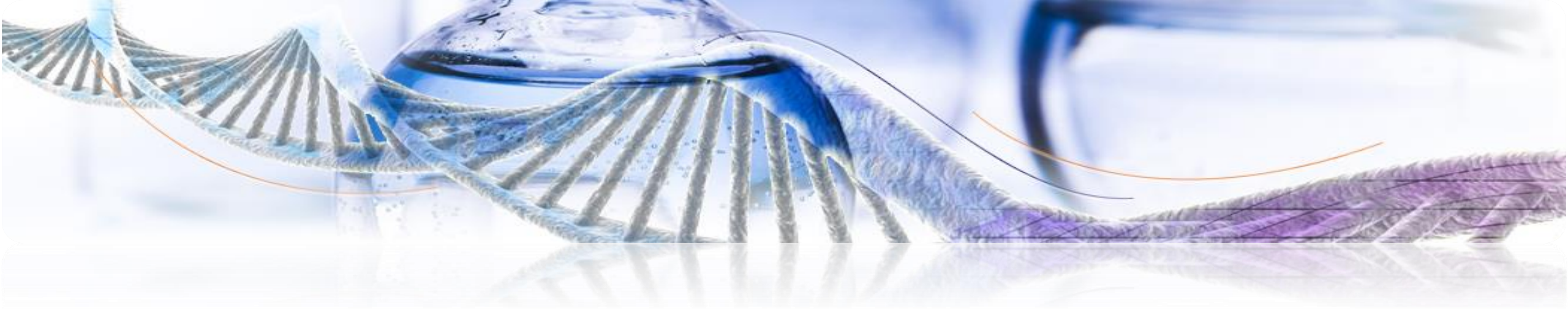

PRO140 SC Monotherapy (MT) Provides Long-Term, Full Virologic Suppression in HIV Patients

Jay Lalezari, Kush Dhody, Ula Kowalczyk, Kazem Kazempour, Nader Pourhassan, and Paul J. Maddon

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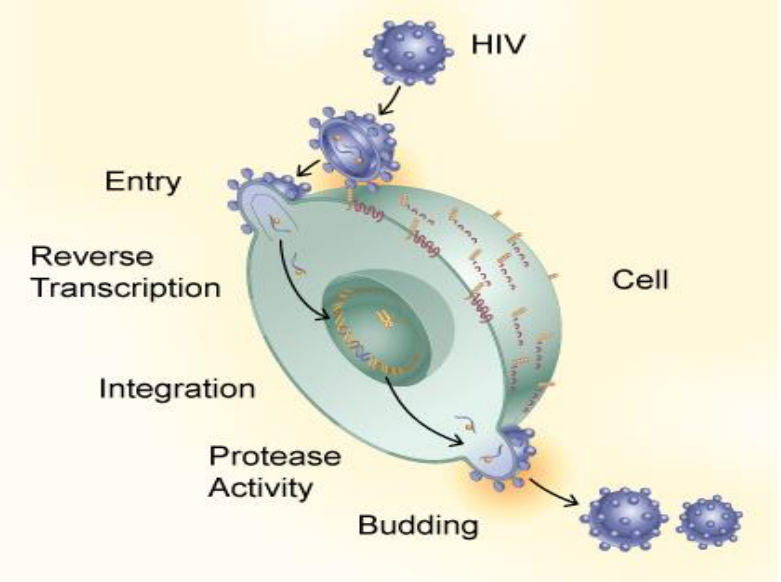
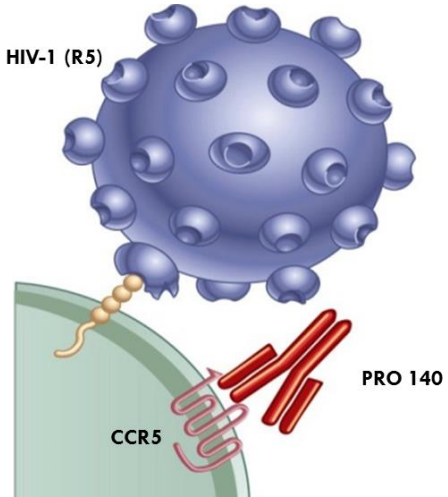
PRO 140 Overview

