



PELAREOREP

a transformative dsRNA immunotherapy platform
for gastrointestinal tumors

April 2026

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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 securities laws (such forward-looking statements and forward-looking information are collectively referred to herein as “forward-looking statements”). Forward-looking statements are statements that are not historical facts, and include, but are not limited to, statements regarding our belief as to the potential, mechanism of action and benefits of pelareorep as a cancer therapeutic, our stated goals and objectives, our anticipated patent protection, our belief in the commercial opportunities for pelareorep, pelareorep’s safety profile, expectations regarding the size and growth of the total addressable market with respect to various types of cancer, expectations regarding future studies and trials, including with respect to the timing, size, benefits, potential, feasibility, and results thereof, and other statements related to anticipated developments in Oncolytics Biotech Inc.’s (“Oncolytics” or the “Company”) 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 occur or be achieved. All forward-looking statements are qualified by the assumptions that are stated or inherent in such forward-looking statements. There can be no assurance that such assumptions will prove to be correct. Forward-looking statements are subject to various known and unknown risks and uncertainties, many of which are difficult to predict and are generally beyond our control, and which may cause the actual results, performance or achievements of Oncolytics, or industry results, to be materially different from any future results, performance or achievements expressed or implied by such forward-looking statements. Some of the important risks and uncertainties that could affect forward-looking statements and cause Oncolytics’ actual results to differ materially from those in the forward-looking statements are described further under the section heading “Item 1A. Risk Factors” of our Annual Report on Form 10-K for the fiscal year ended December 31, 2025, and subsequent filings. Investors should consult Oncolytics’ quarterly and annual filings and current reports 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.

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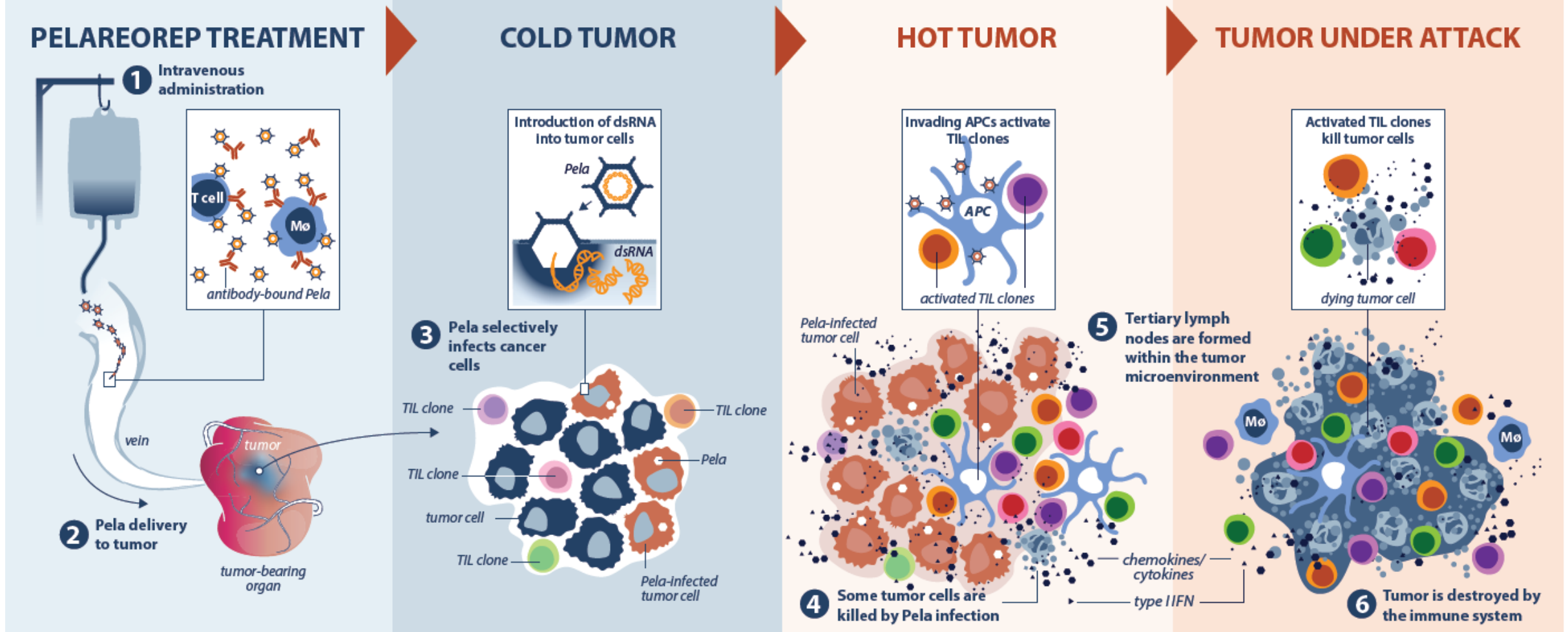
MISSION

We will leverage our proprietary product candidate, pelareorep (pela), an investigational first-in-class double-stranded RNA immunotherapeutic agent, to establish a platform immunotherapy for the treatment of gastrointestinal (GI) tumors.

We believe GI tumors are the largest unmet medical need in oncology and seek to provide patients across multiple GI tumors with a tolerable immunotherapy that increases the chances they will live longer lives.

