A Phase 2 Study of PLK1 Inhibitor, Onvansertib, in Combination with Abiraterone and Prednisone in Patients with Abiraterone-Resistant Metastatic Castration-Resistant Prostate Cancer (mCRPC)

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With prior successes in oncology, the next step for Trovagene, Inc. is to seek FDA approval for the use of Onvansertib in patients with advanced prostate cancer. In this Phase 2 study, patients with mCRPC were treated with abiraterone and prednisone plus Onvansertib (20 mg/kg/day). The study was designed to evaluate the efficacy and safety of Onvansertib in combination with abiraterone and prednisone. The primary endpoint was overall survival (OS), and secondary endpoints included time to PSA decline, time to PSA triple, PSA nadir, and PSA progression-free survival (PPFS).

Enrollment status as of January 31st 2020

<table>
<thead>
<tr>
<th>Arm</th>
<th>Number of Patients</th>
<th>Number of Eligible Patients</th>
<th>Number of Patients Evaluable</th>
<th>Number of Patients with Onvansertib (n=7) with AR T878A</th>
<th>Number of Patients with Onvansertib (n=7) with V7+</th>
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<tbody>
<tr>
<td>A</td>
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<td>C</td>
<td>8</td>
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Study Design:
- **Dosing Regimen:** Abiraterone daily + Onvansertib (20 mg/kg) on days 1 to 4 + prednisone (10 mg) on days 1 to 28.
- **Duration:** 28 days cycle.
- **Efficacy Endpoints:**
  - **OS:** Time from randomization to death or last follow-up.
  - **PPFS:** Time from randomization to first documented disease progression or death.

Efficacy in Abiraterone-Resistant Patients

- **Efficacy observed in 38% (n=12/32) of patients remaining on treatment at 12 weeks across arms.**
- **Overall, 43% (13/30) of patients achieved partial response (PR) or stable disease (SD) following 12 weeks of treatment with onvansertib + abiraterone.** Response to treatment was evaluated based on PSA values, radiographic, and imaging endpoints.

- **Onvansertib-induced CTC decrease was associated with progression-free survival (PPFS).**
  - **CTC, count, reported as favorable or unfavorable (≤ versus >750 CTCs/mL; blood, respective).**
  - **A Phase 2 study of PLK1 inhibitor, Onvansertib, in combination with abiraterone and prednisone in patients with abiraterone-resistant mCRPC.**
  - **At baseline, 25% (7/30) had favorable CTC with median of 70 CTC/mL.**
  - **Of the 12 favorable CTC patients, 12/12 had a decrease in CTC following onvansertib treatment.**

- **Conversely, median time on treatment for patients with increase CTC (n=15) was 5 months, and none of the patients remain on treatment.**

- **Efficacy observed in patients with abiraterone-resistant AR alterations.**
  - **All mechanisms of resistance to abiraterone include the expression of the constitutively active AR splice variant AR-V7.**
  - **Onvansertib has a shorter progression-free survival and overall survival in NCI60 to treat with abiraterone plus Onvansertib.**
  - **Combination of abiraterone and PLK1 inhibitor (V7) reduces AR and AR-V7 protein expression in CTC cell lines.**

- **Phase 2 trial design and objectives.**

- **Safety assessment:**
  - **Overall, across both arms (A and B), 62% (13/21) of response (SD + PR) was observed in patients evaluable for efficacy (completed 12 weeks of treatment). 6 patients were lost to treatment due to toxicity.**
  - **Onvansertib-induced profound CTC decrease in patients with unfavorable CTC count (n=7) decreased survival by 6 patients. CTC decrease was associated with prolonged response to treatment and progression-free survival.**

- **Safety assessment:**
  - **In both arms (A and B) in combination with abiraterone and prednisone.**
  - **A more continuous dosing schedule (Arm C – onvansertib 12 mg/kg on days 1 of a 24-day cycle) is planned, and currently under IRB review to evaluate safety and efficacy.**

- **Adding onvansertib to enzalutamide patients resistant to abiraterone (rising PSA) validates pre-clinical studies and shows promise as a new therapeutic option.**