
**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): April 7, 2016

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)).
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Item 7.01 Regulation FD Disclosure

On April 7, 2016, ZIOPHARM Oncology, Inc., or the Company, will present the attached presentation at the Jefferies 2nd Annual Immuno-Oncology Summit in Boston, Massachusetts.

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 April 7, 2016

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: April 7, 2016

INDEX OF EXHIBITS

**Exhibit
No.**

Description

99.1 Presentation of the Company dated April 7, 2016

ZIOPHARM

Jefferies Immuno-Oncology Summit

April 2016



ZIOPHARM Oncology

*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. 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.*

Rapid Clinical Development

THE UNIVERSITY OF TEXAS
**MD Anderson
Cancer Center**



DNA Engine & Research
INTREXON®

PBL and IL-12
(via Intrexon)

**NATIONAL
CANCER
INSTITUTE**

Clinical Collaborators



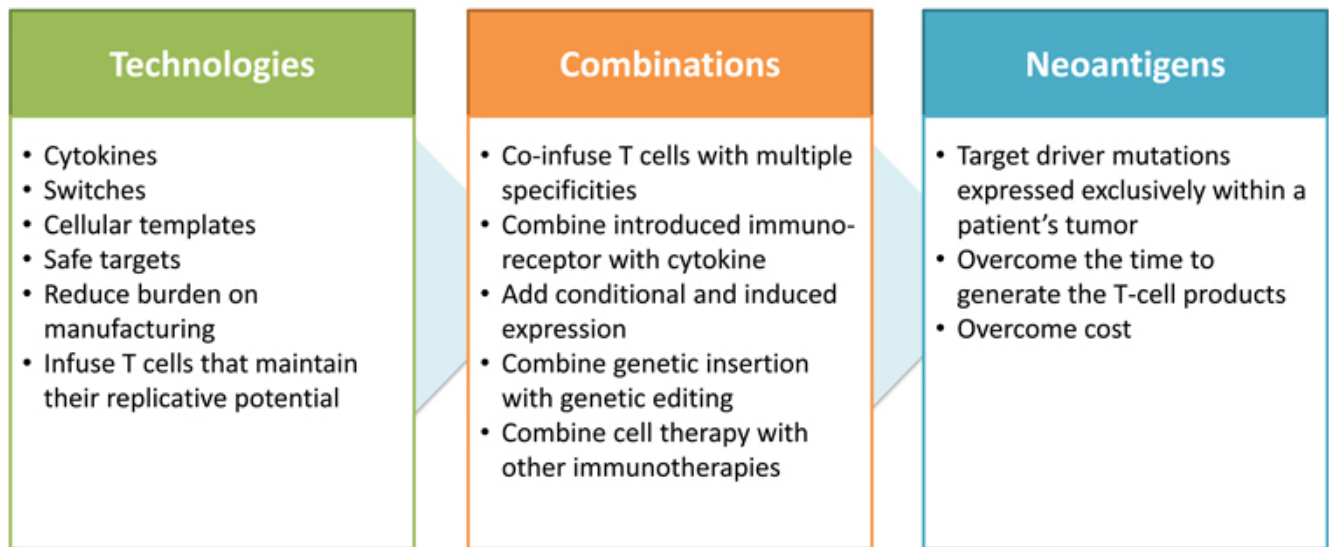
CAR-T Collaboration (via Intrexon)

Biopharmaceutical
business of Merck KGaA,
Darmstadt, Germany



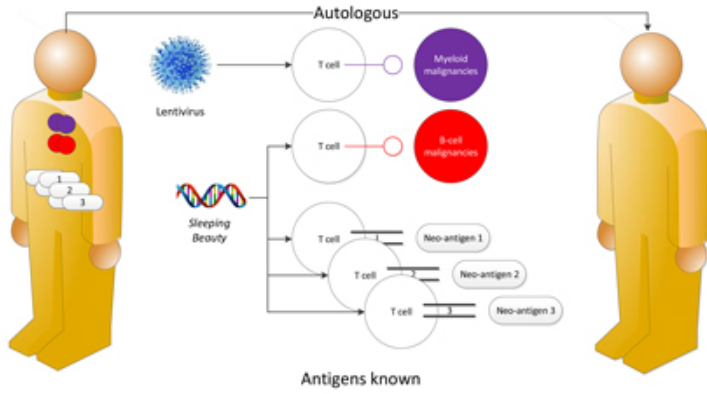
Laurence Cooper, MD, PhD

- Named CEO in May 2015
- Developed *Sleeping Beauty* technology in-licensed by ZIOP/XON in Jan 2015
- Previously professor pediatric oncology at MD Anderson Cancer Center: expertise in immunotherapy, led bone marrow transplant program