PELAREOREP MECHANISM OF ACTION

<p>Intravenous pela evades neutralization by associating with mononuclear cells in the blood and is delivered to the tumor.</p>	<p>Pela selectively infects and replicates in tumor cells with RAS pathway mutations. Pela replication produces dsRNA in tumor cells.</p>	<p>Pela infection kills some tumor cells by cell lysis and initiates an inflammatory response, through activation of chemokines and cytokines creating a "hot" tumor.</p>	<p>The pela-initiated inflammatory response results in activation and expansion of TIL clones that can attack and kill the tumor.</p>
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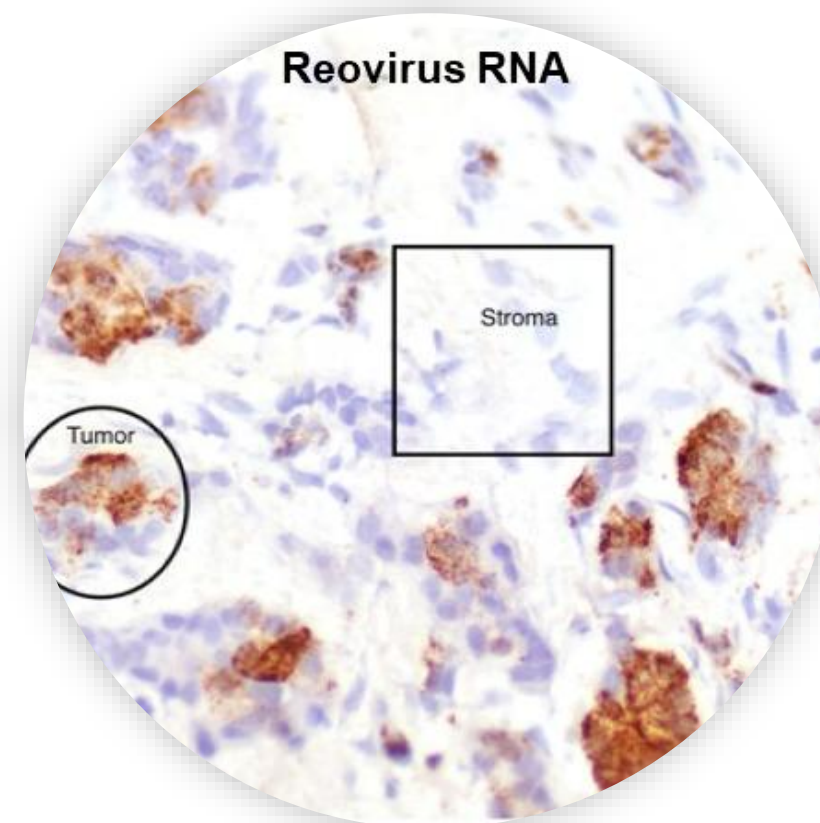


PELAREOREP HAS BEEN OBSERVED TO REPLICATE IN ALMOST ALL EVALUATED TUMORS

Pela is found in almost all on-treatment tumor biopsies

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

Pela RNA is found in tumor but not stromal cells



Brown staining: PELA RNA

- Berkeley, et al. Can Immunol Res. 2018
- Adair, et al. Sci Transl Med. 2012
- Mahalingam, et al. British J Can. 2023
- Ilett, et al. Ther 2009
- Ilett, et al. Clin Cancer Res. 2011
- Phillips, et al. Oncolytic Virother. 2018

PELAREOREP SINGLE-AGENT ACTIVITY

REO 004 and REO 005 - Dose escalation studies of IV pelareorep in refractory metastatic solid tumors



REO 004

(N=18; Cancers: ovarian, colon, breast, cervical, sarcoma, carcinoid, prostate, lung)

- Pelareorep: 1×10^8 to 3×10^{10} TCID₅₀ per dose
- DCR = 45% (1 PR + 7 SD in 18 total patients)
- PR in metastatic breast cancer patient after 5 cycles



REO 005

(N=33; Cancers: bladder, head & neck, lung, sarcoma, pancreas, prostate, renal, colon, skin, gastric, endometrium, esophagus)

- Pelareorep: 1-5 doses per 28-day cycle; 1×10^8 to 3×10^{10} TCID₅₀ per dose
- Responses:
 - 8 SD including 4 with reduction in tumor size
 - 2 CRC patients had SD and reductions in CEA levels for 3 and 6 months
 - A prostate cancer patient had a 51% decrease in PSA



NU 18101

(Pelareorep + pembrolizumab in 2L mPDAC (no chemotherapy, all tumors MSS))

- Checkpoint inhibitors have shown no efficacy in MSS mPDAC
- ORR = 8%; DCR = 42%
- Tumor response comparable to chemotherapy indicating pelareorep activity

SAFETY PROFILE

Pela has been evaluated in

>20 Oncolytics-sponsored studies and several externally sponsored studies (NCI, CCTG, etc.)

Multiple cancer indications (breast, pancreatic, colorectal, myeloma, brain, etc.)

>1,200 patients treated, including >300 patients with GI tumors

Most common PELA-adverse reactions:

- “Flu-like” symptoms: Fever, chills, headache, fatigue, myalgia, cough, anorexia
- GI symptoms also common: Nausea, diarrhea, vomiting
- Lymphopenia, neutropenia, thrombocytopenia also common, but rarely clinically significant
- No maximum tolerated dose (MTD) identified
- Adverse events usually last <6 hours and can be managed with OTC medications

Results from a pooled safety analysis (2017):

- A total of 563 patients were studied
- Fatigue was the most common grade ≥ 3 treatment-related adverse event (TRAE) (<10%)
- Grade ≥ 3 neutrophil count decreased and/or WBC decreased (<20%)
- Addition of pelareorep did not increase the frequency or severity of grade ≥ 3 TRAEs
- Most common serious TRAEs (<5%): fever, febrile neutropenia, sepsis and flu-like syndrome
- Considered “generally well-tolerated”

MARKET OPPORTUNITIES

Gastrointestinal cancer is the fastest growing cancer in the world in people under 50 years old



2L Metastatic Colorectal Cancer (mCRC)

- ~ 1,900,000 patients globally¹
- ~ \$20 billion total addressable market with 4.7% CAGR to 2033²
- RAS mutant patient population high unmet medical need
- 15% mCRC 5-year survival rate³



≥2L unresectable Squamous Cell Anal Carcinoma (SCAC)

- ~ 54,000 patients globally⁴
- ~ \$2.3 billion total addressable market by 2035, growing at 7.7% CAGR 2025-2035⁵
- Evolving standard of care with very few treatment options
- 36% mSCAC 5-year survival rate⁶



1L Metastatic Pancreatic Ductal Adenocarcinoma (mPDAC)

- ~ 500,000 patients globally⁷
- ~ \$3 billion total addressable market with 15% CAGR to 2032⁸
- Chemotherapy standard of care with no approved immunotherapy
- 3% mPDAC 5-year survival rate⁹

A microscopic image showing a cluster of cells with bright blue fluorescence. The cells are arranged in a somewhat circular pattern, with some cells appearing more prominent than others. The background is dark, making the glowing cells stand out.

