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): December 16, 2015

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

Delaware	**001-33038**	**84-1475642**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

One First Avenue, Parris Building 34, Navy Yard Plaza Boston, Massachusetts	**02129**
(Address of Principal Executive Offices)	**(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)).

Item 7.01 Regulation FD Disclosure

On December 16, 2015, ZIOPHARM Oncology, Inc., or the Company, will present the attached presentation during a previously announced conference call to be held at 4:30 PM eastern time to provide a corporate update and discuss the Company's 2016 outlook.

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

Exhibit No.	Description
99.1	Presentation of the Company dated December 16, 2015

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/ Caesar J. Belbel

Name: Caesar J. Belbel

Title: Chief Operating Officer, Executive Vice President, Chief Legal Officer and Secretary

Date: December 16, 2015

INDEX OF EXHIBITS

Exhibit No.	Description
99.1	Presentation of the Company dated December 16, 2015

EXHIBIT 99.1

ZIOPHARM

Review and Outlook

December 16, 2015

ZIOPHARM Oncology

Forward-looking Statements

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, 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.*

Immuno-oncology: Introduction

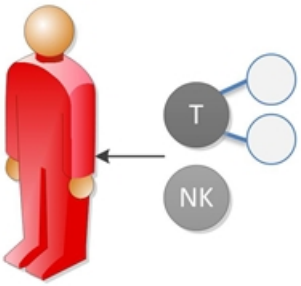
ZIOPHARM Oncology

Tumor resistance is a hallmark of cancer and thus multiple modalities are needed with different mechanisms of action to overcome tumor escape

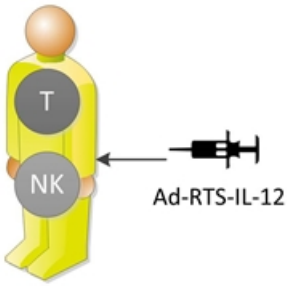
Native immune response unable to treat cancer because the endogenous programming language in T cells and NK cells is muted by cancer

Current Clinical Approaches

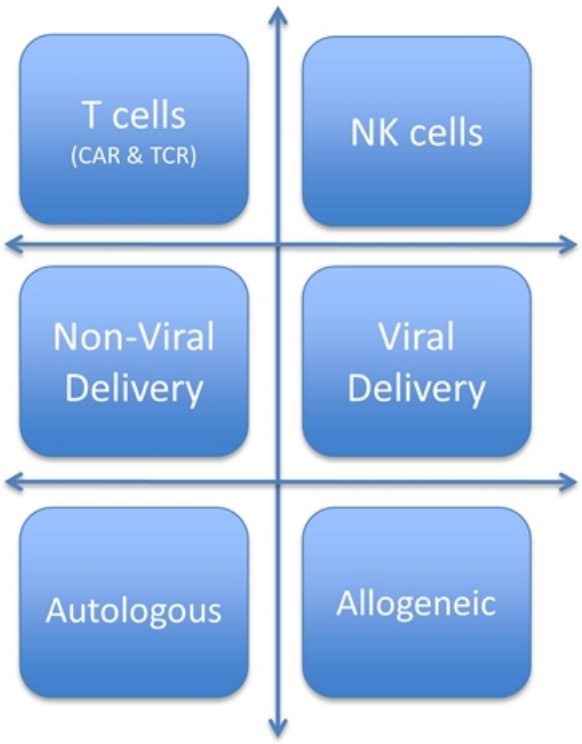
Administer modified immune cells to provide effective anti-tumor response



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



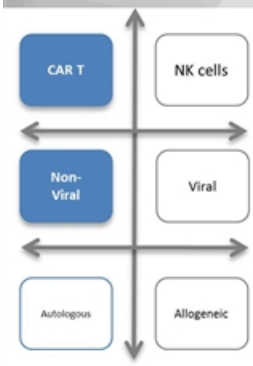
Broad Approach Against Cancer



- ZIOPHARM applying multiple modality and multi-delivery approach that encompasses viral & non-viral mechanisms, differentiating it from many other players in adoptive cellular therapy today
- Positioned to leap frog into leadership in hematological and solid tumor settings with viable commercial strategies that surpass limitations of 1st and 2nd generation approaches

