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

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**FORM 8-K**

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

**Date of report (Date of earliest event reported): January 15, 2014**

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

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**Delaware**  
(State or Other Jurisdiction  
of Incorporation)

**001-33038**  
(Commission  
File Number)

**84-1475672**  
(IRS Employer  
Identification No.)

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

**02129**  
(Zip Code)

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

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

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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)).
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**Item 8.01 Other Events**

On January 15, 2014, ZIOPHARM Oncology, Inc., or the Company, will present the attached discussion of the Company's synthetic-biology development strategy and milestones at the 32nd Annual J.P. Morgan Healthcare Conference in San Francisco, California, being held on January 13 - 16, 2014.

A copy of the above referenced presentation is filed as Exhibit 99.1 to this Current Report on Form 8-K.

**Item 9.01 Financial Statements and Exhibits**

(d) Exhibits

<u>Exhibit No.</u>	<u>Description</u>
99.1	Presentation of the Company dated January 15, 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 Finance, Chief Accounting Officer and Treasurer

Date: January 15, 2014

**INDEX OF EXHIBITS**

**Exhibit  
No.**

**Description**

99.1 Presentation of the Company dated January 15, 2014



# **ZIOPHARM Oncology**

## The Future of Cancer Therapy

J.P. Morgan 32nd Annual Healthcare Conference  
January 2014

Jonathan Lewis, MD, PhD, Chief Executive Officer

# Forward-Looking Statements

This presentation contains certain **forward-looking information about ZIOPHARM Oncology** 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 any of our therapeutic candidates 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 which indications; whether any of our therapeutic candidates will be successfully marketed if approved; whether our DNA-based biotherapeutics 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 pharmaceutical and biotechnology companies; the development of and our ability to take advantage of the market for DNA-based biotherapeutics; 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 periodic and interim reports filed with the SEC including, but not limited to, our Annual Report on Form 10-K for the fiscal year ended December 31, 2012, and our Quarterly Report on Form 10-Q for the fiscal quarter ended June 30, 2013. Our audience is 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.



## Clinical-stage, synthetic-biology oncology company

- Gene based therapies regulating protein expression and controlling cellular function
- Clear leader in *in vivo* control of gene regulation and expression
- Technology channel partner Intrexon Corp. (NYSE: XON)

## Phase 2 program: Ad-RTS-IL-12

- High intratumoral expression of IL-12
- Targeting multiple cancers, including melanoma, breast cancer and glioma
- Multiple new clinical studies planned through 2015

## Technology platform driving clinical program

- Enabling multigenic approach to immunotherapy and cancer therapy
- Multiple INDs planned through 2015



# Why Focus on Synthetic DNA-Based Medicine?

Synthetic DNA is DNA that is intelligently and intentionally designed for a specific function.

## Synthetic DNA enables:

- creation of **new therapies** with targeted biofunction
- **precise control** of biologic concentration and dosing
- **better therapeutic index** through controlled protein delivery and cellular targeting
- **economically feasible approach** to combination biologic therapies

