Voreloxin is a first-in-class Anticancer Quinolone Derivative (AQD) that intercalates DNA and inhibits topoisomerase II, inducing apoptosis. Clinical activity has been observed in ovarian cancer and acute myeloid leukemia. Results are reported from a fully enrolled ongoing Phase 2 study of 3 dose levels of single-agent voreloxin in patients with primary or secondary platinum-resistant or refractory ovarian cancer. **Study Design:** Patients may have received up to 3 prior platinum regimens plus one additional non-platinum platinum analog regimen. An ECOG PS of 0-1 was required. 48 mg/m^2 (Cohort A, N=65), or 60 mg/m^2 (Cohort B, N=37), or 75 mg/m^2 (Cohort C, N=38) patients by slow (≤150) mg/m^2 escalation. **Results:** Objective responses were observed in all cohorts with similar response rates. Four CRs and 14 PRs were achieved in 143 patients for an overall response rate (ORR) of 11%. Seventy-four patients (52%) experienced disease control (CR + PR + SD for ≥12 weeks; median PFS 60 days (55% CI 53 – 104 days). The study included 44 women who had failed prior Doxil treatment in addition to platinum-based therapies. Four PRs were seen in Doxil failures (60 CR%, 12 PR%) and 2 PRs (8%) of these patients achieved disease control. Median PFS is 60 days (95% CI 53 – 120 days) for women who have failed Doxil. Final median PFS is available for Cohort A (60 mg/m^2 [gqw]), estimate for Cohorts B (75 mg/m^2 [gqw]) and C (75 mg/m^2 [gqw] are considered preliminary as patients remain on study. The median PFS for Cohort A was 60 days (95% CI 53 – 104 days). The median PFS for Cohort B is similar, 84 days (95% CI 54 – 161 days). The median PFS for Cohort C has increased to 106 days (95% CI 54 – 187 days). There was a significant difference in PFS among the 3 dose cohorts (p = 0.019, logrank test). PFS was significantly greater in the 60 and 75 mg/m^2 cohorts vs 48 mg/m^2. Six patients remain on study in Cohort B; 10 patients continue on study in Cohort C. Overall, the adverse event profile was similar across cohorts and the drug was generally well-tolerated. No new toxicities were identified. Intracellular neutropenia was increased in Cohort C (75 mg/m^2) (57%) weeks. The incidence of intracellular neutropenia was < 10% in Cohorts A and B, and 25% in Cohort C. The intracellular neutropenia was clinically manageable and was within the range of other commonly used agents. Across all cohorts, the most common Grade 3 or higher adverse events were dermatitis (23%), fatigue (20%), neutropenia (12%), anemia (10%), nausea (7%), vomiting (6%), and hypokalemia (5%). **Conclusions:** Objective responses of 14 patients (11%) were observed in all cohorts with similar response rates (11%). Seventy-four patients (52%) experienced disease control (CR + PR + SD for ≥12 weeks). There was a significant difference in PFS among the 3 dose cohorts (p = 0.019, logrank test). PFS was significantly greater in the 60 and 75 mg/m^2 cohorts vs 48 mg/m^2. Forty-four patients (32%) had failed Doxil in addition to having demonstrated resistance to prior platinum-based therapies. Four PRs were observed (9%) with 34% disease control (CR + PR + SD for ≥12 weeks). PFS was not statistically different between Doxil failures and non-Doxil failures. Overall, the adverse event profile was similar across cohorts and the drug was generally well-tolerated but febrile neutropenia increased to 26% Cohort C. The febrile neutropenia was clinically manageable and was within the range of other commonly used agents. Sixteen patients remain on study in Cohorts B and C. Sixteen patients remain on study in Cohorts B and C.

**Voreloxin has a Validated Mechanism of Action With Distinct Advantages Over Anthracyclines**

**Voreloxin Interferes with DNA Topoisomerase II With Distinct Advantages Over Anthracyclines**

**Voreloxin, a first-in-class Anticancer Quinolone Derivative (AQD), acts as a single agent demonstrating clinical activity in platinum-resistant ovarian cancer as well as in patients who have progressed on Doxil.**

**Voreloxin was generally well-tolerated in this difficult to treat patient population.**

The increased incidence intracellular neutropenia seen in 75 mg/m^2 (23%) was manageable and similar to other approved agents. This overall ORR of 12% and median PFS of 64 days is similar to other commonly used agents in platinum-resistant patients. DRF for Doxil failures was 9% with 64% experiencing disease control (CR + PR + SD for ≥12 weeks). PFS was not statistically different from those who had not failed Doxil (p = 0.73). Further development of voreloxin as a single agent or in combination, is warranted in platinum-sensitive and resistant ovarian cancer, including the Doxil failure setting.