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NASDAQ: XBIO

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Corporate Presentation  
June 2019

Enhancing lives with  
transformative therapies

## Forward-Looking Statements

This presentation contains forward-looking statements for purposes of the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. All statements contained in this presentation other than statements of historical facts may constitute forward-looking statements within the meaning of the federal securities laws. These statements can be identified by words such as "expects," "plans," "projects," "will," "may," "anticipates," "believes," "should," "intends," "estimates," and other words of similar meaning. Any forward-looking statements contained herein are based on current expectations, and are subject to a number of risks and uncertainties. These forward-looking statements include, but are not limited to, statements regarding the acquisition and development of the CAR T technology, such as the anticipated effects of the acquisition on the Company's position in the development of new oncology therapeutics, the expected leveraging opportunities resulting from the acquisition, the expected results of the XCART technology, and the Company's future plans for the XCART clinical program and development efforts in the area of CAR T therapy after the acquisition is consummated. Many factors could cause our actual activities or results to differ materially from the activities and results anticipated in forward-looking statements. Important factors that could cause actual results to differ materially from such plans, estimates or expectations include, among others, (1) that one or more closing conditions to the acquisition of the CAR T technology, including certain regulatory approvals, may not be satisfied or waived, on a timely basis or otherwise, or that the required approval by the stockholders of the Company may not be obtained; (2) the condition that the Company have adequate financing to fund its future working capital obligations may not be met; (3) the risk that the acquisition may not be completed on the terms or in the time frame expected by the Company, or at all; (4) unexpected costs, charges or expenses resulting from the acquisition; (5) uncertainty of the expected financial performance of the Company following completion of the acquisition; (6) failure to realize the anticipated benefits of the acquisition; (7) the ability of the Company to implement its business strategy; (8) the occurrence of any event that could give rise to termination of the acquisition; and (9) other risk factors as detailed from time to time in the Company's reports filed with the SEC, including its annual report on Form 10-K, periodic quarterly reports on Form 10-Q, periodic current reports on Form 8-K and other documents filed with the SEC. In addition, forward-looking statements may also be adversely affected by general market factors, competitive product development, product availability, federal and state regulations and legislation, the regulatory process for new product candidates and indications, manufacturing issues that may arise, patent positions and litigation, among other factors. The forward-looking statements contained in this presentation speak only as of the date the statements were made, and the Company does not undertake any obligation to update forward-looking statements, except as required by law.

## Forward-Looking Statements

### **ADDITIONAL INFORMATION AND WHERE TO FIND IT**

In connection with the acquisition, the Company has filed and had declared effective with the Securities and Exchange Commission (the "SEC"), a registration statement on Form S-4 that includes a combined definitive proxy statement/prospectus. This communication is not a substitute for any proxy statement, prospectus registration statement, or other documents the Company may file with the SEC in connection with the acquisition. **INVESTORS AND SECURITY HOLDERS ARE URGED TO READ CAREFULLY AND IN THEIR ENTIRETY THESE DOCUMENTS, ANY AMENDMENTS OR SUPPLEMENTS TO THESE DOCUMENTS, AND OTHER DOCUMENTS FILED BY THE COMPANY WITH THE SEC IN CONNECTION WITH THE ACQUISITION, BECAUSE THESE DOCUMENTS CONTAIN IMPORTANT INFORMATION.** Investors and security holders will be able to obtain free copies of these materials and other documents filed with the SEC by the Company through the website maintained by the SEC at [www.sec.gov](http://www.sec.gov). Investors and security holders may also obtain free copies of the documents filed by the Company with the SEC by directing a written request to Xenetic Biosciences, Inc., 40 Speen Street, Suite 102, Framingham, MA 01701 or by calling 781-778-7720.

### **PARTICIPANTS IN THE SOLICITATION**

This communication is not a solicitation of a proxy from any investor or security holder. The Company, its respective directors, executive officers and other members of its management and employees may be deemed to be participants in the solicitation of proxies from shareholders of the Company in connection with the acquisition. Information regarding the persons who may, under the rules of the SEC, be deemed participants in the solicitation of proxies in connection with the acquisition, including a description of their direct or indirect interests, by security holdings or otherwise, will be set forth in the relevant materials when filed with the SEC. Information regarding the directors and executive officers of the Company is contained in its Annual Report on Form 10-K for the year ended December 31, 2018, which was filed with the SEC on March 29, 2019 as amended on April 30, 2019, and its Registration Statement on Form S-4 including a combined proxy statement/prospectus, which was filed on March 29, 2019, as amended and declared effective on May 22, 2019. These documents can be obtained free of charge from the sources indicated above.

