

Trovagene Presents Phase 2 Data Demonstrating the Ability of Onvansertib to Overcome Zytiga®-Resistance and Provide Clinical Benefit for mCRPC Patients

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- Onvansertib demonstrates efficacy in Zytiga®-resistant metastatic castration-resistant prostate cancer (mCRPC) across known androgen receptor resistance mechanisms

- Onvansertib-induced decreases in circulating tumor cells (CTCs) is a surrogate for efficacy and associated with greater progression-free survival in mCRPC patients

- Onvansertib shows promise as new therapeutic option to extend the duration of response to Zytiga® and other androgen receptor signaling inhibitors (ARSi)

SAN DIEGO, Feb. 13, 2020 /PRNewswire/ -- **Trovagene, Inc.** (Nasdaq: TROV), a clinical-stage, oncology therapeutics company developing onvansertib for the treatment of various cancers including prostate, colorectal, and leukemia, today announced positive data from its ongoing Phase 2 trial of onvansertib in combination with Zytiga® (abiraterone – Johnson & Johnson)/prednisone, all administered orally, for the treatment of patients with Zytiga®-resistant metastatic castration-resistant prostate cancer (mCRPC).

The clinical data, featured in a poster presentation today at the American Society for Clinical Oncology (ASCO) 2020 Genitourinary Cancers Symposium in San Francisco, further demonstrates the efficacy of onvansertib in patients who develop resistance to first-line treatment with Zytiga®. Onvansertib addresses Zytiga® resistance across known androgen receptor (AR) resistance mechanisms. In patients with AR alterations, 86% had decreases in PSA levels with the addition of onvansertib to daily Zytiga®.

"Metastatic castration-resistant prostate cancer is the second leading cause of cancer-related death among men in the United States, and unfortunately many patients are in desperate need of new treatment options," said study principal investigator Dr. David Einstein, Genitourinary Oncology Program, Beth Israel Deaconess Medical Center. "These data show that adding onvansertib to abiraterone in metastatic castration-resistant prostate cancer patients with an early resistance to abiraterone validates pre-clinical studies and shows potential as a new therapeutic option."

"We are very encouraged by the significant decreases in circulating tumor cells (CTCs) with the addition of onvansertib, given that these changes in CTCs are an accepted surrogate prognostic factor for efficacy and survival," said Dr. Mark Erlander, Chief Scientific Officer at Trovagene. "In addition, observing efficacy in patients that have tumors exhibiting known mechanisms of resistance to ARS inhibitor, Zytiga®, suggests that onvansertib's activity could extend to overcoming resistance to other ARS inhibitors such as Xtandi® and Erleada®."

Key Presentation Highlights:

Efficacy

- Overall, across both arms (A and B), a 63% (12 of 19) response (Stable Disease – SD and Partial Response – PR) was observed in patients evaluable for efficacy (completed 12 weeks of treatment with onvansertib + Zytiga® (abiraterone)/prednisone); 6 patients have been on treatment for ≥7 months
 - Arm B (onvansertib dosed daily on days 1-5 in a 14-day cycle)
 - 80% (4 of 5) patients had SD at 12 weeks, with 3 patients achieving the efficacy endpoint (PSA stabilization) and 3 patients remain on treatment
 - 60% (3 of 5) patients have or had progression-free survival of >7 months
 - Arm A (onvansertib dosed daily on days 1-5 in a 21-day cycle)
 - 57% (8 of 14) patients had SD or PR at 12 weeks, with 5 patients achieving the efficacy endpoint (PSA stabilization) and 4 patients remain on treatment
 - 21% (3 of 14) patients have or had progression-free survival; 2 patients remain on treatment for >1 year
- Onvansertib-induced circulating tumor cell (CTC) decrease is associated with progression-free survival
 - CTC count, reported as favorable or unfavorable (<5 versus ≥5 CTC/7.5mL of blood, respectively) is a prognostic factor for survival in CRPC and the conversion from unfavorable to favorable is associated with improved survival
 - At baseline, 25 (78%) patients had unfavorable CTC count with median of 19 CTC/7.5mL
 - 10 of the unfavorable patients were re-analyzed after 12 weeks of treatment
 - 5 (50%) patients had a ≥80% CTC decrease, including 2 AR-V7+ patients
 - 4 (40%) patients converted from unfavorable to favorable CTC level (<5 CTC/7.5mL)
 - 3 (30%) patients had no detectable CTC
 - Median time on treatment for patients with decrease CTC (n=4) is 7 months to-date, with 4 patients remaining on treatment
 - Conversely, median time on treatment for patients with increase CTC (n=5) was 5 months, and none of these patients remain on treatment
- Efficacy observed in patients with Zytiga®-resistant androgen receptor (AR) alterations
 - AR mechanisms of resistance to abiraterone include the expression of the constitutively active AR splice variant AR-V7 and the AR gain-of-function point mutation T878A
 - Among the 19 patients who completed the 12-week treatment (Arm A + B):
 - 5 patients were AR-V7+ at baseline
 - 2 patients had AR T878A mutations at baseline
 - Onvansertib showed efficacy in patients with AR alterations (N=7):
 - 6 (86%) patients had a decrease in PSA levels with the addition of onvansertib
 - 4 (57%) patients had SD or PR at 12 weeks with 3 (43%) patients achieving the primary efficacy endpoint
 - 3 patients have or had progression-free survival of >7 months, 2 patients remain on treatment

