UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
PURSUANT TO SECTION 13 OR 15(d)
OF THE SECURITIES EXCHANGE ACT OF 1934

Date of report (Date of earliest event reported): May 22, 2014

ZIOPHARM Oncology, Inc.
(Exact Name of Registrant as Specified in Charter)

Delaware	**001-33038**	**84-1475672**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

One First Avenue, Parris Building 34, Navy Yard Plaza Boston, Massachusetts	**02129**
(Address of Principal Executive Offices)	**(Zip Code)**

(617) 259-1970
(Registrant's telephone number, including area code)

Not applicable
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425).

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12).

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b)).

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c)).

Item 7.01 Regulation FD Disclosure

On May 22, 2014, ZIOPHARM Oncology, Inc., or the Company, announced the presentation of results demonstrating the potent anti-tumor and anti-cancer stem cell (CTC) effects of Ad-RTS-IL-12 in a glioma (brain cancer) model, and in other preclinical and clinical settings. The presentation, titled "Intratumoral Regulated Expression of IL-12 as a Gene Therapy Approach to Immunotherapy," was presented in an oral session at the 17th Annual Meeting of the American Society of Gene and Cell Therapy, held May 21-24 in Washington, D.C.

A copy of the above referenced press release is furnished as Exhibit 99.1 to this Current Report on Form 8-K and a copy of the above referenced presentation is furnished as Exhibit 99.2 to this Current Report on Form 8-K. This information, including the information contained in the press release furnished as Exhibit 99.1 and the presentation furnished as Exhibit 99.2, shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, and is not incorporated by reference into any of the Company's filings, whether made before or after the date hereof, regardless of any general incorporation language in any such filing.

Item 9.01 Financial Statements and Exhibits

(d) Exhibits

Exhibit No.	Description
99.1	Press release of the Company dated May 22, 2014
99.2	Presentation of the Company dated May 22, 2014

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

ZIOPHARM Oncology, Inc.

By: /s/ Kevin G. Lafond
Name: Kevin G. Lafond
Title: Vice President, Chief Accounting Officer and Treasurer

Date: May 22, 2014

INDEX OF EXHIBITS

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99.1	Press release of the Company dated May 22, 2014
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Exhibit 99.1

ZIOPHARM Announces Oral Presentation Highlighting Ad-RTS-IL-12
Results Correlated with Reducing Cancer Stem Cells in the Brain
at ASGCT 17th Annual Meeting

BOSTON, MA – May 22, 2014 – ZIOPHARM Oncology, Inc. (Nasdaq: ZIOP), a biopharmaceutical company focused on the development and commercialization of new cancer therapies, announced today results demonstrating the potent anti-tumor and anti-cancer stem cell (CTC) effects of Ad-RTS-IL-12 in a glioma (brain cancer) model, and in other preclinical and clinical settings. Ad-RTS-IL-12 is a novel DNA-based therapeutic candidate for the controlled expression of IL-12, an important protein for stimulating an anti-cancer T cell immune response. The presentation, titled "Intratumoral Regulated Expression of IL-12 as a Gene Therapy Approach to Immunotherapy," was presented in an oral session at the 17th Annual Meeting of the American Society of Gene and Cell Therapy (ASGCT), held May 21-24 in Washington, DC.

Results from human and laboratory studies of Ad-RTS-IL-12 demonstrate that precise control of IL-12 gene expression levels can be achieved using Intrexon Corporation's (NYSE: XON) RheoSwitch Therapeutic System® (RTS®). Rapid, tight modulation of in vivo expression of IL-12 using the activator ligand veledimex was demonstrated across these studies. When IL-12 expression is "switched on" it rapidly leads to expression and an immune response. This immune response is characterized by an increase in tumor infiltrating lymphocytes with system wide immune activation. This modulated immune response has resulted in anti-tumor effects in both injected and systemic non-injected legions in Phase 1 and Phase 2 studies of Ad-RTS-IL-12 in subjects with melanoma and breast cancer.

The data presented today further demonstrate that Ad-RTS-IL-12 has potent anti-cancer effects in a glioma model, showing both a reduction in tumor mass and prolonged survival when compared to existing treatment standards. The data also show a significant reduction in brain cancer stem cells, as measured by dramatically reduced nestin levels. Brain cancer stem cells are thought to play a critical role in recurrence and metastasis.

"Ad-RTS-IL-12 seems to offer precise control over a potent immuno-oncology weapon, the IL-12 cytokine," said Antonio Chiocca, MD, PhD, Prof. and Chairman of Neurosurgery at Brigham and Women's Hospital and Harvard Medical School. "With malignant glioma in particular, delivery of IL-12 is one of several promising experimental approaches being tested, but unlike other therapies the ability to control IL-12 expression in vivo may prove to be ground breaking. This is increasingly being demonstrated both in preclinical models, as well as in the clinic, where patients are showing reversal of immuno-toxicity, including cytokine storm, and then resume therapy." He continued: "IL-12's role in reducing cancer stem cells is also very encouraging, as the role of these cells in recurrence and metastasis is increasingly well understood. I look forward to further data from these clinical and preclinical programs, as well as to the initiation of a Phase 1 study of Ad-RTS-IL-12 in brain cancer."