## Transformative acquisition of the XCART platform positions Xenetic to address high value oncology market

### XCART Platform<sup>1</sup>

#### Expanding the Potential of CAR T Cell Therapy

- Proof-of-mechanism and preclinical evidence of target specificity
- Pursuing academic collaboration for early program development
- Over \$5 billion initial market opportunity in B-cell non-Hodgkin lymphoma<sup>2</sup>

## Experienced Management Team

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### **Jeffrey F. Eisenberg**

Chief Executive Officer & Director

Life Sciences executive with over 20 years of successful track record in value creation in both private and public companies; former CEO of Noven Pharmaceuticals and responsible for 2 product launches and led Noven's Novogyne Women's Health joint venture with Novartis

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### **Curtis Lockshin, Ph.D.**

Chief Scientific Officer

20 years Biotech/Pharma management experience, including discovery, preclinical and clinical development and commercial manufacturing; former CEO of SciVac Therapeutics, CTO of VBI Vaccines and VP of Corporate R&D Initiatives for OPKO Health

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### **James F. Parslow, MBA, CPA**

Chief Financial Officer

Over 30 years of experience providing financial and business leadership to biotech, manufacturing, technology, business-to-business e-commerce and cleantech industries



# Board of Directors

**Adam Logal**

Chairman

CFO, OPKO Health; Former Director, VBI Vaccines; Nabi Biopharmaceuticals

**Dmitry Genkin**

Director

Former Head of Pharmavit, one of Russia's largest pharmaceutical companies; Chairman, PJSC Pharmsynthez

**James Eric Callaway, Ph.D.**

Director

Seasoned CEO within the venture-backed community and current CEO of Kalgene; Former Head of Development, Elan Pharmaceuticals

**Roman Knyazev**

Director

Senior Investment Manager, Rusnano; Chairman, Pharmsynthez, PETAR and Nanolek; Director, SynBio

**Firdaus Jal Dastoor, FCS**

Director

Fellow Member of The Institute of Company Secretaries of India; Group Director of the Poonawalla Group of Companies

**Roger Kornberg, Ph.D.**

Director

Winzer Professor of Medicine in the Department of Structural Biology at Stanford University; Nobel Prize in Chemistry - Molecular Basis of Eukaryotic Transcription

**Jeffrey F. Eisenberg**

Chief Executive Officer & Director

## Scientific Advisory Board

### **Dr. Matthew Frigault**

Medical Oncologist in the Hematologic Malignancy Program at the Massachusetts General Hospital Cancer Center, as well as Assistant Director of the Cellular Immunotherapy Program, serves as Instructor at Harvard Medical School.

### **Prof. Dr. Franco Cavalli**

Former Scientific Director, Institute of Oncology of Southern Switzerland (IOSI), Head of Organizing Committee of International Conference on Malignant Lymphoma (ICML), Chairman of Scientific Committee of the European School of Oncology (ESO) and of the World Oncology Forum (WOF), Founder of the International Extranodal Lymphoma Study Group (IELSG).

### **Dr. Alexander Gabibov**

Head of the Shemyakin & Ovchinnikov Institute of Bioorganic Chemistry at the Russian Academy of Science. Dr. Gabibov holds several senior positions in the Biochemistry sphere in both Russia and France. In 2008, he was appointed President of the Russian Biochemical and Molecular Biology Society. In 2009, Dr. Gabibov took up the role of Foreign Correspondent at the National Academy of Pharmacy in France.

### **Dr. Guenther Koehne**

Internationally recognized cancer specialist and current Chief of Blood & Marrow Transplant and Hematologic Oncology at the Miami Cancer Institute; noteworthy reputation for his work in adoptive immunotherapeutic approaches with antigen-specific, donor-derived T lymphocytes in the treatment of viral complications following allogeneic transplants and has developed new approaches to the treatment of patients with high-risk multiple myeloma.

