CLINICAL TRIAL REPORT ERRATA

A Prospective, Randomized, Double-Blind, Placebo-Controlled Phase 3 Study of VGX-3100 Delivered Intramuscularly Followed by Electroporation With CELLECTRA™ 5PSP for the Treatment of HPV-16 and/or HPV-18 Related High-Grade Squamous Intraepithelial Lesion (HSIL) of the Cervix
REVEAL 1 Trial
(Randomized Evaluation of VGX-3100 and Electroporation for the Treatment of Cervical HSIL)

PROTOCOL NUMBER
HPV-301

Errata Date and Version: 17 NOV 2023, 2.1

CONFIDENTIAL

1. Reason for the Errata

This errata describes a correction to the VGX-3100 HPV-301 Clinical Trial Report (dated 31 Mar 2023). Errors were identified that impact seven (7) summaries (Table 14.2.3.2, Table 14.2.3.3, Table 14.2.3.5, Table 14.2.7.1, Table 14.2.7.2, Table 14.2.7.3, and Table 14.2.7.4) that were provided to Inovio and used to develop the Clinical Trial Report for the HPV-301 study. Many of the estimates and confidence intervals on these tables were updated, and the interpretation of some of the results also changed due to updated data in the tables of TLFs.

2. Impact to the Clinical Trial Report and Synopsis

The impact to the Clinical Trial Report and Synopsis is minor and impacts interpretation of 2 secondary efficacy endpoints.

Virologic clearance of HPV-16 and/or HPV-18 from noncervical anatomic locations at Week 36 (Table 14.2.7.1, Table 14.2.7.2, and Table 14.2.7.3).

Virologic clearance of HPV-16 and/or HPV-18 from noncervical anatomic locations at Week 36 by history of exposure to prophylactic HPV vaccines (Table 14.2.7.4).

In three (3) tables (Table 14.2.3.2, Table 14.2.3.3, and Table 14.2.3.5), many of the estimates and confidence intervals on these tables were updated, however, the interpretation of the results did not change due to the updated data in the tables.

3. Changes to the Appendices and the Clinical Trial Report Table of Contents

In Section 14.2 of the Clinical Trial Report, Table 14.2.3.2, Table 14.2.3.3, Table 14.2.3.5, Table 14.2.7.1, Table 14.2.7.2, Table 14.2.7.3, and Table 14.2.7.4 have been updated and the same tables have been updated in the Table of Contents.

4. Changes to the Clinical Trial Report Body and Synopsis

4.1 Changes to the Clinical Trial Report Synopsis

Changes from the original text are noted below - ~~strike-through text~~ indicates deleted text and ***bold italics*** text indicates newly added text.

Secondary Efficacy Endpoints

Virologic clearance of HPV-16 and/or HPV-18 from noncervical anatomic locations at Week 36**:** In the ITT Population, the percentage of responders (i.e., subjects with virologic clearance of HPV-16 and/or HPV-18 from noncervical anatomic locations at Week 36) was 20.3% in the VGX-3100 + EP group as compared with ~~9.5~~ ***11.1***% in the placebo + EP group. ~~In the mITT Population, the percentage of responders was 24.8% in the VGX-3100 + EP group as compared with 10.7% in the placebo + EP group.~~ The lower bound of the 95% CI for the difference in percentage of responders in the ~~m~~ITT Population ***did not*** exceed~~ed~~ zero (0), ***providing no evidence for efficacy of VGX-3100 + EP compared with placebo + EP in achieving virologic clearance of HPV-16 and/or HPV-18 from noncervical anatomic locations at Week 36 in the ITT Population.*** ~~indicating superior efficacy of VGX-3100 + EP in achieving virologic clearance of HPV-16 and/or HPV-18 from noncervical anatomic locations at Week 36 in mITT Population.~~ The results of the ***mITT and*** PP Population supported the ~~m~~ITT Population results.

Subgroup Analysis

Subgroup analyses of the primary and secondary efficacy endpoints were conducted by history of exposure to prophylactic HPV vaccines (yes, no). Histopathological regression of cervical HSIL and virologic clearance of HPV-16 and/or HPV-18 at Week 36 were also assessed by stratification factors.

