REOLYSIN® and Immune Checkpoint Inhibitors: rationale for combination therapy

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VP Clinical Development

March 25th , 2015

Forward Looking Statements

This presentation contains certain forward looking statements relating to the company's financial results, business prospects and the development and commercialization of REOLYSIN®, a therapeutic reovirus. These statements are based on management's current expectations and beliefs and are subject to a number of factors which involve known and unknown risks, delays, uncertainties and other factors not under the company's control which may cause actual results, performance or achievements of the company to be materially different from the results, performance or other expectations implied by these forward looking statements.

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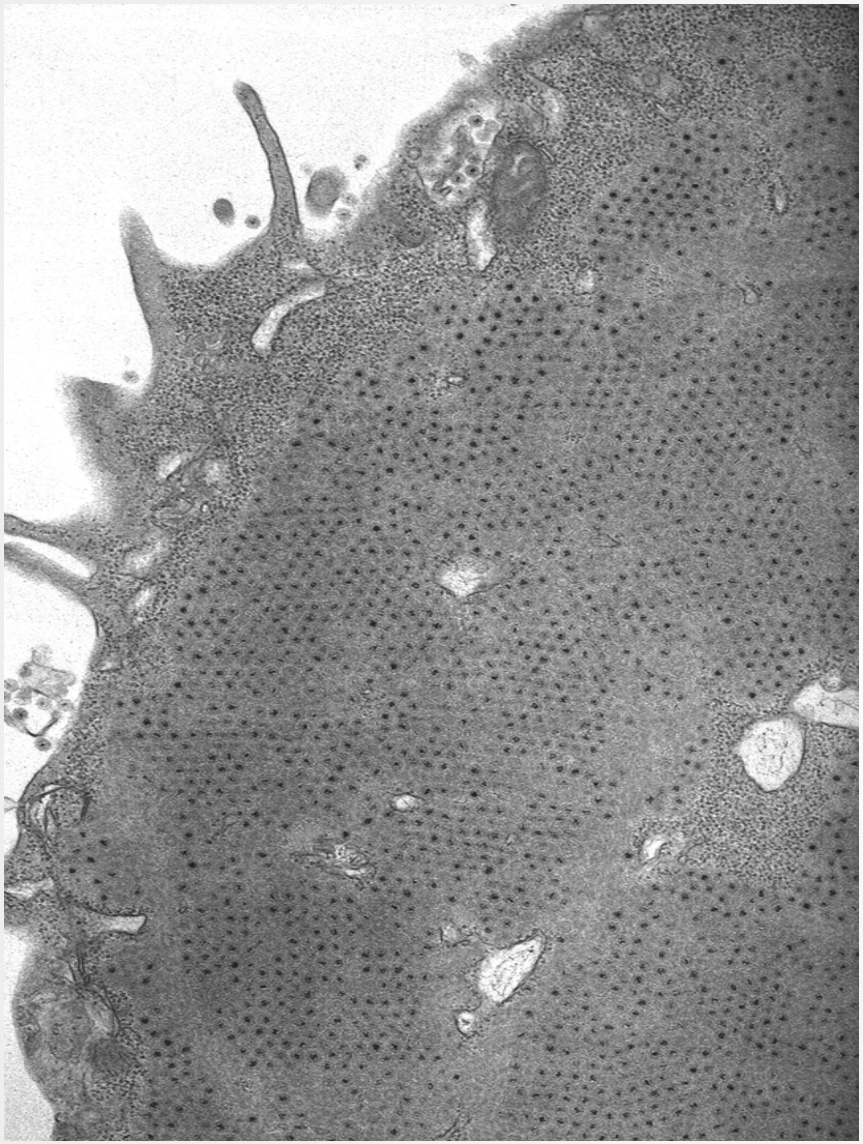
REOLYSIN®: Background

Oncolytics Biotech Inc.

- The Company is focused on the development of an oncolytic virus for use as a cancer therapeutic
- The Company's product, REOLYSIN®, is a proprietary isolate of reovirus type 3 Dearing, currently being investigated in many randomised clinical studies across a variety of cancer indications
- USAN: pelareorep