Non-Viral Delivery: *Sleeping Beauty*

ZIOPHARM Oncology



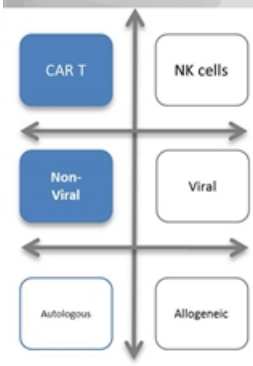
"The Sleeping Beauty transposon-transposase system represents a unique non-viral system for introducing genes encoding T-cell receptors and chimeric antigen receptors into lymphocytes that can be of great value in the development of personalized immunotherapies for patients with cancer."

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

- *Sleeping Beauty* (SB) non-viral DNA delivery system offers unique approach to adoptive cellular therapies including CARs & TCRs
- SB has potential to eclipse limitations associated with viral delivery including point of care, cost of goods, and customization of patient-specific TCRs
- After successful first-in-human study, a Phase I trial with next-gen CAR design utilizing SB system initiated at MDACC
- We anticipate further clinical evaluation of SB as we endeavor to optimize and fully leverage this platform

Sleeping Beauty First-in-man Study

ZIOPHARM Oncology



Long term follow-up data from 1st generation non-viral SB technology tested in two separate trials infusing CAR+ T cells *after* hematopoietic stem-cell transplantation (HSCT)

T-cell survival	Average # of days	Maximum days
Autologous	201*	360
Allogeneic	51	180

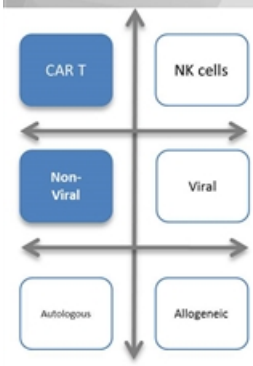
** Compares favorably versus 5 of 7 other CD19 studies presented at ASH*

Patient groups	Summary
Autologous	83%, 3-yr PFS compared with 49% historical controls
Allogeneic (all)	63%, 1-yr OS compared with 20-34% historical controls
Allogeneic (haploidentical)	75%, 1-yr OS and no GVHD despite large numbers of T cells infused

- Auto: Blood 125, 2579-2581 (2015)
- Allo: Curr Hematol Malig Rep 7, 144-152 (2012)

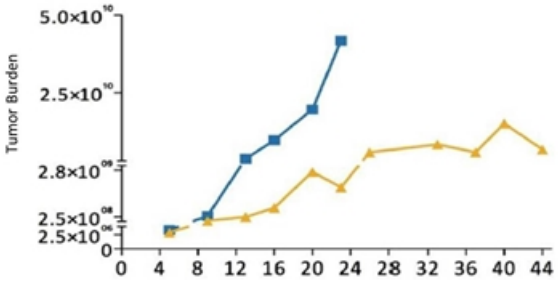
Sleeping Beauty: Next-generation CARs

ZIOPHARM Oncology



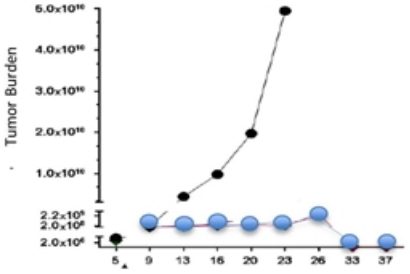
Next-gen CD19 CAR utilizing SB platform with improved design for anti-tumor response demonstrates superior *in vivo* activity pre-clinically

Established Disease Model



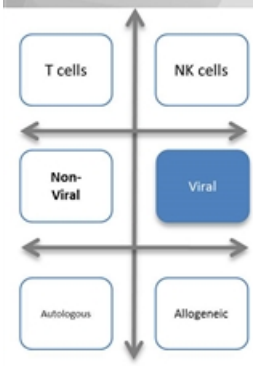
Combination of **CAR signaling with IL-15 cytokine** shows bolstered immune response and improved persistence pre-clinically

