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Oncolytics Biotech Inc.

(ONCY-NASDAQ)

ONCY: Initiating Coverage of Oncolytics Biotech; A Focused Path to Unlocking the Potential of Pelareorep

Based on our probability-adjusted DCF model that takes into account potential future revenues for pelareorep in SCAC, mCRC, and mPDAC, ONCY is valued at $6.00 per share. This model is highly dependent upon the continued clinical success of pelareorep and will be adjusted accordingly based on

Current Price (04/07/26)	$0.96
Valuation	**$6.00**

OUTLOOK

We are initiating coverage of Oncolytics Biotech, Inc. (ONCY) with a valuation of $6.00. Oncolytics is entering a critical phase of its development following a strategic reset that has sharpened focus on two leading indications with clear biological rationale and potential regulatory pathways. Early clinical data across multiple tumor types support pelareorep's ability to enhance anti-tumor immune responses, particularly in immunotherapy-resistant settings. The company's near-term trajectory is likely to be defined by its upcoming FDA interaction in squamous cell anal carcinoma (SCAC), which could establish the feasibility of a single-arm registrational strategy. With a focused pipeline, defined catalysts, and increasing validation of the oncolytic virus class, Oncolytics offers a compelling risk/reward profile. We see the next several months as particularly important in shaping both development strategy and investor perception.

SUMMARY DATA

52-Week High	**$1.42**
52-Week Low	**$0.33**
One-Year Return (%)	**93.92**
Beta	**0.98**
Average Daily Volume (sh)	**735,093**
Shares Outstanding (mil)	**116**
Market Capitalization ($mil)	**$112**
Short Interest Ratio (days)	**1**
Institutional Ownership (%)	**7**
Insider Ownership (%)	**0**
Annual Cash Dividend	**$0.00**
Dividend Yield (%)	**0.00**
5-Yr. Historical Growth Rates	
Sales (%)	**N/A**
Earnings Per Share (%)	**N/A**
Dividend (%)	**N/A**
P/E using TTM EPS	**N/A**
P/E using 2026 Estimate	**-4.0**
P/E using 2027 Estimate	**-4.5**

Risk Level	**Above Avg.**
Type of Stock	**Small-Value**
Industry	**Med-Biomed/Gene**

ZACKS ESTIMATES

Revenue
(in millions of $)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2025	0.0 A	0.0 A	0.0 A	0.0 A	0.0 A
2026	0.0 E	0.0 E	0.0 E	0.0 E	0.0 E
2027					0.0 E
2028					0.0 E

Earnings per Share

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2025	-$0.08 A	-$0.07 A	-$0.14 A	-$0.04 A	-$0.30 A
2026	-$0.06 E	-$0.06 E	-$0.06 E	-$0.06 E	-$0.24 E
2027					-$0.23 E
2028					-$0.21 E

WHAT'S NEW

We are initiating coverage of Oncolytics Biotech with a valuation of $6.00. Oncolytics is a clinical-stage immuno-oncology company advancing pelareorep, a systemically delivered oncolytic virus that selectively replicates in cancer cells and enhances anti-tumor immune responses. Pelareorep has been evaluated across multiple tumor types and combination regimens and has demonstrated the ability to induce tumor-directed immune activation, including increased T-cell infiltration and upregulation of immune checkpoint pathways, supporting its positioning as a potential immune priming agent in combination with checkpoint inhibitors.

Following a strategic reset under new management in June 2025, the company has narrowed its focus to GI indications, specifically second-line metastatic colorectal cancer (mCRC) and second-line or later unresectable squamous cell anal carcinoma (SCAC). This transition reflects a deliberate shift toward indications with both strong biological rationale and clearly defined regulatory pathways, as well as a capital-efficient development strategy centered on combination therapy with established immuno-oncology agents. In particular, both mCRC and SCAC represent tumor types where checkpoint inhibitors alone have demonstrated limited efficacy, creating an opportunity for therapies capable of enhancing tumor immunogenicity and restoring sensitivity to immunotherapy.

A key element of this strategy is Oncolytics' engagement with the FDA to pursue a single-arm pivotal study in SCAC, a rare disease setting with high unmet need and no clearly established standard of care in later lines of therapy. This approach is expected to be informed by the regulatory precedent potentially established by Replimune Group, whose oncolytic immunotherapy RP1 is currently under FDA review (PDUFA date: April 10, 2026) based on data from a single-arm study in anti–PD-1–refractory melanoma. A favorable outcome for RP1 would represent a significant validation not only of the oncolytic virus class, but also of a capital-efficient regulatory pathway based on response-driven endpoints in high unmet need populations.

Oncolytics is scheduled to meet with the FDA in mid-April, positioning the company to potentially incorporate regulatory feedback informed by the outcome of the RP1 review into its own development strategy. We view this sequence of events as a critical near-term inflection point, with the potential to meaningfully impact both the design and timeline of Oncolytics' SCAC program, as well as broader investor perception of the oncolytic virus space.

- **Regulatory precedent may unlock an approval pathway in SCAC.** A potential approval of RP1 based on single-arm data could establish a clear framework for ONCY to pursue a similar strategy in a rare, high unmet need indication, significantly reducing development timelines and capital requirement.
- **Pelareorep is a differentiated immunotherapy backbone with multi-modal activity.** The therapy combines selective viral replication, immunogenic cell death, and systemic immune activation, positioning it as a potential sensitizer to checkpoint inhibitors in immunologically "cold" tumors such as MSS colorectal cancer and SCAC.
- **Focused development strategy improves probability of success.** The company has transitioned from a diffuse pipeline to a targeted approach centered on two indications with strong mechanistic rationale and defined regulatory pathways, enabling more efficient allocation of capital and resources.
- **Attractive risk/reward driven by near-term catalysts.** The April 2026 FDA meeting, the outcome of the RP1 PDUFA decision, and continued clinical updates from ongoing studies represent key drivers of potential revaluation in the near to intermediate term.

INVESTMENT THESIS

Oncolytics Biotech, Inc. (ONCY) is a clinical-stage immuno-oncology company developing pelareorep, an oncolytic viral therapy that is derived from an unmodified type 3 Dearing (T3D) reovirus that selectively replicates in tumor cells while showing single-agent activity in a wide variety of tumors. Following a change in management in mid-2025, the company has reset the development pathway for pelareorep and will focus on gastrointestinal (GI) cancers, with an initial focus on squamous cell anal carcinoma (SCAC) followed by long-term platform expansion into metastatic colorectal cancer (CRC) and metastatic pancreatic ductal adenocarcinoma (mPDAC).

The company has an upcoming mid-April meeting with the U.S. Food and Drug Administration (FDA) in which it will seek to clarify the development pathway for pelareorep in SCAC, including the potential for a single-arm pivotal study. Support for that pathway could be supplied by the approval of RP1 in anti-PD-1 resistant melanoma, which has a PDUFA date of Apr. 10, 2026. Alignment with the FDA on that pathway could lead to a BLA filing within two years.

Program	Collaborator	Combination	Phase 1	Phase 2	Registration-Enabling Phase 3	Anticipated Milestone
2L CRC						
RAS-mutated Biomarker-focused study	TBD	chemo + bev +/- pela				Launch 1H 2026
≥2L SCAC						
GOBLET cohort 4 ≥2L Unresectable SCAC	Roche	pela + atezo				Final data readout expected 1H 2026
Pivotal Study	TBD	pela + CPI				Potential single-arm study launch Q3 2026
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				Initial data readout expected 2H 2026

Source: Oncolytics Biotech, Inc.

Regulatory Precedent Based on Replimune's RP1

Strong support for the Oncolytics investment thesis is derived from the potential for a regulatory precedent to be established by Replimune Group, whose lead oncolytic immunotherapy RP1 is currently under review by the U.S. FDA with a PDUFA date of April 10, 2026. Notably, the Biologics License Application (BLA) for RP1 in anti–PD-1–failed melanoma is supported primarily by data from the single-arm IGNYTE study, positioning it as a potential test case for the acceptability of non-randomized registrational strategies in the oncolytic virus space.