About ZIOPHARM Oncology, Inc.:

ZIOPHARM Oncology is a Boston, Massachusetts-based biotechnology company employing novel gene expression and control technology to deliver DNA for the treatment of cancer. ZIOPHARM's technology platform employs Intrexon Corporation's RheoSwitch Therapeutic System® technology to turn on and off, and precisely modulate, gene expression at the cancer site in order to improve the therapeutic index. This technology is currently being evaluated in Phase 2 clinical studies of the immune system cytokine interleukin-12 for the treatment of breast cancer and advanced melanoma. Multiple new Investigational New Drug Applications for new targets using synthetic biology technology are expected through 2015. ZIOPHARM is also developing novel small molecules as potential cancer therapeutics.

Forward-Looking Safe Harbor Statement:

This press release contains certain forward-looking information about ZIOPHARM Oncology, Inc. that is intended to be covered by the safe harbor for "forward-looking statements" provided by the Private Securities Litigation Reform Act of 1995, as amended. Forward-looking statements are statements that are not historical facts. Words such as "expect(s)," "feel(s)," "believe(s)," "will," "may," "anticipate(s)" and similar expressions are intended to identify forward-looking statements. These statements include, but are not limited to, statements regarding our ability to successfully develop and commercialize our therapeutic products; our ability to expand our long-term business opportunities; financial projections and estimates and their underlying assumptions; and future performance. All of such statements are subject to certain risks and uncertainties, many of which are difficult to predict and generally beyond the control of the company, that could cause actual results to differ materially from those expressed in, or implied or projected by, the forward-looking information and statements. These risks and uncertainties include, but are not limited to: whether Ad-RTS-IL-12, palifosfamide, darinaparsin, indibulin, or any of our other therapeutic products will advance further in the clinical trials process and whether and when, if at all, they will receive final approval from the U.S. Food and Drug Administration or equivalent foreign regulatory agencies and for which indications; whether Ad-RTS-IL-12, palifosfamide, darinaparsin, indibulin, and our other therapeutic products will be successfully marketed if approved; whether any of our other therapeutic product discovery and development efforts will be successful; our ability to achieve the results contemplated by our collaboration agreements; the strength and enforceability of our intellectual property rights; competition from other pharmaceutical and biotechnology companies; the development of, and our ability to take advantage of, the market for our therapeutic products; our ability to raise additional capital to fund our operations on terms acceptable to us; general economic conditions; and the other risk factors contained in our periodic and interim SEC reports filed from time to time with the Securities and Exchange Commission, including but not limited to, our Annual Report on Form 10-K for the fiscal year ended December 31, 2013 and our Quarterly Report on Form 10-Q for the quarter ended March 31, 2014. Readers are cautioned not to place undue reliance on these forward-looking statements that speak only as of the date hereof, and we do not undertake any obligation to revise and disseminate forward-looking statements to reflect events or circumstances after the date hereof, or to reflect the occurrence of or non-occurrence of any events.

Contact:

Lori Ann Occhiogrosso
Director of Corporate Communication
ZIOPHARM Oncology, Inc.
617-259-1987
locchiogrosso@ziopharm.com

INTRATUMORAL REGULATED EXPRESSION OF IL-12 AS A GENE THERAPY APPROACH TO IMMUNOTHERAPY

John Nemunitis[1], John A. Barrett[2], Francois Lebel[2], Thomas D. Reed[3], E. Antonio Chiocca[4], Antonio M. Omuro[5], Larry Norton[5], Jonathan Lewis[2]

[1]Mary Crowley Cancer Research Centers, Dallas, TX, United States, 75201
[2]ZIOPHARM Oncology Inc., Boston, MA, United States, 02129
[3]Intrexon Corporation, Germantown, MD, United States, 20876
[4]Brigham and Woman's Hospital, Harvard Medical School, Boston, MA, United States, 02115
[5]Memorial Sloan-Kettering Cancer Center, New York, NY, United States, 10065

Background & Rationale IL-12 in Glioma

- Tumors escape the immune system through the process of immunoediting. Thus, restoration of the immune system's ability to detect the tumor should result in improved treatment outcomes.
- Localized IL-12 administration has been shown to have antitumor activity that is mediated by direct tumor cell cytotoxicity, and enhancement of immuno-regulatory activities including activation of anti-tumor natural killer (NK) cells, $CD4^+$ T cells and $CD8^+$ T cells.

Background & Rationale IL-12 in Glioma

- Roy & Kranz (University of Illinois) IL-12. *Journal of Immunology,* 2000, 165: 7293–7299. **Model**: SV11 Transgenic mouse administered recombinant mIL-12 i.c. **Findings**: Increased survival infiltration of activated CD8 and CD4 T cells.

- Vom Berg & Becher (University of Zurich) J Exp Med, 2013, 210: 2803-2811. **Model:** GL261 transduced to constitutively express IL-12 i.c. **Findings:** Increased survival combination of IL-12 + CTLA4 elicits decrease Tregs while increasing Teff.

- Dimeco & Olivi **(**Johns Hopkins School of Medicine & Istituto Nazionale Tumori, Milan, Italy*)* *J Neurosurg* 2000, 92:419–427, **Model*:*** Rat 9L gliosarcoma cells expressing IL-12. **Findings**: Local delivery of IL-12 in rat brain prolongs survival in animals challenged i.c. with a malignant glioma cells.

