Ziopharm ONCOLOGY

A New Day for Ziopharm Oncology

October 9, 2018

Forward-Looking Statements

This presentation contains certain forward-looking information about Ziopharm Oncology, Inc. that is intended to be covered by the safe harbor for "forward-looking statements" provided by the Private Securities Litigation Reform Act of 1995, as amended. Forward-looking statements are statements that are not historical facts, and in some cases can be identified by terms such as "may," "will," "could," "expects," "plans," "anticipates," and "believes." These statements include, but are not limited to, statements regarding the expected benefits of the strategic transaction including entry into an exclusive license agreement with Precigen, Inc., the progress, timing and results of preclinical and clinical trials involving the Company's product candidates including the development of Sleeping Beauty-modified TCRs and CD19-specific CAR-T therapies, the expected timing for the Company's response to the U.S. Food and Drug Administration (FDA) in regards to its investigational new drug (IND) application for its third-generation Phase 1 trial to evaluate CD19-specific CAR-T therapies under technology referred to as point-of-care, the expected timing for the filings or amendments of IND applications for its other product 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-hIL-12, TCR and NK cell-based therapies, or any of our other therapeutic candidates will advance further in the preclinical or clinical trials process and whether and when, if at all, they will receive final approval from the FDA or equivalent foreign regulatory agencies and for which indications; whether chimeric antigen receptor T cell (CAR^+ T) approaches, Ad-RTS-hIL-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, 2017, and subsequent reports that the Company may file with the Securities and Exchange Commission. 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.

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Agenda (beginning 8 am ET October 9, 2018)

- On the Call
  - Laurence Cooper, MD, PhD, CEO
  - David Mauney, MD, EVP, CBO and Interim COO
  - David Connolly, VP, Corporate Communications and IR
  - Rob Hadfield, General Counsel
- Introduction / Overview
  - Laurence Cooper
- Terms of New Agreement
  - David Mauney
- Clinical Programs Update
  - Laurence Cooper
- Q&A

The New Ziopharm

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The “New Ziopharm” with Full Autonomy

- Immunotherapy pipeline focused on solid tumors
- New, simplified licensing agreement with Intrexon/Precigen
- Preferred stock issued to Intrexon fully retired
- Revised Board of Directors
- Strategic flexibility for corporate development, sublicensing
- Aligned financial incentives and resources

Refined Focus on Controlled IL-12 *Sleeping Beauty* for All TCR Targets and Two CAR Targets

Exclusive worldwide rights

Platform #1
Controlled IL-12

Ad-RTS-hIL-12 plus veledimex for brain cancer, other solid tumors

- Monotherapy
- Combination with immune checkpoint inhibitors
- Optionality on next-gen delivery

Platform #2
Sleeping Beauty

Sleeping Beauty

- **TCRs targeting neoantigens for solid tumors**
- CD19-specific CAR and second unnamed CAR target

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The New Ziopharm
Terms of New Agreement

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Historic Overview of Ziopharm and Intrexon Relationship

- January 2011 – Intrexon and Ziopharm enter into Exclusive Channel Collaboration (ECC)* agreement
  - Established 50-50 share of net profits; Ziopharm is Intrexon's exclusive oncology partner; Limited sub-licensing rights
- January 2015 – Intrexon, Ziopharm and MD Anderson announce Exclusive Licensing Agreement for CAR-T, TCR, NK Cell programs specifically for development of nonviral adoptive cell therapies
- March 2015 – Intrexon-Ziopharm announce global CAR-T collaboration with Merck KGaA
- June 2016 – Intrexon and Ziopharm renegotiate ECC
  - 80-20 Ziopharm-Intrexon sales royalties (changed from 50-50); 50-50 on sub-licensing agreement remains; Intrexon received $120M in preferred stock plus 12% annually
- January 2017 – Intrexon and Ziopharm announce Collaborative Research and Development Agreement (CRADA) with National Cancer Institute (NCI) – *Sleeping Beauty*-modified TCRs for solid tumors
- March 2017 – Intrexon announces restructuring, formation of Precigen for all health care assets
- October 2018 – ECC terminated, replaced with new licensing agreement

* Intrexon transferred rights to Precigen when it was launched in 2017
** Now, with the exception of CD19

