

## Overview

*Cytokines are small, multifunctional proteins that play critical roles in controlling development and regulating the body's responses to disease and infection. The therapeutic benefits of cytokines are well known, and several cytokines are currently marketed for the treatment of cancer and infectious diseases.*

Lorus has discovered that interleukin-17E (IL-17E) has potent anticancer properties against a range of solid tumors. IL-17E (IL-25) is a recently identified proinflammatory cytokine that induces a TH2-type immune response, which includes the expansion of eosinophils through the production of IL-5, and elevated gene expression of IL-4 and IL-13 in multiple tissues.

Lorus initially identified an anticancer role for IL-17E through examination of the anticancer mechanism of Virulizin®, which is a biological response modifier that Lorus is developing for the treatment of pancreatic cancer. We have subsequently shown that administration of purified recombinant IL-17E to mouse models of

human tumors results in a significant decrease in the size of tumors. This anticancer effect has been demonstrated using both mouse and human forms of IL-17E. Based on these findings, Lorus is developing human IL-17E as a novel form of immunotherapy for the treatment of solid tumors.

## Pre-clinical Efficacy Studies

### ✿ IL-17E has a potent antitumor activity in a variety of cancer in vivo models

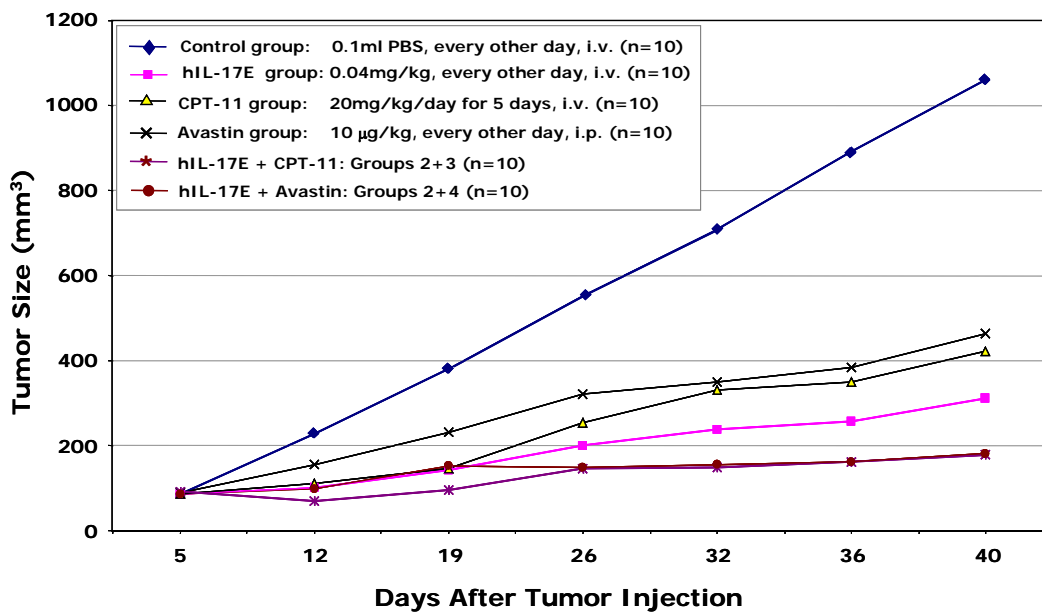
In preclinical studies, IL-17E shows exceptional *in vivo* antitumor activity in a variety of mouse models of human solid tumors, including non-small cell lung cancer, colon cancer, ovarian cancer, pancreatic cancer and malignant melanoma. When compared to marketed anticancer drugs currently used to treat these cancers, IL-17E showed equivalent or superior efficacy as a single agent.

CANCER TYPE	IL-17E ACTIVE AS SINGLE AGENT*	IL-17E COMBINATION STUDIES*
NSCLC	✓	Taxotere® or Tarceva®
Colon Cancer	✓	CPT11 or Avastin®
Ovarian Cancer	✓	Cisplatin
Malignant Melanoma	✓	Dacarbazine
Pancreatic Cancer	✓	Gemcitabine

\*Tumor sizes (volumes and weights) from IL-17E-treated mice were significantly smaller (p < 0.01) than those from tumor-bearing mice treated with PBS.

IL-17E was also effective when used in combination with these drugs, and demonstrated antitumor efficacy that was superior to either agent alone. Illustrated below is an example study demonstrating potent antitumor activity of IL-17E alone or in combination in mice harboring human colon adenocarcinoma (HT29) xenografts. These studies indicate the potential use of IL-17E to treat a range of solid tumors, both alone and in combination with existing therapeutics. In addition, IL-17E shows a dose-dependent antitumor response, and has equivalent potency when given by multiple routes of administration, including intraperitoneal, subcutaneous, and intravenous routes.