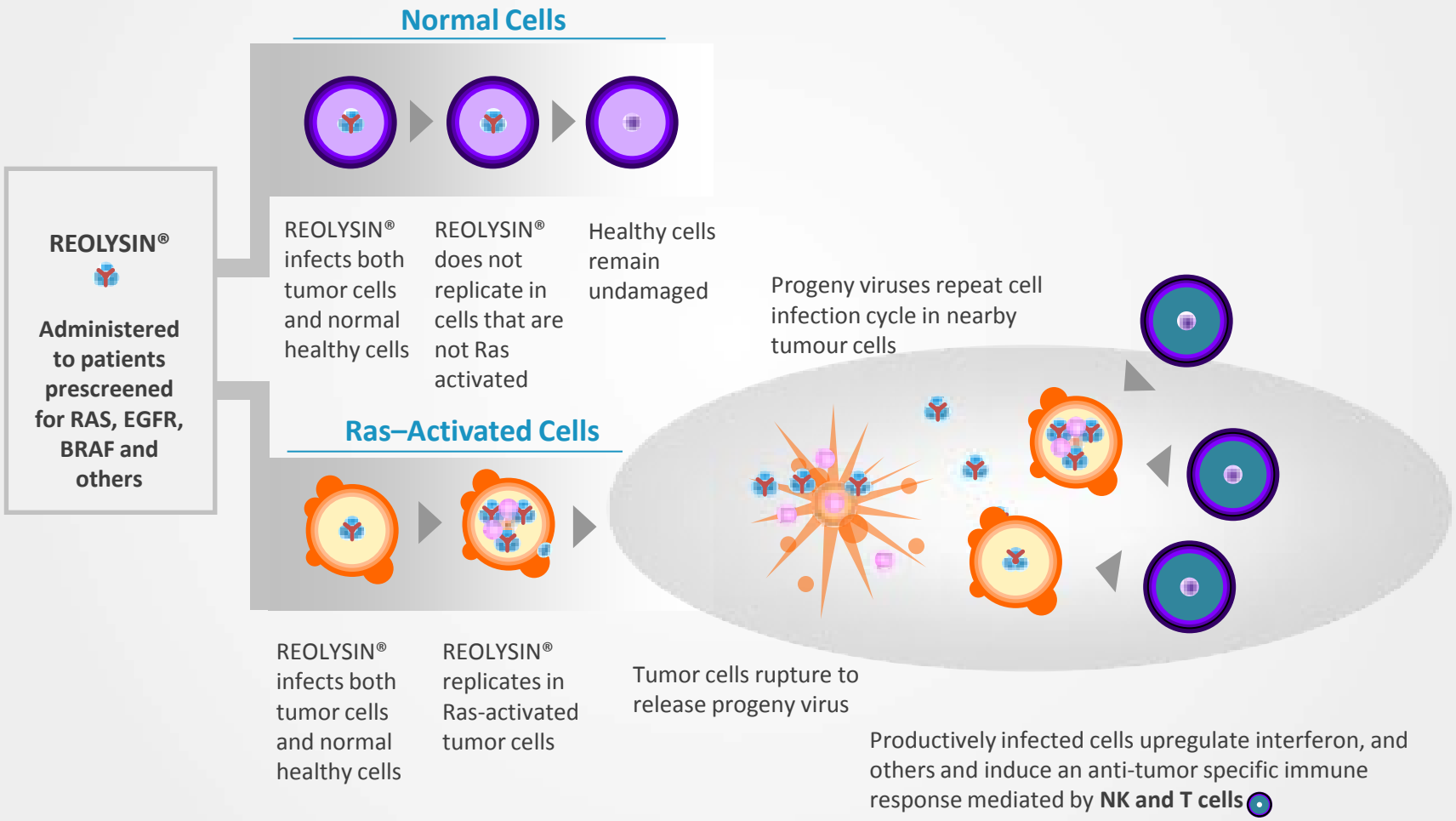
Reovirus Replication



- Fully replication-competent
- Mammalian permissive which allows effective modeling in murine, canine, and non-human primate models
- Viral replication is exclusively cytoplasmic

Kras mutated colorectal cancer cell line infected with reovirus. Picture courtesy of Dr. Scott Wadler.

REOLYSIN® Mechanism of Action



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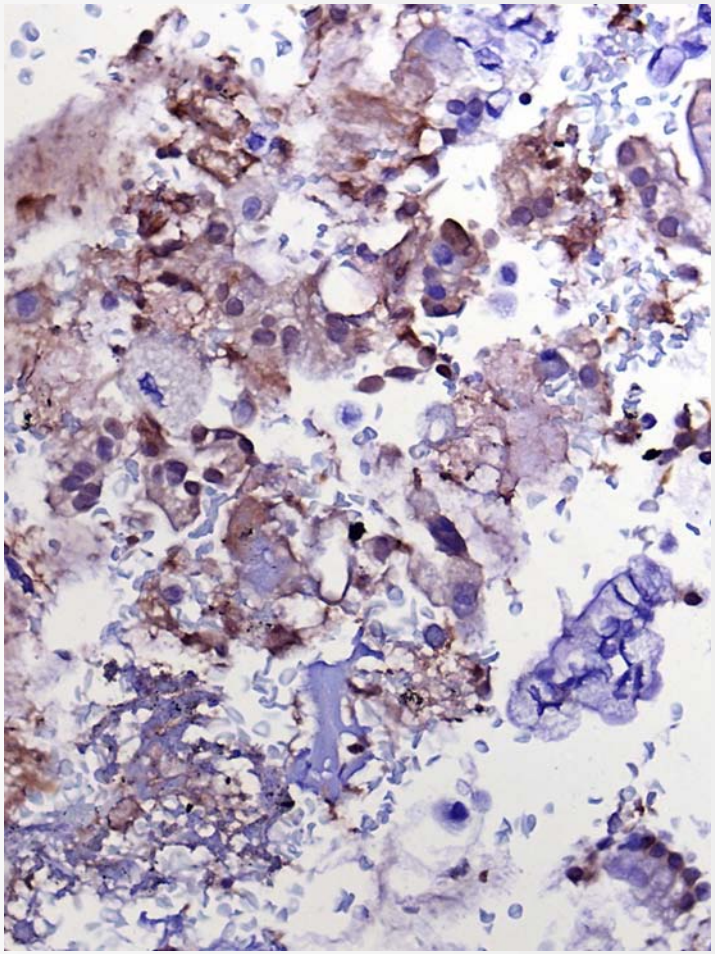
REOLYSIN®: Clinical Development