Among subjects with no history of exposure to prophylactic HPV vaccine, VGX-3100 + EP showed superior efficacy as compared with placebo + EP in the following efficacy measures:

- Histopathological regression of cervical HSIL and virologic clearance of HPV-16 and/or HPV-18 at Week 36
- Virologic clearance of HPV-16 and/or HPV-18 at Week 36
- Histopathological regression of cervical HSIL to normal and virologic clearance of HPV-16 and/or HPV-18 at Week 36
- Histopathological regression of cervical HSIL to normal at Week 36**.**
- ~~Virologic clearance of HPV-16 and/or HPV-18 from noncervical anatomic locations at Week 36.~~

There was no evidence for efficacy of VGX-3100 + EP as compared with placebo + EP ~~The percentage of responders for VGX-3100 + EP and placebo + EP was similar~~ with respect to ***the*** following efficacy measures, irrespective of previous exposure to prophylactic HPV vaccine:

- Histopathological regression of cervical HSIL at Week 36
- Nonprogression of cervical HSIL to cervical carcinoma at Week 36~~.~~
- ***Virologic clearance of HPV-16 and/or HPV-18 from noncervical anatomic locations at Week 36.***

4.2 Changes to the Clinical Trial Report Body

Changes from the original text are noted below - ~~strike-through text~~ indicates deleted text and ***bold italics*** text indicates newly added text.

6.2 Secondary Efficacy Results

6.2.2 Virologic Clearance of HPV-16 and/or HPV-18 at Week 36

The percentage of responders in each treatment group based on the virologic clearance of HPV-16 and/or HPV-18 at Week 36 is summarized for the ITT, mITT, and PP Populations in Table 6-4.

For all ***three (***3***)*** populations, the percentage of responders (subjects with virologic clearance of HPV-16 and/or HPV-18 at Week 36) was higher in the VGX-3100 + EP group as compared with the placebo + EP group. The lower bound of the 95% CI for the difference in percentage of responders exceeded zero (0), ***providing*** ~~indicating~~ ***evidence for*** superior efficacy of VGX-3100 + EP in achieving virologic clearance of HPV-16 and/or HPV-18 at Week 36.

Table 6-1: Virologic Clearance of HPV-16 and/or HPV-18 at Week 36

	VGX-3100 + EP	**Placebo + EP**	**Difference in Percentage (95% CI)[a] (VGX-3100 + EP) – (Placebo + EP)**
ITT Population	138	63	
Subjects contributing analysis data	138	63	
Responders, n (%)[b]	47 (34.1)	10 (15.9)	18.2 (5.1, 29.4)
mITT Population	134	63	
Subjects contributing analysis data	13***0***~~1~~	62	
Responders, n (%)[b]	47 (3***6***~~5~~.***2***~~9~~)	10 (16.1)	***20***~~19~~.***0***~~7~~ (6.***6***~~4~~, 31.***6***~~2~~)
PP Population	124	60	
Subjects contributing analysis data	12***1***~~2~~	60	
Responders, n (%)[b]	46 (3***8***~~7~~.***0***~~7~~)	10 (16.7)	21.***3***~~0~~ (7.***5***~~2~~, 33.***3***~~0~~)

Abbreviations: CI: Confidence Interval; EP: Electroporation; HPV: Human Papilloma Virus; ITT: Intent-to-Treat, mITT: Modified Intent-to-Treat; n: Number of Subjects; PP: Per Protocol.

a: 95% CI was based on the method of Miettinen and Nurminen.

b: A responder was defined as a subject with no evidence of HPV-16 and/or HPV-18 at the Week 36 timeframe. Also, a subject who underwent excision or whose cervix was biopsied at any time on or after her initial dose and before her Week 36 timeframe was considered a nonresponder. The efficacy timeframe is defined by HPV testing at any time starting from 14 days prior to the protocol-specified target date of Week 36. The first tissue removal sample within the timeframe determined the histology endpoint. The most recent HPV clearance result prior to tissue removal, which included results from the same date, within the timeframe determined the HPV clearance endpoint.