Established Disease Model



Ad-RTS-IL-12 + Veledimex Clinical Update

ZIOPHARM Oncology



Early brain tumor data encouraging (N=7)

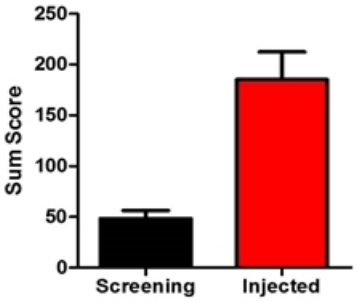
- Patients enrolled at multiple centers
- Biomarkers as expected
- Neurotoxicity minimal
- "On-target toxicities" as expected and promptly reversible upon stopping veledimex →

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)

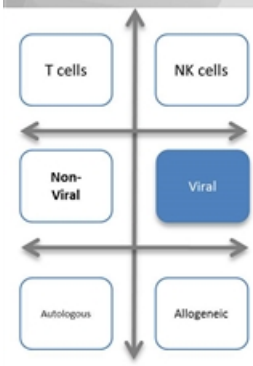
- First patient achieved 12 week PFS endpoint
- Patient accrual accelerating with 5 patients enrolled during fourth quarter
- Looking for confirmation of increased memory T cells as seen in previous trials →
- "On-target toxicities" as expected and promptly reversible upon stopping veledimex

Increased memory T cells within melanoma lesions



Sum Score is the frequency of specifically stained cells multiplied by the staining intensity

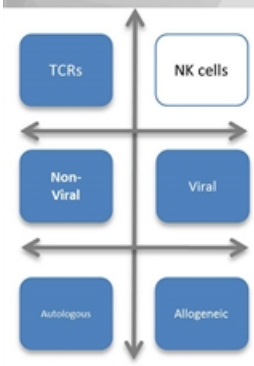
Ad-RTS-IL-12 + Veledimex Control & Safety



- 52 patients treated to date in 4 different human studies
- SAEs and Grade 3 related toxicities are rapidly reversible upon discontinuation of veledimex
- Four cases of Cytokine Release Syndrome (drug related)
  - Reversible with discontinuation of veledimex and supportive care
  - No anti-IL-6 required (Tocilizumab)
  - No vasopressors required
- No drug related deaths
- Pattern observed in current GBM and Breast Cancer studies is predictable, consistent and reversible