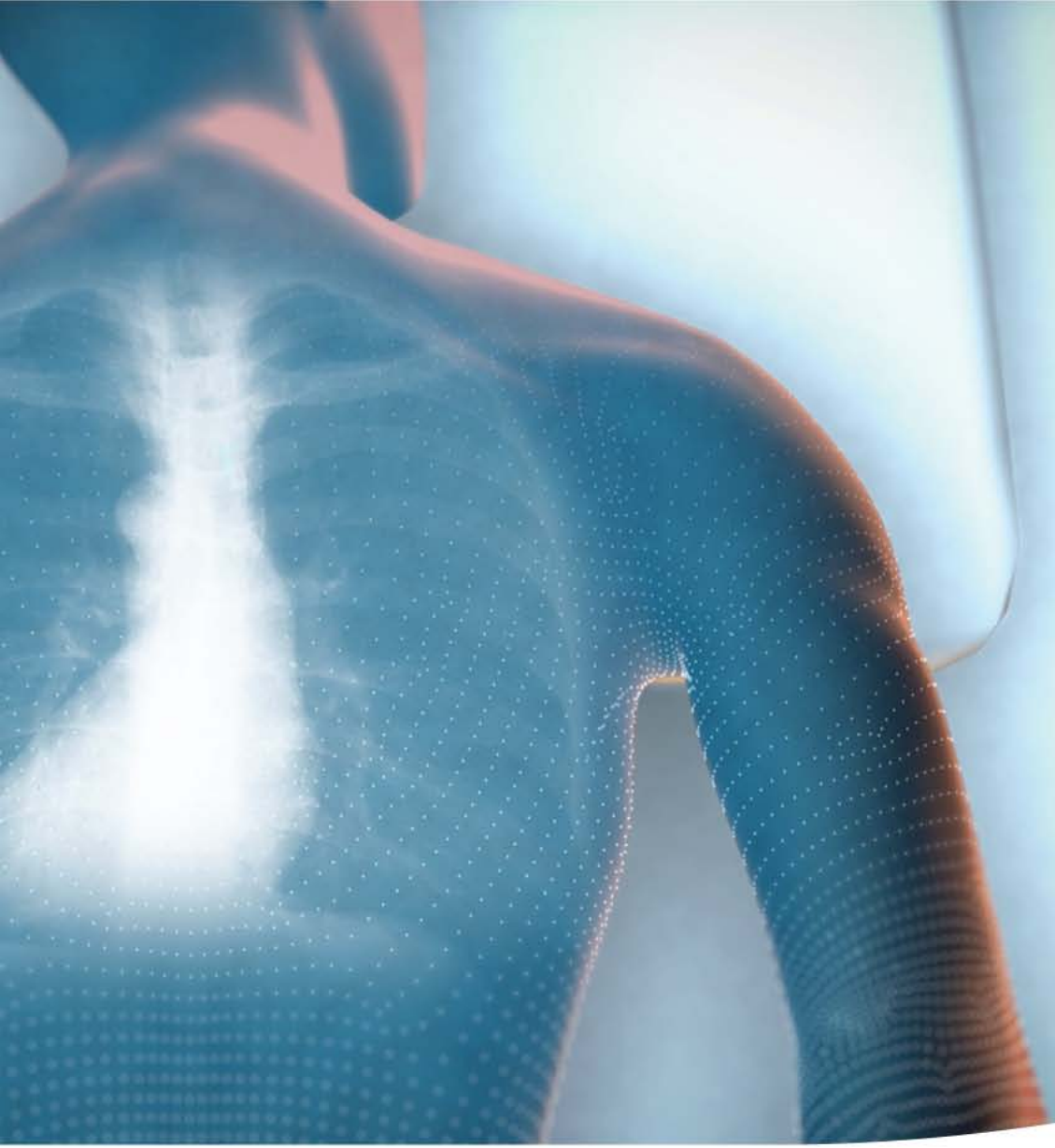
- Phase I studies were conducted in various tumour types without reaching an MTD; highest total weekly dose reached was 1.5×10^{11} $TCID_{50}$ IV
- Synergistic with cytotoxic compounds or radiotherapy (RT), both of which promote delivery to the interior of a tumor, viral protein translation, and apoptosis of tumor cells
- Objective responses are seen in tumors with known Ras pathway activation
- Safety profile:
  - Minimal hematological or liver toxicity
  - Characteristic flu-like symptoms
  - Administered on an outpatient basis
  - BSL2 with no major precautions



Picture courtesy of Drs. Mahalingham and Nuovo (REO 017 study of Gemcitabine and REOLYSIN® in pancreatic cancer with known KRAS mutation)

