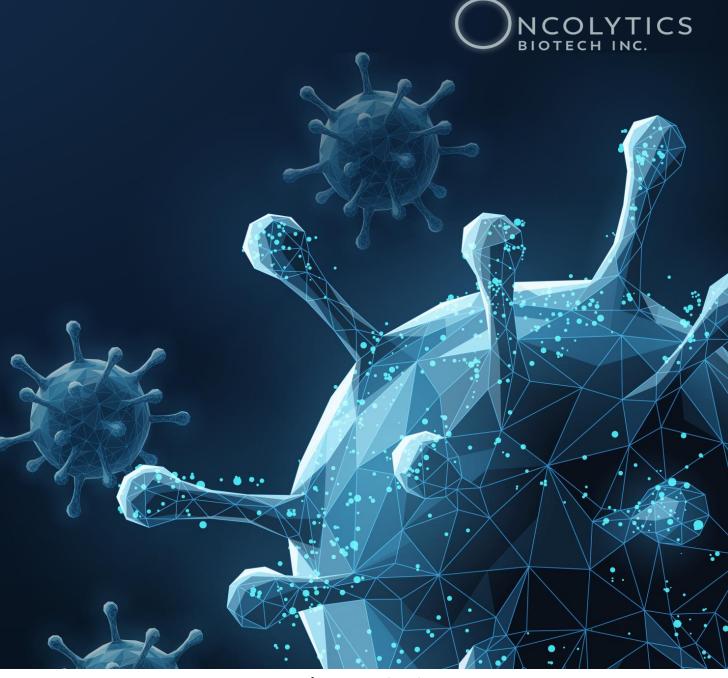
Investor Presentation

November 2023





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 forwardlooking information are collectively referred to herein as "forward-looking statements"). Forward-looking statements contained in this presentation include statements regarding our stated goals and objectives; our anticipated cash runway; our belief as to the potential, mechanism of action and benefits of pelareorep as a cancer therapeutic; our belief that pelareorep's ability to enhance a range of oncology treatments can open large markets; our advancement towards key near-term milestones; our potential registration opportunities in breast and pancreatic cancer and the next steps associated therewith and the anticipated timing thereof; our potential for collaborations with industry leaders; our development strategy; our plans, next steps and expectations relating to pelareorep and CAR T therapy; our upcoming milestones and catalysts; our market opportunities; and other statements related to anticipated developments in Oncolytics' business and technologies. In any forward-looking statement in which Oncolytics expresses an expectation or belief as to future results, such expectations or beliefs are expressed in good faith and are believed to have a reasonable basis, but there can be no assurance that the statement or expectation or belief will be achieved. Such forward-looking statements involve known and unknown risks and uncertainties, which could cause Oncolytics' actual results to differ materially from those in the forward-looking statements. Such risks and uncertainties include, among others, the availability of funds and resources to pursue research and development projects, the efficacy of pelareorep as a cancer treatment, the success and timely completion of clinical studies and trials. Oncolytics' ability to successfully commercialize pelareorep, uncertainties related to the research and development of pharmaceuticals, uncertainties related to the regulatory process and general changes to the economic environment. In particular, we may be impacted by business interruptions resulting from COVID-19 coronavirus, including operating, manufacturing supply chain, clinical trial and project development delays and disruptions, labour shortages, travel and shipping disruption, and shutdowns (including as a result of government regulation and prevention measures). It is unknown whether and how Oncolytics may be affected if the COVID-19 pandemic persists for an extended period of time. We may incur expenses or delays relating to such events outside of our control, which could have a material adverse impact on our business, operating results and financial condition. Investors should consult Oncolytics' quarterly and annual filings with the Canadian and U.S. securities commissions for additional information on risks and uncertainties relating to the forward-looking statements. Investors are cautioned against placing undue reliance on forward-looking statements. The Company does not undertake to update these forward-looking statements, except as required by applicable laws.

Oncolytics At-A-Glance



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

Exchanges	Nasdaq: ONCY / TSX: ONC
Market Cap.	Approx. \$126M
Cash, cash equivalents, & marketable securities	CDN \$40M (USD \$29.2M) Based on FX as of Nov. 6, 2023
Shares Outstanding	73,398,847
Fully Diluted	88,282,459
Cash Runway	12+ months
HQ	San Diego, CA, US Calgary, AB, Canada

Pelareorep: Unleashing the Power of the Immune System to Fight Cancer





Opportunity: Two Registrational Opportunities That are Phase 3-ready

Favorable Phase 2 data from over 120 HR+/HER2- mBC and 120 metastatic PDAC patients Signals of efficacy including ORR, PFS, OS seen across multiple studies for both indications



Pelareorep is an IV-Delivered Immunotherapy That Works Systemically

Enhances T cell infiltration and PD-L1 upregulation by introducing dsRNA into cancer cells, allowing the immune system to identify/target primary and metastatic cancers for destruction



Strong Clinical Data to Advance into Licensure-Enabling Studies

Randomized Phase 2 mBC data show *statistically significant near doubling of survival* and 50% improvement in mPFS Phase 1/2 data in PDAC show *substantial improvements in ORR, mPFS, mOS compared to historical control trials*



Pelareorep's Demonstrated Clinical Synergy with Multiple Oncology Treatments

Chemotherapy-pelareorep combinations have demonstrated efficacy signals in breast cancer and pancreatic cancer Synergy with checkpoint inhibitors-pelareorep seen in breast cancer, pancreatic cancer, colorectal cancer, anal cancer



Advancing Towards Key Near-term Milestones Supported by World-class Collaborators

BRACELET-1 mBC OS data continues to mature; advancing to licensure-enabling studies in breast & pancreatic cancer Clinical collaborators include *Pfizer*, *Merck*, *Roche*, *and Incyte*

Pelareorep's Immune-mediated MOA Positions it to be a Platform Molecule



The Inability of the Immune System to Recognize and Infiltrate Tumors Limits the Impact of Many Drug Classes Pelareorep Offers a Potential Solution to Immunosuppressive Tumor Microenvironments (TMEs)

Underlying Characteristics of Pelareorep's Immune-mediated Mechanism of Action Immunosuppressive TMEs Lack of pre-existing T cells Generates new reactive T cell clones Induces T cell expansion and tumor Lack of T cell expansion and mobilization infiltration Upregulates tumor PD-L1 expression Low tumor PD-L1 expression

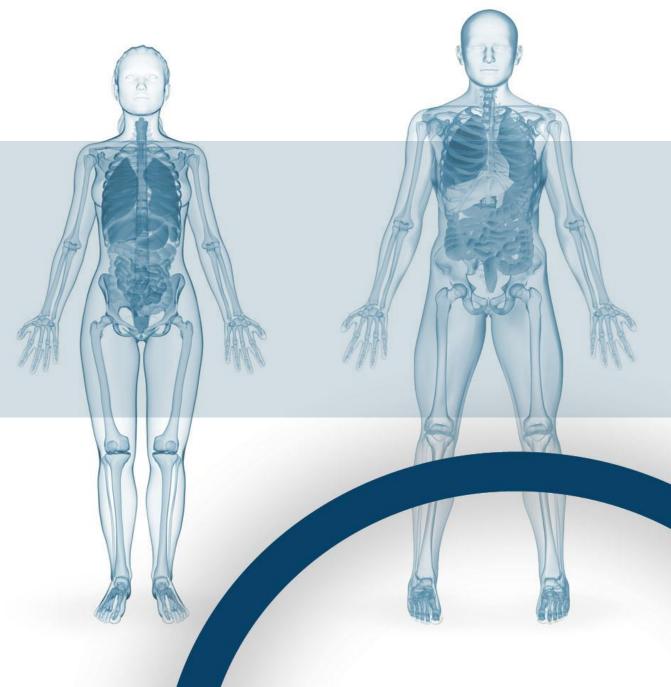
Pipeline Includes Two Registration Opportunities



	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 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 in HR+ / HER2-Breast Cancer





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

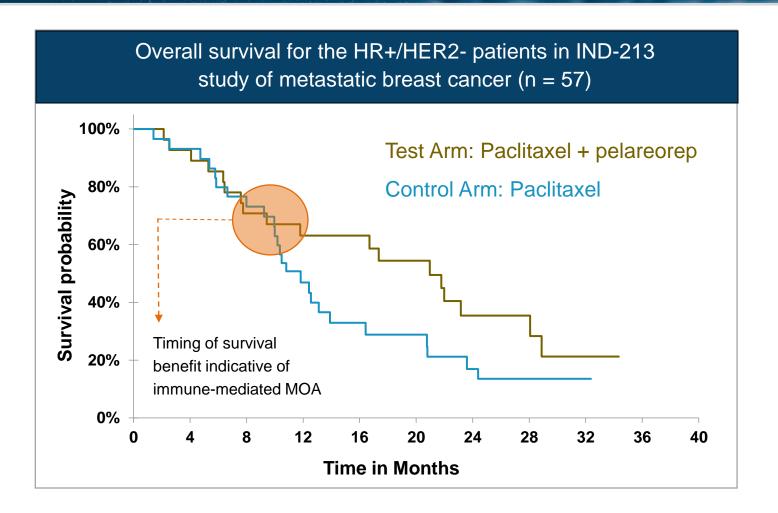


Phase 2 All Subtypes (n = 74)