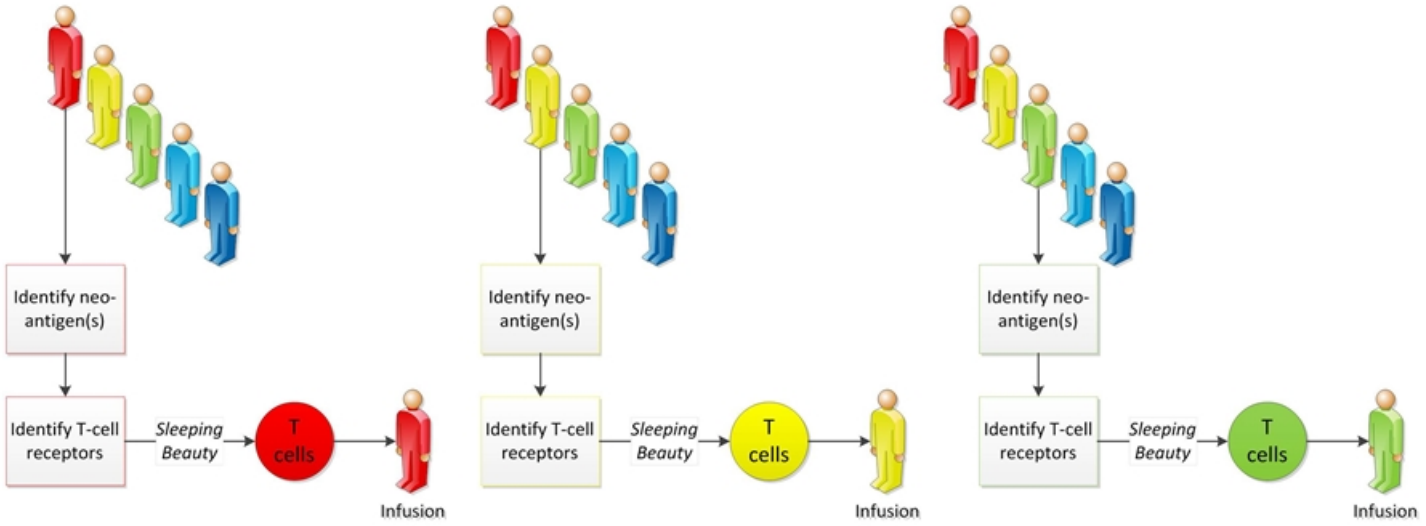
T Cell Receptors

ZIOPHARM Oncology



TCR+ T cells

- Target intracellular TAAs dependent on HLA
- "Private" intra-cellular antigens (neo-antigens)



Beyond T cells: Natural Killer Cells

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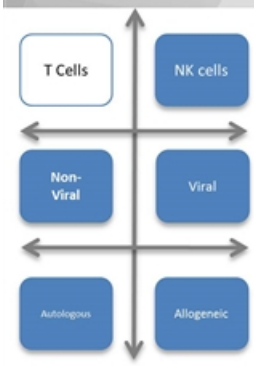
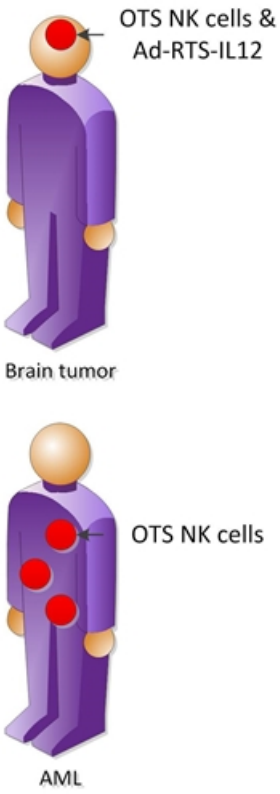


NK cells

- Target tumors with loss of HLA
- Killing is independent of a target antigen

– Proof-of-principle trials ongoing at MDACC infusing autologous and allogeneic NK cells generated using feeder cells
  - SNO 2015: Brain tumor
  - ASH 2015: AML & MM

– Launching trials infusing off-the-shelf NK cells for AML and brain tumor



Therapies for GvHD

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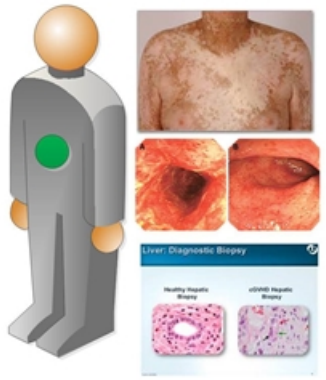
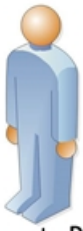
INTREXON®



Recipient
Acute GVHD
Chronic GVHD



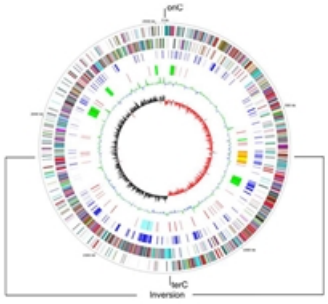
Donor

Regulatory T cells

Genetic modification

Regulatory T cells

IL-2



L. lactis

Genetic modification

IL-2

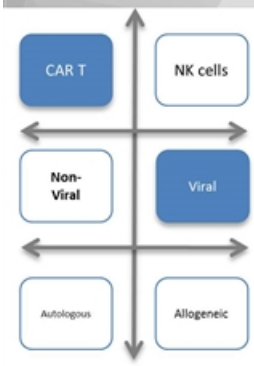
Peter Emtage, Ph.D.

