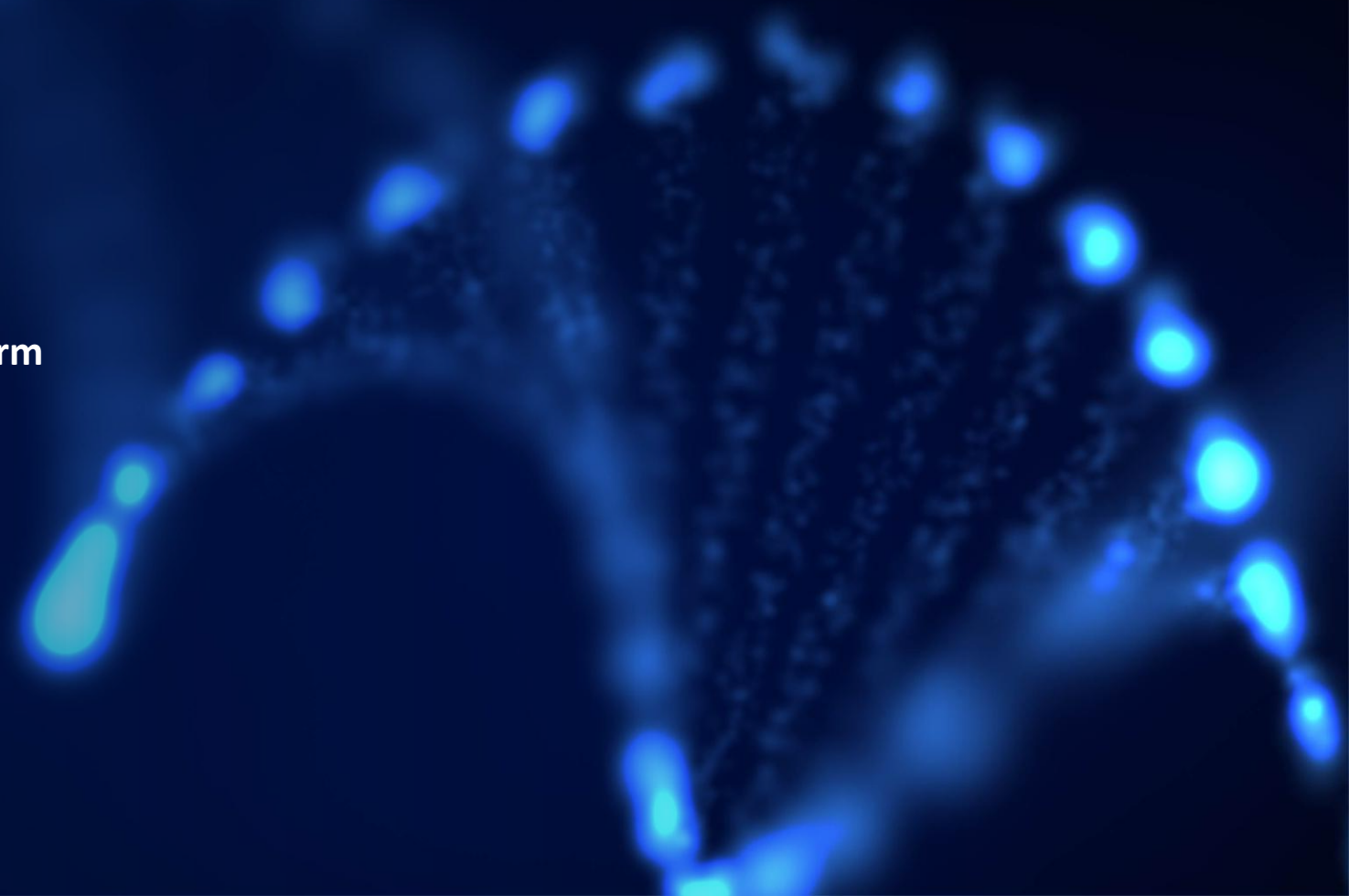
Oncolytics Biotech

PELAREOREP

a transformative dsRNA immunotherapy platform for gastrointestinal tumors



September 2025

Forward-Looking Statements

This presentation contains forward-looking statements within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended, and forward-looking information under applicable Canadian securities laws (such forward-looking statements and forward-looking information are collectively referred to herein as "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