Pelareorep Clinical Development

CLINICAL POC ACROSS TARGETED INDICATIONS GUIDES STRATEGIC SEQUENCING



Targeted indication	SOC benchmark*	Pela Data	Delta
2L mCRC (RAS-mutated)	OS: 11.2 mo, PFS: 5.7 mo ORR: 6-11% ^{1,2}	OS: 27 mo, PFS: 16.6 mo ORR: 33% ⁹	~ 2-3x
≥2L SCAC	ORR: 11-24% ³⁻⁶ DOR: 9.5 months ³	ORR: 30% DOR: 17 months	~ 1.5-3x
1L mPDAC	2-year OS rate: ~ 9% ^{7, 8}	2-year OS rate: ~ 22% ⁶	~ 2.5x

Development sequencing, short-term to long-term



2L mCRC: biomarker-driven study in RAS-mutated population to offset costs while validating the platform potential

≥2L SCAC: fastest potential registration path with controlled study in rare disease with few treatment options

1L mPDAC: could be only registration-directed study with an immunotherapy candidate in indication; will seek partnership for study

mPDAC: metastatic pancreatic ductal adenocarcinoma; mCRC: metastatic colorectal cancer; SCAC: squamous cell carcinoma of the anal canal; pela: pelareorep; IST: investigator-sponsored trial; 1L: First-Line; 2L: Second-Line; SOC: standard of care; OS: overall survival; PFS: progression-free survival; ORR: objective response rate; DOR: duration of response *Benchmarks do not represent a head-to-head analysis, caution should be exercised when comparing data against unrelated studies or trials. 1. Bennouna J. Lancet Oncol (14):29-37, 2013. 2. Iwamoto S. Ann Oncol. Jul; 26(7): 1427-33, 2015. 3. Rao S, et al. Phase II study of retifanlimab in patients (pts) with squamous carcinoma of the anal canal (SCAC) who progressed following platinum-based chemotherapy. Annals of Oncology. 2020 September. 4. Marabelle A, et al. Pembrolizumab for previously treated advanced anal squamous cell carcinoma: results from the non-randomised, multicohort, multicentre, phase 2 KEYNOTE-158 study. Lancet Gastroenterol Hepatol. 2022 May;7(5):446-454. 5. Lonardi S, et al. Randomized phase II trial of avelumab alone or in combination with cetuximab for patients with previously treated, locally advanced, or metastatic squamous cell anal carcinoma: the CARACAS study. J Immunother Cancer. 2021 November;9(11):e002996. 6. Morris V, et al. Nivolumab for previously treated unresectable metastatic anal cancer (NCI9673): a multicentre, single-arm, phase 2 study, The Lancet Oncology, Volume 18 Issue 4, 2017. 7. https://oncolyticsbiotech.com/press_releases/oncolytics-biotech-highlights-transformative-pelareorep-survival-data-in-multiple-tumors-and-commitment-to-registration-enabling-studies/. 8. Mahalingam G, et al. A Phase II Study of Pelareorep (REOLYSIN®) in Combination with Gemcitabine for Patients with Advanced Pancreatic Adenocarcinoma. Cancers (Basel). 2018 May 25;10(6):160. 9. Goel, et al. Mol Cancer Ther (19): 1148-56, 2020

CLINICAL DEVELOPMENT PIPELINE

Program	Collaborator	Combination	Phase 1	Phase 2	Registration-Enabling Phase 3	Anticipated Milestone
2L CRC						
RAS-mutated Biomarker-focused study	TBD	chemo + bev +/- pela	[Progress bar: ~60%]			Preliminary Data Expected Q4 2026
≥2L SCAC						
GOBLET cohort 4 ≥2L Unresectable SCAC		pela + atezo	[Progress bar: ~70%]			Final data readout expected 2H 2026
Pivotal Study	CPI Partner Expected	pela + CPI	[Progress bar: ~85%]			Expect to seek partnership for study
1L PDAC						
Pivotal Study	CPI Partner Expected	pela + GnP +/- CPI	[Progress bar: ~85%]			Expect to seek partnership for study
GOBLET cohort 5 Newly Diagnosed PDAC	 	pela + mFOL +/- atezo	[Progress bar: ~50%]			Initial data readout expected 2H 2026

Colorectal Cancer Program



EFFICACY RESULTS IN COLORECTAL CANCER DEMONSTRATED ACROSS MULTIPLE STUDIES



REO 022 study in 2L KRAS mutant mCRC results more than double historical third-party benchmarks^{1, 2, 3}:

- PFS: 16.6 months vs 5.7 months (pelareorep + FOLFIRI + bevacizumab vs. FOLFIRI + bevacizumab)
- OS: 27.0 months vs 11.2 months (pelareorep + FOLFIRI + bevacizumab vs. FOLFIRI + bevacizumab)
- ORR: 33% vs 6-11% (pelareorep + FOLFIRI + bevacizumab vs. FOLFIRI + bevacizumab)



Data from GOBLET in 3L mCRC met predefined efficacy criteria and exceed historical third-party benchmarks^{4, 5, 6, 7}:

- 40% DCR and 33% 12-month survival rate
- PFS: 2.8 month and median OS: 8.0 months



