

Oncolytics Biotech

PELAREOREP

a transformative dsRNA immunotherapy platform
for gastrointestinal tumors

September 2025

This presentation contains forward-looking statements within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended, and forward-looking information under applicable Canadian securities laws (such forward-looking statements and forward-looking information are collectively referred to herein as "forward-looking statements"). Forward-looking statements 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' 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 3. Key Information – D. Risk Factors" of our Annual Report on Form 20-F for the fiscal year ended December 31, 2024. 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.

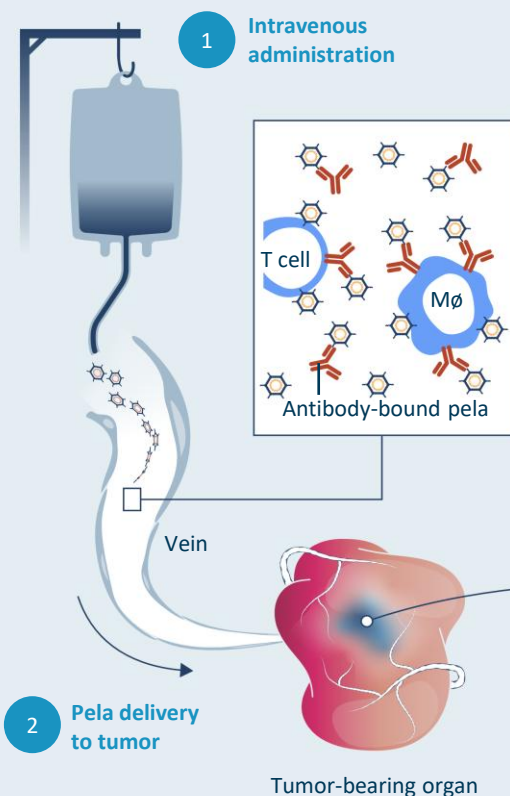
MISSION

We will leverage our proprietary product candidate, pelareorep (pela), a 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

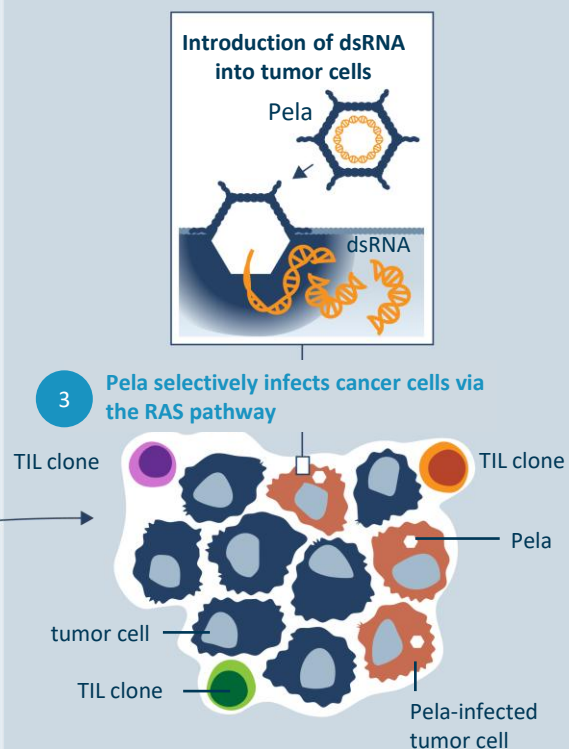
Pelareorep Treatment

Intravenous pela evades neutralization by associating with mononuclear cells in the blood and is delivered to the tumor.