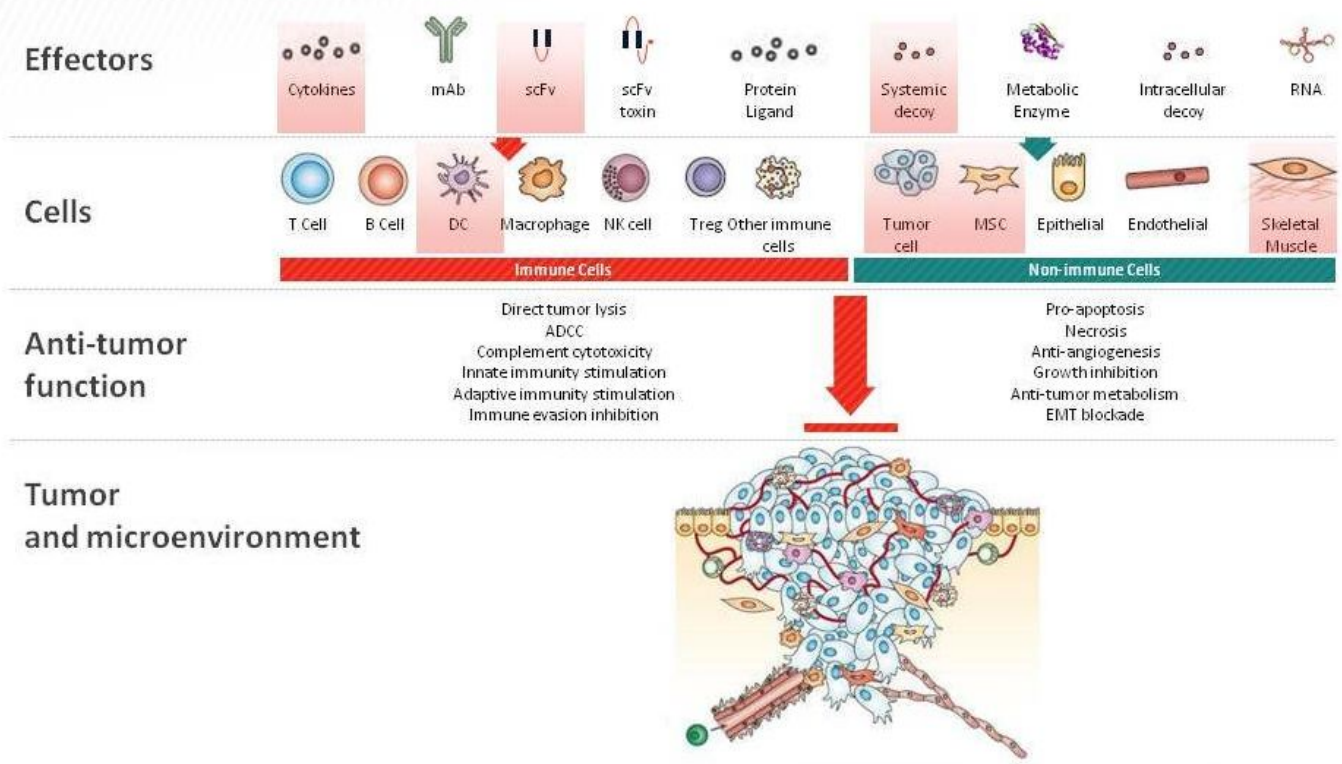




# Molecular and Cellular Oncology DNA-Coded Toolset



ZIOPHARM Oncology



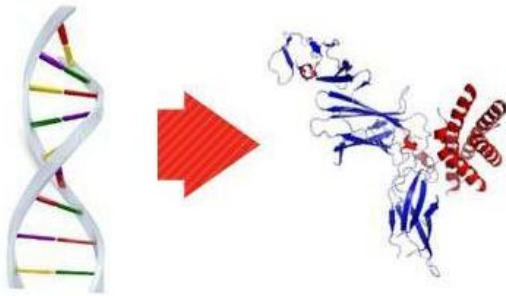
# The Power of Intrexon's RheoSwitch® Technology



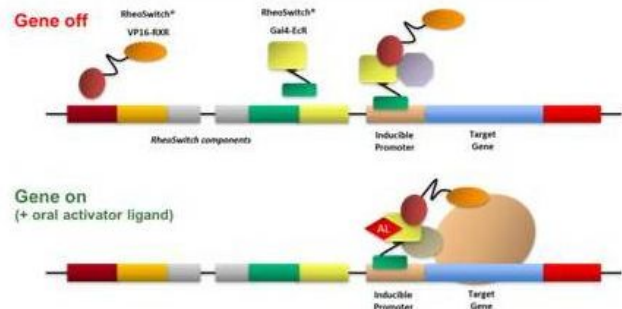
ZIOPHARM Oncology

**Controlled Expression and Delivery of Therapeutic Proteins with RheoSwitch®:**  
This is the most advanced clinical method to turn genes on and off

