
**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, 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 January 13, 2016, ZIOPHARM Oncology, Inc., or the Company will present the attached presentation at the 34th Annual J.P. Morgan Healthcare Conference in San Francisco, California being held on January 11 – 14, 2016.

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 press release 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 13, 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: January 11, 2016

INDEX OF EXHIBITS

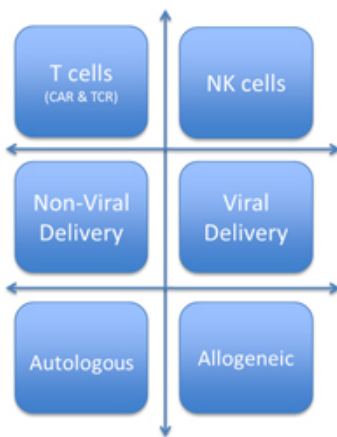
<u>Exhibit No.</u>	<u>Description</u>
99.1	Presentation of the Company dated January 13, 2016

ZIOPHARM
34th Annual J.P. Morgan
Healthcare Conference
January 2016



*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, 2014, and our Quarterly Report on Form 10-Q for the quarter ended September 30, 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.*

Unique Technology Toolbox



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

- ZIOPHARM (NASDAQ: ZIOP) applying combinations that encompass viral & non-viral mechanisms, differentiating it from other players in adoptive cellular therapy today
- We are uniquely situated with:
 - Viral delivery of cytokine
 - T-cell therapy
 - Non-viral and viral delivery of CARs
 - NK-cell therapy
 - Autologous and allogeneic products
 - And combinations of these therapies
- Maturing proof-of-concept data, multiple trial launches in 2016 and 2017
- Well capitalized: Cash and equivalents of \$163.8 million (Q3 2015)
 - Sufficient to fund our planned operations into Q1 2018

Tumor resistance is a hallmark of cancer:

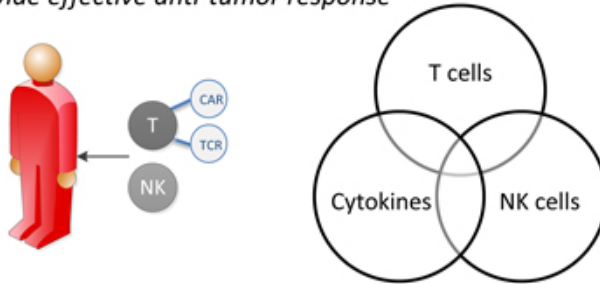
Many therapies, including combination approaches, with different mechanisms of action are needed to overcome tumor escape

Native immune response unable to treat cancer:

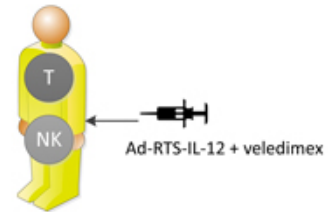
Because the endogenous programming language within T cells and NK cells is muted by cancer

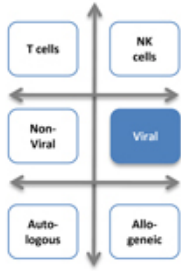
Current Clinical Approaches leading to combination immunotherapy

Administer modified immune cells to provide effective anti-tumor response



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





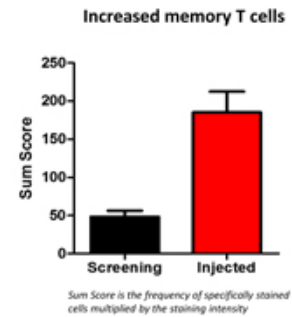
Early brain tumor data encouraging (N=7)

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

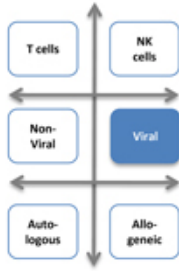
Adverse Event	Grade ≥ 3
Aseptic Meningitis	1 (14%)
Leukopenia	1 (14%)
Neutropenia	1 (14%)
Thrombocytopenia	1 (14%)
Vomiting	1 (14%)