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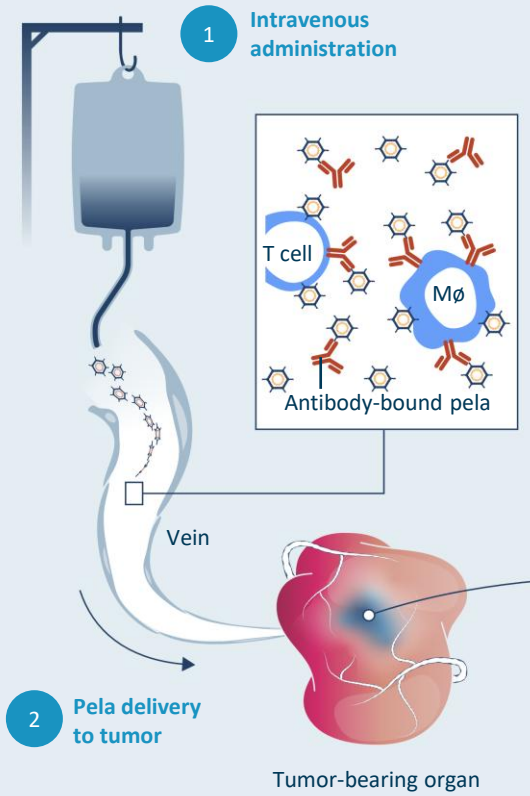
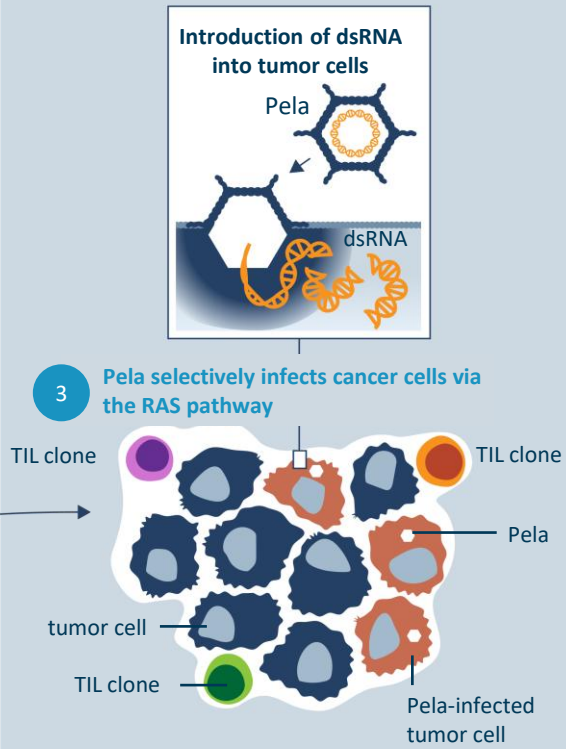
Pelareorep Treatment