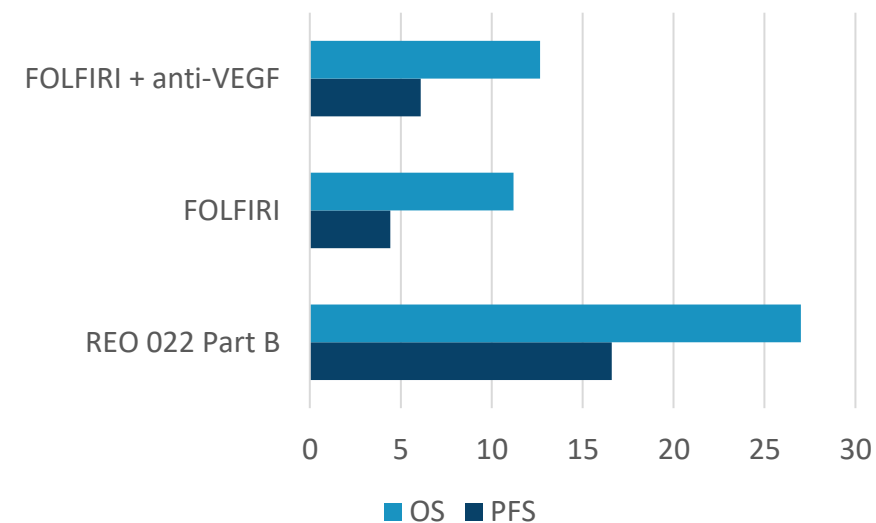
Translational data from REO 022 and REO 013 studies support observed benefit^{1, 7, 8, 9}:

- Viral replication and immune activation shown in mCRC tumors
- Dendritic cell maturation and CD8+ T cell activation alter TME and enabled tumors to respond to treatment

REO 022 STUDY: 2L KRAS-mutant MSS mCRC

The combination of pelareorep with SOC has equated to ORR, PFS, and OS that is 2-3X SOC⁴

Design	Phase 1 dose escalation
Population	15 Part B patients; Metastatic or advanced KRAS-mutated colorectal cancer; Refractory to oxaliplatin
Treatment	pelareorep + FOLFIRI + bevacizumab (Avastin [®])
Endpoints	Efficacy (PFS, OS), safety



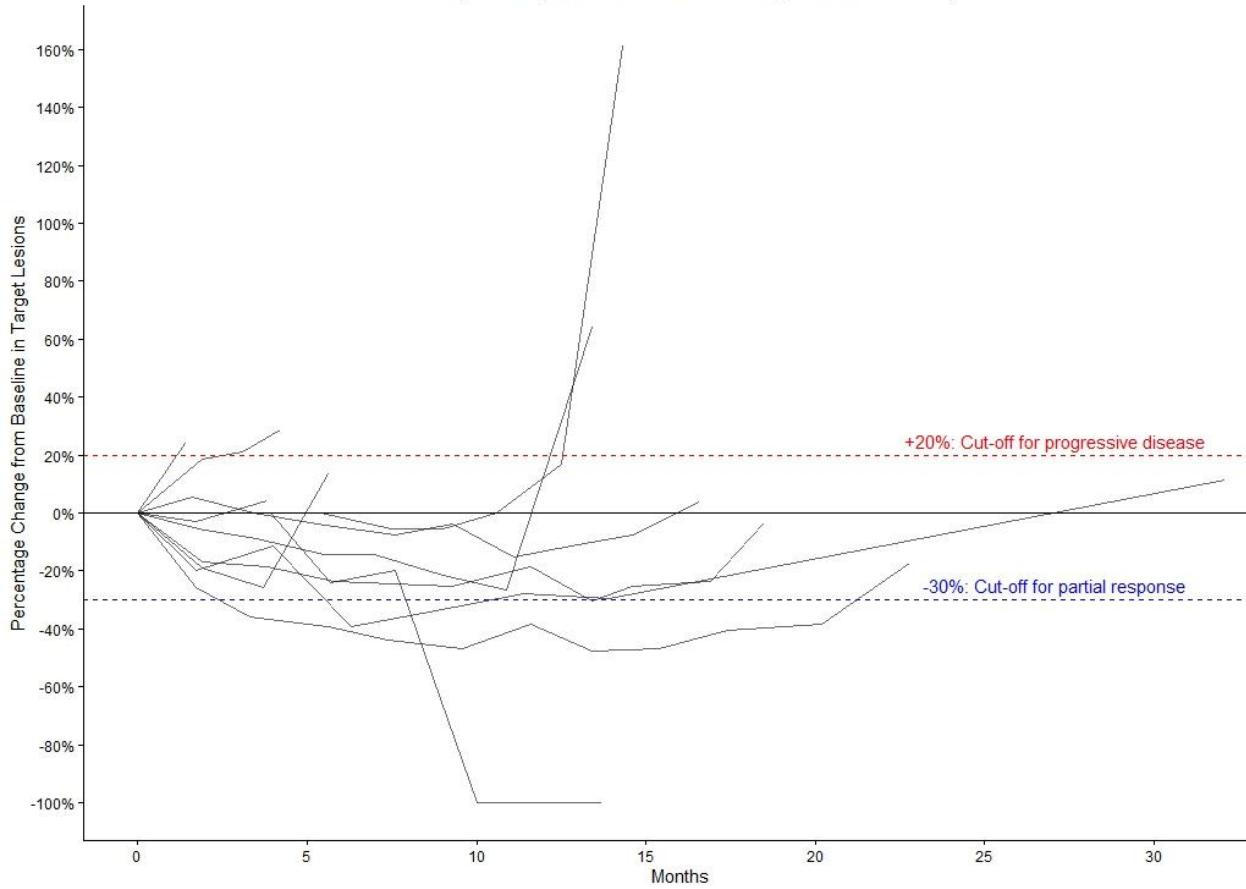
	REO 022 Part B	FOLFIRI ¹	FOLFIRI + Ramucirumab ¹	FOLFIRI ²	FOLFIRI + Aflibercept ²	FOLFIRI ³	FOLFIRI + Bevacizumab ³
OS (months)	27.0	11.7	13.3	12.1	13.5	9.8	11.2
PFS (months)	16.6	4.5	5.7	4.67	6.9	4.1	5.7
ORR	33%	12.5%	13.4%	11.1%	19.8%	4%	5%

