Poster Board Number: SATURDAY - AAR LB15

# Primary Efficacy Results of PRO 140 SC in a Pivotal Phase 2b/3 Study in Heavily Treatment-Experienced HIV-1 Patients

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## Introduction

- 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
- Potently inhibits CCR5-mediated HIV-1 entry without blocking the natural activity of CCR5 *in vitro*
  - High genetic barrier to virus resistance
- PRO 140 broadly inhibits genotypically diverse viruses *in vitro*
  - Wild-type and multidrug-resistant HIV-1
  - viruses resistant to maraviroc (SELZENTRY®)
  - Both laboratory and low-passage clinical strains
- No dose-limiting toxicity in animals and generally well tolerated in clinical studies
- Potent, long-term antiviral activity in clinical studies
- Designated FDA Fast Track drug candidate

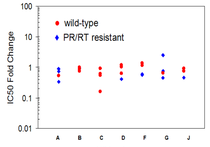



**Figure 1**. PRO 140 $IC_{50}$ Fold Changes For HIV Subtypes

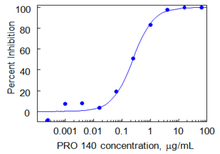



**Figure 2.** PRO 140 Concentration - Viral Inhibition Curve

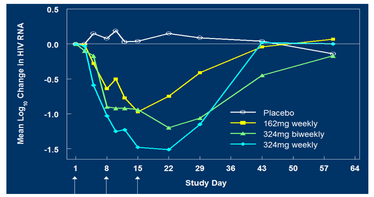



**Figure 3.** Antiviral Activity of Short-Term Monotherapy with PRO 140

## Methods and Materials

- The PRO 140_CD02 study was designed to evaluate efficacy, safety, and tolerability of PRO 140 in conjunction with an existing failing antiretroviral therapy (ART) regimen for one week and Optimized Background Therapy (OBT) for 24 weeks.
- The primary efficacy endpoint for this study was proportion of participants with a $0.5\log_{10}$ or greater reduction in HIV-1 RNA viral load from baseline at the end of the 1-week double-blind treatment period.

**Key Inclusion Criteria for CD02 study:**

- age ≥18 years
- Exclusive R5-tropic virus (HIV-1 Trofile™ Assay)
- Plasma HIV-1 RNA ≥ 400 copies/mL at Screening
- Treatment-experienced with documented resistance to at least one ART drug within three drug classes or within two drug classes and have limited treatment option.

**Key Exclusion Criteria for CD02 study:**

- CXCR4-tropic virus or Dual/Mixed tropic (R5X4) virus
- Any active infection or malignancy requiring acute therapy
- No viable treatment options
- ≥ Grade 3 DAIDS lab abnormality
- Any vaccination within 2 weeks prior to the first study dose

### Study Design Schematic

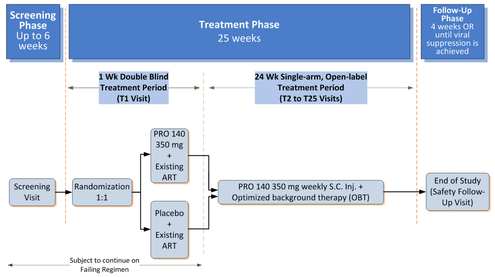



**Figure 4**. Study Design Schematic

### Study Subject Disposition*

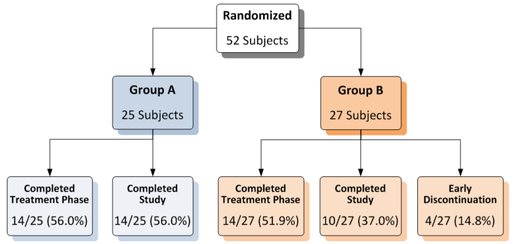



**Figure 5**. Study Subject Disposition

* Data as of 20/Mar/2018. The study is currently ongoing.

