A Phase 1 Study of PRL-02, a Long-Acting IM Depot Injection of Abiraterone Decanoate in Patients with Prostate Cancer

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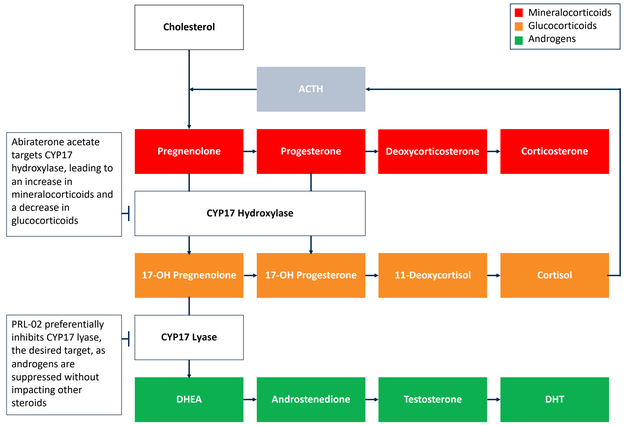
BACKGROUND

- PRL-02 is a long-acting IM depot injection of abiraterone decanoate, a novel prodrug of abiraterone
- PRL-02 preferentially inhibits CYP17 lyase, which blocks androgens without harmful increases in mineralocorticoids or depletion of steroids in the glucocorticoid pathway **(Figure 1)**
- In a castrate monkey model, PRL-02 depressed testosterone (T) through 14 weeks to levels comparable to clinical results with oral abiraterone acetate (AA) but with lower and less variable plasma exposures[1]
- Nonclinical data study results suggest that PRL-02 has the potential for a superior therapeutic index and safety profile compared to oral AA[2]

Figure 1. Metabolic Pathway of Cholesterol to Androgens – Abiraterone Acetate and PRL-02 Effects



OBJECTIVE

We present results of an ongoing dose-escalation Phase 1 study evaluating the safety and efficacy of PRL-02

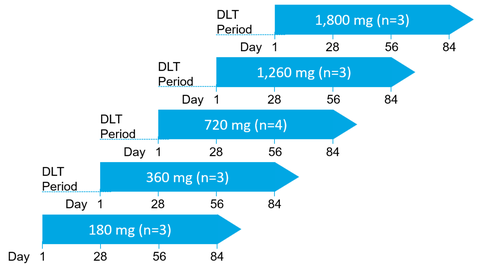
METHODS

- The phase 1 trial uses a standard 3+3 dose escalation design (DLT period = 28 days) intended to identify a RP2D with adequate suppression of T (≤1 ng/dL) for a minimum of 84 days **(Figure 2)**
- PRL-02 is administered as an IM injection every 84 days (1 cycle)
- Patients with biochemical relapse, mCSPC, or mCRPC and had a prior orchiectomy or ongoing GnRH analogue therapy for at least 3 months and a screening T level 2 - 50 ng/dL are included
- Patients with prior treatment with a CYP17 inhibitor and/or concurrent treatment with an AR blocking agent are excluded

METHODS-CONTINUED

- T levels are taken every 7 days starting from Day 1 during Cycle 1 and every 28 days in Cycles 2-4
- PSA is taken at Day 1 of Cycle 1 and Day 84 of all cycles

Figure 2. PRL-02 Phase 1 Trial Study Design (N=16)[1]



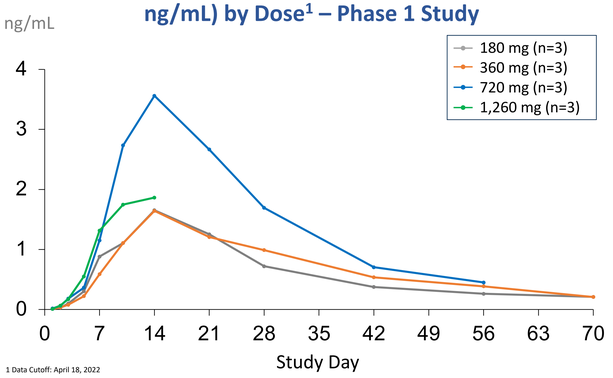
1 Data Cutoff: July 29, 2022

RESULTS

- At the data cutoff of July 29, 2022, 16 patients median age 68 (6 mCRPC, 10 mCSPC) were treated at 5 dose levels: 180 mg, 360 mg, 720 mg, 1,260 mg, and 1,800 mg; 3 patients had prior docetaxel
- There was a mean maximum abiraterone plasma concentration of 1.65 ng/mL, 1.64 ng/mL, 3.56 ng/mL, and 1.86 ng/mL for the 180 mg, 360 mg, 720 mg, and 1,260 mg doses, respectively **(Figure 3)**
- PSA responses were dose-dependent and reported at dose levels of 720 mg and above **(Figure 4)**
- Although plasma abiraterone exposure was low, continued dose-dependent T suppression **(Figure 5)** was observed in all patients
- Nine patients in whom data is available achieved either a 90% reduction in T or values ≤1 ng/dL at Cycle 1 Day 28
- At the dose levels of 1,260 mg and below, no changes in progesterone or corticosterone were observed
- Preliminary data suggests that the 1,260 mg dose shows more lyase selectivity
- Although serial radiology was not prospectively required per protocol, there was radiographic improvement in 4 patients with data available **(Figure 4)**
- PRL-02 was well tolerated with no treatment-emergent adverse effects (TEAE) that qualified as DLTs, treatment-related serious AEs **(Table 1)**, signs of mineralocorticoid excess or related liver enzyme elevations, treatment discontinuations due to TEAEs, or TEAEs related to PRL-02 with severity greater than CTCAE G2
- There were 4 related G2 events including insomnia, fatigue, loss of appetite, and hot flashes

