

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): January 11, 2018

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

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)

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)).

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act (17 CFR 230.405) or Rule 12b-2 of the Exchange Act (17 CFR 240.12b-2).

Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

**Item 7.01**                      **Regulation FD Disclosure**

On January 11, 2018, ZIOPHARM Oncology, Inc., or the Company, will present the attached presentation at the 36<sup>th</sup> Annual J.P. Morgan Healthcare Conference in San Francisco, California being held on January 8 – 11, 2018.

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	<a href="#">Presentation of the Company dated January 11, 2018</a>

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, 2018



## The Next Generation of Immunotherapy Platforms

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

January 2018

## Forward-Looking Statements

*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<sup>+</sup> T) approaches, Ad-RTS-IL-12, TCR and NK cell-based therapies, or any of our other therapeutic candidates will advance further in the preclinical 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<sup>+</sup> 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, 2016 and our Quarterly Report on Form 10-Q for the quarter ended September 30, 2017. 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.*

## Two Distinct Platforms, Multiple Opportunities

### Control of IL-12

#### Weaponize existing immune system

- IL-12: master regulator of immune system
- RheoSwitch® controls local dosing
- Immune checkpoint inhibitor combination with nivolumab
- Multiple cancer indications beginning with GBM



### *Sleeping Beauty*

#### Implement new immune system

- Most clinically advanced non-viral platform
- Point-of-care (P-O-C): fraction of cost in a fraction of the time
- Scalable

# Two Platforms Drive Next Generation Immunotherapy

	Target	Indication	Preclinical	Phase 1	Phase 2	Pivotal		
<b>Controlled IL-12</b>	<b>Ad-RTS-hIL-12</b> Multicenter	GBM	[Progress bar: Preclinical, Phase 1, Phase 2, Pivotal]					
		GBM & OPDIVO® (nivolumab)	[Progress bar: Preclinical, Phase 1]					
		GBM Stereotactic Treatment	[Progress bar: Preclinical, Phase 1]					
		Pediatric Brain Tumor	[Progress bar: Preclinical, Phase 1]					
<i>Sleeping Beauty</i>	CAR	CD19 2 <sup>nd</sup> Gen shortened manufacture	[Progress bar: Preclinical, Phase 1]				THE UNIVERSITY OF TEXAS <b>MD Anderson Cancer Center</b> Making Cancer History®	
		CD19 3 <sup>rd</sup> Gen CAR with mblL15 (P-O-C)	[Progress bar: Preclinical, Phase 1]					
		CD33	[Progress bar: Preclinical, Phase 1]					
	Merck Targets	Undisclosed	[Progress bar: Preclinical, Phase 1]				Merck KGaA Darmstadt, Germany	
		P-O-C	[Progress bar: Preclinical, Phase 1]					
	TCR	<i>Sleeping Beauty</i> neoantigen	Solid tumors	[Progress bar: Preclinical, Phase 1]				NIH NATIONAL CANCER INSTITUTE
		<i>Sleeping Beauty</i> neoantigen and cytokine	TBD	[Progress bar: Preclinical, Phase 1]				
	NK cells	Genetically engineered	TBD	[Progress bar: Preclinical, Phase 1]				

P-O-C = Point-of-Care





## **CONTROLLED IL-12**

**First Market: A New Paradigm for Recurrent Glioblastoma**





# Glioblastoma: Global Opportunity for Controlled IL-12



## Frontline Therapy



**Recurrence = 90%**

**US – 11,151<sup>1</sup>**

**EU – 13,118<sup>2</sup>**



**Recurrent GBM**

Average time to death  
remains **5 to 8 months**

1. <http://www.abta.org/about-us/news/brain-tumor-statistics/>  
2. GlobalData information, June 2016

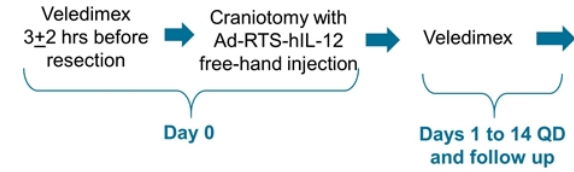
# Multicenter Phase 1 Study Evaluates Ad-RTS-hIL-12 Plus Veledimex in Patients with Recurrent Glioblastoma