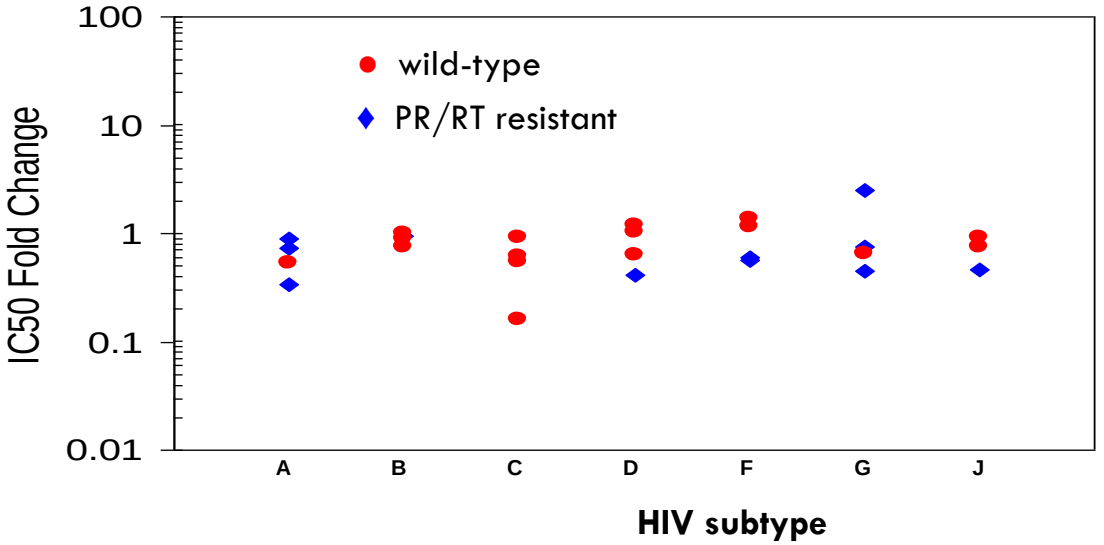
- Humanized IgG4 monoclonal antibody that blocks HIV-1 from entering and infecting healthy immune cells
- Binds CCR5 with high affinity
  - Chemokine receptor that mediates trafficking/activation of immune cells
  - Entry co-receptor for the most prevalent strains (R5) of HIV-1
  - Validated target for HIV-1 therapy
- Potently inhibits CCR5-mediated HIV-1 entry without blocking the natural activity of CCR5 *in vitro*
  - High genetic barrier to virus resistance
- No dose-limiting toxicity in animals and generally well tolerated in man
- Potent, long-term antiviral activity in clinical studies
- Designated FDA Fast Track drug candidate