The IGNYTE trial enrolled patients with advanced melanoma who had experienced confirmed progression on prior anti–PD-1 therapy, including a substantial proportion with prior exposure to both PD-1 and CTLA-4 inhibitors (NCT03767348). This represents a heavily pretreated population with limited therapeutic options and historically poor outcomes, making it an appropriate setting for regulatory flexibility. The study evaluated RP1 in combination with nivolumab, with objective response rate (ORR) and duration of response (DOR) as key endpoints.

Updated data from IGNYTE demonstrated a 33.6% ORR across the full study population, including a 16.4% complete response (CR) rate (Replimune Group). Responses were observed across multiple clinically relevant subgroups, including patients with primary resistance to prior checkpoint inhibitors.

Importantly, responses were not only frequent but also durable, with a median duration of response of approximately 24.8 months, suggesting meaningful and sustained clinical benefit in a refractory setting. These results compare favorably to historical benchmarks in anti–PD-1–refractory melanoma, where response rates to subsequent therapies are typically in the low double digits and often lack durability (Zimmer *et al*., 2017).

From a regulatory perspective, several features of the IGNYTE dataset align with established criteria for accelerated approval based on single-arm studies. First, the study targets a population with high unmet medical need, where no clearly effective standard of care exists following failure of checkpoint inhibitors. Second, the observed response rates substantially exceed historical controls, providing a basis for inferring clinical benefit. Third, the durability of response (approaching two years in median duration) supports the likelihood that these responses are clinically meaningful rather than transient.

The FDA has repeatedly granted accelerated approvals in oncology based on objective response rate and duration of response from single-arm studies in high unmet need settings, including checkpoint inhibitors, CAR-T therapies, and targeted agents (e.g., pembrolizumab, tisagenlecleucel, larotrectinib). In this context, RP1 represents a logical extension of this regulatory framework into the oncolytic virus class.

Importantly, the IGNYTE study also provides evidence that oncolytic immunotherapy can overcome resistance to prior checkpoint blockade. Patients who had demonstrated progression on anti–PD-1 therapy achieved markedly higher response rates when treated with RP1 in combination with nivolumab compared to their immediate prior line of therapy, supporting the concept that oncolytic viruses can restore immune sensitivity in otherwise refractory disease. This mechanistic validation further strengthens the case for regulatory acceptance, as it demonstrates a clear and differentiated therapeutic effect rather than incremental benefit.

A potential approval of RP1 based on IGNYTE would therefore represent a category-defining regulatory event, establishing that (i) oncolytic viruses can achieve clinically meaningful outcomes in checkpoint-refractory populations, and (ii) single-arm studies utilizing ORR and DOR endpoints may be sufficient to support registration in appropriately selected indications.

Implications for Oncolytics

Oncolytics' development strategy in SCAC is explicitly designed to align with the regulatory pathway being tested by RP1. SCAC is a rare malignancy, often associated with HPV infection, with limited treatment options in the second-line or later unresectable setting. While immune checkpoint inhibitors, including retifanlimab, have been approved in both first-line (in combination with chemotherapy) and subsequent-line settings, the overall treatment paradigm remains poorly defined. In particular, the clinical utility of sequential PD-1 inhibition following progression on prior checkpoint-based therapy is uncertain, and real-world treatment patterns remain heterogeneous. Outcomes following progression on first-line chemotherapy remain poor, reinforcing a setting of high unmet need that is broadly analogous to anti-PD-1-refractory melanoma.

The company has indicated that its upcoming FDA meeting (scheduled for mid-April 2026) will focus on the potential to pursue a single-arm pivotal study in SCAC, leveraging objective response rate and durability as primary endpoints. Critically, the timing of this meeting, just days after the RP1 PDUFA date, suggests a deliberate strategy to incorporate regulatory feedback informed by the outcome of the RP1 review.

If RP1 is approved on the basis of single-arm data, Oncolytics is well positioned to argue that a similar evidentiary standard should be applied to pelareorep in SCAC. The parallels between the two programs are notable:

- Both involve oncolytic immunotherapies combined with checkpoint inhibitors

- Both target checkpoint-refractory or limited-option populations
- Both rely on ORR and DOR as primary efficacy endpoints
- Both address indications with high unmet need and limited standard therapies

While differences in tumor biology and prevalence will be considered by regulators, the fundamental logic underlying accelerated approval (e.g., robust and durable responses in a high-need population can justify early approval) would apply equally in SCAC if supported by compelling data.

From an investment perspective, this creates a clear, event-driven pathway for Oncolytics. A positive regulatory outcome for RP1 would not only validate the oncolytic virus class but also materially increase the probability that Oncolytics can pursue a capital-efficient, single-arm development pathway in SCAC. Conversely, a negative outcome would raise the evidentiary bar and likely necessitate a more traditional randomized trial design, increasing both development timelines and capital requirements.

Pelareorep

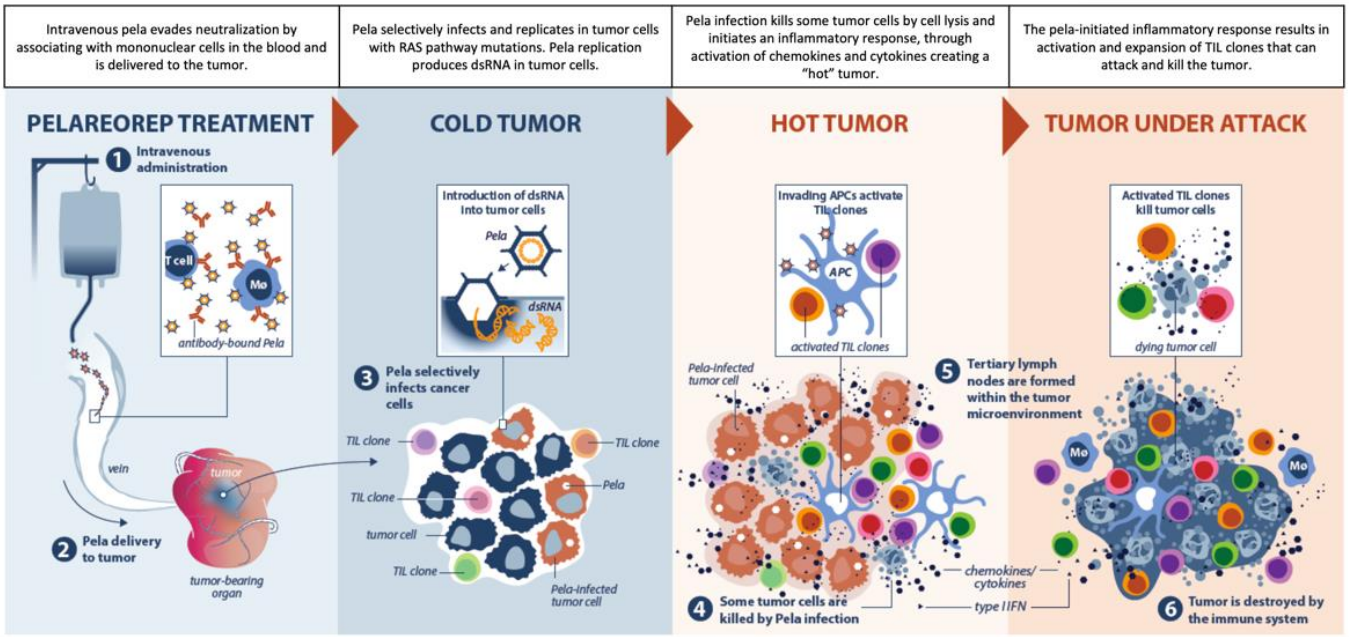
Pelareorep is a proprietary formulation of a naturally occurring, non-enveloped double-stranded RNA (dsRNA) virus derived from Reovirus, a ubiquitous pathogen that is typically asymptomatic in humans but possesses intrinsic oncolytic properties (Carew *et al*., 2013). Unlike many engineered viral platforms, pelareorep is a wild-type virus whose tumor selectivity arises from its ability to exploit oncogenic signaling–mediated defects in antiviral defense pathways (Phillips *et al*., 2018). This biological selectivity has been extensively characterized in preclinical and translational studies and forms the basis for its development as a systemically administered immuno-oncology agent.