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



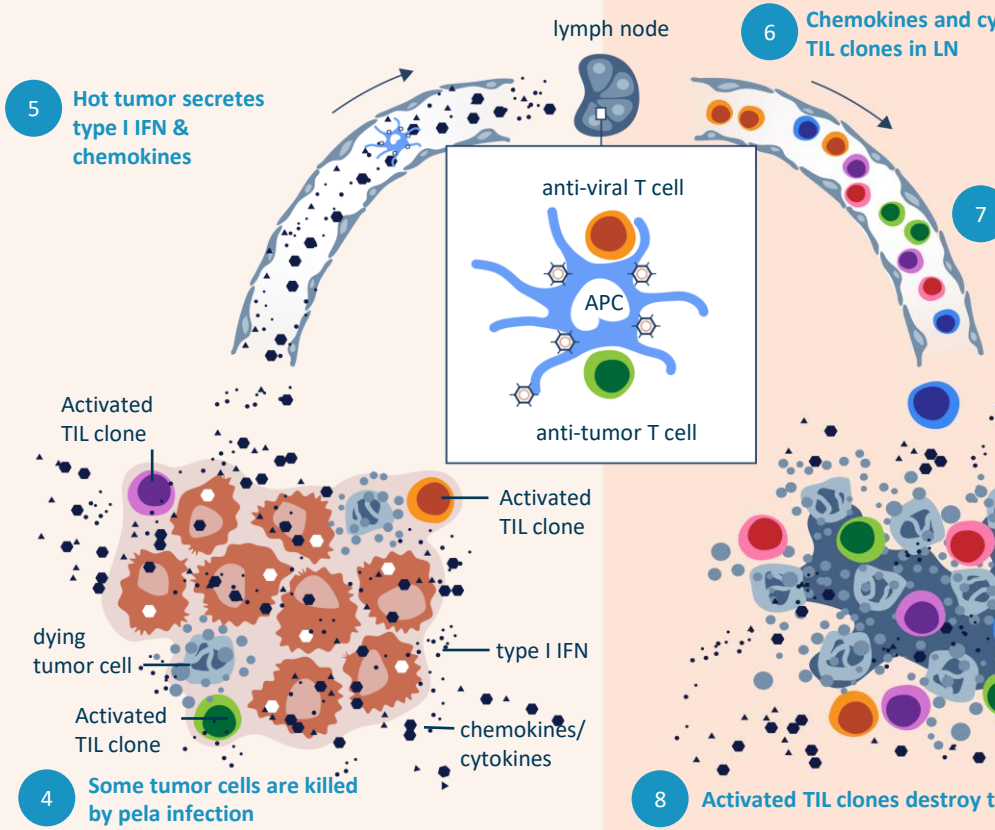
Cold Tumor

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.

Pela – pelareorep | dsRNA – double-stranded RNA | TIL clone – Unique tumor-infiltrating lymphocyte | APC – antigen presenting cell | LN – lymph node | Mø – monocyte

PELAREOREP REPLICATES IN ALMOST ALL TUMORS

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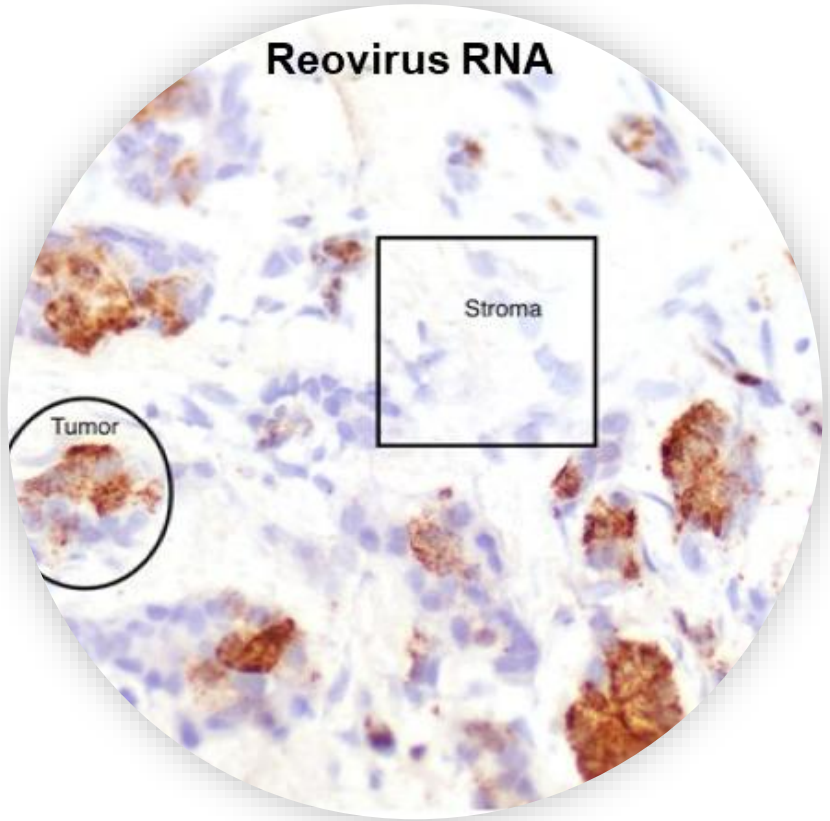
Pela is found in almost all on-treatment tumor biopsies		
Indication treated with IV Pela	# of biopsied tumors	# Pela-positive biopsies
Pancreatic ductal adenocarcinoma	**12**	**12**
Metastatic colorectal cancer	**12**	**11**
Head and neck cancer	**3**	**3**
Gliomas/metastatic brain tumors	**9**	**8**
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. . 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"

