



Ziopharm ONCOLOGY

37th Annual J.P. Morgan
Healthcare Conference
January 2019

Forward Looking Statement

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Ziopharm Transformed

4Q2018 Accomplishments

- Redefined license agreement with Intrexon and Precigen in October 2018
- Eliminated \$157M of preferred stock issued to Intrexon
- Raised \$50M from existing investors
- No debt, funded to achieve milestones into 2Q2020
- Regeneron collaboration for Controlled IL-12
- Formation of Eden BioCell to expand CD19 CAR-T business to Greater China

2019 and beyond

- **Executional excellence**
- **All programs in clinic in 2019**
 - 5 clinical trials
- **In-house capabilities: Expanding laboratory and manufacturing in Houston**

Ziopharm's Three Pillars

To deliver end-to-end and scalable TCR-T cell therapy to treat solid tumors

To solve the current commercial limitations of cost and scalability of approved CAR-T

To harness the power of IL-12 as a drug to address difficult-to-treat solid tumors with precision

Strong Partnerships in Place

NATIONAL
CANCER
INSTITUTE

& Steven Rosenberg

Infusing TCR-T cells
targeting solid tumor
neoantigens with
Sleeping Beauty
technology

MDAnderson
~~Cancer~~ Center®

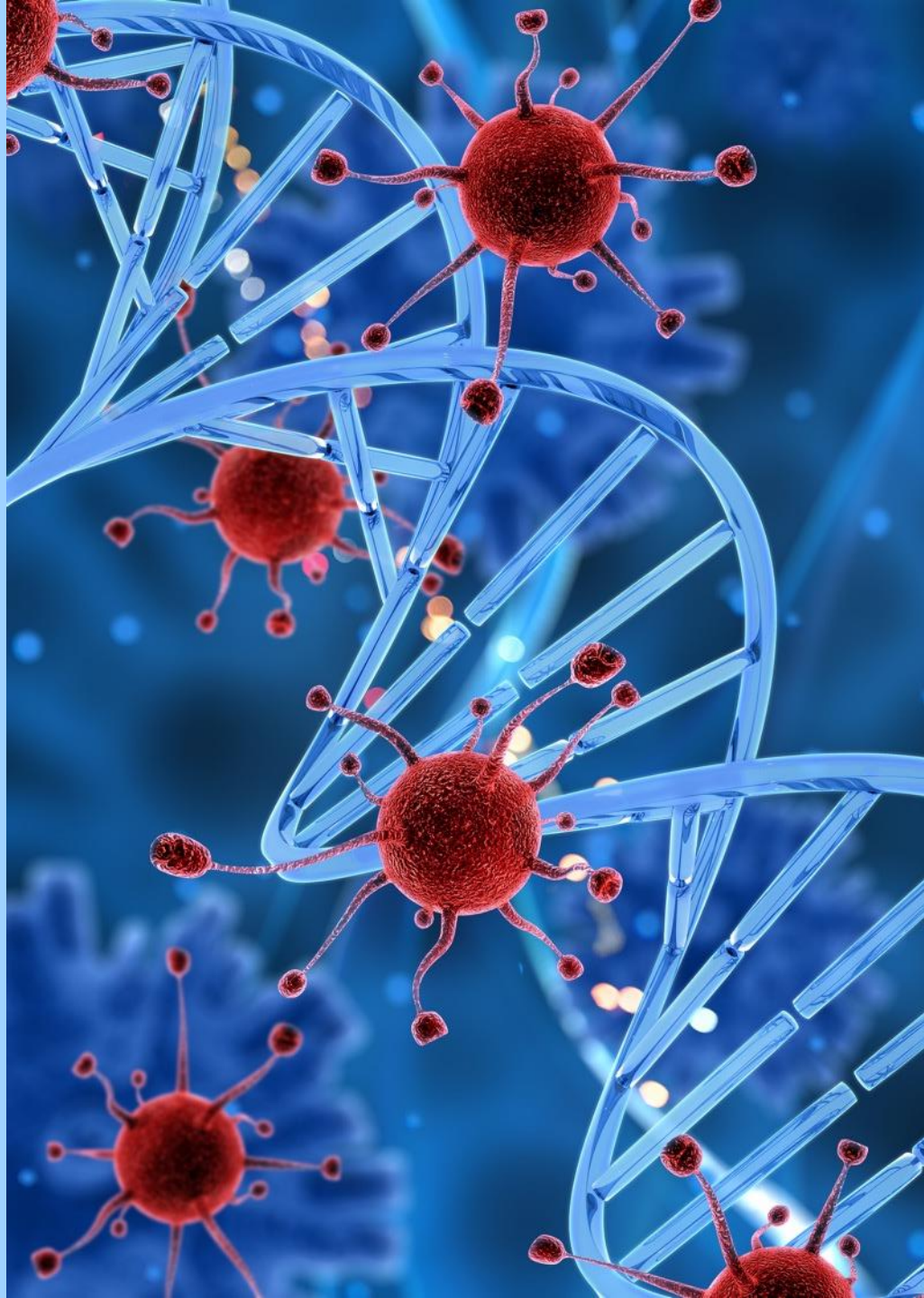
Deploying ***Sleeping
Beauty*** CD19-
specific CAR-T for
very rapid
manufacturing

