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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 11, 2017**

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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)

**84-1475642**  
(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 7.01 Regulation FD Disclosure**

On January 11, 2017, ZIOPHARM Oncology, Inc., or the Company, will present the attached presentation at the 35<sup>th</sup> Annual J.P. Morgan Healthcare Conference in San Francisco, California being held on January 9 – 13, 2017.

A copy of the above referenced presentation is furnished as Exhibit 99.1 to this Current Report on Form 8-K. This information, including the information contained in the presentation furnished as Exhibit 99.1, 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

<u>Exhibit No.</u>	<u>Description</u>
99.1	Presentation of the Company dated January 11, 2017

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: Sr. Vice President Finance, Chief

Accounting Officer and Treasurer

Date: January 11, 2017

**INDEX OF EXHIBITS**

<b><u>Exhibit No.</u></b>	<b><u>Description</u></b>
99.1	Presentation of the Company dated January 11, 2017



**ZIOPHARM Oncology**

**35<sup>th</sup> Annual J.P. Morgan  
Healthcare Conference**

January 11, 2017

## Forward-looking Statements

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*This presentation 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, and in some cases can be identified by terms such as "may," "will," "could," "expects," "plans," "anticipates," and "believes." These statements include, but are not limited to, statements regarding the progress, timing and results of preclinical and clinical trials involving the Company's drug candidates, and the progress of the Company's research and development programs. 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 by, the forward-looking statements. These risks and uncertainties include, but are not limited to: whether chimeric antigen receptor T cell (CAR T) approaches, Ad-RTS-IL-12, TCR and NK cell-based therapies, or any of our other therapeutic candidates will advance further in the pre-clinical or 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 chimeric antigen receptor T cell (CAR T) approaches, Ad-RTS-IL-12, TCR and NK cell-based therapies, and our other therapeutic products will be successfully marketed if approved; the strength and enforceability of our intellectual property rights; competition from other pharmaceutical and biotechnology companies; 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, 2015, and our Quarterly Report on Form 10-Q for the quarter ended September 30, 2016. 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.*



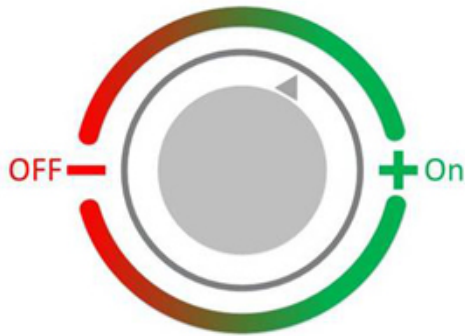
# Cost and Control

The next generation of DNA-based immunotherapies will need to master cost and control

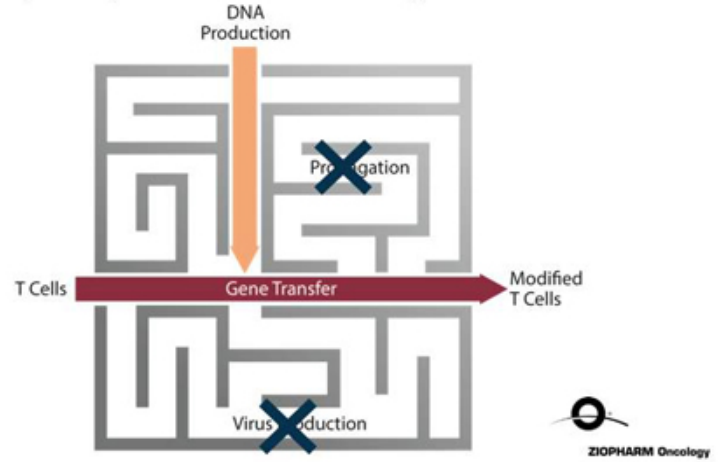


# ZIOPHARM Has Clinically-Validated Genetic Engineering Tools to *Increase Control, Reduce Complexity, and Manage Costs*

The RheoSwitch Therapeutic System<sup>®</sup> gene switch enables precise control over gene expression *in vivo*