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New License for Exclusive Rights to Controlled IL-12, *Sleeping Beauty* TCRs and *Sleeping Beauty* CD19-CAR

Controlled IL-12 Platform

- **Exclusive rights** to Ad-RTS-hIL-12 plus veledimex
- Ziopharm **gains optionality for next-generation technologies** for RTS-IL-12

Sleeping Beauty Platform

- **Exclusive rights** to T cells genetically modified with *Sleeping Beauty* to express TCRs
- **Exclusive rights** to *Sleeping Beauty* CD19-specific CAR-T and rights to second unnamed CAR target

Ziopharm gains broad sub-licensing rights providing flexibility to pursue partnerships with lower sub-licensing fees to Precigen, than previous ECC agreement

Non-exclusive rights to pursue additional programs

Milestone payments upon commencement of later stage clinical and regulatory milestones

Tiered royalty payments based on net sales

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Additional Terms of 2018 Licensing Agreement with Precigen

- Preferred stock valued at approximately $156.9 million* retired
- R.J. Kirk resigns from Ziopharm Board of Directors
- Ziopharm retains collaboration with MD Anderson Cancer Center and the approximately $31.7 million** available from prepayments
- Ziopharm will assume full control of CRADA with NCI for TCRs
- CAR-T development by Precigen remains subject to Merck KGaA
  - Precigen retains worldwide rights to CD33 and all other CAR targets, excluding Ziopharm's CD19 and 2nd unnamed CAR target with *Sleeping Beauty* platform
  - Ziopharm receives capped royalties on Precigen CAR products

* As of Sept. 30, 2018
** As of June 30, 2018

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The New Ziopharm
Clinical Programs Update

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Focused on Controlled IL-12, *Sleeping Beauty*-TCRs to Target Solid Tumors plus Two CAR Targets

Controlled IL-12: Turning cold tumors hot by activating patient's immune response

	Indication	Preclinical	Phase 1	Phase 2	Phase 3
Ad-RTS-hIL-12 + veledimex	rGBM	Monotherapy (expansion)			
	rGBM	In combination w/ OPDIVO®			
	Pediatric brain tumor	Monotherapy			
	New indication	Initiated in 1H2019			

Sleeping Beauty: Non-viral genetic modification of TCR-T cells and CAR-T cells to infuse an immune response

TCRs targeting neoantigens	Multiple solid tumors	IND 4Q2018	NIH NATIONAL CANCER INSTITUTE
CAR-T	Leukemia/lymphoma	CD19 2nd Gen shortened manufacture	THE UNIVERSITY OF TEXAS MD Anderson Cancer Center Making Cancer History®
	Leukemia/lymphoma	3rd Gen w mbIL15 (P-O-C) IND in 2H2019	
	Unnamed target*		

P-O-C = "Point-of-Care" for very rapid manufacturing
* Ziopharm holds rights to second, unnamed CAR target

Initiated Planned

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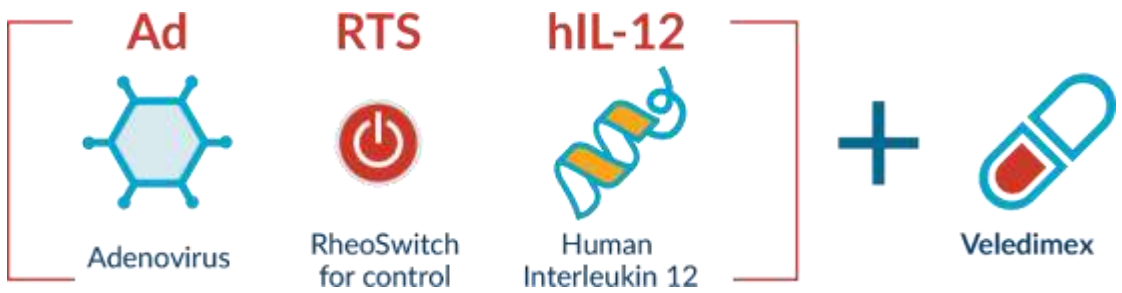
Controlled IL-12 Platform for Brain Tumors