Vice President, Immunology

Intrexon Corporation

ZIOPHARM Oncology

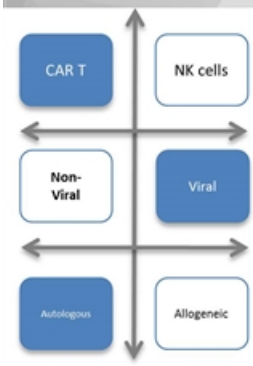
Viral Delivery Approach in CAR T

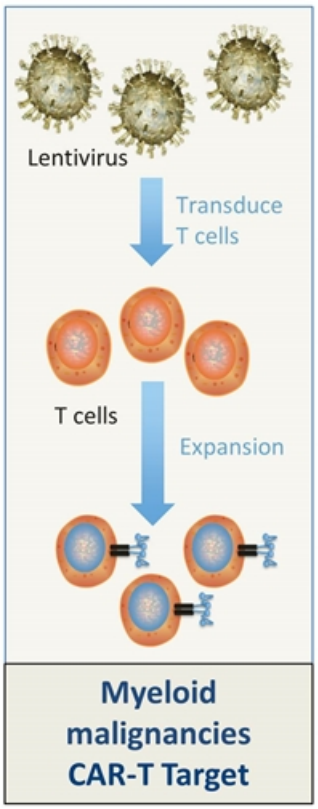


- Ziopharm and Intrexon utilizing lenti-viral delivery in "white space" tumors outside of the very competitive landscape of CD19+ hematological malignancies
- Rapidly advancing clinical candidates for Myeloid malignancies and multiple myeloma (MM) and anticipate clinical starts in 2016 representing near term inflection point
- Malignancies outside of the CD19 space offer a similar development timeline to those seen in ALL and other CD19 tumors
- Considering current treatments available to patients with relapsed and refractory disease in Myeloid malignancies and MM, anticipate an expedited regulatory process

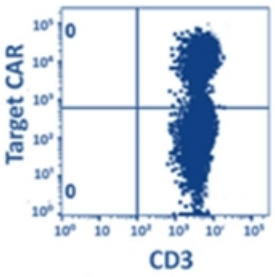
Targeting Myeloid Malignancies with Lenti CAR+ T cells