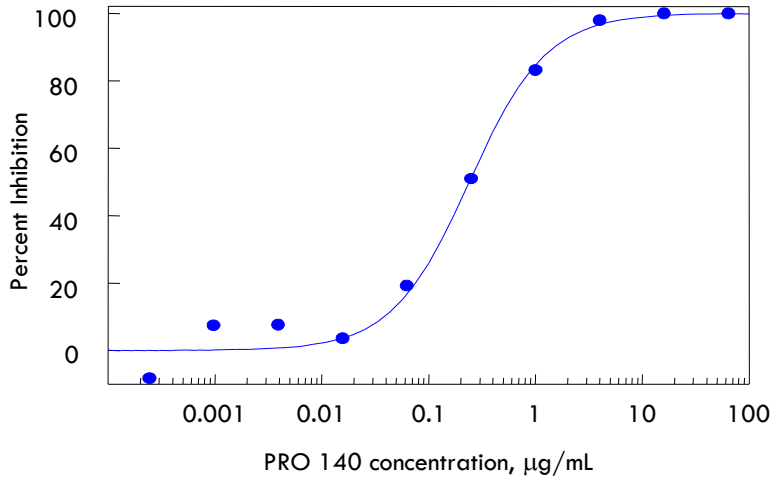




PRO 140 Broadly Inhibits HIV-1 *In Vitro*

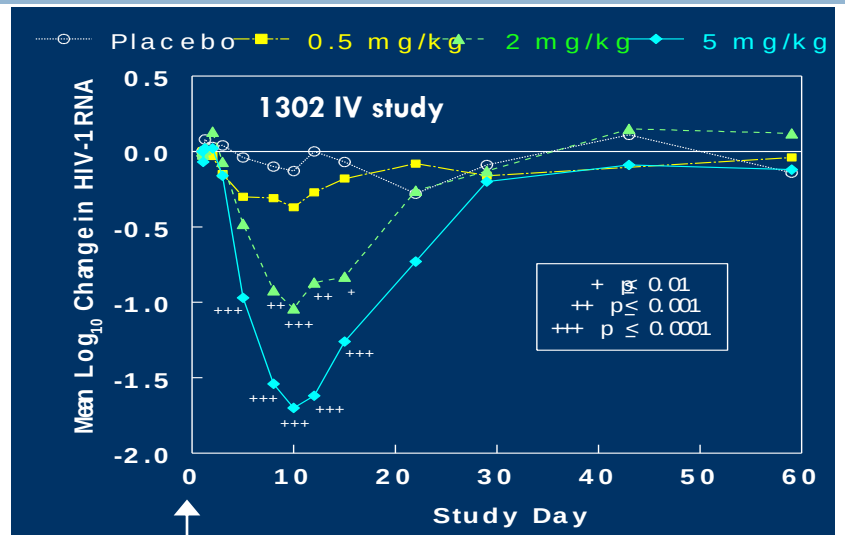
- **R5 antiviral spectrum**
  - Genotypically diverse HIV-1
  - Wild-type and multidrug-resistant HIV-1
  - Viruses resistant to SELZENTRY® (maraviroc)
  - Adult and pediatric viruses
- **Cell/assay systems**
  - Monogram Biosciences (LabCorp) Trofile® assay
  - Cell-cell fusion assays
  - PBMC assays
  - T cells, macrophages, dendritic cells
  - Cells from racially diverse donors