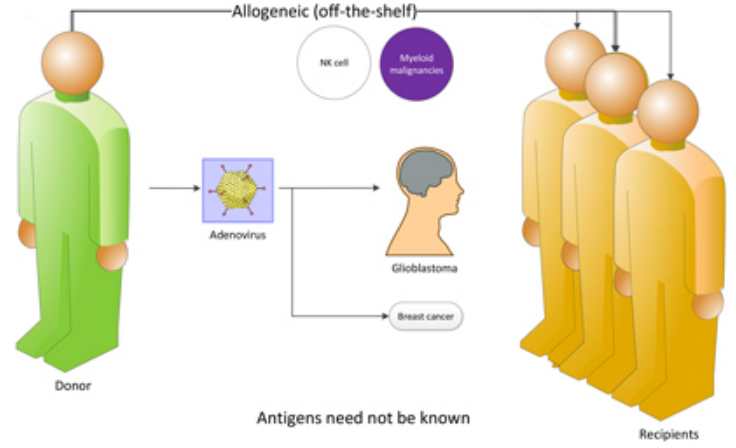


Understanding targets and delivering immunotherapies

Patient-derived platforms

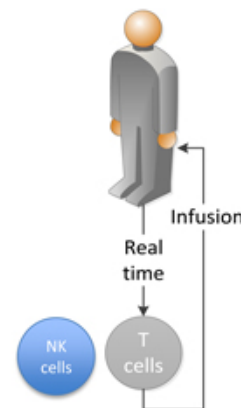


Off-the-shelf platforms



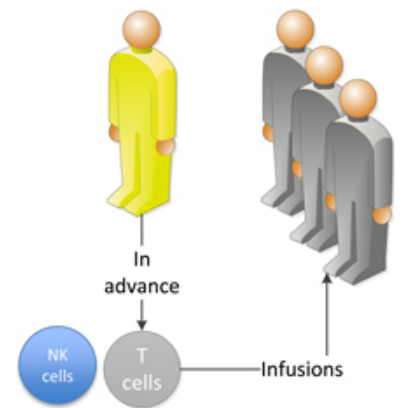
- Implementing manufacturing processes for both autologous and allogeneic settings
- RTS[®] and switches will address off-target effects, especially in solid tumors
- Continued optimization of manufacturing process to improve performance
 - Shortened manufacturing of CAR T cells shows superior *in vivo* activity
- Leveraging manufacturing through
 - MDACC
 - CMOs

Patient-derived (autologous)



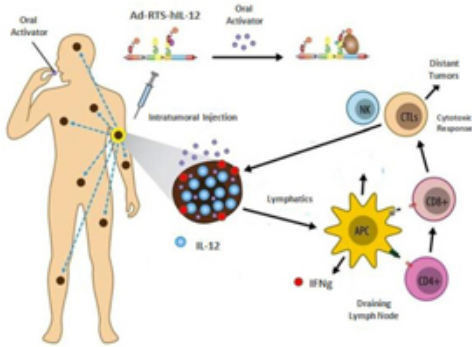
Shorten manufacturing time to produce T or NK cells

Off-the-shelf (allogeneic)



Match one donor with multiple recipients. Generate large numbers of T or NK cells with retained capacity to proliferate.