Patient responses were durable, median duration of response was 19.5 months

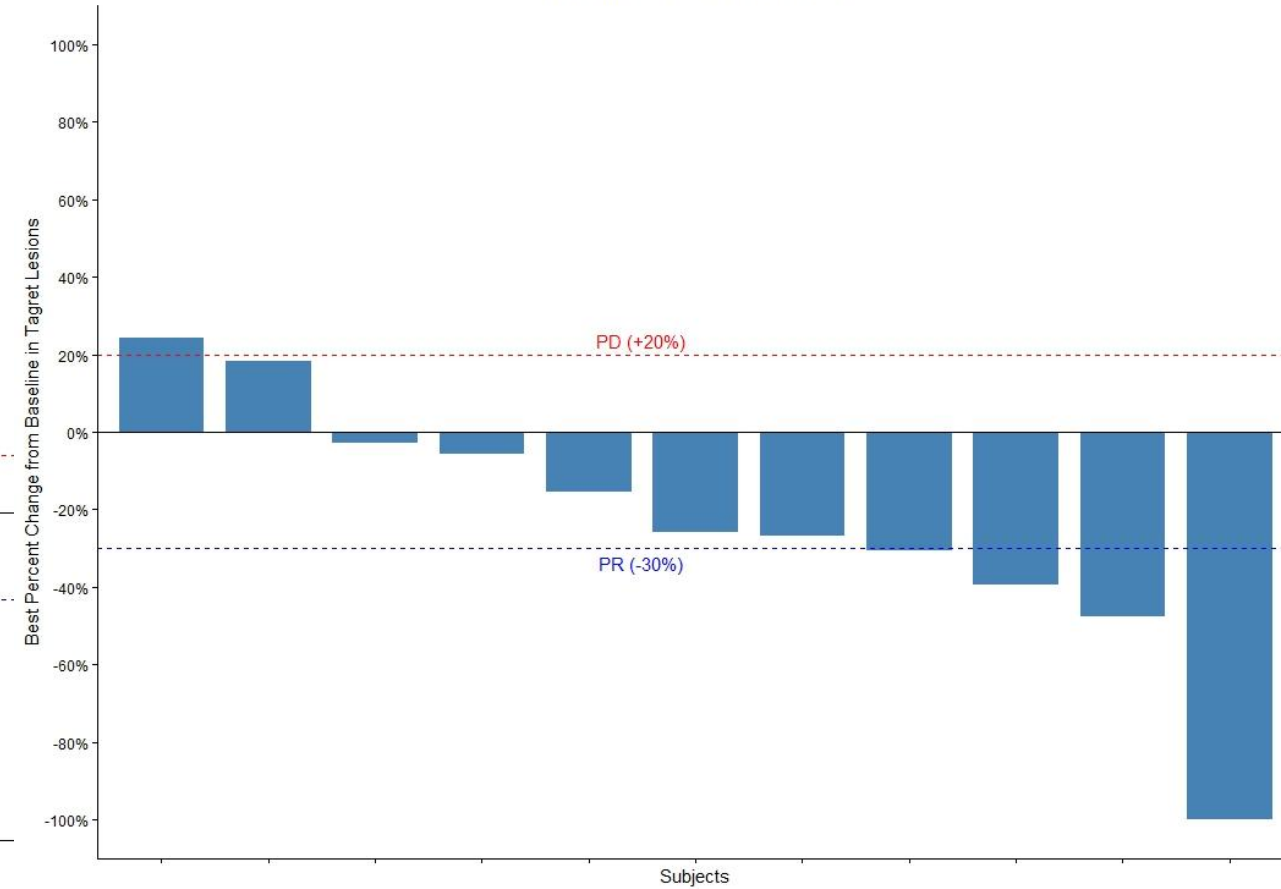
2L: second-line; MSS: microsatellite-stable; mCRC: metastatic colorectal cancer SOC: standard of care; FOLFIRI: leucovorin, fluorouracil, irinotecan; OS: overall survival; PFS: progression-free survival; ORR: objective response rate
 Goel, et al. Mol Cancer Ther (19): 1148-56, 2020; 1. Tabernero J. Lancet Oncol (16):499-508, 2015 2. Van Cutsem E. J Clinical Oncol (30):3499-506, 2012 3. Bennouna J. Lancet Oncol (14):29-37, 2013. 4. This is a cross-study comparison and not based on any head-to-head clinical trials. Cross-study comparisons are inherently limited and may suggest misleading similarities and differences. The values shown in the cross-study comparisons are directional and may not be directly comparable.

REO 022 SPIDER & WATERFALL PLOTS¹

Change in target lesion size over time (REO 022: Part B)