Source: Table 14.2.3.1, Table 14.2.3.2, and Table 14.2.3.3; Listing 16.2.3.1.3.

A ~~The~~ sensitivity analysis for virologic clearance of HPV-16 and/or HPV-18 at Week 36 is summarized for the PP Population in Table 14.2.3.5.

The percentage of responders (subjects with virologic clearance of HPV-16 and/or HPV-18 at Week 36) was higher in the VGX-3100 + EP group (4***3***~~1~~.***8***~~0~~%) as compared with the placebo + EP group (1***8***~~6~~.***3***~~7~~%). The difference in percentage of responders (95% CI) was 2***5***4.***5***~~3~~ (1***1***~~0~~.***2***4, 3***7***~~6~~.***7***~~3~~). The lower bound of the 95% CI for the difference in percentage of responders exceeded zero (0), ***providing evidence for*** ~~indicating~~ superior efficacy of VGX-3100 + EP in achieving virologic clearance of HPV-16 and/or HPV-18 at Week 36.

6.2.6 Virologic Clearance of HPV-16 and/or HPV-18 from Noncervical Anatomic Locations at Week 36

The percentage of responders in each treatment group based on the virologic clearance of HPV-16 and/or HPV-18 from noncervical anatomic locations at Week 36 is summarized for the ITT, mITT, and PP Populations in Table 6-8.

For all ***three (***3***)*** populations, the percentage of responders (subjects with virologic clearance of HPV-16 and/or HPV-18 from noncervical anatomic locations at Week 36) was higher in the VGX-3100 + EP group as compared with the placebo + EP group. ~~For the mITT and PP Populations, the lower bound of~~ ***The lower bound of the*** 95% CI for the difference in percentage of responders ***did not exceed zero (0),*** ~~exceeded zero (0), indicating superior efficacy of VGX-3100 + EP~~ ***providing no evidence for efficacy*** in achieving virologic clearance of HPV-16 and/or HPV-18 from noncervical anatomic locations at Week 36 in these populations.

Table 6-2: Virologic Clearance of HPV-16 and/or HPV-18 from Noncervical Anatomic Locations at Week 36

	VGX-3100 + EP	Placebo + EP	Difference in Percentage (95% CI)[a] (VGX-3100 + EP) – (Placebo + EP)
ITT Population	138	63	
Subjects contributing analysis data	138	63	
Responders, n (%)[b]	28 (20.3)	~~7~~***6*** (~~11~~***19***.~~1~~***15***)	~~9~~***10***.~~2~~***28*** (~~-2~~***-20***.~~4~~***45***, ~~1~~***18***~~2~~***20***.~~8~~***81***)
mITT Population	134	63	
Subjects contributing analysis data	11~~0~~***03***	5~~2~~***26***	
Responders, n (%)[b]	28 (2~~5~~***54***.~~5~~***58***)	~~7~~***6*** (1~~3~~***30***.~~5~~***57***)	1***24***.~~0~~***01*** (~~-~~1.~~8~~***83***, 2~~3~~***34***.~~6~~***69***)
PP Population	124	60	
Subjects contributing analysis data	10~~3~~***37***	5~~1~~***15***	
Responders, n (%)[b]	2~~6~~***67*** (25.2)	~~7~~***6*** (1~~3~~***30***.~~7~~***79***)	1***14***.~~5~~***53*** (~~-2~~***-21***.~~5~~***53***, 2~~3~~***35***.~~4~~***45***)

Abbreviations: CI: Confidence Interval; EP: Electroporation; HPV: Human Papilloma Virus; ITT: Intent-to-Treat; mITT: Modified Intent-to-Treat; n: Number of Subjects; PP: Per Protocol.

a: 95% CI was based on the method of Miettinen and Nurminen.

b: A responder was defined as a subject with no evidence of HPV-16 and/or HPV-18 on specimens from noncervical anatomic locations at the Week 36 timeframe. The efficacy timeframe was defined by HPV testing at any time starting from 14 days prior to the protocol-specified target date of Week 36. The first HPV clearance result within the timeframe determined the endpoint.

