Building on the successes of the original SU2C Epigenetics Dream Team, the team is continuing to apply epigenetic therapies in combination with other treatments to multiple types of cancer, with clinical trials in three categories: immune sensitization, chemo sensitization, and novel target strategies.

In its immune sensitization work, the team has combined epigenetic agents with immune checkpoint therapy in lung, blood, and multiple solid cancer patients.

The team’s chemo sensitization strategy involves testing a new epigenetic agent on chemotherapy-resistant colorectal cancer.

And the novel targeting strategies category comprises two projects: a trial using an epigenetic agent with a PARP inhibitor in acute myeloid leukemia patients, and a study of combining a vitamin C supplement with epigenetic agents in blood cancer patients.

The team has reported the following progress:

**December 2018**

- The team has enrolled 64 patients in their amended Legacy Lung Cancer Project.
- The team is testing the benefit of combining an epigenetic drug with an anti-PD-L1 antibody to treat patients with myelodysplastic syndrome. No dose-limiting toxicities and immune-related adverse events were observed in their Phase I study. The trial is now in Phase II.
- Promising results have been observed in their Phase II trial in colorectal cancer where they are testing whether an epigenetic drug can reverse resistance to the chemotherapy agent called irinotecan.
- 24 patients with Acute Myeloid Leukemia (AML) have been enrolled in a Phase I clinical trial (target for Phase I: 36) in which the safety of combining an epigenetic drug and a PARP inhibitor is being tested. Extended survival has been observed in a few patients.

**June 2018**

- The Legacy Lung Cancer Project continues. The protocol was modified to: 1) move checkpoint therapy up front for simultaneous administration with each cycle of epigenetic therapy, and 2) give six months of epigenetic therapy (instead of two) to patients who stay on trial. Almost all patients on combined therapy are tolerating the initial cycles.
Team Progress Updates

- Myelodysplastic Syndrome (MDS) Project: Nine MDS patients have been enrolled in a clinical trial in which patients are treated with immunotherapy.

- Multiple Solid Tumor (MST) Project: This trial is enrolling at USC, where three patients are on treatment; two additional clinical sites will soon be activated.

- The colorectal cancer (CRC) trial is almost fully accrued. Ninety-one of 96 patients have been enrolled.

- Eighteen patients with acute myeloid leukemia (AML) have been enrolled in a phase I clinical trial to test the safety of combining an epigenetic drug and a PARP inhibitor.

- The EV-1 pilot trial in MDS/AML has reached the target patient accrual of 20 patients, and the team is analyzing blood samples.

- The EV-2 trial enrollment has begun for a cohort of subjects who have clonal cytopenia of undetermined significance, a precursor to MDS. So far the trial has enrolled 22 patients.

December 2017

- Enrolled 67 patients with advanced colorectal cancer in a clinical trial testing the epigenetic drug guadecitabine.

- Enrolled 20 MDS/AML patients in the clinical trial combining an epigenetic drug with vitamin C. The Team has observed that a single 500 mg Vitamin C tablet given daily was sufficient to restore normal vitamin C blood levels in the patients.

- Enrolled 15 patients with AML in a Phase I clinical trial where the safety of combining an epigenetic drug and a PARP inhibitor, is being tested. Extended survival has been observed in 4 patients.

- Continued clinical trials in lung cancer and MDS.

June 2017

- Continued to enroll patients in clinical trials.

- Completed enrollment in EVITA pilot project of randomized vitamin C supplementation in combination with epigenetic therapy in MDS and AML patients.

December 2016

- Continued to move forward with clinical trials in lung cancer, MDS, colorectal cancer, and AML, and the EVITA project on Vitamin C supplementation.
June 2016

- Continued to move forward with trials in lung cancer, acute myeloid leukemia, and myelodysplastic syndrome, testing whether epigenetic agents can sensitize the tumors to subsequent treatment.

- Began preclinical phase testing of an inhibitor of a gene called the enhancer of Zeste 2 polycomb repressive complex 2 subunit (EZH2i) in combination with chemotherapy in small cell lung cancer cell lines and mouse models. EZH2 is frequently over-expressed in a wide variety of cancer types.

- Began preclinical work on EVITA (Epigenetics, Vitamin C, and Abnormal Hematopoiesis). In this project, the Team will evaluate whether supplementation with Vitamin C (to restore normal Vitamin C levels) will improve the effects of epigenetic therapy in patients with MDS/AML.

December 2015

- Enrolled patients in a clinical trial to test a combination of epigenetic agents to see whether they sensitize lung cancer patients to immune checkpoint therapy.

June 2015

- Finished Phase I of a trial in colorectal cancer (begun during the first iteration of the Dream Team) to determine safety, efficacy, and appropriate dosing of combined SGI-110 and irinotecan.