Eden BioCell

Expanding ***Sleeping
Beauty*** CD19-
specific CAR-T for
very rapid
manufacturing into
Greater China

REGENERON

**Advancing
Controlled IL-12**
in combination with
Libtayo for recurrent
GBM



Sleeping Beauty TCR-T Program

T cells genetically modified to express neoantigen-specific TCRs represent the best opportunity for targeting metastatic solid tumors

- **The best TCRs are unique for each patient**
- **T cells with multiple specificities (multiple TCRs) are required to prevent relapse**

Sleeping Beauty Scalability

Solves the manufacturing challenge of targeting neoantigens

Problem: **1 patient** may need treatment with **6 TCRs** requires 6 separate T-cell gene transfer events



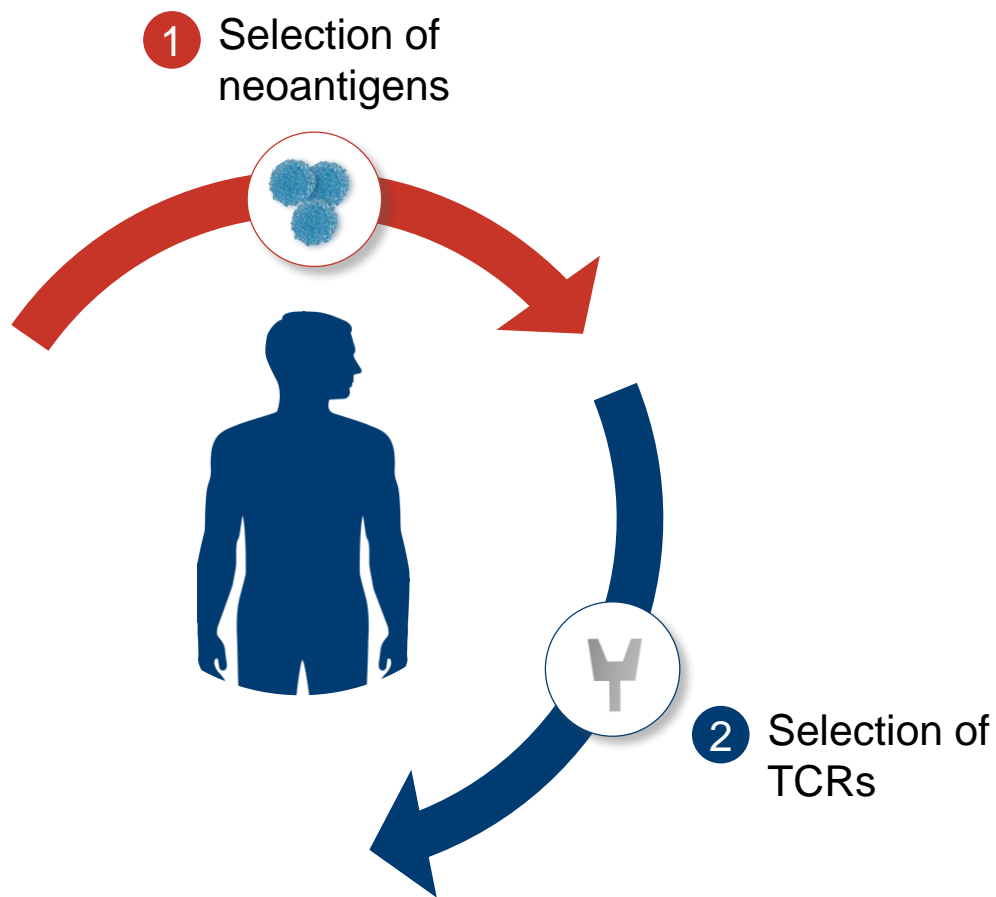
~\$1.5M to generate six TCRs from lentivirus for each patient*

Bigger Problem: **10 patients** with **60 TCRs** requires 60 separate gene transfer events, **60 different viruses**

