SYNOPSIS OF ABBREVIATED CLINICAL STUDY REPORT (REO 018)

Company: Oncolytics Biotech Inc. **Name Of Finished Product:** TBD **Name of Active Substance:** Pelareorep (formerly known as REOLYSIN)	(FOR NATIONAL AUTHORITY USE ONLY)

Study Title:
Randomized, Double-blind, Multicenter Phase 3 Study of Intravenous Administration of REOLYSIN® (Reovirus Type 3 Dearing) in Combination with Paclitaxel and Carboplatin versus the Chemotherapy Alone in Patients with Metastatic or Recurrent Squamous Cell Carcinoma of the Head and Neck who have Progressed On or After Prior Platinum-Based Chemotherapy

Study Phase: 3

First Patient First Treatment/Last Patient Last Treatment:
August 9, 2010/March 15, 2013

Investigators/Centers/Countries:
Multicenter study with sites in Belgium (3 centers), Canada (3), France (4), Germany (1), Greece (3), Hungary (2), Italy (3), Poland (3), Portugal (1), Russia (10), Slovenia (1), Spain (5), United Kingdom (6), and United States (11).

Publications (reference):
None

Primary Study Objective:
Compare overall survival for the treatment regimens in the entire study population, in the subgroup of patients with recurrent loco-regional disease (with or without metastases) and in the subgroup of patients with metastatic disease without measured local recurrence at time of randomization.

Secondary and Tertiary Objectives:

Secondary

1. Compare progression free survival for the treatment regimens in the entire study population, in the subgroup of patients with recurrent loco-regional disease (with or without metastases) and in the subgroup of patients with metastatic disease without measured local recurrence at time of randomization.
2. Compare Objective Response (Complete Response (CR) + Partial Response (PR)) rate and Clinical Benefit Rate (CR + PR + Stable Disease (SD)) for the treatment regimens

in the entire study population, in the subgroup of patients with recurrent loco-regional disease (with or without metastases) and in the subgroup of patients with metastatic disease without measured local recurrence at time of randomization.
3. Compare the safety and tolerability of the treatment regimens in the study population.

Tertiary

1. Compare Best % Tumor Specific Response in loco-regional disease and metastatic disease for the treatment regimens in the entire study population, in the subgroup of patients with recurrent loco-regional disease (with or without metastases) and in the subgroup of patients with metastatic disease without measured local recurrence at time of randomization.

Study Design:
Randomized, placebo controlled, double blind study.

Number of Patients (planned and enrolled):
Planned: < 170 evaluable patients. Enrolled: 167 patients.

Diagnosis and Main Criteria for Inclusion:
Measureable recurrent or metastatic squamous cell carcinoma of the head and neck (SCCHN) that had progressed within 190 days of platinum-based first line treatment for advanced SCCHN. Patients were not allowed to have received prior taxanes for the treatment of SCCHN.

Test Drug/ Batch No:
Pelareorep/160-10006, 160-10007, 160-11006, 160-11007, 160-12001, 160-12002, 160-12007

Reference Drug/ Batch No:
Placebo (0.9% Sodium chloride) prepared from investigators' local supplies.

Study Treatment Dose/Route/Regimen/Duration:

- Day 1 of each 21-day treatment cycle: 3 x 10^{10} 50% tissue culture infective dose ($TCID_{50}$) intravenous (IV) pelareorep/placebo, 175 mg/m^2 IV paclitaxel, and area under the curve (AUC) 5 mg/mL min IV carboplatin
- Days 2-5 of each treatment 21-day cycle: 3 x 10^{10} $TCID_{50}$ IV pelareorep/placebo

Patients received up to 8 cycles of combination treatment. Pelareorep/placebo monotherapy could be continued thereafter according to the same schedule (3 x 10^{10} $TCID_{50}$ IV on Days 2-5 of each treatment 21-day cycle) at the discretion of the investigator.
Dose delays and reductions were allowed for certain toxicities as defined in the protocol. Treatment was continued until disease progression, unacceptable toxicity, or patient or investigator decision to discontinue.