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

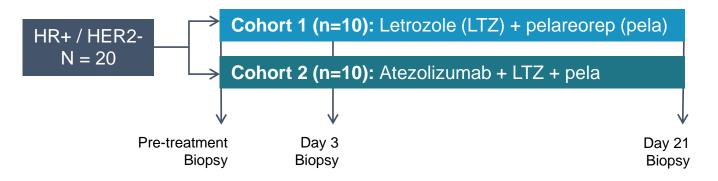


Near doubling of mOS in HR+/HER2- patients with pelareorep treatment

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



AWARE-1 Window-of-opportunity Study Design

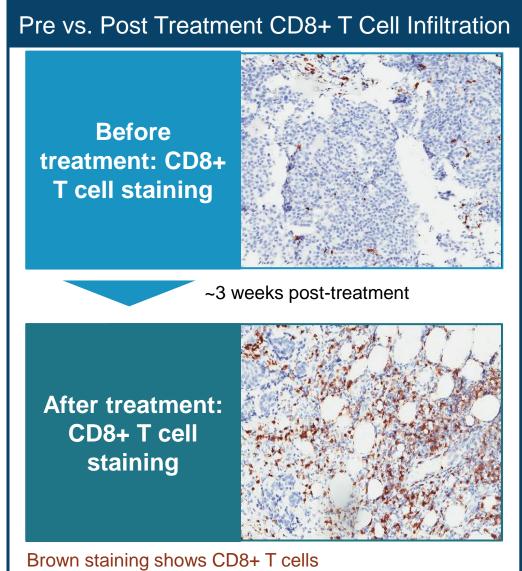


Objective

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

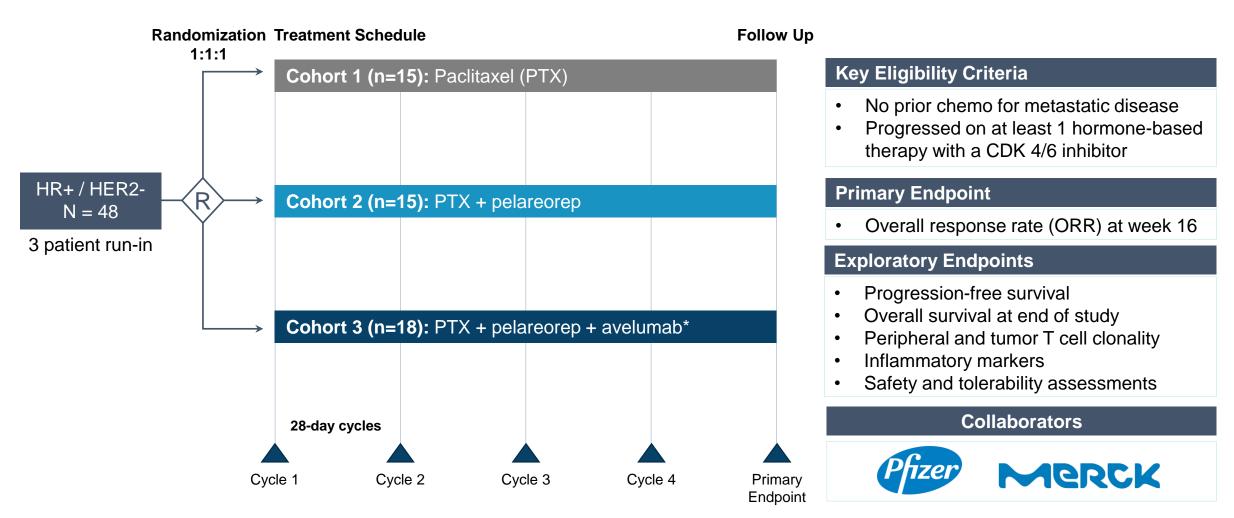
Key Takeaways

-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



Phase 2 BRACELET-1 Study: Designed to Confirm IND-213's Positive Results and Inform Registrational Trial Design





Patients receive treatment for at least 4 cycles until disease progression

BRACELET-1 Data Show Robust Improvements in PFS and ORR in Pelareorep + Paclitaxel Arm¹



Response ²	Paclitaxel (PTX) Monotherapy (Cohort 1, n=15)	PTX + Pelareorep (Cohort 2, n=16)	PTX + Pelareorep + Avelumab (Cohort 3, 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: -, -)		
Key Translational Finding	Statistically significant increase in T cell expansion in cohort 2, but not cohort 3				

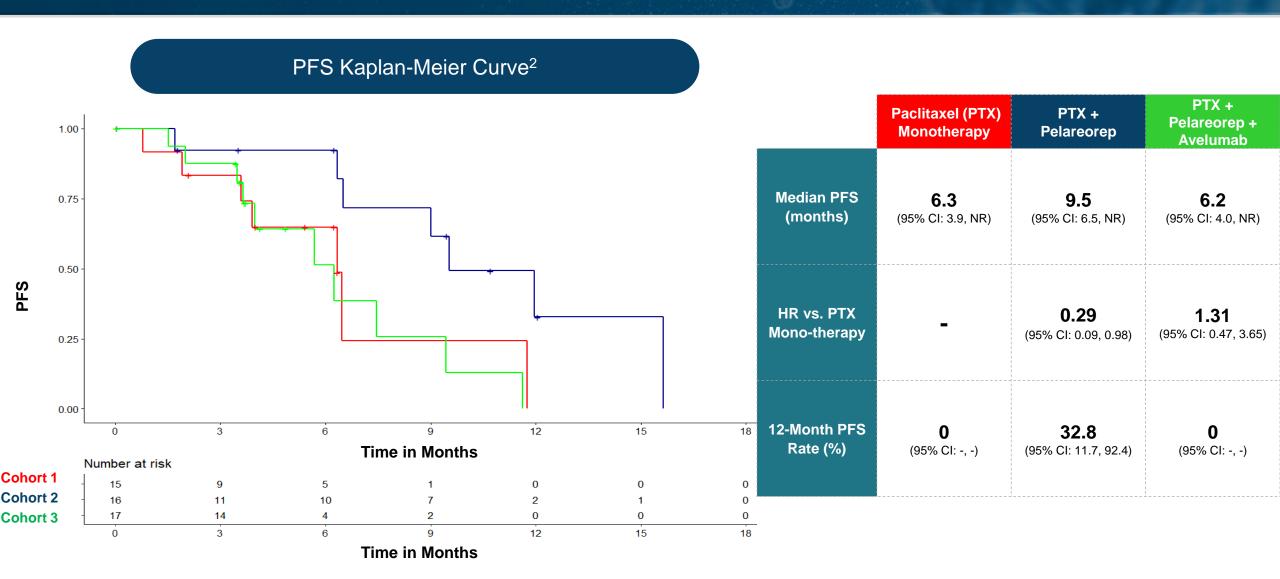
¹Data from a March 3, 2023 cut-off date. Numbers presented may change as they are derived from an unlocked database.

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.

BRACELET-1 Robust Improvement in PFS in Pelareorep + Paclitaxel Arm¹



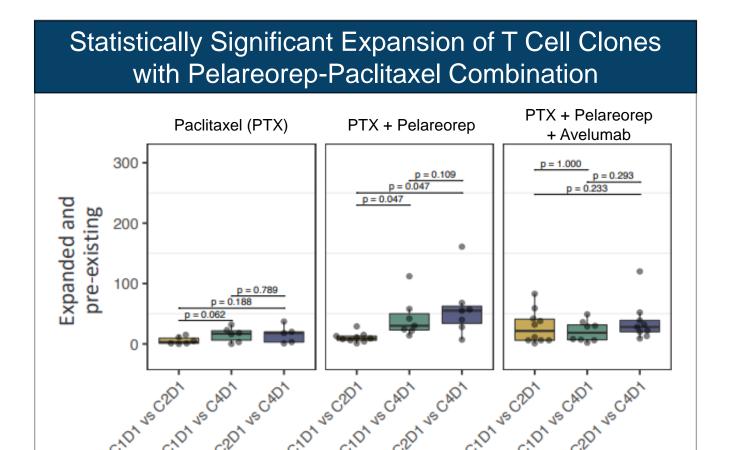


¹Data from a March 3, 2023 cut-off date. Numbers presented may change as they are derived from an unlocked database.

