WE ARE PLEASED TO ANNOUNCE A SEMINAR PRESENTED BY

Bruce A. Littlefield, Ph.D.
Distinguished Scientist and Head of Translational Medicine, Eisai

“Discovery and Development of Eribulin, a Macrocyclic Ketone Analog of Halichondrin B, for Treatment of Advanced Breast Cancer”

Thursday, March 31, 2016 at 9:00 AM
Astellas Conference Room, SLSRC 3410/3430
Refreshments will be served at 8:45 AM

Marine natural products represent rich sources of novel compounds for drug discovery. Owing to their roles in chemical defense, marine natural products are often remarkably potent in order to overcome highly diluting ocean environments. Halichondrin B (HB), originally isolated from the sponge Halichondria okadai, is one such compound. Early reports of HB’s remarkable antitumor activity led to significant interest in developing it as a new anticancer drug, but limited natural supplies ultimately foiled such efforts. Fortunately, the total synthesis of HB plus the discovery that its anticancer activity resided in its macrolactone “right half” moiety provided an opportunity to develop structurally simplified, fully synthetic analogs. Eribulin, a synthetic analog of HB’s right half, retains HB’s high potency with low/sub-nM activity against cancer cells in vitro. In vivo, eribulin induces tumor regression and long-term survival of nude mice bearing human tumor xenografts. Mechanistically, eribulin is a novel microtubule dynamics inhibitor that disrupts mitotic spindle formation, causing cell death by apoptosis after 10-12 hours of irreversible mitotic blockage. Unexpectedly, recent findings have shown that eribulin also has significant effects on tumor biology that are unrelated to its antimitotic activities. Eribulin (as Halaven®) is now approved for clinical use in the United States and 58 other countries worldwide for treatment of certain patients with advanced breast cancer. This lecture will provide an overview of eribulin’s discovery and development, its mechanisms of action, and the preclinical pharmacology results that led to its evaluation in human clinical trials for cancer.

Bio: Dr. Littlefield serves as Distinguished Scientist and Head, Translational Medicine at Eisai, a global pharmaceutical company headquartered in Tokyo. Since joining Eisai in 1990, Dr. Littlefield has overseen numerous natural product-based oncology drug discovery programs. One such program, initiated at Eisai by Dr. Littlefield in 1992 together with Professor Yoshito Kishi of Harvard, was based on the marine sponge natural product halichondrin B. This program led to development of eribulin (Halaven®), currently approved in 59 countries worldwide for treatment of certain patients with advanced breast cancer. Dr. Littlefield has published widely in the cancer research literature, holds numerous patents in the same field, and is a frequent lecturer at universities and scientific conferences in the US and abroad. In addition to working at Eisai, Dr. Littlefield has held faculty positions at both Yale and Harvard Medical Schools, most recently 2009-2011, when he temporarily joined Harvard to oversee scientific development of a new natural products research program, before returning to Eisai in 2011.