Source: Table 14.2.7.1, Table 14.2.7.2, and Table 14.2.7.3; Listing 16.2.3.1.3.

6.3 Subgroups

6.3.7 Virologic Clearance of HPV-16 and/or HPV-18 from Noncervical Anatomic Locations at Week 36

The percentage of responders in each treatment group based on virologic clearance of HPV-16 and/or HPV-18 from noncervical anatomic locations at Week 36 by history of exposure to prophylactic HPV vaccines is summarized for the ITT Population in Table 14.2.7.4.

Among subjects with history of exposure to prophylactic HPV vaccine, 21.4% ***(3)*** subjects in the VGX-3100 + EP group and 33.3% ***(1)*** subject in the placebo + EP group were considered responders. The difference in percentage of responders (95% CI) was -11.9 (-63.7, 29.6). The ***lower bound of the*** 95% CI did not exclude zero (0), ***providing no evidence for*** ~~indicating similar~~ ***superior*** efficacy ~~of VGX-3100 + EP and placebo + EP~~ in ***achieving*** ~~causing~~ virologic clearance of HPV-16 and/or HPV-18 from noncervical anatomic locations at Week 36 in subjects who had previously received prophylactic HPV vaccine.

Among subjects with no history of exposure to ***a*** prophylactic HPV vaccine, 20.2% ***(25)*** subjects in the VGX-3100 + EP group ***(N=138)*** and ***10***~~8~~.***0***~~3~~% ***(6)*** subjects in the placebo + EP group ***(N=63)*** were considered responders. The difference in percentage of responders (95% CI) was 1***0***~~1~~.***2***~~8~~ (***-1***~~0~~.***6***~~5~~, 2***0***~~1~~.***1***4). The lower bound of the 95% CI ***did not*** exceed~~ed~~ zero (0), ~~indicating superior efficacy of VGX-3100 + EP in causing~~ ***providing no evidence for efficacy in achieving*** virologic clearance of HPV-16 and/or HPV-18 from noncervical anatomic locations at Week 36 in subjects who had previously not received prophylactic HPV vaccine.

6.8 Efficacy Conclusion

6.8.2 Secondary Efficacy Endpoints

Virologic clearance of HPV-16 and/or HPV-18 from noncervical anatomic locations at Week 36: In the ITT Population, the percentage of responders (i.e., subjects with virologic clearance of HPV-16 and/or HPV-18 from noncervical anatomic locations at Week 36) was 20.3% in the VGX-3100 + EP group as compared with ***11***~~9~~.***1***~~5~~% in the placebo + EP group. ~~In the mITT Population, the percentage of responders was 24.8% in the VGX-3100 + EP group as compared with 10.7% in the placebo + EP group.~~ The lower bound of the 95% CI for the difference in percentage of responders in the ~~m~~ITT Population ***did not*** exceed~~ed~~ zero (0), ***providing no evidence for superior efficacy of VGX-3100 + EP compared with placebo + EP in achieving virologic clearance of HPV-16 and/or HPV-18 from noncervical anatomic locations at Week 36 in the ITT Population.*** ~~indicating superior efficacy of VGX-3100 + EP in achieving virologic clearance of HPV-16 and/or HPV-18 from noncervical anatomic locations at Week 36 in mITT Population.~~ The results of the ***mITT and*** PP Population supported the ~~m~~ITT Population results.

6.8.3 Subgroup Analysis

Subgroup analyses of the primary and secondary efficacy endpoints were conducted by history of exposure to prophylactic HPV vaccines (yes, no). Histopathological regression of cervical HSIL and virologic clearance of HPV-16 and/or HPV-18 at Week 36 were also assessed by stratification factors.