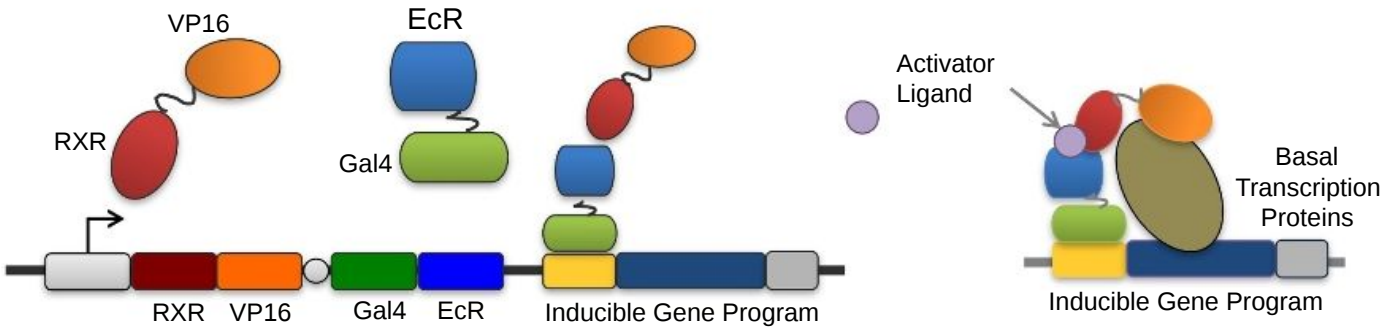
- Sonabend & Lesniak (University of Chicago). *Anti-Cancer Drugs* 2008, 19:133–142. **Model:** GL-261 orthotopic glioma model. **Findings:** Synergy in survival with locally administered pmIL-12/PPC + biodegradable carmustine

- Markert & Whitley (University of Alabama) *Journal of Virology* 2012,86: 5304–5313 **Model:** 4C8 glioma cells orthotopic B6D2F1 mouse. **Findings:** Hsv mutant M002 expressing IL-12 demonstrated prolonged survival vs. control

- Liu & Yu (Cedars Sinai Medical Center) *Cancer Gene Therapy* (2002) 9, 9–15 **Model:** GL-26 orthotopic mouse. Ad5-mIL-12 **Findings:** Survival was significantly prolonged in Ad-mIL-12–treated animals with increased CD4+ and CD8+ T- cell infiltration

Inducible Gene Regulation: RheoSwitch Therapeutic System®

RheoSwitch Therapeutic System® (RTS®) is a 3-component transcriptional regulator

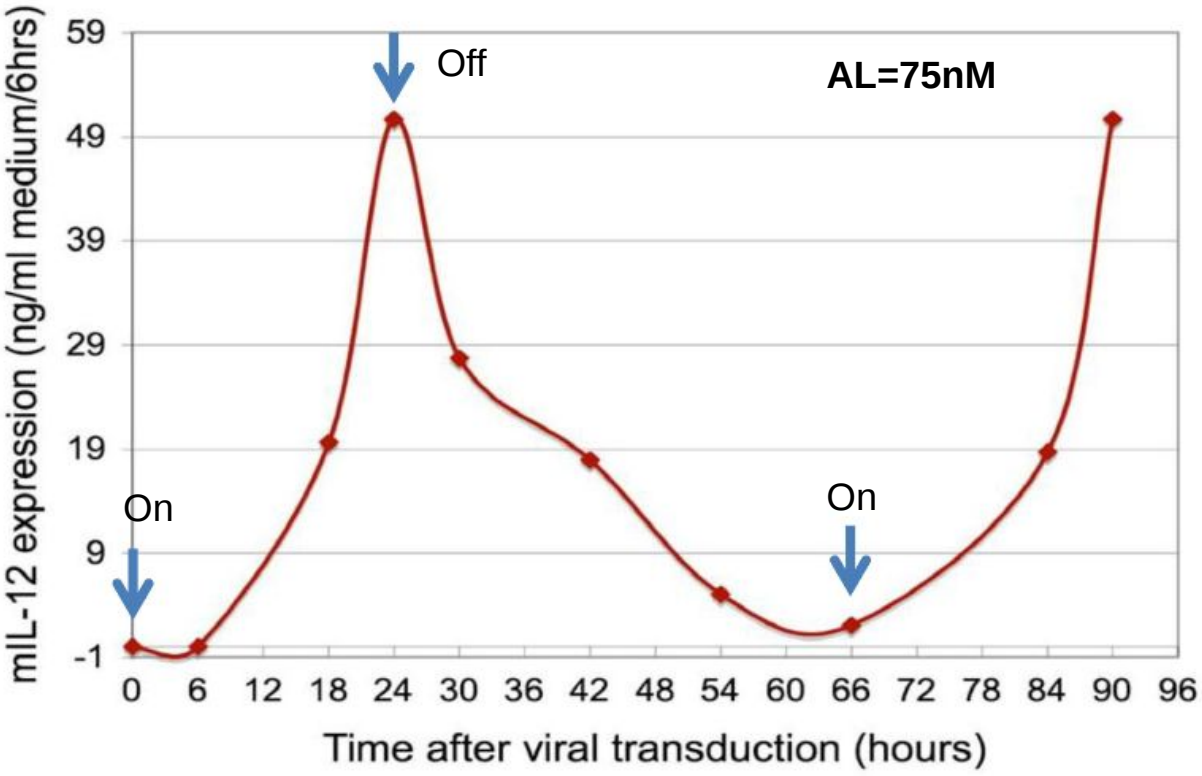


1. **The Switch Components:** The RTS® gene program includes 2 receptor protein fusions: VP16-RXR and Gal4-EcR. They form unstable and unproductive heterodimers in the absence of any ligand.