## Ad-RTS-hIL-12

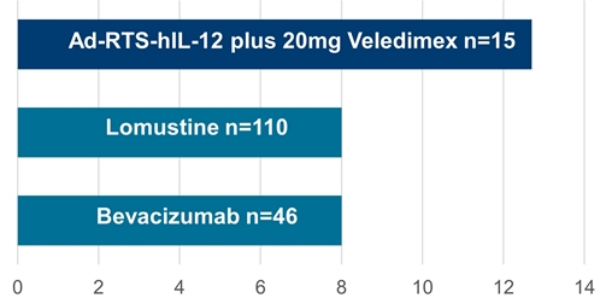
A replication-incompetent adenoviral vector administered via a single injection into the tumor and engineered to express and control hIL-12, a powerful cytokine that stimulates an immune anti-tumor response.



Patients scheduled for SOC resection/craniotomy



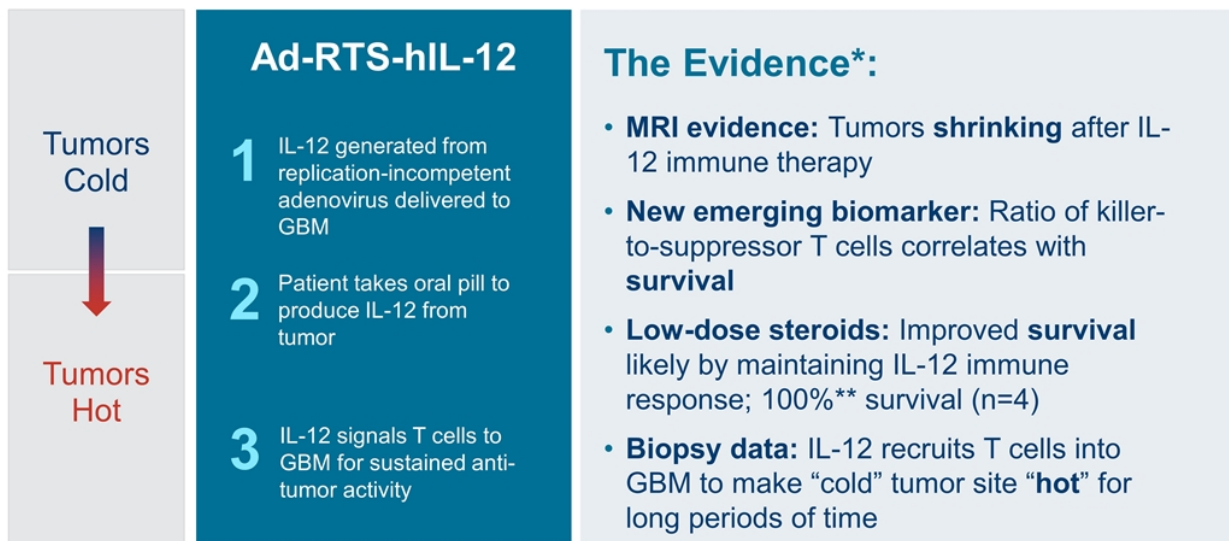
## Median Overall Survival (months)



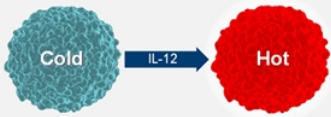
Ad-RTS-hIL-12 + v data as of October 18, 2017; Data for lomustine and bevacizumab from randomized phase 2 study (BELOB).