Randomized Clinical Trial Program for REOLYSIN®: Active Studies

Trial	Phase	Sponsor	n	Enrollment Status
IND 213: Intravenous REOLYSIN® in Combination with Paclitaxel in Patients with Advanced or Metastatic Breast Cancer	II	NCIC CTG	100	>60% complete
IND 211: Intravenous REOLYSIN® in Combination with Docetaxel or Pemetrexed in Patients with Previously-Treated Advanced or Metastatic Non-Small Cell Lung Cancer (NSCLC)	II	NCIC CTG	150	>90% complete
IND 210: Intravenous REOLYSIN® in Combination with FOLFOX-6 Plus Bevacizumab (Avastin®) in Patients with Advanced or Metastatic Colorectal Cancer	II	NCIC CTG	100	complete
IND 209: Intravenous REOLYSIN® in Combination with Docetaxel in Patients with Recurrent or Metastatic Castration-Resistant Prostate Cancer	II	NCIC CTG	80	>90% complete
GOG-0186H: Intravenous REOLYSIN® in Combination with Paclitaxel for Patients with Persistent or Recurrent Ovarian, Fallopian Tube or Primary Peritoneal Cancer	II	NCI/GOG	110	complete
NCI-8601: Intravenous REOLYSIN® in Combination with Carboplatin and Paclitaxel for Patients with Metastatic Pancreatic Cancer	II	NCI	70	complete



REOLYSIN®, PD-1 and PD-L1

REOLYSIN®, PD-1 and PD-L1

- REOLYSIN® induces the up-regulation of PD-1 and PD-L1 in target tissues
- PD-L1 and PD-1 overexpression is strongly associated with productive reoviral infection

REOLYSIN® for the Treatment of Brain Tumors

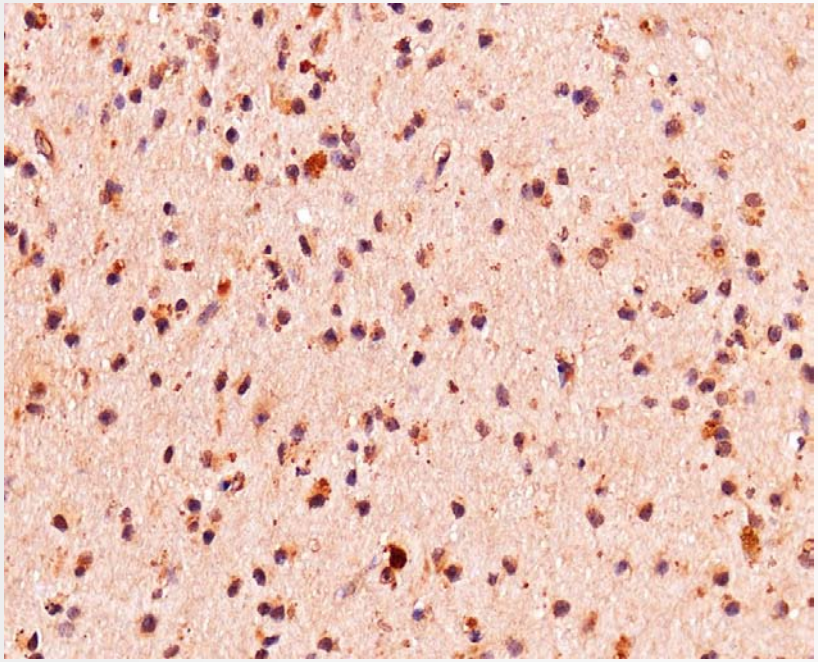
- REO 013b is an open-label, single arm, translational clinical study of REOLYSIN® as single IV infusion to nine patients with high grade glioma or metastatic brain tumours prior to planned surgical resection of the target tumours

Presence of Reoviral Protein, PD-1, and PD-1 (REO 013b Study)

