P – 297 CanStem303C trial: A Phase 3 Study of napabucasin (NAPA) in combination with 5-fluorouracil (5-FU), leucovorin, and irinotecan (FOLFIRI) in adult patients (pts) with previously treated metastatic colorectal cancer (mCRC) - Trial in progress

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Introduction: NAPA is an oral investigational agent, which has been hypothesized to inhibit cancer stemness pathways, including STAT3 pathway implicated in cancer stem-cell viability. Preclinical studies suggest that NAPA may sensitize cancer cells to chemotherapeutics, including 5-FU and irinotecan. Encouraging anticancer activity in advanced CRC was observed in a phase 1b/2 study (NCT02024607). In the subset of FOLFIRI-naive patients with an on-study RECIST evaluation, disease control rate (DCR) was 85% (33/39) and objective response rate (ORR) was 21% (8/39).1 On the basis of these data, a phase 3 trial is being conducted in North America, Europe, Australia, and Asia.

Methods: This randomized, multicenter, open-label study (NCT02753127) will assess the efficacy of NAPA + FOLFIRI vs FOLFIRI in pts with mCRC (N = 1250). Addition of bevacizumab (bev) to FOLFIRI backbone is permissible per investigator decision. Pts must have failed 1 prior line of therapy with oxaliplatin and a fluoropyrimidine +/- bev for metastatic disease. Pts are randomized 1:1 to receive NAPA 240 mg PO BID plus FOLFIRI bi-weekly (5-FU at 400 mg/m 2 bolus followed by 1200 mg/m 2 continuous infusion, leucovorin 400 mg/m 2, and irinotecan 180 mg/m 2) , or FOLFIRI biweekly. Patients are stratified by geography (North America/Western Europe/Australia vs. Japan/Korea vs. rest of the world), time to progression on 1st-line therapy (<6 months vs. ≥6 months), RAS mutation status (mutant vs. wild type), bev as part of study treatment (yes vs. no), and primary tumor location (left vs. right colon). Treatment will continue until disease progression or another discontinuation criterion. The primary endpoint is overall survival (OS) in the general study population (HR 0.80 for OS improvement from 12.54 to 15.68 months); secondary endpoints include progression free survival (PFS), ORR and DCR, safety and quality of life. Blood and tumor archival tissue will be assessed for PK and biomarker analyses. An interim analysis for non-binding futility set at HR > 1 will be performed on OS at 50% of events (424). Additionally, early efficacy analysis based on OS will be performed at the time of the interim analysis. Should the trial not stop at time of the interim analysis, study will continue to final analysis at 850 events. Study enrollment is ongoing with >50% of planned patients enrolled to date.