At the core of pelareorep's tumor selectivity is its interaction with the cellular antiviral protein kinase pathway, particularly Protein Kinase R, a dsRNA-activated kinase that serves as a key mediator of host defense against viral infection (Strong *et al*., 1998). In normal cells, reovirus infection leads to activation of PKR, phosphorylation of eIF2α, and subsequent inhibition of protein translation, effectively aborting viral replication. However, in malignant cells with activated RAS signaling, a hallmark of many solid tumors, PKR activation is suppressed, allowing efficient viral protein synthesis and replication (Coffey *et al*., 1998). This phenomenon, first described in seminal studies by Coffey ***et al***. and Strong ***et al***., has since been validated across multiple tumor models and is now recognized as a central mechanism by which reovirus selectively replicates in cancer cells while sparing normal tissue (Maitra *et al*., 2012).

Following entry into permissive tumor cells, pelareorep undergoes active replication, leading to cell death through a combination of direct cytopathic effects (Roner *et al*., 2007), apoptosis (Tyler *et al*., 1998), and necrotic pathways (Berger *et al*., 2013). Importantly, this process is not immunologically silent; rather, it induces a form of immunogenic cell death (ICD) characterized by the release of tumor-associated antigens (TAAs), damage-associated molecular patterns (DAMPs), and viral pathogen-associated molecular patterns (PAMPs), including dsRNA intermediates. These signals serve as potent activators of antigen-presenting cells, particularly dendritic cells, which internalize tumor antigens and initiate adaptive immune responses. This dual function of direct tumor lysis coupled with antigen release positions pelareorep as both a cytotoxic agent and an *in situ* 'cancer vaccine'.

In parallel, pelareorep infection activates innate immune sensing pathways through recognition of viral RNA by pattern recognition receptors such as Toll-like receptor 3 (TLR3), RIG-I, and MDA5 (Levy *et al*., 2011; Stuart *et al*., 2018). Engagement of these receptors leads to downstream activation of interferon regulatory factors and production of type I interferons (IFN-α and IFN-β), as well as a broad array of pro-inflammatory cytokines and chemokines. This innate immune activation promotes recruitment and activation of natural killer (NK) cells, macrophages, and dendritic cells, creating a highly inflamed tumor microenvironment conducive to immune-mediated tumor clearance. While interferon signaling can theoretically limit viral replication, preclinical and clinical evidence suggests that the net effect is enhancement of anti-tumor immunity, particularly when pelareorep is used in combination with immune checkpoint inhibitors (Rajani *et al*., 2016).

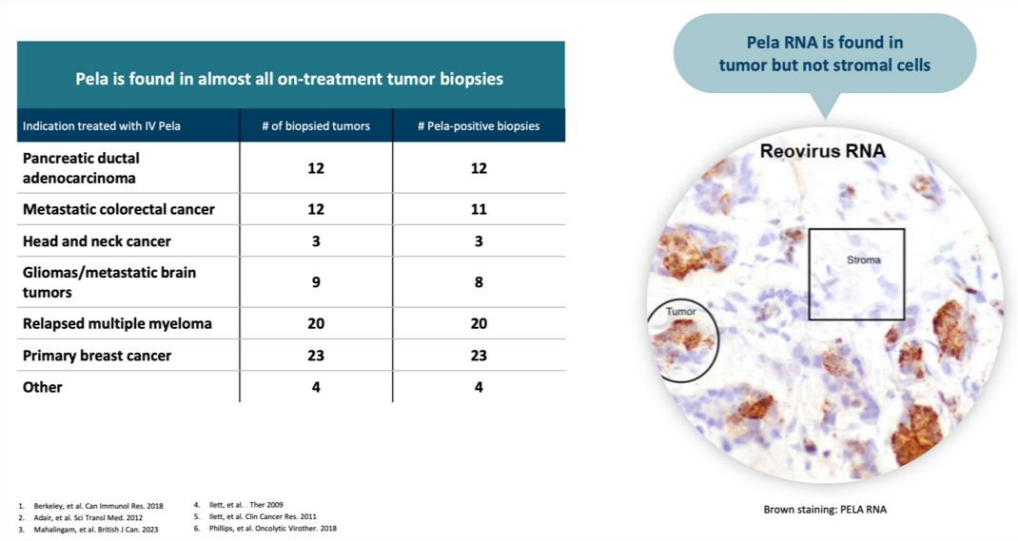
An important downstream consequence of pelareorep-mediated tumor lysis and innate immune activation is the priming of adaptive anti-tumor immunity (Gujar *et al.*, 2014). Dendritic cells that have internalized tumor antigens migrate to regional lymph nodes, where they present antigenic peptides via major histocompatibility complex (MHC) molecules to naïve T cells, leading to activation and clonal expansion of tumor-specific CD8+ cytotoxic T lymphocytes. These effector T cells can then traffic systemically and mediate killing of both infected and uninfected tumor cells, enabling a broader anti-tumor response beyond the initial sites of viral replication. This immune-mediated systemic anti-tumor response has been observed in both preclinical models and clinical studies of oncolytic viruses, including pelareorep (Müller *et al.*, 2020). An overview of the proposed mechanism of action of pelareorep is given below.



Source: Oncolytics Biotech, Inc.

Importantly, pelareorep has demonstrated the ability to modulate the tumor microenvironment in ways that are particularly relevant to overcoming resistance to immune checkpoint blockade. Many solid tumors, including microsatellite stable (MSS) CRC, are characterized by low baseline T-cell infiltration and limited responsiveness to therapies targeting the PD-1/PD-L1 pathway (Ganesh *et al.*, 2019). Pelareorep infection has been shown to increase infiltration of CD8+ T cells, upregulate expression of interferon-stimulated genes, and induce PD-L1 expression on tumor cells, effectively converting immunologically "cold" tumors into "hot," inflamed tumors that are more susceptible to checkpoint inhibition (Mahalingam *et al.*, 2018). This provides a strong mechanistic rationale for combining pelareorep with PD-1/PD-L1 inhibitors, as the virus addresses upstream limitations in antigen presentation and T-cell priming while checkpoint inhibitors release downstream inhibitory signals on activated T cells.

A key differentiating feature of pelareorep relative to many other oncolytic virus platforms is its ability to be administered intravenously, enabling systemic delivery to both primary and metastatic tumor sites. Following infusion, pelareorep has been shown to associate with circulating immune cells, including monocytes and dendritic cells, which can serve as carriers to facilitate delivery to tumor tissue and potentially shield the virus from rapid neutralization by pre-existing antibodies (Adair *et al.*, 2012). The following figure provides an overview of the clinical studies that have demonstrated that intravenously administered pelareorep can be detected within tumor biopsies, but not in stromal tissue, confirming successful trafficking to tumor sites and supporting its utility in metastatic disease settings. This systemic delivery capability is particularly relevant in gastrointestinal malignancies such as colorectal cancer, where metastatic lesions are often distributed across organs such as the liver and lungs and may not be amenable to intratumoral injection approaches.



Source: Oncolytics Biotech, Inc.

In summary, pelareorep is a wide-ranging immunotherapy that incorporates direct oncolysis with robust activation of both innate and adaptive immunity. By selectively replicating in RAS-activated tumor cells, inducing immunogenic cell death, and reshaping the tumor microenvironment to enhance T-cell infiltration and checkpoint sensitivity, pelareorep functions as an immune primer capable of overcoming key mechanisms of resistance in poorly immunogenic tumors. These mechanistic attributes are particularly well aligned with the biological characteristics of mCRC, SCAC, and mPDAC, providing a strong scientific foundation for Oncolytics' focused clinical development strategy.

Metastatic Colorectal Cancer

Metastatic colorectal cancer (mCRC) remains a major global health burden and a leading cause of cancer-related mortality, with approximately 150,000 new cases diagnosed annually in the United States and a substantial proportion of patients ultimately developing metastatic disease (Siegel *et al.*, 2024). Despite incremental advances in systemic therapy, outcomes for patients with advanced disease remain poor, particularly in the second-line and later settings, where median overall survival from the initiation of second-line therapy is approximately 14-15 months in real-world population (Hess *et al.*, 2019).