Early breast cancer data encouraging (N=6)

- First patient achieved 12 week PFS endpoint
- Patient accrual accelerating with 5 patients enrolled during fourth 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



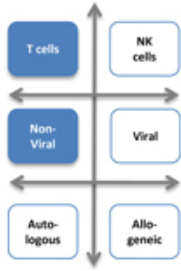
Control and Safety*

- 52 patients treated to date in 4 different human studies
- SAEs and Grade 3 related toxicities are rapidly reversible upon discontinuation of veledimex
- Pattern observed in current GBM and Breast Cancer studies is predictable, consistent and reversible

Next Steps

- Monotherapy
 - Complete current trials
 - Determine optimal dose
- Combination therapy with checkpoint inhibitors
 - Pre-clinical data demonstrates improved anti-tumor response in mice with glioma
 - Abstract submitted ASGCT May 2016

*As of Dec 15, 2015

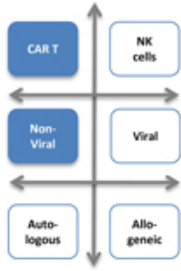


“The Sleeping Beauty transposon-transposase system represents a unique non-viral system for introducing genes encoding T-cell receptors and chimeric antigen receptors into lymphocytes that can be of great value in the development of personalized immunotherapies for patients with cancer.”

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

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
- Pathway to overcome regulatory hurdles

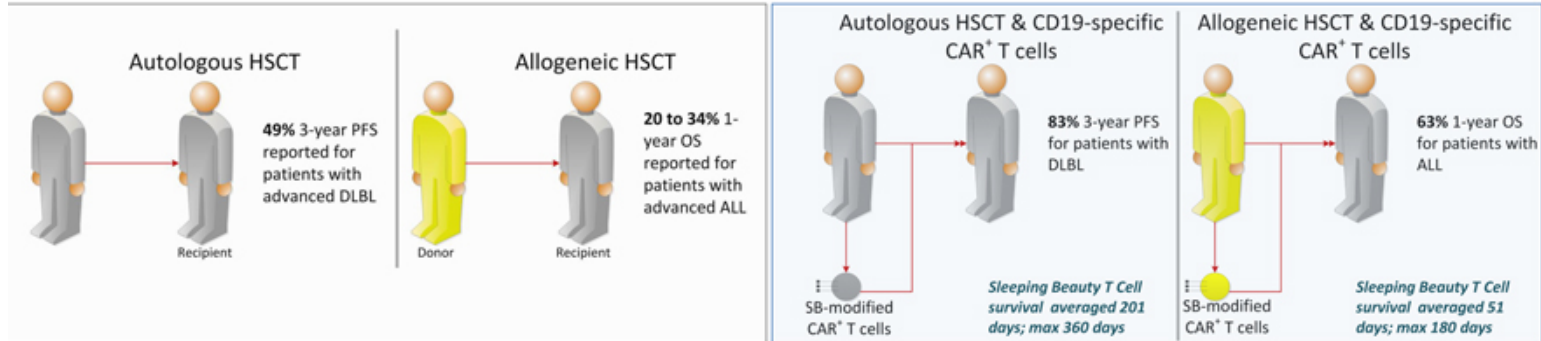


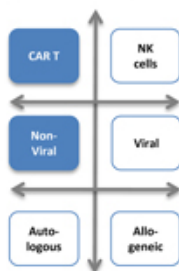
Long term follow-up data from 1st generation *Sleeping Beauty* platform in two trials infusing CAR⁺ T cells *after* hematopoietic stem-cell transplantation (HSCT)

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

Historical Controls

Sleeping Beauty

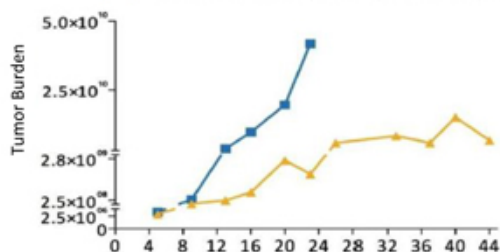




Next-gen CARs utilizing *Sleeping Beauty* demonstrating superior pre-clinical in vivo activity