ZIOPHARM Oncology

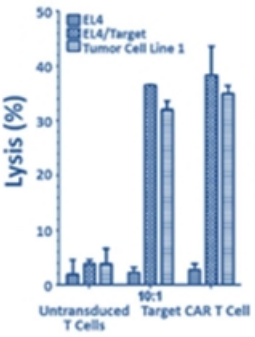




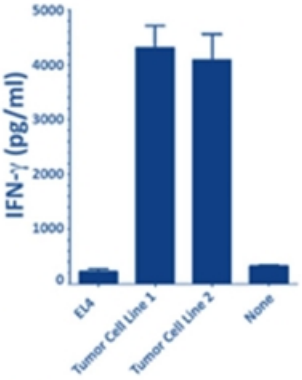
CAR expression



Cytotoxicity

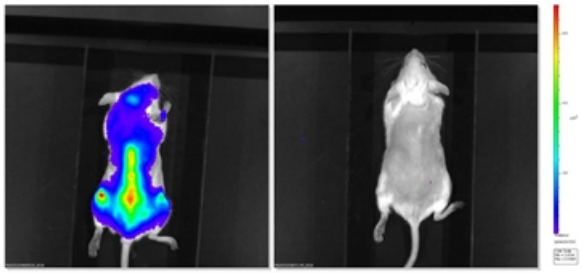


IFNγ production



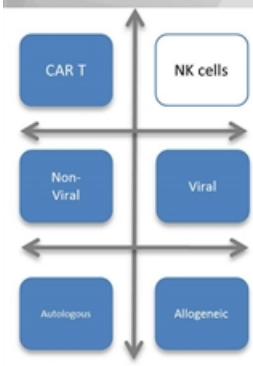
In vivo Tumor Cell Model

Saline Treated | Target CAR Treated

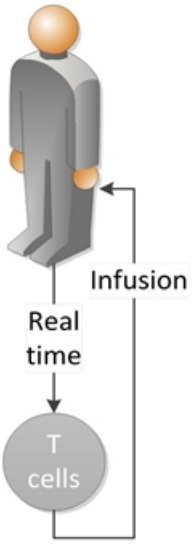


Autologous & Allogeneic Approach in Myeloid Malignancies

ZIOPHARM Oncology

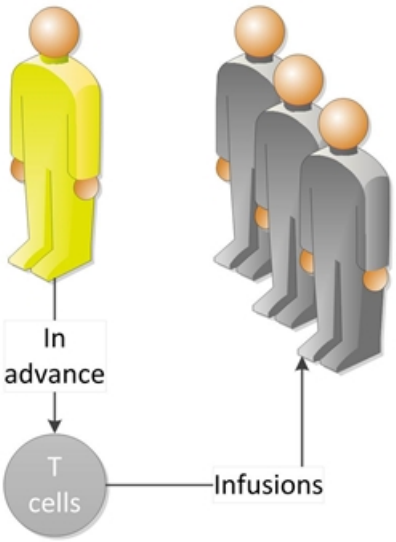


Patient-derived (autologous)



Shorten manufacturing time to produce T cells

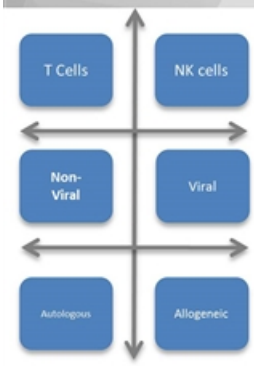
Off-the-shelf (allogeneic)



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

Targeting Solid Tumor Malignancies

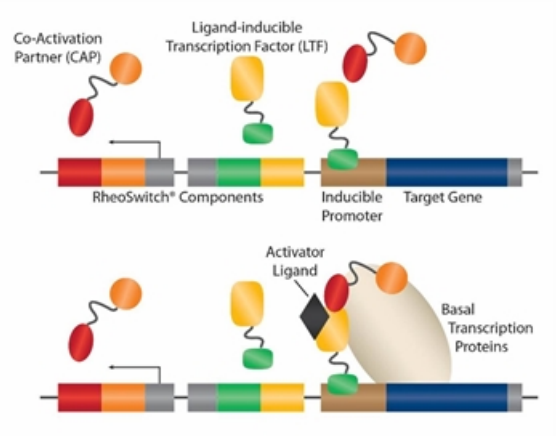
ZIOPHARM Oncology



Outside of hematological malignant disease we have a number of solid tumor programs that target various tumor types:

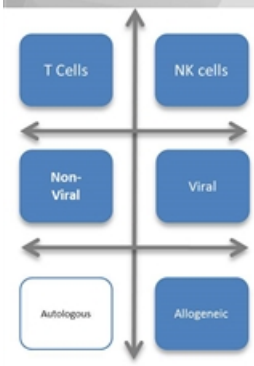
- GBM
- Neuroblastoma
- Breast
- Prostate
- Colorectal
- Gastric
- Head and neck

Addressing Off-target Effects



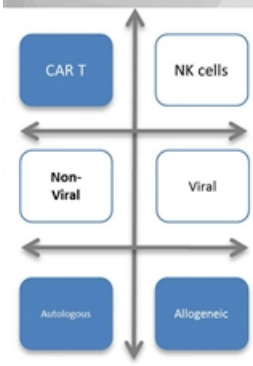
- We believe that all CAR and TCR companies will need to address off-target effects in solid tumors.
- To address these off target effects we are testing and implementing switch controllable gene expression modules as well as target discovery
- Considerable strides are being made addressing off-target issues through RTS® platform and other switch technologies

“Off the Shelf” Therapies



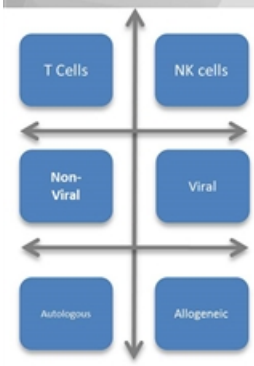
- Developing a strategy for “off the shelf” which we believe will be an important advancement for patient and commercial success
- We believe that modulating both aspects of transplant biology is critical for success in the “off the shelf” space
  - Prevention of Graft-versus-Host-Disease (GvHD) that is currently under evaluation in the clinic
  - Approaches to reduce Host-versus-Graft-Disease (HvGD)
  - Approaches to reduce rejection of infused immune cells
  - Approaches to maintain survival of infused immune cells