## Gene Expression



## RheoSwitch®



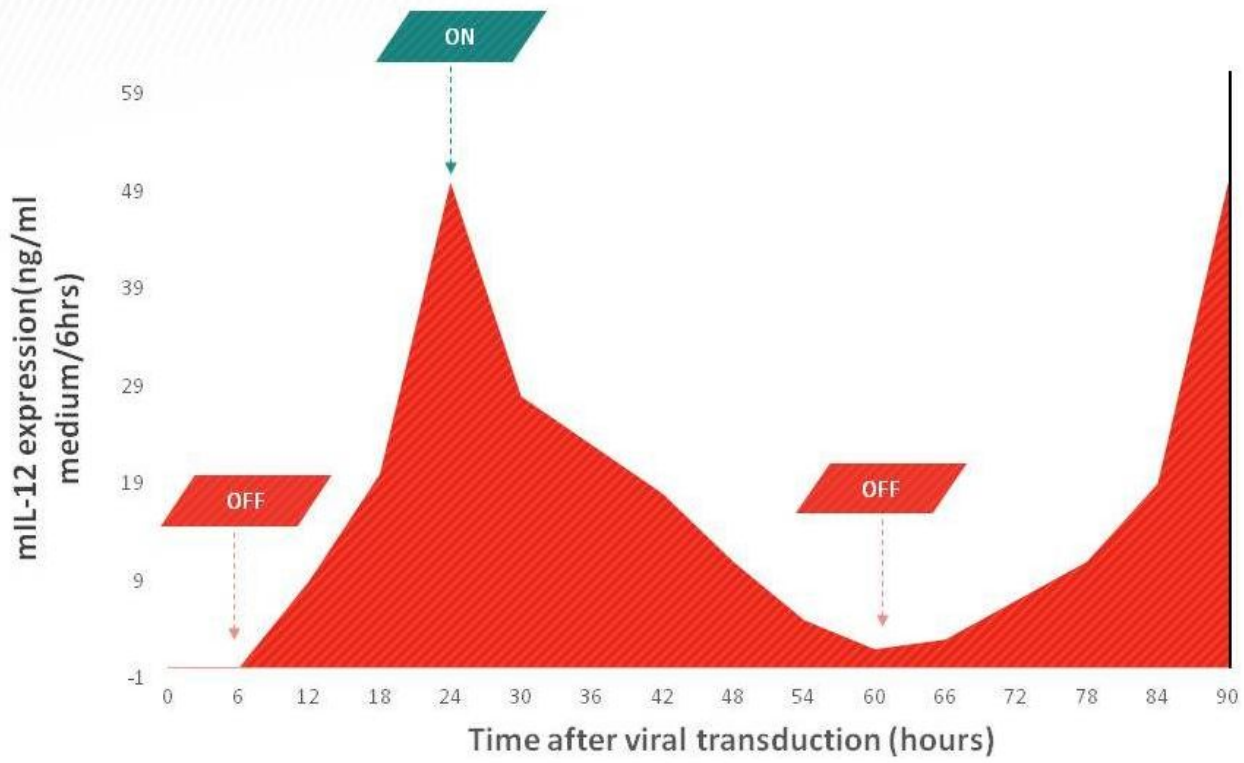
- Local
- High Potency
- Monogenic/Multigenic

- Dose-control
- Orally activated biologic on/off switch

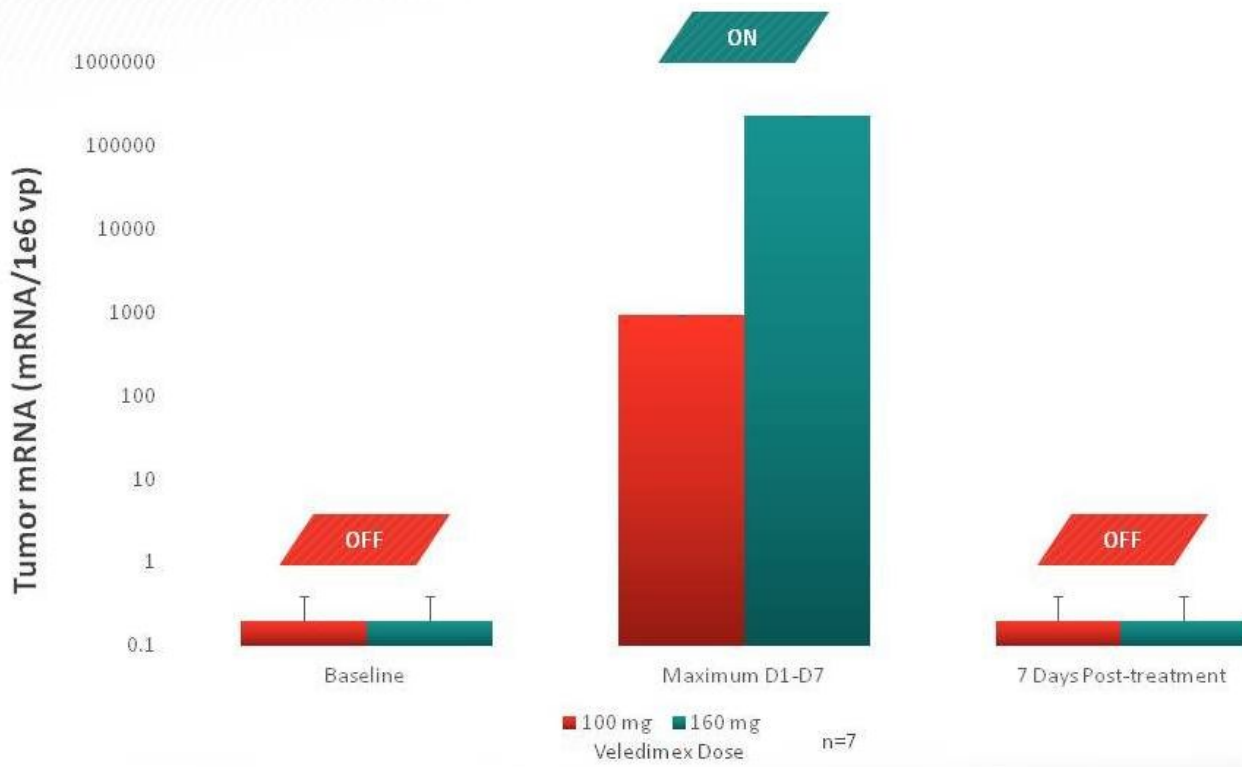
# IL-12 Production is Modulated by Veledimex (Activator Ligand) in HT 1080 Cells