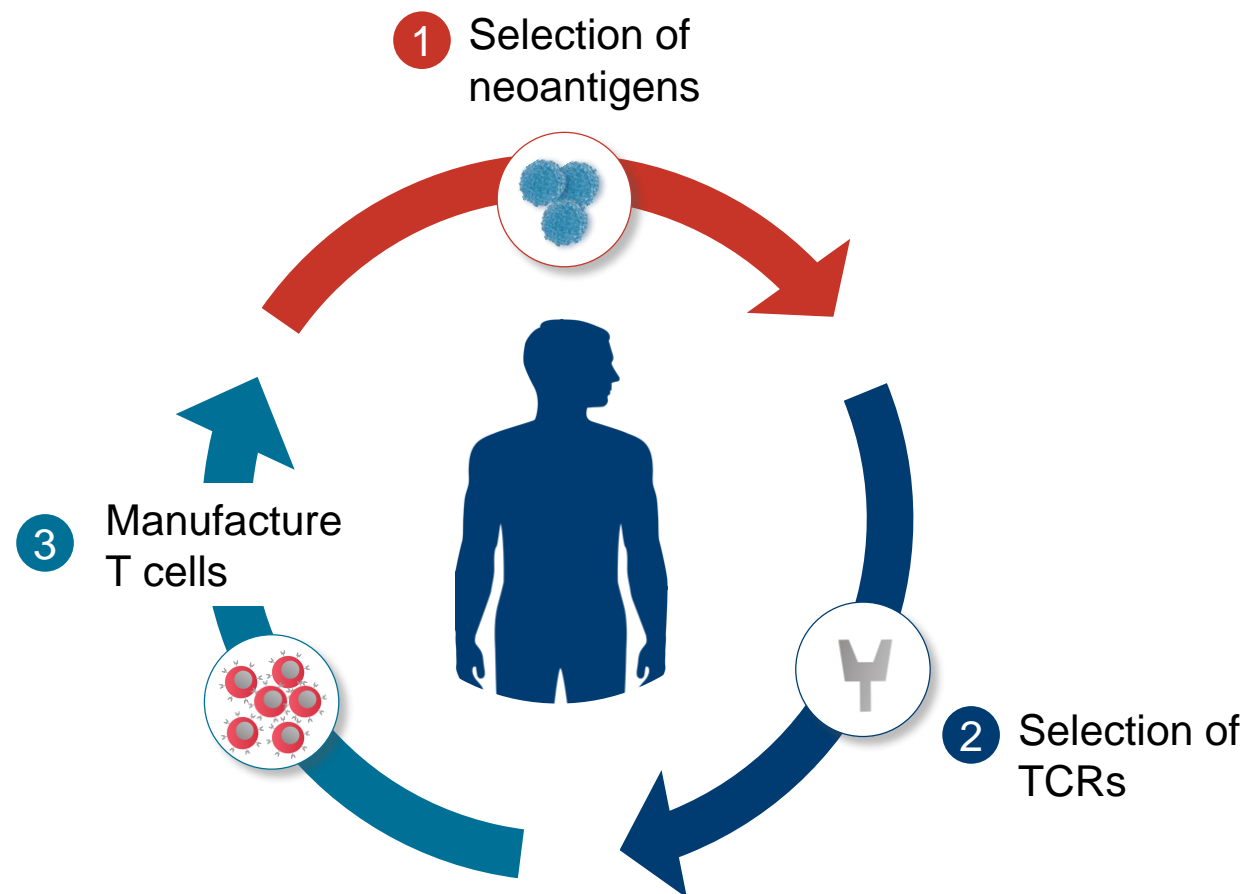
Non-viral solution is scalable:

- To express **multiple unique TCRs** to target multiple neoantigens
- To produce Multiple TCRs **meet demands of tumor target diversity** within one patient
- To reduce costs and avoid virus with **manufacturing** using **DNA plasmids**

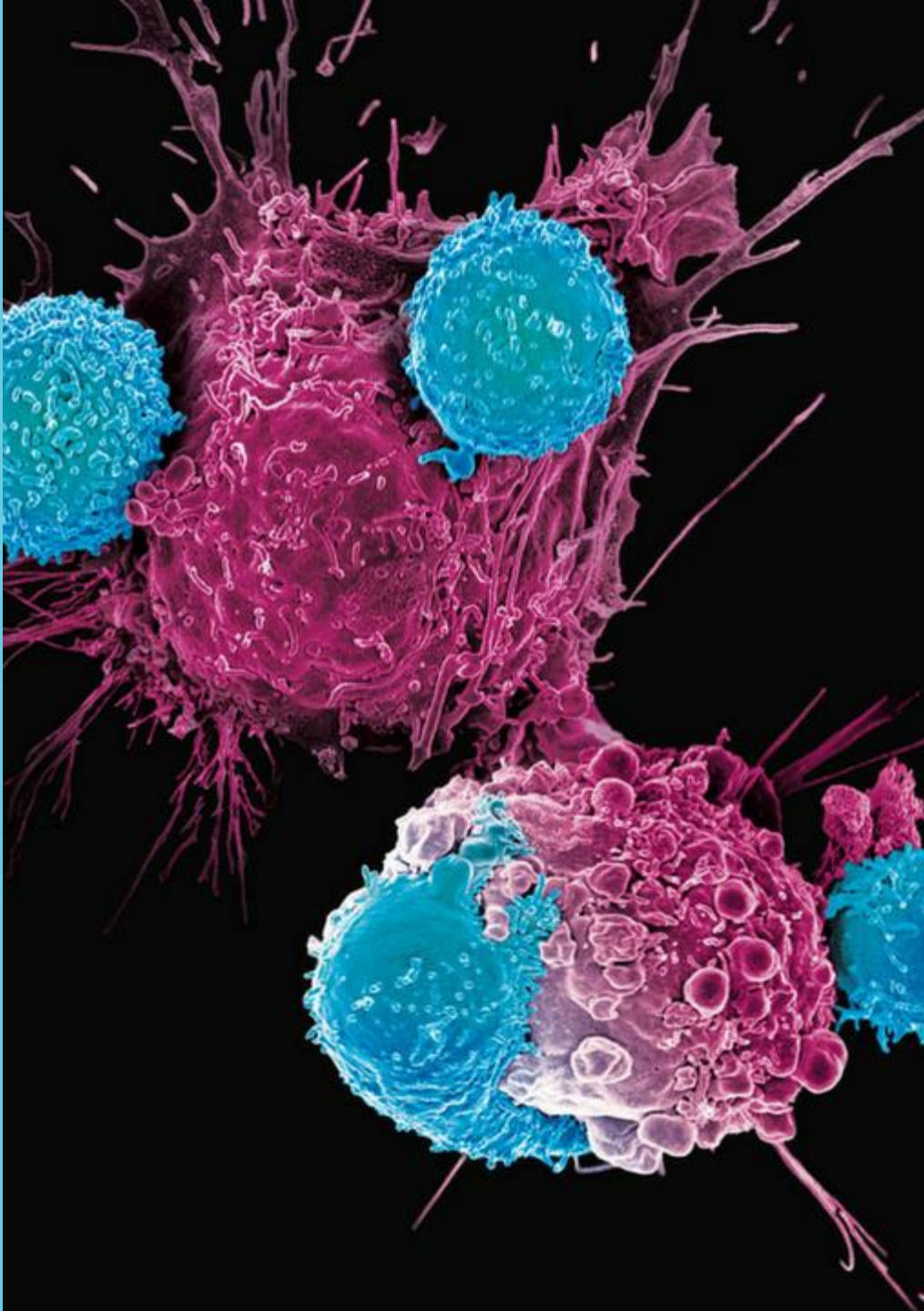
Ziopharm Collaborating with NCI on End-to-end Solution to Target Solid Tumors



