Interim Results in a Phase 2b/3 Pivotal Study of PRO 140 in Treatment Experienced HIV-1 Patients with Multiple ARV Class Resistance

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PRO 140: Overview

- PRO 140 is a humanized IgG4 monoclonal antibody that blocks HIV-1 from entering and infecting immune cells by binding to CCR5 with high affinity
  - High genetic barrier to virus resistance
- PRO 140 broadly inhibits genotypically diverse viruses
  - Wild-type and multidrug-resistant HIV-1
  - Viruses resistant to SELZENTRY® (maraviroc)
- No dose-limiting toxicity in animals and generally well tolerated in clinical studies
- Potent, long-term antiviral activity
- Designated FDA Fast Track drug
Study Title:
A Randomized, Double-blind, Placebo-controlled, Multi-center Trial of PRO 140; Followed by Single-arm combination of PRO 140 with Optimized Background Therapy in Treatment-Experienced HIV-1 Patients.

Patient Population:
- Exclusive CCR5-tropic virus
- Failing on ongoing antiretroviral therapy
- Have documented genotypic or phenotypic resistance within three drug classes (or within two drug classes with limited treatment options)

Study Design: Two-part Study
- Part 1 – Patients who are failing on existing ART will receive a single dose of PRO 140 or placebo plus their failing ART and the viral load assessed at one week [Week 1]
- Part 2 – All patients will then begin an optimized background regimen (OBT) along with weekly doses of PRO 140 for 24 weeks
**HIV-Infected patient population:**
Treatment-experienced Patients who are poorly controlled on their current ART.

Subject to continue on Failing Regimen

**Randomization 1:1**

**Screening Visit**

**PRO 140 350 mg + Existing ART**

**Placebo + Existing ART**

**Screening Phase**
Up to 6 weeks

1 Wk Double Blind Treatment Period
T1 Visit

24 Wk Single-arm, Open-label Treatment Period
T2 to T25 Visits

**Treatment Phase**
25 weeks

**Follow-Up Phase**
4 weeks OR until viral suppression is achieved*

*Optimized background therapy (OBT) is chosen on the basis of a subject’s resistance test results and treatment history.*

**End of Study (Safety Follow-Up Visit)**

*or up to maximum of 6 months after experiencing Treatment Failure (TF) if the treating physician does not feel that there is an antiretroviral regimen that will regain full viral suppression.*
PRO 140_CD02 Study: Disposition and Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Statistic</th>
<th>PRO 140_CD02 Study (N = X)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>Median</td>
<td>54.0</td>
</tr>
<tr>
<td></td>
<td>Min - Max</td>
<td>33-63</td>
</tr>
<tr>
<td>Time since HIV Diagnosis (yrs)*</td>
<td>Median</td>
<td>23</td>
</tr>
<tr>
<td></td>
<td>Min - Max</td>
<td>5-36</td>
</tr>
<tr>
<td>Baseline CD4 cell count</td>
<td>Median</td>
<td>246</td>
</tr>
<tr>
<td></td>
<td>Min - Max</td>
<td>10-1133</td>
</tr>
<tr>
<td>Gender</td>
<td>Male, n (%)</td>
<td>XX (78.2)</td>
</tr>
<tr>
<td>Race</td>
<td>Non-Caucasian, n (%)</td>
<td>X (30.4)</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>Hispanic or Latino, n (%)</td>
<td>X (21.7)</td>
</tr>
</tbody>
</table>

N = number of eligible subjects within the population and the denominator for percentages
n = number of subjects (or observations) within the population and the numerator for percentages
* data missing for 2 subjects

Foot Notes:
*aScreen failure rate mainly attributed to d/m tropism, insufficient resistance and viral load
*bOne subject withdrew consent; one subject withdrawn due to d/m tropism
PRO 140_CD03, Phase 2b/3 Monotherapy Study

- **Study Title:** A Multicenter Study to Assess the Safety and Efficacy of PRO 140 as Long-Acting Single-Agent Maintenance Therapy for 48 Weeks in Patients with CCR5-tropic HIV-1 infection

- **Target Enrollment:** 300 subjects

- **Study Population:** Virally suppressed HIV-infected patients with CCR5-tropic virus

- **Study Design:** Patients who are on **stable highly active antiretroviral therapy (HAART)** for at least 6 months will receive PRO 140 monotherapy for up to 48 weeks

- **Study Status:** Enrollment target of 100 patients by end of 2Q17 & 300 by 4Q17

- **Safety Data:** Provides the safety data for the Pivotal Combination Trial CD02
PRO 140 350mg SC was generally well-tolerated

- No drug-related SAEs
- No discontinuation due to AEs
- No pattern of toxicity
- Injection site reactions
  - Most common AE which occurred in <10% of patients
  - Infrequent, mild, transient, and self-resolving
- No dose-limiting toxicity in preclinical or clinical studies
PRO 140: Conclusions and Path Forward

- **PRO 140_CD02 Phase 2b/3 Pivotal Study**
  - Ongoing Pivotal Combination study
  - Enrollment target of 30 patients by end of 2Q17
  - PRO 140 in combination with other ARV agents, in treatment-experienced patients infected with CCR5-tropic virus who have documented multi-ARV class resistance and evidence of HIV-1 replication despite ongoing therapy

- **Two Other PRO 140 Monotherapy studies are ongoing:**
  - **PRO 140 CD03 Phase 2b/3 Monotherapy Study**
    - Enrollment target of 100 patients by end of 2Q17 & 300 by 4Q17 with leading subject completed 24 weeks on PRO 140 Monotherapy
  - **PRO 140 CD01-Extension Study**
    - Nine (9) patients ongoing with leading subject completed 142 weeks on PRO 140 Monotherapy
    - Eight of 9 patients have completed over 2.5 years on PRO 140 monotherapy