The treatment landscape for mCRC is highly stratified by molecular characteristics, most notably microsatellite instability (MSI) status. A small subset of patients (~5%) harbor mismatch repair–deficient (dMMR) or microsatellite instability–high (MSI-H) tumors, which are characterized by high tumor mutational burden and robust immune infiltration. These tumors respond favorably to immune checkpoint inhibitors targeting the PD-1/PD-L1 pathway, with durable responses observed in a meaningful proportion of patients (Le *et al.*, 2015). However, the vast majority of mCRC patients (~95%) have microsatellite stable (MSS) disease, which is characterized by low neoantigen burden, minimal baseline T-cell infiltration, and a profoundly immunosuppressive tumor microenvironment. In this population, checkpoint inhibitors have demonstrated little to no clinical activity as monotherapy, representing a major unmet need in oncology (Ganesh *et al.*, 2019).

Standard treatment for MSS mCRC in the second-line setting typically involves cytotoxic chemotherapy regimens such as FOLFIRI or FOLFOX in combination with targeted agents, including anti-VEGF therapies (e.g., bevacizumab) or anti-EGFR antibodies in RAS wild-type disease. While these approaches can provide incremental benefit, response rates are modest and durability is limited, and few therapies meaningfully alter the underlying immunobiology of the disease. As such, there is significant interest in strategies capable of sensitizing MSS tumors to immunotherapy, particularly by increasing tumor immunogenicity and promoting T-cell infiltration.

Recent therapeutic development in mCRC reflects this shift toward immune modulation and combination strategies, although progress has been uneven. Newly approved agents such as Fruquintinib have demonstrated incremental survival benefit in the refractory setting, but do not address the fundamental challenge of immune resistance. Similarly, targeted therapies such as KRAS G12C inhibitors (e.g., Sotorasib in combination with EGFR blockade) have shown encouraging activity, but are limited to small molecularly defined subpopulations representing a minority of patients.

Consequently, a growing portion of the development pipeline is focused on novel immunotherapy combinations designed to overcome resistance in MSS disease, including dual checkpoint blockade strategies, myeloid-targeting agents, and personalized approaches such as neoantigen-directed vaccines. Despite these efforts, many approaches rely on downstream immune modulation and have yet to consistently demonstrate the ability to generate robust and durable responses in "cold" tumors.

Within this evolving landscape, therapies capable of directly initiating anti-tumor immune responses may offer a differentiated approach. Oncolytic viruses such as pelareorep are uniquely positioned in this regard, as they combine direct tumor cell lysis with activation of innate and adaptive immunity, potentially addressing the central limitation of MSS colorectal cancer. By increasing antigen presentation, promoting T-cell infiltration, and upregulating checkpoint pathways, pelareorep may function as an upstream immune primer that enhances responsiveness to checkpoint inhibition and other immunotherapies.

The following table includes a selection of approved and emerging therapies in mCRC to help visualize pelareorep's positioning within the broader treatment landscape, with a focus on mechanism of action, target population, and stage of development.

Company	Therapy	Mechanism	Target Population	Stage	Key Takeaway
Amgen	Sotorasib + Panitumumab	KRAS G12C inhibitor + EGFR	KRAS G12C mCRC (~3–4%)	Approved / Late-stage	Highly targeted; limited to small subset
Takeda	Fruquintinib	VEGFR TKI	Refractory mCRC	Approved	Modest survival benefit; not immunologic
BioNTech	Individualized mRNA vaccines	Neoantigen vaccine	MSS + adjuvant CRC	Phase II	Personalized IO; early-stage, complex
Agenus	Botensilimab + Balstilimab	CTLA-4 + PD-1	MSS mCRC	Phase II	Dual IO approach; early efficacy signals
Roche	Tiragolumab combos	TIGIT + PD-L1	Broad CRC	Phase II/III	Checkpoint expansion; mixed results
Merck	Pembrolizumab combos	PD-1 combinations	MSS mCRC	Phase II/III	Backbone IO; limited MSS efficacy

Sources: Company documents; Zacks SCR

Pelareorep in mCRC

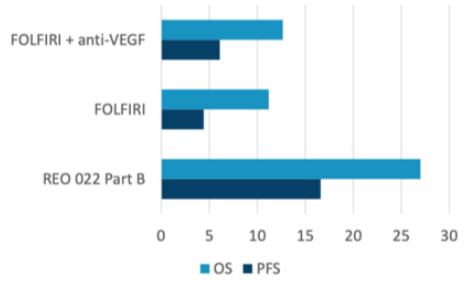
Pelareorep is mechanistically well suited to address the challenges of mCRC treatment. As discussed previously, reovirus selectively replicates in tumor cells with activated RAS signaling, which is altered in approximately 40–50% of colorectal cancers. This results in tumor cell lysis and release of tumor-associated antigens. More importantly, pelareorep has been shown to induce a pro-inflammatory tumor microenvironment characterized by increased CD8+ T-cell infiltration, activation of interferon signaling pathways, and upregulation of PD-L1 expression. This provides a strong mechanistic rationale for combining pelareorep with checkpoint inhibitors, as the virus addresses upstream limitations in antigen presentation and immune activation while checkpoint blockade releases downstream inhibitory signals on T cells.

Clinical evaluation of pelareorep in mCRC has been conducted directly in combination with standard-of-care second-line therapy, most notably irinotecan-based chemotherapy (FOLFIRI) plus bevacizumab (Goel *et al.*, 2020). In a multi-center phase I study in patients with KRAS-mutant, oxaliplatin-refractory mCRC, pelareorep was administered intravenously in combination with FOLFIRI and bevacizumab, demonstrating both biological activity and encouraging efficacy signals. At the recommended phase II

dose, the combination produced a median progression-free survival (PFS) of 16.6 months and a median overall survival (OS) of 27.0 months, substantially exceeding historical expectations for second-line therapy in this population, as shown in the following figure. Importantly, correlative analyses confirmed intratumoral viral replication, dendritic cell maturation, and activation of cytotoxic T cells, providing direct translational evidence of pelareorep's proposed immune-mediated mechanism of action.

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

Design	Phase 1 dose escalation
Population	15 Part B patients; Metastatic or advanced KRAS-mutated colorectal cancer; Refractory to oxaliplatin
Treatment	pelareorep + FOLFIRI + bevacizumab
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%

Source: Oncolytics Biotech, Inc.

These results compare favorably to established benchmarks for FOLFIRI plus bevacizumab in the second-line setting. Across prospective trials and real-world studies, objective response rates for FOLFIRI-based regimens in previously treated mCRC are typically in the range of ~6–11%, with median PFS of approximately 5–7 months and median OS of approximately 11–13 months (Bennouna *et al.*, 2013; Iwamoto *et al.*, 2015). While cross-trial comparisons should be interpreted with caution, the magnitude of improvement observed with pelareorep, particularly in a molecularly defined, poor-prognosis KRAS-mutant population, suggests the potential for meaningful clinical benefit beyond cytotoxic therapy alone.

Mechanistically, these findings are consistent with preclinical and translational data demonstrating that pelareorep can enhance chemotherapy efficacy through both direct oncolysis and immune modulation. The observed activation of dendritic cells followed by expansion of cytotoxic T-cell populations in treated patients provides evidence that pelareorep is not simply additive to chemotherapy, but may fundamentally alter the tumor microenvironment and restore anti-tumor immune activity in a setting otherwise characterized by immune resistance. Taken together, the combination of strong biological rationale and early clinical signal supports continued development of pelareorep as a novel adjunct to standard-of-care therapy in second-line mCRC, particularly in KRAS-mutant and microsatellite stable disease where therapeutic options remain limited.

From a commercial perspective, mCRC represents a large and well-established market opportunity, with substantial unmet need in the MSS population. Given the limited efficacy of existing therapies and the absence of effective immunotherapy options for the majority of patients, even modest improvements in response rates or durability could translate into meaningful clinical and economic value. As such, pelareorep's ability to modulate the tumor microenvironment and enhance responsiveness to immunotherapy positions it as a potentially differentiated approach in a highly competitive but inadequately served indication.