NCI: National Cancer Institute; Canadian Cancer Trials Group

Gutierrez, A.A., et al., Pooled data analysis of the safety and tolerability of intravenous pelareorep in combination with chemotherapy in 500 + cancer patients, Annals of Oncology, Volume 28, V422, September 2017

MARKET OPPORTUNITY WITHIN PELAREOREP'S INDICATIONS

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

1L Metastatic Pancreatic Ductal Adrenal Carcinoma (mPDAC)

- ~ 500,000 patients globally[1]
- ~ $3 billion total addressable market with 15% CAGR to 2032[2]
- Chemotherapy standard of care with no approved immunotherapy
- 3% mPDAC 5-year survival rate[3]

2L Metastatic Colorectal Cancer (mCRC)

- ~ 1,900,000 patients globally[4]
- ~ $12 billion total addressable market with 4% CAGR to 2030[5]
- KRAS mutant patient population high unmet medical need
- 15% mCRC 5-year survival rate[6]

2L unresectable Squamous Cell Anal Carcinoma (SCAC)

- ~ 30,000 patients globally[7]
- ~ $1 billion total addressable market with 6% CAGR to 2032[8]
- Evolving standard of care with very few treatment options
- 35% mSCAC 5-year survival rate[9]

1. Kian-Huat Lim et al. Avutometinib/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-naive 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

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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/.

CLINICAL DEVELOPMENT PIPELINE

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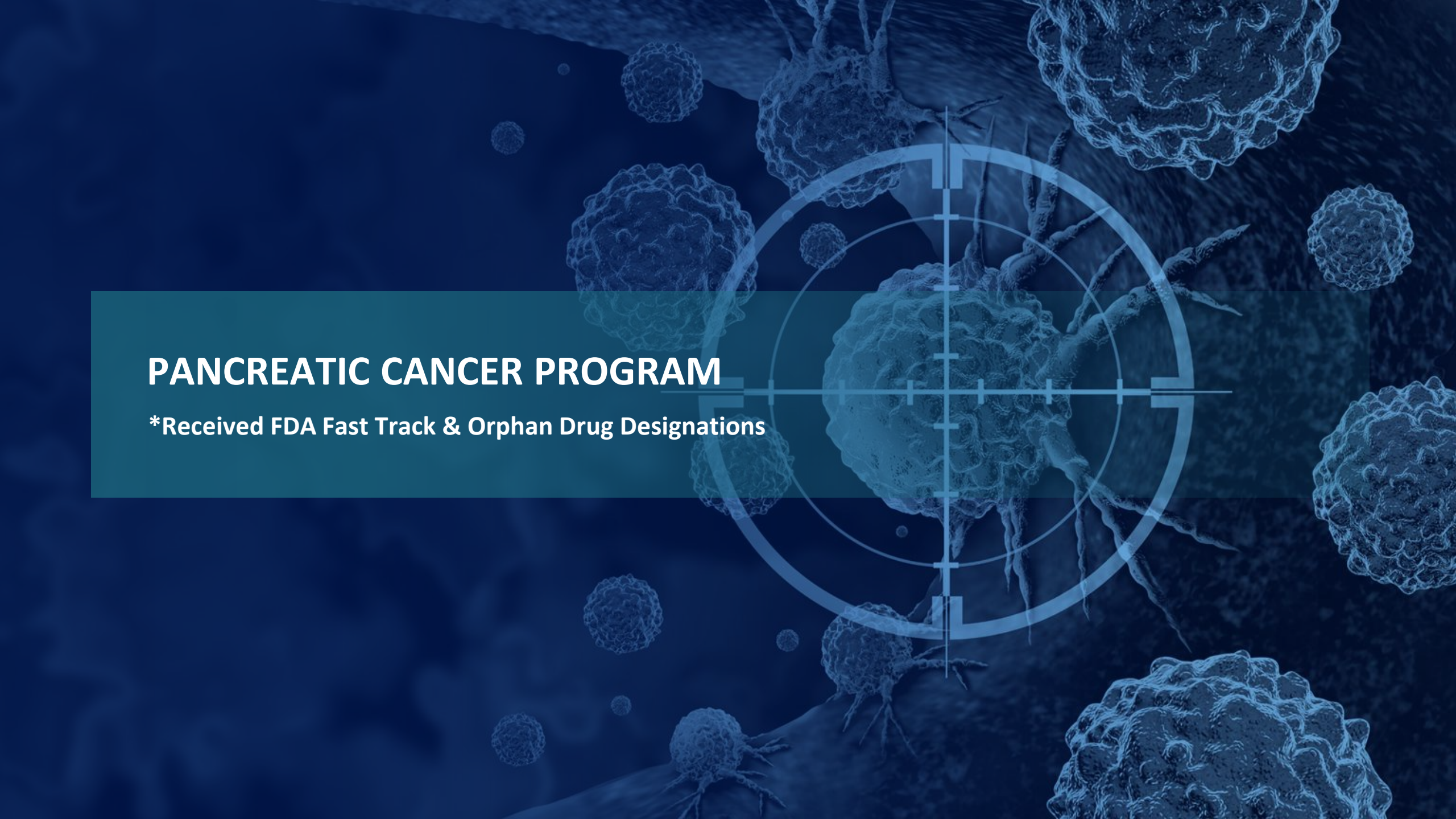
Near-term rare disease approval path in SCAC and long-term platform expansion in CRC and PDAC