		Preclinical	Phase I	Phase II	
Ad-RTS-IL-12	GBM				
	Breast Cancer				
	Pediatric				
	GBM + Checkpoint				
CAR					
CD19 1 st Generation	Leukemia/Lymphoma				
CD19 2 nd Generation					
CD19 3 rd Generation with cytokine					
Myeloid malignancies target	Undisclosed				
Merck Target 1	Undisclosed				
Merck Target 2	Undisclosed				
Off-the-shelf myeloid malignancies target	Undisclosed				
NK Cells					
Primary NK cells	AML				
Combination with Ad-RTS-IL-12	Brain Cancer				
Genetically-engineered	TBD				
TCR					
<i>Sleeping Beauty</i> TCR	TBD				Target 2016
<i>Sleeping Beauty</i> TCR and cytokine	TBD				Target 2017
Other					
Regulatory T Cells	GvHD				
Modified Bacteria (microbiome)	GvHD				



Next Steps

- Combination therapy with checkpoint inhibitors
 - Pre-clinical data demonstrates improved anti-tumor response in mice with glioma
 - Abstract at ASGCT May 2016

Early brain tumor data encouraging (N=7)*

- Patients enrolled at multiple centers
- Biomarkers supportive of activity
- Neurotoxicity minimal and manageable
- “On-target toxicities” as expected and promptly reversible upon stopping veledimex

Early breast cancer data encouraging (N=6)*

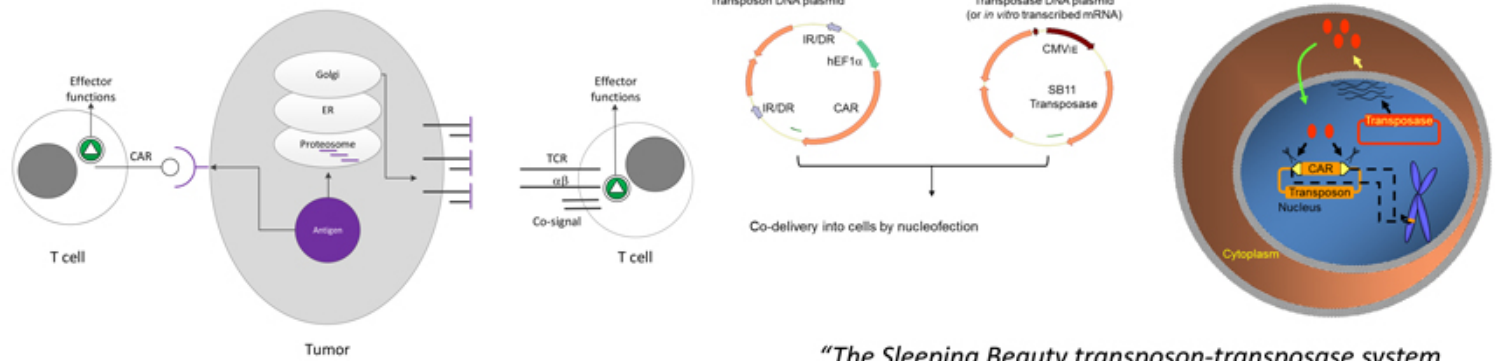
- First patient achieved 12 week PFS endpoint
- Patient accrual accelerating with 5 patients enrolled during 4th quarter
- Looking for confirmation of increased memory T cells as seen in previous trials
- “On-target toxicities” as expected and promptly reversible upon stopping veledimex

*As of Dec 15, 2015

Updated data at ASGCT 2016

Updated data for both studies at ASCO 2016

T cells genetically modified with tumor-specific CAR or TCRs



Advantages of *Sleeping Beauty* non-viral platform:

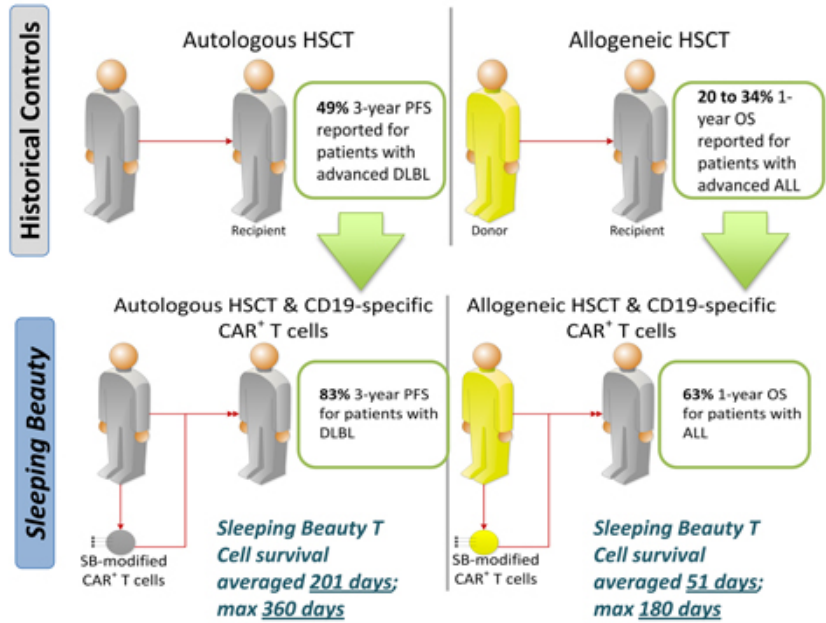
- Provides conduit to targeting solid tumor neo-antigens using T-cell receptors
- Lowers the cost of generating genetically modified T cells
- Has the potential to generate T cells with minimal *ex vivo* processing