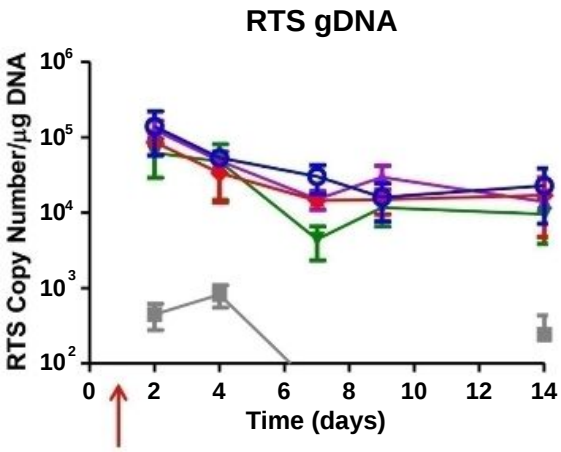
2. **The Inducible Promoter:** A customizable promoter to which basal transcription proteins are recruited and the target gene is transcribed.

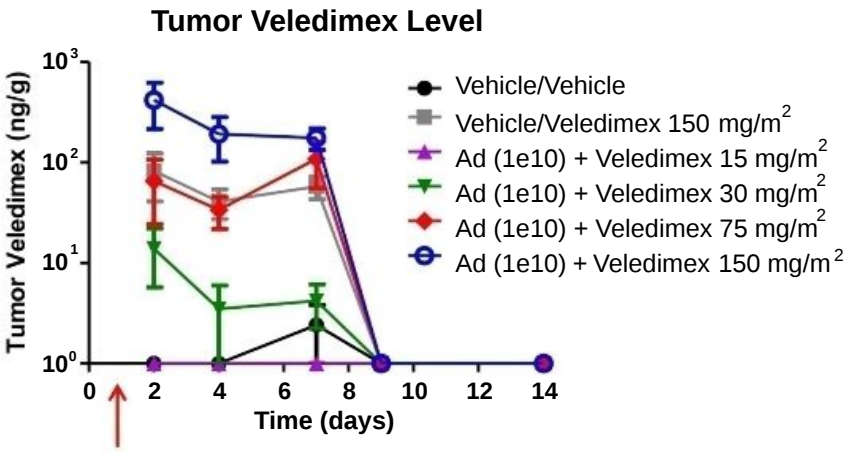
3. **The Activator Ligand (veledimex):** An ecdysone analog, diacylhydrazine-based small molecule functions as an activator. In the presence of the ligand, the protein heterodimer changes to a stable conformation and binds to the inducible promoter.

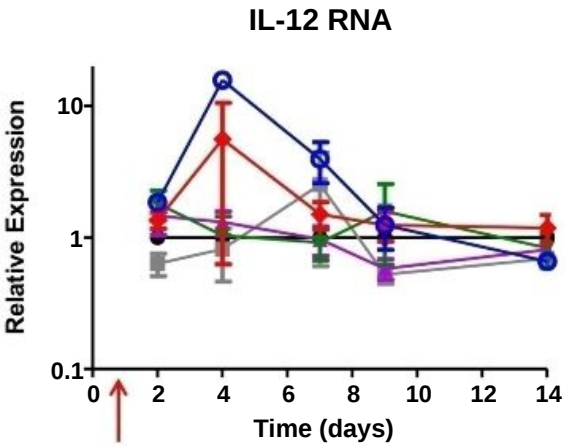
IL-12 Production is Modulated by Activator Ligand in HT 1080 Cells

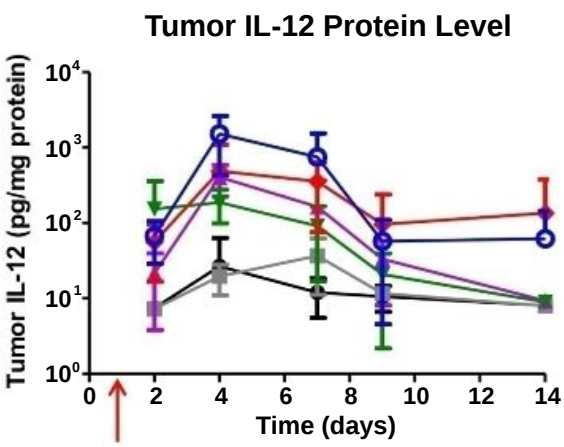


Dose-Dependent Increase in Expression of Tumor IL-12 mRNA & IL-12 Protein in Response to Veledimex

