**LOCOREGIONAL DISEASE CONTROL IN METASTATIC MELANOMA: EXPLORATORY ANALYSES FROM PHASE 2 TESTING OF INTRARESIDENTIAL ROSE BENGAL (PV-10)**

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Pre-Treatment Day 7 Week 8 Week 16

**RESULTS**

Number of PV-10 treatment cycles: mean of 1.8 per subject (median of 2 cycles)

Adverse Events were Generally Mild to Moderate Severity, Transient and Locoregional to the Injection Site (Table 2)

**Locoregional Blistering was Experienced by 40% of Subjects**

- 2% of subject experienced CTGA Grade 3 blisters, 10% Grade 2 and 1% Grade 3 (includes one report of possible Grade 1 “Transient” Phototoxicity)
- Typically presented as tense bullae within 7 days of PV-10 treatment
- Close agreement with no apparent relationship to sequence of PV-10 administration
- Generally resolved within 4 weeks with or without medication intervention

**Robust Response was Observed in Infected Lesions**

- Against HSV Targeted Lesions, 58% achieved 15% or 12% SD
- Per-subject response summarized in Table 3
- OR in 34 of 54 subjects (67%) when all tumors treated or only bystanders uninfected

**EXAMPLES OF CLINICAL RESPONSE – SINGLE TREATMENT**

**EXAMPLES OF CLINICAL RESPONSE – MULTIPLE TREATMENTS**

**EXPLANATORY ANALYSES**

Trends in OR and DFS Consistent Across Sub-Groups by Untreated Disease Burden

Table 4. (Table 4)

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**Clinical Evidence**

- Magnitude and duration of response inversely related to untreated tumor burden
- Blistering may be indicative of system general immunologic response
- Regression of untreated bystanders strongly correlated with OR of Target lesions
- Regression of other untreated Unrelated Disease observed in subjects with OR of Target lesions, 4% OR 1-year survival in Stage III(Ki67) subjects
- Enhanced survival to 30 observed with PV-10 in these subgroups (Med Rev 20; 49, 2010)
- All clinical evidence consistent with non-clinical data demonstrating tumor-specific immunologic response
- Clinical study underway at F. Lee Mothet Cancer Center to elucidate immunologic signaling (NCT01640999)

**Non-Clinical Evidence**

- Synergy with anti-CTLA-4 (AAL 2013 Annual Meeting, abstract 4755)
- Regration of system wide and/or sentinel tumors (Dye, Dix, 2013, AAD)
- Adoptive transfer of immunity via T cells (Dye et al 2013, AAD)

**CONCLUSIONS**

PV-10 is Well Tolerated, Electrifying Rapid, Durable Response in Inherited Tumors

- Exceptional outcome seen all (or substantially all) lesions are injected
- Robust control of refractory tumor burden demonstrated across all studies sites
- Subjects from 5 centers treated after 52 weeks despite limited dosing schedule of protocol
- Additional intervention needed for long term control of recurrent disease
- Remarkable systemic healing/tissue remodeling evident with PV-10 adaption
- Approachable to many commonly existent cancer
- Abilitate mechanism extends to solid tumors accessible to injection (e., hepatic, nervous)
- Numerous additional studies treated under expanded access (90+ subjects to date)

PV-10 Offers Unique Immunomodulatory Potential

- Safety and efficacy compare favorably with existing and emerging therapies
- PV-10 combines rapid reduction in tumor burden with induction of tumor-specific immunity
- Potential for rapid disease control in cutaneous patients with locally advanced metastases
- Induced immunity has the potential to delay, reverse or prevent progression of disease/metastatic disease
- Safety profile makes PV-10 an attractive candidate for combination strategies in advanced disease

**MOUNTING EVIDENCE OF SYSTEMIC IMMUNOLOGIC ACTIVITY**

**STUDY OVERVIEW**

- rEC672 (modified REC672) assessment of Target and Bystander Lesions
- Up to 10 Target Lesions (cutaneous or subcutaneous) followed for objective response change in sum of largest diameters
- Disease progression or DFS and OR measured against baseline
- New, non-clinically significant cutaneous or subcutaneous lesions presenting within initial 16 weeks could be treated as Non-Target Lesions (provided total number of HMs ≥ 10)
- Subjects withdrawing prior to week 4 of assigned PD

**DEMOGRAPHIC DATA**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Subjects %</th>
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<td>Disease Location</td>
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