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Annual Report to the Environmental Protection Agency and Ministry of Primary Industries (NZ)

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Table of Contents

1 List of Abbreviations

AE	Adverse Event
CNS	Clinical Network Services
EPA	Environmental Protection Agency
GMO	Genetically Modified Organism
MPI	Ministry of Primary Industries
NZ	New Zealand
OGTR	Office of the Gene Technology Regulator (Australia)
SAE	Serious Adverse Event
SIV	Site Initiation Visit
VIG	Vaccinia Immunoglobulin

2 Introduction

In accordance with Control 7 of the "EPA-MPI compliance expectations for APP202601 controls". *The New Zealand sponsor must submit a report that shows compliance with the above controls, to the EPA and MPI, six months after the commencement of the Phase 3 clinical trial, then on or before 30 June every year thereafter until the conclusion of the Phase 3 clinical trial*.

This is the fourth annual report to the Environmental Protection Agency (EPA) and Ministry of Primary Industries (MPI) regarding the Genetically Modified Organism (GMO) "Pexa-Vec", approved for use in a clinical trial on the 27th October 2015. This report outlines a summary of the evidence/information demonstrating compliance provided to the EPA and MPI, for the period of approximately 12 months after the third annual report submitted on the 04th June 2019.

3 Compliance Measures

All appropriate personnel have been trained in the handling of this GMO product in accordance with Controls 1, 2 and 3 (records can be provided to the EPA on request). In addition, according to Control 1 (Note 1), the date(s) de-identified trial participants were intratumorally administered with Pexa-Vec, including the name of the practitioner who administered Pexa-Vec and where the administration occurred (trial site), has been recorded in a master checklist. The signed master checklist can be provided to the EPA and MPI on request. This is listed on each IT injection preparation and administration sheet and the master checklist will be the site delegation log which lists who is registered to perform the study and their roles/responsibilities.

In accordance with Control 5, there have been no occurrences of Pexa-Vec-induced adverse effects resulting from confirmed events of Pexa-Vec transmission from Pexa-Vec treated individuals to untreated individuals or animals, notifiable to the EPA/MPI. Standard safety blood samples as per the protocol are sent to a central lab in Singapore.

4 Adverse Events

During this reporting period (30th May 2019 to 17th June 2020), there have been 0 patients treated with Pexa-Vec, giving a total of 25 patients treated since the trial commenced.

There have been no reports of AEs/SAEs resulting from confirmed events of transmission to date and there is no requirement under the EPA controls to report AE/SAEs that do not result in transmission. Treatment-emergent treatment-related SAE listings are available on request.

No transmission to other persons or animals have been reported to date. All patients were given biohazard containers and trained on pustule management in accordance with EPA-MPI controls. The development of pustules following Pexa-Vec administration is deemed expected. No other concerns have been noted.

In accordance with Control 6, adequate stocks (at least 2 doses) of Vaccinia Immunoglobulin (VIG) and cidofovir, within their expiry dates, are stored at the Auckland clinical trial site and will be for the duration of the trial. Practically speaking, this equates to 12 vials of VIG where 8.4 vials are needed for a 70 kg person. Therefore, 12 vials would cover one dose for a large or average person and 2 doses for small (up to 50 kg) patients. Two vials of cidofovir should equate to 2 doses.

Currently, as of 17th June 2020, there are no remaining vials of VIG, cidofovir and Pexa-Vec at the site.

On 02 August 2019, the trial was recommended to be discontinued per the recommendation of the IDMC. The IDMC identified no new safety risks associated with Pexa-Vec treatment, however, based their decision on a pre-planned futility analysis where the interim results suggested that the study was not going to meet the primary objective of improving OS by the time of the final analysis. Hence, this is the last report to be submitted.