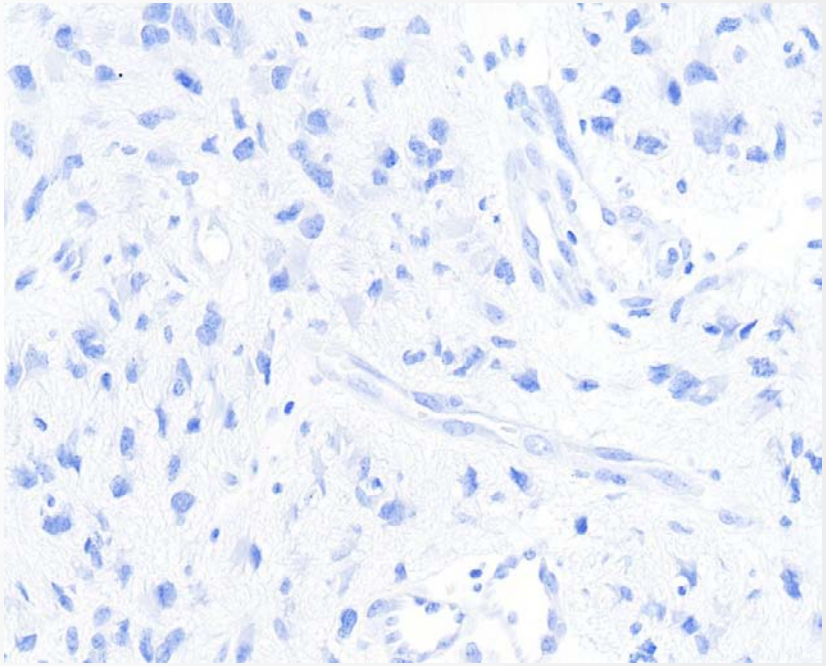
Case	Diagnosis	Reoviral Protein	PD-L1	PD-1
1	glioblastoma	1+	2+	2+
2	adenocarcinoma (colon metastasis)	1+	2+	2+
3	glioma, grade 3	1+	2+	2+
4	glioma, grade 3	negative	0	1+
5	melanoma metastasis	negative	1+	2+
6	glioblastoma	1+	2+	2+
7	glioblastoma	negative	weak	0
8	glioblastoma	1+	1+	2+
9	melanoma metastasis	2+	3+	2+
10 (control)	adenocarcinoma (breast metastasis)	negative	0	0
11 (control)	glioblastoma	negative	0	0
12 (control)	glioblastoma	negative	0	0
13 (control)	glioblastoma	negative	0	0
14 (control)	glioblastoma	negative	0	0
15 (control)	adenocarcinoma (ovarian metastasis)	negative	0	weak

REOLYSIN® Increases PD-L1 Expression

- Glioblastomas treated with REOLYSIN®: productive reoviral infection showed increases in PD-L1 expression (brown is +)



GBM Treated with REOLYSIN®

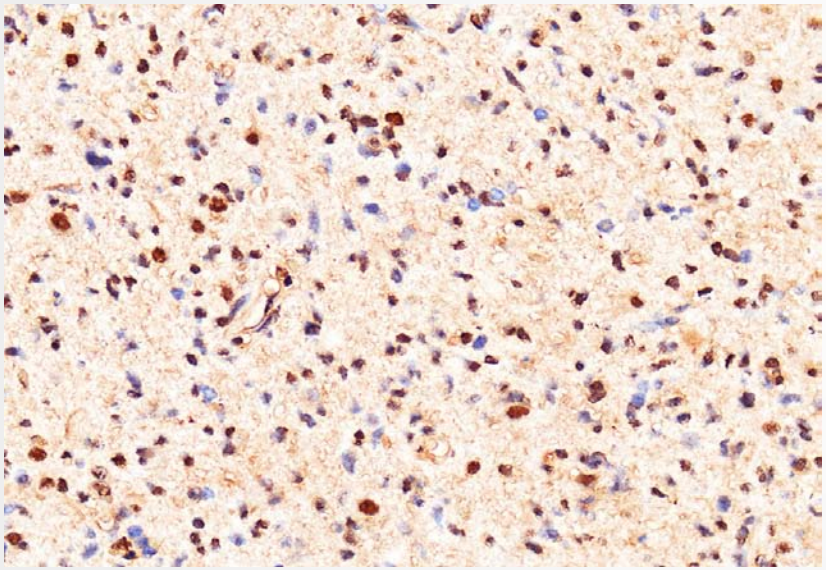


Control GBM (Untreated)

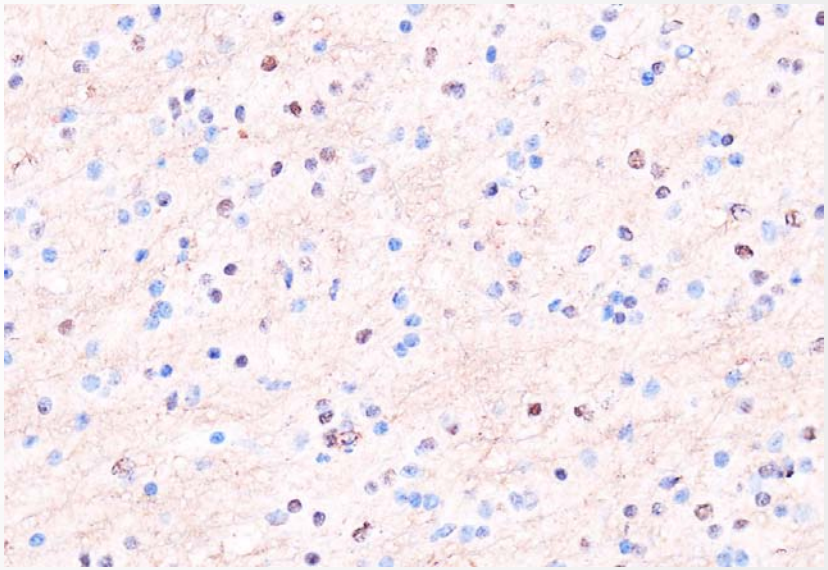
Courtesy of Dr. Gerard Nuovo of the OSU Comprehensive Cancer Center and Phylogeny, Inc.