Collaboration with Merck KGaA in CAR-T



- 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

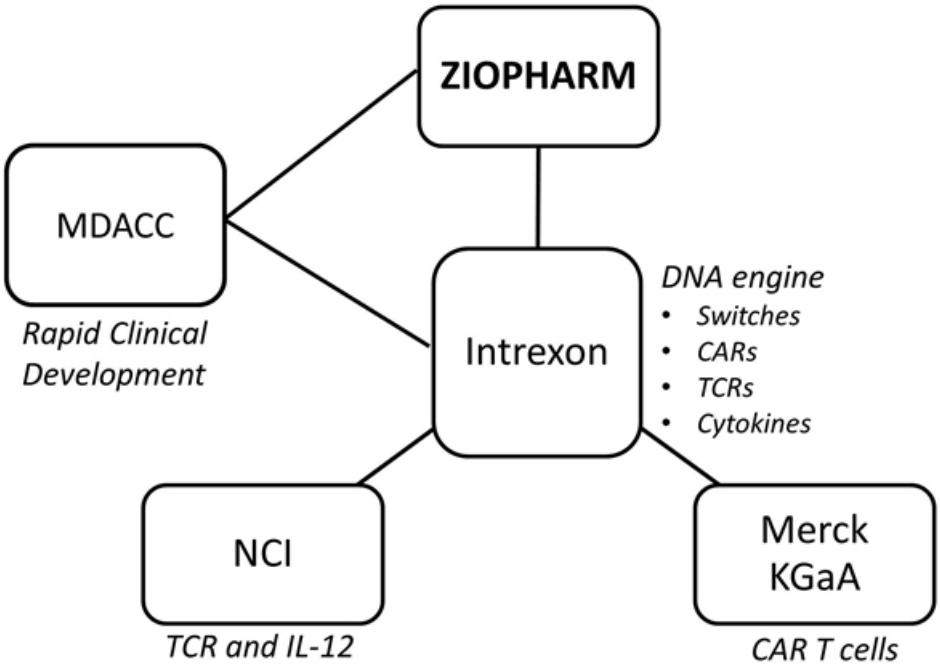
Collaboration with MDACC

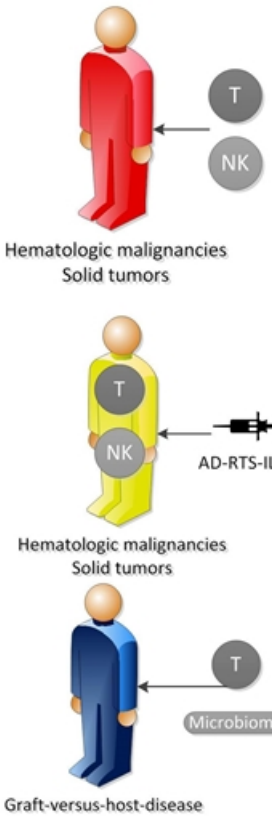


- Fully leveraging our clinical collaboration with MDACC to rapidly evaluate various strategies
- Development is not limited to competitive CARs or TCRs
- Exploring cutting edge immunology to harness the full capability of gene modified adoptive cell types, such as various immune-modulatory strategies driving T 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

