
**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): September 10, 2015

ZIOPHARM Oncology, Inc.

(Exact Name of Registrant as Specified in Charter)

Delaware
(State or Other Jurisdiction
of Incorporation)

001-33038
(Commission
File Number)

84-1475672
(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)).
-
-

Item 7.01 Regulation FD Disclosure

On September 10, 2015, ZIOPHARM Oncology, Inc., or the Company, will present the attached presentation of its immuno-oncology programs at the 2015 Wells Fargo Healthcare Conference in Boston, Massachusetts, being held on September 9 - 10, 2015.

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 September 10, 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/ Kevin G. Lafond

Name: Kevin G. Lafond

Title: Vice President, Chief Accounting Officer and Treasurer

Date: September 10, 2015

INDEX OF EXHIBITS

**Exhibit
No.**

Description

99.1 Presentation of the Company dated September 10, 2015

Wells Fargo Healthcare Conference

SEPTEMBER 2015



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 10Q for the quarter ended June 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.*

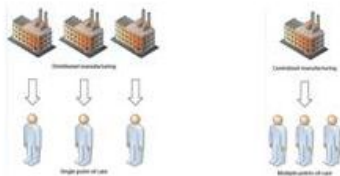
- NASDAQ: ZIOP
- Robust synthetic immunology pipeline
 - Virotherapy & adoptive cell therapy
 - Multiple partnerships
- Differentiated technology platforms
 - Gene switch, non-viral integration and viral-based delivery
- Multiple trial launches in 2015/2016
- Well capitalized
 - Cash and equivalents of \$176.1 million (Pro forma)
 - Sufficient to fund our planned operations into Q1 2018

Delivering on the Premise and Promise of Gene and Immune-based Therapies

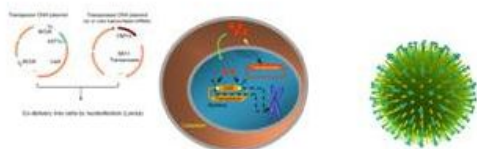
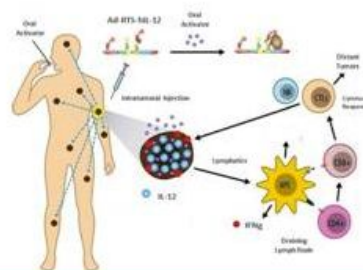
- ✓ Fully Aligned with research and development (Intrexon)
- ✓ Big pharma partnership (CARs)
- ✓ Bio-processing for next-generation products
- ✓ Aligned with academic centers for manufacturing of cells for investigator-initiated trials
- ✓ Contract manufacturing for ZIOP-sponsored trials in place
- ✓ Established suite of correlative studies
- ✓ Undertaking multi-center gene therapy trials
- ✓ Multi-faceted approach to gene therapy (non-viral and viral)
- ✓ Ability to manipulate the immune response *in situ* (generate immune response within patient)
- ✓ Ability to provide an immune response (infuse immune cells)
- ✓ Ability to manipulate virus after infusion
- ✓ Ability to manipulate immune cells after infusion
- ✓ Immune cells targeting tumor through CAR, TCR, and NK
- ✓ Infuse patient-derived immune cells
- ✓ Infuse 3rd party (allogeneic) immune cells

Cell Therapy

CAR-T, TCR and NK Cells
Autologous and Allogeneic

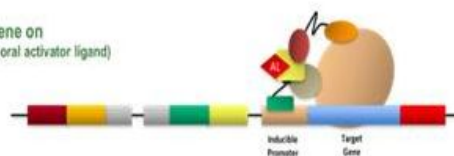


Virotherapy



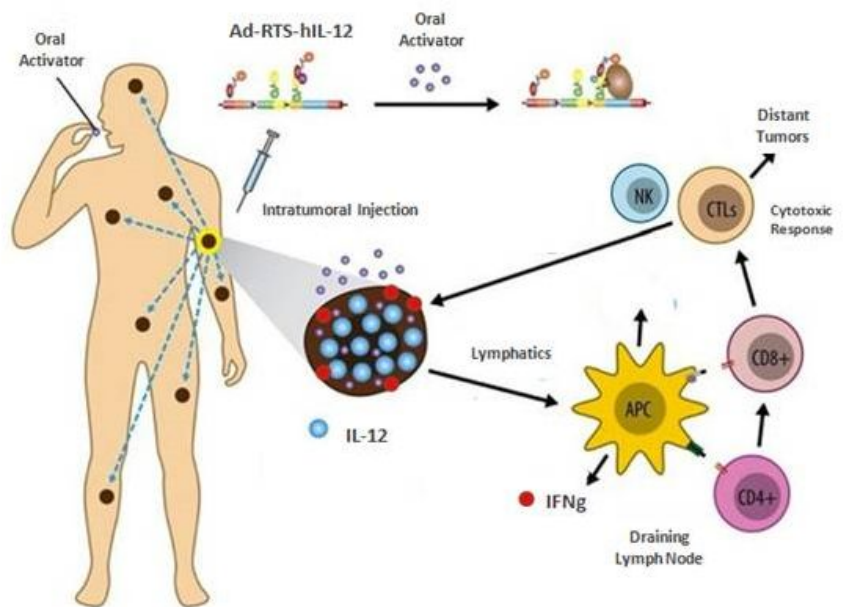
Viral & Non-viral Gene Integration

Gene on
(+ oral activator ligand)