Waterfall Plot - REO 022 Part B

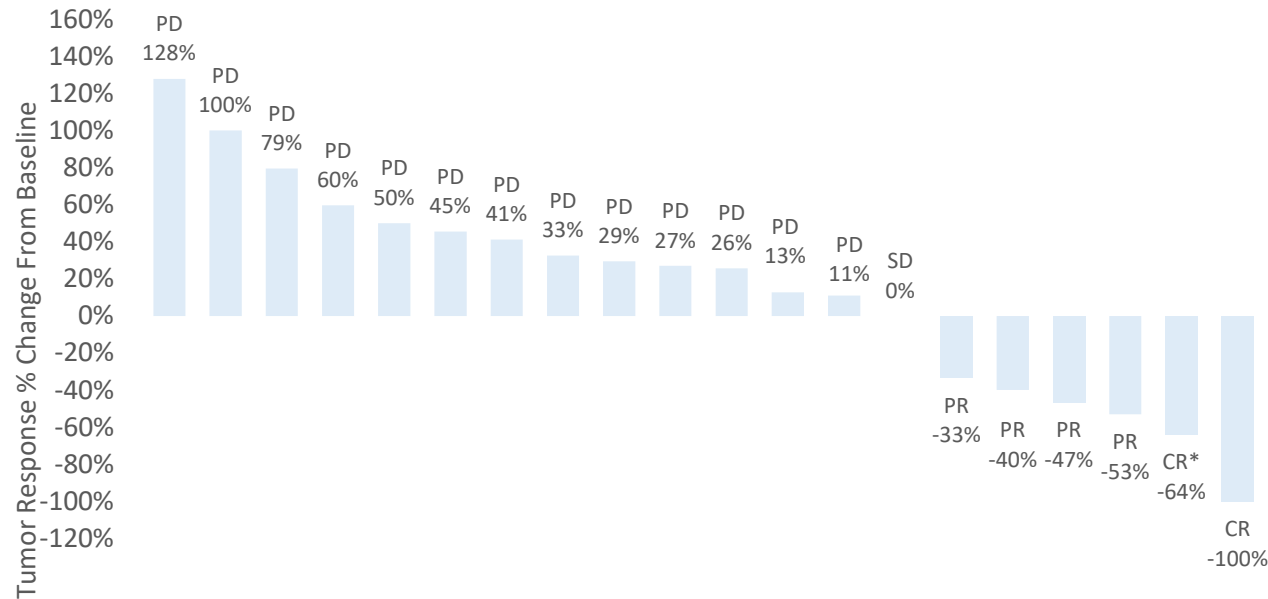


Anal Cancer Program



GOBLET COHORT 4 DATA: PELA + ATEZO IN $\geq 2L$ SCAC

Strong efficacy signal with immunotherapy combination without chemo in difficult cancer



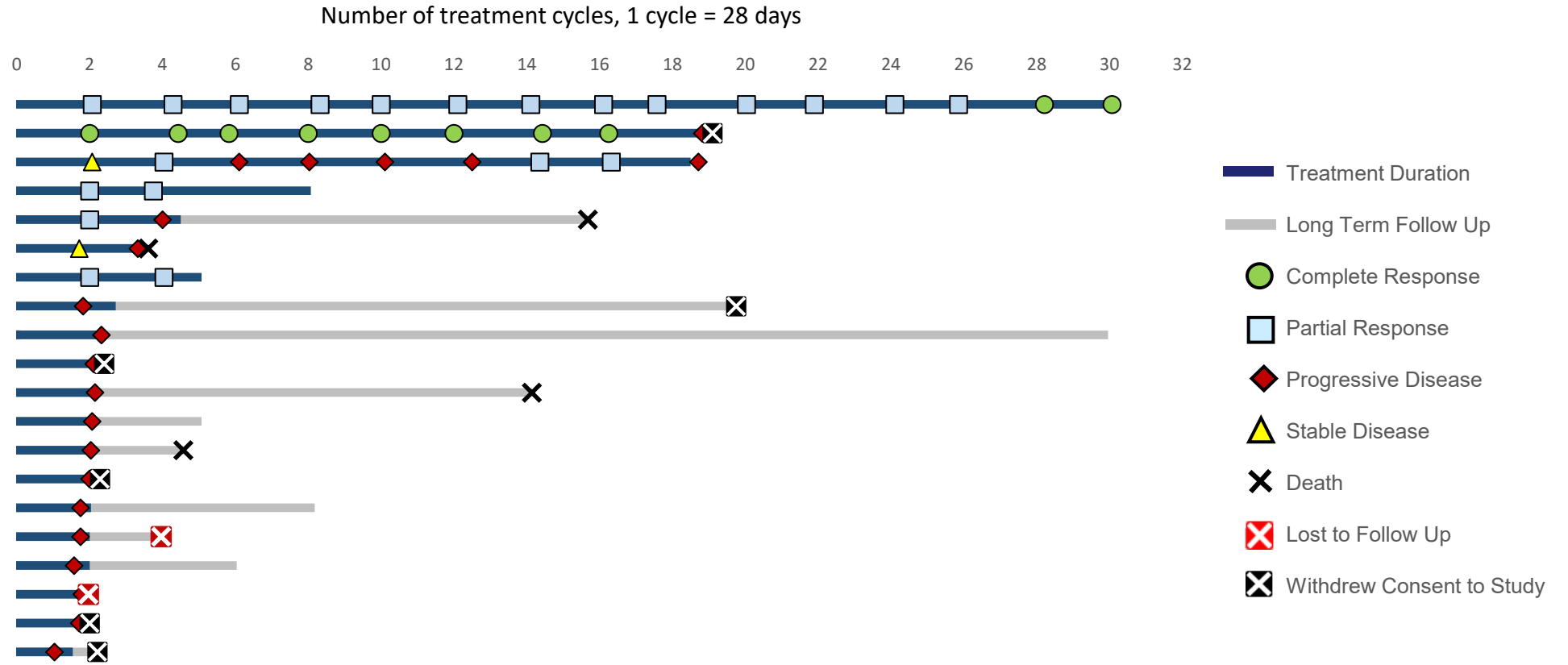
- 30% ORR in 20 evaluable $\geq 2L$ patients
- 29% ORR in 14 evaluable $\geq 3L$ patients
- Durable responses:
 - 1 CR lasting 15 months
 - 1 prolonged, ongoing response lasting 28 months that culminated in a CR
 - Compared to 9.5 months for the current approved therapy¹

ORR: objective response rate; 2L: second-line; SCAC: squamous cell carcinoma of the anal canal; pela: pelareorep; atezo: atezolizumab; DCR: disease control rate; CR: complete response; PR: partial response; PD: progressive disease; SD: stable disease