- Monotherapy of Ad-RTS-hIL-12 + veledimex has shown improved survival benefit of 12.7 months median overall survival (mOS) in 15 patients*; Low-dose steroid use improved survival
  - Adult: Phase 1 expansion cohort with 20 mg of veledimex underway to expand clinical data
    - Seven patients treated to date
  - Pediatrics: Wide open for drug development
    - First pediatric patient survival past 10-month mark reported as of August 2018; Second patient treated in September
- Combination trial with OPDIVO (nivolumab): Biopsy, biomarker data supportive of combination
  - Actively enrolling; three patients treated to date; up to 18 planned



- Administered intratumorally at resection
- Oral veledimex modulates and turns on/off local expression of IL-12

** mOS of 12.7 months at 12.9 months follow-up compares favorably to historical controls of 5 to 8 months mOS. Was presented in "A Phase 1 study of Ad-RTS-hIL-12 + veledimex in adult recurrent glioblastoma," at 2017 Society of Neuro-Oncology by Antonio Chiocca, M.D., Ph.D., Brigham and Women's / Dana-Farber Cancer Center*

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Market Opportunity for IL-12 in rGBM – Three Paths to Commercialization to be Explored

Monotherapy

- Adult rGBM
- Pediatric gliomas

Combination with anti-PD-1

- Adult rGBM

~70,000
new adult cases world wide each year

12,390[1]
new cases in the U.S. each year

14,576[2]
new cases in Europe each year

Recurrence = 90%
US – 11,151[1]
EU – 13,118[2]

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

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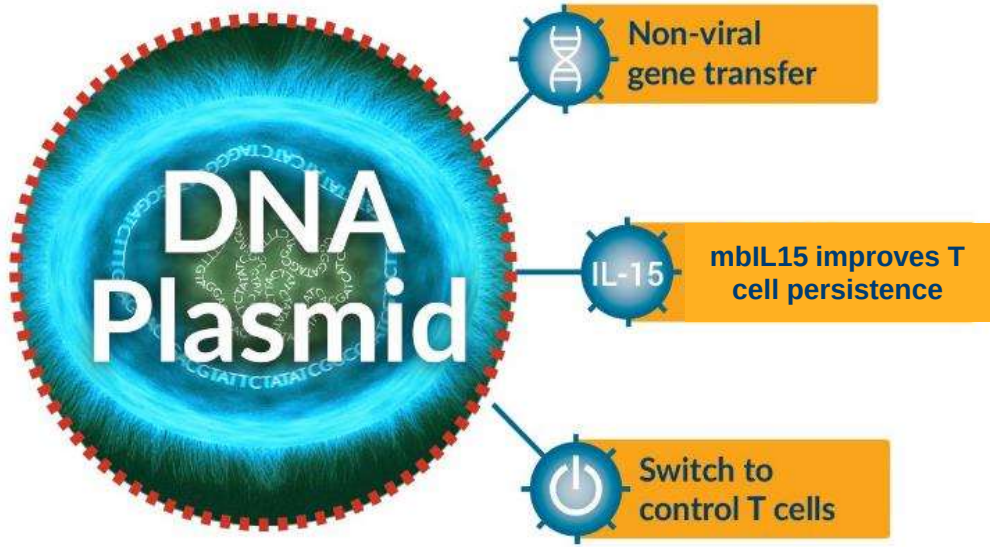
Status of Investigational New Drug Application for Third-Generation Trial to Evaluate CD19-specific CAR-T Therapy

- Per disclosures in June and August 2018, FDA requested additional pre-clinical process development, placed clinical hold on IND
- Guidance update on “point-of-care” (“P-O-C”):
  - FDA mandated a 70% cell viability threshold
  - Ziopharm and MD Anderson executing on cell viability improvements
  - Anticipate filing amended IND in 2H2019
- Second-generation *Sleeping Beauty* trial at MD Anderson Cancer Center ongoing
  - Dosing, CAR design, reduced manufacturing and release testing time
  - Encouraging clinical data

Genetic modification of T cells with *Sleeping Beauty* system to produce T cells in < 2 days