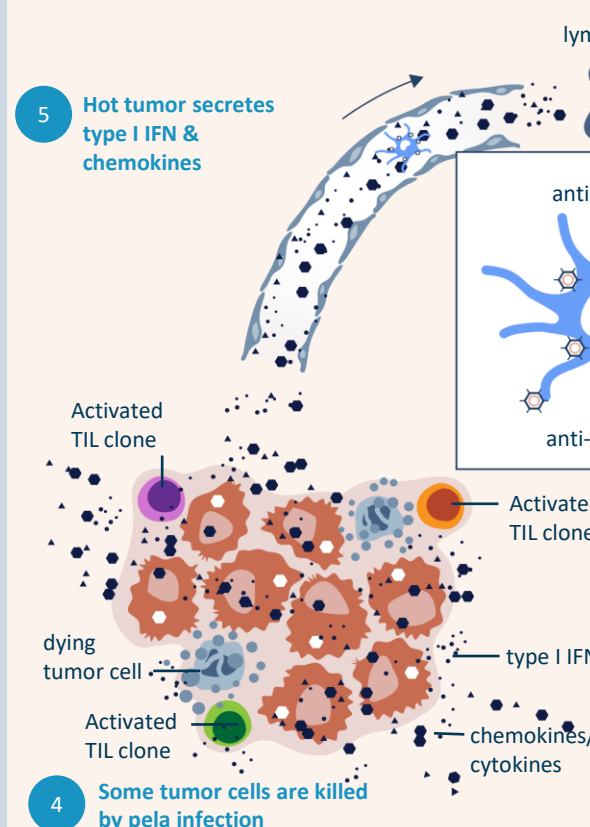
Cold Tumor

Pela selectively infects and replicates in tumor cells with RAS pathway mutations. Pela replication produces dsRNA in tumor cells.



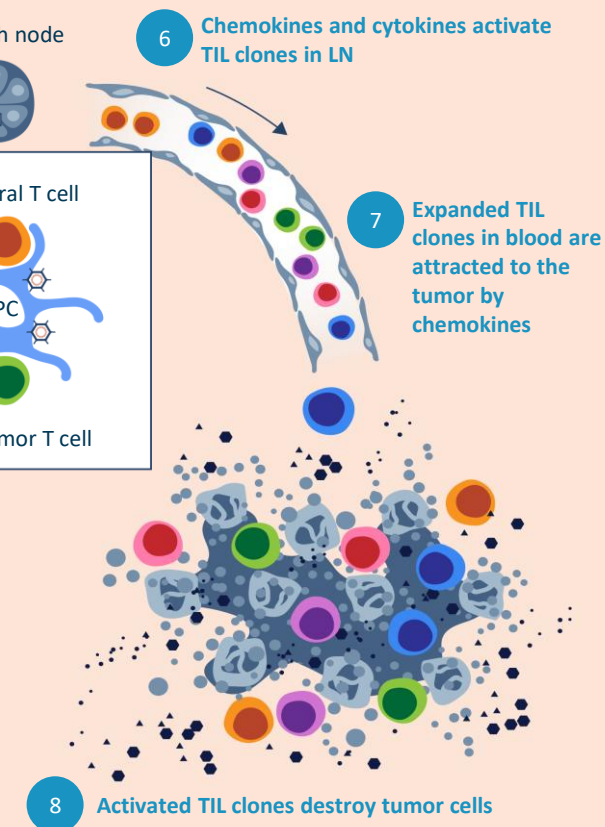
Hot Tumor

Pela infection kills some tumor cells by cell lysis and initiates an inflammatory response, through activation of chemokines and cytokines creating a "hot" tumor.



Tumor Under Attack

The pela-initiated inflammatory response results in activation and expansion of TIL clones that can attack and kill the tumor.