²Data include all patients enrolled in trial. Response data presented by Člark et al. at ASCO 2023 included the 45 randomized patients and excluded participants in the three-patient safety run-in. PFS: Progression-free survival; CI: Confidence interval; NR: Not reached; HR: Hazard ratio

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

IND-213 and BRACELET-1 Patient Populations



BRACELET-1 Population is Representative of Current Standard-of-care

All BRACELET-1 Patients Received Prior Hormone-based Therapy with a CDK 4/6 Inhibitor

		IND-213				
		PTX	PTX + Pela	PTX	PTX + Pela	PTX + Pela + Ave
HR+ / HER2- BC	n	29	28	15	16	17
Non-HR+ / HER2- BC	n	9	8	0	0	0
# of prior chemotherapy for	1	42%	31%	0%	0%	0%
advanced / metastatic /	2	18%	17%	0%	0%	0%
recurrent disease ¹	3	2.6%	0%	0%	0%	0%
	1	26%	31%	33%	44%	35%
# of prior hormone-based	2	29%	11%	47%	44%	29%
therapy	3	8%	17%	13%	0%	24%
	4+	11%	6%	7%	13%	12%
	0	34%	47%	67%	69%	59%
ECOG PS	1	53%	47%	33%	31%	41%
	2	13%	6%	0%	0%	0%

Pelareorep Displayed a Generally Favorable Safety Profile



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)	
G	irade	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

BRACELET-1 Summary: Advancing to Registrational Study



Efficacy Data 31.3% ORR at week 16 with pelareorep + paclitaxel (PTX) vs. 20% with PTX monotherapy

37.5% Confirmed ORR Over Course of Trial with pelareorep + paclitaxel (PTX) vs. 13% with PTX monotherapy

Median PFS of **9.5 months** with pelareorep + PTX vs **6.3 months** with PTX monotherapy (HR=0.29)

Translational Data

Statistically significant expansion of T cell clones seen with pelareorep + paclitaxel combination

Safety Data

Generally favorable and manageable safety profile consistent with prior studies

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



Registration Could Address a Critical Unmet Need





Significant SOC limitations

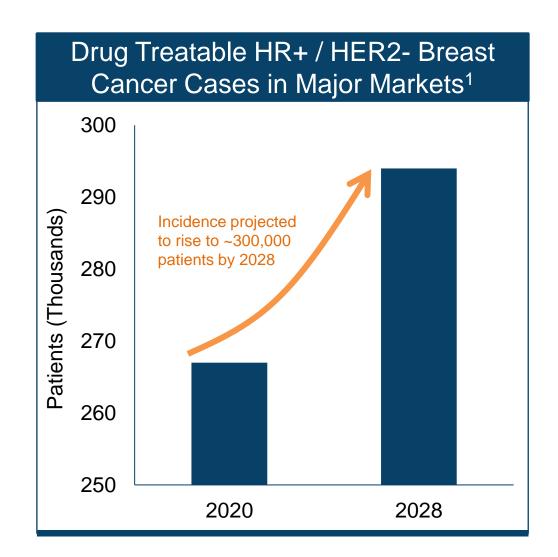
Currently approved therapies are unable to produce a meaningful survival advantage

HR+ / HER2- Collaborators

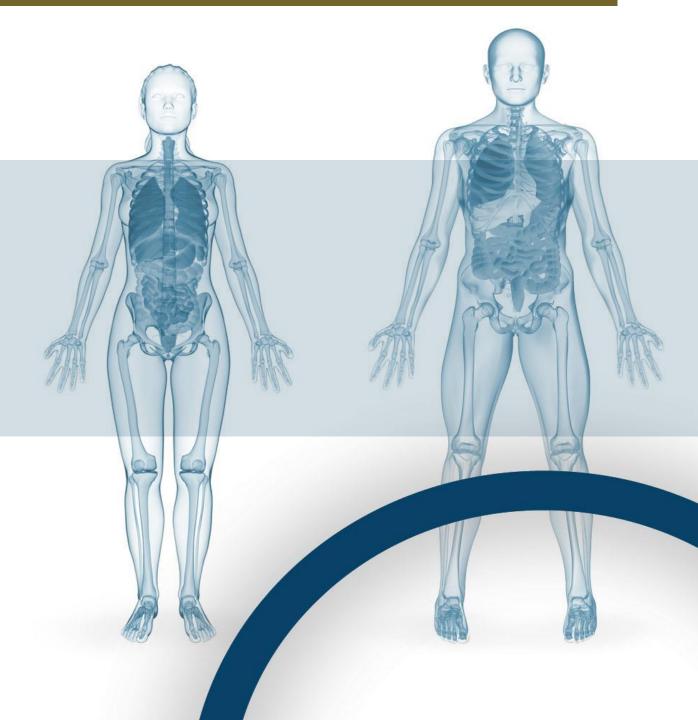








Pelareorep in First-Line Advanced / Metastatic Pancreatic Cancer





Effective Therapies For Pancreatic Cancers are an **Urgent Unmet Need**



Estimates project ~135,000 metastatic, drug-treatable, 1L cases in major markets by 2028¹

Chemotherapy Provides Limited Efficacy

Historical control trials evaluating gemcitabine combined with nab-paclitaxel as a first-line treatment for pancreatic cancer show an average ORR of ~25%²⁻⁵

Mono- or Combo-therapies with ICIs Are Not Effective for >99% of Patients

Immune checkpoint inhibitors (ICIs) only benefit the <1% of pancreatic cancer patients that are classified as "MSI-high" 6

Poor Prognosis

Shortcomings of current treatments contribute to a dismal 11.5% five-year survival rate for pancreatic cancer patients per the U.S. National Cancer Institute

Several Pelareorep-based Combinations, Including With Checkpoint Inhibitors, Have Been Evaluated in First and Second-line Patients



Pelareorep has been administered to 129 PDAC patients in 4 completed and 1 ongoing study:

First-line studies

Study	N	CPI	Treatment regimen
REO 017	34	-	pelareorep + gemcitabine
NCI 8601	52	-	pelareorep + carboplatin + paclitaxel
REO 029 ¹	19	+	pelareorep + gemcitabine/nab-paclitaxel + atezolizumab

Second-line studies

Study	N	CPI	Treatment regimen
REO 024	11	+	pelareorep + chemotherapy ² + pembrolizumab
NU 18I01	13	+	pelareorep + pembrolizumab

REO 017: Pelareorep + Chemotherapy Generated Median Overall and Landmark Survival Rates 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)

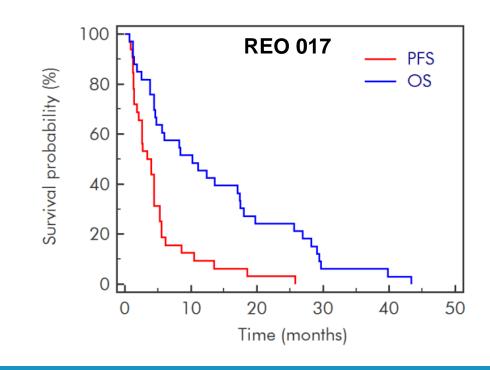
Treatment: Gemcitabine (Days 1, 8) + pelareorep (Days 1, 2 & Days 8, 9)

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



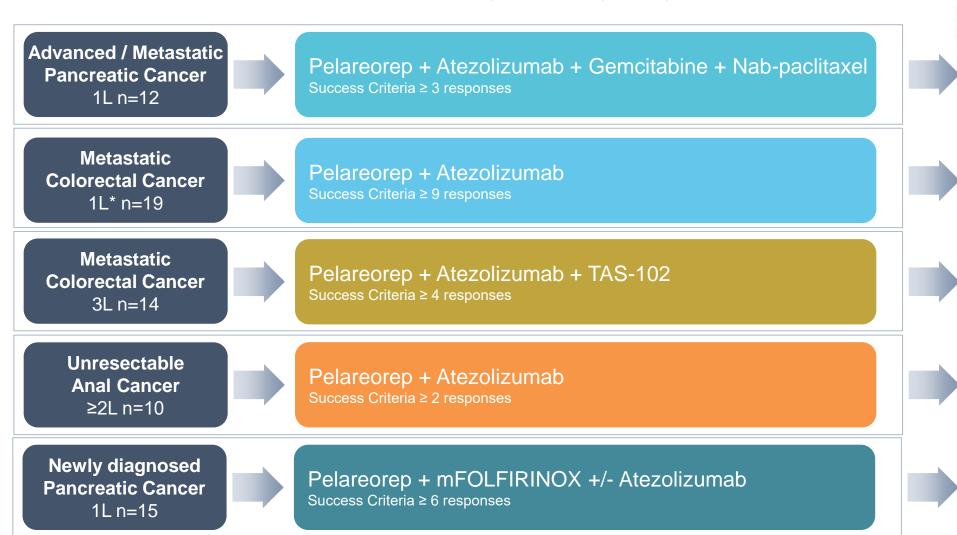
Key Takeaways*:

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

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

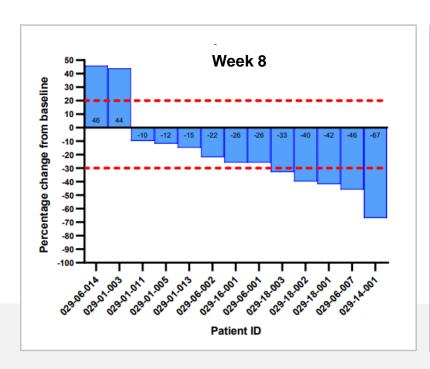
Exploratory Endpoints:

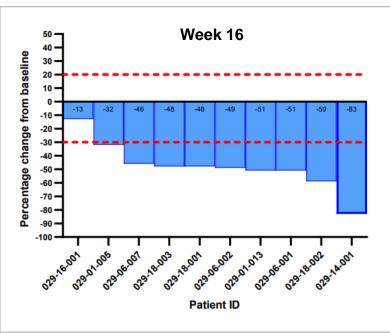
T cell clonality

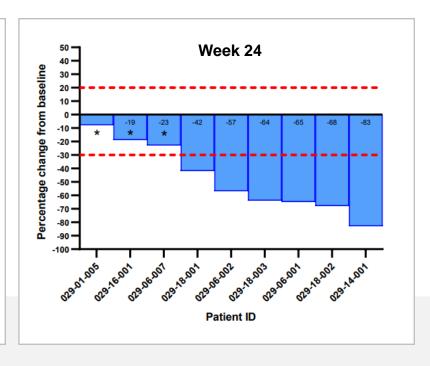
CEACAM6 expression

GOBLET Tumor Responses at Weeks 8, 16, and 24







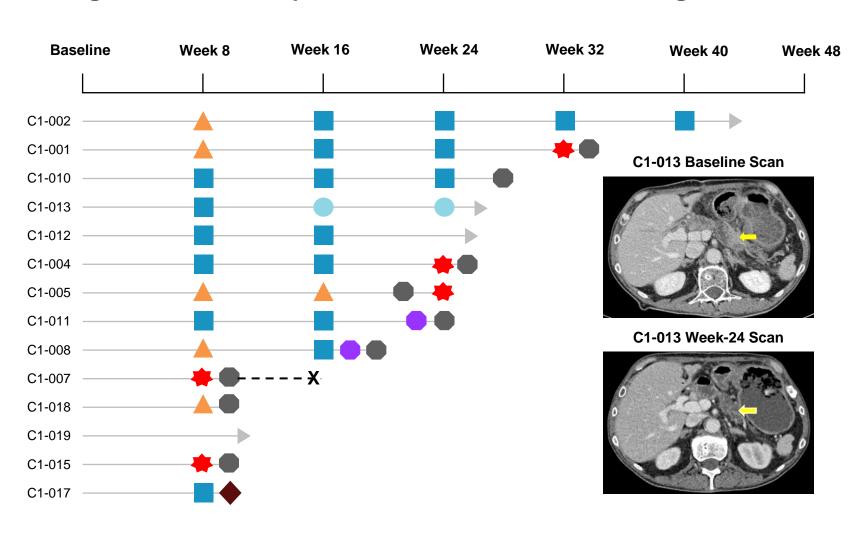


- Numbers indicate the percent change in target lesion size from baseline
- Dotted lines represent cut-offs for progressive disease (+20%) or partial response (-30%)
- (*) indicates patients with PD

Interim Data from Pancreatic Cancer Cohort Showed ORR of 69% in Evaluable Patients (n = 13)



Average ORR of ~25% reported in historical control trials of gemcitabine + Nab-paclitaxel¹⁻⁴



- Complete response (CR)
- Partial response (PR)
- ▲ Stable disease (SD)
- Progressive disease (PD)
- End of treatment
- Withdrawn from study
- Serious adverse event
- x Death

Best responses for the 13 evaluable patients at cut-off date: CR=1, PR=8, SD=2 and PD=2.

Conclusions from Pancreatic Cancer Studies and the Pathway to Registration

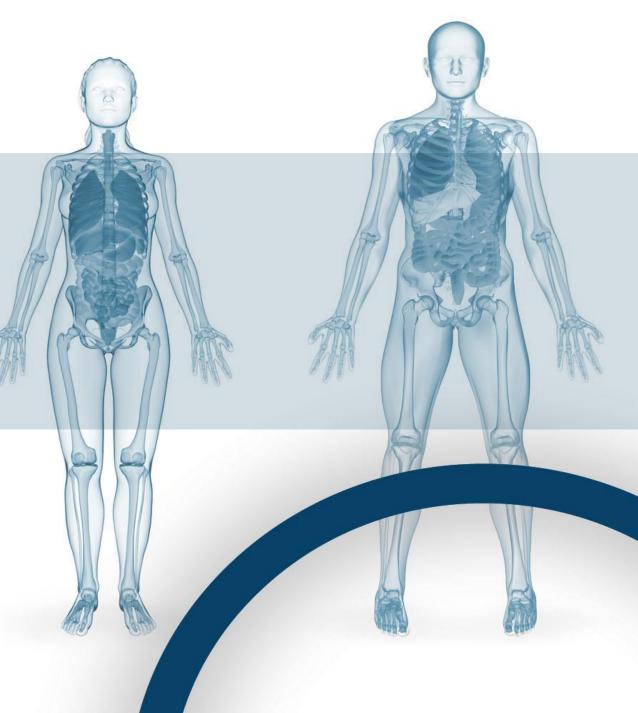


Pelareorep administered to 129 pancreatic cancer patients with no safety concerns, multiple studies show pelareorep infects tumors and modifies the TME to stimulate both innate and adaptive immune responses

Pelareorep + chemotherapy provides a promising survival benefit in the absence of checkpoint inhibitors

- Pelareorep + checkpoint inhibitor has demonstrated activity in the <u>absence of chemotherapy</u> in second line MSS pancreatic cancer patients
- When combined with a checkpoint inhibitor, pelareorep + chemotherapy produces a more profound effect
- With Fast Track designation and a promising data set from multiple studies, a licensure-enabling study is the next logical step using the combination of pelareorep + gemcitabine/nab-paclitaxel + a checkpoint inhibitor

Pancreatic Cancer Action
Network Grant Enables
Opportunity to Address Both
Standard of Care Populations





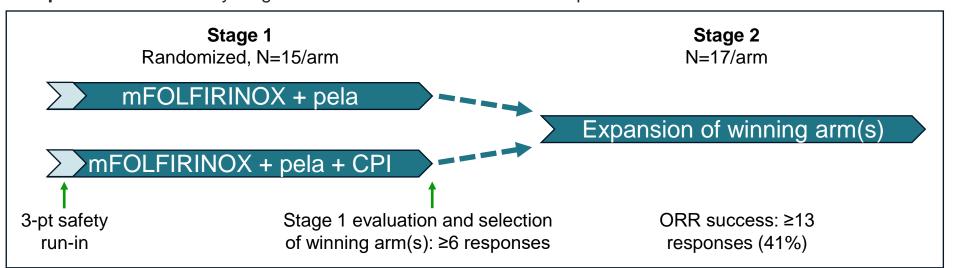
PanCAN \$5M Therapeutic Accelerator Award Grant Opens Both Standard of Care Markets in Pancreatic Cancer



- > Currently, mFOLFIRINOX and gemcitabine + nab-paclitaxel are the standards of care for pancreatic cancer patients.1
- The \$5M Therapeutic Accelerator Award grant allows exploration for an efficacy signal in patients receiving mFOLFIRINOX
- Metastatic first and second-line drug-treatable pancreatic cancer patients estimated to reach 168,000 in the US and major European markets by 2028.¹

Design Phase 1/2 randomized Simon two-stage screened selection design

Population Newly diagnosed metastatic PDAC measurable per RECIST 1.1



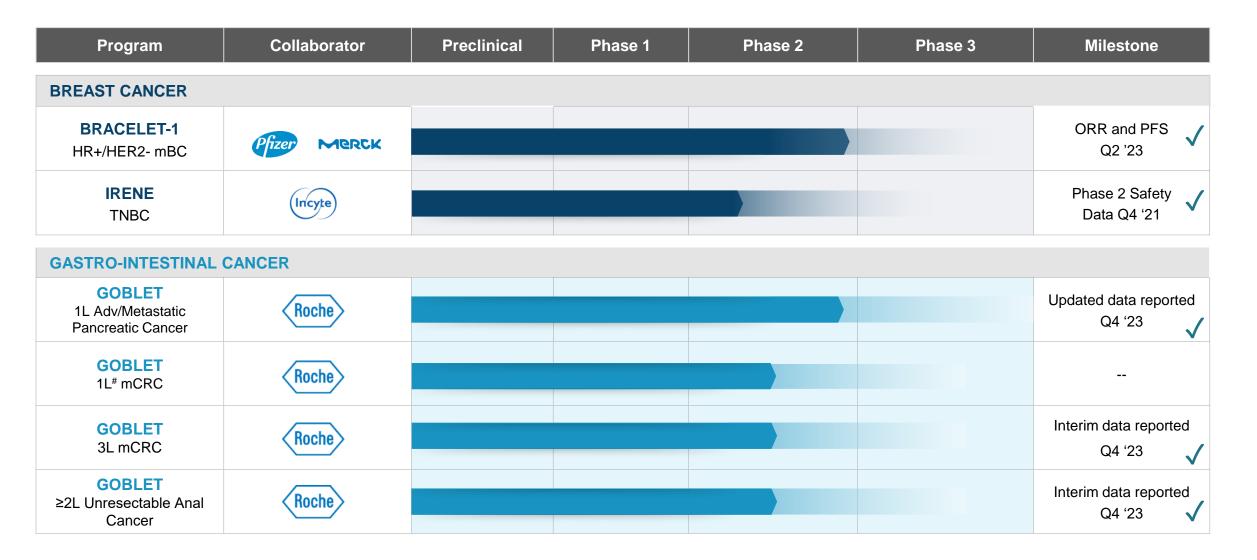
If both arms succeed:

Treatment selected for further development will be based on:

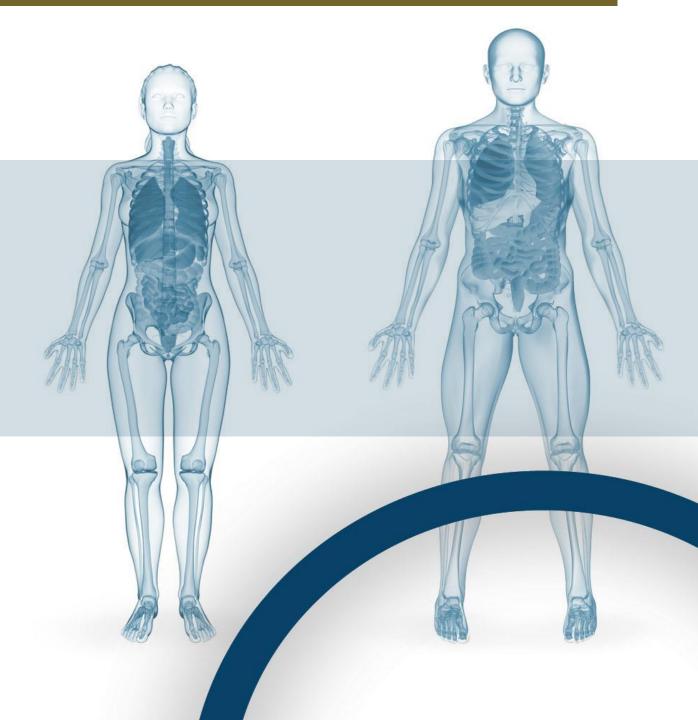
- Relative efficacy
- Safety, tolerability
- Health economic considerations

Clinical Studies Leverage Pelareorep's Platform Potential and Collaborations With Industry Leaders





Pelareorep as an Enabling Technology for CAR T Cell Therapy in Solid Tumors





Pelareorep: An Enabling Technology For CAR T Cell Therapy in Solid Tumors





Current Challenges for CAR T Cell Therapy in Solid Tumors



- Early CAR T cell exhaustion: CAR T cells are short lived with responses that are not durable
- Pelareorep-loaded CAR T cells are long lasting, and can be reactivated with a pelareorep boost

2 Antigen escape

Pelareorep can promote antigen cross presentation

Impaired CAR T cell trafficking to the tumor

Pelareorep can promote the expression of chemokines that recruit lymphocytes to the tumor

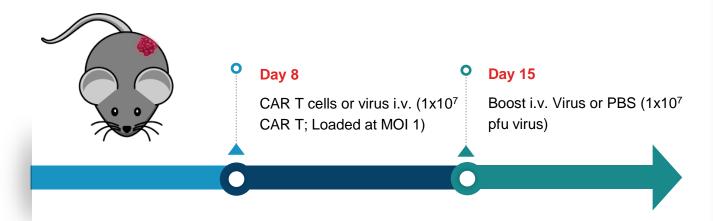
A Immunosuppressive tumor microenvironment

Pelareorep can preferentially activate chemokines that recruit CD8+ T cells rather than Tregs

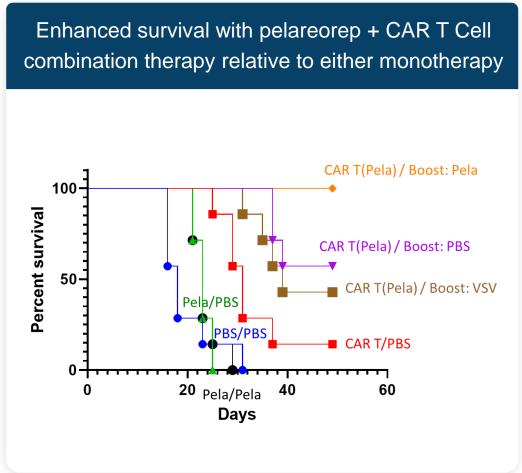
Synergistic Anti-Cancer Activity of Pelareorep Combined With CAR T Cell Therapy in Solid Tumors





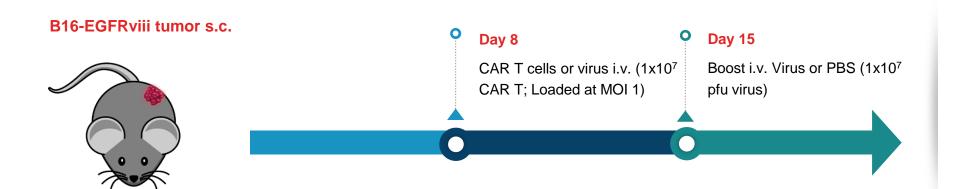


Collaboration between Oncolytics and researchers at the Mayo Clinic and Duke University evaluated pelareorep and CAR T cell combination therapy in a murine solid tumor model

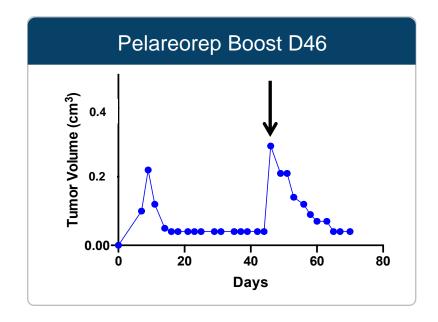


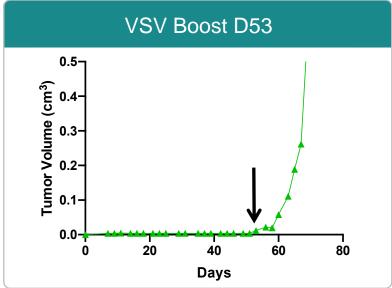
Tumors Which Recur Can Be Treated With a Further Boost of Homologous Virus But Not Heterologous Virus

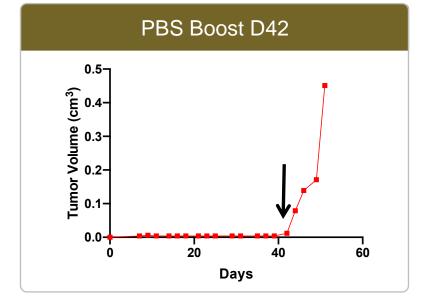




In three mice, tumors recurred around day 40-50. When recurrent tumors started to grow (>0.2cm in diameter) they were administered a further i.v. injection of 10⁷ pfu pelareorep, PBS or VSV-GFP (arrows).







CAR T Conclusions and Next Steps





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



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

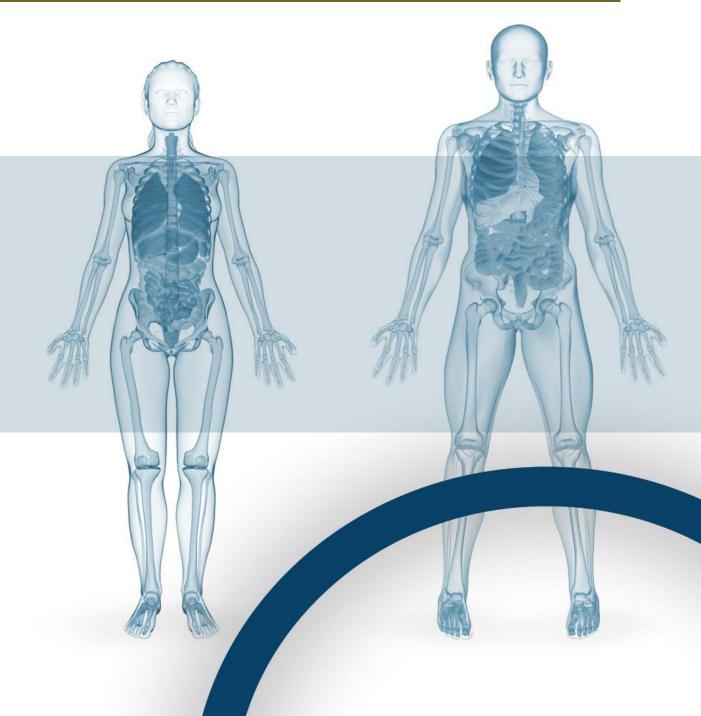


Pelareorep has the potential to broaden the applicability of CAR T cells for solid tumors