Potential advantage over off-the-shelf

- Third-party OTS cells require lymphodepletion, but mbIL15 may enable avoidance

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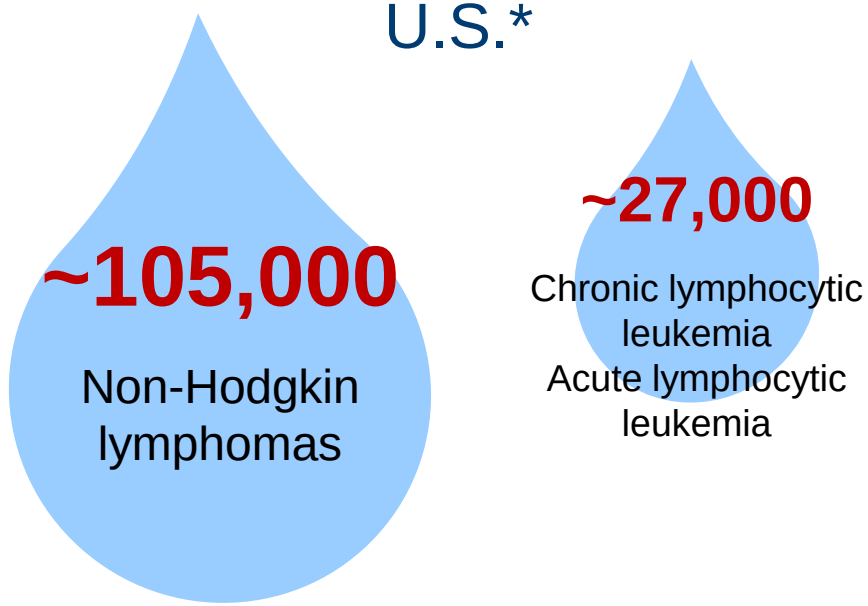
Market Opportunity for CD19-Specific CAR-T

"Point-of-care"

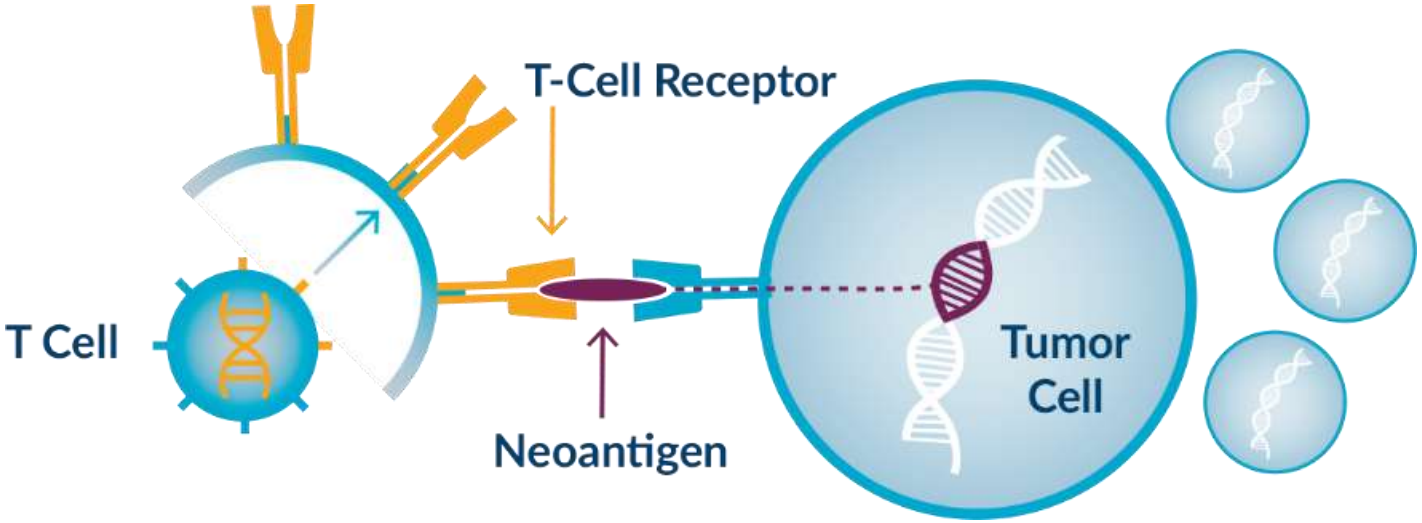
- Reduced cost and complexity with < 2-day manufacturing
- Potential to avoid lymphodepletion with SB system and mbIL15