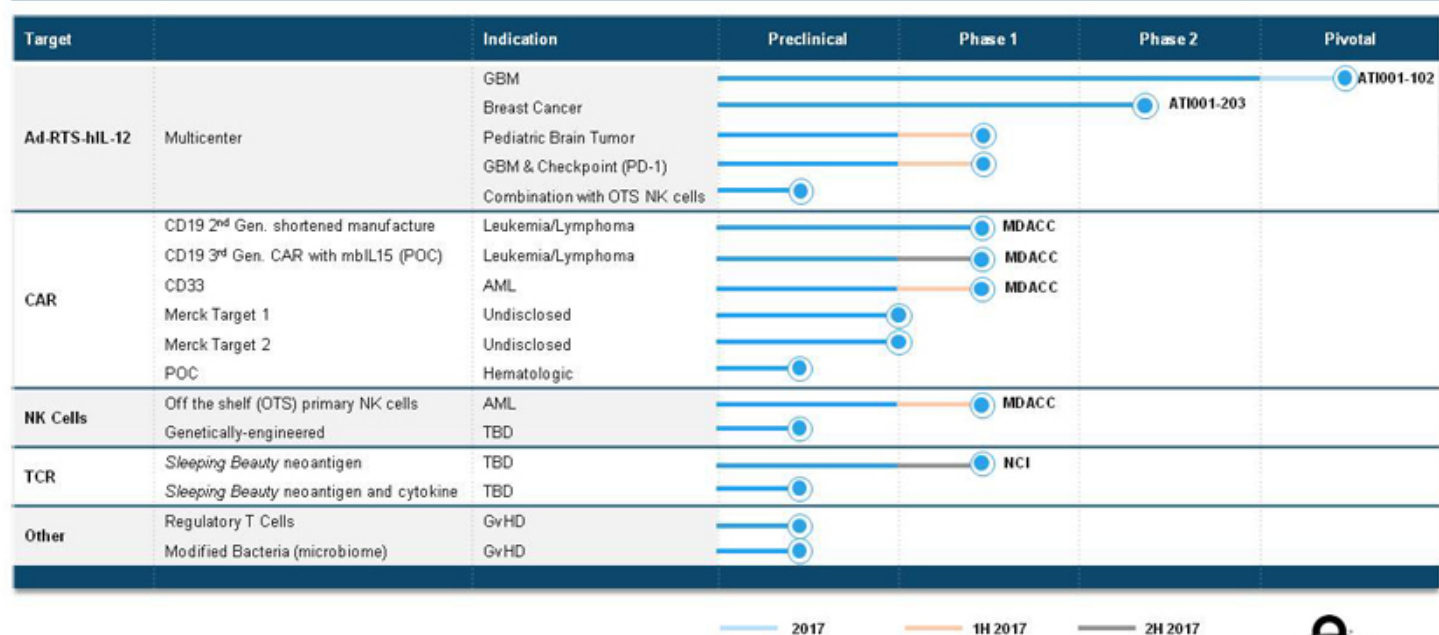


Non-viral *Sleeping Beauty* system has the potential to eliminate many GMP steps in cell manufacturing *ex vivo*, thereby reducing complexity of manufacturing