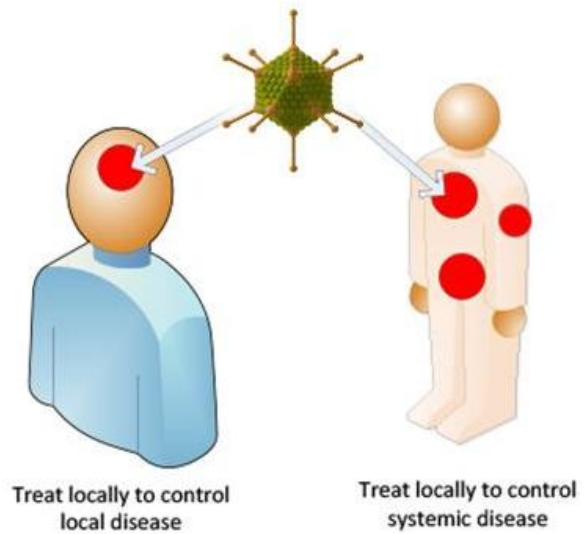


RTS® Gene Switches

- Adenoviral vector engineered to express IL-12 utilizing RheoSwitch Therapeutic System® (RTS®) gene switch
- Injected intra-tumor with IL-12 expression controlled via administration of oral activator ligand veledimex
- Regulated intra-tumoral expression of IL-12 promotes activation of tumor-infiltrating lymphocytes to drive cytotoxic immune response against distant tumors

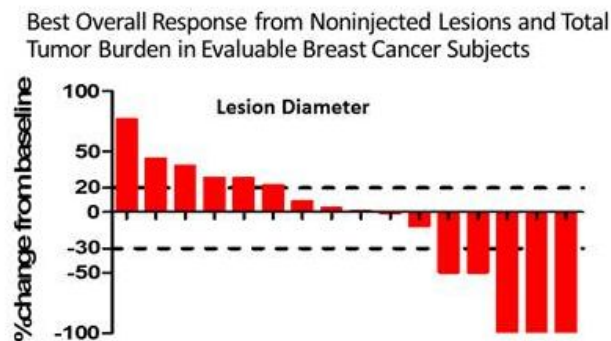


- Improved persistence and survival in tumor microenvironment
- Limits on-target, off-tumor toxicities
- Administer virus locally to achieve systemic anti-tumor effects (Breast)
- Administer virus locally to achieve local anti-tumor effects (GBM)



Ad-RTS-IL-12 Gene Therapy Clinical Response To Date

- Expression of functional IL-12 in human subjects by direct intra-tumoral injection of Ad-RTS-hIL-12 + oral veledimex generates downstream IFN γ production and rapid systemic elevation of IL-10 and IP-10
- Documented **systemic immune activation and clinical effect** in advanced, heavily pretreated melanoma and breast cancer patients
- Adverse event profile, including cytokine release syndrome, of Ad-RTS-hIL-12 + veledimex is predictable, controllable, and **fully and rapidly reversible on stopping veledimex**. Several subjects then restarted on veledimex



A Multi-Center Gene Therapy Study

Phase 1 Study of IL-12 Gene Therapy in Recurrent or Progressive Glioblastoma/Grade III Malignant Glioma



N = 72

Recurrent or progressive glioblastoma or Grade III malignant glioma

Stratified according to clinical indication for tumor resection: Resection plus injection vs. stereotactic injection alone

A single cycle of Ad-RTS-hIL-12 + escalating veledimex

10 : Safety and tolerability

20 : Determine MTD and immune response, including ORR, PFS and OS

Early Response Data Expected in 4Q 2015

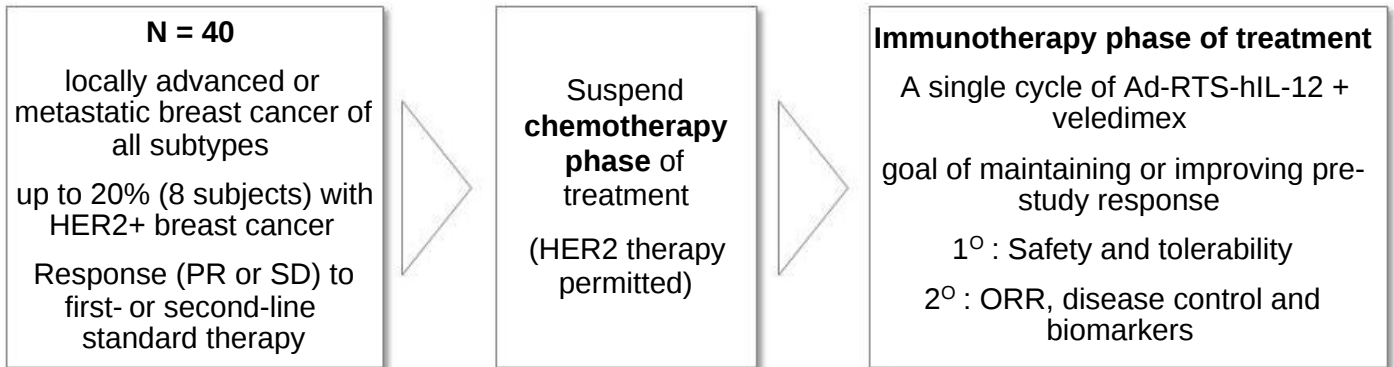
Phase 1b/2 Study of IL-12 Gene Therapy in Locally Advanced/Metastatic Breast Cancer



ZIOPHARM Oncology

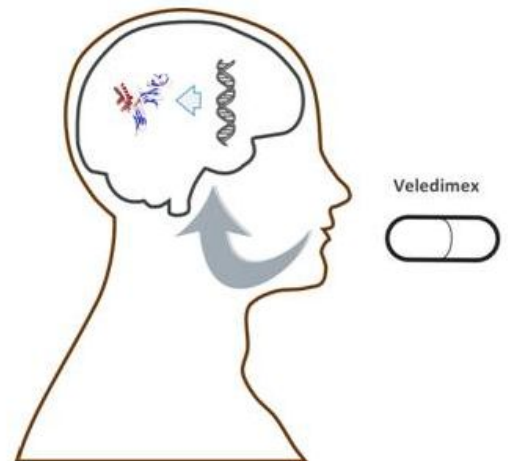


Memorial Sloan Kettering
Cancer Center.