Estimated new cases of lymphomas and leukemias in U.S.*



- *Updated Data on Blood Cancers, 2018,* Leukemia & Lymphoma Society
- CA Cancer J Clin. 2016 Sep 12 [Epub ahead of print]

Sleeping Beauty Provides Manufacturing Solution for Autologous Personalized TCR-T Therapies Targeting Neoantigens for Each Patient



Neoantigens → the key to targeting solid tumors

Intracellular antigens that are unique to each patient's cancer

TCRs	T cells	TCR+ T cells	*Sleeping Beauty*
• Neoantigens can only be recognized by TCRs (& not CARs)	• Infuse autologous T cells as cannot be targeted by off-the-shelf T cells	• Eliminate bulky solid tumors with infusions of genetically modified T cells	• The gene therapy platform to express multiple TCRs in T cells

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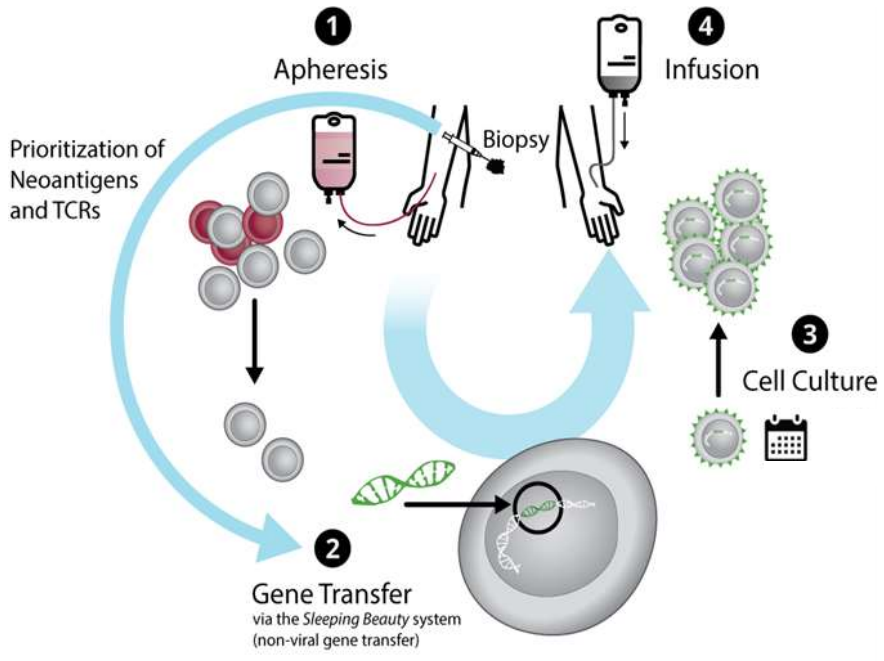
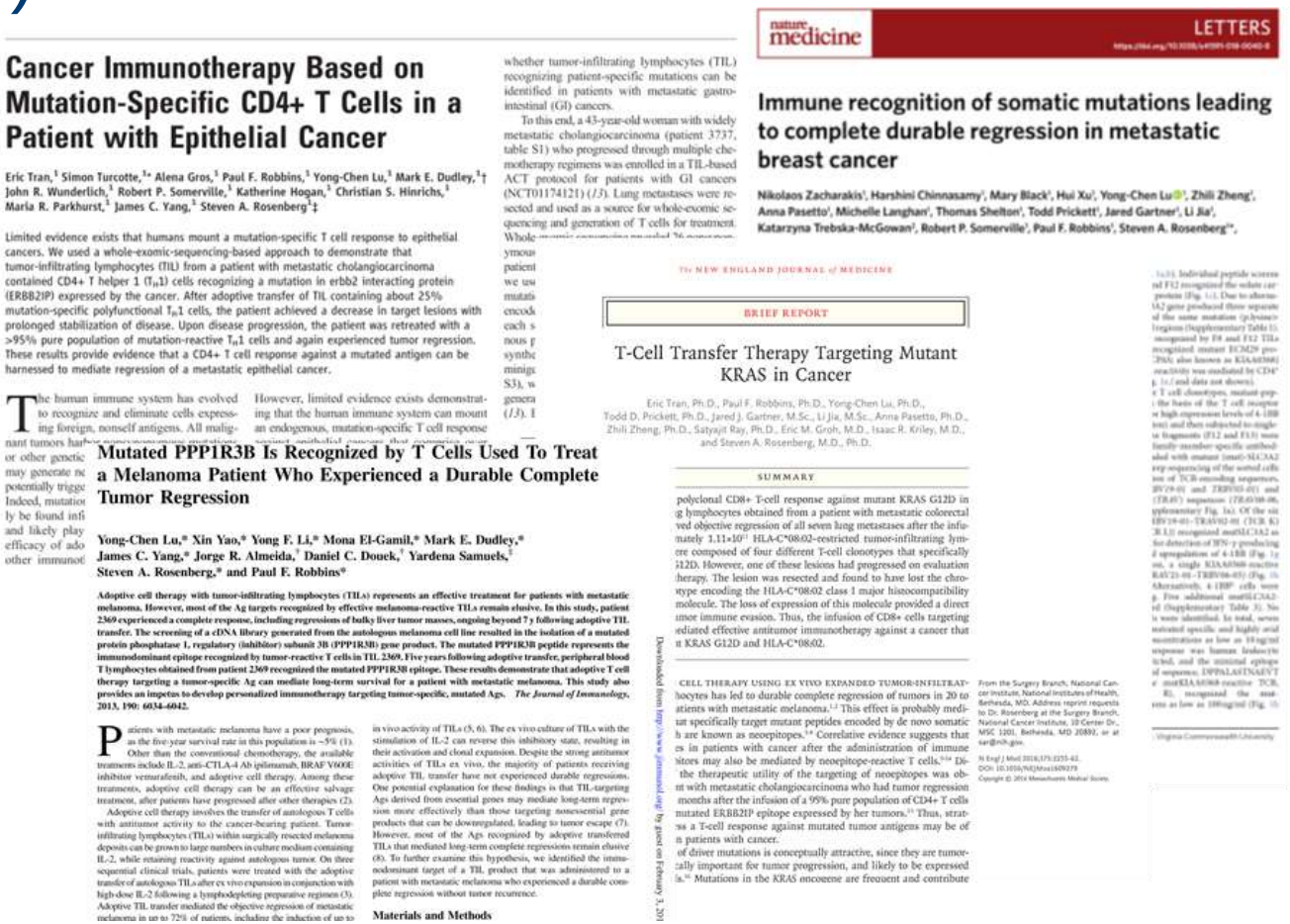
T cells Targeting Neoantigens has Demonstrated Clinical Success in Solid Tumors (History on our Side)