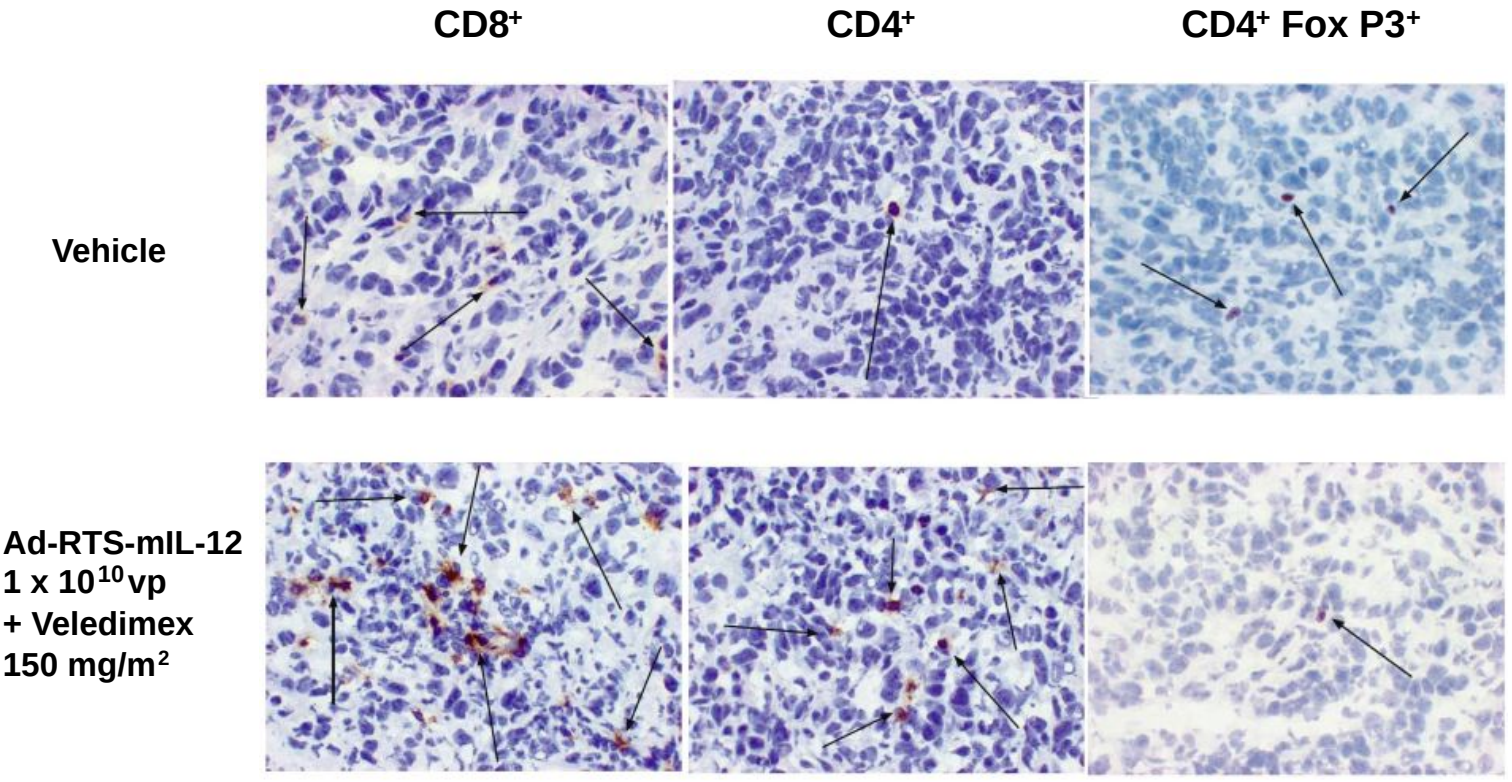




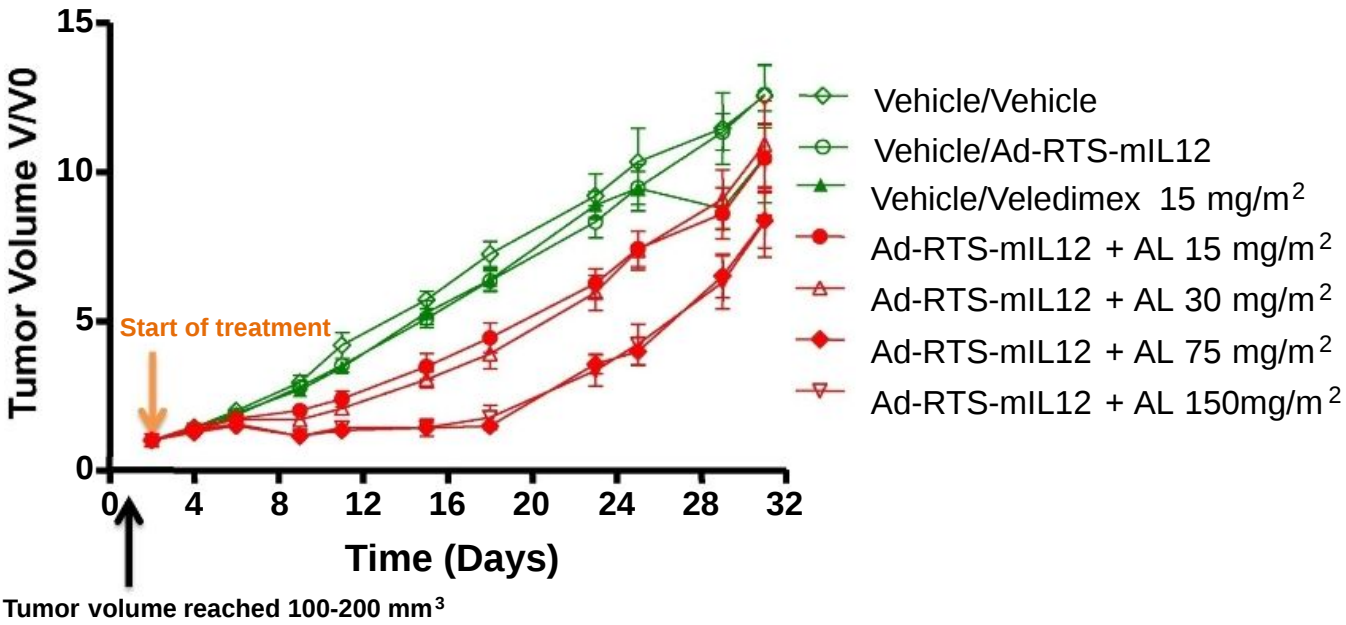




Ad-RTS-mIL-12 + Veledimex Increases Tumor CD8$^+$ & CD4$^+$ While Decreasing CD4$^+$ Fox P3$^+$ TILs in the 4T1 Syngeneic Mouse



Dose-Dependent Anti-Tumor Activity of Ad-RTS-mIL-12 + Veledimex (AL) in Murine 4T1 Model



Tumor volume reached 100-200 mm^3

Clinical Observations to Date

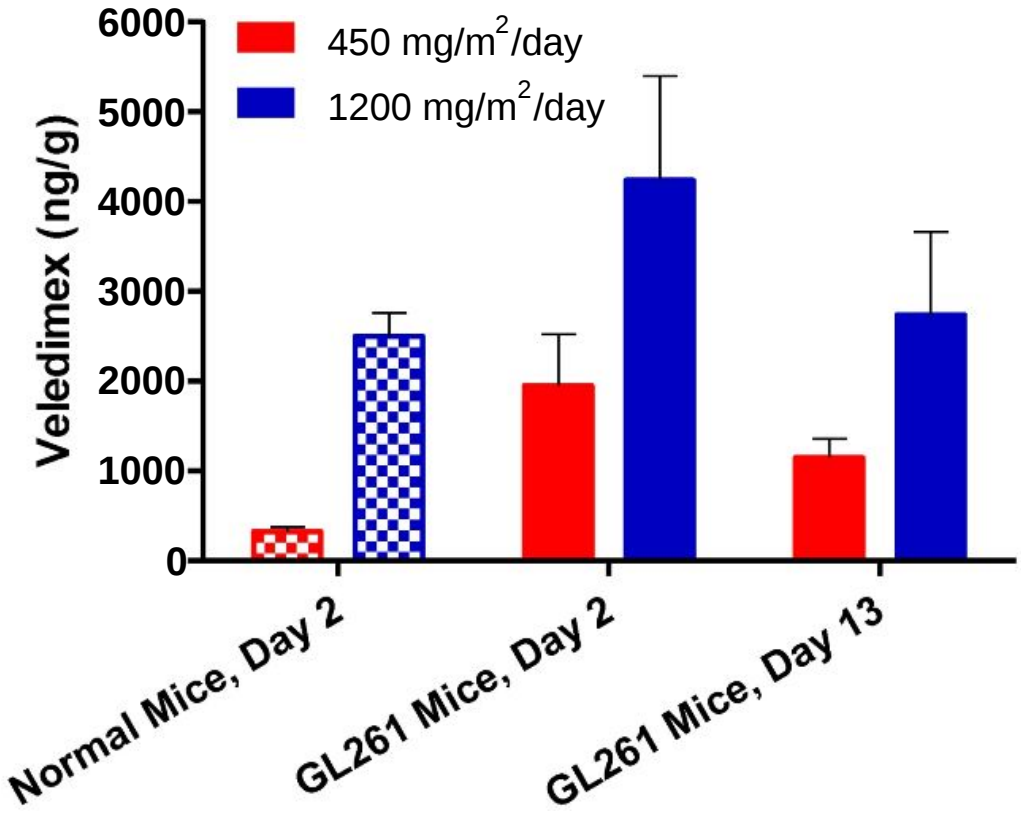
We can control gene expression to achieve a systemic immune response

- High expression of IL-12 mRNA in tumors, tightly controlled by veledimex dose
- Tumor biopsies show increased tumor infiltrating lymphocytes in both injected and systemic non-injected lesions

We have seen systemic and fully reversible toxicity

- Serious adverse events are mechanism-based and consistent with immunotherapy (Fever, N&V, leukopenia, increased LFTs, hyponatremia, cytokine release response)
- Serious adverse events reversed within days after stopping veledimex dosing
- Subjects who have had IL-12 expression turned “off” have been redosed, and IL-12 turned “on” again

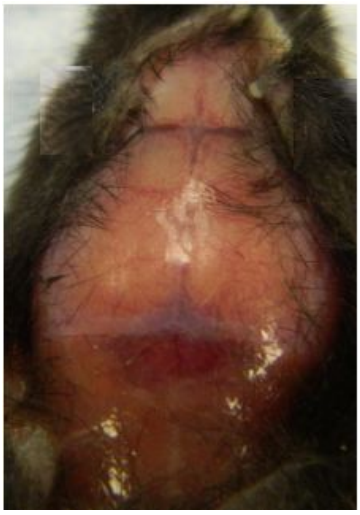
Higher Veledimex Levels Normal and in GL261 Orthotopic Glioma Mouse Brains