Established Disease Model

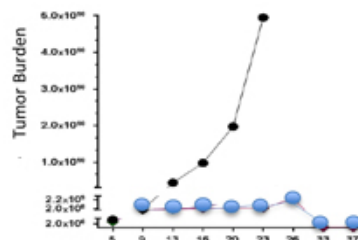
— Prior *Sleeping Beauty* CAR design
— Modified *Sleeping Beauty* CAR design



Next-gen CD19 CAR-T with improved design for improved persistence and anti-tumor response

Established Disease Model

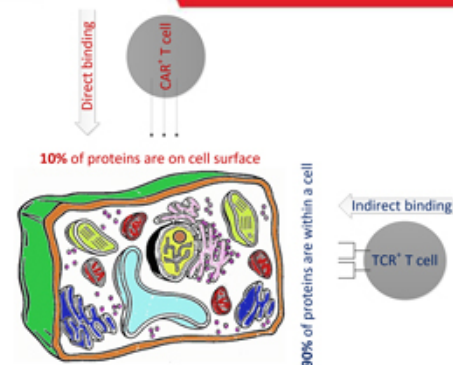
● No T cells
● Modified CAR & mIL-15



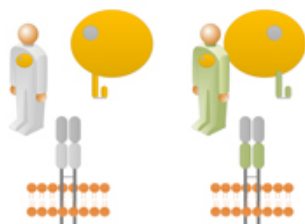
Combination of CAR-T and IL-15 cytokine signaling improves persistence and bolsters immune response

Tumor-Associated Antigens (TAAs)

- Majority TAAs (90%) are intracellular versus only ~10% of proteins expressed on the surface of cells
- Presented by human leukocyte antigen (HLA)
- Minority of patients share HLA
- Most TAAs are not shared between recipients, i.e. **neo-antigens**
- Driver mutations and linked to cancerous behavior



Multiple TCRs needed to target same intracellular antigen in different individuals



Approach for developing therapies

- Targeting most TAAs will be via T-cell receptors (TCRs)
- Targeting intracellular TAAs requires multiple TCRs to benefit multiple patients
- Targeting neo-antigens requires that the T-cell products are personalized to that one antigen in that individual patient.

Sleeping Beauty: This non-viral approach is the key for targeting intracellular antigens by TCRs



Non-viral <i>Sleeping Beauty</i>	Viral delivery
Provides conduit to targeting solid tumor intracellular neo-antigens via multiple TCRs	While established for CARs, viral approaches have limited appeal for targeting multiple intracellular antigens via TCRs
Cost effective approach	High cost approach
Rapid manufacture	Labor intensive, slow manufacture
Customizable, able to swap in different receptors	Challenging to customize

nature
medicine

PERSPECTIVE

Prospects for gene-engineered T cell immunotherapy for solid cancers

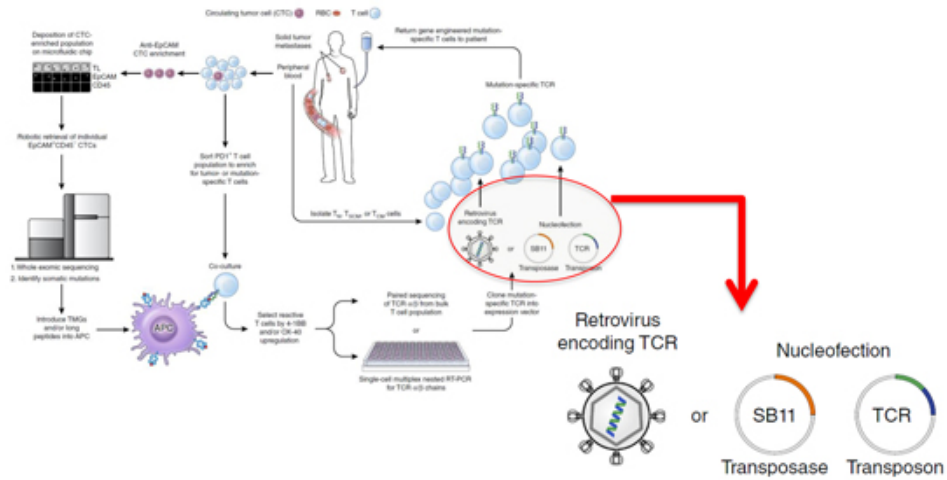
Christopher A Klebanoff, Steven A Rosenberg & Nicholas P Restifo