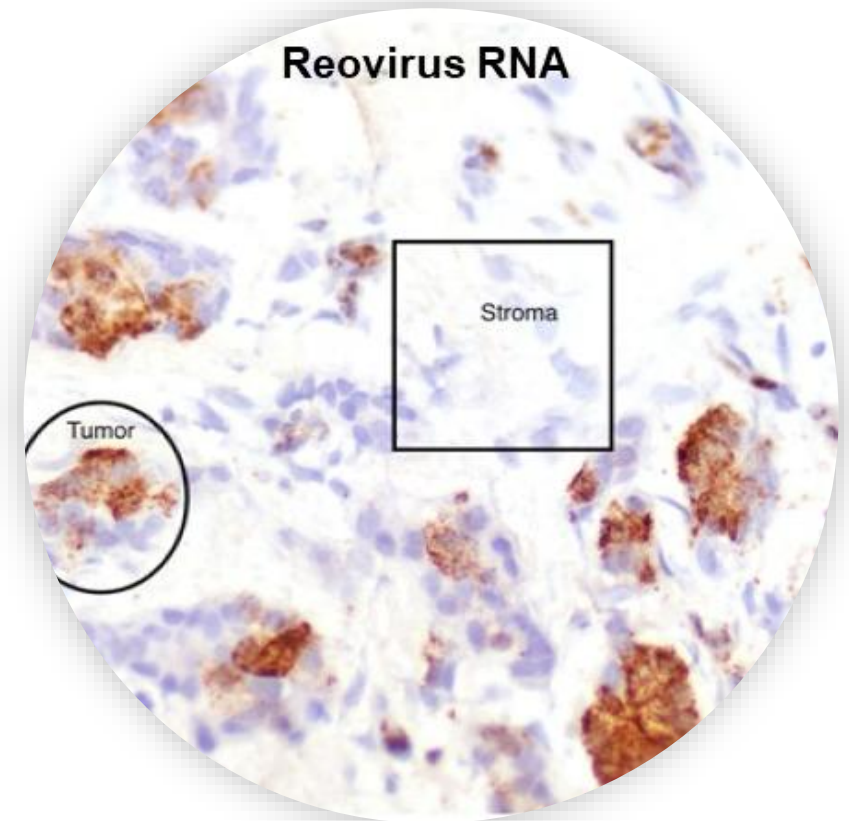
PELAREOREP REPLICATES IN ALMOST ALL TUMORS

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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

1. Berkeley, et al. Can Immunol Res. 2018
2. Adair, et al. Sci Transl Med. 2012
3. Mahalingam, et al. British J Can. 2023
4. Ilett, et al. J Ther 2009
5. Ilett, et al. Clin Cancer Res. 2011
6. Phillips, et al. Oncolytic Virother. 2018

BROAD CLINICAL EXPERIENCE AND WELL-UNDERSTOOD SAFETY PROFILE

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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 “safe and well-tolerated”

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



1L Metastatic Pancreatic Ductal Adenocarcinoma (mPDAC)

- ~ 500,000 patients globally¹
- ~ \$3 billion total addressable market with 15% CAGR to 2032²
- Chemotherapy standard of care with no approved immunotherapy
- 3% mPDAC 5-year survival rate³



2L Metastatic Colorectal Cancer (mCRC)

- ~ 1,900,000 patients globally⁴
- ~ \$12 billion total addressable market with 4% CAGR to 2030⁵
- KRAS mutant patient population high unmet medical need
- 15% mCRC 5-year survival rate⁶



2L unresectable Squamous Cell Anal Carcinoma (SCAC)

- ~ 30,000 patients globally⁷
- ~ \$1 billion total addressable market with 6% CAGR to 2032⁸
- Evolving standard of care with very few treatment options
- 35% mSCAC 5-year survival rate⁹

1. Kian-Huat Lim et al. Avutemetinib/defactinib and gemcitabine/nab-paclitaxel combination in first-line metastatic pancreatic ductal adenocarcinoma: Initial safety and efficacy of phase 1b/2 study (RAMP 205).. JCO 42, 4140-4140(2024). 2. <https://www.fortunebusinessinsights.com/pancreatic-cancer-treatment-market-101989>. 3. Wainberg, Zev A et al. NALIRIFOX versus nab-paclitaxel and gemcitabine in treatment-naïve patients with metastatic pancreatic ductal adenocarcinoma (NAPOLI 3): a randomised, open-label, phase 3 trial, The Lancet, Volume 402, Issue 10409, 1272 – 1281. 4. <https://www.wcrf.org/preventing-cancer/cancer-statistics/colorectal-cancer-statistics/>. 5. <https://media.market.us/colorectal-cancer-therapeutics-market-news/>. 6. <https://www.cancer.org/cancer/types/colon-rectal-cancer/detection-diagnosis-staging/survival-rates.html>. 7. Araradian C, Walsh M, Standage H, Tsikitis VL. Advances in the Management, Treatment, and Surveillance of Anal Squamous Cell Cancer. Cancers. 2025; 17(8):1289. 8. <https://www.marketresearchfuture.com/reports/anal-cancer-market-1530>. 9. <https://www.cancer.org/cancer/types/anal-cancer/detection-diagnosis-staging/survival-rates.html>