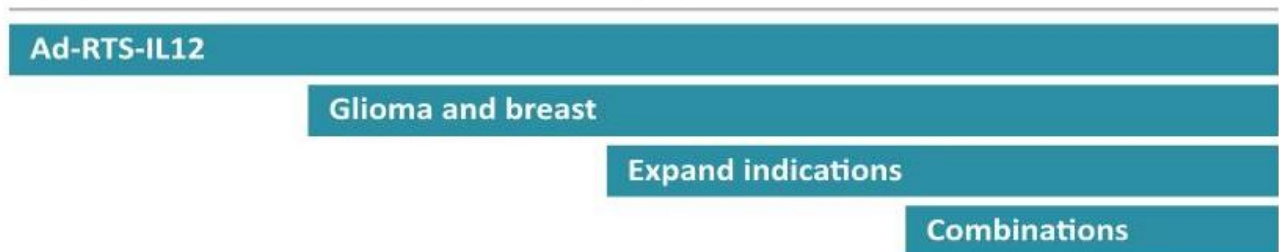
Early Response Data Expected in 4Q 2015

- Demonstrated the ability of Veledimex to cross blood-brain barrier in animal models (AACR 2014)
- Proof-of-concept in humans being explored in ongoing multi-center gene therapy trial
- Combination therapies
- Veledimex for activation of genetically modified T cells in brain



2015

2016



CAR⁺ T cells

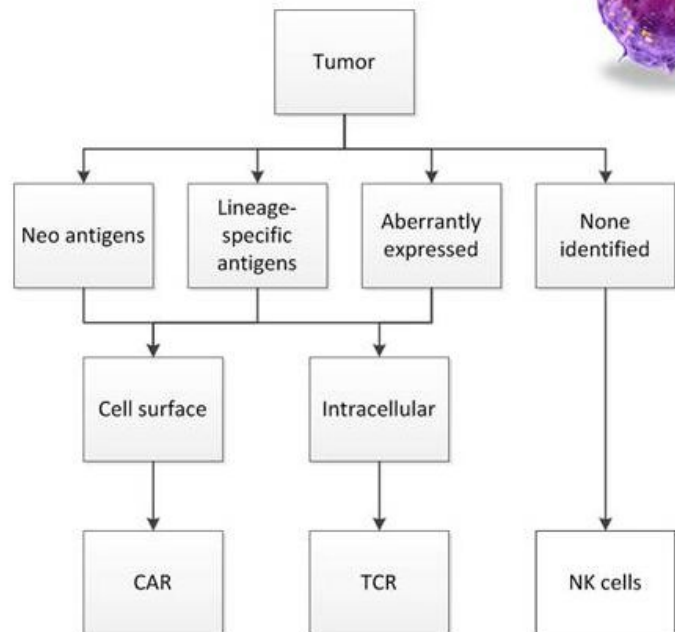
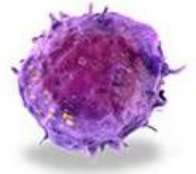
- Target cell surface tumor-associated antigens (TAAs) independent of HLA
- “Public” cell surface antigens

TCR⁺ T cells

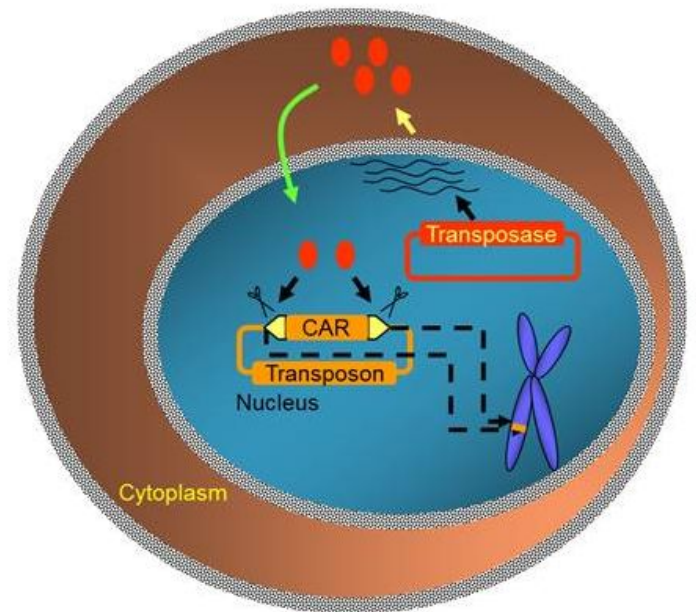
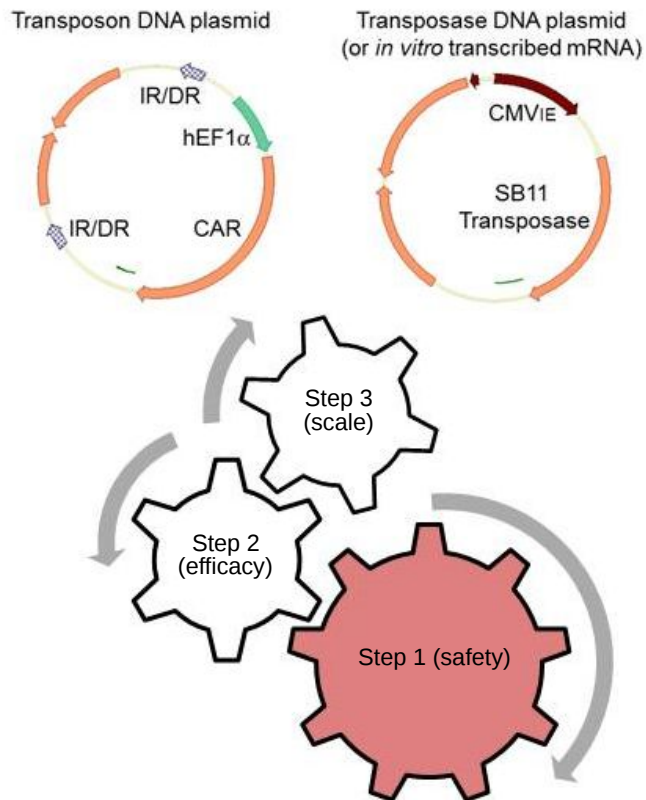
- Target intracellular TAAs dependent on HLA
- “Private” intra-cellular antigens

