Interim Results of the Extension Phase of a Phase I/IIa Trial of a Therapeutic CMV Vaccine Against Recurrent Glioblastoma (GBM)

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Background
- Cytomegalovirus (CMV) antigens are reported in >90% of GBMs
- "Foreign" tumor-associated viral antigens are inherently immunogenic
- gB and pp65 antigens are the most frequent CMV targets for CD4+ and CD8+ T-cells
  - CD8+ T cells are critical for killing of tumor cells
  - CD4+ effector memory (CCR7-CD45RA-) cells preferentially migrate to the tumor microenvironment and are critical for CD8+ T cell persistence and function
- Targeting CMV as a foreign viral antigen has the potential to harness, re-stimulate, and re-focus pre-existing anti-CMV immunity to clear CMV+ tumors
- VBI-1901 is a bivalent gB/pp65 enveloped virus-like particle (vLP) formulated with GM-CSF and given as an intradermal injection
- VBI-1901 is currently in a Phase I/IIa clinical trial in recurrent GBM patients

About VBI-1901
Rationally-designed vaccine immuno-therapeutic for CMV+ solid tumors

Schematic

Antibody Target
gB (CD4+), pp65 (CD8+)

T Cell Targets
Treatment of CMV+ solid tumors, notably glioblastoma

Target Indication
Targets multiple antigens, each with multiple epitopes, to promote broad immunity & avoid tumor escape

Rationale
Co-administered with GM-CSF via intradermal route

Phase I/IIa Trial Design
Two-part, multi-center, open-label, dose-escalation study of VBI-1901 in patients with recurrent GBM

PART A : Dose-Escalation Phase
Patient population: Recurrent GBM (any # of recurrences)

Study Arm 3: High Dose
10.0 µg + GM-CSF
N=6
VS.
Study Arm 2: Intermediate Dose
2.0 µg + GM-CSF
N=6

Study Arm 1: Low Dose
0.4 µg + GM-CSF
N=6

Outcome Measures : Part A & B
- Safety
- Immunogenicity: (1) T-cell immunity (gB, pp65), (2) serum anti-gB antibody titers, (3) other immune biomarkers
- Tumor and clinical responses: Based on MRIs and survival data
- Quality of life: Change from baseline

PART B: Extension Phase
Patient population: First Recurrent GBM

Study Arm 1: 10.0 µg + GM-CSF (i.d.)
N=10

Study Arm 2: 10.0 µg + GSK’s AS01b Adjuvant System (i.m.)
N=10

ClinicalTrials.Gov identifier: NCT03382977

Enrollment Status
As of Nov. 18, 2019
- Enrollment of 18 subjects across all dose levels in Part A completed in December 2018 – 0 dose-limiting toxicities (DLTs) were observed
  - Median age of enrolled patients was 57.5, 49.0, and 53.5 years in the Low-, Intermediate-, and High-Dose cohorts, respectively (range 39 – 66 years)
- Enrollment of 10 subjects in the Part B 10.0 µg + GM-CSF arm is ongoing – to-date four (4) patients have been enrolled
  - Median age of enrolled patients is 61.5 years (range 50 – 63 years)
- Karnofsky Performance Scale (KPS) score is similar across all cohorts in Part A and those enrolled to-date in Part B (80, 70, 85, and 85 in the Low-, Intermediate-, and High-Dose cohorts in Part A, and the patients enrolled in Part B, respectively)
- Initiation of enrollment of 10 subjects in the 10.0 µg + AS01b arm is expected around year-end 2019, subject to FDA acceptance of the amended protocol and investigational site institutional review board approvals

Impact of Vaccination on Tumor Response & CMV-Specific Immunity—Patient-Specific Responder Data

Table: Tumor Responders in High-Dose Cohort

<table>
<thead>
<tr>
<th>Subject</th>
<th>Available Data on Enrolled Subjects</th>
<th>Tumor Responders in High-Dose Cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subject 03</td>
<td>1 recurrence</td>
<td>Subject 04-002</td>
</tr>
<tr>
<td>Subject 04</td>
<td>1 recurrence</td>
<td>Subject 03-007</td>
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<tr>
<td>Subject 05</td>
<td>1 recurrence</td>
<td>Subject 03-006</td>
</tr>
<tr>
<td>Subject 06</td>
<td>1 recurrence</td>
<td>Subject 03-003</td>
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</tbody>
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Tumor Responses (Magnetic Resonance Imaging – MRI)

- ~33% reduction in tumor seen to-date
- Stable Disease (SD) based on 2 consecutive scans
- Presumed pseudo-progression based on 1st MRI
- Surgical resection to assess PD versus T cell infiltration/tumor necrosis
- ~60% reduction seen in Lesion 1
- Lesion 2 appeared after 4.5 months, defined PD per protocol, though patient was clinically stable
- ~60% reduction seen in Lesion 2 with associated cyst required surgical resection of lesions
- Initial tumor progression later presumed to be pseudo-progression due to subsequent tumor stabilization (atypical of rGBM)

ELISPOT T Cell Responses

CD8+ T Cell Responses

- Data not available

CD4+ Effector Memory T Cell Responses

- Data not available

Conclusions
- No dose-limiting toxicities (DLTs) or vaccine-related safety signals observed
- First patient enrolled in Part B had evidence of stable disease, with 33% tumor reduction to-date
- Robust CD8+ & CD4+ T cell responses induced in some patients receiving High (10µg) dose in both Parts A & B of trial
- Further characterization of baseline biomarkers and immunologic responses are ongoing to assess potential vaccine and tumor responders
- Correlations between immunological biomarkers and tumor/clinical responses will be refined as more patients are enrolled in Part B of the trial

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