### **Dr. Davide Rossi**

Deputy Head of the Division of Hematology and co-chair of the Clinical Lymphoid Tumors Investigation Program (CLIP) at the Institute of Oncology of Southern Switzerland (IOSI), Head of the Experimental Hematology research program at the Institute of Oncology Research (IOR), Member of Organizing Committee of the International Conference on Malignant Lymphoma. Dr. Rossi's translational research focuses on lymphomas and chronic lymphocytic leukemia.

# XCART Platform<sup>1</sup>

Expanding the Potential  
of CAR T Cell Therapy

<sup>1</sup> Acquisition, subject to the satisfaction of the closing conditions, is expected to close in the first half of 2019. Please see our Registration Statement on Form S-4 for more details.



# CAR T Cell Therapy is Driving New Breakthroughs in the Treatment of Cancer

## 2 Approved CAR T Therapies

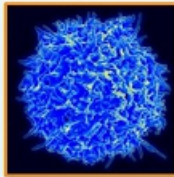
 **KYMRIAH**<sup>®</sup>  
(tisagenlecleucel) Suspension for IV infusion

 **YESCARTA**<sup>®</sup>  
(axicabtagene ciloleucel) Suspension for IV infusion

## Advancing Development

**~40** companies developing CAR T therapy<sup>1</sup>

**>240** CAR T trials registered on clinicaltrials.gov<sup>2</sup>



**CBS** New CAR T Treatment Giving Hope To Some Cancer Patients



**Forbes** CAR T Cell Therapy Is Here to Stay

**Newsweek** With Latest Gene Therapy Approval, a New Medical Era Has Officially Arrived


# CAR T Value Indicators Suggest Potential Significant Upside

## Acquisitions

 cell design labs acquired by  GILEAD for **\$567M<sup>1</sup>**

 Juno acquired by  Celgene for **\$9B<sup>2</sup>**

 Kite acquired by  GILEAD for **\$11.9B<sup>3</sup>**

Company	Lead Program	Phase	MKT Cap <sup>4</sup>
 ATARA BIO <sup>4</sup>	EBV+ PTLD following HCT	Phase 3	<b>\$1B</b>
 cellectis	UCART19	Phase 1	<b>\$658M</b>
 Ziopharm ONCOLOGY	rGBM & Libtayo <sup>*</sup>	Phase 1	<b>\$672M</b>
 MITSUBISHI	MB-101 IL13Rα2-specific CAR	Phase 1/2	<b>\$130M</b>

## Licensing Agreements

 Bellicum PHARMACEUTICALS agreement with  Agensys

 Pfizer agreement with  cellectis **\$80M upfront & up to \$185M per product**

 abbvie 4 year agreement with  Calibr

 Johnson-Johnson agreement with  Nanjing Legend for **\$350M**

## XCART Has the Potential to Transform CAR T Therapy

### XCART

- XCART constructs can target patient-specific tumor neoantigens
- Established proof-of-mechanism in B-cell lymphomas
- Potential to address various target and tumor types
- Proprietary cell-based CAR screening platform
- Proprietary autocrine technology licensed from Scripps (originating in Richard Lerner's lab)
- Compatible with current up- and down-stream CAR T manufacturing processes
- Applicable to a wide range of CAR T constructs
- Enables rapid identification of functional CARs & TCRs





## SCIENCE ADVANCES | RESEARCH ARTICLE

### CANCER

## Autocrine-based selection of ligands for personalized CAR-T therapy of lymphoma

Alexey V. Stepanov<sup>1</sup>, Oleg V. Markov<sup>2</sup>, Ivan V. Chernikov<sup>2</sup>, Danil V. Gladkikh<sup>2</sup>, Hongkai Zhang<sup>3,4</sup>, Teresa Jones<sup>3</sup>, Alexandra V. Sen'kova<sup>2</sup>, Elena L. Chernolovskaya<sup>2</sup>, Marina A. Zenkova<sup>2</sup>, Roman S. Kalinin<sup>1</sup>, Maria P. Rubtsova<sup>2</sup>, Alexander N. Meleshko<sup>6</sup>, Dmitry D. Genkin<sup>7</sup>, Alexey A. Belogurov Jr.<sup>1</sup>, Jia Xie<sup>3\*</sup>, Alexander G. Gabibov<sup>1\*</sup>, Richard A. Lerner<sup>3\*</sup>

We report the development of a novel platform to enhance the efficacy and safety of follicular lymphoma (FL) treatment. Since lymphoma is a clonal malignancy of a diversity system, every tumor has a different antibody on its cell surface. Combinatorial autocrine-based selection is used to rapidly identify specific ligands for these B cell receptors on the surface of FL tumor cells. The selected ligands are used in a chimeric antigen receptor T cell (CAR-T) format for redirection of human cytotoxic T lymphocytes. Essentially, the format is the inverse of the usual CAR-T protocol. Instead of being a guide molecule, the antibody itself is the target. Thus, these studies raise the possibility of personalized treatment of lymphomas using a private antibody binding ligand that can be obtained in a few weeks.