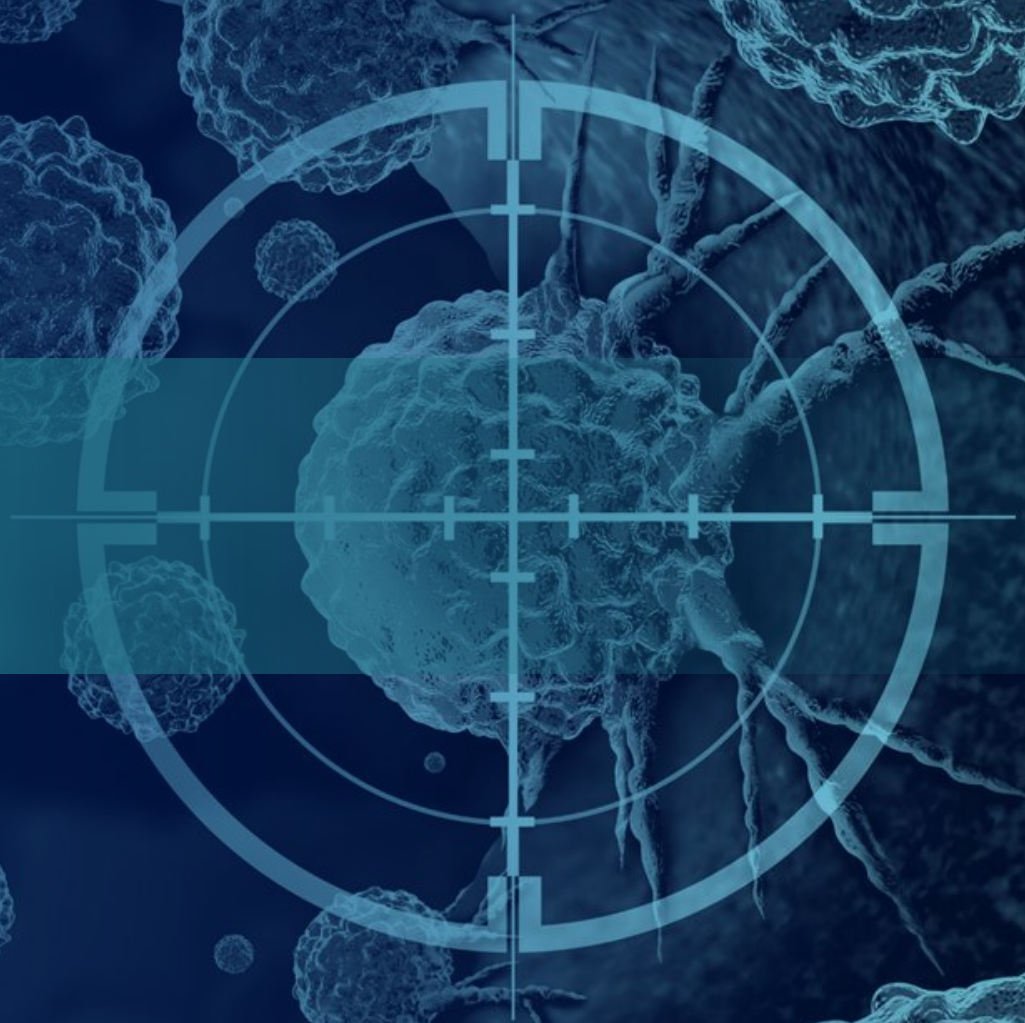
*Complete response (CR) recorded by the investigator based on RECIST version 1.1 criteria and a reduction in the size of the malignant lymph node target lesions to normal and the disappearance of all non-target lesions

1. Rao S, et al. A phase II study of retifanlimab (INCMGA00012) in patients with squamous carcinoma of the anal canal who have progressed following platinum-based chemotherapy (POD1UM-202). ESMO Open. 2022 Aug;7(4):100529.

GOBLET COHORT 4 SWIMMER PLOT - 20 EVALUABLE PATIENTS



Pancreatic Cancer Program



CONSISTENT SURVIVAL BENEFIT OBSERVED IN MULTIPLE 1L MPDAC STUDIES



Clinical results of pelareorep in first-line mPDAC studies

Company (Study)	Description (Patients)	1-Year Survival	2-Year Survival	Notes
Oncolytics (REO 017)	Pelareorep + Gemcitabine (34 patients)	45% vs. 22%	24% vs. 4%	DCR: 83% vs. 33% Single arm vs. gemcitabine benchmark
Oncolytics/NCI (NCI 8601)	Paclitaxel/Carboplatin + Pelareorep (36 patients) vs. Paclitaxel/Carboplatin (37 patients)	34% vs. 28%	20% vs. 6%	Randomized study vs. control arm (excluding crossover)
Oncolytics (REO 029 – Cohort 1)	Pelareorep + Gemcitabine/ Nab-Paclitaxel + atezolizumab (13 patients)	45% vs. 35%	N/A	ORR: 62% vs. 23% Single arm vs. gemcitabine/ nab-paclitaxel benchmark
Oncolytics (REO 029 – Cohort 5)	Pelareorep + modified FOLFIRINOX +/- atezolizumab (enrollment completed)	TBD	TBD	