NK cells

- Target tumor with loss of HLA
- No “antigens”

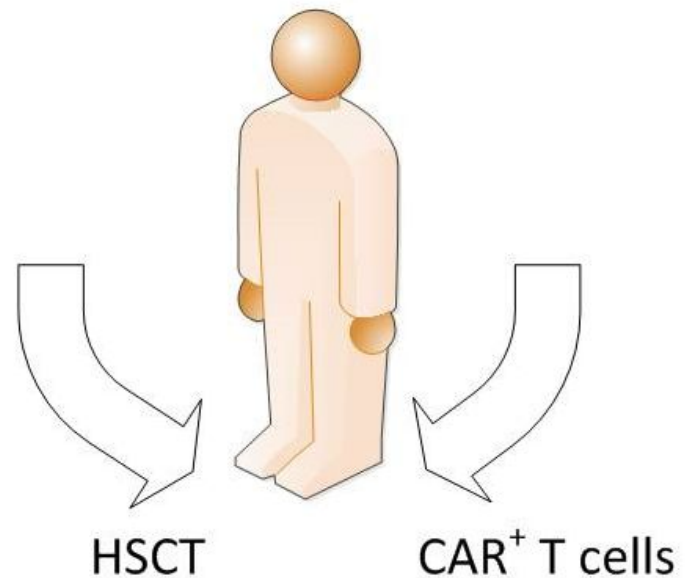


Sleeping Beauty (SB) Non-viral Gene Integration



Pre-emptive donor lymphocyte Infusion with CD19-directed CAR⁺ T cells infused after **autologous** hematopoietic stem-cell transplantation (HSCT)

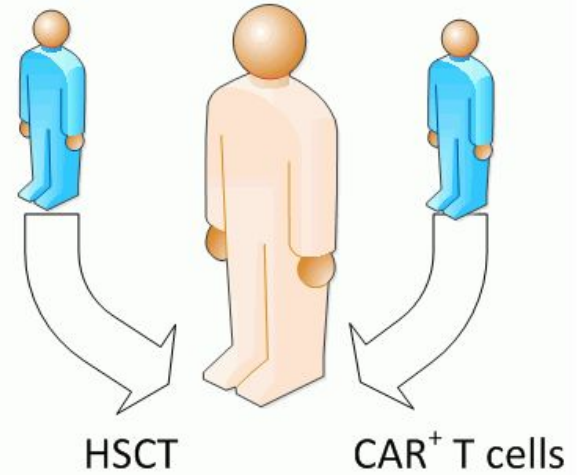
- Population** 7 patients with advanced non-Hodgkin lymphoma (NHL)
- Safety** Patients have not demonstrated any acute or late toxicity to CAR⁺ T-cell infusions
- Efficacy** 100% of patients remain alive following a single CAR⁺ T-cell infusion with a median follow-up of 24 months
- 86% of patients (n=6) remain alive and in complete remission (CR)



Trial at MDACC; Will be submitted for publication

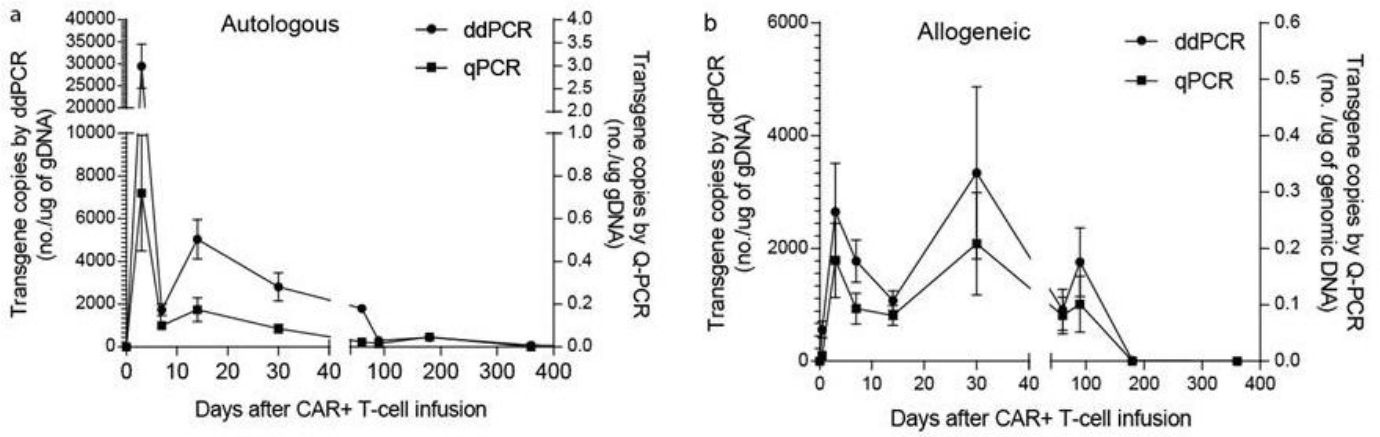
Pre-emptive donor lymphocyte infusion with CD19-directed, CAR⁺ T cells infused after **allogeneic** HSCT

- Population** 19 patients with advanced CD19⁺ ALL (n=17) or NHL (n=2)
- Safety** 3 patients developed GVHD which is lower than the expected range after allogeneic HSCT alone
- Efficacy** 58% of patients (n=11/19) remain in complete remission (CR) and 10/19 remain alive and in CR (1 death in CR) following CAR⁺ T-cell infusion with a median follow-up of 6.5 months post transplant among survivors.
- Among 8 patients who received haplo-HCST and CAR, 100% of remain alive and 75% remain in remission
- Rate of CMV reactivation after CAR⁺ T-cell administration was 24% vs. 41% previously reported for our patients without infusion