Safety

- Safety lead-in cohort was completed in Arm A at 24 mg/m² and is ongoing in Arm B at 18 mg/m²
- Most frequent G3/G4 AEs were expected, on-target, reversible hematological (anemia, neutropenia, thrombocytopenia and leukopenia), associated with the mechanism of action of onvansertib
 - Hematological AEs were reversible and effectively managed by dose delay, dose reduction and/or growth factor support
- Grade 3 hypophosphatemia was reported in 3 patients, next cycle treatment was delayed for 2 patients to allow recover

Conclusions

- Overall, across both arms (A and B), a 63% (12 of 19) response (SD + PR) was observed in patients evaluable for efficacy (completed 12 weeks of treatment); 6 patients have been on treatment for ≥7 months
- Onvansertib induced profound CTC decreases in patients with unfavorable CTC count (>80% decrease in 5 of 10 patients tested); CTC decrease was associated with prolonged response to treatment and progression-free survival
- 6 of 7 patients with AR alterations (AR-V7+ or AR T878A) had an immediate decrease in PSA following onvansertib treatment; efficacy (SD+PR) was achieved in 57% (4 of 7) patients
- In both arms (A and B) onvansertib in combination with abiraterone was safe and well-tolerated
- A more continuous dosing schedule (Arm C – onvansertib 12 mg/m² on days 1-14 of a 21-day cycle) is planned to evaluate safety and efficacy
- Adding onvansertib to abiraterone in mCRPC patients resistant to abiraterone (rising PSA) validates pre-clinical studies and shows promise as a new therapeutic option

About the Phase 2 Trial of Onvansertib in Metastatic Castration-Resistant Prostate Cancer

The trial is a Phase 2 open-label study of onvansertib in combination with Zytiga® (abiraterone acetate)/prednisone, all administered orally, in patients with metastatic castration-resistant prostate cancer (mCRPC), showing signs of disease progression demonstrated by two rising PSA values separated by at least one week, while on Zytiga® ([NCT03414034](#)). The primary efficacy endpoint is the proportion of patients achieving disease control after 12 weeks of study treatment, as defined by lack of prostate specific antigen (PSA) progression in patients who are showing signs of early progressive disease (rise in PSA but minimally symptomatic or asymptomatic) while currently receiving abiraterone acetate and prednisone. The trial is being conducted by Beth Israel Deaconess Medical Center (BIDMC), Dana-Farber Cancer Institute (Dana-Farber), and Massachusetts General Hospital Cancer Center (MGH). David Einstein, MD, Genitourinary Oncology Program at BIDMC, is the principal investigator for the trial.

About Onvansertib

Onvansertib is a first-in-class, third-generation, oral and highly-selective adenosine triphosphate (ATP) competitive inhibitor of the serine/threonine polo-like-kinase 1 (PLK1) enzyme, which is over-expressed in multiple cancers including leukemias, lymphomas and solid tumors. Onvansertib targets the PLK1 isoform only (not PLK2 or PLK3), is orally administered and has a 24-hour half-life with only mild-to-moderate side effects reported. Trovogene believes that targeting only PLK1 and having a favorable safety and tolerability profile, along with an improved dose/scheduling regimen will significantly improve on the outcome observed in previous studies with a former panPLK inhibitor in AML.