"The Sleeping Beauty transposon-transposase system represents a unique non-viral system for introducing genes encoding T-cell receptors and chimeric antigen receptors into lymphocytes that can be of great value in the development of personalized immunotherapies for patients with cancer."

Steven A. Rosenberg M.D., Ph.D.
December 2015

Long term follow-up data from 1st generation *Sleeping Beauty* platform in two trials infusing CAR⁺ T cells *after* hematopoietic stem-cell transplantation (HSCT)

- Showed favorable PFS and OS trends in both autologous and allogeneic cohorts
- Non-viral *Sleeping Beauty* T-cell survival compared favorably versus viral approaches

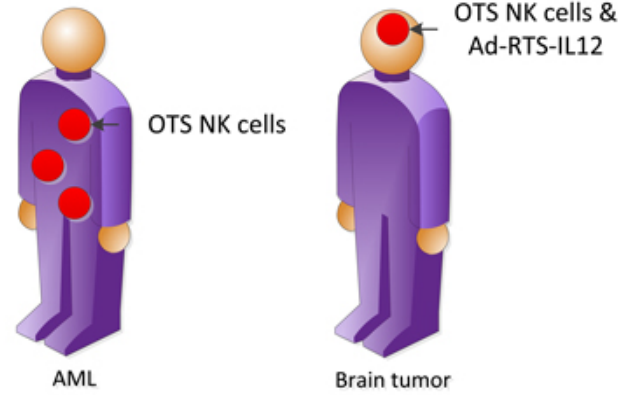


- Exclusive agreement to develop and commercialize CAR-T cancer therapies
- 2 novel CAR T targets nominated
- Merck KGaA, Darmstadt, Germany to lead IND filing and pre-IND interactions, clinical development and commercialization
- Intrexon and ZIOPHARM retain ability to explore targets independently, granting Merck KGaA opt-in rights during clinical development
- Economics divided evenly between ZIOPHARM and Intrexon
 - \$413 million per product in milestones
 - Tiered royalties up to lower-double digits on net sales

Natural killer (NK) cells

- Target tumors, *e.g.*, with loss or mismatch of HLA
- Killing is independent of a specific (known) target antigen
- Cytokines, *e.g.*, IL-12 are “fuel” for NK cells
- Build on promising proof-of-principle trials ongoing at MDACC infusing autologous and allogeneic NK cells manufactured using feeder cells

Launching Phase 1 trials of off-the-shelf NK cells for AML and brain tumors in 2016 & 2017



PERSPECTIVE

nanomedicine

Prospects for gene-engineered T cell immunotherapy for solid cancers

Christopher A. Klebanoff, Steven A. Rosenberg & Nicholas P. Restifo

Adoptive transfer of receptor-engineered T cells has produced impressive results in treating patients with B cell leukemia and lymphomas. This success has captured public imagination and drove academic and industrial researchers to develop similar ‘‘off-the-shelf’’ receptors targeting shared antigens in epithelial cancers, the leading cause of cancer-related deaths. However, the successful treatment of large numbers of people with solid cancers using this strategy is unlikely to be straightforward. Receptor-engineered T cells have the potential to cause lethal toxicity from on-target recognition of normal tissues, and there is a paucity of truly tumor-specific antigens shared across tumor types. Here we offer our perspective on how expanding the use of genetically restricted T cells to treat the majority of patients with solid cancers will require major technical, manufacturing and regulatory innovations centered around the development of antigenic gene therapies targeting private somatic mutations.