Phase 3 randomized control trial to initiate this year

# Why Do Patients Benefit?

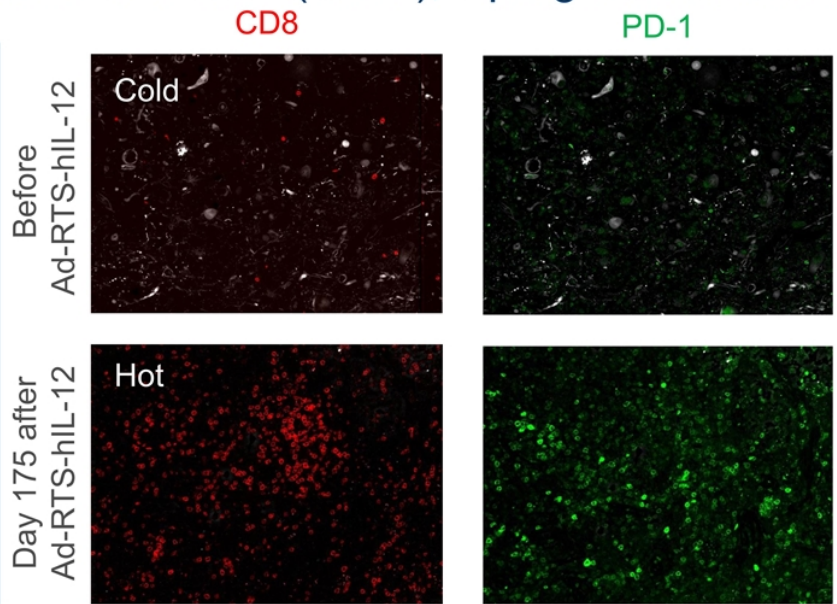


# Biopsies Show New Influx of Killer T cells (CD8<sup>+</sup>), Upregulation of PD-1



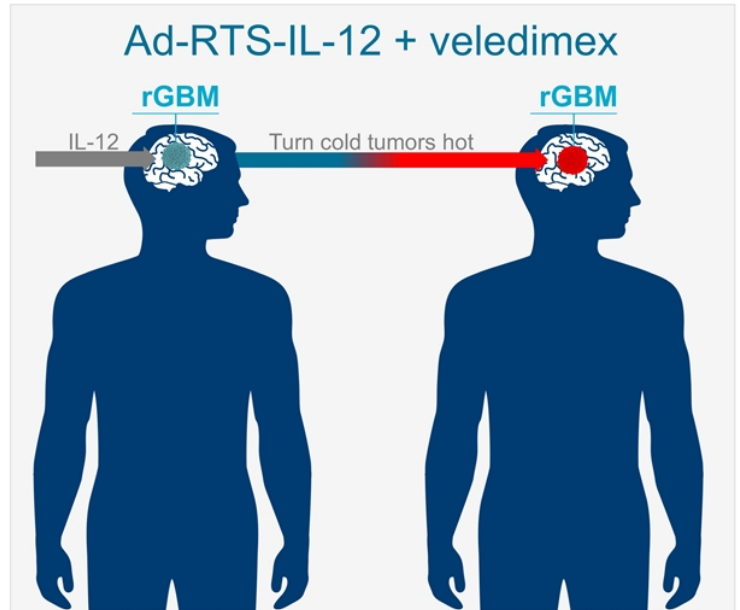
3/3 Subjects	IFN $\gamma$ : Mean $\pm$ SEM (pg/g)	
	Serum (pg/mL)	Tumor (pg/g)
Baseline	0.0 $\pm$ 0.0	4.2 $\pm$ 2.6
Days 130-175	0.0 $\pm$ 0.0	226 $\pm$ 138

Biopsies at four-plus months after IL-12 activation by veledimex reveal new infiltrates of T cells active in 3 of 3 patients