## Results

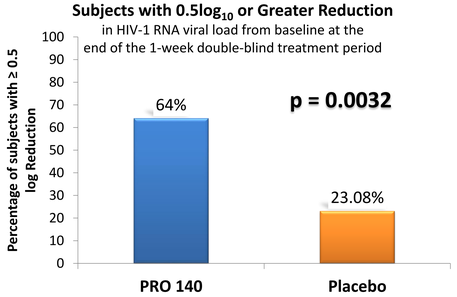
### Baseline Characteristics*

| Parameter | Characteristics | Total N=52 |
|---|---|---|
| Age | Median | 53.5 |
| | Min - Max | 33.0-63.0 |
| Gender | Male, n (%) | 38 (73.1) |
| | Female, n (%) | 14 (26.9) |
| Race | Asian, n (%) | 1 ( 1.9) |
| | Black or African American, n (%) | 24 (46.2) |
| | Caucasian, n (%) | 27 (51.9) |
| Ethnicity | Not Hispanic or Latino, n (%) | 39 (75.0) |
| | Hispanic or Latino, n (%) | 13 (25.0) |
| Time since HIV Diagnosis (Years) | Median | 21.5 |
| | Min - Max | 4.0-37.0 |
| Peak Viral Load (copies/mL) | >100000, n (%) | 18 (34.6) |
| Lowest CD4+ Cell Count (cells/$mm^3$) | <200, n (%) | 22 (42.3) |
| | 200-500, n (%) | 27 (51.9) |
| Number of ART Drugs Exposure Prior to Enrollment | Mean (SD) | 11.0 (4.3) |
| | Min - Max | 3.0 – 20.0 |
| Number of ART Drugs with Documented Resistance | Mean (SD) | 9.2 (4.8) |
| | Min - Max | 0.0 – 25.0 |
| HIV-1 RNA Level ($Log_{10}$ Copies/mL) | Mean (SD) | 21104(40287) |
| | Median | 2814 |
| CD4+ Cell Count | Mean (SD) | 297.8(220.9) |
| | Median | 247.5 |

N = number of eligible subjects within the population and the denominator for percentages
n = number of subjects within the group and the numerator for percentages

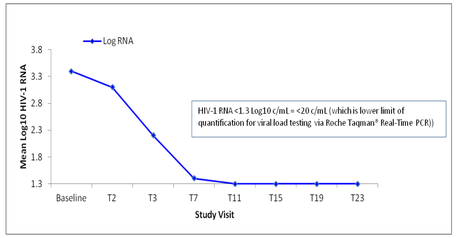
## Primary Efficacy Endpoint

**Subjects with $0.5\log_{10}$ or Greater Reduction**
in HIV-1 RNA viral load from baseline at the end of the 1-week double-blind treatment period




**Graph 1.** Reduction in HIV-1 RNA copies/mL

### HIV-1 RNA Levels ($Log_{10}$ copies/mL) Overtime




**Graph 2.** HIV-1 RNA Levels ($Log_{10}$ copies/mL) Overtime

### Mean Change from Baseline in CD4+ Cell Count at Week 25

| Visit | Statistic | PRO 140 N=52 Result | Change from Baseline [1] |
|---|---|---|---|
| Baseline | n | 52 | |
| | Mean (SD) | 297.8(220.9) | |
| | Median | 247.5 | |
| | Min - Max | 4.0 - 1133.0 | |
| Week 25 | n | 35 | 35 |
| | Mean (SD) | 404.1(287.8) | 84.3(185.5) |
| | Median | 360.0 | 64.0 |
| | Min - Max | 89.0 - 1519.0 | 312 - 784 |

[1] Change from baseline is based on patients with paired values

### Additional Key Endpoints

- Anti-PRO 140 antibodies were not detected
- Favorable PRO 140 PK profile that allows once-weekly dosing
- No change in co-receptor tropism at virologic rebound

## Safety Summary

- Generally well-tolerated
- No discontinuation due to AEs
- No pattern of toxicity
- Administration-site reactions were infrequent, mild, transient, and self-resolving (in <10% of subjects)
- No dose-limiting toxicity in preclinical or clinical studies

### Summary of All AEs

| Parameter | Total N = 52 n (%) |
|---|---|
| Subjects with ≥ 1 AE | 32 (61.5) |
| Subjects with ≥ 1 Related [1] AE | 7 (13.5) |
| Subjects with ≥ 1 Severe AE | 5 ( 9.6) |
| Subjects with ≥ 1 Serious AE | 8 (15.4) |
| Subjects with ≥ 1 Related [1] Serious AE | 0 ( 0.0) |
| Deaths | 0 ( 0.0) |
| Subjects with discontinuation due to AE | 0 ( 0.0) |
| All AEs | 138 |
| All Related [1] AEs | 17 |
| All Severe AEs | 12 |
| All Serious AEs | 15 |
| All Related [1] Serious AEs | 0 |

N = Number in the population (denominator for percentages, where applicable)
n = Number of subjects (numerator for percentages, where applicable)
[1] Related = Probably, Possibly, Definitely related to the study treatment.
Note: A subject is counted only once within each category. If there is more than one event within the category, the worst-case assessment is tabulated.

## Conclusions and Path Forward

- **PRO 140 CD02 Study**
  - Significant viral load reduction for subjects treated with PRO 140, in comparison to placebo-treated subjects, was observed after a single SC injection.
  - Subjects with ≥ 0.5 log10 copies/mL reduction:
    - 64% in the PRO 140 treated group
    - 23.08% in the placebo group
  - PRO 140 also demonstrated the long-term ability to suppress viral load.
  - Additionally, PRO 140 offers patients an alternate route of administration. The therapy can be self-administered subcutaneously on a weekly basis. This is expected to increase treatment compliance by eliminating the burden of daily pills or frequent clinic visits.
- A roll-over study, **PRO 140 CD02-Extension,** was designed to extend a subject's access to PRO 140 treatment when, in the opinion of the treating physician, PRO 140 was required to form a viable suppressive regimen.
  - To date, 35 subjects have entered the extension study.

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