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## 2018 SEBASTIANSTRONG RESEARCH GRANT

### **Clinical Trial of Disulfiram to Overcome Chemotherapy Resistance In Sarcomas**

*PI: Matteo Trucco, MD, University of Miami's Sylvester Comprehensive Cancer Center*

SebastianStrong Foundation's grant to Dr. Matteo Trucco will test the safety and ability of adding disulfiram to chemotherapy to overcome the resistance to chemotherapy seen in relapsed sarcomas. Metastasis and relapse are the major cause of death from pediatric bone and muscle tumors (sarcomas). Current chemotherapy can kill the majority of sarcoma cells, but often some are able to survive the chemotherapy and give rise to new cancers (relapse) or spread throughout the body (metastasis). We have been using the same chemotherapy for pediatric sarcomas for decades. Sarcoma cells that express high levels of an enzyme called Aldehyde Dehydrogenase (ALDH) have proven to be resistant to chemotherapy. The drug disulfiram, used safely for over 50 years for the treatment of alcoholism, blocks ALDH and laboratory tests have shown that it makes sarcoma cells more sensitive to chemotherapy. This is the first step in developing disulfiram as a way to make current treatment more effective against pediatric sarcoma.

UPDATE 1: "With the support of the SebastianStrong Foundation combined with support from similar foundations, we secured the funding necessary to conduct a clinical trial testing the ability of a drug called disulfiram (Antabuse) to overcome the resistance to chemotherapy seen in several sarcomas. Disulfiram blocks an enzyme called Aldehyde Dehydrogenase. This enzyme has been found to make cancer cells resistant to many of the chemotherapy drugs used to treat pediatric sarcomas. By blocking this enzyme, we hope to make chemotherapy more effective in treating those cancers, and in time potentially enable doses to be reduced leading to less toxic treatments. With all the necessary funding secured, we are in the process of obtaining approval by the University and the FDA to conduct the trial and contract with laboratories to perform the drug and enzyme measurements necessary to assure we are hitting the target."

UPDATE 2: "Our clinical trial adding the alcoholism drug disulfiram (Antabuse) to chemotherapy to target the cells that are resistant to the chemotherapy is in development. We have secured funding from other organizations which, combined with



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the award from the SebastianStrong Foundation, will allow us to purchase the drugs and cover the costs of conducting the trial and necessary laboratory testing to better understand how the disulfiram is working and which patients are likely to benefit. We are about to submit a Letter of Interest (LOI) to the National Pediatric Cancer Foundation (NPCF) to consider opening the trial through the Sunshine Project Consortium which includes 20 of the top Pediatric Cancer Centers in the country. Opening the trial through this consortium would make this treatment available to more patients and help complete the trial more quickly. The trial was presented at the annual NPCF summit in February, was well received and we were invited to submit the LOI for consideration. We have also partnered with Dr. Kurt Weiss, whose laboratory is leading the studying of disulfiram in sarcomas, to perform the necessary experiments testing the response to the disulfiram treatment in tumor samples. Independently, disulfiram was found to be one of the most active drugs in 2 of 3 pediatric sarcomas screened against 215 FDA-approved drugs. While the process of developing a clinical trial is frustratingly slow, we continue to make progress and anticipate opening the trial either locally or nationally in the near future.”