Viral approach
to manufacturing TCR-T



Sleeping Beauty approach
to manufacturing TCR-T



Sleeping Beauty
**CD19-specific
CAR-T Program**

The Problem: CAR-T Therapy Today

Viable business model remains elusive

High cost and reimbursement dynamic is likely **unsustainable**

Centralized manufacturing adds **logistical complexities**

Significant time required to deliver to patients

The Solution: *Non-viral Sleeping Beauty* ≤ 2-day manufacturing

- **Local, very rapid, simplified, scalable manufacturing**
- **Bioengineering resting T cells with CAR and membrane-bound IL-15 keeps them “young”**
- **mbIL15 may avoid lymphodepletion**
- **Deliver low numbers of T cells and expand in the body, to avoid cytokine release syndrome**
- **CD19-specific approved CAR target for autologous T cells**

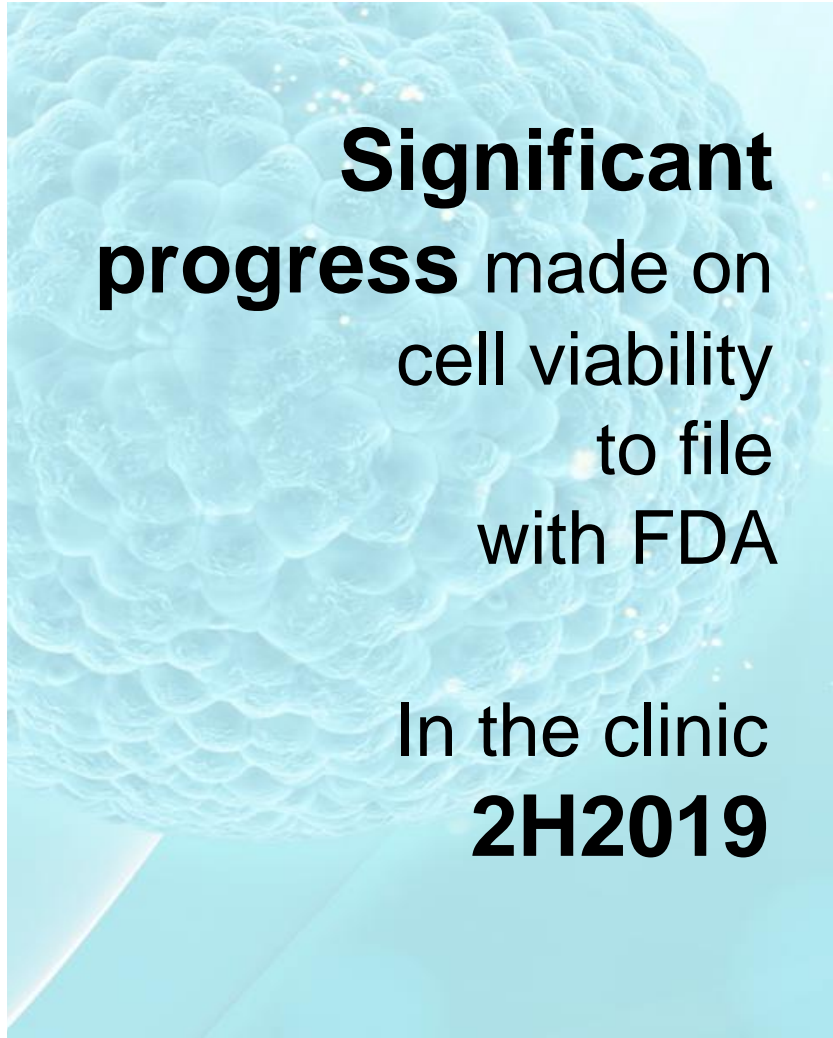
Strategy for Very-Rapid Manufacturing of CAR-T

✓ Demonstrated *Sleeping Beauty* with CD19-specific CAR-T

✓ Value to Ziopharm

- CD19: Fully-funded with Eden BioCell
- CD19: Fully-funded at MD Anderson
- Undisclosed: Additional validated target