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# Market Opportunity – Non-Hodgkin Lymphoma Therapeutics

Estimated 2018 US Incidence of NHL: 75,000<sup>1</sup>

## Indolent Lymphomas

### Follicular Lymphoma (FL):

**US Incidence** ~15K/year  
 Second most common subtype of NHL in the US (~20% of all NHL Cases)

- Majority of Follicular Lymphoma (FL) cases remain *incurable* with standard therapies
- Most patients undergo relapses over time, often with increasing frequency and aggressiveness

## Aggressive Lymphomas

### Diffuse Large B-Cell Lymphoma (DLBCL):

**US Incidence** ~30K/year  
 Most common subtype of NHL in the US (~40% of all NHL cases)

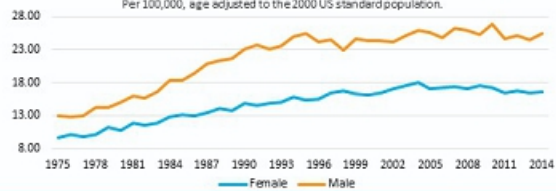
- ~ 50% Of *Refractory & Relapsed* DLBCL have poor prognoses:<sup>2</sup>
  - ORR: 26% (7% CR)
  - Median OS: 6.3 months

### Global Market for Non-Hodgkin Lymphoma<sup>3</sup>



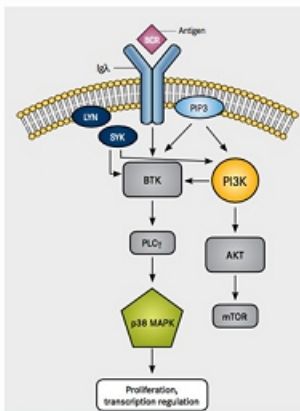
### Trends in NHL Incidence Rates, 1975-2014<sup>3</sup>

Per 100,000, age adjusted to the 2000 US standard population.



## Engineered to target a patient- and tumor-specific neoantigen

### B-cell Receptor (BCR) on an Individual Patient's Lymphoma Cells



### BCR Signaling Pathway

- Central regulator of B-cell function
- Promising anticancer drug target in lymphomas

### BCR Expressed by Clonal B-cell Tumor

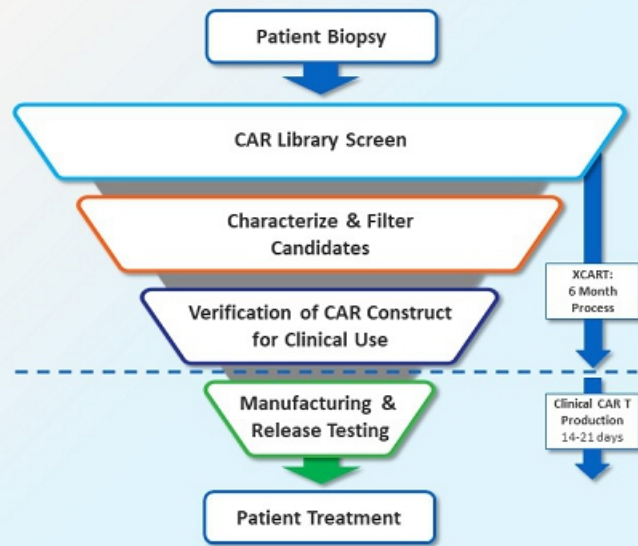
- Pivotal driver of tumor pathways
- Patient- and tumor-specific antigen