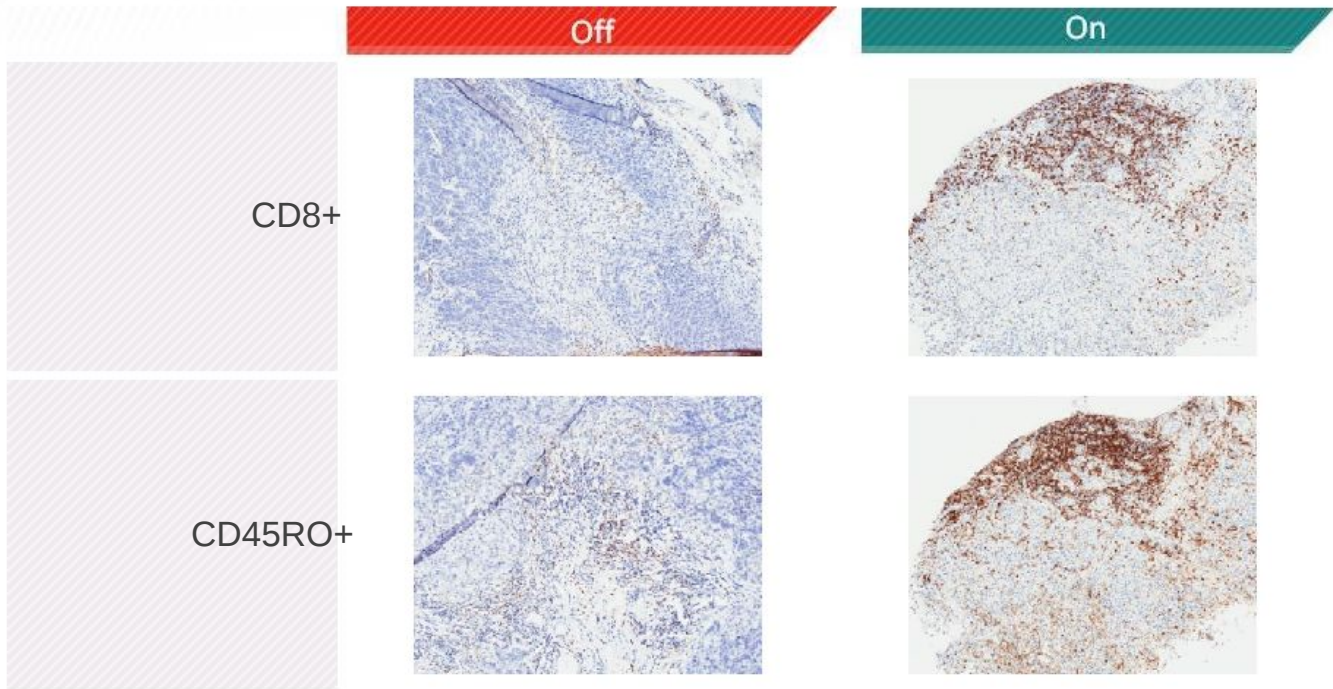
ZIOPHARM Oncology



# Veledimex Tightly and Precisely Controls the Expression of IL-12 $\beta$ RNA in the Tumor



# Cytotoxic T Cells & Memory T Cells (TILs) Significantly Increase in Tumors Following Ad-RTS-IL-12 Treatment



Images were obtained using an Aperio ScanScope XT whole-slide imager and digitized at 20x.