Onvansertib has demonstrated synergy in preclinical studies with numerous chemotherapies and targeted therapeutics used to treat leukemias, lymphomas and solid tumor cancers, including irinotecan, FLT3 and HDAC inhibitors, taxanes and cytotoxins. Trovogene believes the combination of onvansertib with other compounds has the potential to improve clinical efficacy in acute myeloid leukemia (AML), metastatic castration-resistant prostate cancer (mCRPC), non-Hodgkin lymphoma (NHL), colorectal cancer and triple-negative breast cancer (TNBC), as well as other types of cancer.

Trovogene has three ongoing clinical trials of onvansertib: A Phase 2 trial of onvansertib in combination with Zytiga® (abiraterone acetate)/prednisone in patients with mCRPC who are showing signs of early progressive disease (rise in PSA but minimally symptomatic or asymptomatic) while currently receiving Zytiga® ([NCT03414034](#)); a Phase 1b/2 Study of onvansertib in combination with FOLFIRI and Avastin® for second-line treatment in patients with mCRC with a KRAS mutation ([NCT03829410](#)) and a Phase 1b/2 clinical trial of onvansertib in combination with low-dose cytarabine or decitabine in patients with relapsed or refractory AML ([NCT03303339](#)). Onvansertib has been granted orphan drug designation by the FDA in the U.S. and by the EC in the European Union for the treatment of patients with AML.

Trovogene licensed onvansertib (also known as NMS-1286937 and PCM-075) from Nerviano Medical Sciences (NMS), the largest oncology-focused research and development company in Italy, and a leader in protein kinase drug development. NMS has an excellent track record of licensing innovative drugs to pharma/biotech companies, including Array (recently acquired by Pfizer), Ignyta (acquired by Roche) and Genentech.

About Trovogene, Inc.

Trovogene is a clinical-stage, Precision Cancer Medicine™ oncology therapeutics company developing drugs that target cell division (mitosis), for the treatment of various cancers including leukemias, lymphomas and solid tumors. Trovogene has intellectual property and proprietary technology that enables the Company to analyze circulating tumor DNA (ctDNA) and clinically actionable markers to identify patients most likely to respond to specific cancer therapies. Trovogene plans to continue to vertically integrate its tumor genomics technology with the development of targeted cancer therapeutics. For more information, please visit <https://www.trovogeneoncology.com>.

Forward-Looking Statements

Certain statements in this press release are forward-looking within the meaning of the Private Securities Litigation Reform Act of 1995. These statements may be identified by the use of words such as "anticipate," "believe," "forecast," "estimated" and "intend" or other similar terms or expressions that concern Trovogene's expectations, strategy, plans or intentions. These forward-looking statements are based on Trovogene's current expectations and actual results could differ materially. There are a number of factors that could cause actual events to differ materially from those indicated by such forward-looking statements. These factors include, but are not limited to, our need for additional financing; our ability to continue as a going concern; clinical trials involve a lengthy and expensive process with an uncertain outcome, and results of earlier studies and trials may not be predictive of future trial results; our clinical trials may be suspended or discontinued due to unexpected side effects or other safety risks that could preclude approval of our product candidates; uncertainties of government or third party payer reimbursement; dependence on key personnel; limited experience in marketing and sales; substantial competition; uncertainties of patent protection and litigation; dependence upon third parties; our ability to develop tests, kits and systems and the success of those products; regulatory, financial and business risks related to our international expansion and risks related to failure to obtain FDA clearances or approvals and noncompliance with FDA regulations. There are no guarantees that any of our technology or products will be utilized or prove to be commercially successful. Additionally, there are no guarantees that future clinical trials will be completed or successful or that any precision medicine therapeutics will receive regulatory approval for any indication or prove to be commercially successful. Investors should read the risk factors set forth in Trovogene's Form 10-K for the year ended December 31, 2018, and other periodic reports filed with the Securities and Exchange Commission. While the list of factors presented here is considered representative, no such list should be considered to be a complete statement of all potential risks and uncertainties. Unlisted factors may present significant additional obstacles to the

realization of forward-looking statements. Forward-looking statements included herein are made as of the date hereof, and Trovogene does not undertake any obligation to update publicly such statements to reflect subsequent events or circumstances.

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