Weill Cornell Medicine

6-Ethylthioinosine for the Treatment of Cancers that Overexpress Adenosine Kinase (ADK)

Lead Inventors:

Ethel Cesarman, M.D., Ph.D.
Professor of Pathology and Laboratory Medicine,
Weill Cornell Medical College

J. David Warren, Ph.D.
Adjunct Associate Professor of Research in
Biochemistry, Weill Cornell Medical College

Business Development Contact:
Jamie Brisbois
Business Development & Licensing Senior Associate

(646) 962-7049
jamie.brisbois@cornell.edu

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Background & Unmet Need

- The γ-herpesvirus KSHV, also called HHV-8, is the etiological agent of Kaposi's sarcoma (KS), multicentric Castleman's disease, and primary effusion lymphoma (PEL)
- KS, the most common malignancy in AIDS patients, is often treatable by antiviral therapy and radiation or chemotherapy
- PEL is a rare HIV-associated non-Hodgkin's lymphoma (NHL) that is largely a highly aggressive and intractable disease, with rapid progression to death
- **Unmet Need:** Specific and effective therapeutics for diseases caused by KSHV

Technology Overview

- **The Technology:** Identification of 6-ethylthioinosine (6-ETI) as a potent inhibitor of cancers that overexpress adenosine kinase (ADK)
- 6-ETI was identified through a high throughput screen of compounds that selectively inhibit NF-κB in a KSHV-infected PEL cell line (LC_{50}=50nM)
- The inventors then demonstrated that 6-ETI is converted into phosphor-6-ETI by ADK, which is commonly overexpressed in several cancers
- **PoC Data:** 6-ETI is highly effective in both PEL and disseminated multiple myeloma (MM) xenograft mouse models, with significant reduction in tumor burden and prolonged survival
- 6-ETI was also demonstrated to be effective against solid tumors that overexpress ADK, including those with resistance to 1L therapies
- 6-ETI is therefore a promising lead compound for targeted treatment of ADK positive cancers

Inventors:
Ethel Cesarman
J. David Warren
Utthara Nayar
Jouliana Sadek

Patents:
US Application Filed

Publications:
Nayar et al. *J Clin Invest.* 2017.

Biz Dev Contact:
Jamie Brisbois
(646) 962-7049
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Technology Applications

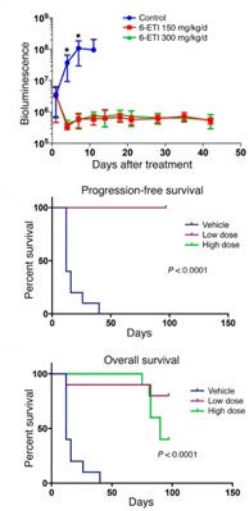
- Treatment of plasma cell malignancies including PEL, PBL, and MM
- Treatment of solid tumors with ADK overexpression, such as NSCLC, colorectal, and pancreatic

Technology Advantages

- Precision medicine approach
- Applicable to multiple tumor types
- Demonstrated efficacy in PEL and MM xenograft models
- Overcomes treatment resistance to gemcitabine and erlotinib in pancreatic and NSCLC cancer

Supporting Data / Figures

PEL Xenograft Mouse Model



Disseminated MM Xenograft Mouse Model

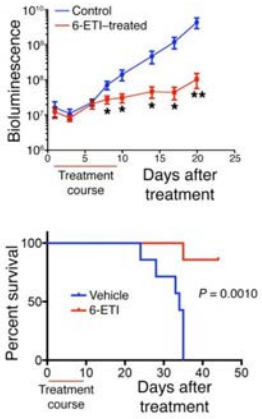


Figure 1: 6-ETI has demonstrated in vivo efficacy in both PEL and MM mouse models.

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