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

Catalysts & Milestones





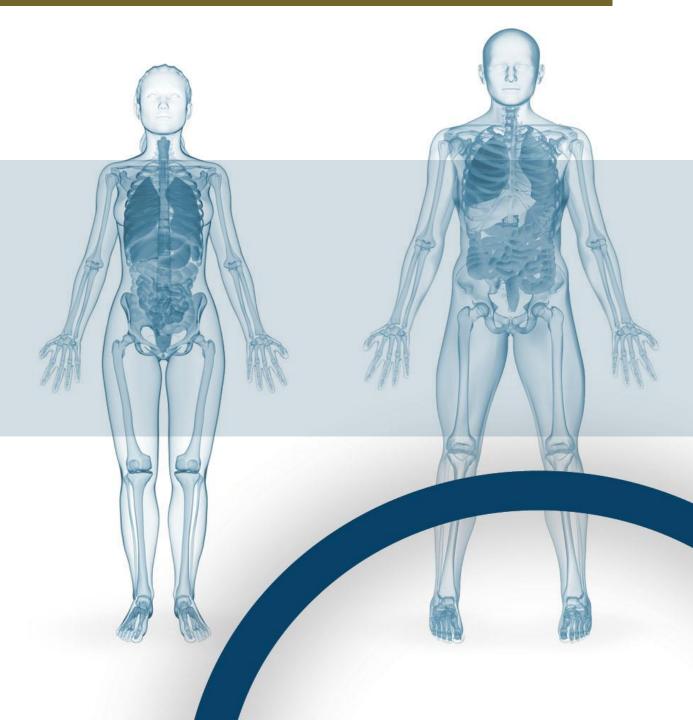
Catalysts & Milestones



Upcoming Catalysts & Milestones	Collaborator(s)	Timing
BRACELET-1 mBC study: ORR and PFS data	Pfizer Merck	
GOBLET PDAC cohort updated efficacy data	Roche	✓
GOBLET metastatic colorectal and advanced anal cohort data	Roche	✓
Guidance for registration path for HR+/HER2- mBC		H1 2024
Initiation of Phase 1/2 PDAC study of pelareorep + mFOLFIRINOX		H1 2024
Adaptive Phase 3 PDAC trial design update		H1 2024

Anticipated Catalysts & Milestones	Collab	orator(s)
BRACELET-1 mBC study: OS data	Pfizer	Merck
Initiation of adaptive Phase 3 PDAC study		

Appendix





Experienced Leadership and Advisory Board



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

MANAGEMENT

Matt Coffey, PhD, MBA

Co-founder, Director, President & CEO

Thomas Heineman, MD, PhD

Chief Medical Officer Denovo, Genocea, Halozyme, GSK

Kirk Look, CA

Chief Financial Officer EY LLP

Andrew de Guttadauro

Global Head of Business Development Amgen, Biogen, Takeda

Allison Hagerman, PEng, PMP

VP of Product Development Visionary Biomedical

NON-EXECUTIVE DIRECTORS

Wayne Pisano, MBA

Chair of the Board, Oncolytics Former President, Sanofi Pasteur

Angela Holtham, MBA, ICD.D

Nabisco Hospital for Sick Children

Bernd R. Seizinger, MD, PhD

Former President & CEO of GPC Biotech Oncology Drug Discovery, BMS

Deborah M. Brown, BSc, MBA

Former President, EMD Serono Canada CCTG

James T. Parsons

Former CFO of Trillium Therapeutics, ProMIS Neurosciences, and Aptose Biosciences

Jonathan Rigby

Group CEO Revolo Biotherapeutics, co-founder of Zogenix, Inc.

SCIENTIFIC ADVISORY BOARD

Dr. Martine Piccart, MD, PhD

Professor of Oncology, Université Libre de Bruxelles BCRF Scientific Advisory Board Co-Founder of Breast International Group (BIG)

Dr. Aleix Prat, MD, PhD

Head, Medical Oncology Department, Hospital Clinic of Barcelona SOLTI - Breast Cancer Research Group

Dr. Padmanee Sharma, MD, PhD

Professor, Department of Genitourinary Medical Oncology MD Anderson Cancer Center KITE, Amgen & BMS IO Network

Dr. Richard Vile, PhD

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



















Robust Intellectual Property Portfolio





153 patents issued worldwide, including 19 US and 7 Canadian19 pending applications worldwide

Reovirus issued patent claims cover:

Compositions of matter comprising reovirus

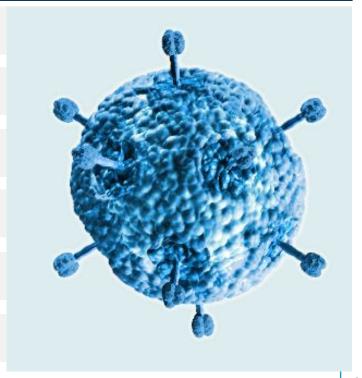
Patent rights extend to at least the end of 2031

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



Competitive Advantages



Delivered Intravenously

Accesses primary and metastatic disease

BSL 2 classification

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

Potentiates multiple immunotherapies

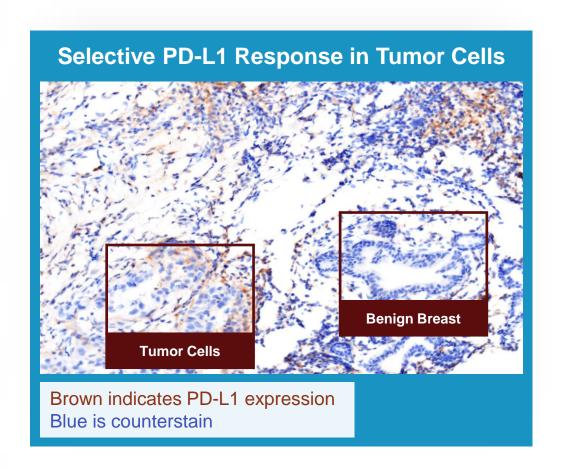
Synergistic potential with both PD-L1 and PD-1 inhibitors, plus other immunotherapies, including CAR T, PARP-1, CDK4/6

Selectively replicates in tumor cells

As shown in multiple clinical studies

Predictive and prognostic biomarkers identified

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



Underlying Biology of Pelareorep's Immunotherapeutic Mechanism of Action

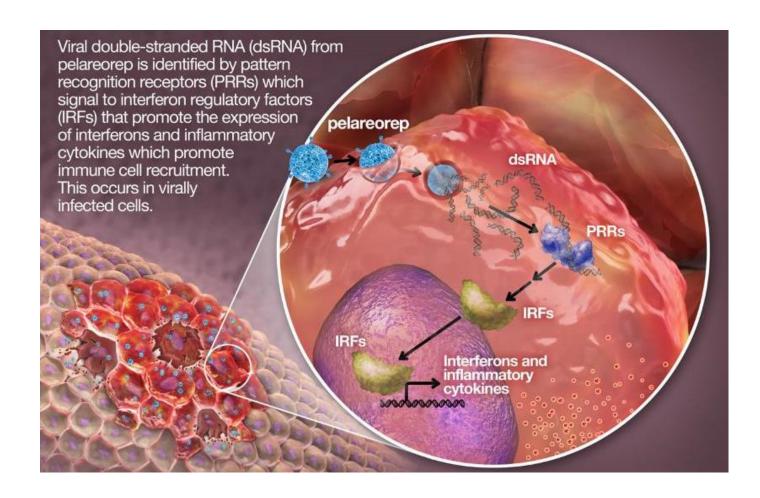


Intravenous administration of pelareorep leads to

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

MORE THAN 40

supporting publications



Pelareorep is Safe and Well-Tolerated



Intravenous



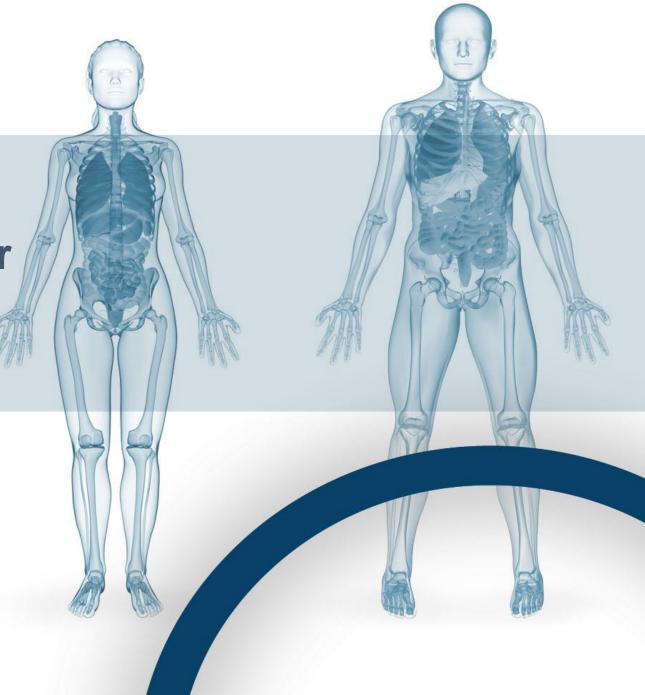
• 1,100 patients treated, 1,000+ intravenously

Monotherapy Toxicity Symptoms

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

No maximum tolerated dose has been reached to date







BRACELET-1 - Robust Improvement in ORR in Pelareorep + Paclitaxel Arm¹



Response ^{2,3}	Paclitaxel (PTX) Monotherapy (Cohort 1, n=15)	PTX + Pelareorep (Cohort 2, n=16)	PTX + Pelareorep + Avelumab (Cohort 3, n=17) ⁴
ORR at Week 16	20%	31.3%	17.6%
Confirmed ORR Over Course of Trial	13.3%	37.5%	17.6%
Disease Control Rate at Week 16 (CR+PR+SD)	46.7%	62.5%	70.6%