Ziopharm provides technology to commercialize T-cell targeting of TCRs

Four steps to success





Cancer Immunotherapy Based on Mutation-Specific CD4+ T Cells in a Patient with Epithelial Cancer

Eric Tran, Simon Turcotte, Alena Gros, Paul F. Robbins, Yong-Chen Lu, Mark E. Dudley, John R. Wunderlich, Robert P. Somerville, Katherine Hogan, Christian S. Hinrichs, Maria R. Parkhurst, James C. Yang, Steven A. Rosenberg

Limited evidence exists that humans mount a mutation-specific T cell response to epithelial cancers. We used a whole-exomic-sequencing-based approach to demonstrate that tumor-infiltrating lymphocytes (TIL) from a patient with metastatic cholangiocarcinoma contained CD4+ T helper 1 (T_H1) cells recognizing a mutation in erbb2 interacting protein (ERBB2IP) expressed by the cancer. After adoptive transfer of TIL containing about 25% mutation-specific polyfunctional T_H1 cells, the patient achieved a decrease in target lesions with prolonged stabilization of disease. Upon disease progression, the patient was retreated with a >95% pure population of mutation-reactive T_H1 cells and again experienced tumor regression. These results provide evidence that a CD4+ T cell response against a mutated antigen can be harnessed to mediate regression of a metastatic epithelial cancer.