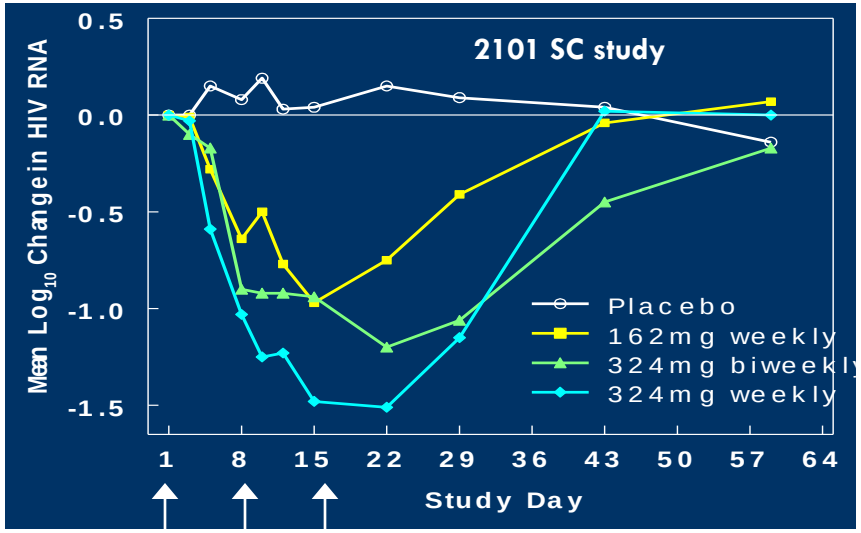


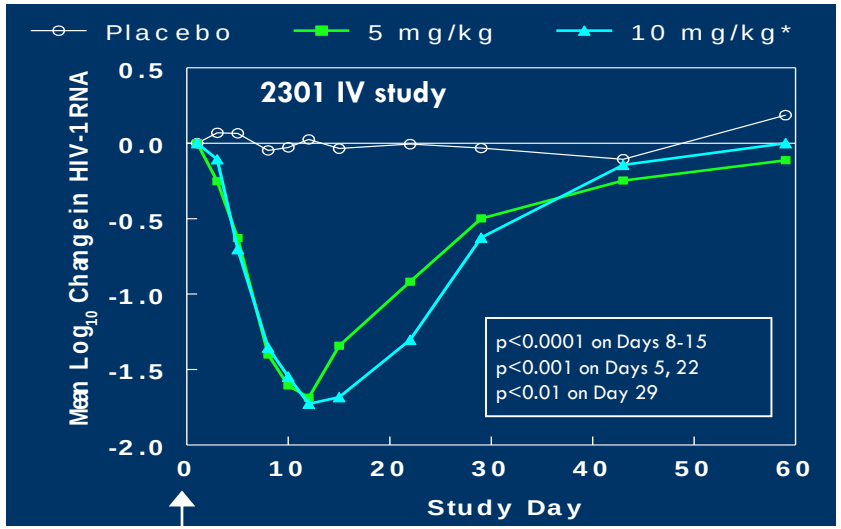


PRO 140 Has Potent and Long-Term Antiviral Activity in Man

- Potent, dose-dependent antiviral effects that are highly statistically significant
- Rapid and prolonged virologic suppression with both IV and SC dosing
- Largest single-dose HIV-1 RNA reductions reported to date







**Data exclude one subject who was reclassified as not having pure R5 virus at screening*

PRO 140_CD01/CD01-Extension Phase 2b Study Design

- Evaluate efficacy, safety, and tolerability for the maintenance of viral suppression in 40 subjects stable on effective combination antiretroviral therapy (ART)
- Subjects were shifted from daily oral ART to weekly subcutaneous (SC) PRO 140 monotherapy for up to 12 weeks (with 1 week overlap of ART + PRO 140)
- Subjects who maintained viral suppression for 12 weeks were allowed to continue PRO 140 monotherapy for an additional 108 weeks under the CD01-Extension Study
- PRO 140 administered as a 350 mg SC injection weekly for up to 120 weeks (12 + 108 weeks) in subjects who do not experience virologic failure (VF) (defined as two consecutive HIV-1 RNA levels of ≥400 copies/ml separated by at least 3 days)