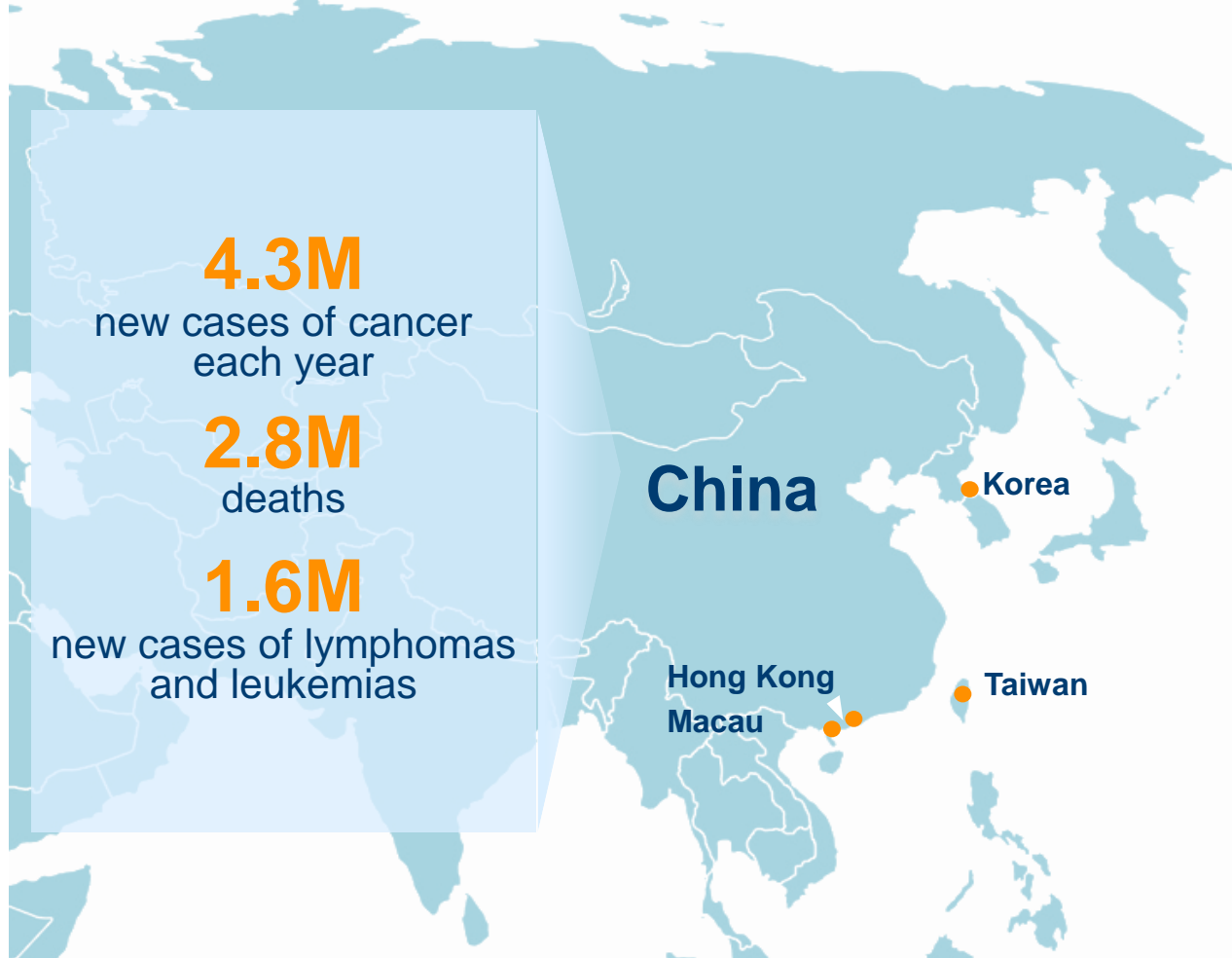
✓ Not pursuing new CAR targets



Significant progress made on cell viability to file with FDA

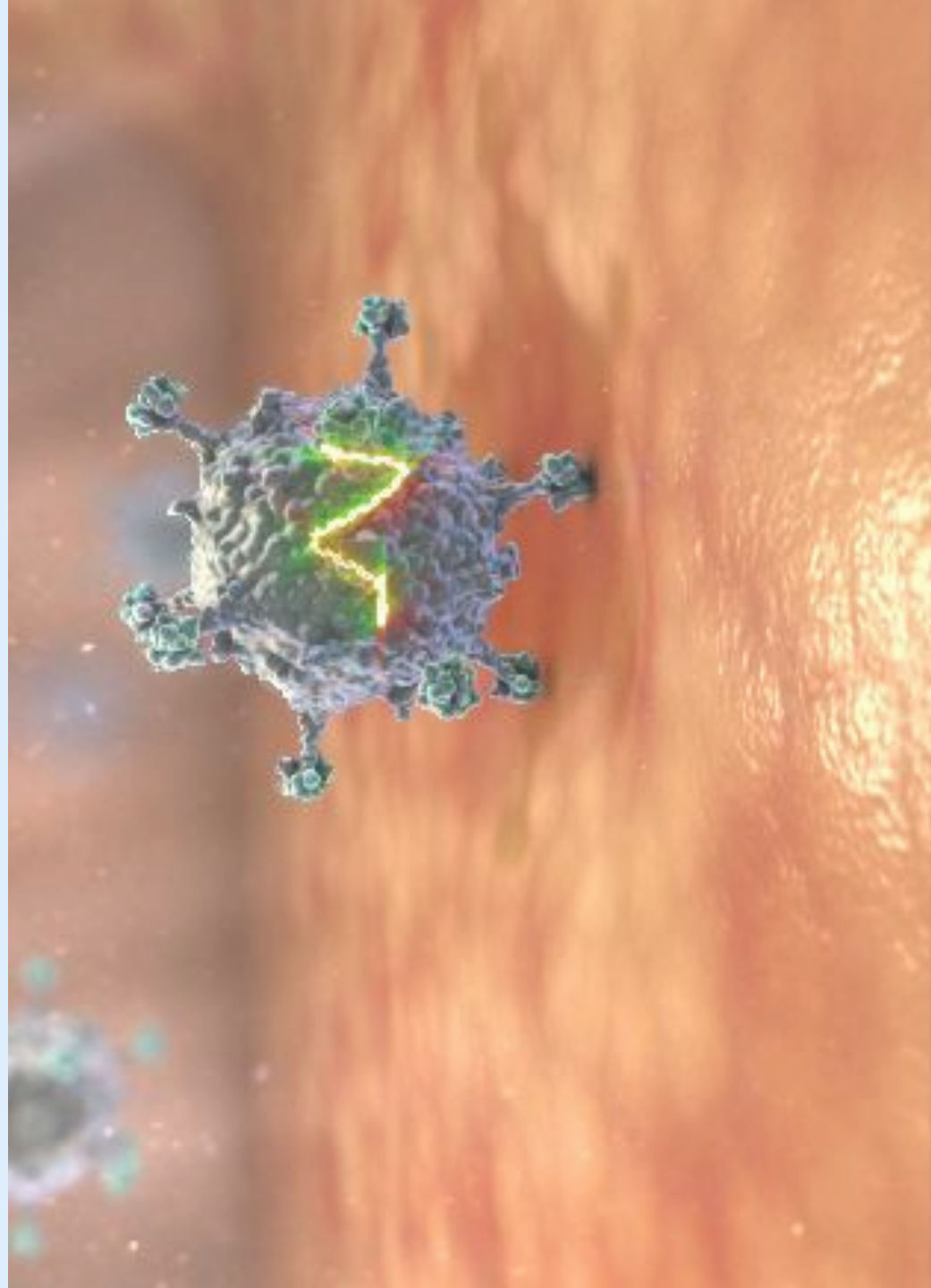
In the clinic
2H2019

Eden BioCell to take CAR-T CD19 to Asian Markets



- *Sleeping Beauty* third-generation for very rapid manufacturing of CD19-specific CAR-T cell therapy licensed to Eden BioCell for Greater China
- Eden BioCell funded with up to \$35 million entirely from TriArm Therapeutics
- Ziopharm and TriArm each have 50 percent ownership

"Cancer Statistics in China, 2015" Wanqing Chen, Ph.D., M.D., et al in CA Cancer J Clinical 2016; 66: 115-132



Controlled IL-12 Platform

Recurrent Glioblastoma is not Curable; A New Rational Approach is Needed



TARGETS ARE UNKNOWN

Current therapies don't work



LOW SURVIVAL RATE

Historical overall survival is 5 to 8 months



IMMUNOTHERAPY BEST APPROACH

Immune system to fight the cancer

THE PROBLEM

Brain tumors exclude or weaken the immune system



THE SOLUTION: IL-12 as a DRUG

Most powerful immuno-stimulant to recruit T cells

IL-12 Delivered into Recurrent Glioblastoma can be Controlled by Ziopharm to Improve Survival

Ad



RTS®*



hIL-12



Veledimex**



Low-dose
steroids***



Median Overall Survival (months)

Ad-RTS-hIL-12 + 20mg Vel + low dose steroids n= 6£

Ad-RTS-hIL-12 + 20mg Veledimex n=15£

Lomustine n=110££

Bevacizumab n=46£££

0 5 10 15 20

* RheoSwitch Therapeutic System®

** 15 daily doses of 20 mg

*** < 20 mg dexamethasone

£: Based on patients and a subset of receiving less than 20mg dexamethasone following surgery, SNO2018 presentation entitled, "A Phase 1 study of Ad-RTS-hIL-12 + veledimex in adults with recurrent glioblastoma: Dose determination with updated overall survival";
££ Wick W, Gorlia T, Bendszus M, et al. Lomustine and Bevacizumab in Progressive Glioblastoma. N Engl J Med 2017;377:1954-63.
£££ Taal, W, et al. Single-agent bevacizumab or lomustine versus a combination of bevacizumab plus lomustine in patients with recurrent glioblastoma (BELOB trial): a randomised controlled phase 2 trial. Lancet Oncology, 2014, 15: 943–953.