# Phase 1/2 Melanoma Study

- Subjects with unresectable stage III/IV melanoma, n=13 (Phase 1) + n= 8 (Phase 2, ongoing)
- Intratumoral injection of Ad-RTS-hIL-12 on Day 1 of each cycle
- Oral administration of veledimex to activate gene expression of hIL-12

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## Primary Objective

Evaluate the safety and tolerability of intratumoral injections of Ad-RTS-hIL-12 in combination with veledimex

## Secondary Objective

Inform the selection of a veledimex dose and regimen for further study in combination with Ad-RTS-hIL-12

# Prominent Tumor Infiltrating Lymphocyte Response Correlates with Biologic Activity

C1D1



C1D16



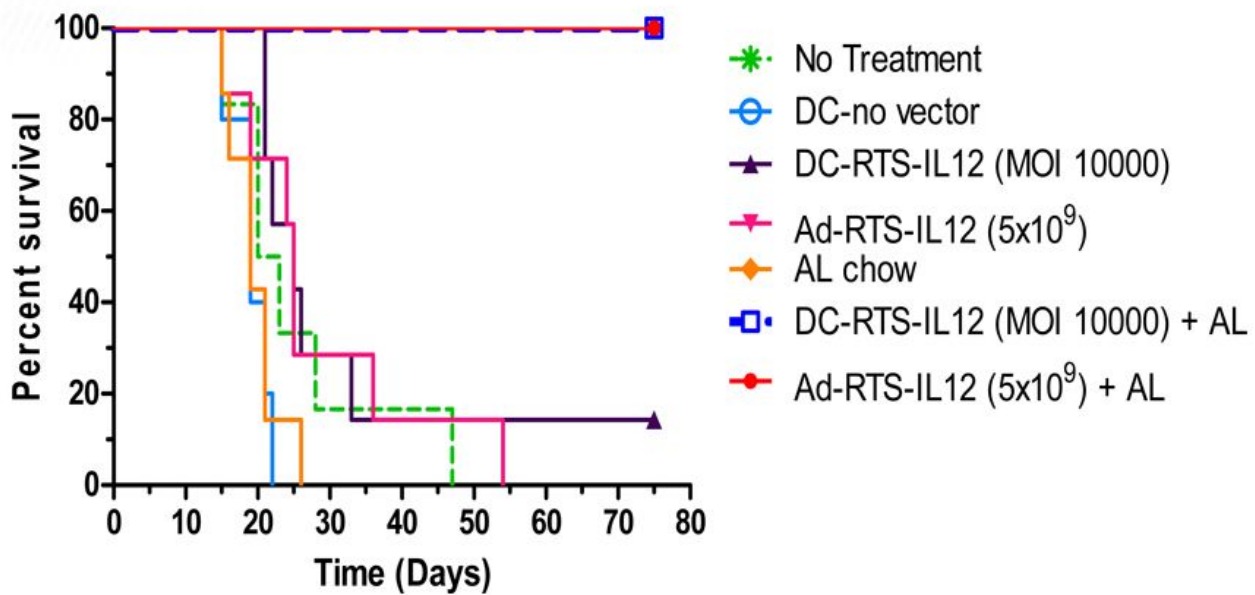
C2D1



- Initial increase in lesion size due to immune response seen at Cycle 1 Day 16
- Lesion was undetectable at Cycle 2 Day 1
- Subject ultimately progressed and was taken off study

# Glioblastoma Multiforme: IL-12 Preclinical Activity

Kaplan Meier Survival in GL261 Orthotopic Syngeneic Mouse Model



Veledimex (AL) dosing Day 4 to EOS at ~ 675 mg/m<sup>2</sup>/day in chow; DC-RTS-IL-12 or Ad-RTS-IL-12 on Day 5  
**100% survival observed with Ad-RTS-IL-12 + AL or DC-RTS-IL-12 + veledimex**