# Addressing Unmet Medical Needs



***Control***

**Ad-RTS-hIL-12 + Veledimex**



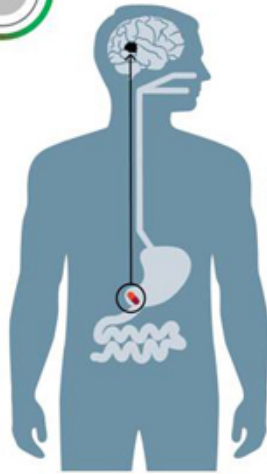
**ZIOPHARM Oncology**

# Control Using the RheoSwitch Therapeutic System<sup>®</sup> (RTS<sup>®</sup>)

Intratumoral injection of Ad-RTS-hIL-12



Veledimex taken by mouth

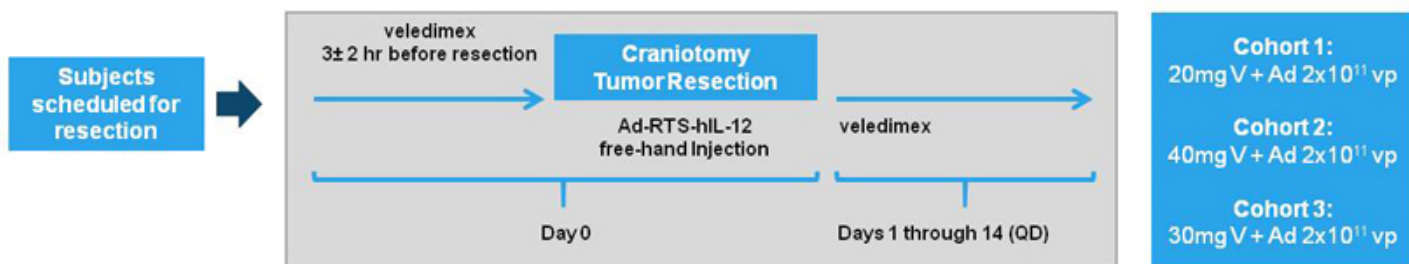


IL-12 production calls in cellular immune response



Cellular immune response shows durability beyond initial IL-12 signaling

# A Study of Ad-RTS-hIL-12 + Veledimex in Subjects With Recurrent or Progressive Glioblastoma



DANA-FARBER/BRIGHAM AND WOMEN'S  
CANCER CENTER

CEDARS-SINAI

UCSF

THE UNIVERSITY OF CHICAGO  
PRITZKER SCHOOL OF MEDICINE

Northwestern Memorial  
Hospital

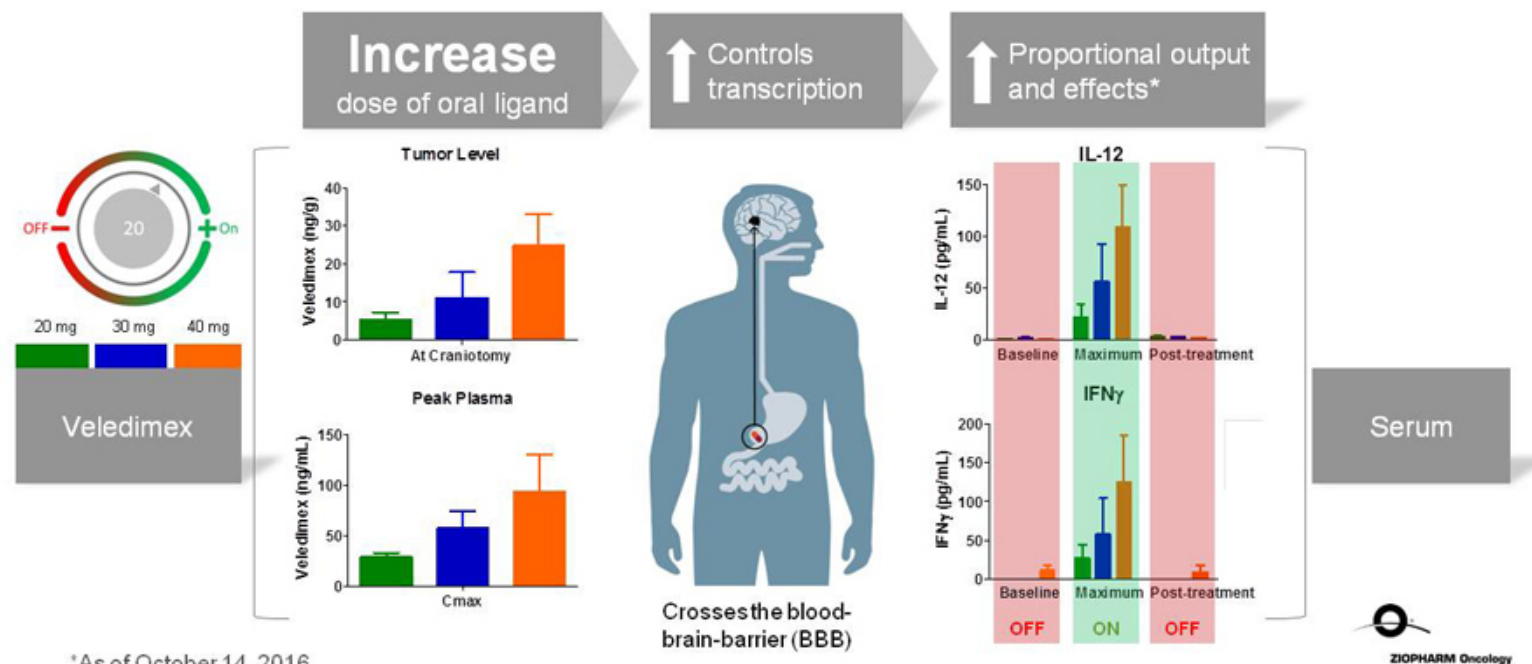


Ability to control IL-12 gene expression in multicenter study

Clinicaltrials.gov: NCT02026271

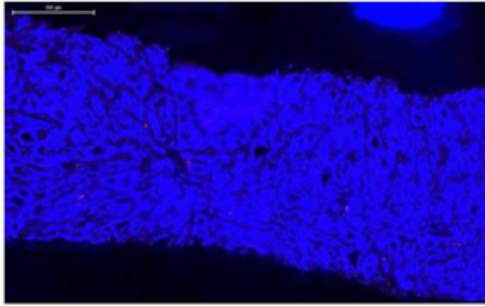


# RTS® Switch Responds to the Presence/Absence and Dose of Veledimex in Recurrent or Progressive Glioblastoma Patients

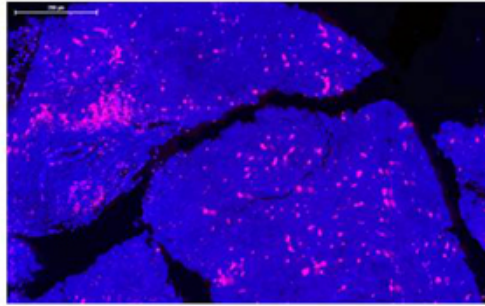


# Ad-RTS-hIL-12 + Veledimex in Subjects With Breast Cancer: Positive Biomarker Data\*

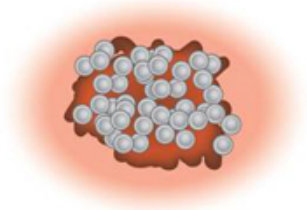
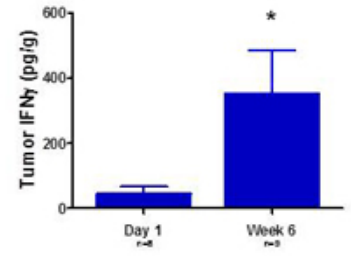
CD8<sup>+</sup> T cells