PELAREOREP CLINICAL DEVELOPMENT

CLINICAL POC ACROSS INDICATIONS GUIDES STRATEGIC SEQUENCING

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Indication	SOC benchmark	Pela Data	Delta
2L mCRC (KRAS mutant)	OS: 11.2 mo, PFS: 5.7 mo ¹	OS: 27 mo, PFS: 16.6 mo	~ 2-3x
≥2L SCAC	ORR: 11-24% ²⁻⁴	ORR: 33%	+ 10-20%
1L mPDAC	2-year OS rate: ~ 9% ⁵	2-year OS rate: ~ 22% ⁵	~ 2.5x

Development
sequencing,
short-term to
long-term

2L SCAC: fastest
registration path with
potential single-arm study
in rare disease with few
treatment options

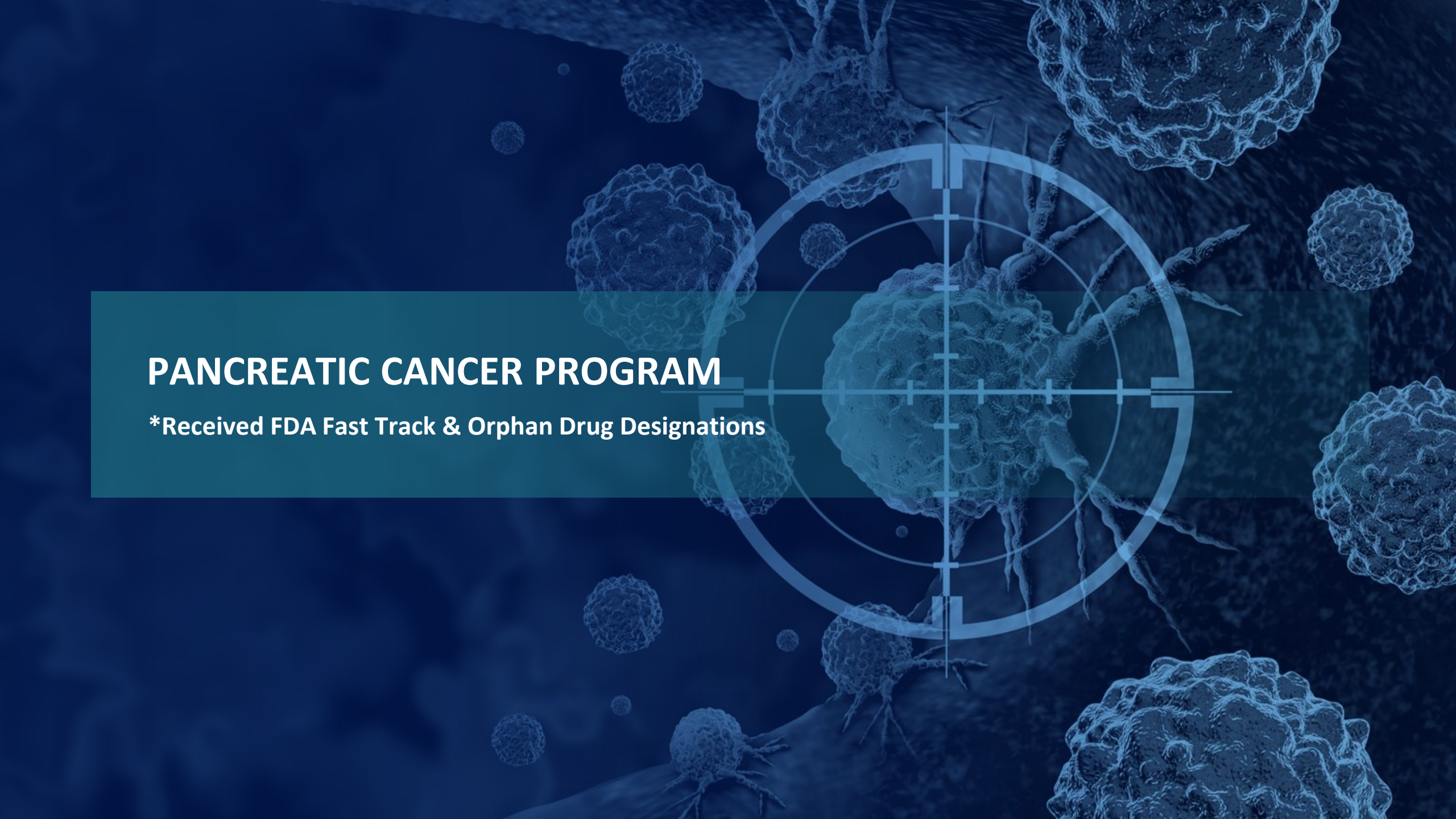
2L mCRC: biomarker-
driven IST in KRAS mutant
population to offset costs
while validating the
platform potential