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

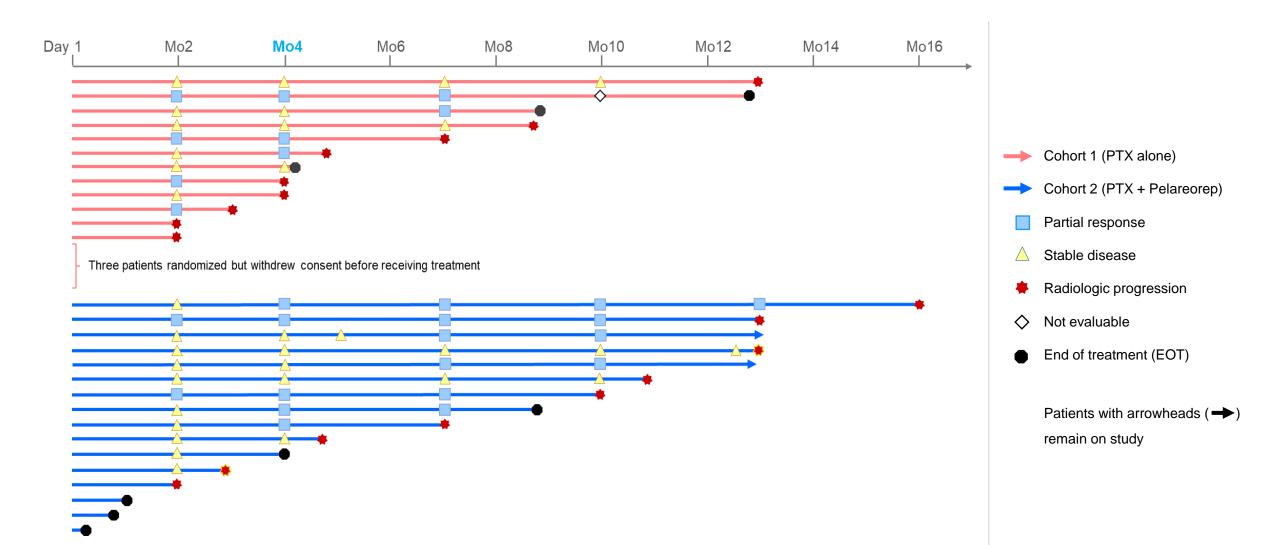
²Response based on RECIST V1.1 investigator assessment.

³Patients who were unevaluable or not assessed were considered non-responders.

⁴Data 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. ORR: Overall response rate; CR: Complete response; PR: Partial response; SD: Stable disease

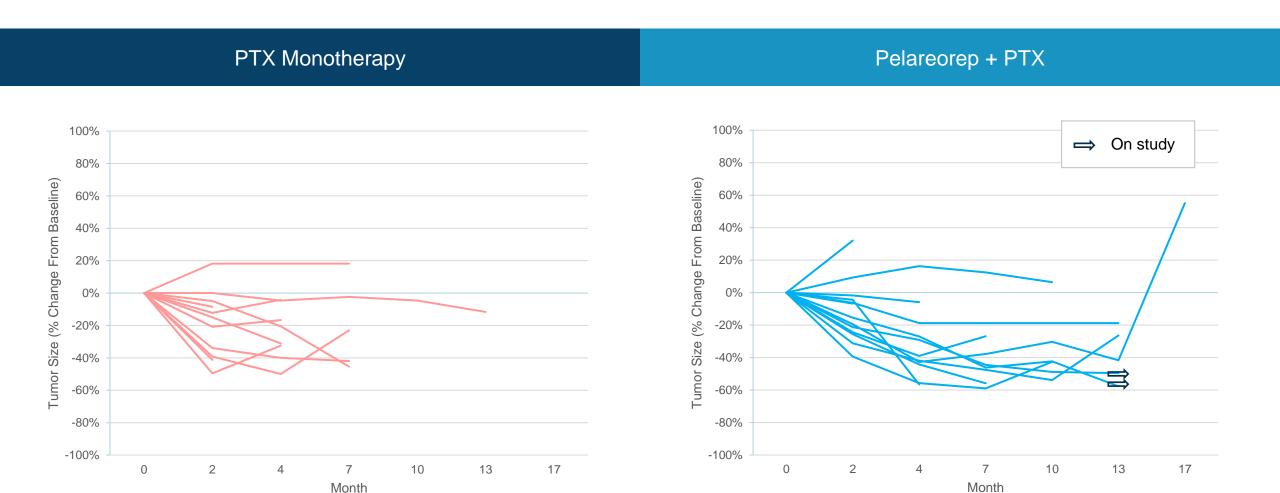
BRACELET-1 Swimmers Plots: PTX vs. Pelareorep + PTX





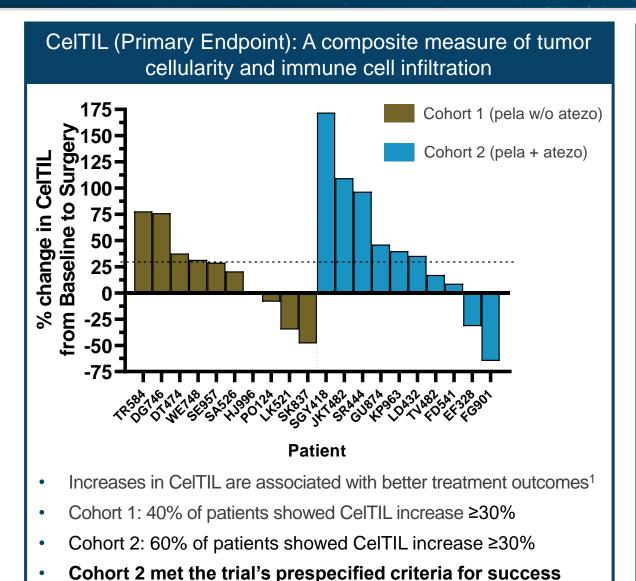
BRACELET-1 Spider Plots: PTX vs. Pelareorep + PTX

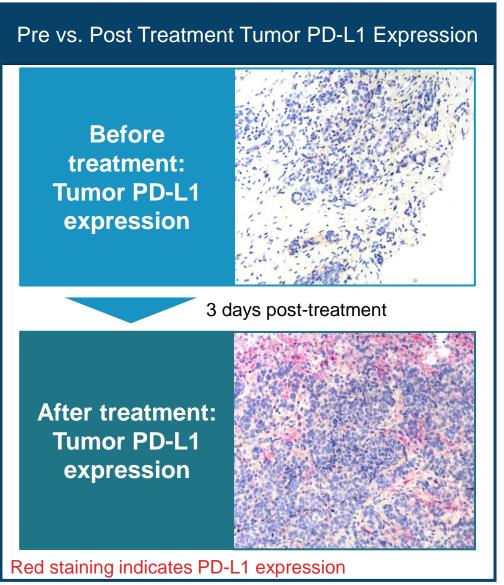




AWARE-1 Achieved Primary Objective







TNBC Market: Additional Opportunity



3,600,000

breast cancer prevalence, U.S. 2017¹

540,000

TNBC prevalence in the US²

62%

of patient are not eligible for immunotherapy based on low PD-L1 expression³

TNBC: Triple-negative breast cancer Sources:

¹NIH SEER. Cancer Stat Facts: Female Breast Cancer. January 18, 2021.

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

³Cortes et al. The Lancet. Vol 396, issue 10265, p1817-1828. December 2020.

TNBC Collaborator

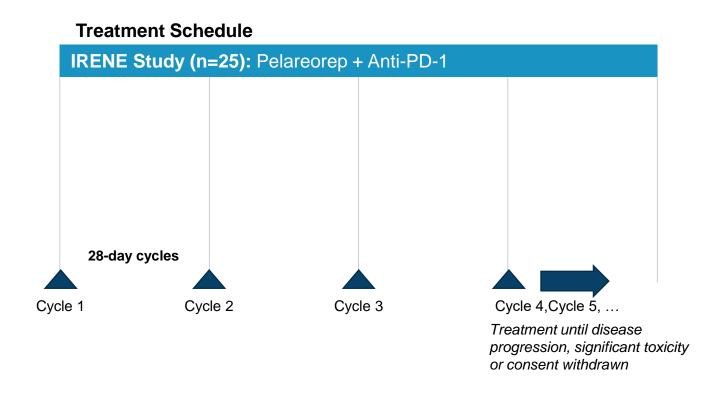




Nearly all patients saw increased PD-L1 expression in the **AWARE-1** study following pelareorep treatment⁴