IL-12 Monotherapy with Low-dose Steroids Expanded Trial

Phase 1: Ad-RTS-hIL-12 plus 20mg of veledimex

- Expansion cohort of monotherapy and guidance for low dose (<20 mg) dexamethasone
- Enrollment (n=25) completed this week
 - 65% of enrolled patients received low-dose steroids

Next Logical Step: Controlled IL-12 in Combination with PD-1 Inhibitors for recurrent GBM

Biomarker-driven studies

Monotherapy resulted in upregulation of PD-1 in tumor microenvironment

Combination with OPDIVO

- **Phase 1** trial of Controlled IL-12 in combination PD-1 antibody OPDIVO® (nivolumab) to treat patients with rGBM
- Enrollment up to 18 patients expected to be complete in 2Q2019

New collaboration with Regeneron Pharmaceuticals

- **Phase 2** trial of Controlled IL-12 in combination with PD-1 antibody Libtayo® (cemiplimab-rwlc) to treat patients with rGBM
- Enroll up to ~30 patients; primary endpoints are safety and efficacy
- Initiate 1H2019

Summary of 2019 Milestones: Two Platforms Solving Critical Problems

	1Q2019	2Q2019	1H2019	Mid-2019	2H2019
	Phase 1 Fully enrolled Controlled IL-12 monotherapy expansion cohort	Phase 1 Fully enrolled Controlled IL-12 in combination with OPDIVO	Phase 2 Initiation Controlled IL-12 in combination with Libtayo	Phase 1 First-in-human trial initiation NCI-led Sleeping Beauty TCR-T-cell trial targeting solid tumors	Phase 1 Trial initiation Sleeping Beauty CD19-specific CAR-T third-generation trial with membrane- bound IL-15
	Controlled IL-12 Platform			Sleeping Beauty Platform	

All Programs in the Clinic in 2019

Sleeping Beauty TCR-T

- Delivers **multiple TCRs** targeting multiple patient-specific neoantigens
- End-to-end *Sleeping Beauty* TCR-T **process is clinically advanced**
- NCI/Rosenberg **partnership** advancing into the clinic

Sleeping Beauty CAR-T

- ***Sleeping Beauty*** platform FDA-**cleared for use in clinical trials**
- **Most clinically advanced** non-viral CAR-T
- MD Anderson and Eden BioCell **partnerships**

Ad-RTS-hIL-12 plus veledimex

- Monotherapy data suggest **survival benefit** and safety
- Biopsy data point to advantages in combining with **checkpoint inhibitors**
- Regeneron **partnership**
- Opportunity for **additional solid tumor indications**