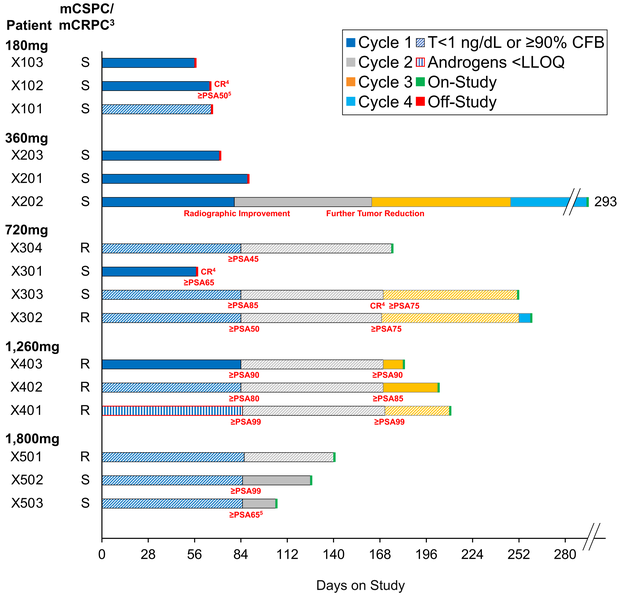
RESULTS-CONTINUED

Figure 3. Plasma Abiraterone Concentration (LLOQ=0.25 ng/mL) by Dose[1] – Phase 1 Study



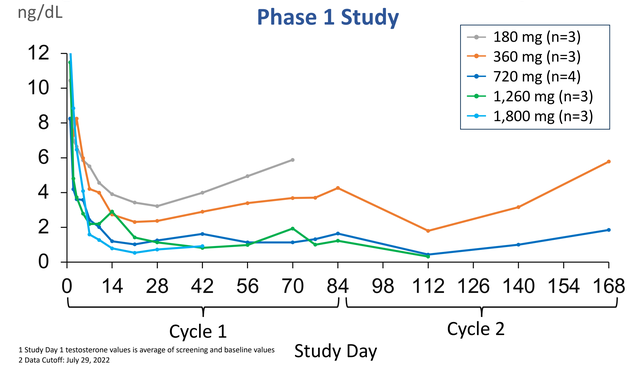
1 Data Cutoff: April 18, 2022

Figure 4. Patient Swim Plot[1] – Phase 1 Study[2]



1 Data Cutoff: August 15, 2022; Patients enrolled by 8/1/22 are included in the analysis
2 Radiology was not prospectively collected and was done as SOC, Data reports are available for 4 patients as indicated
3 mCSPC = S, mCRPC = C
4 Complete Response
5 C1D1 PSA values used as baseline values for response calculation. A post-baseline PSA value of 0.01 was used for response calculation if the post-baseline value was <LLOQ (0.02)

Figure 5. Serum Testosterone Concentration[1] by Dose[2] – Phase 1 Study



1 Study Day 1 testosterone values is average of screening and baseline values
2 Data Cutoff: July 29, 2022

Table 1. Overall Summary of Adverse Events (AEs) by Dose[1]

Number (Percent) of Patients

Adverse Event Category	Dose (mg) 180 (n=3)	360 (n=3)	720 (n=4)	1,260 (n=3)	1,800 (n=3)
Any TEAE[2]	2 (66.7)	2 (66.7)	4 (100.0)	2 (66.7)	3 (100.0)
Treatment-Related TEAE[2]	2 (66.7)	0 (0.0)	2 (50.0)	2 (66.7)	1 (33.3)
Serious TEAE[2]	0 (0.0)	0 (0.0)	0 (0.0)	1 (33.3)	1 (33.3)
Treatment-Related Serious AE[2]	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
TEAE[2] that Qualify as a Dose-Limiting Toxicity	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Fatal Events	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

1 Cutoff 7/29/2022 with updates made based on the Safety database
2 Treatment Emergent Adverse Effect

CONCLUSIONS

- PRL-02 was well tolerated, with minimal adverse effects observed at all doses
- Dose-dependent and durable T suppression was observed; this was associated with PSA response and evidence of radiologic improvement

IMPLICATIONS

Available clinical data confirms the potential for a superior therapeutic index and improved patient convenience. This hypothesis will be tested in Phase 2 once the RP2D has been identified. The study is ongoing

References:
1. Moore et al. *J Clin. Oncology*. 2021.
2. Moore et al. *J Clin. Oncology*. 2022.

Acknowledgments:
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