Unfavorable evidence that an entirely immunologic approach can cause regression of a wide array of human cancers has come from the recent success of using monoclonal antibodies (mAbs) targeting checkpoints of immune activation, including cytotoxic T lymphocyte-associated protein 4 (CTLA-4) and programmed cell death protein 1 (PD-1) (ref. 1). This includes patients affected with an ever-expanding list of malignancies, including melanoma^{2,3}, renal cell carcinoma⁴, lung cancer^{5,6}, bladder cancer⁷, ovarian cancer⁸, Hodgkin lymphoma⁹ and gastrointestinal (GI)- and endometrial cancer associated with defects in DNA mismatch repair¹⁰. Despite different mechanisms of action, these immunosuppressive inhibitors with the activation and expansion of tumor-infiltrating T cells¹¹.

Because T cells are often one of the final effectors of immune-mediated cancer regression, strategies that directly use tumor-infiltrating T cells as a therapy have been developed¹². In this approach, tumor-adjacent and distant (ACT) T cells are expanded in vitro and genetically immunoregulatory components of a tumor and are infused in large numbers into the cancer patient (up to 10¹¹ cells). Immunologic gene transfer of a cancer gene into T cells to obtain tumor-infiltrating lymphocytes (TILs) has demonstrated tumor reactivity with variable

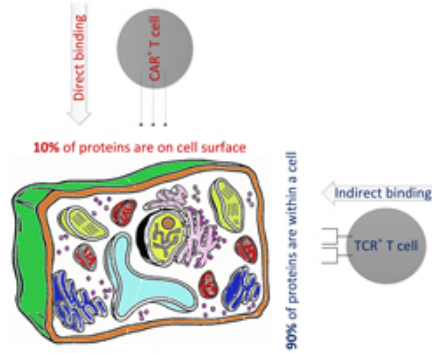
frequency in a range of cancers, including melanoma^{13,14}, glioma¹⁵, lung¹⁶ and human papilloma virus-associated malignancies¹⁷. TIL infusion can induce durable complete responses (CRs)^{18,19}, including in patients for whom other immunotherapies have failed²⁰. Despite demonstrable efficacy, use of TILs outside the context of clinical trials performed at academic medical centers has proven challenging.

Progress in gene engineering technologies has simplified the generation of autologous T cells, increasing rates of the practical harvest that have limited with dissemination of ACT using TIL cells. Gene engineering obviates the requirement for surgery because T cells can be isolated from the blood and receptors conferring specificity for tumor-associated antigens can be introduced using viral and non-viral integrative techniques²¹. Thus, autologous T cells can potentially be made on a large scale using commercial production methods. Indeed, recent experience with adoptive T cell gene-modified cell product for prostate cancer demonstrated the feasibility of having a private immune cell collected, sent to a central manufacturing facility, and returned back for re-infusion to a patient that passed US Food and Drug Administration (FDA) regulatory approval²².

Finally, genetic modifications of T cells have a track record of safety. Transposon- and lentiviral vectors have been used most commonly in antigen receptor gene therapy trials. Despite concerns about the possibility of insertional mutagenesis²³, introduction of antigen receptors into tumor-bearing T cells has been used to treat several hundred patients without evidence of clonal expansion or transformation²⁴.

Collectively, a framework of manufacturing feasibility, regulatory precedent and vector safety is now in place and it is possible to envision treating large numbers of cancer patients using gene-engineered T cells. Recent success with gene-modified T cells targeting the B cell lineage differentiation antigen CD19 in a range of B cell malignancies has focused attention on using similar ‘‘off-the-shelf’’ antigen receptors to treat patients with advanced solid cancers. In this Perspective, we offer our appraisal of how adoptive immunotherapy using receptor-engineered T cells can cause meaningful clinical benefit for patients with advanced epithelial cancers, the leading cause of cancer-related death²⁵.