Thank you

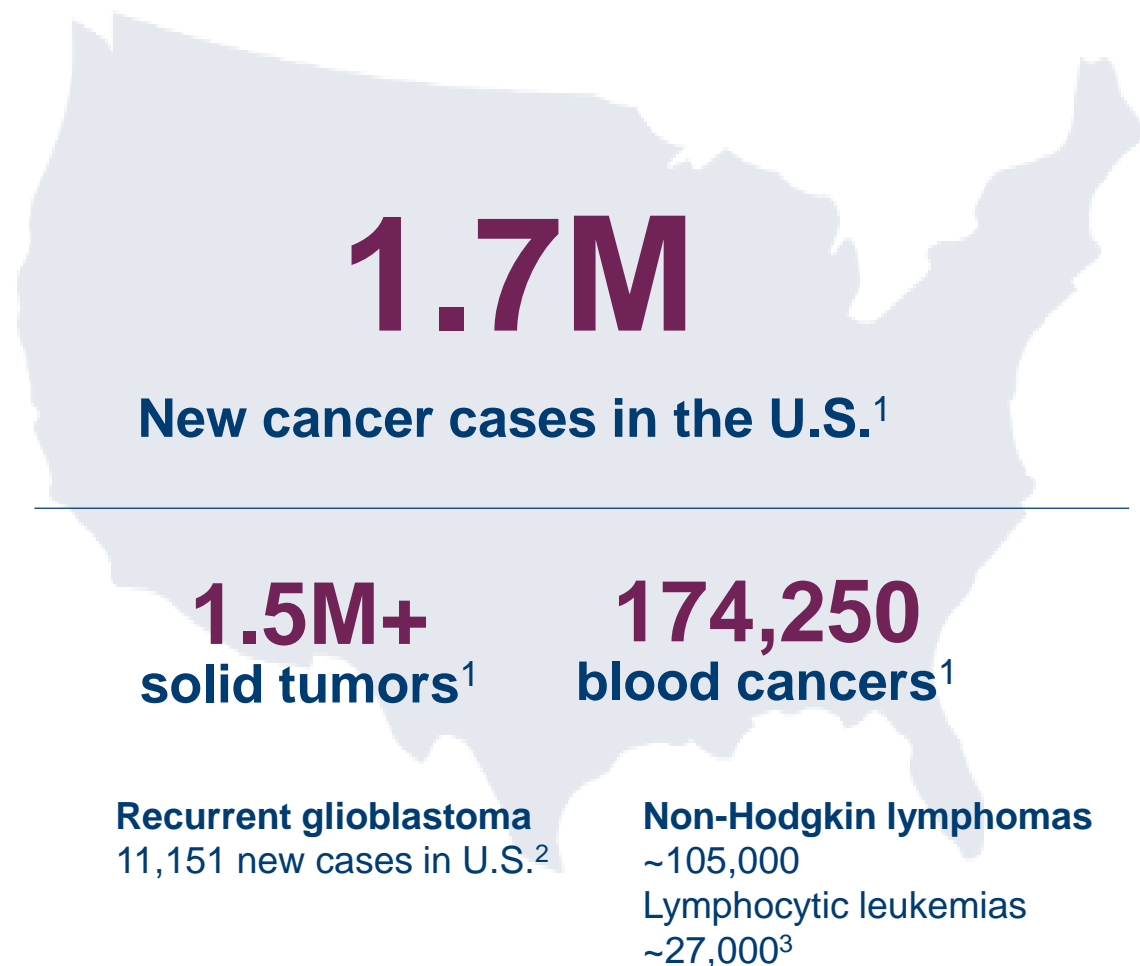


Appendix

Pipeline Overview

Asset	Indication	Phase 1 / 2	
<i>Sleeping Beauty</i> TCRs targeting neoantigens	Multiple solid tumors	Treat patients mid-2019	
<i>Sleeping Beauty</i> CAR-T	Leukemia/lymphoma	2 nd Generation CD19	
	Leukemia/lymphoma	3 rd Gen CD19 with mblL15 2H2019	
	Unnamed target*		
Ad-RTS-hIL-12 + veledimex	rGBM	Monotherapy (expansion)	
	rGBM	In combination w/ OPDIVO®	
	rGBM	In combination w/ LIBTAYO® 1H2019	
	Pediatric brain tumor	Monotherapy	

Significant Unmet Need and Opportunity Across Platforms



Sleeping Beauty TCR-T
for solid tumors

Sleeping Beauty CAR-T
for CD19⁺ blood cancers

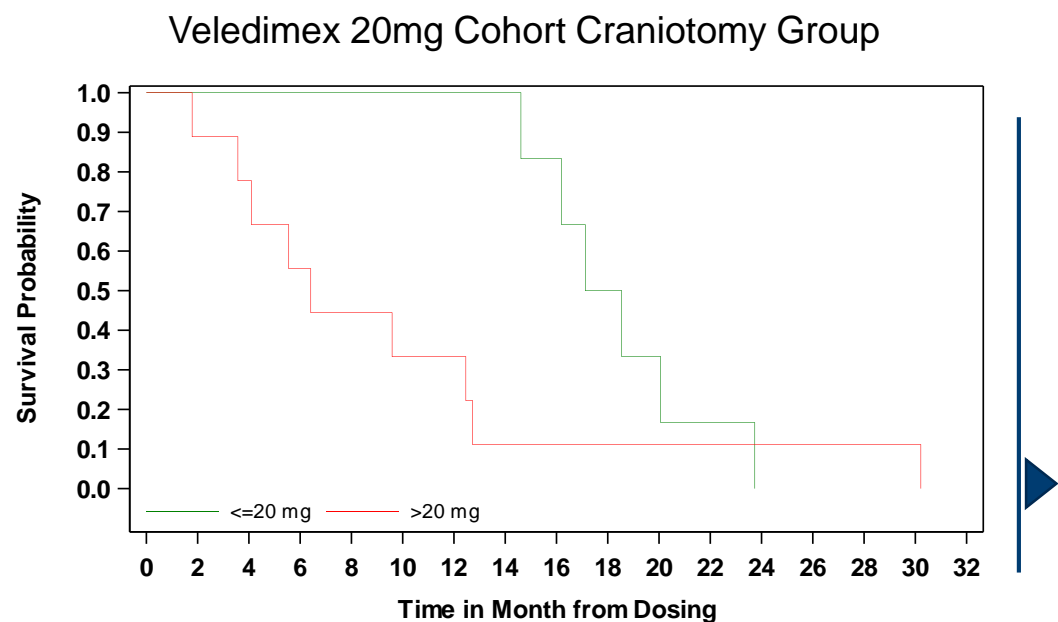
Controlled IL-12
for recurrent glioblastoma

1. 2018, International Agency on Research for Cancer, *Cancer Facts & Figures*, 2018, American Cancer Society

2. GlobalData information, June 2016

3. Updated Data on Blood Cancers, 2018, Leukemia & Lymphoma Society

Low Doses of Dexamethasone with Controlled IL-12 Shown to Improve Survival Compared to Higher Doses



Cohort	Dexametha sone Use (Days 0-14)	mOS (mos.)	Lower bound	Upper bound	Mean F/U	No. Events
20 mg V Craniotomy	≤20 mg	17.8	14.6	23.7	18.4	6
	>20 mg	6.4	1.8	12.7	9.6	9

Clear separation of survival curves favoring low dose steroids

SNO2018 presentation entitled, “A Phase 1 study of Ad-RTS-hIL-12 + veledimex in adults with recurrent glioblastoma: Dose determination with updated overall survival”

Ziopharm's Exclusive Rights for Cancer Treatment

Sleeping Beauty TCR-T

- Exclusivity for all IP for TCR products for neoantigens, including *Sleeping Beauty* and mblL15
- Exclusivity for *Sleeping Beauty* for all TCRs (public and shared)

Sleeping Beauty CAR T

- Exclusivity for *Sleeping Beauty* CAR-T targeting CD19 with mblL15 and kill switch
- Exclusive rights to second, unnamed but highly validated CAR target with mblL15 and kill switch

Ad-RTS-hIL-12 plus veledimex with RheoSwitch

- Exclusivity as monotherapy or in combination therapy

Exclusive license provides development autonomy

Updated Financials

Condensed Consolidated Balance Sheet

Cash, cash equivalents and short term investments as of Sept. 30, 2018, plus net proceeds from \$50 million private financing which closed on Nov. 13, 2018.	\$79 M
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At MD Anderson Cancer Center from prepayment for programs to be conducted by the Company as of Sept. 30, 2018	\$29.6M
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Current plans and resources will be sufficient to fund planned operations into the second quarter of 2020 and pre-payments to MD Anderson fund planned programs there into 2020