Baseline: Cold Tumor



6 Weeks: Inflamed Tumor



\*European Society for Medical Oncology 2016

## Interim Study Results

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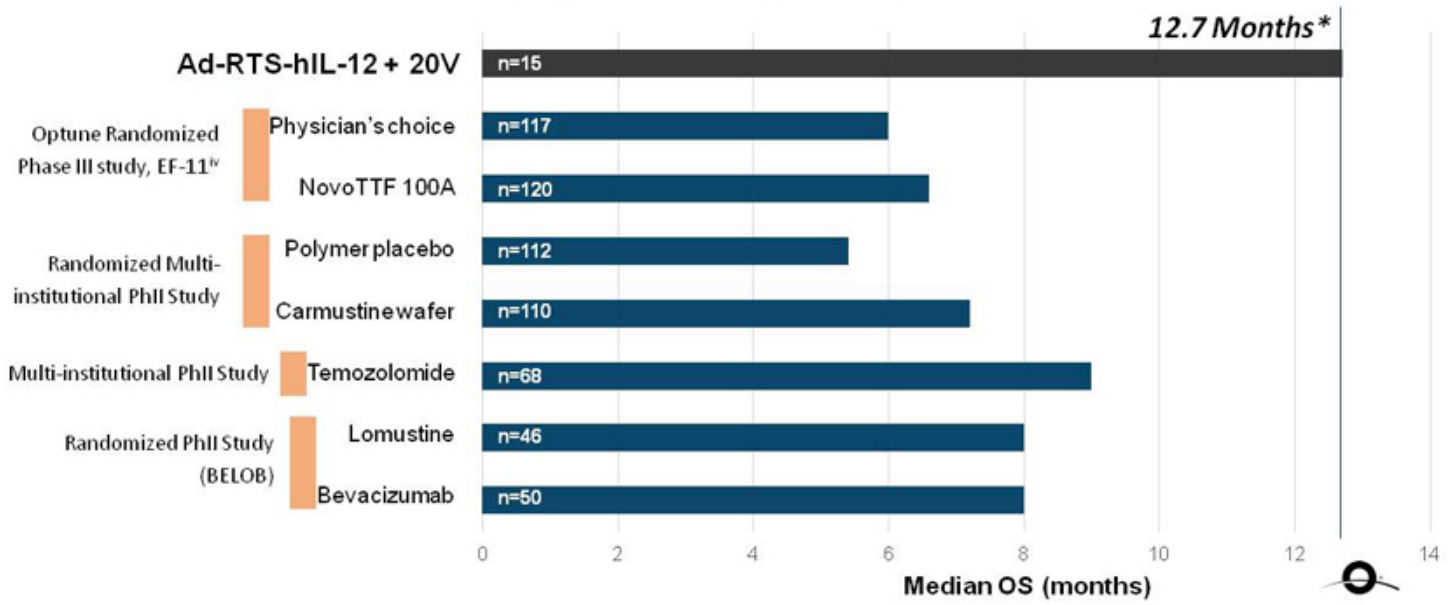
- Based on tolerability and survival benefit (median OS=12.7 months, n=15), 20 mg was selected for an expansion cohort and we are following patients' overall survival data\*
- Ad-RTS-hIL-12 + veledimex is well tolerated and suggests a survival benefit over historical controls at 6, 9, and 12 months (median OS=9.6 months, n=25)
- Toxicities were tolerable, predictable and reversible upon discontinuing veledimex
- There is a strong correlation between veledimex dose, BBB penetration, and IL-12 production
- These data demonstrate that the RTS<sup>®</sup> gene switch works in humans toggling not only as a switch to turn on and off the production of IL-12, but also as a rheostat to control the level of IL-12

\* As of January 6, 2017



# Interim Median Overall Survival (mOS) Relative to Historical Controls

## Studies in recurrent GBM



\* As of January 6, 2017



# Registration Pathway for Recurrent Glioblastoma



## Registration Pathway

- **End-of-Phase 2** face-to-face meeting with FDA in early Q1 2017
- Determine design of **pivotal trial** to be **initiated in 2017**

### Glioblastoma

**74,000** new cases annually worldwide

**12,120** in the U.S. in 2016

Recurrence rates are **~90%**

Less than **10%** of patients are alive at 5 years

Source: World Health Organization, American Cancer Society, Central Brain Tumor Registry of the United States

## Clinical Studies with Ad-RTS-hIL-12 + Veledimex in 2017

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Based on strong preclinical data previously presented at ASGCT and SNO in 2016, advance to the clinic:

- **Combination with checkpoint inhibitor**
  - Open stereotactic arm of the Phase 1 GBM study and then combine with checkpoint inhibitor in adult recurrent glioblastoma – 1H 2017
- **Pediatric trial for brain tumors**
  - Open initially for supratentorial disease and then diffuse intrinsic pontine gliomas (DIPG) – 1H 2017

Strategic focus on brain cancer trials; Pause breast cancer study in 2017

# ***Cost and Control***

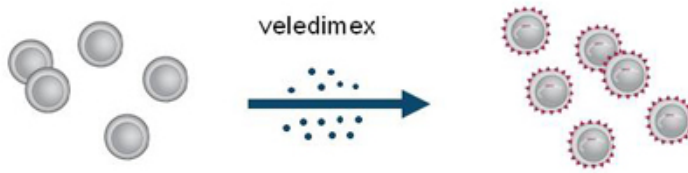
Competitive Edge in Cell Therapy



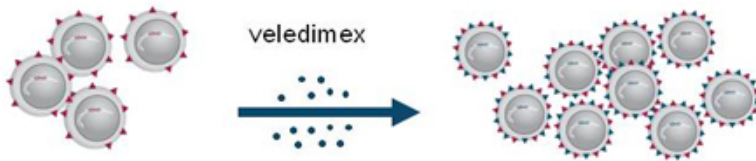
**ZIOPHARM Oncology**

# Control of T Cells Through Advanced Genetic Engineering

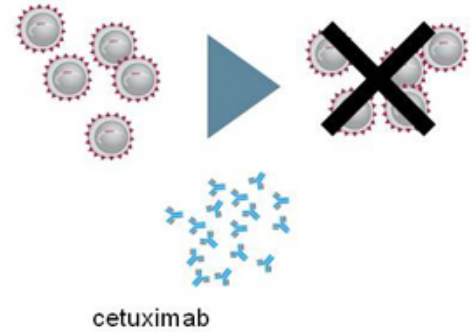
CAR is conditionally expressed under RTS<sup>®</sup> switch