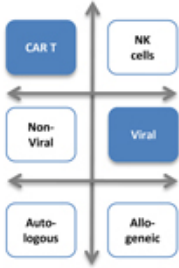
Adoptive transfer of receptor-engineered T cells has produced impressive results in treating patients with B cell leukemias and lymphomas. This success has captured public imagination and driven academic and industrial researchers to develop similar 'off-the-shelf' receptors targeting shared antigens on 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 redirected T cells to treat the majority of patients with solid cancers will require major technical, manufacturing and regulatory innovations centered around the development of autologous gene therapies targeting private somatic mutations.

Nat Med. 2016 Jan 6;22(1):26-36.

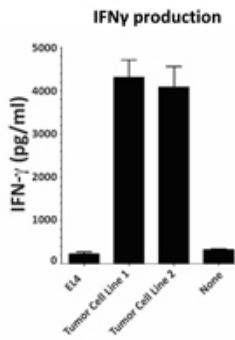
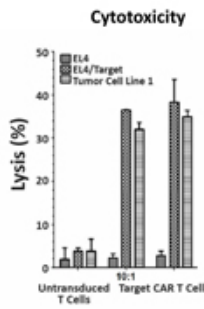
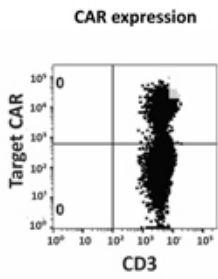
"Success for cell-based immunotherapies may come from the arduous task of targeting the unique set of mutations that cause each patient's cancer"

"Presently, use of the Sleeping Beauty (SB) transposon / transposase system has advanced farthest in clinical development"

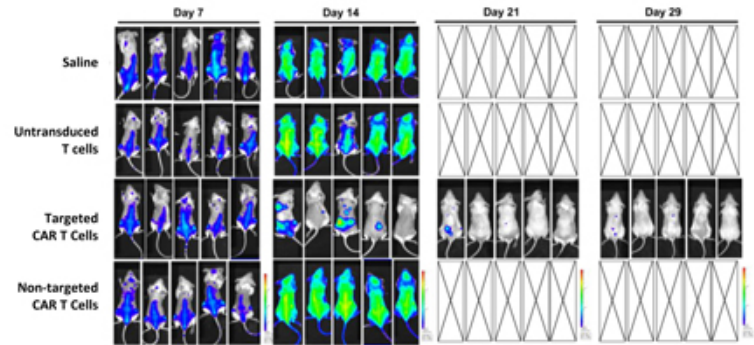


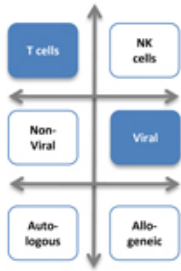


- Ziopharm is utilizing Intrexon's lentiviral platform for immunotherapy of tumors with unmet needs outside of the crowded viral CAR T treatment landscape for CD19⁺ malignancies
- Rapidly advancing a CAR T target for myeloid malignancies:
 - Encouraging pre-clinical data including CAR expression, cytotoxicity, and IFN- γ production
 - Clinical trial is planned for 2016