To follow up on the REO 022 results, Oncolytics recently initiated a Phase 2 trial in second-line, RAS-mutated, microsatellite-stable mCRC patients. The patients will be randomized into one of two groups:

bevacizumab and FOLFIRI or pelareorep, bevacizumab, and FOLFIRI. The study is powered for statistical significance with each arm expected to enroll 30 patients. The primary endpoint of the trial is objective response rate (ORR), with PFS, OS, safety, and biomarker analysis as other endpoints. Preliminary data could be available by the end of 2026.

Squamous Cell Anal Carcinoma

Squamous cell anal carcinoma (SCAC) is a relatively rare malignancy, with approximately 9,000–10,000 new cases diagnosed annually in the United States, but its incidence has been steadily increasing over the past several decades (Siegel *et al*., 2024). The disease is strongly associated with infection by high-risk human papillomavirus (HPV), particularly HPV-16, which drives oncogenesis through expression of viral oncoproteins that promote immune evasion and cellular transformation (Lin *et al*., 2018).

While early-stage SCAC can often be treated effectively with chemoradiation, outcomes for patients with unresectable or metastatic disease are significantly worse. First-line treatment has historically consisted of platinum-based chemotherapy (e.g., carboplatin plus paclitaxel), which can achieve response rates in the range of 60-80%, although a substantial proportion of patients ultimately experience disease progression (Gondal *et al*., 2023). More recently, the treatment landscape has begun to evolve with the incorporation of immune checkpoint inhibitors, including the approval of retifanlimab in combination with chemotherapy in the first-line setting. Despite this progress, outcomes following progression remain poor, and treatment patterns In the second-line and later setting are not well defined, with no universally adopted standard of care.

Immune checkpoint inhibitors have been evaluated in SCAC given its viral etiology and presumed immunogenicity. Agents targeting the PD-1/PD-L1 pathway, including nivolumab and pembrolizumab, have demonstrated modest activity in previously treated patients, with objective response rates generally in the range of 11-24% and a mean duration of response of 9-10 months (Morris *et al*., 2017; Marabelle *et al*., 2022; Rao *et al*., 2022). While retifanlimab is also approved as a monotherapy in the post-platinum setting, the clinical benefit of sequential PD-1 inhibition following progression on prior checkpoint-based therapy remains uncertain, and real-world utilization appears variable. As a result, the majority of patients derive limited benefit from currently available therapies, highlighting the need for combination strategies capable of enhancing immune activation and overcoming resistance mechanisms.

Recent clinical development efforts in SCAC have increasingly focused on combination immunotherapy approaches designed to augment checkpoint inhibitor activity. These include combinations of checkpoint inhibitors with chemotherapy, radiation, and other immune-modulating agents, as well as HPV-targeted therapeutic vaccines aimed at generating tumor-specific immune responses. Despite growing interest, the pipeline remains relatively limited compared to more common malignancies, with few late-stage assets and a lack of clearly differentiated therapeutic approaches.

Within this context, the treatment landscape in SCAC remains underserved but strategically attractive, characterized by high unmet medical need, regulatory flexibility in rare diseases, and the potential for approval pathways based on response-driven endpoints. Importantly, many emerging approaches seek to enhance immune activation indirectly, and few therapies directly address the upstream limitations in antigen presentation and immune priming that may underlie resistance to checkpoint inhibition.

The following table includes a selection of approved and emerging therapies in SCAC to help visualize pelareorep's positioning within the broader treatment landscape, with a focus on mechanism of action, target population, and stage of development.

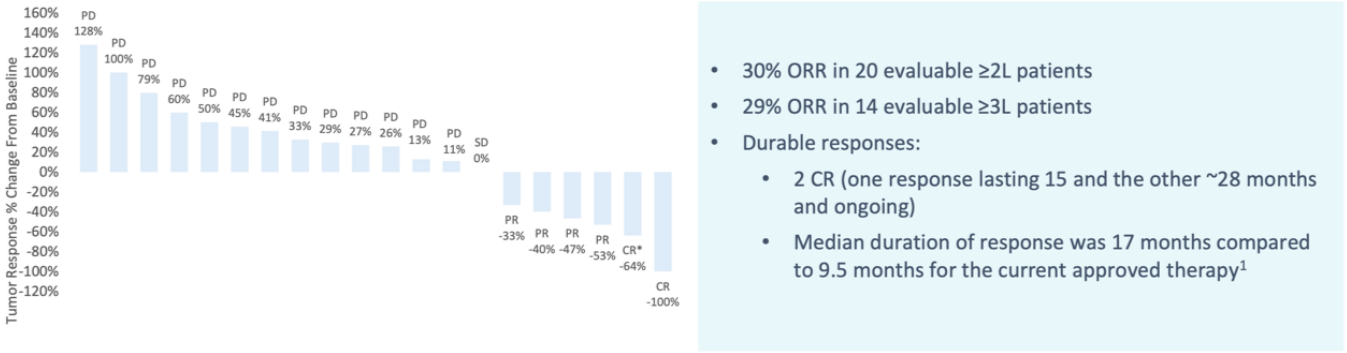
Company	Therapy	Mechanism	Setting	Stage	Key Takeaway
Merck	Pembrolizumab	PD-1 inhibitor	2L+ SCAC	Approved	ORR ~10–20%; limited durability
Bristol Myers Squibb	Nivolumab	PD-1 inhibitor	2L+ SCAC	Approved	Similar modest activity
Incyte	Retifanlimab	PD-1 inhibitor	1L + chemo; 2L+ mono	Approved	Expands IO use; sequencing post-PD-1 remains unclear
Roche	Atezolizumab combos	PD-L1 inhibitor	SCAC	Early-stage	Combination strategies emerging
Inovio Pharmaceuticals	VGX-3100	HPV-targeted DNA vaccine	HPV+ cancers	Phase II/III	Virus-targeted immunotherapy

Sources: Company documents; Zacks SCR

Pelareorep in SCAC

Pelareorep has been evaluated in SCAC in the GOBLET study, an ongoing multi-cohort clinical trial investigating pelareorep in combination with checkpoint inhibition and chemotherapy, as appropriate, across gastrointestinal malignancies (NCT07280377). In Cohort 4, pelareorep was combined with the PD-L1 inhibitor atezolizumab in patients with second-line or later SCAC, representing a heavily pretreated population with limited therapeutic options. Updated data from this cohort demonstrated evidence of clinical activity, including a 30% overall response rate and a median 17-month duration of response.

Notably, the pattern of response observed in GOBLET Cohort 4 is consistent with pelareorep's proposed mechanism as an immune primer. Treatment was associated with tumor shrinkage across multiple patients, including both partial responses and prolonged stable disease, suggesting that the combination of pelareorep and checkpoint inhibition may overcome resistance mechanisms that limit the efficacy of PD-1/PD-L1 blockade alone. While cross-trial comparisons should be interpreted cautiously, the observed activity compares favorably to historical benchmarks for checkpoint inhibitor monotherapy in this setting, where response rates are generally low and disease control is limited.



Source: Oncolytics Biotech, Inc.

From a mechanistic perspective, these findings are highly consistent with the biology of both pelareorep and SCAC. As an HPV-driven malignancy, SCAC expresses viral antigens that can serve as targets for immune recognition, but effective anti-tumor immunity is often constrained by insufficient antigen presentation and limited T-cell infiltration. Pelareorep's ability to induce immunogenic cell death, activate dendritic cells, and promote expansion of tumor-specific cytotoxic T cells provides a clear rationale for its use in this setting. In addition, the upregulation of PD-L1 and increased immune infiltration observed with pelareorep treatment may enhance the activity of checkpoint inhibitors such as atezolizumab, resulting in a more robust and durable anti-tumor response.

Importantly, the clinical signal observed in GOBLET Cohort 4 has meaningful implications for Oncolytics' regulatory strategy. Given the rarity of SCAC, the lack of established second- or third-line standards of

care, and the precedent for approval based on response-based endpoints in high unmet need populations, these data support the feasibility of a single-arm pivotal study evaluating pelareorep in combination with checkpoint inhibition. When viewed in the context of the potential regulatory precedent being established by Replimune Group, the GOBLET dataset provides an early but important proof-of-concept that pelareorep can generate clinically meaningful responses in a population where existing therapies have limited efficacy.