REOLYSIN® Increases PD-1 Expression

- Glioblastomas treated with REOLYSIN®: productive reoviral infection showed increases in PD-1 expression (brown is +)



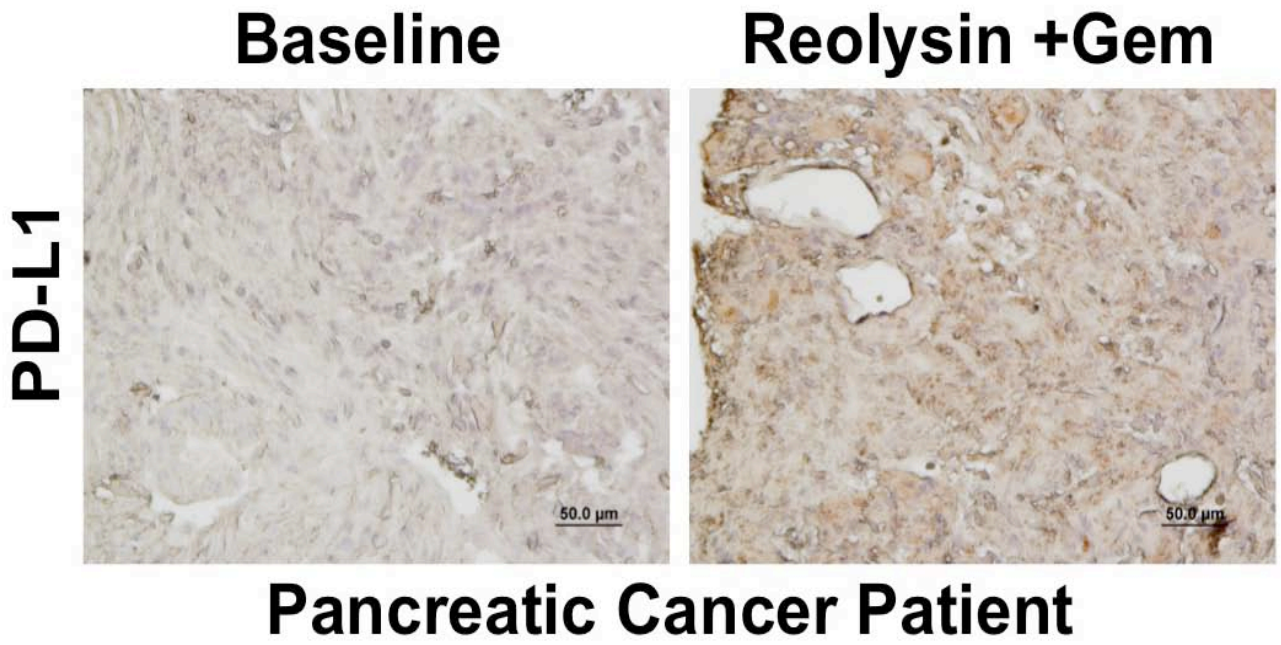
GBM Treated with REOLYSIN®



GBM Treated with REOLYSIN®, But No Productive Infection

Courtesy of Dr. Gerard Nuovo of the OSU Comprehensive Cancer Center and Phylogeny, Inc.

REO 017: Gemcitabine and REOLYSIN® Induced PD-L1 Expression (25 cycles)



Courtesy of Dr. Steffan T. Nawrocki, Department of Medicine, CRTC at University of Texas Health Science Center at San Antonio