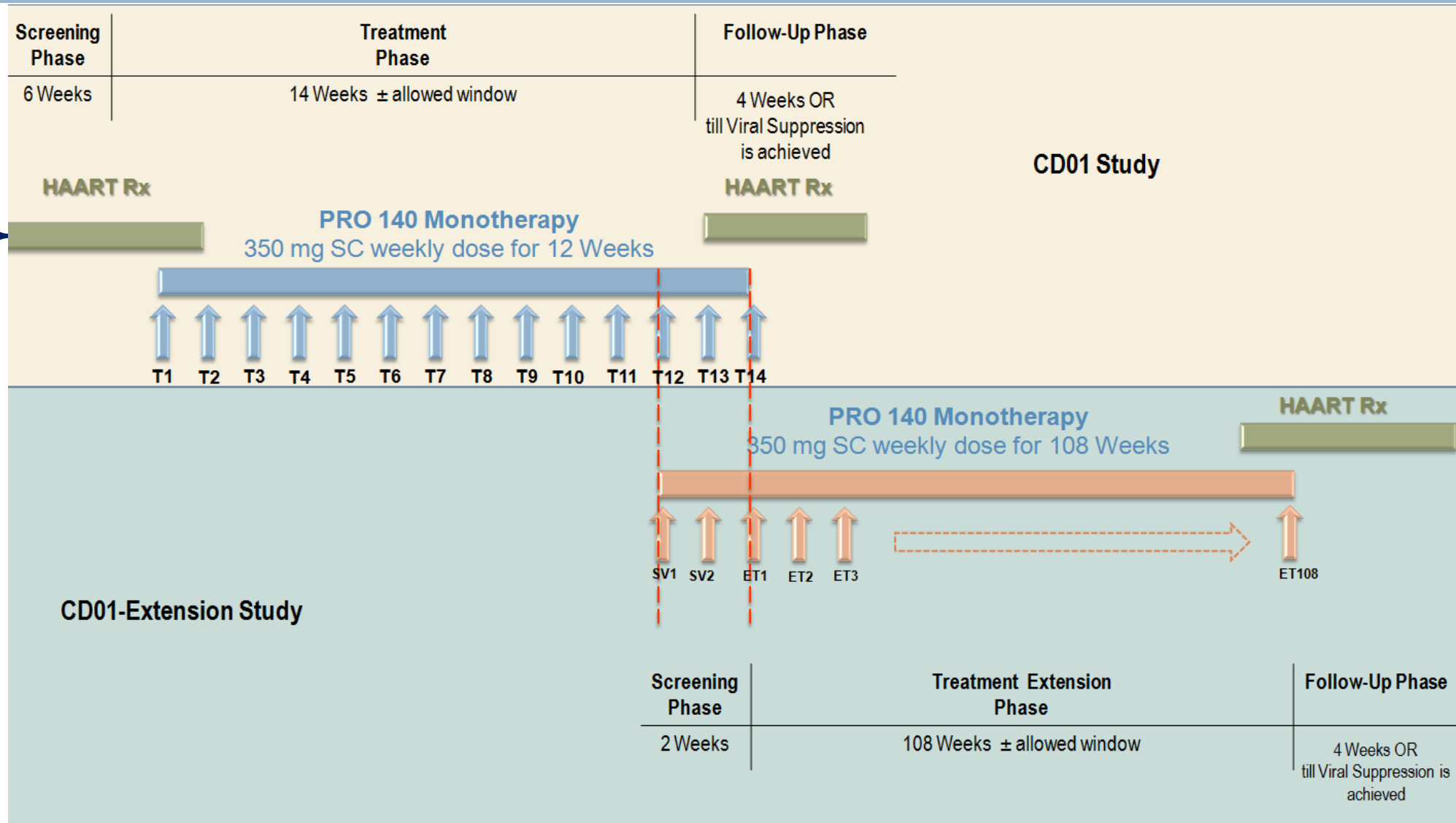
PRO 140_CD01/CD01-Extension Phase 2b Study Design

Inclusion Criteria:

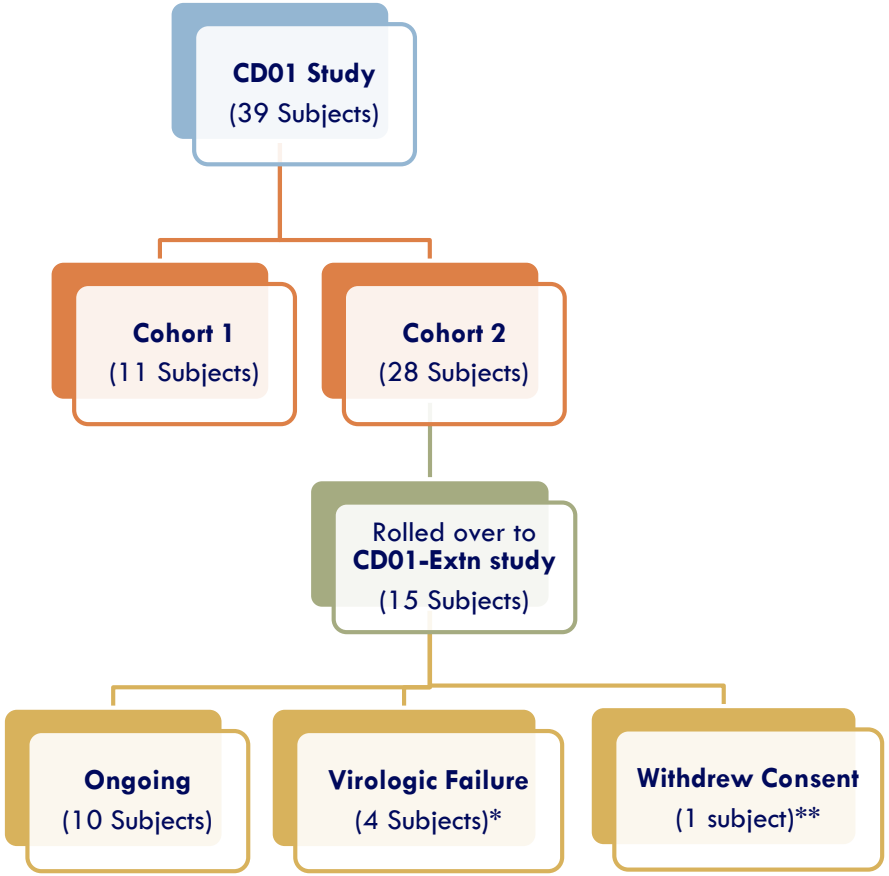
- age ≥18 years
- on stable ART regimen for 12 months and no change in last 4 wks prior to Screening
- Exclusive R5-tropic virus (Trofile™ DNA Assay)
- Plasma HIV-1 RNA <100 c/mL at Screening and no documented detectable viral loads within the last 12 months prior to Screening
- Nadir CD4 count >200 c/mm^3
- CD4 count >350 c/mm^3 at Screening

Exclusion Criteria:

- Hepatitis B
- AIDS-defining illness
- ≥ Gr 4 DAIDS lab abnormality



Disposition and Baseline Characteristics



Characteristic	Statistic	PRO 140_CD01 Study (N = 39)	PRO 140_CD01-Extension Study (N = 15)
Age (years)	Median	55.0	55.3
	Min - Max	26-72	26-68
Time since HIV Diagnosis (yrs)	Median	19.0	13.0
	Min - Max	2-37	2-37
Baseline CD4 cell count	Median	609	586
	Min - Max	365-1240	365-1059
Gender	Male, n (%)	36 (92.3)	13 (86.7)
Race	Non-Caucasian, n (%)	9 (23.0)	3 (20.0)
Ethnicity	Hispanic or Latino, n (%)	7 (17.9)	3 (20.0)

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

* 3/4 subjects showed increase in HIV-1 RNA levels while on concomitant antibiotics/antiviral/antifungal treatment for concurrent infection

** withdrew consent at week 47 (with HIV-1 RNA <40 c/mL) due to relocation

CD01 Study: 1 enrolled subject was considered not eligible since DNA Trofile result was subsequently corrected to D/M at Screening Visit

CD01-Extn Study: 1 subject was considered not eligible as subject experienced virologic failure prior to first extension treatment

PRO 140 Antiviral Activity

Ongoing Subjects in CD01-Extension Phase 2b Study

Standard HIV-1 RNA Assay (Abbott RealTime)
[LabCorp]

Subject ID	Last known viral load results (copies/mL) after completing 70 Weeks of Monotherapy
01-025	TND
01-027	TND
01-037	TND
01-038	<40
01-052	TND
01-053	TND
01-057	TND
01-061	TND
01-064	<40
01-066	<40

TND: Target not detected

Single-Copy HIV-1 RNA Assay
[Dr. John Mellors Laboratory, Univ. of Pittsburg]

Subject ID	Lowest known single-copy viral load results (copies/mL)
01-025	0.45
01-027	0.3
01-037	0.3
01-038	Not performed
01-052	3.2
01-053	0.5
01-057	0.3
01-061	0.3
01-064	2.3
01-066	39.9