Pancreatic Ductal Adenocarcinoma

Pancreatic ductal adenocarcinoma (PDAC) is among the most aggressive and treatment-refractory solid tumors, characterized by late-stage diagnosis, dense stromal architecture, and a profoundly immunosuppressive tumor microenvironment. Five-year survival remains below 10%, and outcomes in metastatic disease are particularly poor despite incremental advances in chemotherapy (Burris III *et al.*, 1997). Standard first-line regimens, including FOLFIRINOX and gemcitabine plus nab-paclitaxel, have demonstrated median overall survival of approximately 8–11 months, but are associated with significant toxicity and limited durability of response. Notably, immune checkpoint inhibitors have failed to demonstrate meaningful activity in unselected PDAC populations, largely due to low tumor mutational burden, poor antigen presentation, and limited baseline T-cell infiltration, establishing PDAC as a canonical example of an immunologically "cold" tumor.

Pelareorep has been extensively evaluated in mPDAC across multiple clinical studies, supporting its role as an immune-priming agent in a historically non-immunogenic tumor type. The biological rationale for its use in PDAC is particularly strong, as activating mutations in RAS are present in approximately 70–90% of pancreatic cancers, enabling selective viral replication and tumor cell lysis (Bryant *et al.*, 2014). A summary of pelareorep's results in mPDAC are in the table below.

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	

Source: Oncolytics Biotech, Inc.

- In the Phase 2 REO 017 trial, pelareorep was combined with gemcitabine in patients with advanced or metastatic PDAC. The study demonstrated a median overall survival of 10.2 months, with 1-year and 2-year survival rates of 45% and 24%, respectively, comparing favorably to historical gemcitabine benchmarks of approximately 22% and 4% (Mahalingam *et al.*, 2020). The disease control rate was also notably high at approximately 83%, suggesting meaningful biological activity even in the absence of high objective response rates. Importantly, pharmacodynamic analyses confirmed intratumoral viral replication and induction of immune signaling pathways, including PD-L1 upregulation, providing direct translational validation of pelareorep's mechanism of action.

- Further evidence was generated in the randomized phase II NCI 8601 study, which evaluated pelareorep in combination with paclitaxel and carboplatin versus chemotherapy alone (Noonan *et al.*, 2016). While median progression-free survival was similar between arms, the addition of pelareorep was associated with improved long-term survival outcomes, including 2-year overall survival rates of approximately 20% versus 6–9% in the control arm, suggesting a potential tail-of-the-curve benefit consistent with immune-mediated effects.

- More recently, the Phase 1b REO 029 study evaluated pelareorep in combination with gemcitabine, nab-paclitaxel, and the PD-L1 inhibitor atezolizumab, representing a multi-modal chemoimmunotherapy approach. In this small but informative cohort, the combination achieved an objective response rate of approximately 62%, substantially exceeding historical benchmarks of ~23% for chemotherapy alone in this setting. Additionally, 1-year survival rates were reported at approximately 45%, again comparing favorably to standard-of-care expectations.

Taken together, these studies provide a consistent body of evidence supporting pelareorep's ability to enhance both chemotherapy and immunotherapy in PDAC. Across trials, a recurring pattern emerges: modest effects on traditional endpoints such as progression-free survival, but meaningful improvements in long-term survival and disease control, consistent with an immune-mediated mechanism of action. This "tail effect" is particularly relevant in PDAC, where durable responses are rare and represent a key unmet need.

Financials and Capital Structure

On March 30, 2026, Oncolytics filed form 10-K with financial results for the year ending December 31, 2025. As expected, the company did not report any revenues in 2025. R&D expenses in 2025 were $13.3 million compared to $15.4 million in 2024. The decrease was primarily due to decreased clinical trial expenses from the completion of the BRACELET-1 study in 2024 and lower manufacturing expenses. G&A expenses in 2025 were $15.4 million compared to $10.1 million in 2024. The increase was primarily due to increased public company-related expenses, personnel-related expenses, and intellectual property expenses.

As of December 31, 2025, Oncolytics had approximately $5.2 million in cash and cash equivalents. Subsequent to the end of the year, the company sold approximately 7.5 million common shares pursuant to the ATM offering agreement with BTIG for net proceeds of approximately $7.6 million. As of March 23, 2026, Oncolytics had approximately 116.1 million common shares outstanding and, when factoring in stock options and warrants, a fully diluted share count of 142.9 million.

Risks to Consider

In addition to the risk factors listed below, investors are encouraged to read the company's 10-K filing that discusses additional risk factors.

Regulatory Risk: A driving force behind the investment thesis in Oncolytics is its ability to pursue a single-arm pivotal study in SCAC, leveraging objective response rate and durability as primary endpoints. This strategy is heavily dependent on regulatory precedent, particularly the outcome of the pending FDA decision on Replimune Group's RP1 program. While a favorable outcome would support the feasibility of this approach, there is no guarantee that the FDA will extend a similar evidentiary standard to pelareorep in SCAC, given differences in tumor biology, study design, and dataset maturity. A negative or more restrictive regulatory outcome for RP1 could raise the evidentiary bar for Oncolytics, potentially requiring a randomized controlled trial to support approval. A change like this would increase development timelines, capital requirements, and execution risk. Even if RP1 is approved, Oncolytics' ability to secure alignment with the FDA on trial design, endpoints, and patient population remains a key risk factor.

Clinical Risk: While pelareorep has demonstrated encouraging signals of biological activity and clinical benefit across multiple studies, much of the data supporting its advancement is from early-phase trials

with small patient cohorts. This is particularly relevant in SCAC, where the GOBLET Cohort 4 dataset represents a limited number of pretreated patients, and in mCRC, where prior studies have not yet been confirmed in large, randomized trials. Early-phase results are inherently subject to variability, and observed response rates, survival outcomes, and biomarker signals may not be reproduced in larger, well controlled studies. In addition, comparison to historical benchmarks introduces potential bias due to differences in patient populations, prior lines of therapy, and study design.

Translational Risk: Pelareorep's mechanism of action is supported by a large volume of preclinical and translational data demonstrating viral replication, immunogenic cell death, and activation of innate and adaptive immune responses. However, the translation of these biological effects into consistent and durable clinical benefit remains uncertain. There is a risk that pelareorep's immune-modulating effects may be necessary but not sufficient to overcome the complex immunosuppressive mechanisms present in solid tumors such as mCRC and mPDAC.

Competitive Risk: The treatment landscape for mCRC, SCAC, and mPDAC is highly dynamic, with numerous ongoing efforts to develop combination immunotherapy strategies, targeted therapies, and novel modalities. In mCRC, multiple approaches are being explored to sensitize MSS tumors to checkpoint inhibitors, including bispecific antibodies, cellular therapies, and other oncolytic virus platforms. In SCAC, checkpoint inhibitors are already approved in certain settings, and additional combinations are under investigation. There is a risk that competing approaches may achieve superior efficacy, more favorable safety profiles, or faster regulatory timelines, potentially limiting pelareorep's commercial opportunity.

Execution Risk: The company's recent strategic reset under new management represents a positive shift toward a more focused and capital-efficient development strategy. However, this transition also introduces execution risk, as the new leadership team must successfully prioritize indications, design registrational studies, and engage with regulatory authorities. The success of this strategy is dependent on disciplined capital allocation, effective clinical trial execution, and timely regulatory interactions. Any delays in study initiation, patient enrollment, or data readouts could impact development timelines. In addition, the company's ability to maintain strategic focus and avoid returning to a more diffuse development approach will be critical to long-term success.

Financial Risk: As a clinical-stage biotechnology company, Oncolytics does not generate product revenue and is dependent on external funding to support its operations. While the company is pursuing a capital-efficient development strategy, advancement of clinical programs requires significant financial resources. Oncolytics may need to raise additional capital through equity offerings, partnerships, or other financing mechanisms. Such activities could result in shareholder dilution and may be sensitive to broader market conditions.