Membrane-bound IL-15 is conditionally expressed under RTS<sup>®</sup> switch



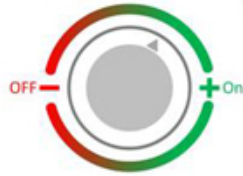
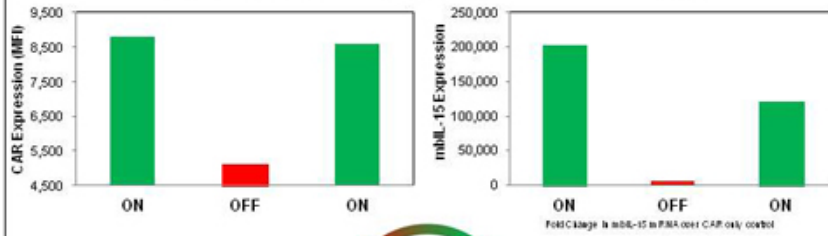
HER1t kill switch is activated by cetuximab in CD33 program



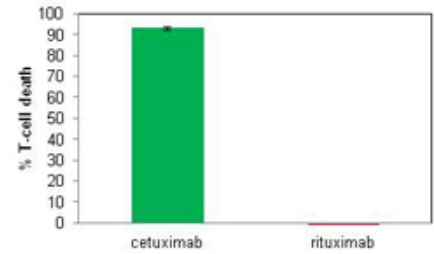
# Control of T Cells with RTS<sup>®</sup> and Kill Switches

## CAR and cytokine (mbIL15) are conditionally expressed under RTS<sup>®</sup> switch

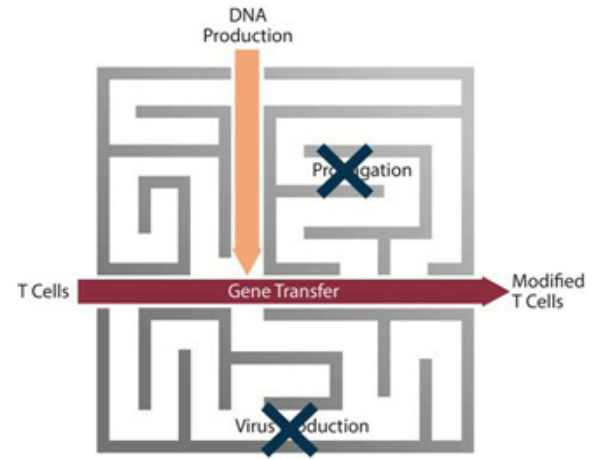
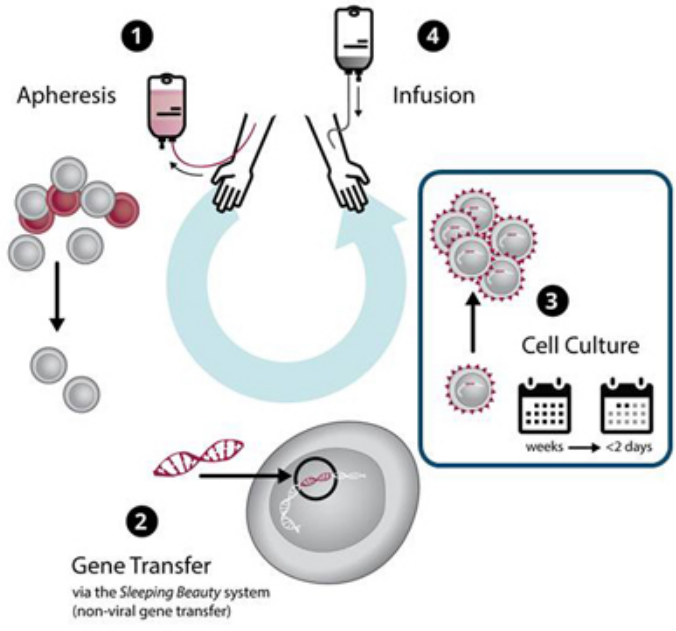
CAR and membrane-bound IL-15 (mbIL15) expression can be turned **ON**, **OFF** and back **ON** by addition or removal of



## HER1t kill switch is activated by cetuximab in CD33 program



# Minimizing Gene Transfer & Culture Time to Achieve Point-of-Care (POC) for Rapid Production of T cells



# ***Cost and Control***

CD19 CAR<sup>+</sup> T: Improving Autologous Cell Therapies

**INTREXON**<sup>®</sup>



**ZIOPHARM Oncology**

# CD19 Autologous CAR<sup>+</sup> T Program Harnessing the Potential of the *Sleeping Beauty* Platform

1<sup>st</sup> generation complete

2<sup>nd</sup> generation ongoing

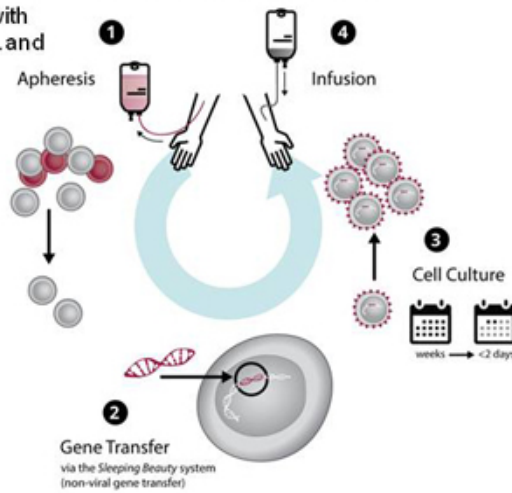
3<sup>rd</sup> generation planned

First-in-human trial utilizing  
*Sleeping Beauty* gene transfer

- Survival rates doubled in comparison with historical controls for patients with NHL and ALL after HSCT\*