PRO 140 Additional Key Endpoints

- CD4 cell counts maintained at stable levels throughout study
- Anti-PRO 140 antibodies were not detected in any subject
- Favorable PRO 140 PK profile that allows once-weekly dosing
- No change in co-receptor tropism at VF
- PhenoSense® Entry Assay results for PRO 140, maraviroc, and AMD3100 showed no significant change in post-treatment IC_{50}, IC_{90} and fold change values compared with baseline results in VF and non-VF group of subjects
- All VF subjects achieved full viral suppression after re-initiation of ART

Safety Analysis I

Overall Summary of Adverse Events (AEs)

Parameters	CD01 Study (N = 40)	CD01-Extn Study (N = 16)
Number of subjects with any reported AE, n(%)	28 (70.0%)	15 (93.8%)
Incidence of all AEs	86	72

N = number of subjects within the population

n = number of subjects (or observations) within the population

Safety Analysis II

Summary of all AEs by Relationship to Study Treatment

Relationship to Study Drug	CD01 Study (N = 40)		CD01-Extn Study (N = 16)	
	Events	n (%)	Events	n (%)
Total	86	28 (70.0%)	72	15 (93.8%)
Definitely Related	7	3 (7.5%)	0	0 (0.0%)
Probably Related	4	4 (10.0%)	0	0 (0.0%)
Possibly Related	14	7 (17.5%)	0	0 (0.0%)
Unlikely	29	4 (10.0%)	17	9 (56.3%)
Unrelated	32	10 (25.0%)	52	6 (37.5%)

Note: Relationship to Study Drug assessment missing for three AEs in the CD01-Extension study

N = number of subjects within the population and treatment group and the denominator for percentages

n = number of subjects (or observations) within the population and treatment group and the numerator for percentages

CD01 Study: All definitely- and probably-related adverse events were local injection site reactions and are of mild or moderate intensity

Safety Analysis III

Summary of all AEs by Severity

Severity Grading	CD01 Study (N = 40)		CD01-Extn Study (N = 16)	
	Events	n (%)	Events	n (%)
Total	86	28 (70.0%)	72	15 (93.8%)
Mild	70	20 (50.0%)	54	8 (50.0%)
Moderate	15	7 (17.5%)	14	6 (37.5%)
Severe*	1	1 (2.5%)	1	1 (6.3%)

Note: Severity grading assessment missing for three AEs in the CD01-Extn study

*Severe AEs are those adverse events that were considered severe or life-threatening or causing death.

N = number of subjects within the population and treatment group and the denominator for percentages

n = number of subjects (or observations) within the population and treatment group and the numerator for percentages

Safety Analysis IV

Overall Summary of Serious Adverse Events (SAEs)

Parameters	CD01 Study (N = 40)	CD01-Extn Study (N = 16)
Number of subjects with any reported SAE, n(%)	1 (2.5%)	1 (6.3%)
Incidence of all SAEs	1	1
SAE, Preferred Term	Transient ischemic attack	Pancreatitis
Relationship to Study Drug	Unrelated	Unrelated

N = number of subjects within the population

n = number of subjects (or observations) within the population

PRO 140 Safety Summary

- Generally well-tolerated both IV and SC
- No drug-related SAEs
- No pattern of toxicity
- Administration-site reactions were infrequent, mild, transient, and self-resolving
- No dose-limiting toxicity in preclinical or clinical studies

PRO 140 Conclusions

- PRO 140 CD01-Extension Phase 2b Study is ongoing; plan to further extend PRO 140 monotherapy duration beyond 120 weeks
- For >1 year, weekly PRO 140 SC 350 mg provided full viral suppression, was well tolerated, and enabled avoidance of potential toxicity of ART while preserving drug options
- These results support further development of PRO 140 as a simple, long-acting, single-agent maintenance therapy after initial ART in selected HIV-1 patients