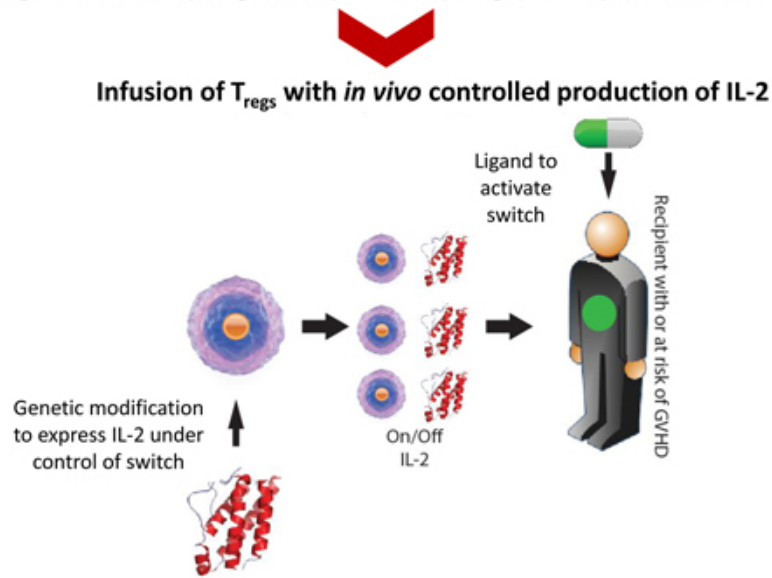


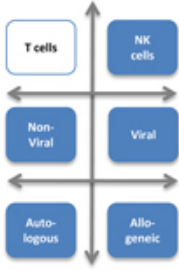
In vivo model for myeloid malignancies CAR-T target





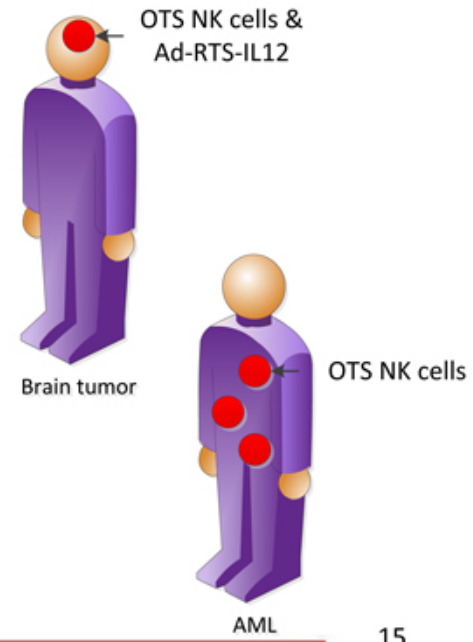
Ziopharm is utilizing lentiviral delivery and Intrexon's proprietary gene control technologies to modify regulatory T cells (Tregs) to express IL-2 for treatment of GvHD

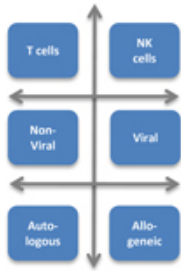




Natural killer (NK) cells

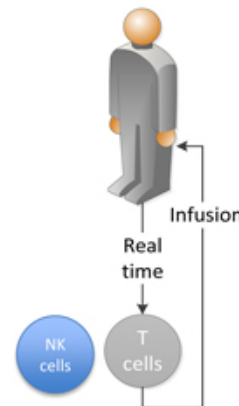
- Target tumors, *e.g.*, with loss or mismatch of HLA
- Killing is independent of a specific (known) target antigen
- Cytokines, *e.g.*, IL-12 are “fuel” for NK cells
- Build on promising proof-of-principle trials ongoing at MDACC infusing autologous and allogeneic NK cells manufactured using feeder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





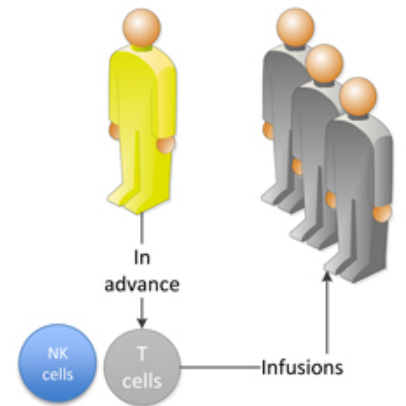
- Implementing manufacturing processes for both autologous and allogeneic settings
- RTS[®] and switches will address off-target effects, especially in solid tumors
- Continued optimization of manufacturing process to improve performance
 - Shortened manufacturing of CAR T cells shows superior *in vivo*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

