BACKGROUND

• PRL-02 is a long-acting IM depot injection of abiraterone decanoate, a novel prodrug of abiraterone - a Long Acting IM Depot Injection of Abiraterone Decanoate in Patients with Prostate Cancer

• 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.

• Nonclinical data study results suggest that PRL-02 has the potential for a superior therapeutic index and safety profile compared to oral AA.

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

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, 720 mg, and 1,260 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 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 PSA 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 (AEs) that qualified as DLTs, 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 (LOQ<0.25 ng/mL) by Dose – Phase 1 Study

Figure 4. Patient Swim Plot – Phase 1 Study

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

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 release, mCSPC, or mCRPC and had a prior orchectomy or ongoing GnRH analogue therapy for at least 3 months and a screening T level ≤ 50 ng/dL are included

• Patients with prior treatment with a CYP17 inhibitor and/or concurrent treatment with an AR blocking agent are excluded

RESULTS-CONTINUED

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

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 response 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


ACKNOWLEDGMENTS

Writing support was provided by Xelay Acumen Group, Inc., and funded by Prooppia Therapeutics, Inc.

For more information contact: info@prooppia.com

Copyright © 2022 Prooppia Therapeutics, Inc.

Presented at the 2022 ESMO Congress, September 9 – 13, Paris, France