## Clinical Conclusions to Date

### Tight control of expression and biologic activity

- High expression of IL-12 mRNA *in tumors, tightly controlled* by veledimex dose
- Increased tumor infiltrating lymphocytes (TILs) observed *in the tumor* microenvironment, suggesting *multiple favorable biologic effects* of IL-12 expression

### On-mechanism and on-target response and toxicity

- *Melanoma: potent biologic activity in injected and non-injected sites*
- *Breast: on-mechanism and on-target toxicity demonstrates powerful manifestation of the immune system controlled by dose-dependent inducible expression of IL-12*
- Adverse events consistent with immunotherapy use and immune response;  
*Serious adverse events reversed* after veledimex dosing stopped

### Optimization of dose and scheduling to refine response and tolerability is ongoing

*“This opens the possibility that, for the first time, we can achieve personalized scheduling as a component of personalized cancer medicine.”*

*Larry Norton, M.D., Deputy Physician-in-Chief for Breast Cancer Programs, Memorial Sloan-Kettering Cancer Center*

# Significant Market Potential for Ad-RTS-IL-12



## Incidence



# IL-12 Next Study Timelines

## Melanoma Phase 2

## Breast cancer Phase 2

## GBM Phase 1

combination study with SOC combination study with SOC dose-escalation study

FPI 1H 2014

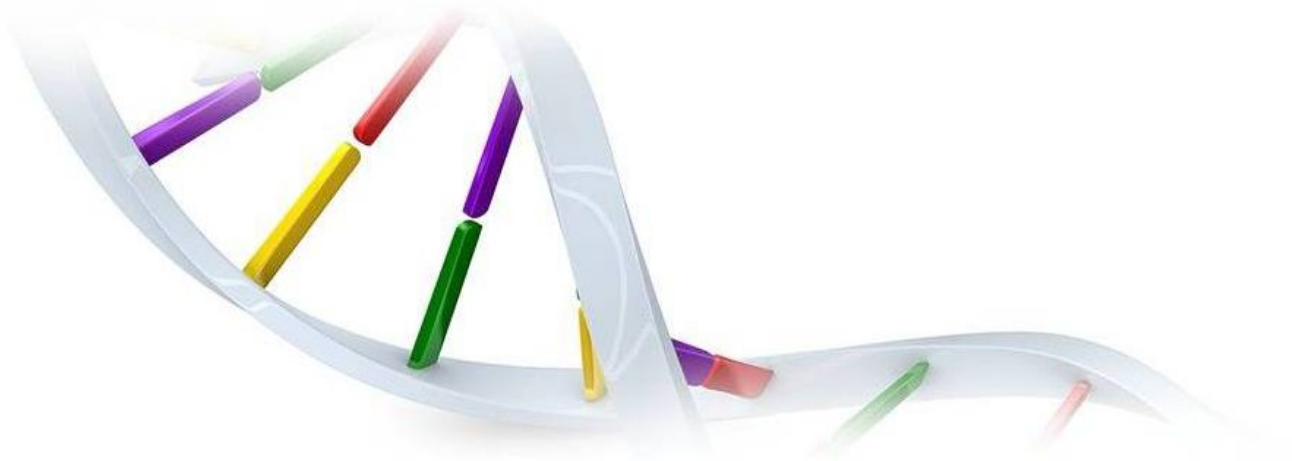
Preliminary data YE 2014

FPI 1H 2014

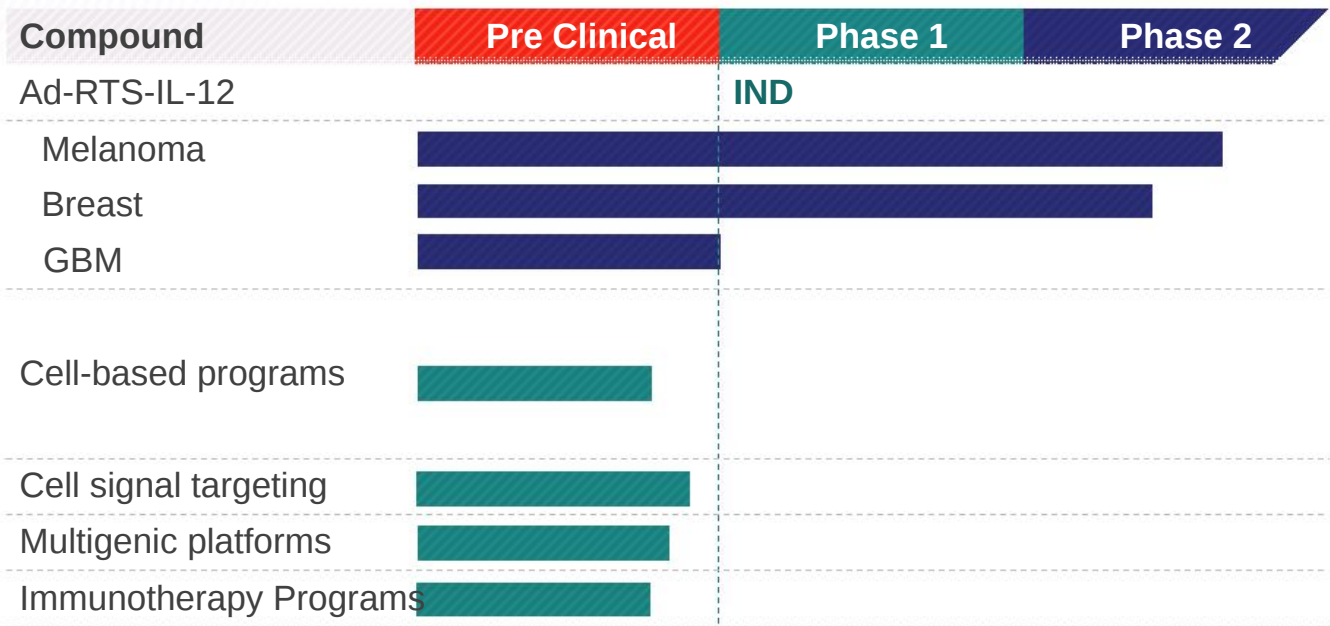
Preliminary data 1H 2015

FPI 1H 2014

Preliminary data YE 2014



# A Growing Oncology Portfolio



# We can intelligently and intentionally construct multi-gene therapies



# Combination Therapies Targeting Multiple Cancers: Potential INDs



ZIOPHARM Oncology

**Human mesenchymal stem cells (hMSCs) genetically modified with multigenic hIL-12, hIFN $\alpha$ , and CTLA4 decoy**

- Potential use of hMSCs for tumor-targeted delivery of multiple RTS $\textcircled{R}$ regulated cancer immunotherapies