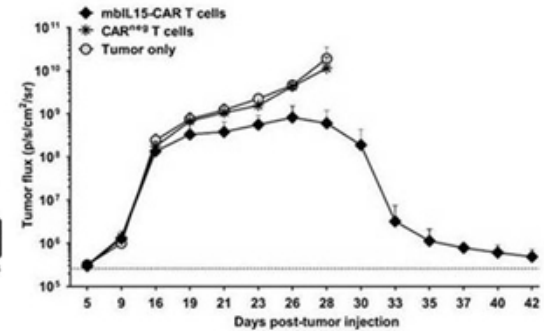


Shortening manufacturing process  
time from 28 days to 14 days



Elimination of *ex vivo* T-cell propagation envisioned  
under POC using switch-controlled mBL15

- Mouse studies show improved leukemia-free survival after infusion of T cells\*\*



\*\* [Proc Natl Acad Sci U S A](#), 2016 Nov 29;113(48):E7788-E7797 &ASH 2016, Publication Number 2807



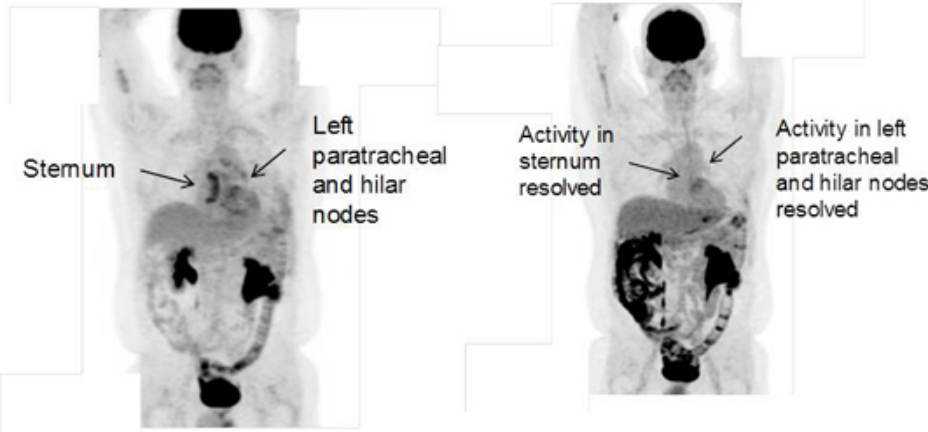
\*J Clin Invest. 2016 Sep 1;126(9):3363-76.



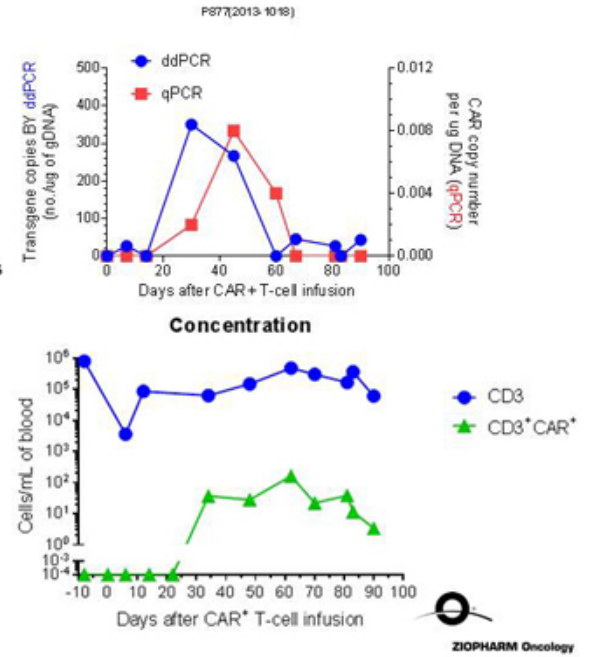
# 2<sup>nd</sup> generation *Sleeping Beauty* Platform E.g., 3-stim, 23-day manufacturing

PET-CT Day -8:  
Extramedullary ALL

PET-CT Day 48:  
Extramedullary ALL resolved



Ongoing CR (currently 90 days) in patient with multiple-relapsed ALL after lymphodepleting chemotherapy





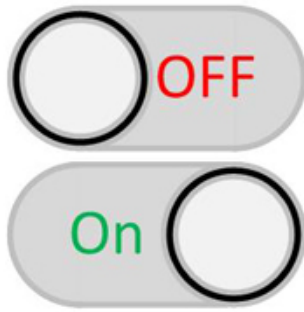
Technologies Extend to Other Immunologic Therapies

**INTREXON**<sup>®</sup>



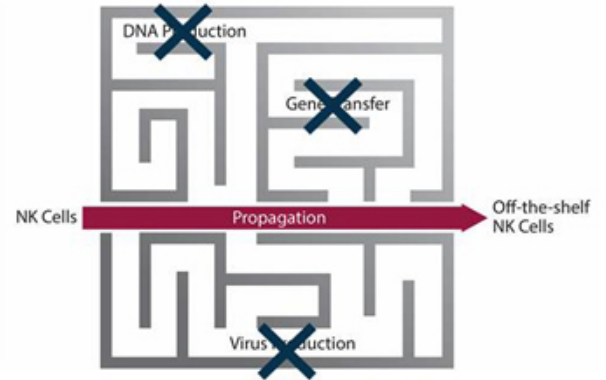
**ZIOPHARM Oncology**

# Targeted Approaches to Treatment of Unmet Need in Acute Myelogenous Leukemia (AML)



## Control: CD33 CAR<sup>+</sup> T program for AML

- Employs lentivirus and kill switch technology
- Relapsed or Refractory, Adult and Pediatric AML
- Trial to open 1H 2017 following FDA review