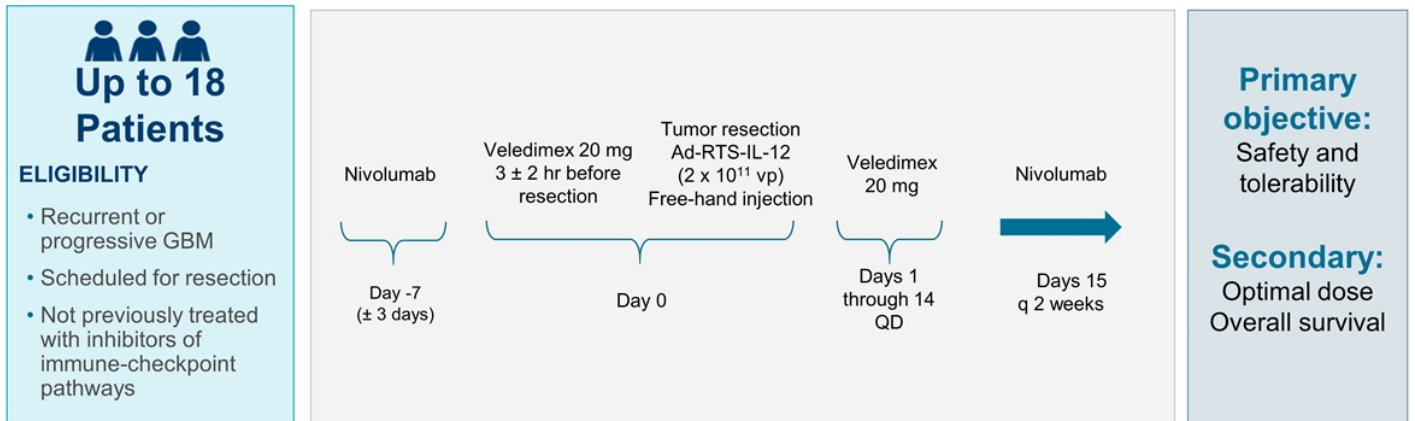
## Rationale for Combination Therapy for rGBM

- Tumors **remain** HOT months after IL-12 therapy
- T-cells **traffic** deep into tumor
- **Reassuring** safety profile

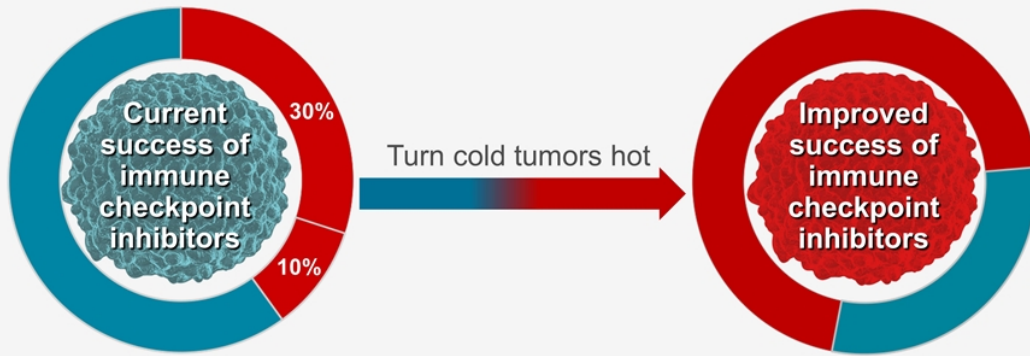


# Phase 1 Trial Initiated to Evaluate Ad-RTS-hIL-12 plus Veledimex in Combination with OPDIVO® (nivolumab) to Treat Patients with rGBM

- Compelling data demonstrating that IL-12 can remodel the tumor microenvironment
- Sustained influx of CD8<sup>+</sup> T cells expressing PD-1
- Combining IL-12 with anti-PD-1 may yield even better anti-tumor responses