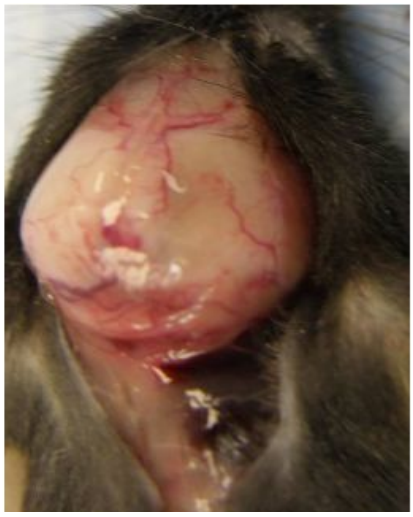
Veledimex levels at 24 hr posttreatment

Effects of Ad-RTS-mIL-12 + Veledimex (AL) in the Orthotopic GL261 Mouse

Normal Mouse

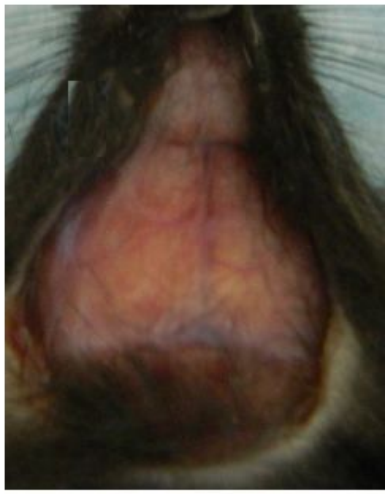


Control Day 20



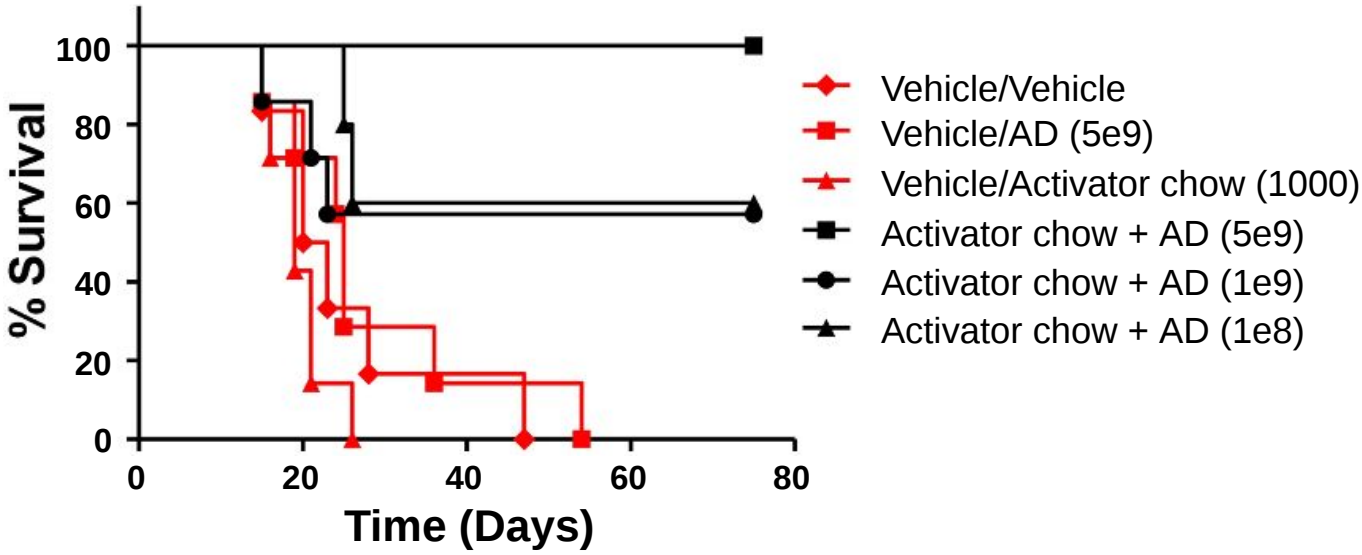
Vehicle
BID x 14

Treatment For 14 days
Day 74 (end of study)