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	Roche; PANCREATIC CANCER ACTION NETWORK	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	Roche	pela + atezo				Data expected Q4 2025; US sites open 1H 2026
Pivotal Study	TBD	pela + CPI				Potential single-arm study launch Q3 2026

PDAC: pancreatic ductal adenocarcinoma; CRC: colorectal cancer; SCAC: squamous cell carcinoma of the anal canal; pela: pelareorep; GnP: gemcitabine + nab-paclitaxel; CPI: checkpoint inhibitor; mFOL: modified FOLFIRINOX; atezo: atezolizumab; IST: investigator-sponsored trial; bev: bevacizumab; 1L: First-Line; 2L: Second-Line



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+FOLFIRINOX+/-Atezolizumab (enrolling; 60 patients expected)	TBD	TBD	

mPDAC: metastatic pancreatic ductal adenocarcinoma; DCR: disease control rate; ORR: overall response rate; NCI: National Cancer Institute

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

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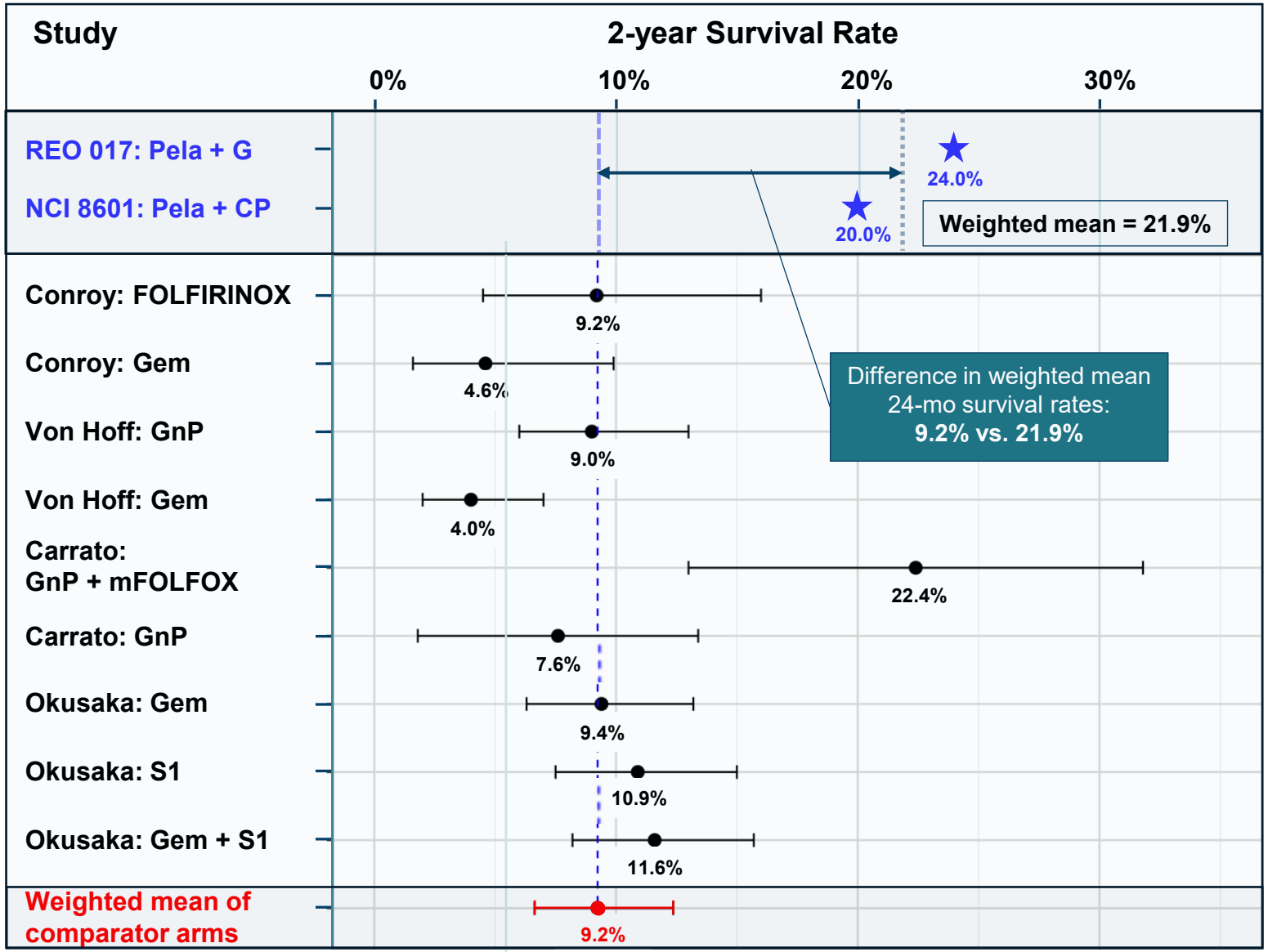
	2-year survival
Pela-based therapy	21.9%
Comparator treatment arms (n=9)	9.2%



Legend

Gem = gemcitabine
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

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

2L: second-line; mCRC: metastatic colorectal cancer; FOLFIRI: fluorouracil, leucovorin, and irinotecan; PFS: progression-free survival; OS: overall survival; 3L: third-line; DCR: disease control rate; TME: tumor microenvironment. 1. Goel, et al. Mol Cancer Ther (19): 1148-56, 2020; 2. Bennouna J. Lancet Oncol (14):29-37, 2013; 3. Ungerechts G et al. Pelareorep + atezolizumab and chemotherapy in third-line (3L) metastatic colorectal cancer (mCRC) patients – Interim results from the GOBLET study, ESMO Congress 2023; 4. Mayer et al. N Engl J Med 2015; 372:1909-1919; 5. Moriwaki et al. The Oncologist 2018; 23(1):7-15; 6. Bachet et al. ESMO Open. 2020 Jun;5(3):e000698.; 7. Adair RA, et al. Cell carriage, delivery, and selective replication of an oncolytic virus in tumor in patients. Sci Transl Med. 2012 Jun 13;4(138):138ra77; 8. El-Sherbiny YM, et al. Controlled infection with a therapeutic virus defines the activation kinetics of human natural killer cells in vivo. Clin Exp Immunol. 2015 Apr;180(1):98-107