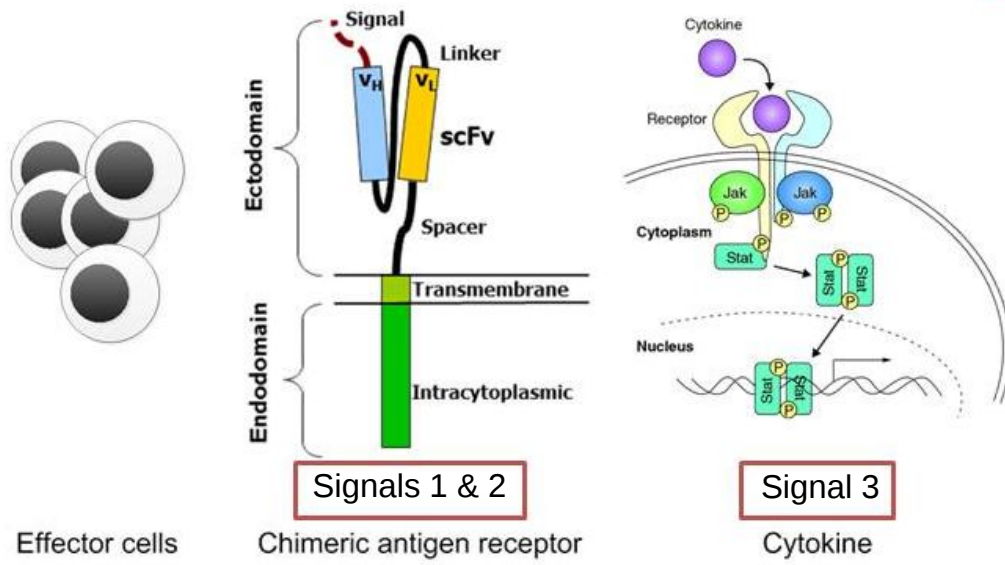
Trial at MDACC, Updated from EHA 2015; Will be submitted for publication
*Wilhelm et al. J Oncol Pharm Practice, 2014, 20:257

Persistence of Infused CAR⁺ T Cells



Trial at MDACC, Updated from EHA 2015; Will be submitted for publication

Improving Therapeutic Potential of CAR⁺ T Cells



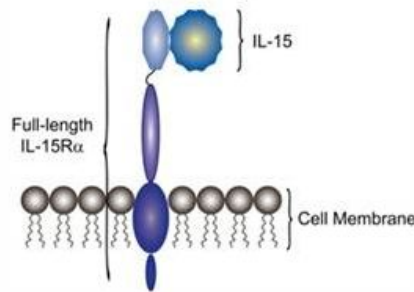
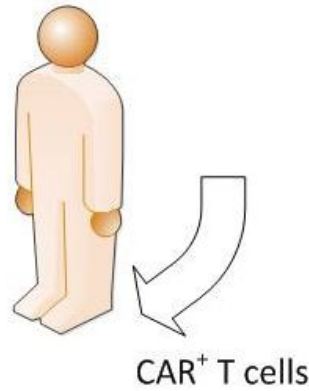
BIOPROCESSING

CAR DESIGN

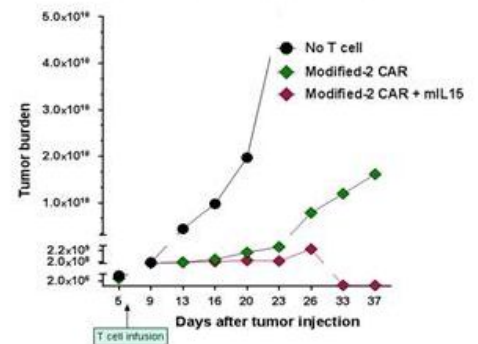
CYTOKINE

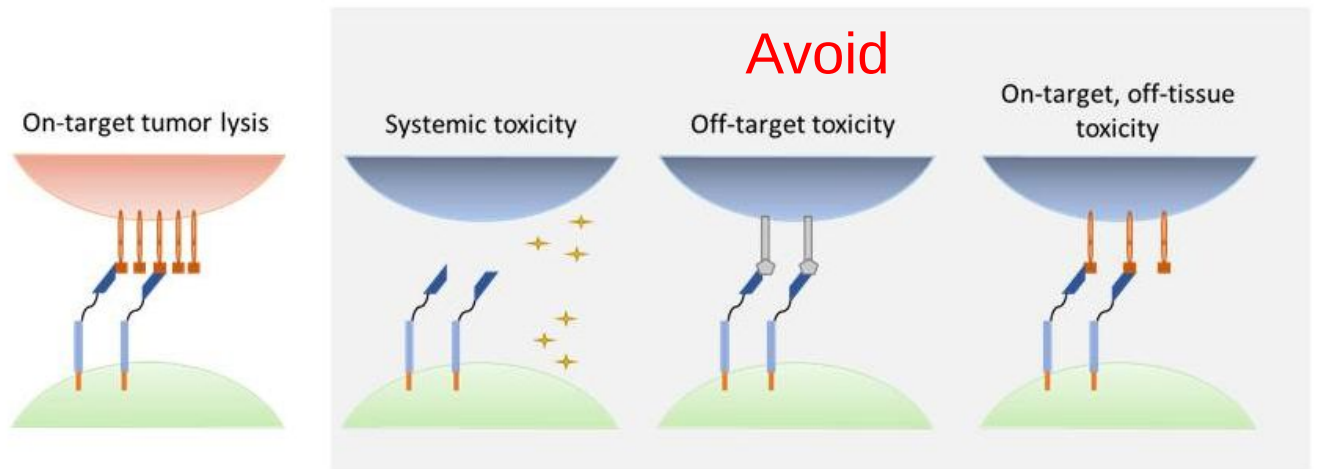
TIME IN CULTURE

1. New CAR designs for patients with hematologic malignancies and solid tumors
2. Combining CAR with cytokines
 - IL-12
 - IL-15
- TCR-based T-cell therapy
- NK-cell immunotherapy



Established Disease Model





How do we achieve on-target anti-cancer activity?