**Growth of Human Colon Adenocarcinoma (HT-29) in CD-1 Nude Mice**

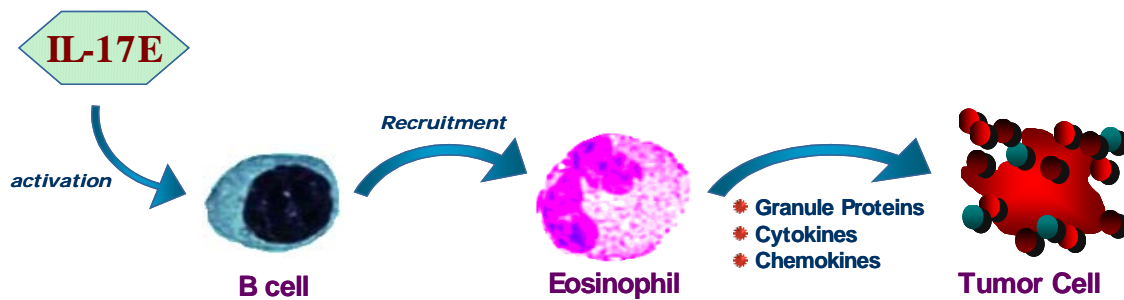


## Toxicity Findings

No significant toxicity (lethality or decreased body weight) has been observed with IL-17E, in conjunction with efficacy studies in mice. While published reports have shown pathological changes associated with IL-17E overexpression or high-dose administration in mice, these effects have not been seen at the dose levels of IL-17E used in our studies. Formal dose-escalation studies are planned to fully examine IL-17E-related toxicities. Lorus is planning to initiate these studies as part of the IND-enabling toxicity program for IL-17E in 2009.

## Mechanism of Action

Lorus is currently elucidating the role of immune factors in the antitumor activity demonstrated by IL-17E. Lorus believes that eosinophils and B cells are essential for IL-17E-mediated antitumor response, and that these cells exert an antitumor effect both directly and indirectly through the activation of other immune factors.



Tumor-bearing mice treated with IL-17E show a significant increase in serum levels of IL-5, as well as increased numbers of eosinophils in peripheral blood, spleen and tumors, as compared to tumor-bearing control mice. IL-17E-treated mice also showed a significant increase in the number of splenic B-cells, as well as an increase in the percentage of activated splenic B cells. Overexpression of IL-17E *in vivo* is known to induce the expression of several proinflammatory cytokines and increase the numbers of eosinophils and B cells.

## Patent Protection

- ▶ PCT application filed on March 2006: Use of Interleukin 17E for the Treatment of Cancer.

## Technology Validation

With our expertise in the development of immune modulators for cancer therapy, Lorus is well positioned to develop IL-17E as a potent and safe anti-cancer agent. Please see our abstract from the 2005 ASCO annual meeting that includes data presented at the meeting:

Benatar T *et al.*, Virulizin induces production of IL-17E to enhance antitumor activity by recruitment of eosinophils into tumors. *Journal of Clinical Oncology*, 2005 ASCO Annual Meeting Proceedings. Vol 23, No 16S (June 1 Supplement), 2005: 2537

[http://www.asco.org/portal/site/ASCO/menuitem.34d60f5624ba07fd506fe310ee37a01d/?vgnextoid=76f8201eb61a7010VqnVCM100000ed730ad1RCRD&vmview=abst\\_detail\\_view&confID=34&abstractID=33909](http://www.asco.org/portal/site/ASCO/menuitem.34d60f5624ba07fd506fe310ee37a01d/?vgnextoid=76f8201eb61a7010VqnVCM100000ed730ad1RCRD&vmview=abst_detail_view&confID=34&abstractID=33909)

## IL-17E Development Plan

Based on the mechanism of action of IL-17E and its effectiveness to inhibit tumor growth in animal models of metastatic cancer, Lorus is developing IL-17E as an immunotherapy for treatment of solid tumors. IL-17E is the second development candidate derived from Lorus' drug discovery program.

The Company has already completed preclinical efficacy and dose response studies. Future studies will include, dose-escalation preliminary toxicology studies, safety pharmacology, CMC and GLP toxicology studies. Based on the outcome of these studies, the Company intends to initiate a Phase I clinical study in solid tumors and further expand into additional cancer indications.

## Market Opportunity

- *IL-17E has a broad antitumor effect with low toxicity.*
- *IL-17E can be used as a single agent or in combination with one or more anti-tumor therapeutics in the treatment of cancer.*

Cytokine-based research is revolutionizing the treatment of inflammatory, infectious, and neoplastic diseases. Many of the original cytokine treatments have given way to more refined approaches as the knowledge and discovery process concerning complex cytokine and chemokine networks becomes further clarified. The increased market penetration of approved drugs targeting cytokines and their receptors has spurred several pharmaceutical companies to devote a portion of their pipelines to the development of these immunotherapeutics.

## Partnering / Cooperation Options

Lorus is seeking for corporate partners interested in further development of IL-17E and academic partners for testing of new applications for this product. We would welcome a partner who will bring expertise and/or funding for further development.

## Contact Information

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