# IL-12 Platform can Combine with Immune Checkpoint Inhibitors Across Oncology



## Broad potential





***SLEEPING BEAUTY***  
**A New Paradigm for Adoptive Cell Therapy**





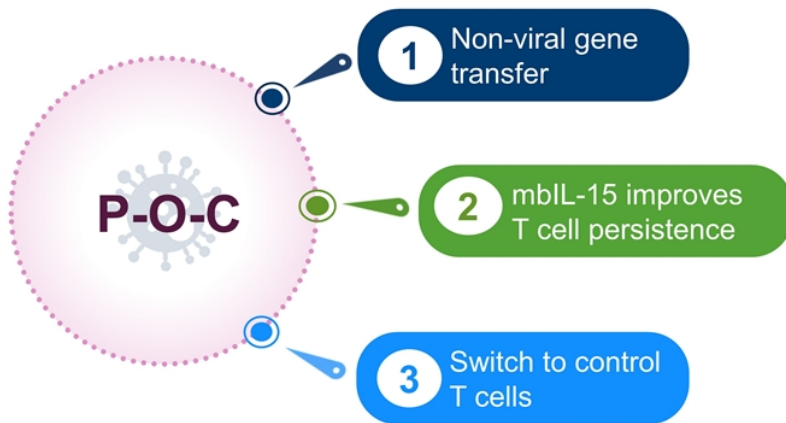
# Two Platforms Drive Next Generation Immunotherapy

	Target	Indication	Preclinical	Phase 1	Phase 2	Pivotal
Controlled IL-12	Ad-RTS-hIL-12 Multicenter	GBM	[Progress bar]			
		GBM & OPDIVO® (nivolumab)	[Progress bar]			
		GBM Stereotactic Treatment	[Progress bar]			
		Pediatric Brain Tumor	[Progress bar]			
Sleeping Beauty	CAR	CD19 2 <sup>nd</sup> Gen shortened manufacture	[Progress bar]		THE UNIVERSITY OF TEXAS <b>MD Anderson Cancer Center</b> Making Cancer History®	
		CD19 3 <sup>rd</sup> Gen CAR with mblL15 (P-O-C)	[Progress bar]			
		CD33	[Progress bar]			
		Merck Targets	[Progress bar]		Merck KGaA Darmstadt - Germany	
	TCR	P-O-C	[Progress bar]			
		Sleeping Beauty neoantigen	[Progress bar]		NIH NATIONAL CANCER INSTITUTE	
	NK cells	Sleeping Beauty neoantigen and cytokine	[Progress bar]			
		Genetically engineered	[Progress bar]			

P-O-C = Point-of-Care



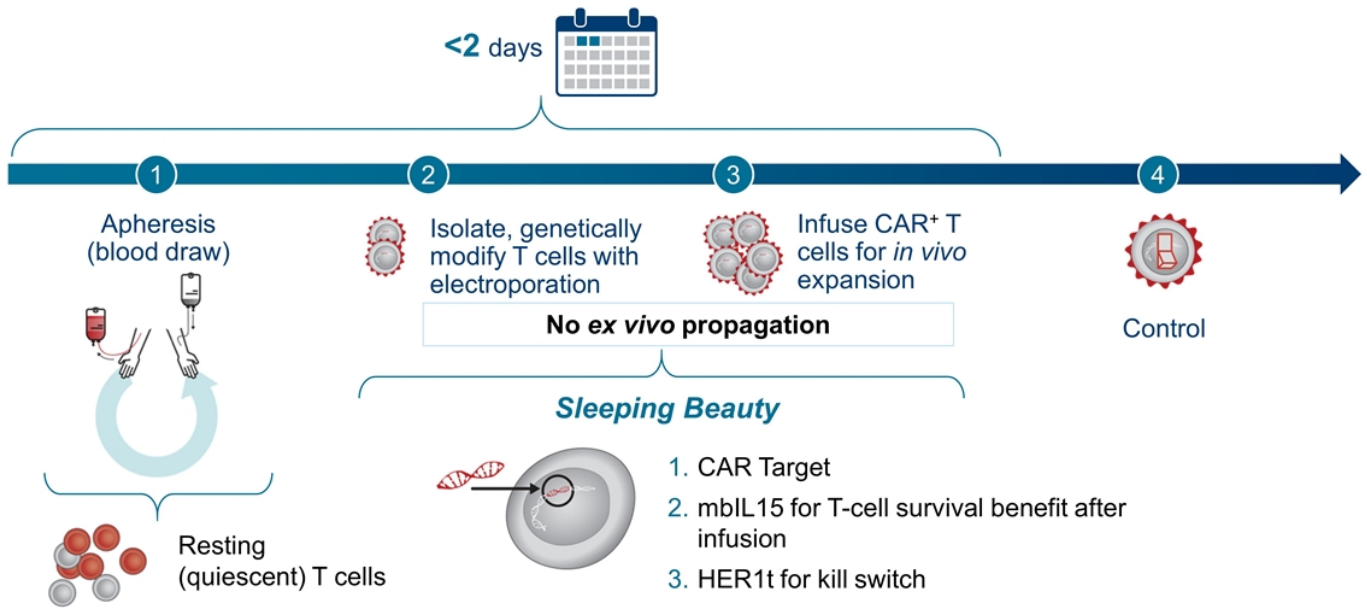
# ZIOP's Vision – Scalable, Lower Cost, High-throughput Platform