Patient-derived (autologous)

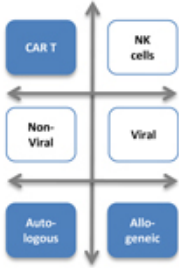


Shorten manufacturing time to produce T or NK cells

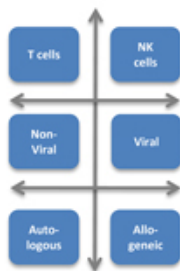
Off-the-shelf (allogeneic)



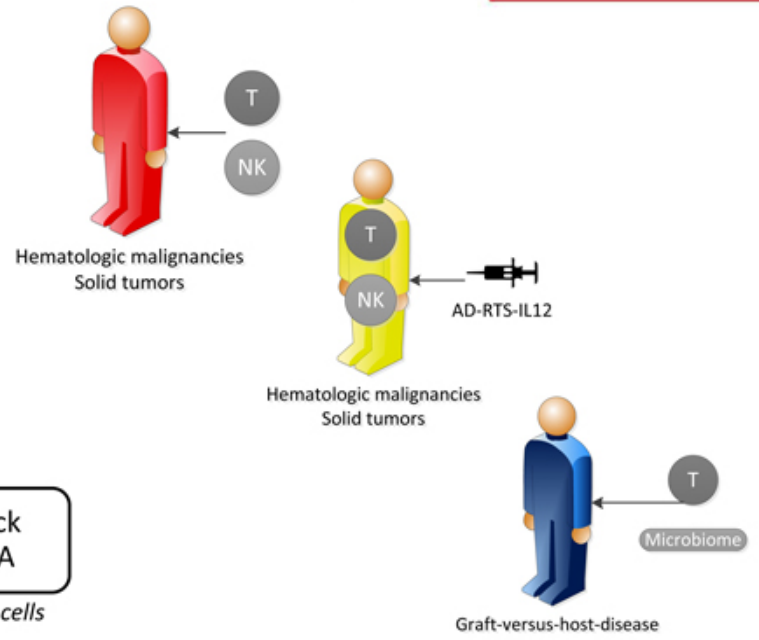
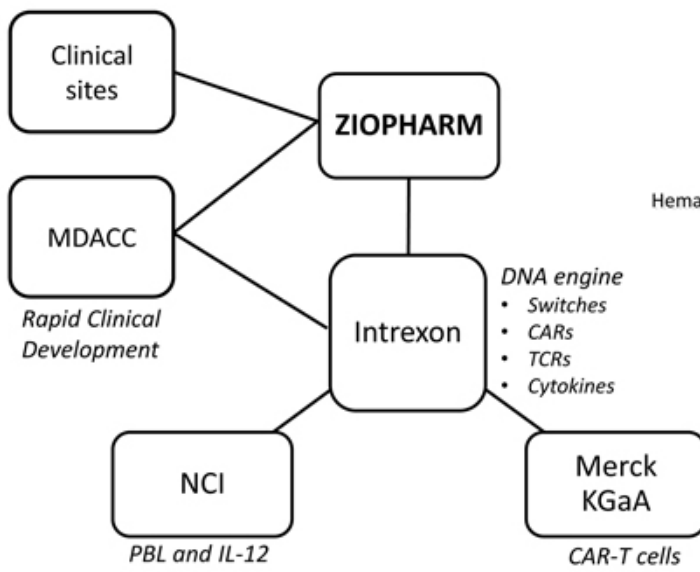
Match one donor with multiple recipients. Generate large numbers of T or NK cells with retained capacity to proliferate.