### Targeting a Patient-Specific BCR with CAR T Therapy

- Imparts high selectivity
- Can overcome limitations of CD19 CAR T therapies

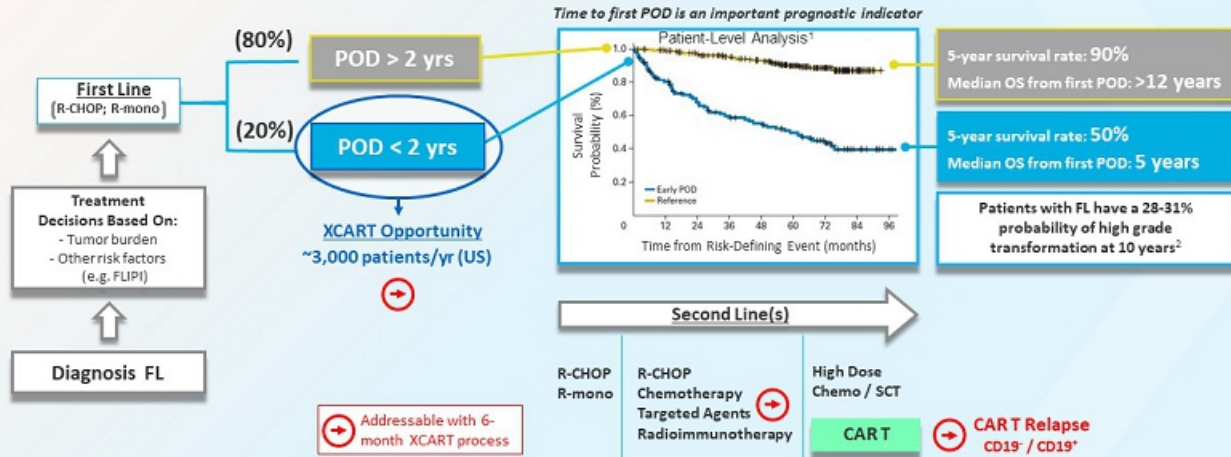


# XCART Clinical Workflow

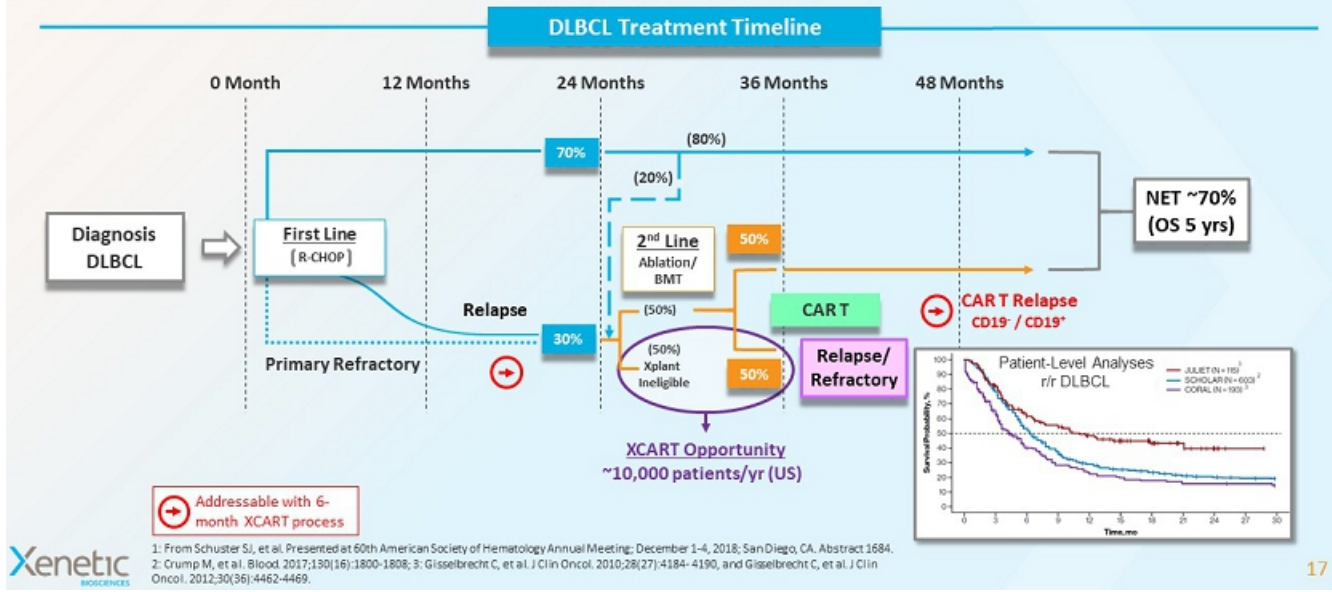


# Unmet Need in Follicular Lymphoma (FL)

## FL Treatment Timeline



# Unmet Need in Diffuse Large B-Cell Lymphoma (DLBCL)

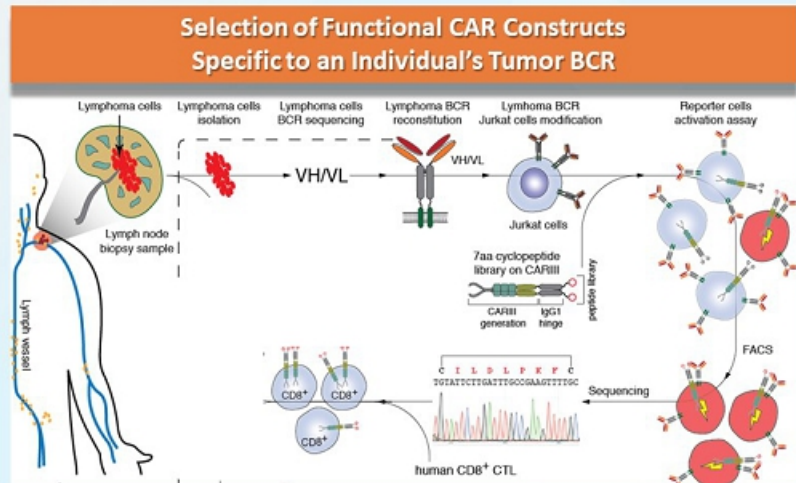


1: From Schuster SJ, et al. Presented at 60th American Society of Hematology Annual Meeting; December 1-4, 2018; San Diego, CA. Abstract 1684.  
 2: Crump M, et al. Blood 2017;130(16):1800-1808; 3: Gisselbrecht C, et al. J Clin Oncol. 2010;28(27):4184-4190, and Gisselbrecht C, et al. J Clin Oncol. 2012;30(36):4462-4469.

# Selection of Functional CAR Constructs Specific to an Individual's Tumor BCR

XCART Proof of Mechanism: Workflow