ZIOPHARM's Partnerships

ZIOPHARM Oncology





Pipeline

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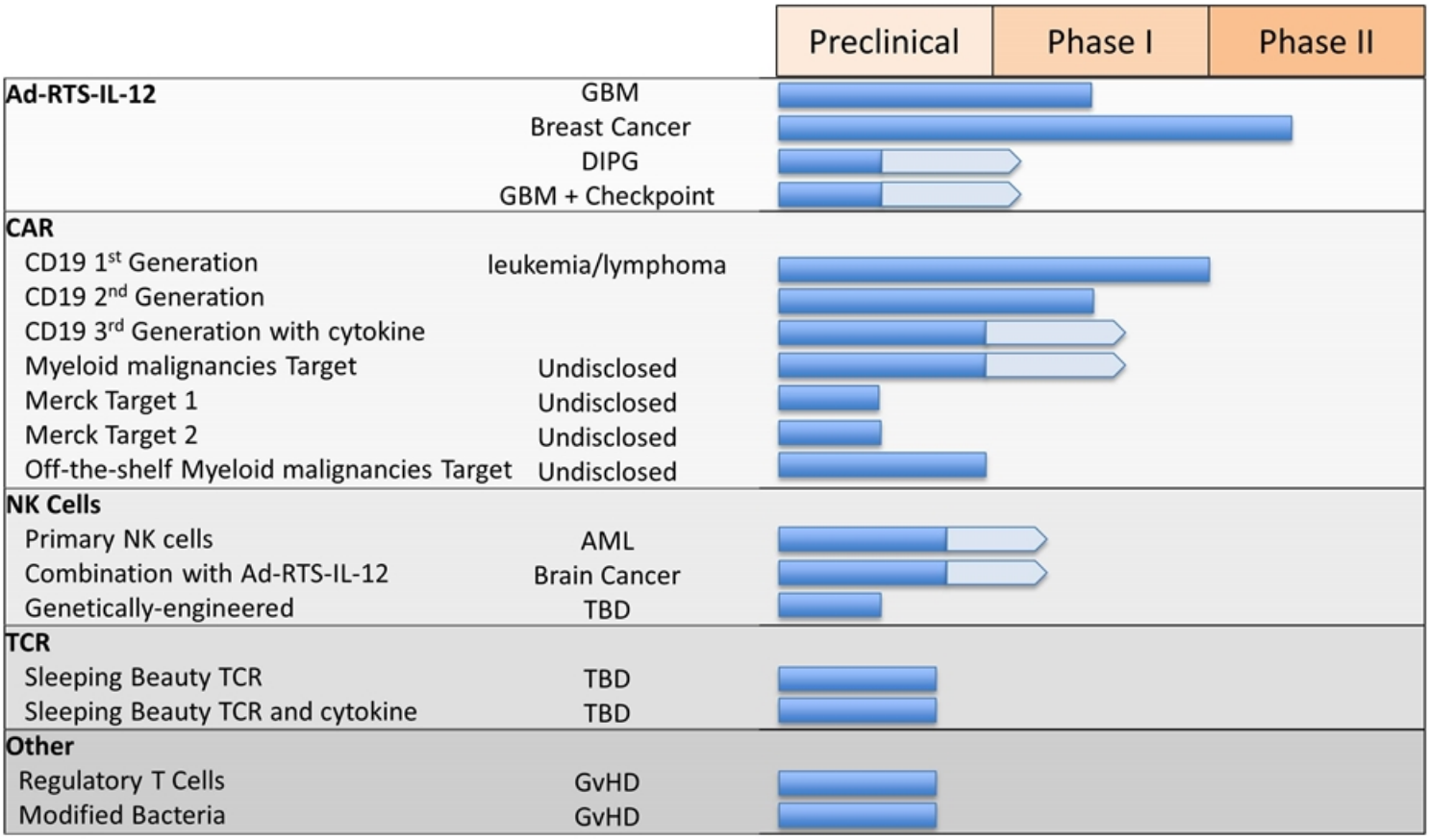

Summary

ZIOPHARM Oncology

- R&D efforts provide us a competitive position in tumors outside of CD19 and an opportunity to take a leadership position as we leverage our immunological and technical expertise
- We are implementing a series of programming languages (operating systems) to control the immune system in humans
  - RheoSwitch® platform
  - Non-viral gene transfer
- This is being tested in multiple opportunities
  - Virus
  - CAR T, TCR, and NK Cells
- ZIOPHARM and Intrexon have the genetic programming tools and multitude of cell products needed in combination to treat cancer

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Review and Outlook

December 16, 2015

ZIOPHARM Oncology