- Exclusive strategic collaboration and license agreement to develop and commercialize CAR-T cancer therapies
 - Biopharmaceutical business of Merck KGaA has nominated its 2 novel CAR T targets; they will 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
 - Upfront payment of \$115 million
 - For first two CAR T targets, up to \$826 million (\$413 million per product) in development and commercial milestones
 - Tiered royalties up to lower-double digits on net sales
 - Merck KGaA may elect additional targets at additional cost
- Up to \$941M in upfront/milestones for two targets recognizes value of CAR T programs and technology
 - De-risks portfolio and adds significant global development expertise

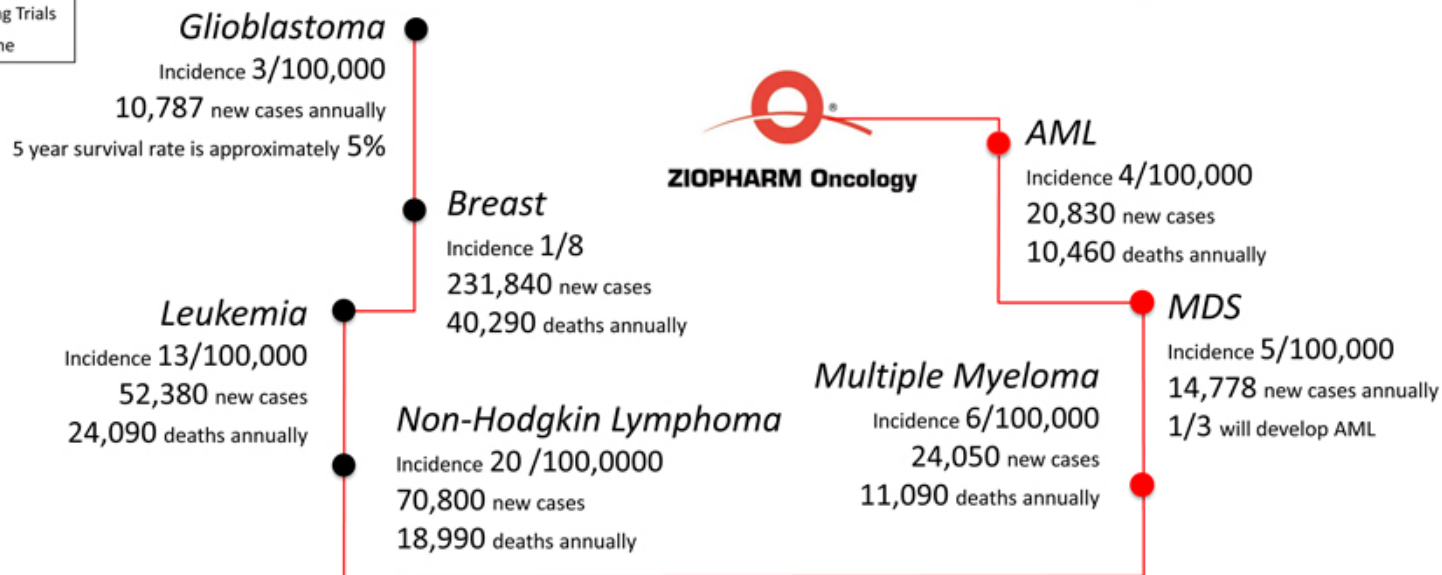


- Fully leveraging our clinical collaboration with MDACC to rapidly evaluate various strategies
- Exploring cutting edge immunology to harness the full capability of gene modified adoptive cell types, such as various immune-modulatory strategies driving T cell or NK cell anti-tumor activity:
 - PD-1 and CTLA-4 knock down
 - Chimeric co-stimulatory receptors
 - Transcription factors
 - Cytokines (IL-2, IL-7, IL-15, IL-21 and IL-12)
 - Chemokines



Addressing unmet medical needs: Solid tumors and hematological malignancies

● Existing Trials
● Pipeline



Refs: Glioblastoma (CBTRUS Report, *Neuro-Oncology* 17:iv1–iv62, 2015); Breast (Cancer Facts & Figures 2015, American Cancer Society); Hematologic Malignancies (Leukemia and Lymphoma Society Facts 2014-2015, based on Cancer Facts & Figures 2014 and SEER Program SEER*Stat Database 2007-2011)

		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				

- 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 modalities
 - Trial initiated with 2nd generation CD19 CAR-T utilizing non-viral *Sleeping Beauty*
 - 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

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