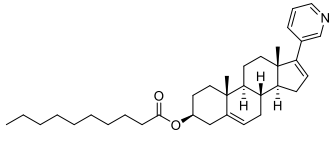
Abstract 337037: A Phase 1/2a, Open-label, Multicenter Study of Intramuscular Abiraterone Decanoate (PRL-02) Depot in Patients with Advanced Prostate Cancer (NCT04729114)

Authors: Tim Warneke[1], Michael R. Kurman[2], Robert Dreicer[3], Daniel J. George[4], Neal Shore[5], William Douglas Figg[6], Robert Schotzinger[7], William R. Moore[1]

[1]Propella Therapeutics, Inc., Pittsboro, NC; [2]Consultant, Wyckoff, NJ; [3]University of Virginia, Charlottesville, VA; [4]Duke Cancer Institute Center for Prostate and Urologic Cancers, Duke University, Durham, NC; [5]Carolina Urologic Research Center, Myrtle Beach, SC; [6]Clinical Pharmacology Program, National Cancer Institute-National Institutes of Health, Bethesda, MD; [7]Consultant, Raleigh, NC

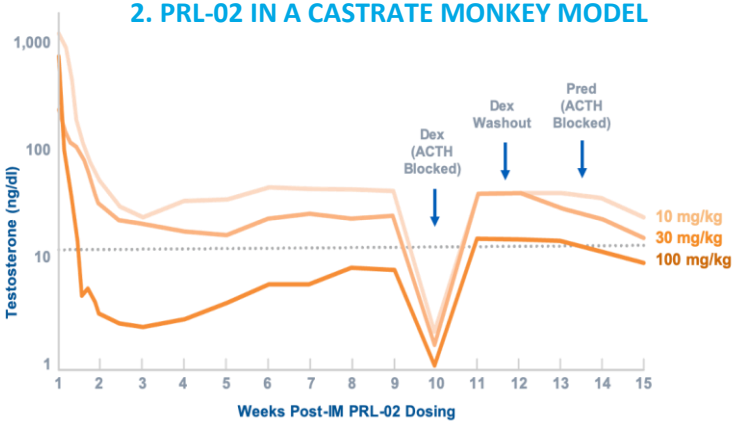
1. BACKGROUND

PRL-02 is a long-acting IM formulation of proprietary abiraterone decanoate being developed for the treatment of patients with prostate cancer. In nonclinical models, PRL-02 has a prolonged duration of action due to slow release of the prodrug into circulation. PRL-02 is expected to provide greater abiraterone bioavailability and less pharmacokinetic variability than oral abiraterone acetate (AA). Results in non-human primate models indicate PRL-02 may provide efficacy (e.g., testosterone suppression) comparable to oral AA, but with lower abiraterone plasma concentrations, potentially leading to a superior therapeutic index and safety profile.



Abiraterone decanoate

2. PRL-02 IN A CASTRATE MONKEY MODEL



Single doses of PRL-02 markedly depress testosterone levels through 14 weeks in castrate monkey model

3. STUDY DESIGN

The Phase 1 portion (Dose Escalation) is a standard 3+3 design intended to identify a recommended Phase 2 dose (RP2D) that adequately suppresses T for a minimum of 12 weeks. The Phase 2a portion (Dose Expansion) will confirm the safety, tolerability and pharmacodynamic effects of the RP2D. In Phase 1, three patients will initially be enrolled at each dose. The starting dose is 180 mg IM (i.e., 1 mL of PRL-02) and dose escalation will proceed with a modified Fibonacci sequence. If none of the patients in a cohort experience a dose-limiting toxicity (DLT), the dose will be escalated in the next cohort of 3 patients.

Main eligibility criteria include:

- Patients with mCSPC, biochemical relapse or oligometastatic prostate cancer. Patients with mCRPC will be allowed in the dose expansion phase
- Orchiectomy or ongoing GnRH analogue therapy for at least 3 months and a screening T level <50 ng/dL
- Prior treatment with abiraterone (or any other CYP17 inhibitor) and current treatment with enzalutamide or any other AR blocking agents are excluded

Patients will undergo scheduled periodic assessments of T levels. Patients may remain on study unless their T is >1 ng/dL on two sequential determinations starting on Day 28 through Day 77 of the first dosing cycle.

Planned Cohort	Dose	Volume
1	180 mg	1 mL
2	360 mg	2 mL
3*	720 mg*	4 mL*
4	1260 mg	7 mL
5	1800 mg	10 mL

*Projected RP2D based on nonclinical models

4. ENDPOINTS

Primary Objective: To determine a RP2D for PRL-02 that adequately suppresses testosterone for ≥ 12 weeks

Other key objectives:

- To evaluate the safety and tolerability of PRL-02
- To evaluate the PK profile of PRL-02
- To evaluate the pharmacodynamic effects of PRL-02 e.g., testosterone, DHEA, DHEA-S, DHT, progesterone, cortisol and ACTH levels
- To evaluate the preliminary efficacy of PRL-02 e.g., PSA, CT scans, bone scans

5. CONCLUSIONS

- PRL-02 is a long-acting IM formulation of abiraterone decanoate, a novel prodrug of abiraterone
- Single doses of PRL-02 have been shown to markedly depress testosterone levels through 14 weeks in a castrate monkey model
- Projected RP2D dose may provide testosterone suppression comparable to 90,000 mg of oral AA needed for that same time period
- The results of this Phase 1/2a study are planned to be presented at a future ASCO conference

PRL-02 VS. 12-Week ORAL AA