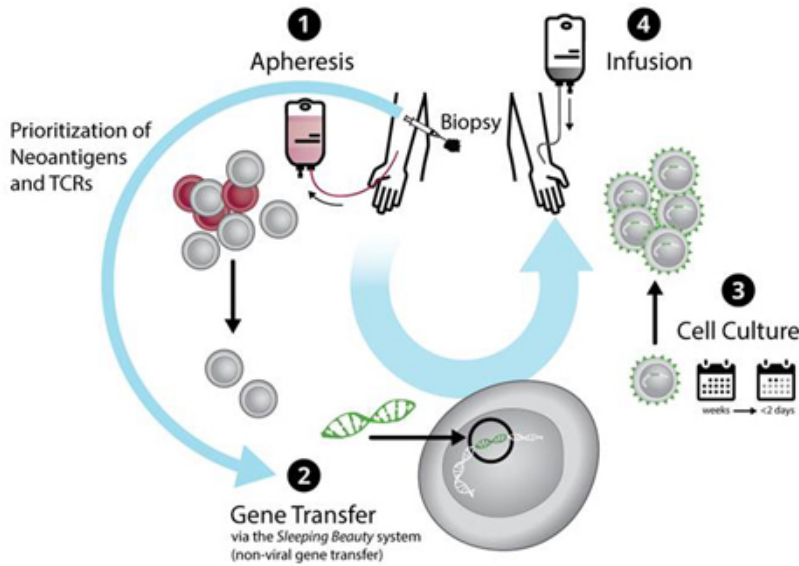
## Cost: Off-the-shelf (OTS) primary NK cells for AML

- Ideal OTS therapy because NK cells do not have TCR
- Medically-fragile elderly patients with AML
- Trial to be opened 1H 2017 following FDA review

Clinical trials planned under our R&D Agreement with MDACC

# Targeting Solid Tumors: ZIOPHARM and Intrexon CRADA With NCI

## Cooperative Research and Development Agreement with the National Cancer Institute Utilizing *Sleeping Beauty* System to Generate T cells Targeting Neoantigens



original article

### Stable, Nonviral Expression of Mutated Tumor Neoantigen-specific T-cell Receptors Using the *Sleeping Beauty* Transposon/Transposase System

David C. Springer, Anna Frenkel, Shiv Sanyal, Mark A. Rothbart, Cyrille J. Cohen, Paul F. Robbins, Laurence P. Cooper, and Steven A. Rosenberg

Immunogenetics unique to each patient's tumor can be recognized by adoptive T cells through their T-cell receptor (TCR) but the low frequency and/or limited differentiation of mutation-specific T cells in tumors can limit their utility as adoptive T-cell therapies. To overcome this problem, we generated a rapid, cost-effective strategy to genetically engineer cancer patient T cells with TCRs using the clinical *Sleeping Beauty* transposon/transposase system. Patient-specific TCRs reactive against HLA-A\*02:01-restricted neoantigens derived from the HLA-DQP7021-restricted melanoma antigen (MAGE) were expressed with routine constant chains and cloned into *Sleeping Beauty* transposons. Patient peripheral blood lymphocytes were cotransfected with SM1 transposase and *Sleeping Beauty* transposons, and transposed T cells were selected by sorting on murine TCRβ (mTCRβ) expression. Rapid expansion of mTCRβ<sup>+</sup> T cells with mutated antigen-specific TCRs was observed in lymphocyte cultures. CD45<sup>RO</sup> expression of effector CD8<sup>+</sup> (CD45RA) and non-differentiated CD8<sup>+</sup> (CD45RA<sup>lo</sup>) T cells. Transposed T cells specifically mounted a polyfunctional response against cognate mutated neoantigens and tumor cell lines. Thus, *Sleeping Beauty* transposition of mutation-specific TCRs can facilitate the use of personalized T-cell therapy targeting unique neoantigens.

**INTRODUCTION**  
 Mutation-specific T cells identify their cells by recognizing long peptide sequences in antigenic T-cell ligands using tumor-infiltrating lymphocytes (TIL) (1). In addition, 50% of the patient-tumor mTCR and mTCRβ (2). Following non-modifiable conditioning regimens, adoptive transfer, cognate

expression of intratumoral disease (3). Biopsies of these mutant T cells revealed that TCR-mutated patient-specific events, was associated with tumor regression (4). Progressive administration of TCR-specific reactive with CD8<sup>+</sup> TCRs resulted in a durable response of melanoma (5). However, tumor regression was observed in patients with TCRs that were not reactive against the neoantigen-specific T cells (6). Therefore, high tumor-specific TCRs are needed to be genetically generated for use in patients with T cells that recognize tumor antigens.

However, the direct use of TCRs with altered antigen specificity is not always feasible. One common method relies on screening multiple independent genes (7). Alternatively, the transposon system, which can be genetically altered to incorporate specific TCR sequences, is a more efficient alternative. This method has been used to generate specific TCRs in mice (8) and in human T cells (9). However, the use of TCRs with altered antigen specificity in human T cells may be limited by non-specific TCR expression (10). Therefore, a strategy to generate and maintain a population of T cells with a unique antigen-specific TCR is needed. This can be achieved by using a non-viral gene transfer system to generate T cells with unique antigen-specific TCRs.