2-YEAR SURVIVAL RATES IN 1L METASTATIC PDAC: COMPARISON TO LANDMARK STUDIES

	2-year survival
Pela-based therapy	21.9%
Comparator treatment arms (n=9)	9.2%

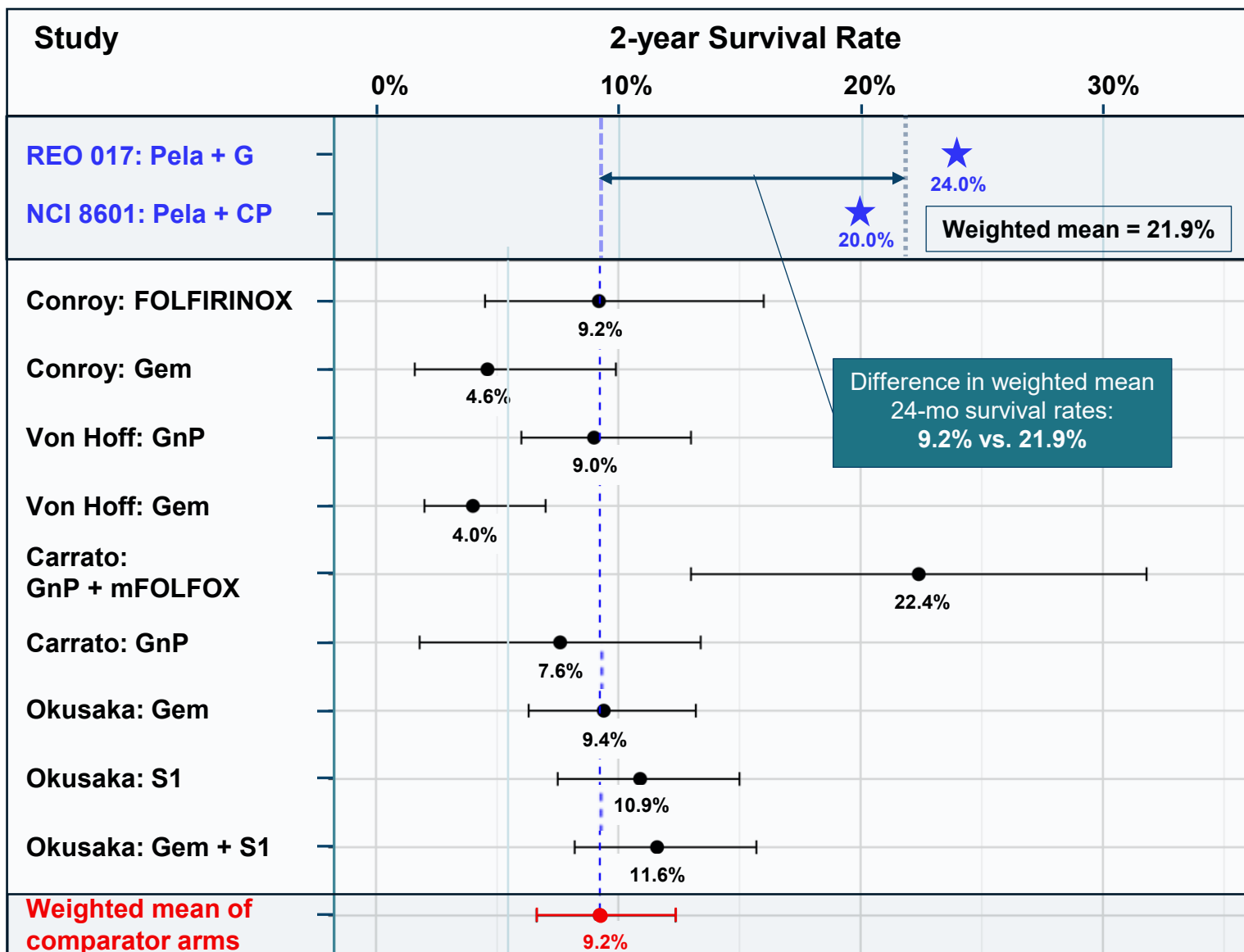
Legend

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

References

FOR ILLUSTRATIVE PURPOSES ONLY – not a head-to-head analysis. Differences exist between subject characteristics and trial designs, and caution should be exercised when comparing data across unrelated studies.

Carrato, et al., NEJM Evid. 2024
 Mahalingam, et al. Cancers. 2018
 Okusaka, et al., Res Clin Oncol. 2017
 Noonan, et al., Mol Ther. 2016
 Von Hoff, et al., NEJM, 2013
 Conroy, et al., NEJM, 2011



Pela-based therapy

Select comparator treatment arms

Difference in weighted mean 24-mo survival rates: 9.2% vs. 21.9%

A microscopic image of cells, likely bacteria or yeast, showing bright blue fluorescence. The cells are arranged in a somewhat circular pattern, with some appearing as individual spots and others as small clusters. The background is dark, making the glowing cells stand out.

Regulatory, Intellectual Property and Manufacturing

REGULATORY AND COMMERCIAL STRATEGY

Regulatory Strategy

- Proof of concept solidly established in three GI tumors
- Focus on most efficient regulatory path in high unmet medical need indications with large commercial potential
- Utilize multiple Fast Track Designations and biomarker driven studies
- Launched biomarker-driven 2L CRC study in RAS-mutated patient population
- ≥2L SCAC study expected to be a pivotal controlled study with a possible accelerated approval based on durable responses
- 1L PDAC study with chemo and CPI expected to focus on overall survival with two experimental arms
- Continue partnership discussions with CPI partners to advance development in multiple indications with clear registration paths

Indication	Design	Trial Activities (estimated)
2L CRC	Randomized; Sponsored	Enrolling patients
≥2L SCAC	Randomized; Partnered	2H 2026
1L PDAC	Randomized; Partnered	Ongoing

Commercial Strategy

- Position pelareorep as a platform in a product in three GI indications
- Expand combination strategy with CPI rechallenge study partners and combine with RAS inhibitors and CAR T therapies

IP PROFILE AND MANUFACTURING CHARACTERISTICS

Intellectual Property

- 137 patents issued worldwide
- New patents expected to extend manufacturing protection to 2044 and method of use protection into 2046
- Composition of matter protection through 2028
- Existing method of use and manufacturing protection through 2031
- Pending filings for proprietary manufacturing methods, certain immunotherapy uses, and synergies with T cell therapies and RAS-related treatments

Manufacturing

- Non-genetically modified Reovirus
- No special handling requirements
- High yield and low COGs
- Made in Carlsbad, California from products generally sourced in the USA
- Transferrable technology and procedures with clean IP ownership profile
- Easy to scale for large studies or commercial launch in multiple indications

INNOVATIVE LEADERSHIP TEAM WITH STRONG IMMUNO-ONCOLOGY, BUSINESS DEVELOPMENT, CLINICAL TRIAL AND FINANCE EXPERTISE



Transactional expert having led more than 50 deals, including \$2 billion Ambrx sale to JNJ in 2024

Jared Kelly
Chief Executive Officer
Board Member



Over 20 years of finance and accounting expertise focused on biotech and public company matters

Kirk Look, CA, MSJ
Chief Financial Officer



Nearly 30 years of drug development experience with an expertise in virology and oncology

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

Expertise in supply chain management, process performance qualification and manufacturing



Allison Hagerman, PEng, PMP, MBT
Chief Technology Officer

Over 30 years of expertise in oncology portfolio optimization and business development transactions



Andrew Aromando
Chief Business Officer

Over 20 years of clinical research and development experience at late-stage biotechs, particularly oncolytic virus companies



John McAdory
EVP, Strategy & Operations





Nasdaq: ONCY