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





Primary Endpoints

- Safety
- Objective response rate

Secondary Endpoints

- PFS
- OS
- Duration of response

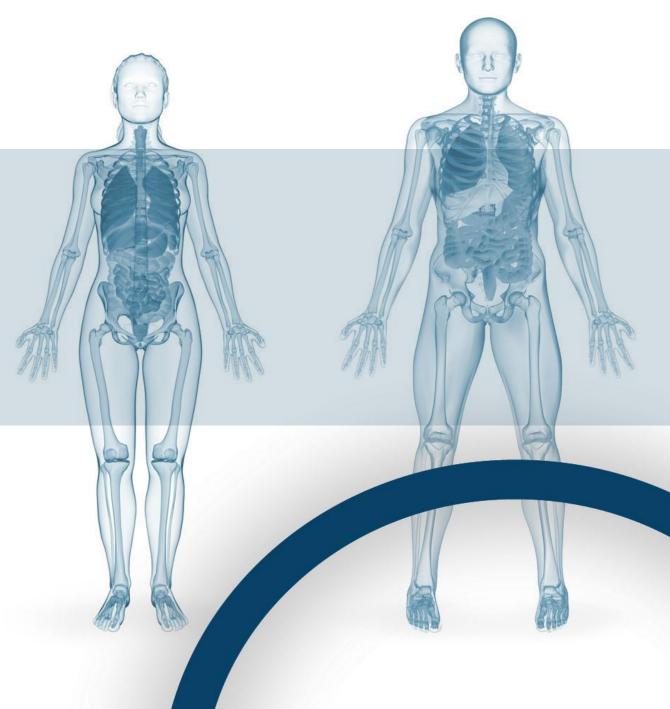
Exploratory Endpoints

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

Collaborator



Expanding the Frontiers of Immunotherapy
Gastrointestinal Cancers
& Hematologic Malignancies





Improved Therapies For Gastrointestinal Cancers Are Needed



4,800,000

Estimated number of new GI cancer cases worldwide in 2018¹

26%

GI cancers account for 26% of global cancer incidence¹

180,000

Estimated new US cases of colon, rectal, pancreatic, anal cancer in 2023²







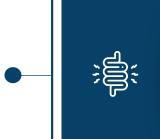
Pela combo therapies have shown:

>90% CBR in KRAS-mutated colorectal cancer patients³

69% ORR and **85% CBR** in pancreatic cancer patients from the GOBLET study

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





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

- A >90% clinical benefit rate in KRAS-mutated colorectal cancer patients¹
- 69% objective response rate and 85% clinical benefit rate in pancreatic cancer patients in the GOBLET study



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

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



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

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

GOBLET PDAC Patient Profiles: Evaluable Patients



Patient #	Age (years)	Sex	ECOG score	Metastases (location)	Target lesion size at baseline (mm)
C1-001	72	F	1	None	65
C1-002	54	M	1	Peritoneum	37
C1-004	63	F	1	Lung	13
C1-005	71	M	0	Liver	79.5
C1-007	54	M	0	Liver	63
C1-008	53	M	0	Liver	187
C1-010	67	M	0	Liver	39.1
C1-011	69	M	0	Liver	15.7
C1-012	49	M	0	Liver	52.1
C1-013	65	M	1	Lymph node	30
C1-015	71	M	0	Liver	24
C1-017	76	F	0	Liver	56
C1-018	54	M	0	Peritoneum	29
C1-019	54	M	0	Liver	39
	Ave: 62.3 yrs	79% male	71% ECOG 0 29% ECOG 1	93%: mets 64%: liver mets	Ave: 52 mm

Anti-PD-1 / PD-L1 Have Shown Limited Efficacy in PDAC



Table 1 | Selected T cell checkpoint-targeted clinical trials in PDAC¹

Target (drug)	Phase	N	Population	Objective Response Rate
PD-L1 (BMS-936559)	1	14	Advanced PDAC, pretreated	0%
PD-1 (pembrolizumab + gemcitabine + nab-paclitaxel)	1	11	Advanced PDAC	18.2%*
CTLA-4 (tremelimumab)	2	20	Advanced PDAC	0%
CTLA-4 (ipilimumab)	2	27	Advanced PDAC, pretreated	0%
CTLA-4 (tremelimumab + gemcitabine)	1	28	Metastatic PDAC, chemotherapy naïve	7%**
CTLA-4 (ipilimumab + gemcitabine)	1	21	Advanced PDAC, 67% pretreated	14%**
PD-L1 (durvalumab) ± CTLA-4 (tremelimumab)	2	65 (33 monotherapy; 32 combination)	Metastatic PDAC, pretreated	0% for monotherapy, 3% for combination
BTK (acalabrutinib) ± PD-1 (pembrolizumab)	2	77 (37 monotherapy; 40 combination)	Advanced PDAC, pretreated	0% for monotherapy, 7.9% for combination
CTLA-4 (ipilimumab) ± GM-CSF- transfected tumor cells (GVAX)	1	30 (15 monotherapy; 15 combination)	Advanced PDAC, pretreated	0%
PD-1 (nivolumab) ± CTLA-4 (ipilimumab) ± MEK (cobimetinib)	1/2	69 (18 monotherapy; 21 dual therapy; 30 triple therapy)	Advanced or metastatic PDAC	0% for monotherapy, 0% for dual therapy, 6.7% for triple therapy

PDAC: Pancreatic ductal adenocarcinoma; *Similar to historical data for gemcitabine + nab-paclitaxel; **Similar to historical data for single-agent gemcitabine.

NU 18I01: Pelareorep + Pembrolizumab Without Chemotherapy Achieved Disease Control in 42% of PDAC Patients



Design: Single-arm; 13 patients enrolled, 12 evaluable for efficacy

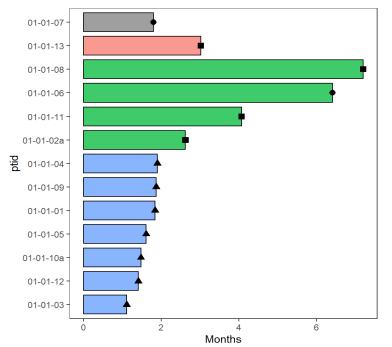
Population: Relapsed metastatic PDAC (2L)

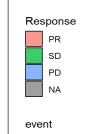
Treatment: Pelareorep (Days 1, 2, 3, 8) [cycle 1]; Days 1, 8, [cycle 2+]) +

pembrolizumab (Day 8)

Primary Endpoint: ORR

Secondary Endpoints: PFS, OS, 1- and 2-year survival rate, DCR, safety





Died with no progression

- RECIST Progression
- Endpoint Progression

Efficacy results in the absence of chemotherapy:

ORR: 8% (1/12); DCR: 42% (5/12)

PFS & OS data to be presented at a later date

Immunomodulatory effects of pelareorep + pembrolizumab:

Pelareorep replication

Increased infiltration of CD8+ T cells & PD-L1+ cells

Reduction in T regs in pts with PR or SD

Key Takeaways:

Demonstrates activity of pelareorep + checkpoint inhibitor <u>without</u> chemotherapy

Provided immunologic rationale for combining pelareorep with a checkpoint inhibitor

Clinical Data Show Pelareorep's Potential in Liquid Tumors



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

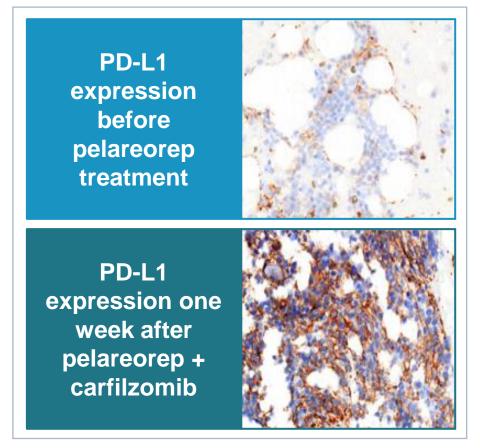
Proof-of-Concept Clinical Data

Pelareorep targets and selectively replicates in MM tumor cells

Achieved a **50% ORR** and **83% CBR** in patients who have failed carfilzomib¹

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

Saw PD-L1 upregulation with pelareorep treatment



Brown staining indicates PD-L1 expression

Development Strategy



Objective:

Pelareorep As An Enabling Technology Across Oncology Drug Classes



Preserve primary focus and resources on advancing breast and pancreatic cancer programs to licensure-enabling studies

2

Leverage collaborations with industry leaders and academia to execute on stated clinical milestones outside of core breast and pancreatic cancer programs



Selectively pursue partnership opportunities to further pelareorep's development as an immunotherapy backbone for combination regimens in other indications

Additional Potential Immunotherapy Opportunities



Bispecific Antibodies¹

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

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

PARP Inhibitors²

Pelareorep and talazoparib synergistically interact to increase cancer cell apoptosis

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

CDK4/6 Inhibitors³

Combining pelareorep with palbociclib led to enhanced immunogenic cell death

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

Business Development Strategy Anchored By Partnerships With Large Pharmaceutical Companies



Objective: Joint Development and Commercialization Partnership

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

Co-Development Study

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

Oncolytics or Investigator Sponsored Trials

 Combination studies with Merck, Roche, Bristol-Myers Squibb, & Incyte

Monetize Certain Geographies

Successful partnership with Adlai Nortye

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