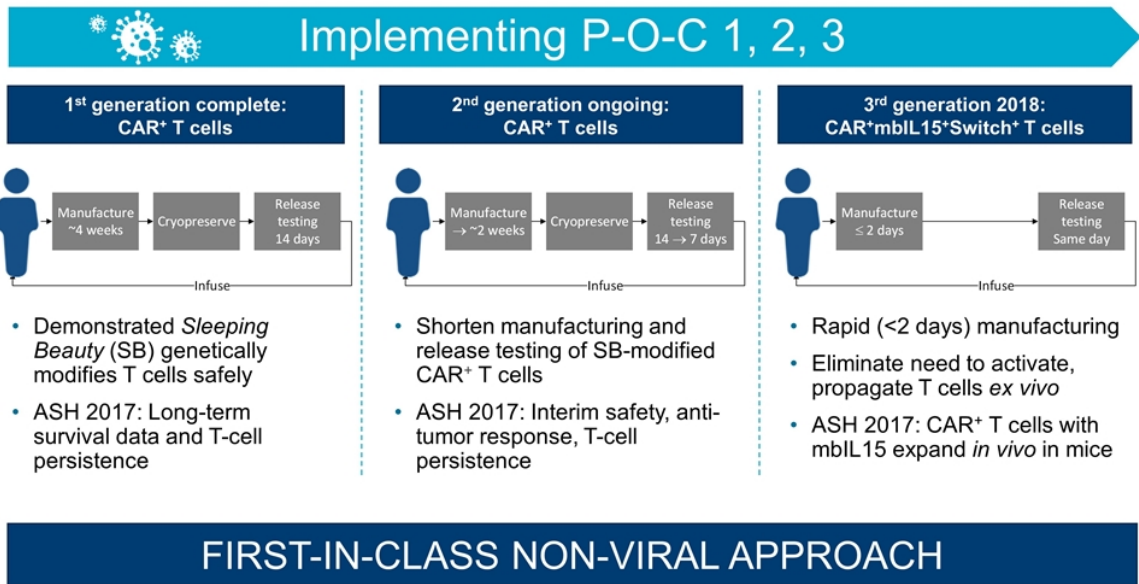
## *Sleeping Beauty* under P-O-C

- Very rapid manufacture
- Scalable process
- Avoids use of virus
- Removes need to grow T cells outside the body
- Reduces costs