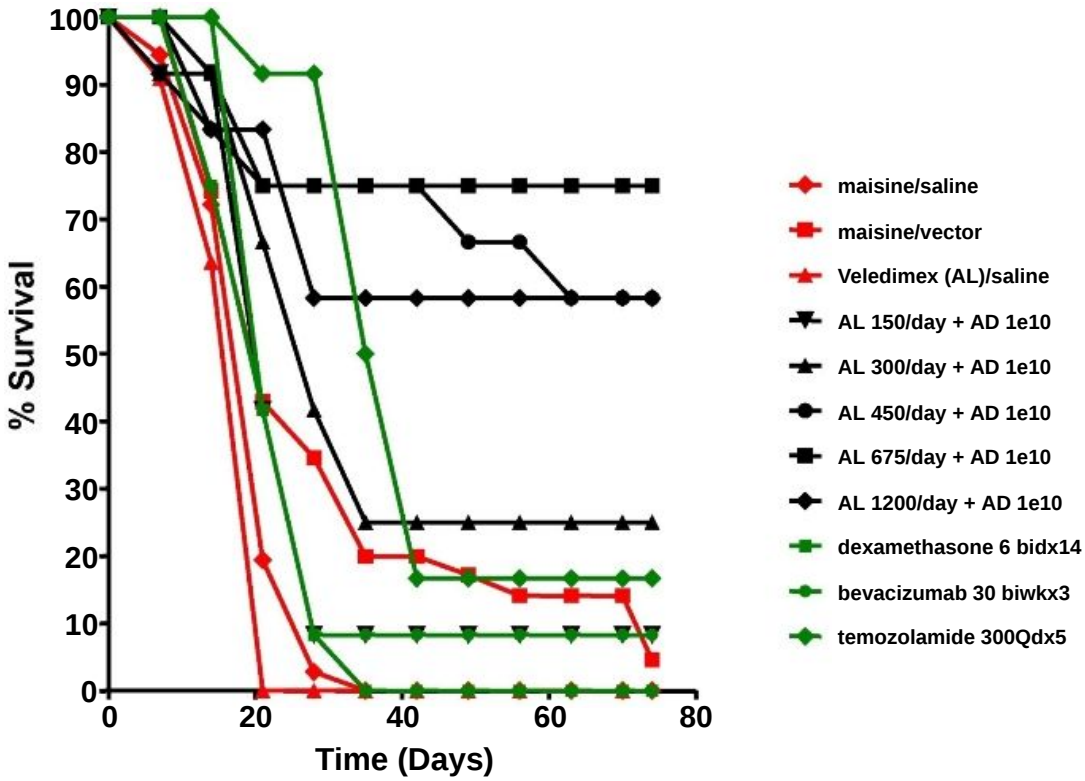
Ad-RTS-mIL-12 $1x10^{10}$vp
+ AL 450 mg/m^2/day
BID x14

Ad-RTS-mIL-12 + Veledimex (in Chow) Results in Increased Survival in the GL261 Orthotopic Glioma Mouse Model



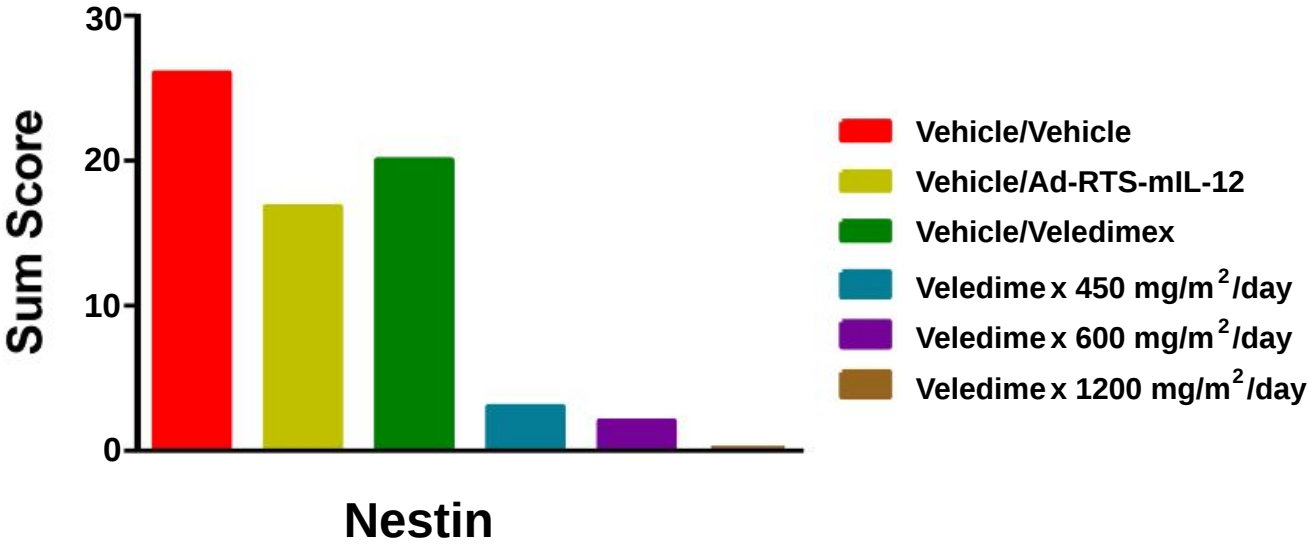
Veledimex administered *ad lib* in chow from Day 4 to EOS at ~ 675 mg/m ^{2}/day
Ad-RTS-mIL12 administered on Day 5

Ad-RTS-mIL-12 + Veledimex (AL) Results in Increased Survival When Compared to Control in the GL261 Orthotopic Glioma Mouse Model



Ad-RTS-mIL12 administered on Day 5 ; Veledimex (mg/m^2) administered BID for 14 days from Day 5;

Ad-RTS-mIL-12 + veledimex significantly reduces brain cancer stem cells in GL-261 Orthotopic Glioma Model



Nestin levels (marker for cancer stem cells)
inverse correlation with survival (Pearson r= 0.92)

Conclusions

- Ad-RTS-mIL-12 + veledimex PO exhibits controllable systemic immune activation in human subjects with melanoma and breast cancer.
- Veledimex exhibits dose-related increases in plasma and brain tissue exposure with no accumulation in brain.
- Ad-RTS-mIL-12 ($1x10^{10}$ vp) + veledimex PO improves survival over temozolomide, dexamethasone and bevacizumab.
- Ad-RTS-mIL-12 + veledimex significantly reduces brain cancer stem cells
- These findings support the utility of localized, regulatable IL-12 production as an approach for the treatment of malignant glioma in human subjects.