Genetic transfer of patient-specific TCRs will likely require a rapid, efficient, and non-viral approach. The *Sleeping Beauty* transposon/transposase system is a candidate for this application because it can integrate into non-coding DNA in a non-specific and non-toxic manner (11). *Sleeping Beauty* transposons are highly efficient in generating TCRs in human T cells (12). *Sleeping Beauty* transposons have been approved for use in clinical trials evaluating the ability of T cells modified with disease

Targeting tumor neoantigens using T cells. *Sleeping Beauty* transposon/transposase system. *Sleeping Beauty* transposons are used to generate T cells with unique antigen-specific TCRs. The *Sleeping Beauty* transposon/transposase system is used to generate T cells with unique antigen-specific TCRs. The *Sleeping Beauty* transposon/transposase system is used to generate T cells with unique antigen-specific TCRs.

Mol Ther. 2016 Jun;24(6):1078-89.



# Undertaking the Pipeline Through Partnerships and Collaborations



INTREXON®

THE UNIVERSITY OF TEXAS  
MDAnderson  
Cancer Center

UCSF THE UNIVERSITY OF TEXAS  
MDAnderson  
Cancer Center

Memorial Sloan Kettering  
Cancer Center.

Northwestern Memorial  
Hospital

DANA-FARBER/BRIGHAM AND WOMEN'S  
CANCER CENTER

THE UNIVERSITY OF  
CHICAGO  
PRITZKER SCHOOL  
OF MEDICINE



CEDARS-SINAI

EMD  
SERONO

NATIONAL  
CANCER  
INSTITUTE

INTREXON®

ZIOPHARM Oncology

## Corporate and Financial Highlights

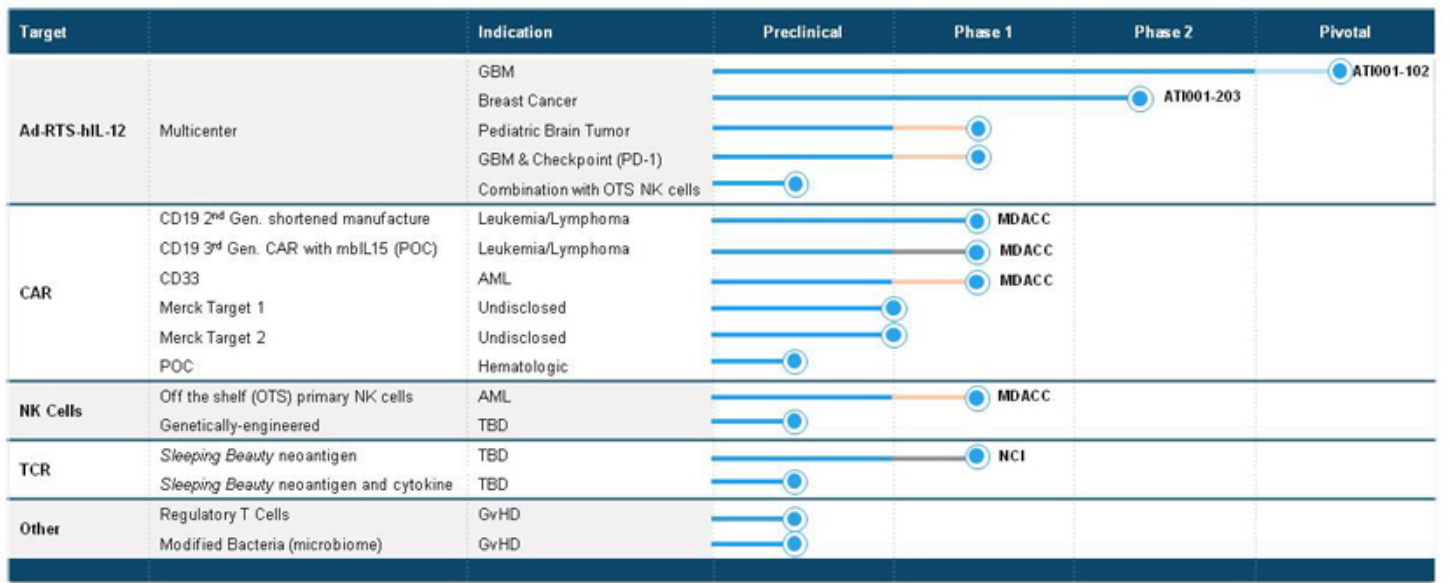
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- Amended Exclusive Channel Collaborations with Intrexon
  - All unpartnered programs divided 80:20 in favor of ZIOPHARM
    - Provides greater reward for investing in development
    - Increases attractiveness to potential strategic partners
  - Sublicensed programs continue to be divided 50:50\*
  - Consideration for new terms is dilutive only under certain developments
- Well Capitalized
  - Approximately \$94.7M in cash as of 3Q16
  - Cash runway into 1Q18
  - Shares outstanding as of November 3, 2016: 131.7M
- Highly Efficient Operations with a Headcount of 35
  - Partnerships support preclinical, clinical and commercial development

\*Includes exclusive agreement with Intrexon for the development and commercialization of CAR-T products with Merck KGaA, Darmstadt, Germany



# Addressing Unmet Medical Needs



2017      1H 2017      2H 2017







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