**Integration of modularized protein engineering technology and the RTS $\textcircled{R}$  platform to develop high-affinity trastuzumab (Herceptin $\textcircled{R}$ ) and cetuximab (Erbix $\textcircled{R}$ ) single-chain variable fragment-Fc proteins for gene therapy**

- Potential use of inducible multigenic systems to treat cancer using multigenic therapeutic antibodies

**RTS $\textcircled{R}$ regulated immunomodulatory proteins expressed from multigenic embedded cellular bioreactor (ECB) using electroporation into skeletal muscle**

- Potential use of ECBs to deliver multiple proteins systemically, under control of RTS $\textcircled{R}$  platform



# Upcoming Milestones



ZIOPHARM Oncology

Program	Milestone	Timing
IL-12	Phase 2 breast cancer study data	2014
	Phase 2 advanced melanoma study data	2014
	Initiate Phase 1/2 glioblastoma multiforme study	1H 2014
	Initiate Phase 2 melanoma combo study	1H 2014
	Initiate Phase 2 breast cancer combo study	1H 2014
New Indications	Report discovery and preclinical data	2014
	Submit INDs for monogenic/multigenic studies	2H 2014 and beyond
Publications and Presentations	Across programs	2014
Corporate	Seek partnering opportunities	Ongoing



## Financial Highlights

Approx. **100 million shares outstanding** (pro forma)

Approx. **\$77.4 million in cash and investments** (pro forma)

No debt

**Channel partner/top shareholder**

 Intrexon Corp. (NYSE: XON)





**Ad-RTS-IL-12 advancing through Phase 2 studies in breast cancer and melanoma**

- On-mechanism and on-target response and toxicity observed
- Expanded data anticipated in late 2014 and in 2015

**Pre-clinical/clinical data on glioblastoma in 2014**

**Poised to launch multiple new studies in 2014 and beyond**

**INDs targeting new gene expression patterns, new cell types and new indications**





# **ZIOPHARM Oncology**

The Future of Cancer Therapy

NASDAQ: ZIOP

Jonathan Lewis, MD, PhD

Chief Executive Officer

[www.ziopharm.com](http://www.ziopharm.com)