Criteria for Evaluation:

Safety: Nature, frequency, severity, and seriousness of adverse events; hematology and blood biochemistry laboratory results.
Efficacy: Best overall disease response reported by the investigator in End of Study case report form.

Statistical Methods:
Due to modifications to the study's original adaptive design and consultation with United States regulatory authorities, the study was terminated early and planned analyses were not conducted. For this reason, study analyses were limited to descriptive summaries of safety data and best overall disease response as reported by the investigator in the case report form.

Safety Results:

	Pelareorep (N=82) n (%)	Placebo (N=81) n (%)
Patients with at Least One AE in the Following Categories:		
Any TEAE	81 (98.8)	77 (95.1)
Grade 3 TEAE	60 (73.2)	53 (65.4)
Grade 4 TEAE	16 (19.5)	18 (22.2)
Serious TEAE	43 (52.4)	34 (42.0)
Treatment-Related TEAE	80 (97.6)	70 (86.4)
Treatment-Related Serious TEAE	23 (28.0)	19 (23.5)
Leading to Death	12 (14.6)	10 (12.3)
Leading to discontinuation of any study drug	27 (32.9)	16 (19.8)

AE: adverse event; TEAE: treatment-emergent adverse event

- AEs occurring with ≥ 10% higher frequency in the pelareorep arm were pyrexia (63.4% vs. 22.2%), anemia (54.9% vs. 44.4%), nausea (48.4% vs 30.9%), asthenia (41.5% vs. 27.2%), diarrhea (31.7% vs. 18.5%), leukopenia (19.5% vs. 4.9%), and chills (18.3% vs. 4.9%).
- The most common Grade ≥ 3 AEs in both treatment arms were anemia (pelareorep arm: 23.2%; placebo arm: 16.0%) and neutropenia (pelareorep: 14.6%; placebo: 13.6%).
- Treatment-related Grade ≥ 3 AEs occurring with ≥ 5% higher incidence in the pelareorep arm compared to the placebo arm were leukopenia (6.1% vs. 0%), fatigue (7.3% vs. 1.2%), and hyponatremia (6.1% vs. 0%).
- The most frequent AE leading to treatment discontinuation was asthenia (pelareorep arm: 6.1%; placebo arm: 0%).
- Serious adverse events occurring in > 2 patients in the pelareorep arm were febrile neutropenia (n=4 in each treatment arm), anemia (pelareorep arm: n=4; placebo arm: n=2), and sepsis (pelareorep: n=3; placebo arm: n=0).
- The proportions of patients experiencing newly occurring Grade ≥ 3 hematological abnormalities were similar in both arms with the exception of absolute neutrophil

counts (pelareorep arm: 25%; placebo arm: 10%) and white blood cell counts (pelareorep: 27%; placebo: 13%).

- The incidences of newly occurring Grade ≥ 3 blood chemistry results were similar between treatment arms.
- 10 patients in each treatment arm (12% per arm) died within 30 days of their last study treatment.

Efficacy Results:

Investigator-Assessed Best Overall Response	Pelareorep (N=82) n (%)	Placebo (N=81) n (%)
Complete Response	0	1 (1.2)
Partial Response	14 (17.1)	16 (19.8)
Stable Disease	43 (52.4)	27 (33.3)
Disease Control [1}	57 (69.5)	44 (54.3)
Disease Progression	16 (19.5)	23 (28.4)
Missing [2]	9 (11.0)	14 (17.3)

[1] Disease control = number of patients with complete response, partial response, or stable disease

[2] Patients for whom no best overall response was reported in the CRF were counted as missing.

Conclusions:

Overall, the safety data collected in this study are in keeping with the addition of an active agent to a combination regimen and the known safety profile of pelareorep. Efficacy data collected in this truncated trial are limited but do not rule out the potential for efficacy in this setting.

Date of Report: 5 May 2022