# Eliminate the Complexity – P-O-C Trial to be Initiated 2018

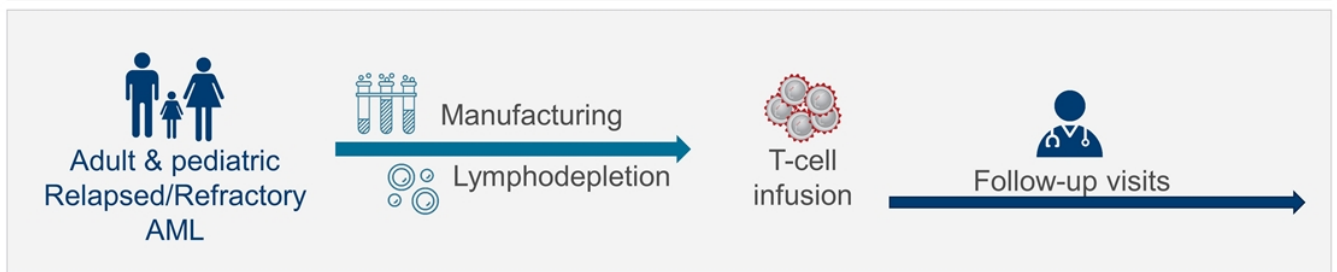


# First Point-of-Care – CD19-Specific CAR<sup>+</sup> T cells

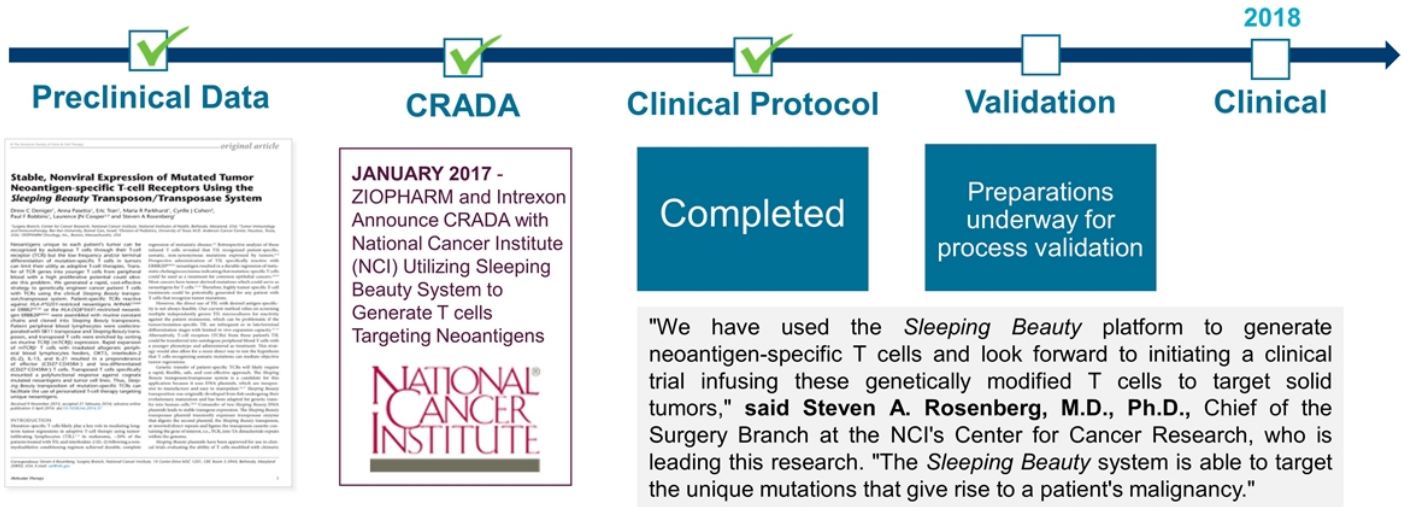


# CAR<sup>+</sup> T Cells Targeting CD33 on AML

- Trial open at MD Anderson Cancer Center to establish CD33 as a target for CAR<sup>+</sup> T cells
- Technology employs lentivirus and kill switch
- Enrollment underway



# NCI Progressing *Sleeping Beauty* to Target Neoantigens in Solid Tumors with TCRs



*original article*

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

Steen A. Rosenberg, Anna Frazier, Shi Sun, Maria R Fakhari, Cynthia Cohen, Paul F. Senter, Lawrence P. Cooper, and Steven A. Rosenberg

**Abstract**

Neoantigen-specific T cells are essential for tumor rejection. However, the generation of neoantigen-specific T cells is limited by the low frequency of neoantigen presentation and the low frequency of T-cell receptor (TCR) gene rearrangement. We have developed a nonviral system for the generation of neoantigen-specific T cells using the *Sleeping Beauty* transposon/Transposase system. This system allows for the stable, nonviral expression of mutated TCR genes in T cells, resulting in the generation of neoantigen-specific T cells. We have demonstrated that this system can be used to generate neoantigen-specific T cells in mice and in human T cells. These cells are stable and functional, and they can be used for adoptive cell transfer. This system provides a powerful tool for the generation of neoantigen-specific T cells for cancer immunotherapy.