Mutated PPP1R3B Is Recognized by T Cells Used To Treat a Melanoma Patient Who Experienced a Durable Complete Tumor Regression

Yong-Chen Lu, Xin Yao, Yong F. Li, Mona El-Gamil, Mark E. Dudley, James C. Yang, Jorge R. Almeida, Daniel C. Douek, Yardena Samuels, Steven A. Rosenberg, and Paul F. Robbins

Adoptive cell therapy with tumor-infiltrating lymphocytes (TILs) represents an effective treatment for patients with metastatic melanoma. However, most of the Ag targets recognized by effective melanoma-reactive TILs remain elusive. In this study, patient 2369 experienced a complete response, including regressions of bulky liver tumor masses, ongoing beyond 7 y following adoptive TIL transfer. The screening of a cDNA library generated from the autologous melanoma cell line resulted in the isolation of a mutated protein phosphatase 1, regulatory (inhibitor) subunit 3B (PPP1R3B) gene product. The mutated PPP1R3B peptide represents the immunodominant epitope recognized by tumor-reactive T cells in TIL 2369. Five years following adoptive transfer, peripheral blood T lymphocytes obtained from patient 2369 recognized the mutated PPP1R3B epitope. These results demonstrate that adoptive T cell therapy targeting a tumor-specific Ag can mediate long-term survival for a patient with metastatic melanoma. This study also provides an impetus to develop personalized immunotherapy targeting tumor-specific, mutated Ags. *The Journal of Immunology*, 2013, 190: 6034-6042.

Immune recognition of somatic mutations leading to complete durable regression in metastatic breast cancer

Nikolaos Zacharakis, Harshini Chinnasamy, Mary Black, Hui Xu, Yong-Chen Lu, Zhili Zheng, Anna Pasetto, Michelle Langhan, Thomas Shelton, Todd Prickett, Jared Gartner, Li Jia, Katarzyna Trebska-McGowan, Robert P. Somerville, Paul F. Robbins, Steven A. Rosenberg

T-Cell Transfer Therapy Targeting Mutant KRAS in Cancer

Eric Tran, Ph.D., Paul F. Robbins, Ph.D., Yong-Chen Lu, Ph.D., Todd D. Prickett, Ph.D., Jared J. Gartner, M.Sc., Li Jia, M.Sc., Anna Pasetto, Ph.D., Zhili Zheng, Ph.D., Satyajit Ray, Ph.D., Eric M. Groh, M.D., Isaac R. Kriley, M.D., and Steven A. Rosenberg, M.D., Ph.D.

Clockwise from top left:

1. Science. 2014 May 9;344(6184):641-5
2. Nat Med. 2018 Jun;24(6):724-730
3. N Engl J Med. 2016, Dec 8;375(23):2255-2262
4. J Immunol. 2013 Jun 15;190(12):6034-42

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NCI Advancing *Sleeping Beauty* to Target Neoantigens in Solid Tumors with TCR-expressing T cells

Preclinical Data

original article

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

CRADA

ZIOPHARM and Intrexon Announce CRADA with NCI

NIH NATIONAL CANCER INSTITUTE

Clinical Protocol

Completed

Validation

Complete 4Q 2018

Patient Data in 2019

- **IND for TCR-T to be submitted in 4Q 2018** (unaffected by CAR program)
- All four steps being tested at NCI
- Multiple solid tumor types can benefit from this approach

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Ziopharm Will be First to Use Non-Viral Approach to Manufacture TCR-T