MANAGEMENT PROFILES

Jared Kelly – Chief Executive Officer and Director

Mr. Kelly recently served as head of legal and corporate strategy at Ambrx and played a central role in its $2 billion sale to Johnson & Johnson. He has managed numerous transactions in the biotech space for companies at various stages of development. After leaving Ambrx, he has served as an advisor to multiple public and private drug development and pharmaceutical companies. Prior to becoming a biotech executive, Mr. Kelly was a sought-after public company lawyer who began his career with Kirkland & Ellis LLP, where he represented various public companies in securities offerings, IPOs and merger transactions. He also served as a partner at Lowenstein Sandler LLP, where his practice focused on representing biotechnology companies in financing transactions, mergers and acquisitions, and other complex transactions. Mr. Kelly received his J.D. and an LL.M. in Securities and Financial Regulation from Georgetown University Law Center, where he was the recipient of multiple honors and fellowships, including the Lane Evans Fellowship and Decrane Scholarship.

Kirk Look, CA, MSJ – Chief Financial Officer

Mr. Look joined Oncolytics as the Company's Controller in April 2003 and assumed the role of Chief Financial Officer in November 2012. Prior to joining Oncolytics, from 2000 to April 2003, Mr. Look was Manager of Audit and Assurance Services with Ernst & Young LLP in Canada. From 1998 to the end of 1999, Mr. Look held the positions of Audit Manager and Senior Accountant at Ernst & Young LLP in Chile. Mr. Look has a Bachelor of Commerce from the University of Calgary and a Master of Science in Jurisprudence Law Degree from the Seton Hall Law School.

Thomas C. Heineman, MD, PhD – Chief Medical Officer

Prior to joining Oncolytics, Dr. Thomas Heineman was Senior Vice President and Head of Clinical Development at Denovo Biopharma. Prior to his time at Denovo, he served as Vice President and Head of Clinical Development at both Genocea Biosciences and Halozyme Therapeutics. At Halozyme, Dr. Heineman was also Head of Translational Medicine and oversaw clinical trials in indications such as breast and pancreatic cancer. Dr. Heineman's experience further extends to big pharma and academia, as he previously worked as Senior Director, Global Clinical Research and Development at GlaxoSmithKline and as an Associate Professor at the Saint Louis University School of Medicine. Dr. Heineman has co-authored over 60 peer-reviewed publications and is board certified in Internal Medicine and Infectious Diseases. He completed his fellowship in Infectious Diseases at the National Institutes of Health and his internship and residency at the University of Maryland. Dr. Heineman earned his MD and PhD in Virology at the University of Chicago.

Allison Hagerman, Peng, PMP, MBT – Chief Technology Officer

A professional engineer focused on biotechnology, Allison Hagerman joined Oncolytics in 2010 and has been integral to the progress of its product development program ever since. Prior to being appointed as Vice President of Product Development, Ms. Hagerman was the Director, Manufacturing and Engineering from 2013-2017 and Project Manager from 2010-2013, during which time she led the process performance qualification for pelareorep drug substance. Ms. Hagerman is a Professional Engineer (P.Eng., APEGA) and Project Management Professional (PMP, PMI). She holds a Master of Biomedical Technology (MBT) degree from the University of Calgary, and B.Sc. degrees in both Chemical Engineering and Biological Sciences.

Andrew Aromando – Chief Business Officer

Andrew Aromando is an accomplished biopharmaceutical executive with over 30 years of industry experience. Prior to Oncolytics, he served in C-level positions for 20 years at multiple oncology-focused biotech and specialty pharmaceutical companies, where he crafted and led corporate strategy, acquired and advanced clinical-stage candidates, developed and executed commercialization plans for marketed products that increased sales, and negotiated successful exits. Mr. Aromando most recently served as Chief Operating Officer at Ambrx Biopharma, where his contributions were instrumental in the $2 billion acquisition of the San Diego-based biotech by Johnson & Johnson. He also served in senior leadership roles at IQVIA, Syneos Health and WCG Clinical, He began his career in field sales at Novartis. Mr. Aromando holds a B.A. from The College of New Jersey and an M.A. from Rutgers University.

VALUATION

We are initiating coverage of Oncolytics Biotech, Inc. (ONCY) with a valuation of $6.00. Oncolytics is a clinical-stage immuno-oncology company developing pelareorep, an oncolytic viral therapy that is derived from an unmodified type 3 Dearing (T3D) reovirus that selectively replicates in tumor cells while showing single-agent activity in a wide variety of tumors. Following a change in management in mid-2025, the company has reset the development pathway for pelareorep and will focus on gastrointestinal (GI) cancers, with an initial focus on squamous cell anal carcinoma (SCAC) followed by long-term platform expansion into metastatic colorectal cancer (mCRC) and metastatic pancreatic ductal adenocarcinoma (mPDAC).

The company has an upcoming mid-April meeting with the U.S. Food and Drug Administration (FDA) in which it will seek to clarify the development pathway for pelareorep in SCAC, including the potential for a single-arm pivotal study. Support for that pathway could be supplied by the approval of RP1 in anti-PD-1 resistant melanoma, which has a PDUFA date of Apr. 10, 2026. Alignment with the FDA on that pathway could lead to a BLA filing within two years.

Pelareorep

Pelareorep is a proprietary formulation of a naturally occurring, non-enveloped double-stranded RNA (dsRNA) virus derived from Reovirus, a ubiquitous pathogen that is typically asymptomatic in humans but possesses intrinsic oncolytic properties. Following entry into permissive tumor cells, pelareorep undergoes active replication, leading to cell death through a combination of direct cytopathic effects, apoptosis, and necrotic pathways that releases multiple immunologically active compounds. Importantly, pelareorep has demonstrated the ability to modulate the tumor microenvironment in ways that are particularly relevant to overcoming resistance to immune checkpoint blockade. Pelareorep infection has been shown to increase infiltration of CD8+ T cells, upregulate expression of interferon-stimulated genes, and induce PD-L1 expression on tumor cells, effectively converting immunologically “cold” tumors into “hot,” A key differentiating feature of pelareorep relative to many other oncolytic virus platforms is its ability to be administered intravenously, enabling systemic delivery to both primary and metastatic tumor sites. This systemic delivery capability is particularly relevant in gastrointestinal malignancies such as colorectal cancer, where metastatic lesions are often distributed across organs such as the liver and lungs and may not be amenable to intratumoral injection approaches.

Pelareorep in SCAC: Pelareorep has been evaluated in SCAC in the GOBLET study, an ongoing multi-cohort clinical trial investigating pelareorep in combination with checkpoint inhibition and chemotherapy, as appropriate, across gastrointestinal malignancies. In Cohort 4, pelareorep was combined with the PD-L1 inhibitor atezolizumab in patients with second-line or later SCAC, representing a heavily pretreated population with limited therapeutic options. Updated data from this cohort demonstrated evidence of clinical activity, including a 30% overall response rate and a median 17-month duration of response. Importantly, the clinical signal observed in GOBLET Cohort 4 has meaningful implications for Oncolytics’ regulatory strategy. Given the rarity of SCAC, the lack of established second- or third-line standards of care, and the precedent for approval based on response-based endpoints in high unmet need populations, these data support the feasibility of a single-arm pivotal study evaluating pelareorep in combination with checkpoint inhibition. When viewed in the context of the potential regulatory precedent being established by Replimune Group, the GOBLET dataset provides an early but important proof-of-concept that pelareorep can generate clinically meaningful responses in a population where existing therapies have limited efficacy.

Pelareorep in CRC: Clinical evaluation of pelareorep in mCRC has been conducted directly in combination with standard-of-care second-line therapy, most notably irinotecan-based chemotherapy (FOLFIRI) plus bevacizumab. At the recommended phase II dose, the combination produced a median progression-free survival (PFS) of 16.6 months and a median overall survival (OS) of 27.0 months,

substantially exceeding historical expectations for second-line therapy in this population. Oncolytics recently initiated a Phase 2 trial in second-line, RAS-mutated, microsatellite-stable mCRC patients. The patients will be randomized into one of two groups: bevacizumab and FOLFIRI or pelareorep, bevacizumab, and FOLFIRI. The study is powered for statistical significance with each arm expected to enroll 30 patients. The primary endpoint of the trial is objective response rate (ORR), with PFS, OS, safety, and biomarker analysis as other endpoints. Preliminary data could be available by the end of 2026.