**JANUARY 2017 - ZIOPHARM and Intrexon Announce CRADA with National Cancer Institute (NCI) Utilizing *Sleeping Beauty* System to Generate T cells Targeting Neoantigens**

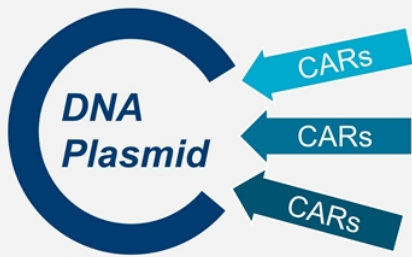
**NATIONAL CANCER INSTITUTE**

**Completed**

**Preparations underway for process validation**

"We have used the *Sleeping Beauty* platform to generate neoantigen-specific T cells and look forward to initiating a clinical trial infusing these genetically modified T cells to target solid tumors," said **Steven A. Rosenberg, M.D., Ph.D.**, Chief of the Surgery Branch at the NCI's Center for Cancer Research, who is leading this research. "The *Sleeping Beauty* system is able to target the unique mutations that give rise to a patient's malignancy."

## *Sleeping Beauty* Platform's Versatility, Multiple Targets

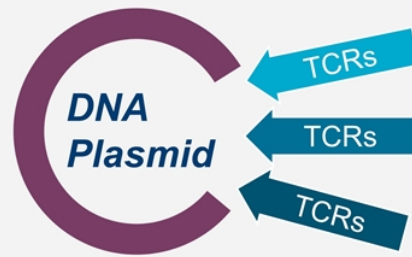


CD19

CD33

Merck KGaA: two targets

Plus others.....



Neoantigens

*Sleeping Beauty* reprograms T cells to target the personalized neoantigens within solid tumors

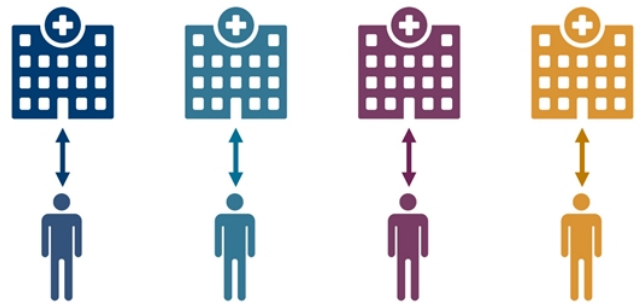
# Changing the Paradigm for Manufacturing Genetically Modified T Cells

## Centralized Manufacturing



Centralized production is necessary due to the use of viral-based gene transfer which is tied to the need for *ex vivo* numeric expansion

## Hospital-based Manufacturing



Distributed production, e.g., in blood banks, envisioned under point-of-care is now possible using non-viral-based gene transfer and undertaking *in vivo* numeric expansion



## Rolling out Point-of-Care at Hospitals – First Hospital Signed Up



### First Hospital Signed Up

- Hospital system holds exclusive regional license
- **Intrexon** and **Ziopharm** receive licensing fees, royalties

The Year Ahead



## Two Platforms with Multiple Milestones in 2018

### Controlled IL-12 with RTS®

#### Off to a great start

- Combination trial with nivolumab
- Stereotactic adult & pediatric trials

#### To be initiated

- Pivotal, randomized control trial

### *Sleeping Beauty*

#### Off to a great start

- 2<sup>nd</sup> Gen. Phase 1 CAR<sup>+</sup> CD19
- Trial evaluating CD33 as a target

#### To be initiated

- P-O-C Phase 1 targeting CD19
- Phase 1 w/ Merck KGaA CAR<sup>+</sup> T cells
- NCI: File IND for Phase 1 study of SB-modified TCRs to target neoantigens

# Financial Update as of Sept. 30, 2017

## Condensed Consolidated Balance Sheet

Cash, cash equivalents and short term investments	\$84.4M
At MD Anderson Cancer Center from prepayment for programs to be conducted by the Company	\$29.4M

Current resources will be sufficient to fund planned operations into the fourth quarter of 2018



**Ziopharm**  
ONCOLOGY

January 2018