1L mPDAC: could be only
registration-enabled study
with an immunotherapy 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; 1. Bennouna J. Lancet Oncol (14):29-37, 2013. 2. 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. 3. 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. 4. 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. 5. https://oncolyticsbiotech.com/press_releases/oncolytics-biotech-highlights-transformative-pelareorep-survival-data-in-multiple-tumors-and-commitment-to-registration-enabling-studies/.

Near-term rare disease approval path in SCAC and long-term platform expansion in CRC and PDAC

Program	Collaborator	Combination	Phase 1	Phase 2	Registration-Enabling Phase 3	Milestone
1L PDAC						
Pivotal Study	Partner Expected	pela + GnP +/- CPI				Expect to seek partnership for study
GOBLET cohort 5 Newly Diagnosed PDAC	 	pela + mFOL +/- atezo				US sites open 1H 2026; fully-enrolled 2H 2026
2L CRC						
KRAS-mutant Biomarker-focused IST	Rutgers University	chemo + bev +/- pela				IST to launch 1H 2026
2L SCAC						
GOBLET cohort 4 ≥2L Unresectable SCAC		pela + atezo				Data expected Q4 2025; US sites open 1H 2026
Pivotal Study	TBD	pela + CPI				Potential single-arm study launch Q3 2026

The background of the slide is a dark blue, textured surface. It features several 3D models of cancer cells, which are irregularly shaped and have a bumpy, textured surface. Some cells have thin, branching structures extending from them. Overlaid on the right side of the image is a white target symbol consisting of two concentric circles and a crosshair with tick marks along the horizontal and vertical axes. The text is located on the left side of the slide, within a semi-transparent dark blue rectangular area.

PANCREATIC CANCER PROGRAM

***Received FDA Fast Track & Orphan Drug Designations**

CONSISTENT SURVIVAL BENEFIT IN MULTIPLE 1L MPDAC STUDIES

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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 (enrolling; 60 patients expected)	TBD	TBD	