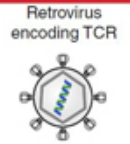
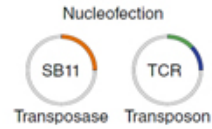
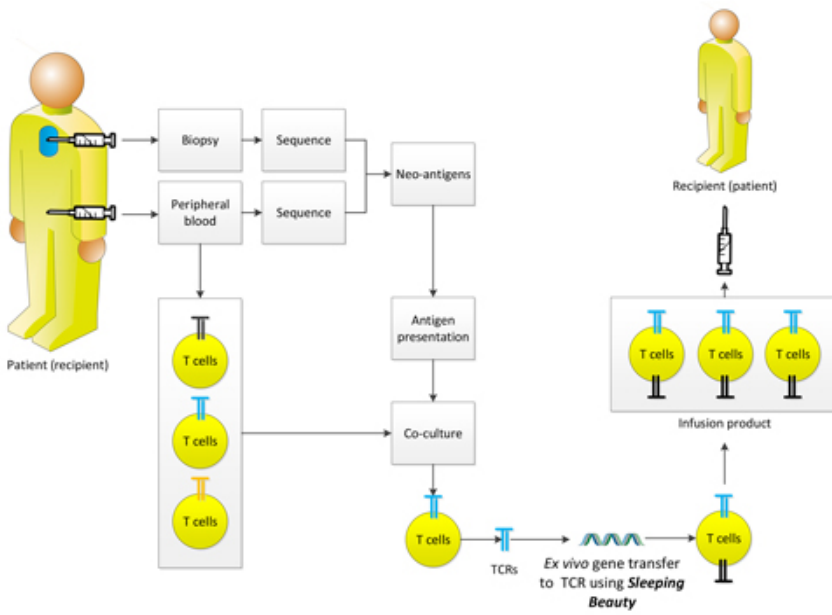
Antigen receptor-engineered T cells
T cell receptors (comprising an antigen-specific T cell specificity toward a patient's cancer can be accomplished by the introduction of one or two types of antigen receptors. In one approach, a cloned T cell receptor (TCR) conferring tumor recognition is inserted into circulating lymphocytes. Similarly to the endogenous TCR expressed by all T cells, genetically introduced TCRs recognize a predominantly processed peptide derived from either a protein or an endogenous non-protein



- “Clinical evidence supports the hypothesis that immunogenic products of somatic mutations unique to each patient’s cancer—so-called neoantigens—are the relevant targets for successful immunotherapies”
- “Success for cell-based immunotherapies may come from the arduous task of targeting the unique set of mutations that cause each patient’s cancer”
- “Presently, use of the Sleeping Beauty (SB) transposon / transposase system has advanced farthest in clinical development”

Nat Med. 2016 Jan 6;22(1):26-36
 Science. 2015 Apr 3;348(6230):62-8
 Science. 2015 Apr 3;348(6230):69-74

Sleeping Beauty: farthest advanced in non-viral clinical development



Non-viral <i>Sleeping Beauty</i>	Viral delivery
Target solid tumor intracellular neo-antigens via multiple TCRs	Limited appeal for targeting multiple intracellular antigens via TCRs
Low cost approach	High cost approach
Rapid manufacture	Labor intensive, slow manufacture
Customizable, able to swap in different receptors	Challenging to customize

- Melanoma: AHNAKmut-TCR
 - AHNAK^{S2580F}(A*0201)
- Melanoma: ERBB2mut-TCR
 - ERBB2^{H473Y}(A*0201)
- Cholangiocarcinoma: ERBB2IPmut-TCR
 - ERBB2IPE805G(DQB*0601)

Accepted manuscript

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Shen C, Zhang J, Ansa-Ponzi F, Liu T, Ma X, Robinson C, Collins J, Cohen P, Paul F, Robbins PD, Cantor H, Cyster J, Gattinoni L, Restifo N, Rosenberg SA, Rosenberg JN

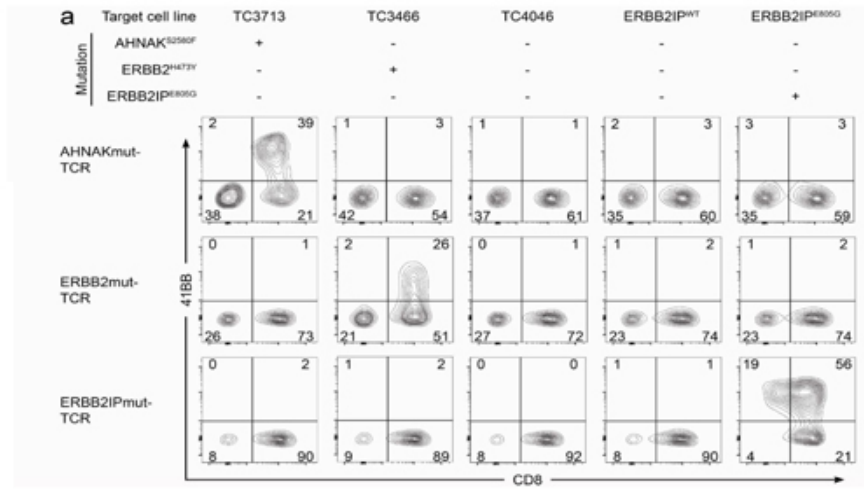
¹Targeted Therapy Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, MD, USA
²Center for Immunology and Immunotherapy, The Ohio State University, Columbus, Ohio, USA
³Department of Pathology, University of Texas MD Anderson Cancer Center, Houston, TX, USA
⁴Genentech Inc., South San Francisco, CA, USA

