

## CS2-2 Chemical Approaches to a Novel Natural Product Pladienolide

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Pladienolide is a novel 12-membered macrolide isolated from *Streptomyces sp.* The compound showed prominent antitumor activities *in vitro* and *in vivo*. Several lines of data indicated that pladienolide has a unique mode of action unlike those of anticancer drugs currently in clinical use. These data encouraged us to search for novel antitumor agents based on this unique lead and we discovered a semi-synthetic derivative of pladienolide, E7107. Now E7107 has been progressed to clinical trials. We also achieved the first total synthesis of pladienolide and target protein identification using derivatives of pladienolide, so called “chemical probes”. These approaches culminated the study of medicinal chemistry on pladienolide and revealed that E7107 is a “first-in-class” compound targeting splicing factor SF3b.