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

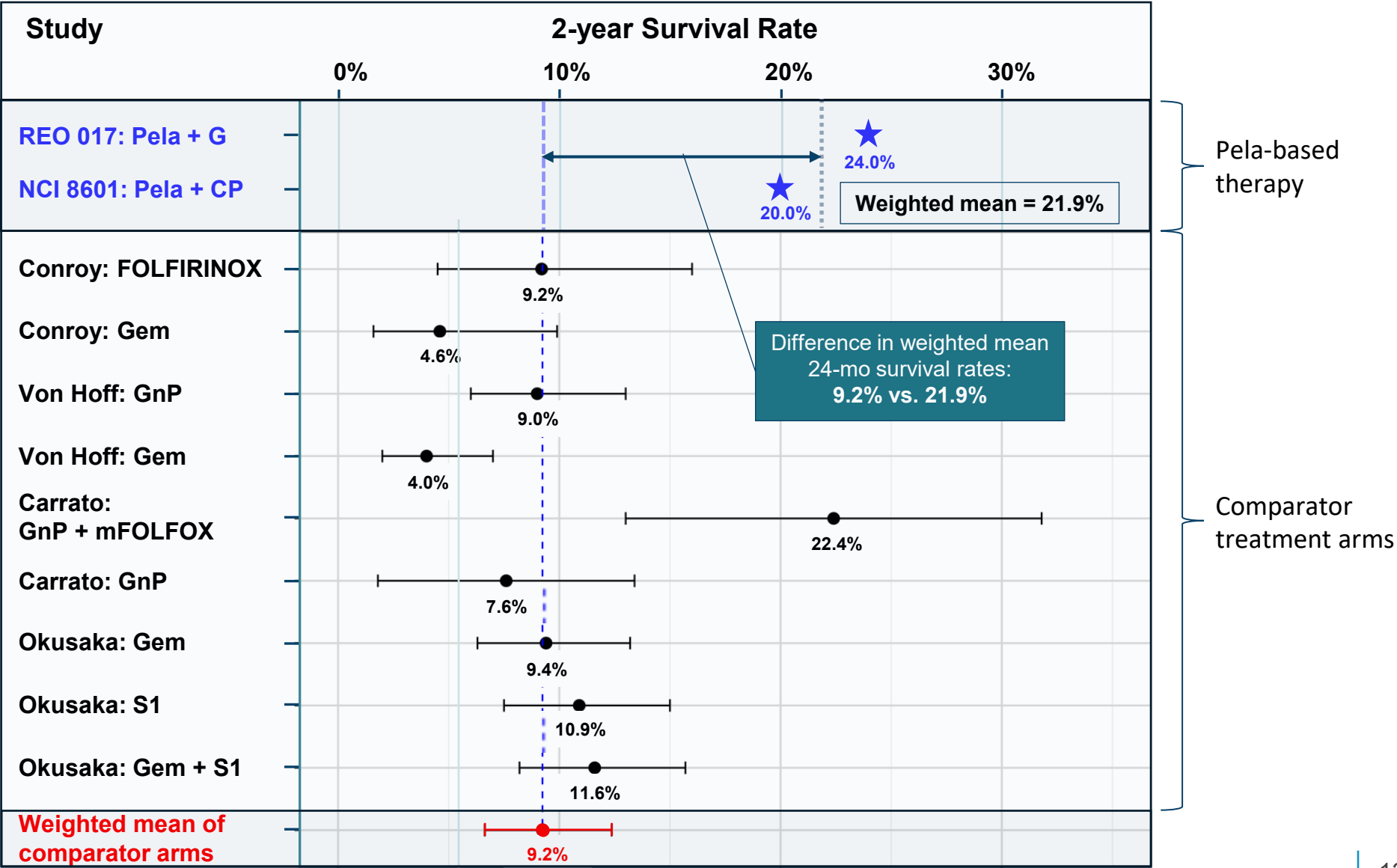
	2-year survival
Pela-based therapy	21.9%
Comparator treatment arms (n=9)	9.2%

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

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



The background of the slide is a dark blue, textured surface. It features several 3D models of cancer cells, which are irregularly shaped and have a bumpy, textured surface. Some cells are larger and more prominent, while others are smaller and scattered. A white, semi-transparent reticle is centered over one of the larger cells. The reticle consists of two concentric circles and a crosshair with small squares at the ends. The text "COLORECTAL CANCER PROGRAM" is written in white, bold, uppercase letters on a dark teal rectangular background that is positioned on the left side of the slide.

COLORECTAL CANCER PROGRAM

EFFICACY OF PELAREOREP IN COLORECTAL CANCER DEMONSTRATED ACROSS MULTIPLE STUDIES

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REO 022 study in 2L KRAS mutant mCRC results more than double historical control trials^{1, 2}:

- 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)



Data from GOBLET in 3L mCRC met predefined efficacy criteria and exceed historical results^{3, 4, 5, 6}:

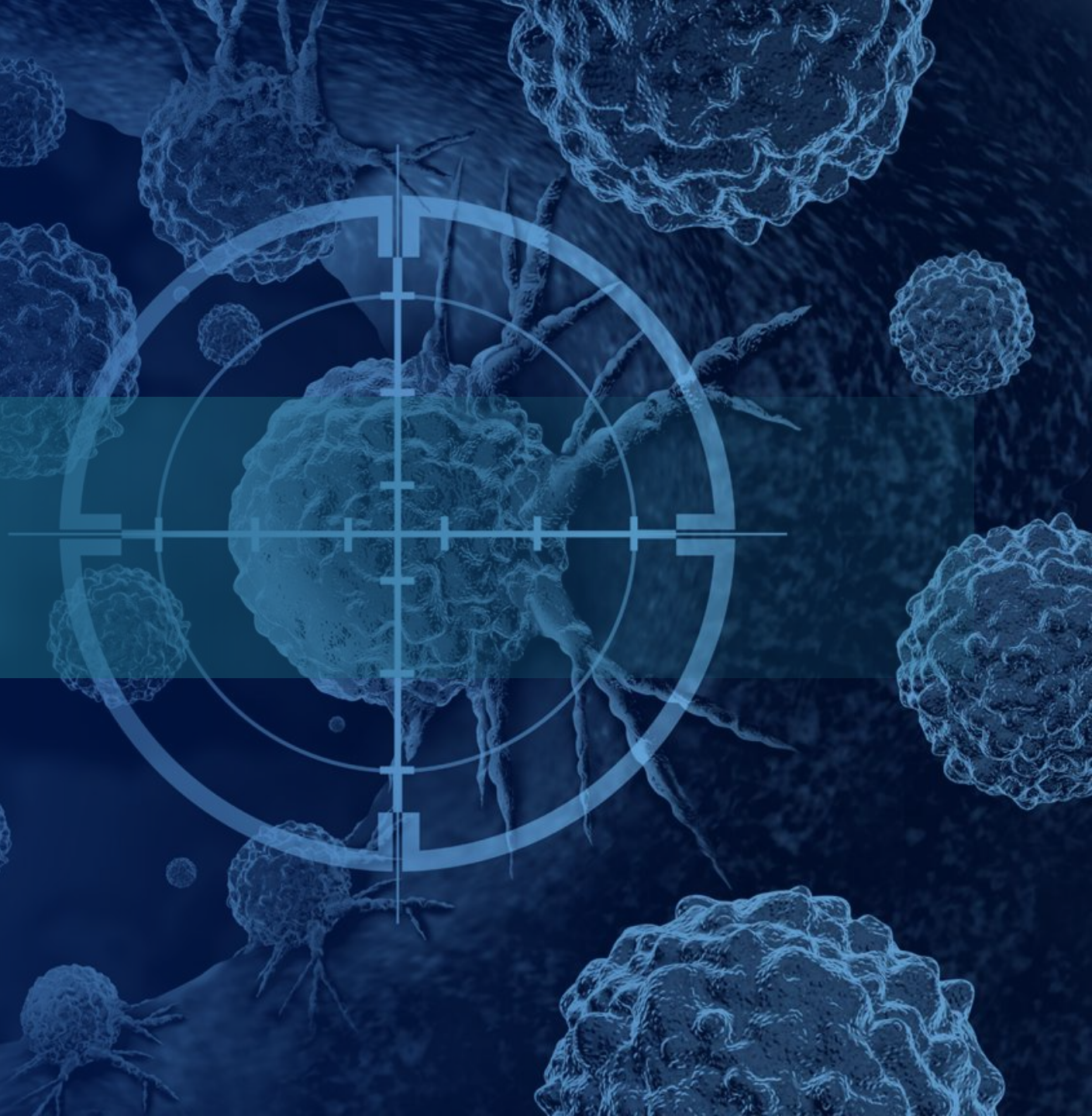
- 40% DCR and 33% 12-month survival rate
- PFS: 2.8 month and median OS: 8.0 months