Strategies to widen therapeutic index to Target Solid Tumors

Target CAR to tumor site

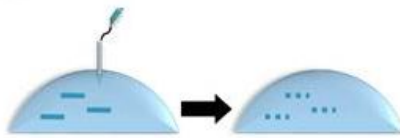


Homing to tumor sites

Limit CAR Expression



Drug-induced suicide



CAR expression by mRNA

Limit CAR Activation



Signal splitting



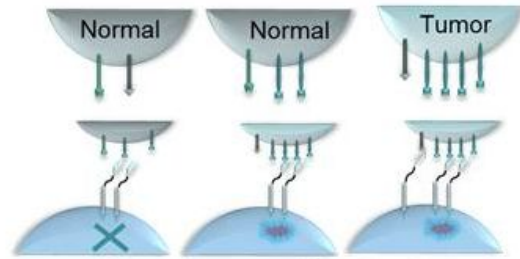
Inhibitory CAR to normal tissue



Recognition of combinatorial epitope

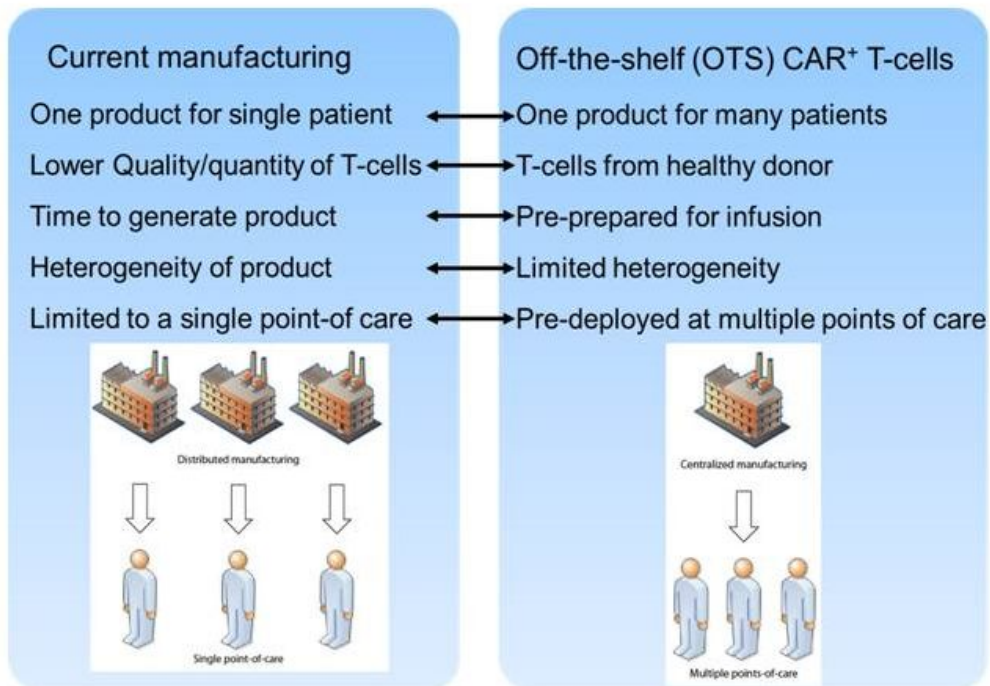


Inducible CAR Expression

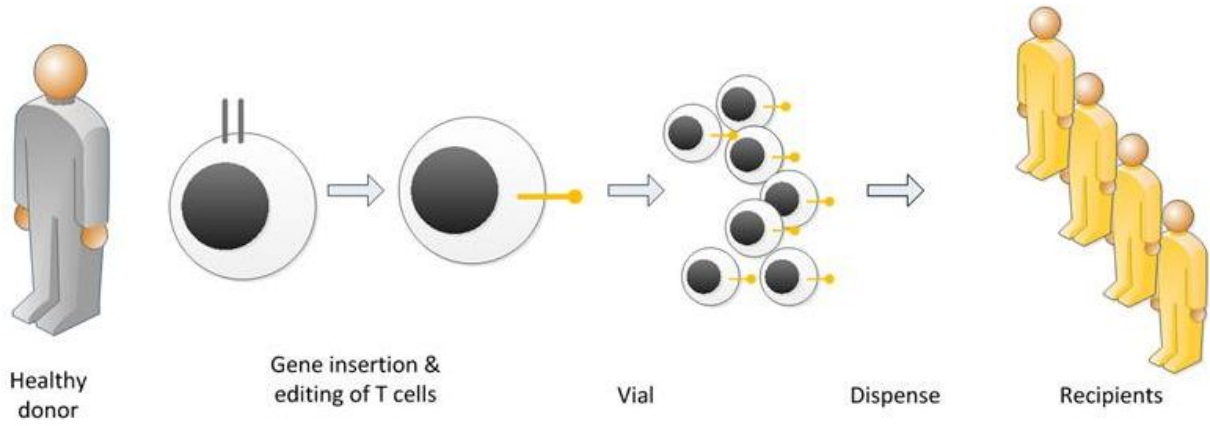


Dependent on antigen density

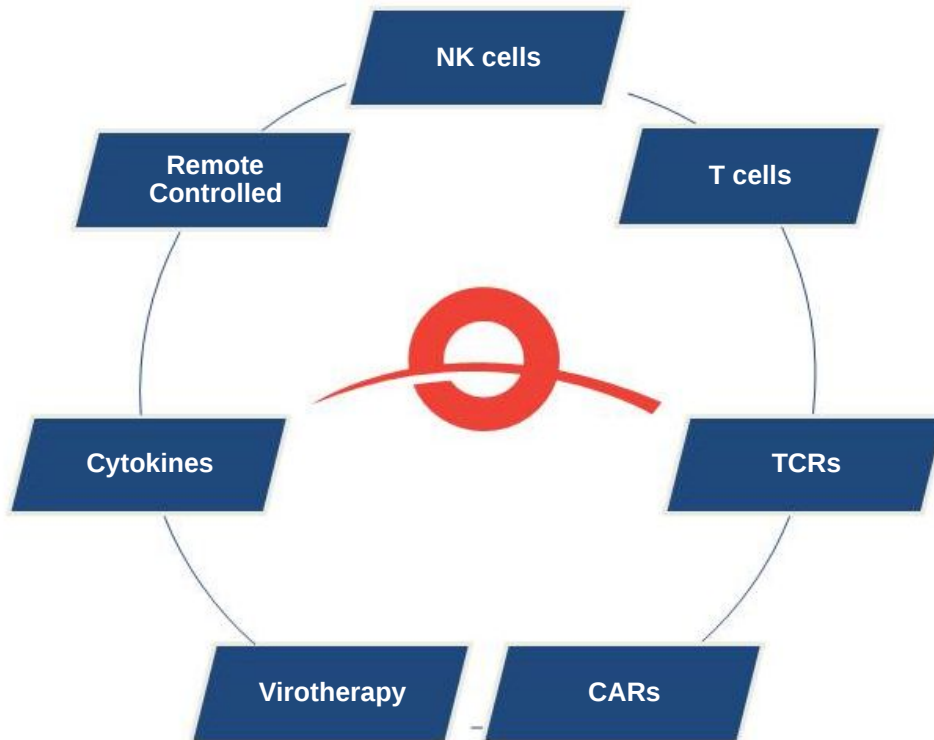


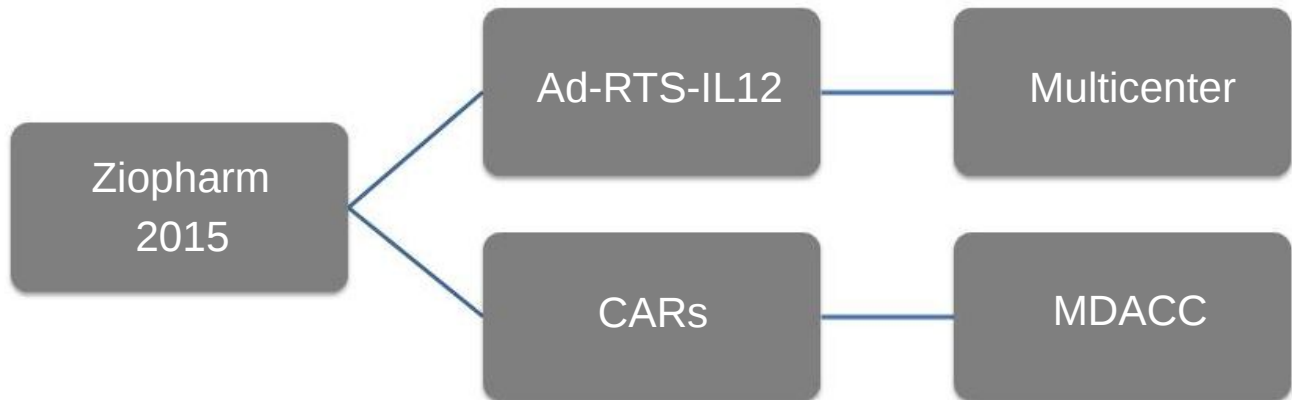


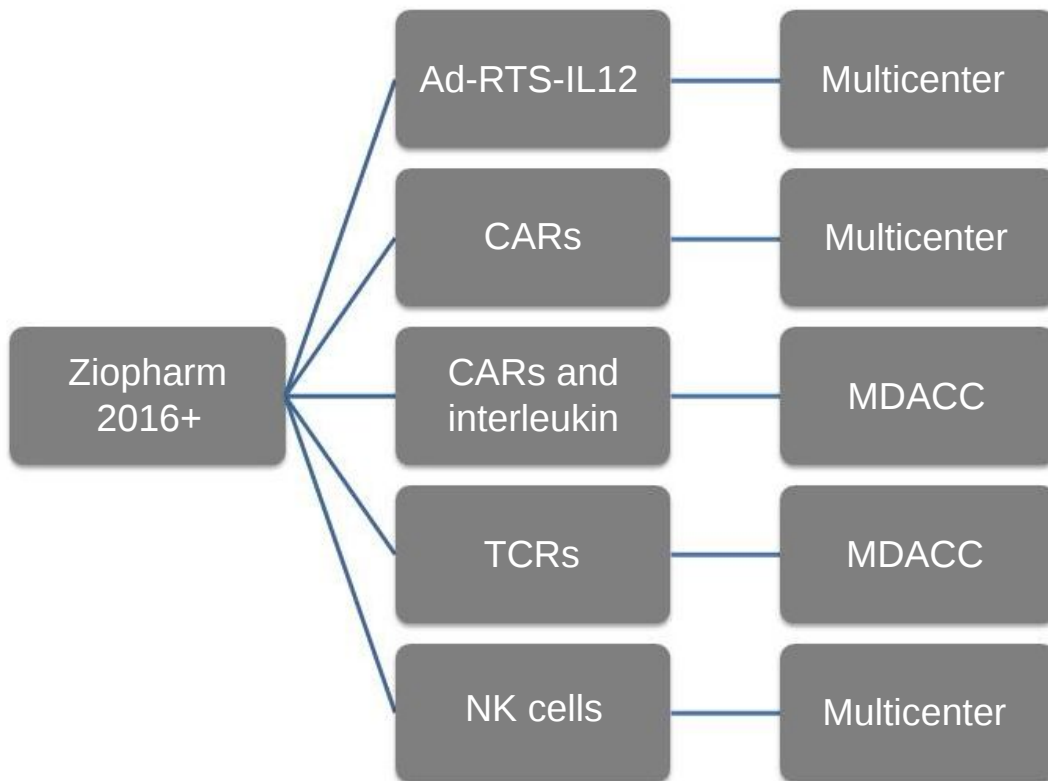
Elimination of Endogenous TCR



Fitting Together the Pieces of the Puzzle







Abstracts

- **European Hematology Association (June 2015)**
 - Donor-derived, CD19-directed, CAR-modified T cells infused after allogeneic hematopoietic stem-cell transplantation as pre-emptive donor lymphocyte infusion in patients with CD19+ malignances
- **CRI-CIMT-EATI-AACR (September 2015)**
 - Demonstration of systemic antitumor immunity via intratumoral regulated expression of IL-12 in advanced breast cancer and melanoma patients