ANAL CANCER PROGRAM

PELA + ATEZO NEARLY TRIPLES ORR IN ≥2L SCAC

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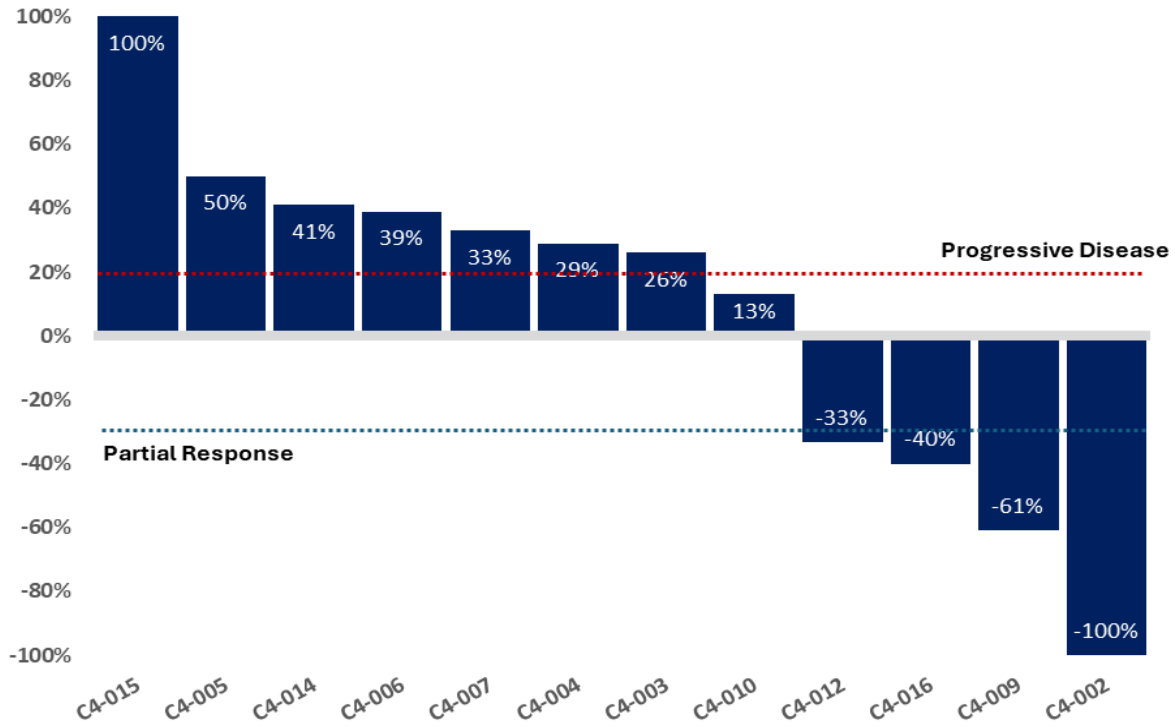
Strong efficacy signal with immunotherapy combination without chemo in difficult cancer



- 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

ORR: objective response rate; 2L: second-line; SCAC: squamous cell carcinoma of the anal canal; pela: pelareorep; atezo: atezolizumab; CR: complete response; PR: partial response

REGULATORY, INTELLECTUAL PROPERTY AND MANUFACTURING

REGULATORY CLARITY BASED ON EXTENSIVE CLINICAL DATA

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

PDAC: pancreatic ductal adenocarcinoma; CRC: colorectal cancer; SCAC: squamous cell carcinoma of the anal canal; CPI: checkpoint inhibitor; mFOL: modified FOLFIRINOX; atezo: atezolizumab; 1L: First-Line; 2L: Second-Line; ORR: objective response rate; PFS: progression-free survival; OS: overall survival: SOC: standard of care

IP PROFILE AND MANUFACTURING CHARACTERISTICS

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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

Patent numbers as of June 30, 2025

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 biotechs

Amy Levin, RN, BSN
VP, Clinical Operations