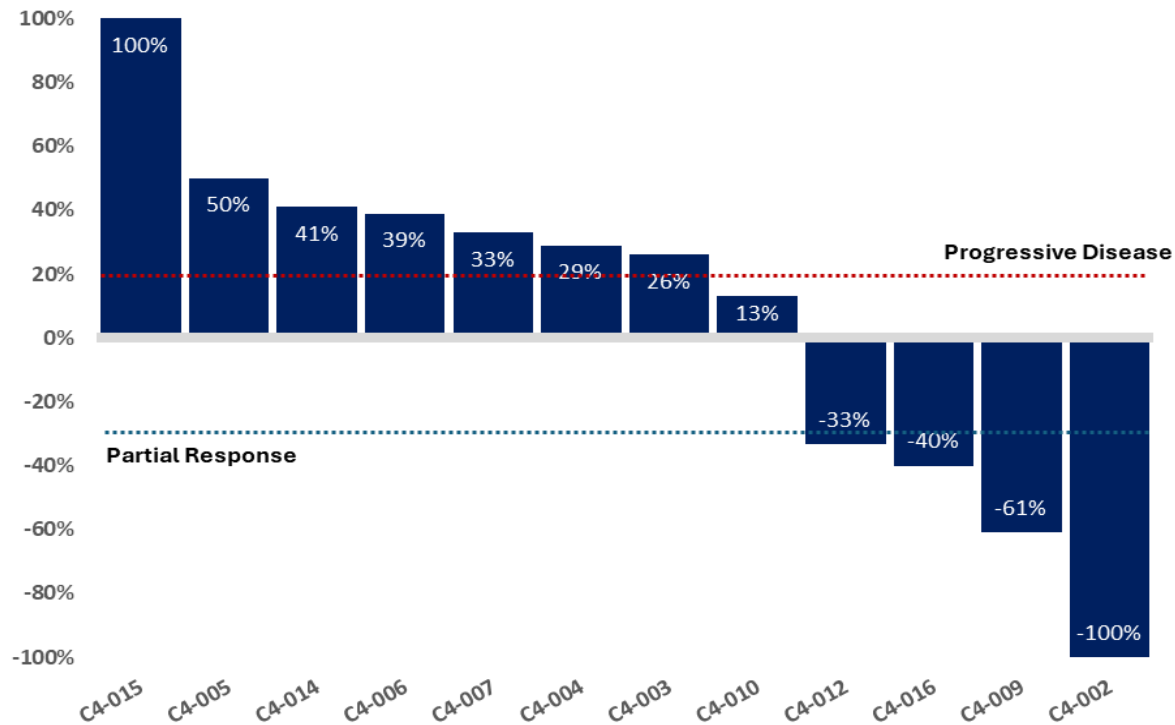
Translational data from REO 022 and REO 013 studies validate observed benefit^{1, 7, 8}:

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

ANAL CANCER PROGRAM



Strong efficacy signal with immunotherapy combination without chemo in difficult cancer



- Durable responses:
 - 1 CR (ongoing at 15 months)
 - 3 PR (one at week 8, week 16, and one ongoing at week 80)
- 33% ORR in 12 evaluable patients (presented at ASCO GI in January 2025)
- Steady enrollment in GOBLET cohort 4 with US sites expected to open by January 2026
- 23 evaluable and potentially evaluable patients as of September 2025 with safety and efficacy update expected in 2H 2025

REGULATORY, INTELLECTUAL PROPERTY AND MANUFACTURING

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 regulatory designations and biomarker driven studies to accelerate registration
- 1L PDAC study with chemo and CPI to focus on overall survival with two experimental arms
- 2L CRC study expected to be biomarker driven IST in KRAS mutant patient population
- 2L SCAC study expected to be a single arm study with an approval based on ORR
- Continue partnership discussions to advance development quickly and efficiently

Indication	Design	Trial Activities (estimated)
1L PDAC	Randomized; Partnered	2H 2025
2L CRC	Randomized; IST	1H 2026
2L SCAC	Single-Arm; Sponsored	1H 2026

Commercial Strategy

- Potential for approvals in three GI indications validates a platform in a product with pelareorep
- Partners interested in launching a platform immunotherapy in GI indications can enter at any point during the clinical development pathway

Intellectual Property

- 147 patents issued worldwide
- New patents expected to extend manufacturing and method of use protection into 2044
- Composition of matter protection through 2028
- Existing method of use and manufacturing protection through 2031
- Pending filings for proprietary manufacturing methods regarding virus harvest and extraction

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

Oncolytics Biotech



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

VP, Product Development

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



Andrew Aromando

Chief Business Officer

Over two decades of
clinical experience,
including at oncology
focused biotech



Amy Levin, RN, BSN

VP, Clinical Operations