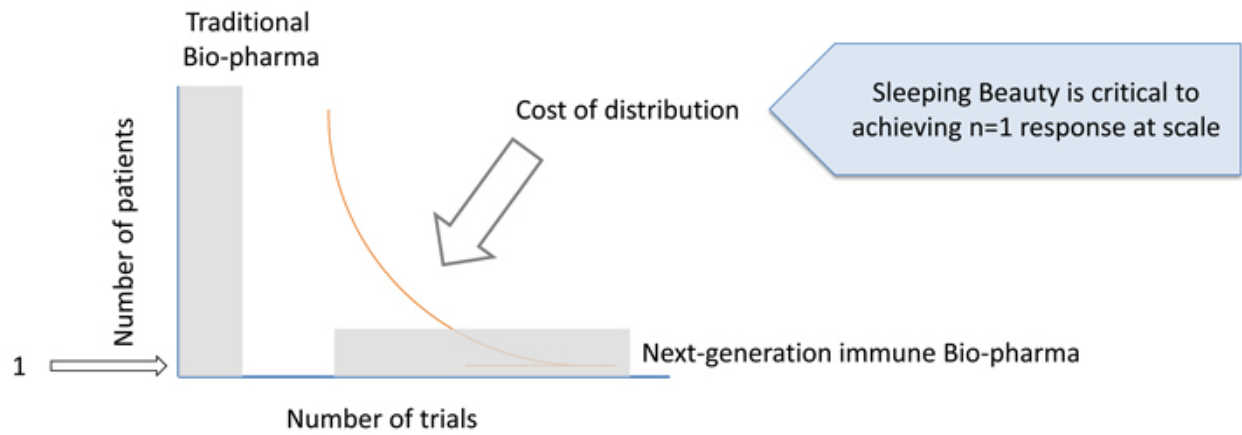
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Short title: Personalized TCRs

Conflict of interest statement: On May 1, 2015, ZIOPHARM was acquired by the Chief Executive Officer of ZIOPHARM Oncology and remains an NCI National Cancer Center on a Non-Profit basis. No other conflicts of interest exist.

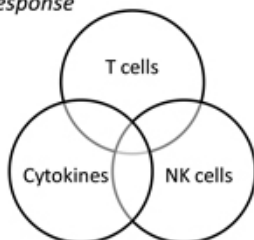
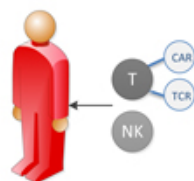
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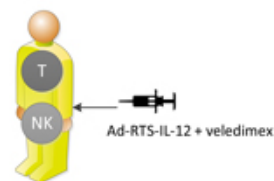


Current Clinical Approaches leading to combination immunotherapy

Administer modified immune cells to provide effective anti-tumor response



Administer IL-12 via controlled gene therapy to bolster endogenous immune response



- We stand alone in our ability to control the delivery of IL-12
- We stand alone in being able to harness non-viral DNA as a method to genetically control T cells
- We are launching multiple immunotherapy trials
 - Trial initiated with 2nd generation CD19 CAR-T utilizing non-viral *Sleeping Beauty* platform
 - Three new trials in 2016: Combination immunotherapy, viral CAR-T, and NK cells
- We are combining different elements of the immune system
- We have an ecosystem to efficiently develop and test new ideas in the clinic
- We have an expanding and unique platform to control the immune system

ZIOPHARM

Jefferies Immuno-Oncology Summit

April 2016



ZIOPHARM Oncology