1. TITLE PAGE

ADDENDUM NUMBER 1

CLINICAL STUDY REPORT

STUDY TITLE: A RANDOMISED PHASE II OPEN-LABEL STUDY WITH A PHASE IB SAFETY LEAD-IN COHORT OF ONCOS-102, AN IMMUNE-PRIMING GM-CSF CODING ONCOLYTIC ADENOVIRUS, AND PEMETREXED/CISPLATIN IN PATIENTS WITH UNRESECTABLE MALIGNANT PLEURAL MESOTHELIOMA

Test Product: ONCOS-102

Sponsor's Responsible Medical Officer: Dr Lone Ottesen MD
Sponsor: Targovax OY
Sponsor address: Vollsveien 19, 1366 Lysaker, Norway

Principal Investigator: Luis Paz-Ares MD
Principal Investigator affiliation: Servicio Oncología Médica, Edificio Maternidad 2ª Planta, Hospital 12 de Octubre, Avda. Andalucía s/n, 28041-Madrid, Spain

Sponsor's Signatory: Dr Lone Ottesen MD, Chief Medical Officer

DocuSigned by:
Lone Ottesen
Signer Name: Lone Ottesen
Signing Reason: I approve this document
Signing Time: 25-Mar-2022 | 8:23:39 AM CET
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Date, Signature

Protocol Number: ONCOS C719 **EudraCT Number:** 2015-005143-13

Study Initiation Date (First Patient First Treatment): 30 June 2016
Study Completion Date (Last Patient 21-Month Follow-up): 28 January 2021
Follow-up Data for Addendum number 1 (End of Survival follow-up): 11 November 2021

Study Phase: Phase II with a Phase Ib safety lead-in cohort

This study was conducted in compliance with International Council for Harmonisation (ICH) Good Clinical Practice (GCP), including the archiving of essential documents.

Final 1.0, 23 March 2022
Addendum 1 to CSR, final 1.0, 25 May 2021

CONFIDENTIAL

REASON FOR ADDENDUM

At the time of completion of the Clinical Study Report (CSR), dated 25 May 2021, 21-months follow-up data was collected and analyzed. The analysis revealed that survival data were still maturing. Final follow-up data has therefore been collected and data up to 30-months (when all patients have been in the study for at least 30 months) is reported in this addendum.

2. SYNOPSIS

Name of Sponsor/Company: Targovax OY
Name of Finished Product: Not applicable
Name of Active Ingredient: ONCOS-102
TITLE OF STUDY: A randomised Phase II open-label study with a Phase Ib safety lead-in cohort of ONCOS-102, an immune-priming GM-CSF coding oncolytic adenovirus, and pemetrexed/cisplatin in patients with unresectable malignant pleural mesothelioma (Protocol Number: ONCOS C719; EudraCT Number: 2015-005143-13)
PRINCIPAL/COORDINATING INVESTIGATOR NAME, NUMBER OF STUDY CENTRES AND COUNTRIES: No new information
PUBLICATION (REFERENCES): None
STUDY PERIOD: Follow-up data for Addendum Number 1 (End of Survival follow-up)**:** 11 November 2021 Since all populations have reached median overall survival no further follow-up data will be collected**.**
PHASE OF DEVELOPMENT: No new information
BACKGROUND AND RATIONALE FOR THE STUDY: No new information
OBJECTIVES: No new information
METHODOLOGY: No new information
NUMBER OF SUBJECTS (planned and analysed): No new information
DIAGNOSIS AND MAIN CRITERIA FOR INCLUSION AND EXCLUSION: No new information
TEST PRODUCT, DOSE, MODE OF ADMINISTRATION, BATCH NUMBERS: No new information
DURATION OF TREATMENT: No new information
CONTROL PRODUCT, DOSE, MODE OF ADMINISTRATION, BATCH NUMBER(S): No new information
ENDPOINTS: No new information
STATISTICAL METHODS: No new information
SUMMARY OF RESULTS AND CONCLUSIONS: ***Efficacy Results:*** <u>Secondary Efficacy Endpoints: Progression-Free Survival and Overall Survival</u> Final survival follow-up information since the 21-months follow-up analysis (CSR dated 25 May 2021) has been collected. The 30-months follow-up analysis (when all patients have been in the study for at least 30 months) is summarised below. <u>Progression-Free Survival (PFS)</u> Since data cut-off for the 21-months analysis no additional patients have progressed and three patients are still censored. With the exception of maximum overall Progression-Free survival time, PFS data were unchanged.