 - Demonstration of systemic antitumor immunity via intratumoral regulated expression of IL-12 as a gene therapy approach to treatment of cancer
 - Bio-engineered Dectin-1 CAR+ T cells to control invasive fungal infection
 - Ex-vivo generation of clinical grade T cells by using activating and propagating feeder cells to cross-link T cell receptor
 - Designing CARs for personalized immunotherapy: rapid assembly of CARs from principal components using “EZ-CAR” platform
 - Transcriptional and epigenetic signatures of ex vivo propagated three distinct TCR V α 1, TCR V α 2 and TCR V α 3 cell subtypes with broad specificity for malignancies

Papers

- Sleeping Beauty Transposition of Chimeric Antigen Receptors Targeting Receptor Tyrosine Kinase-Like Orphan Receptor-1 (ROR1) into Diverse Memory T-Cell Populations. PLoS One. 2015 Jun 1;10(6):e0128151 PMID: 26030772
- Genetic Engineering of T Cells to Target HERV-K, an Ancient Retrovirus on Melanoma. Clin Cancer Res. 2015 Mar 31. [Epub ahead of print] PMID: 25829402
- Moving from tinkering in the garage to assembly line production: the manufacture of genetically modified T cells expressing chimeric antigen receptors (CARs) comes on line. Cancer Gene Ther. 2015 Mar;22(2):64-6. PMID: 25675874
- Manufacture of T cells using the Sleeping Beauty system to enforce expression of a CD19-specific chimeric antigen receptor. Cancer Gene Ther. 2015 Mar;22(2):95-100. PMID: 25591810
- Tuning Sensitivity of CAR to EGFR Density Limits Recognition of Normal Tissue While Maintaining Potent Antitumor Activity. Cancer Res. 2015 Sep 1;75(17):3505-18. PMID: 26330164

...With More to Come for 2015

CRI-CIMT-EATI-AACR Immunotherapy Conference September 16-19, NY, NY

SITC November 4-8, National Harbor, MD

SNO November 19-23, San Antonio, TX

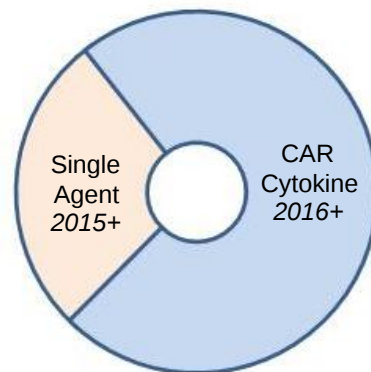
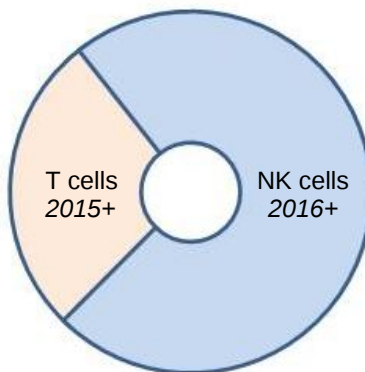
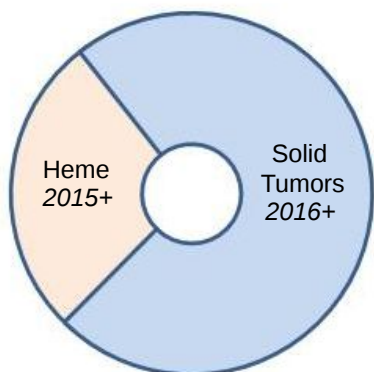
CAR-T Summit November 12-13, Boston, MA

ASH December 5-8, Orlando FL

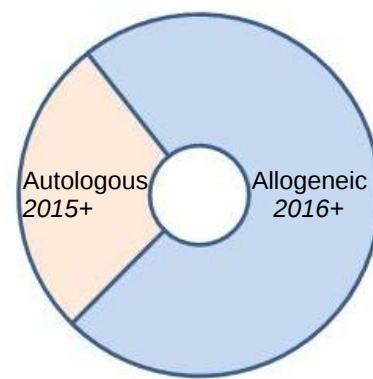
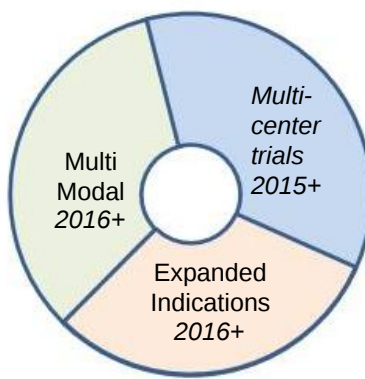
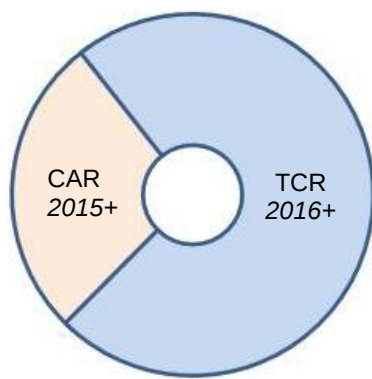
SABCS December 9-12, San Antonio TX

Additional papers

Adoptive Cell Therapy



Virotherapy



Wells Fargo Healthcare Conference

SEPTEMBER 2015



ZIOPHARM Oncology