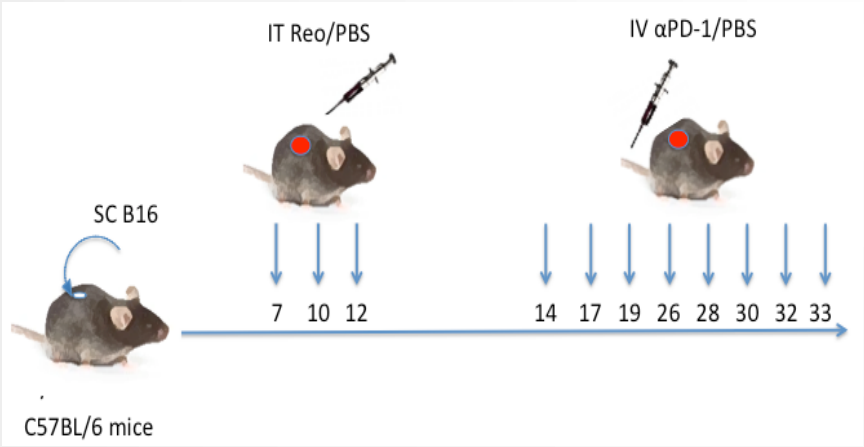
Reovirus and the PD-L1 blockade

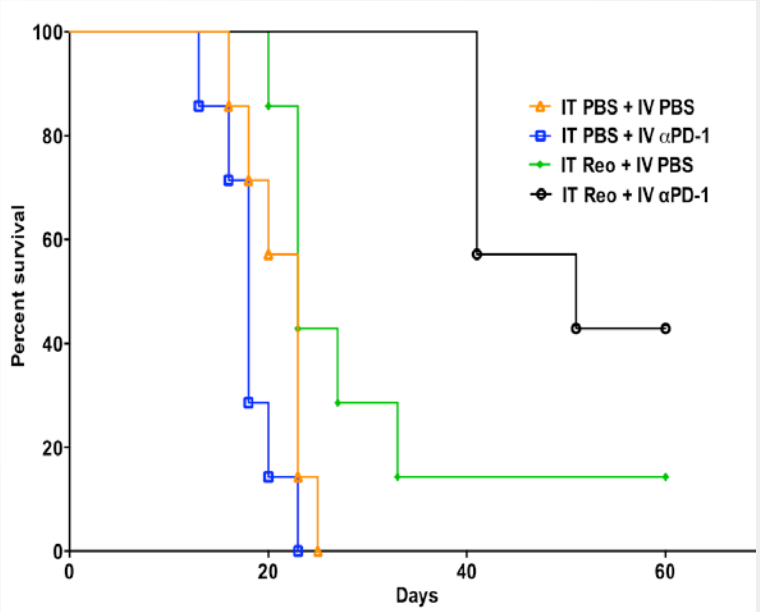
- Reovirus upregulates PD-L1 on the surface of breast, kidney and lung cell lines.
- The combination of reovirus and sunitinib further enhances the expression of PD-L1 in breast and lung cancer cell lines
- This combination increases cell killing in breast and lung cancer cell lines

Mostafa et al. 2014: Don Morris group, University of Calgary (AACR Tumor Immunology Conference poster)

REOLYSIN® and Anti-PD-1 Combination Therapy

- The combination of intratumoural REOLYSIN® with an anti-PD-1 Ab results in prolonged survival of mice with melanoma.





Rajani et al. 2014: Richard Vile group (Conference poster)

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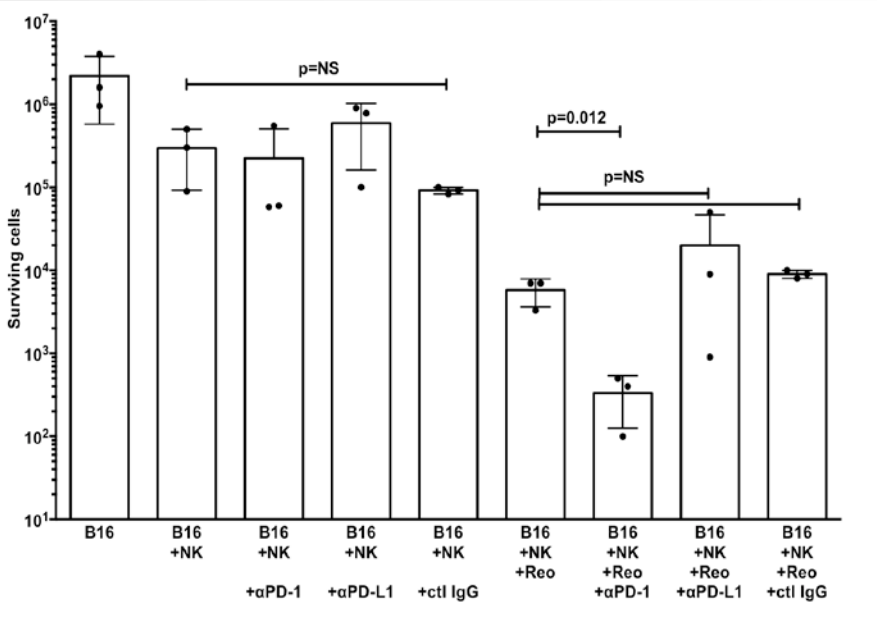
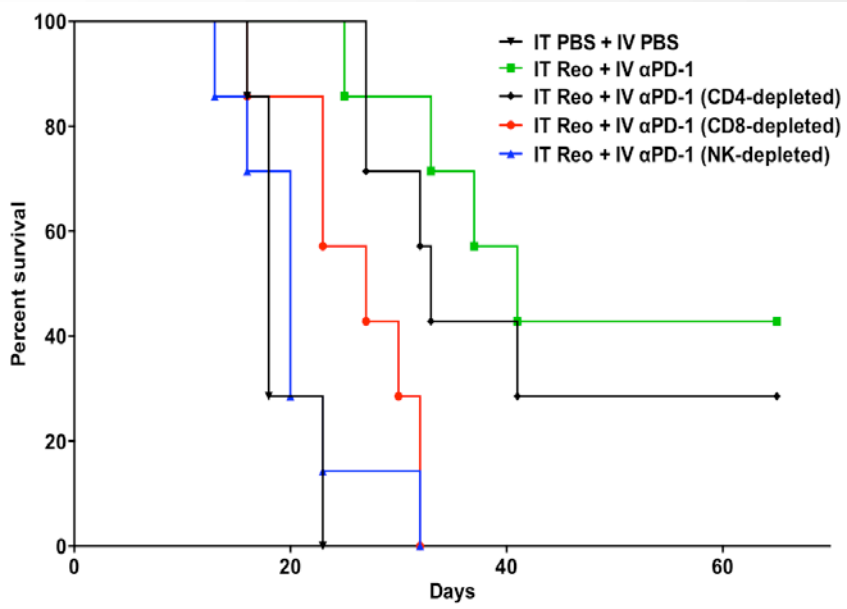
REOLYSIN® and Anti-PD-1 Combination Therapy

- The combination of REOLYSIN® with an anti-PD-1 Ab augments tumor-specific NK responses and attenuates tumor-specific immunosuppression, resulting in significant survival benefits in C57BL/6 mice with established SC B16 tumors (melanoma).





