

Docket #: S21-064

Synthesis of EBC-46 (tigilanol tiglate) and Analogs for Treatment of Cancer and Other PKC-related Diseases

Stanford scientists in Dr. Paul Wender's lab have developed a novel method to synthesize tigilanol tiglate (EBC-46) and related compounds from readily available starting materials. This synthesis of EBC-46, a highly selective protein kinase C (PKC) modulator FDA-approved for treatment of veterinary cancer with remarkable in vivo activity against cancer and other PKC-related diseases, represents the first scalable and sustainable laboratory methodology for obtaining a clinical supply of this valuable small molecule.

PKC modulators like bryostatin have shown great promise for treating a variety of diseases and medical problems ranging from cancer to HIV eradication to Alzheimer's, multiple sclerosis and wound healing. EBC-46 is a potent, isoform-selective PKC modulator with an 88% cure rate in veterinary cancers and ongoing clinical studies to treat head and neck squamous cell carcinomas in humans. The only current supply of this molecule is from the rare tree *Fontainea picrosperma* which is found only in a small, remote rainforest in Australia.

This new methodology developed by the Wender lab describes the semi-synthesis of EBC-46 from an abundant and readily available starting material instead. Not only does this invention allow for a steady clinical supply for the use and study of EBC-46, it also enables synthetic access to numerous tiglianes, daphnanes and their novel analogs that were previously impossible to make from the natural product as isolated from nature.

Stage of Development

Molecule is FDA-approved for treating veterinary cancer, showing an 88% cure rate, and is currently being tested in humans with encouraging results. Proof-of-concept synthesis of EBC-46 in the laboratory successful and ready for scale-up to GMP

production.

Applications

- Synthesis of a potent PKC modulator EBC-46 for the treatment of cancer in animals and humans and as a cell therapy adjuvant
- Synthesis of a potent PKC modulator EBC-46 for its potential to treat HIV and Alzheimer's
- Synthesis of EBC-46 analogs for facilitating wound healing
- Synthesis of EBC-46 analogs as adjuvants to enhance antigen targeted therapies
- Synthesis of numerous bioactive tiglianes, daphnanes and their novel analogs previously unavailable by existing synthetic routes
- Synthesis of EBC-46 for life science supply companies who provide the compound to labs studying PKC activation

Advantages

- FDA-approved drug with remarkable cure rates in veterinary cancer (88%) and encouraging results in human trials
- More sustainable and environmentally-friendly source of EBC-46 than previous natural source from *Fontainea picrosperma*, especially given the susceptibility of proposed plantations to climate change, the plant's required reliance on pollinators to produce fruit and seed, the plant's susceptibility to pathogens and the susceptibility of proposed plantations to land development.
- Semi-synthetic methodology enables greater exploration of EBC-46 analogs not synthetically accessible from the natural product, enabling broader structure-activity studies

Publications

- Zachary O. Gentry et al. ,[Synthesis and preclinical evaluation of tigilanol tiglate analogs as latency-reversing agents for the eradication of HIV](#). *Sci. Adv.* 11, eads1911 (2025).

- Hadhazy, Adam. [Cancer-fighting compound shows immense potential to eradicate HIV](#). *Stanford Report*, January, 2025.
- Wender, P.A., Gentry, Z.O., Fanelli, D.J. et al. [Practical synthesis of the therapeutic leads tigilanol tiglate and its analogues](#). *Nat. Chem.* (2022). <https://doi.org/10.1038/s41557-022-01048-2>
- Hadhazy, Adam. [Breakthrough in the production of an acclaimed cancer-treating drug achieved by Stanford researchers](#). *Stanford News* 2022
- [Technology Networks Drug Discovery](#)

Patents

- Published Application: [WO2022192521](#)
- Published Application: [20240132460](#)

Innovators

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