Pelareorep in mPDAC: Pelareorep has been extensively evaluated in mPDAC across multiple clinical studies, supporting its role as an immune-priming agent in a historically non-immunogenic tumor type. In the Phase 2 REO 017 trial, pelareorep was combined with gemcitabine in patients with advanced or metastatic PDAC. The study demonstrated a median overall survival of 10.2 months, with 1-year and 2-year survival rates of 45% and 24%, respectively, comparing favorably to historical gemcitabine benchmarks of approximately 22% and 4%. More recently, the Phase 1b REO 029 study evaluated pelareorep in combination with gemcitabine, nab-paclitaxel, and the PD-L1 inhibitor atezolizumab. In this small but informative cohort, the combination achieved an objective response rate of approximately 62%, substantially exceeding historical benchmarks of ~23% for chemotherapy alone in this setting. Additionally, 1-year survival rates were reported at approximately 45%, again comparing favorably to standard-of-care expectations.

Valuation

We value Oncolytics using probability-adjusted peak sales estimates for each of the three core indications of SCAC, mCRC, and mPDAC, discounted to present value using a 15% rate, and applying a 3.0x multiple to risk-adjusted revenues, which is consistent with comparable clinical-stage oncology assets. For each indication, we model for peak sales to be seven years following approval.

- For SCAC, we model a 2028 BLA filing and a 2029 launch enabled by a potential single-arm registration pathway, with peak U.S. sales of approximately $250 million and peak E.U. sales of approximately $150 million. We estimate a 60% probability of approval for this indication. This leads to an NPV in SCAC of $169 million.

- For mCRC, we model for a 2030 BLA filing and a 2031 launch with peak U.S. sales of approximately $1.1 billion and peak E.U. sales of approximately $700 million. We estimate a 50% probability of approval for this indication. This leads to an NPV in mCRC of $477 million.

- For mPDAC, we model for a 2030 BLA filing and a 2031 launch with peak U.S. sales of approximately $1.2 billion in the U.S. and peak E.U. sales of approximately $800 million. We estimate a 30% probability of approval for this indication. This leads to an NPV in mPDAC of $371 million.

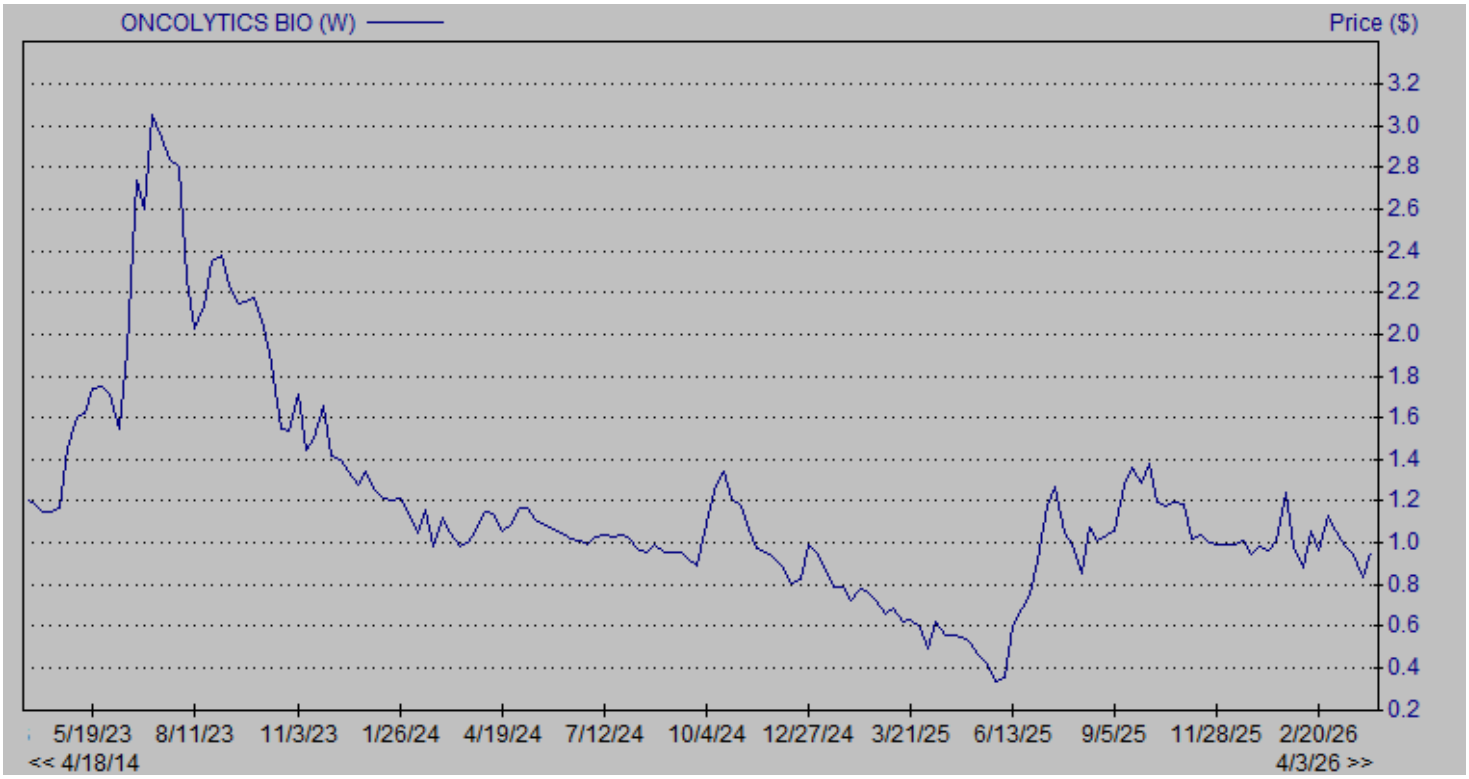
Combining the contributions from each product results in a total NPV of just over $1 billion. Adding in the current cash position ($5 million) and the potential cash from warrant exercises ($42 million) and dividing by the fully diluted share count, plus an additional 20 million shares for dilution, leads to a valuation of $6.00 per share.

PROJECTED FINANCIALS

Oncolytics Biotech, Inc.	2025 A	1Q E	2Q E	3Q E	4Q E	2026 E	2027 E	2028 E
SCAC	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
mCRC	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
mPDAC	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Grants & Collaborative Revenue	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Total Revenues	**$0.0**	**$0.0**	**$0.0**	**$0.0**	**$0.0**	**$0.0**	**$0.0**	**$0.0**
Research & Development	$13.3	$3.2	$3.4	$3.6	$3.8	$14.0	$17.0	$20.0
General & Administrative	$15.4	$4.0	$4.0	$4.0	$4.0	$16.0	$17.0	$18.0
Other Expenses	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Operating Income	($28.7)	($7.2)	($7.4)	($7.6)	($7.8)	($30.0)	($34.0)	($38.0)
Non-Operating Expenses (Net)	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$1.0
Pre-Tax Income	($28.7)	($7.2)	($7.4)	($7.6)	($7.8)	($30.0)	($34.0)	($37.0)
Income Taxes Paid	($0.1)	$0.2	$0.0	$0.2	$0.0	$0.3	$0.0	$1.0
Net Income	**($28.8)**	**($7.0)**	**($7.4)**	**($7.4)**	**($7.8)**	**($29.7)**	**($34.0)**	**($36.0)**
Translation Adjustments	($0.1)	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$1.0
Total Comprehensive Gain/Loss	**($28.90)**	**($7.03)**	**($7.40)**	**($7.43)**	**($7.80)**	**($29.66)**	**($34.00)**	**($35.00)**
Net Loss per Share	**($0.30)**	**($0.06)**	**($0.06)**	**($0.06)**	**($0.06)**	**($0.24)**	**($0.23)**	**($0.21)**
Basic Shares Outstanding	95.9	110.0	120.0	130.0	140.0	125.0	150.0	175.0

Source: Zacks Investment Research, Inc. *David Bautz, PhD*

HISTORICAL STOCK PRICE



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