Among subjects with no history of exposure to prophylactic HPV vaccine, VGX-3100 + EP showed superior efficacy as compared with placebo + EP in the following efficacy measures:

- Histopathological regression of cervical HSIL and virologic clearance of HPV-16 and/or HPV-18 at Week 36

- Virologic clearance of HPV-16 and/or HPV-18 at Week 36
- Histopathological regression of cervical HSIL to normal and virologic clearance of HPV-16 and/or HPV-18 at Week 36
- Histopathological regression of cervical HSIL to normal at Week 36**.**
- ~~Virologic clearance of HPV-16 and/or HPV-18 from noncervical anatomic locations at Week 36.~~

There was no evidence for efficacy of VGX-3100 + EP as compared with placebo + EP ~~The percentage of responders for VGX-3100 + EP and placebo + EP was similar~~ with respect to ***the*** following efficacy measures, irrespective of previous exposure to prophylactic HPV vaccine:

- Histopathological regression of cervical HSIL at Week 36
- Nonprogression of cervical HSIL to cervical carcinoma at Week 36~~.~~
- ***Virologic clearance of HPV-16 and/or HPV-18 from noncervical anatomic locations at Week 36.***

12 Discussion and Conclusion

12.1 Discussion

Up to 13,000 women in the US alone are diagnosed with cervical cancer each year, with an estimated 4,120 deaths [4]. HPV-16 is the most common high-risk genotype and combined with HPV-18 these two (2) genotypes are estimated to cause about 70% of all cervical cancers [5, 6]. VGX-3100 is being developed as a nonsurgical therapeutic option for the precancerous precursor to cervical cancer, cervical HSIL, and the underlying pathogenic HPV infection. VGX-3100 contains plasmids that encode HPV-16 E6/E7 and HPV-18 E6/E7 antigens. VGX-3100 is delivered *in vivo* using the CELLECTRA™ 5PSP EP device.

This Phase 3 clinical trial, HPV-301, employed a prospective, randomized, double-blind, placebo-controlled design to demonstrate the efficacy, safety, and tolerability of VGX-3100 followed by EP in women with cervical HSIL associated with HPV-16 and/or HPV-18. The clinical trial consisted of a screening period (up to 10 weeks), treatment and follow-up period (36 weeks), and long-term follow-up period (52 weeks). The total duration of participation in the clinical trial for each subject was up to 98 weeks.

A total of 201 subjects were randomly assigned to receive either 6 mg (in 1 mL) VGX-3100 (138 subjects) or placebo (63 subjects), IM followed by EP. Subjects were randomly assigned in a stratified manner according to: 1) CIN severity observed in the biopsy specimens at screening (CIN2 vs. CIN3), 2) BMI category (≤25 kg/m^2 vs. >25 kg/m^2) on Day 0, and 3) age category (<25 years vs. ≥25 years) on Day 0. The first clinical trial treatment was administered on Day 0, the second at Week 4, and the third (final) at Week 12.

The mean age of the subjects was 31.5 years. Majority of the subjects (77.1%) were White, and not Hispanic or Latino (82.6%). The mean BMI was 25.07 kg/m^2. The demographic and baseline characteristics were similar across both the treatment groups.

Most subjects in both treatment groups received all 3 doses of clinical trial treatment with EP: 93.5% subjects in the VGX-3100 + EP group and 96.8% subjects in the placebo + EP group.

The primary efficacy endpoint was no evidence of cervical HSIL on histology (i.e., biopsy or excisional treatment) and no evidence of HPV-16 and/or HPV-18 in cervical samples by type-specific HPV testing at Week 36 visit. In the ITT Population, the percentage of responders was 22.5% in the VGX-3100 + EP group as compared with 11.1% in the placebo + EP group. The difference between the responders in the two (2) groups was not statistically significant (one-sided p-value = 0.029). In the mITT Population, the percentage of responders was 23.7% in the VGX-3100 + EP group as compared with 11.3% in the placebo + EP group. The difference between the responders in the two (2) groups was statistically significant (one-sided p-value = 0.022). Of the 4 subjects excluded from the mITT Population (VGX-3100 + EP group), two (2) subjects had not received any IP and two (2) other subjects had received only one (1) dose of the IP. The results of the PP Population and the sensitivity analysis in the PP Population supported the mITT Population results.