Overall Survival (OS)
At the time of the 30-month follow-up analysis (when all patients had been in the study for at least 30 months) seven patients were still alive (five in the Experimental group and two in the Control group). Three patients have died since the 21-month analysis: One in the Experimental group and two in the Control group.

The latest available data available for OS are summarised below.

Overall survival rate for the Intent-to-Treat (ITT) population was calculated at 30 months as 34.3% (95% confidence interval [CI]: 14.9, 54.8) and 18.2% (95% CI: 2.9, 44.2) in the Experimental and Control Group, respectively.
For chemotherapy naïve (first-line) patients, 30-month survival rate was 34.1% (95% CI: 9.1, 61.6) and 0.0% in the Experimental and Control Group, respectively. For chemotherapy non-naïve patients, 30-month survival rate was 33.3% (95% CI: 7.8, 62.3) and 40.0% (95% CI: 5.2, 75.3) in the Experimental and Control Group, respectively.

For patients in the Phase II randomised part of the study only, overall survival rate at 30 months was 34.3% (95% CI: 11.6, 58.7) and 18.2% (95% CI: 2.9, 44.2) in the Experimental and Control Group, respectively.
For chemotherapy naïve (first-line) patients, 30-month survival rate was 33.3% (95% CI: 5.6, 65.8) and 0.0% in the Experimental and Control Group, respectively. For chemotherapy non-naïve patients, 30-month survival rate was 33.3% (95% CI: 4.6, 67.6) and 40.0% (95% CI: 5.2, 75.3) in the Experimental and Control Group, respectively.

Median OS (mOS) for the ITT population was 16.6 months (95% CI: 5.0, 30.4) in the Experimental Group and 18.3 months (95% CI: 3.1, 28.9) in the Control Group.
For chemotherapy naïve (first-line) patients, mOS was 20.3 months (95% CI: 6.3, NA) in the Experimental Group and 13.5 months (95% CI: 3.1, 22.4) in the Control Group.
For chemotherapy non-naïve patients, mOS was 10.4 months (95% CI: 4.3, 31.5) in the Experimental Group and 28.9 months (95% CI: 3.0, NA) in the Control Group.

For patients in the Phase II randomised part of the study, only mOS was 19.3 months (95% CI: 4.6, NA) in the Experimental Group and 18.3 months (95% CI: 3.1, 28.9) in the Control Group.
For chemotherapy naïve (first-line) patients, mOS was 25.0 months (95% CI: 1.4, NA) in the Experimental Group and 13.5 months (95% CI: 3.1, 22.4) in the Control Group.
For chemotherapy non-naïve patients, mOS was 14.4 months (95% CI: 4.5, NA) in the Experimental Group and 28.9 months (95% CI: 3.0, NA) in the Control Group.

Conclusions:
At the time of the final 30-month analysis, there were still three patients who had not progressed, and seven patients still alive. The median PFS (mPFS) was unchanged at this update, whereas the maximum individual PFS was extended with the longer follow-up. Additional survival follow-up information allowed 30-months survival rate to be calculated. In addition, mOS was calculated for all populations, including the chemotherapy naïve (first-line) patients in the Experimental group and the non-chemotherapy naïve patients in the Control group. Therefore, no further survival data will be collected.

Efficacy was a secondary endpoint in this study and the study was not dimensioned to detect statistically significant differences on efficacy endpoints. Of note, this additional follow-up analysis strengthens a trend towards extended survival in first-line chemotherapy-naïve patients who receive ONCOS-102 in addition to standard of care chemotherapy.

DATE AND VERSION OF THIS REPORT:
Final 1.0, 23 March 2022 (Addendum 1 to CSR Final 1.0, 25 May 2021)