PRO 140 (leronlimab) 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 activity of CCR5 in vitro.

High genetic barrier to virus resistance.

PRO 140 (leronlimab) broadly inhibits genotypically diverse viruses in vitro.

Wild-type and multidrug-resistant HIV-1.

Virus resistant to maraviroc (SLEVZENT®).

The laboratory and non-clinical studies included in Phase I/II studies showing potent, long-term antiretroviral activity in clinical studies.

No dose-limiting toxicity in animals and generally well tolerated following intravenous administration of single doses of 0.5 to 10 mg/kg or up to 700 mg weekly doses as subcutaneous (SC) injection in clinical studies. The longest duration of exposure lasting more than 4 years at 350 mg SC weekly doses.

Designated FDA Fast Track drug candidate.

Methods and Materials

Patients were shifted from combination antiretroviral therapy to weekly PRO 140 (leronlimab) monotherapy for 48 weeks during the Treatment Phase with the one week overlapping of existing retreatral regimen and PRO 140 (leronlimab) at the beginning of the study treatment.

Patients who experienced virologic failure were given the option of receiving a higher dose of PRO 140 under rescue arm or returning to their prior ART regimen.

The first ~150 eligible subjects were enrolled to receive PRO 140 (leronlimab) 350 mg SC weekly injection in a single-arm study. Subsequently, another ~150 subjects were randomized 1:1 to PRO 140 (leronlimab) 350mg (Group A) or PRO 140 (leronlimab) 525mg (Group B). An additional ~200 subjects will be randomized 1:1 to PRO 140 (leronlimab) 525mg (Group B) or PRO 140 (leronlimab) 700mg (Group C).

Key Inclusion Criteria

Age ≥ 18 years

Receiving combination antiretroviral therapy for last 24 weeks.

Exclusive R5-tropic virus (Trulite™ DNA assay).

Plasma HIV-1 RNA <50 c/mL at screening and no documented detectable viral loads (≥50 c/mL) within the last 24 weeks prior to Screening.

Nadir CD4 count >200 cells/mm³.

CD4 count ≥50 cells/mm³ at ≥24 weeks preceding and at Screening.

Key Exclusion Criteria

Hepatitis B

A history of an AIDS-defining illness

2 Grade 4 DADIS lab abnormality.

Conclusions and Path Forward

Based on preliminary results, the majority of patients receiving higher doses of PRO 140 (525 or 700 mg) as single-agent maintenance therapy (SAMP) were able to maintain virologic suppression.

Pharmacokinetic parameters demonstrated dose proportionality over the range of these three doses tested in this study.

Additionally, there were no significant anti-drug antibodies to PRO 140 (leronlimab) detected in subjects.

Now that response rates for higher doses are more aligned with standard of care and the drug has been generally well-tolerated, PRO 140 (leronlimab) could be a paradigm shift in the treatment of HIV as an single-agent maintenance therapy.

In 2019, CytoDyn is targeting a BLA submission for PRO 140 (leronlimab) in treatment of HIV-1 in treatment-experienced patients with CCR5-tropic virus and demonstrated evidence of HIV-1 replication despite ongoing antiretroviral therapy with documented genotypic or phenotypic drug resistance. As the results from the recently completed CO22 study demonstrated that the proportion of subjects in the PRO 140 (leronlimab) group with reductions ≥ 2 5 log10 copies/mL was significantly higher than those in the placebo group (p<0.0032).

Prior clinical experience of PRO 140 (leronlimab) in over 65 subjects has provided a strong foundation for upcoming clinical trials for cancer and graft vs. host disease (GvHD) indications.