Results for the secondary endpoint of histopathological regression of cervical HSIL at Week 36 were similar to those of the primary endpoint. For other secondary efficacy endpoints including virologic clearance of HPV-16 and/or HPV-18 at Week 36; histopathological regression of cervical HSIL to normal and virologic clearance of HPV-16 and/or HPV-18 at Week 36; ***and*** histopathological regression of cervical HSIL to normal at Week 36~~; and virologic clearance of HPV-16 and/or HPV-18 from noncervical anatomic locations at Week 36~~, the percentage of responders was higher in the VGX-3100 + EP group as compared with placebo + EP group and the lower bound of the 95% CI of the difference between responder percentages ~~in the two (2)~~ groups generally exceeded zero (0) ***providing evidence for superior efficacy of VGX-3100 + EP group compared with the placebo + EP group***. For the secondary endpoint of nonprogression of cervical HSIL to cervical carcinoma at Week 36 ***and virologic clearance of***

HPV-16 and/or HPV-18 from noncervical anatomic locations at Week 36, the lower bound of the 95% CI for the difference in percentage of responders in the ITT Population did not exceed zero (0), providing no evidence for efficacy in achieving efficacy measures for both ~~treatment groups showed similar response rates~~. ***The results of the mITT and PP Population supported the ITT Population results for both efficacy measures.***

In subgroup of subjects with no history of exposure to prophylactic HPV vaccine, the response rate in VGX-3100 + EP was higher as compared with placebo + EP for the efficacy endpoints of histopathological regression of cervical HSIL and virologic clearance of HPV-16 and/or HPV-18 at Week 36; virologic clearance of HPV-16 and/or HPV-18 at Week 36; histopathological regression of cervical HSIL to normal and virologic clearance of HPV-16 and/or HPV-18 at Week 36; ***and*** histopathological regression of cervical HSIL to normal at Week 36~~; and virologic clearance of HPV-16 and/or HPV-18 from noncervical anatomic locations at Week 36~~. The percentage of subjects with histopathological regression of cervical HSIL and virologic clearance of HPV-16 and/or HPV-18 at Week 36 was higher in the VGX-3100 + EP group as compared with the placebo + EP group for all stratification combinations. The difference in percentage of responders was highest (5.8%) in subjects who were ≥25 years of age and had BMI ≤25 kg/m^2 and CIN2.

The impact of prior miRNA and DNA methylation, colposcopy, cytology, and HPV result, baseline immunoscore, and baseline biomarker status on histopathologic regression of cervical HSIL and virologic clearance of HPV-16 and/or HPV-18 at Week 36 was evaluated. At the individual subject level, Day 0 and Week 8 miRNA and Day 0 and Week 15 DNA methylation values did not significantly influence the odds of the response, except the Day 0 methylated NKAIN2, for which the odds of response increased as the Day 0 NKAIN2 increased. Baseline immunoscore also did not significantly influence the odds of the response. The odds of achieving a response at Week 36 were higher if the prior colposcopy and cytology result showed an improvement as compared with no change or possible progression. The odds of achieving a response at Week 36 were also higher if HPV had cleared from the cervical lesions at Weeks 8, 15, and 28. VGX-3100 + EP demonstrated superior efficacy for histopathological regression of cervical HSIL and virologic clearance of HPV-16 and/or HPV-18 at Week 36 in subjects with baseline biomarker status positive when compared with placebo + EP but did not have the same impact in subjects with baseline biomarker status negative. The percentages of subjects with no evidence of cervical HPV-16 and/or HPV-18 at Week 62 and Week 88 were higher in the VGX-3100 + EP group as compared with the placebo + EP group; however, the difference between the groups decreased over time.

Patient-reported outcome measures (SF-36, EQ-5D-5L, Week 40 QoL responses) were overall similar in the VGX-3100 + EP and placebo + EP groups.