Neoantigens

Likely, best chance to target solid tumors

TCR-T

Undertaken using the cutting edge science at NCI

Sleeping Beauty

Superior technology to commercialize TCR-T

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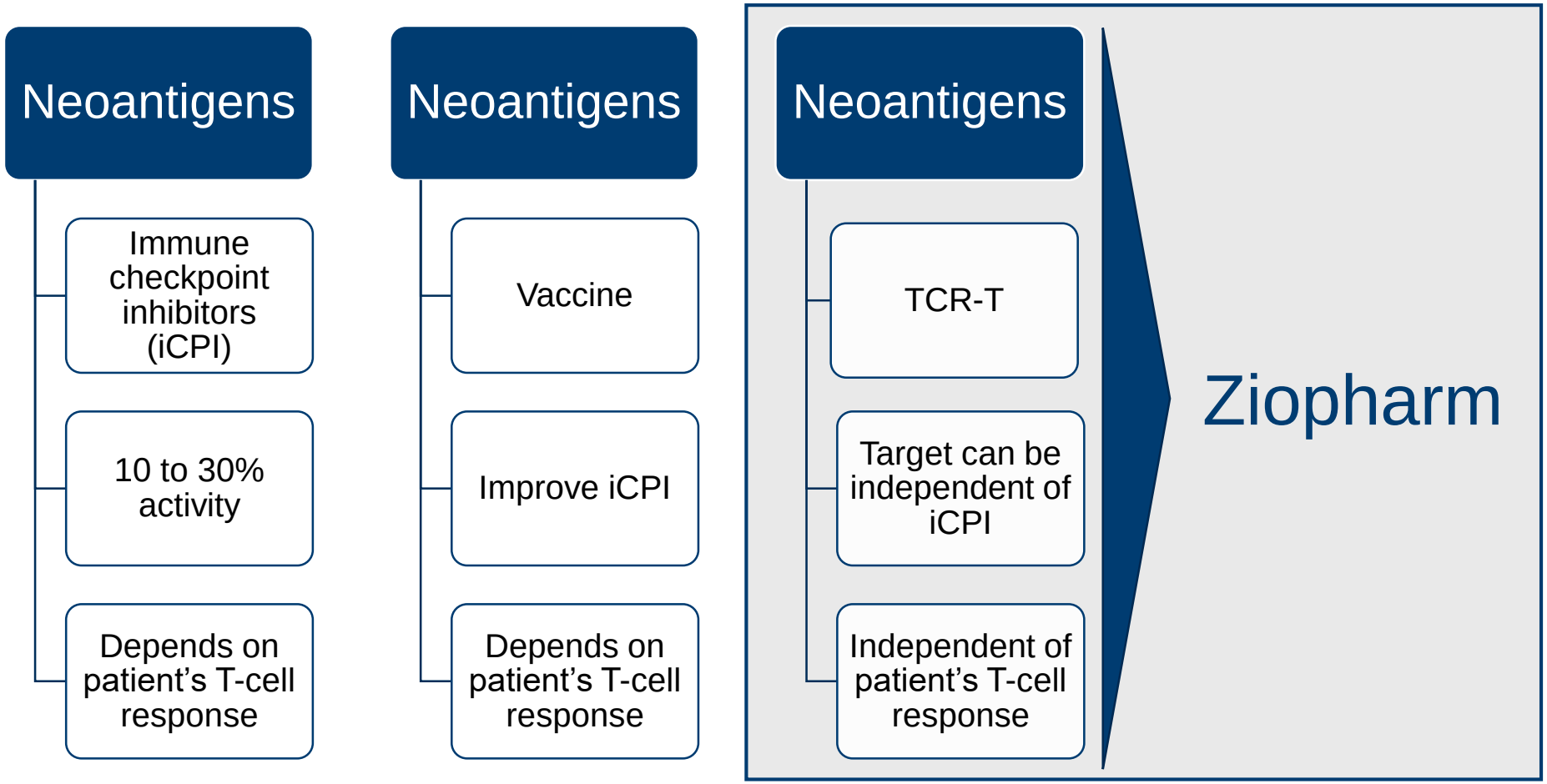
Market Opportunity for TCR-T in Solid Tumors

Prospect of TCR-T dwarfs the opportunity for CAR-T



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New Day

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Key Investment Highlights: Expected Milestones and Value Inflection Points

New Ziopharm on Day 1

- ✓ Large platform opportunities currently in clinic and more in 2019
- ✓ Strategic autonomy
- ✓ Preferred stock retired
- ✓ Three new board members with 75+ years experience in life sciences

- **Fourth Quarter 2018**
  - NCI to submit IND for TCR
  - Updated IL-12 data at Society of Neuro-Oncology
  - Additional board members
- **First Half 2019**
  - Complete enrollment in IL-12 monotherapy expansion and in IL-12 combo trial with nivolumab
  - Initiate new phase 1 trial for IL-12 and immune checkpoint inhibitor
  - Begin enrollment in TCR trial with SB-modified T cells
  - Data updates across all programs
  - Investor & Analyst Day
- **2H19**
  - Resubmit third-generation (“P-O-C”) CD19 CAR T IND

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