Rajani et al. 2014: Richard Vile group (Conference poster)

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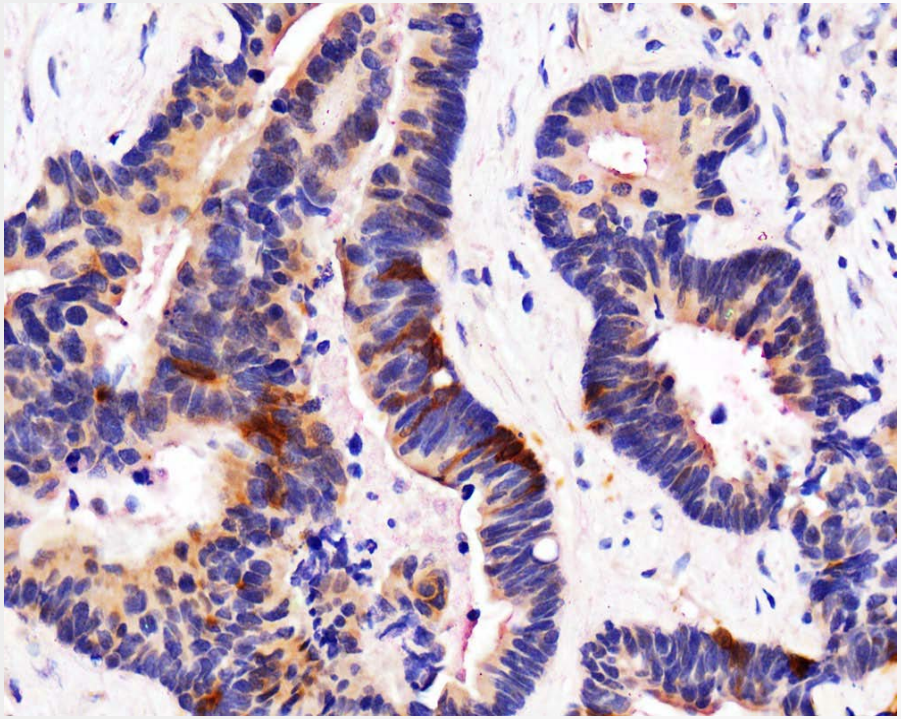
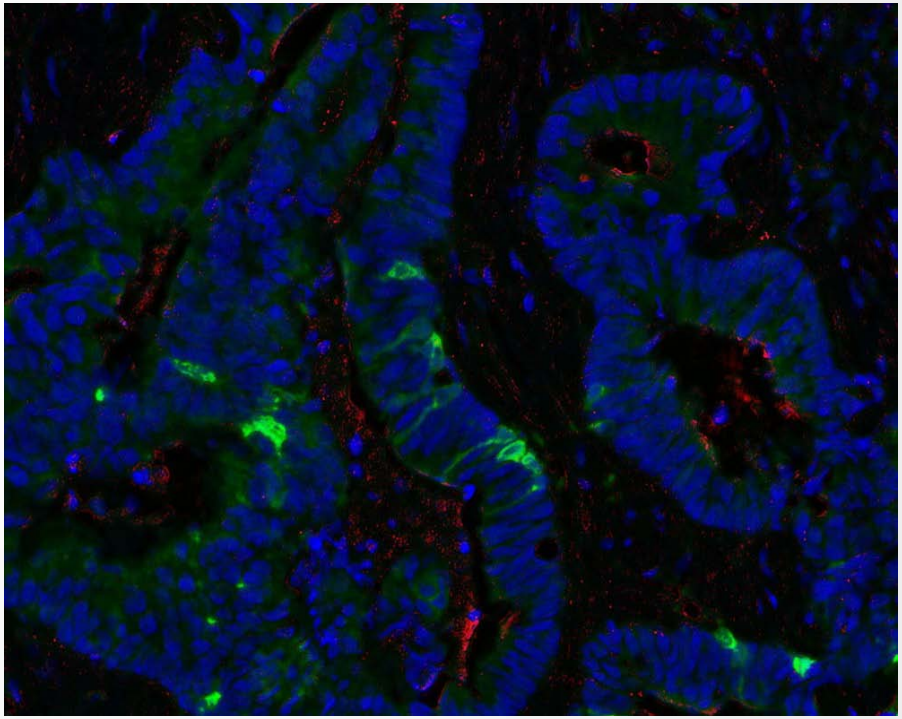
REO 013b: Co-Expression of NK Cells and Productive Reoviral Infection

- Reoviral protein expression is seen in same areas as NK cells in brain metastases from colorectal cancer.



red = reovirus protein; brown = cKIT



red = reovirus protein; green = cKIT; blue = hematoxylin

Courtesy of Dr. Gerard Nuovo, OSU Comprehensive Cancer Center and Phylogeny, Inc.

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