VGX-3100 was immunogenic as seen from the geometric means of the reciprocal endpoint titers, which were several-fold higher in the VGX-3100 + EP group as compared with the placebo + EP group at Weeks 8, 15, and 36 for both HPV-16 E7 and HPV-18 E7. Anti-HPV-16 E6 and anti-HPV-18 E6 antibodies were not assayed. A notable increase from baseline was seen in the SFU/10^6 PBMCs of HPV-16 E6, HPV-16 E7, HPV-18 E6, HPV-18 E7, and related combinations in the VGX-3100 + EP group as compared with the placebo + EP group at all postbaseline timepoints (Weeks 8, 15, and 36). All parameters including CD8+CD137+perforin+, CD8+CD38+perforin+, and CD8+CD69+perforin+ showed an increase in the VGX-3100 + EP group indicating greater cellular immune responses (as measured by activated CD8+ T cells with lytic potential) on flow cytometry as compared with the placebo + EP group at Week 15. Changes from baseline to Week 36 in CD8+, CD103+, FoxP3+, and perforin+ cells in cervical tissue normal epithelium, normal stroma, CIN2/3 epithelium, and CIN2/3 stroma were small and generally similar between the treatment groups.

Device performance was evaluated using the number of successful and unsuccessful EP attempts. Most (>95%) EP attempts, in both VGX-3100 + EP and placebo + EP groups, were successful. The small number of unsuccessful attempts (4.1% and 3.1% in VGX-3100 + EP and placebo + EP groups, respectively) were most commonly due to Array problems or an error message received from the device.

Overall, IM injection of VGX-3100 or placebo followed by EP was well-tolerated by subjects with HPV-16 and/or HPV-18 associated HSIL of cervix. The safety findings were in-line with those seen with VGX-3100 and closely related DNA plasmid products. The TEAEs of injection-site pain, headache, fatigue, injection-site erythema, injection-site pruritus, myalgia, and injection-site swelling were most commonly reported during the clinical trial. Most TEAEs were CTCAE grade 1 or 2 in intensity. Most common TEAEs of grade ≥3 included injection-site pain and headache. One (1) subject died during the clinical trial on Day 450, 365 days after Dose 3 of VGX 3100 + EP due to the unrelated TEAE of pulmonary embolism. Through the clinical trial, no TEAEs related to abnormal laboratory results were reported. Vital signs and physical examination were found to be normal in most subjects and few AEs were reported due to abnormal vital signs or physical examination findings.

4.3 Changes to the Appendices

In Section 14.2 of the Clinical Trial Report, Table 14.2.3.2, Table 14.2.3.3, Table 14.2.3.5, Table 14.2.7.1, Table 14.2.7.2, Table 14.2.7.3, and Table 14.2.7.4 have been updated and are included here.

14.2 Efficacy Data

Number	Title
Table 14.2.3.2	Virologic Clearance of HPV-16 and/or HPV-18 at Week 36 mITT Population
Table 14.2.3.3	Virologic Clearance of HPV-16 and/or HPV-18 at Week 36 PP Population
Table 14.2.3.5	Virologic Clearance of HPV-16 and/or HPV-18 at Week 36 - Sensitivity Analysis PP Population
Table 14.2.7.1	Virologic Clearance of HPV-16 and/or HPV-18 from Noncervical Anatomic Locations at Week 36 ITT Population
Table 14.2.7.2	Virologic Clearance of HPV-16 and/or HPV-18 from Noncervical Anatomic Locations at Week 36 mITT Population
Table 14.2.7.3	Virologic Clearance of HPV-16 and/or HPV-18 from Noncervical Anatomic Locations at Week 36 PP Population
Table 14.2.7.4	Virologic Clearance of HPV-16 and/or HPV-18 from Noncervical Anatomic Locations at Week 36 by History of Exposure to Prophylactic HPV Vaccines ITT Population

5. Signature Page

STUDY TITLE: A Prospective, Randomized, Double-Blind, Placebo-Controlled Phase 3 Study of VGX-3100 Delivered Intramuscularly Followed by Electroporation With CELLECTRA™ 5PSP for the Treatment of HPV-16 and/or HPV-18 Related High-Grade Squamous Intraepithelial Lesion (HSIL) of the Cervix

STUDY NUMBER: HPV-301

I have read this report and confirm that to the best of my knowledge it accurately describes the results of the study.

Sponsor's Responsible Medical Officer:

SIGNATURE: DocuSigned by: _____ Date

Signer Name: Jeffrey Skolnik
Signing Reason: I approve this document
Signing Time: 17-Nov-2023 | 9:18:03 AM EST
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