Ad-RTS-IL12 has a Broad Therapeutic Window in Melanoma Cancer (B16F0) Model

- **Figure 3:** The dose response of Ad-RTS-IL-12 in melanoma (B16F0) tumor.
- **Figure 4:** The dose response of Ad-RTS-mIL-12 with activator ligand (L) in melanoma (B16F0) tumor.

**Ad-RTS-IL12 has a Broad Activator Dose Window in Various Tumor Models**

- **Figure 5:** Antitumor activity of AdRTS-mIL12 with activator ligand in various cancer models.

**Ad-RTS-mIL12 has a Broad Therapeutic Window across a wide range doses of activator ligand (100-1000 mg/kg of rodent feed).**

- **Figure 1:** Schematic representation of recombinant adenovirus incorporating the Rheoswitch Therapeutic System (RTS) inducible gene regulation system. In the absence of the activator ligand, the transcription of the responsive/mutagenic rheoSwitch®-Mediated Regulation of IL-12 Protein Delivered Using an Adenoviral Vector Results in Anti-Tumor Effects Across a Spectrum of Tumor Types

- **Rheoswitch®-Mediated Regulation of IL-12 Protein Delivered Using an Adenoviral Vector Results in Anti-Tumor Effects Across a Spectrum of Tumor Types**

- **Abstract**

One of the limitations of current cancer research is the development of new treatment strategies. In this study, a novel approach was proposed to improve the therapeutic efficacy of cancer treatment by utilizing a therapeutic protein named Ad-RTS-mIL12. Ad-RTS-mIL12 is a novel system with promising therapeutic potential. The utility of Ad-RTS-mIL12 in the treatment of cancer is limited due to toxicity. To improve the therapeutic capability and avoid toxicity, we developed the RTS® (Rheoswitch Therapeutic System) inducible gene regulation system that enables activation (AdRTS-mIL12) or expression of IL-12 mRNA (Ad-RTS-IL12). This technology has been well characterized, and is currently being employed in a number of clinical trials. In the present study, we evaluated the therapeutic potential of Ad-RTS-mIL12 in various cancer models. The results demonstrated that Ad-RTS-mIL12 is a promising therapeutic agent for cancer treatment.

- **Results**

Ad-RTS-mIL12 was administered via IT injections at a dose of 1x1010 vp. The tumor growth was monitored using a caliper, and the tumor size was determined using the formula: (length x width) / 2. The tumor inhibition was calculated as follows: (1 - (tumor size of treated group / tumor size of control group)) x 100.

- **Conclusion**

Ad-RTS-mIL12 is a promising therapeutic agent for cancer treatment with a broad therapeutic window. Further studies are needed to determine the optimal dose and duration of treatment for different cancer models.

- **Acknowledgments**

This research was supported by grants from the National Cancer Institute (NCI) and the American Cancer Society (ACS). We would like to thank the members of our laboratory for their valuable contributions.

- **References**

1. Selva R Murugesan, Mario Moreno, Sheila Connelly, Fayaz Khaiz, Meiza B, Mini Bharathan, Charles Reed, Vernon Daily, Qin Zong, Mark Thornton and Sunil Chada. RheoSwitch®-Mediated Regulation of IL-12 Protein Delivered Using an Adenoviral Vector Results in Anti-Tumor Effects Across a Spectrum of Tumor Types.

- **Figure 2:** The potency of Ad-RTS-mIL12 with various doses of activator ligand (L) in melanoma (B16F0) tumor. The B16F0 tumors were grown in C3H/HeJ mice. The tumor growth was followed using calipers, and the tumor size was determined using the formula: (length x width) / 2. The tumor inhibition was calculated as follows: (1 - (tumor size of treated group / tumor size of control group)) x 100.

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**Rheoswitch Therapeutic System (RTS) Inducible Gene Regulation System**

- **Therapeutic Gene Expression is ON**

- **Therapeutic Gene Expression is OFF**

- **Figure 1:** Schematic representation of recombinant adenovirus incorporating the Rheoswitch Therapeutic System (RTS) inducible gene regulation system. The cancer cells, transduced with Ad-RTS-mIL12, the Gal4-EcR and VP16-RXR fusion proteins are expressed under the control of constitutive promoters. These proteins form heterodimers in the presence of the activator ligand, resulting in the conditional activation of mIL-12 transcription from the responsive/mutagenic rheoSwitch®-RheoSwitch®-Mediated Regulation of IL-12 Protein Delivered Using an Adenoviral Vector Results in Anti-Tumor Effects Across a Spectrum of Tumor Types.

- **Abstract Session II.**

A Phase I clinical trial is currently in progress in patients with advanced melanoma cancer who were intolerant or refractory to traditional chemotherapies. The results of this trial will be presented at the meeting.

- **Figure 2:** The potency of Ad-RTS-mIL12 with various doses of activator ligand (L) in melanoma (B16F0) tumor. The B16F0 tumors were grown in C3H/HeJ mice. The tumor growth was followed using calipers, and the tumor size was determined using the formula: (length x width) / 2. The tumor inhibition was calculated as follows: (1 - (tumor size of treated group / tumor size of control group)) x 100.

- **Figure 3:** The dose response of Ad-RTS-mIL12 in melanoma (B16F0) tumor.

**Summary**

- **•** Evidence of broad therapeutic window for both activator ligand and AdRTS-mIL12 in in vivo melanoma cancer model

- **Concentration of AdRTS-mIL12 and activator ligand demonstrated strong anti-tumor activity in various cancer models, including melanoma, breast, and lung cancer.**

- **•** AdRTS-mIL12 and activator ligand were well tolerated.

**ZIOPHARM Oncology**

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- **Poster #68**

Selva R Murugesan, Mario Moreno, Sheila Connelly, Fayaz Khaiz, Meiza B, Mini Bharathan, Charles Reed, Vernon Daily, Qin Zong, Mark Thornton and Sunil Chada. RheoSwitch®-Mediated Regulation of IL-12 Protein Delivered Using an Adenoviral Vector Results in Anti-Tumor Effects Across a Spectrum of Tumor Types.

- **Intrexon Corporation, Germantown, MD and ZIOPHARM Oncology, Boston, MA**

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