- Lymph node biopsy sample is isolated from a patient with follicular lymphoma
- Collected tumor cells used for identification of malignant BCR genes - then reconstituted as membrane-bound tumor BCRs using PDGFR as membrane anchor
- The reconstituted tumor BCR, co-expressed with the CAR library on surface of Jurkat cell line, are used as reporter-cell system for selection of tumor BCR-targeting ligand
- Following several rounds of panning, selected peptide ligands (fused to chimeric antigen receptor), are sequenced and may be directly used for generation of therapeutic T lymphocytes modified by BCR-specific CAR

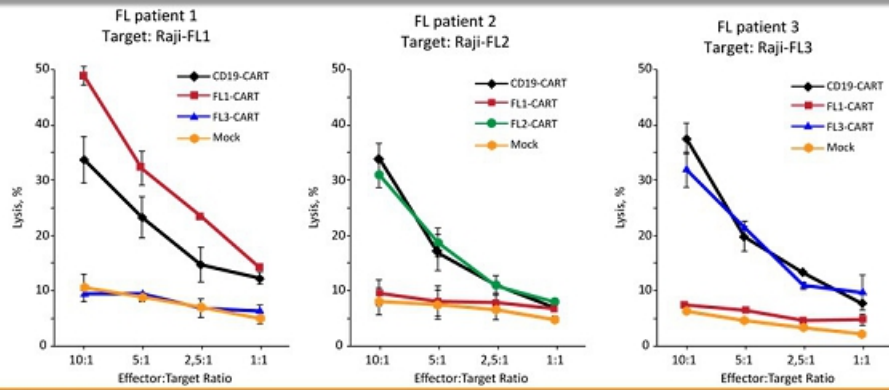


# Cyclopeptide-CAR T Cells Selectively Kill Raji Cell Lines Expressing Target BCRs

XCART Proof-of-Mechanism: Patient Specificity

- Human CD8+ T cells were transduced with Lentiviral vectors coding for one of pepFL1-CAR, pepFL2-CAR, pepFL3-CAR or CD19-CAR constructs

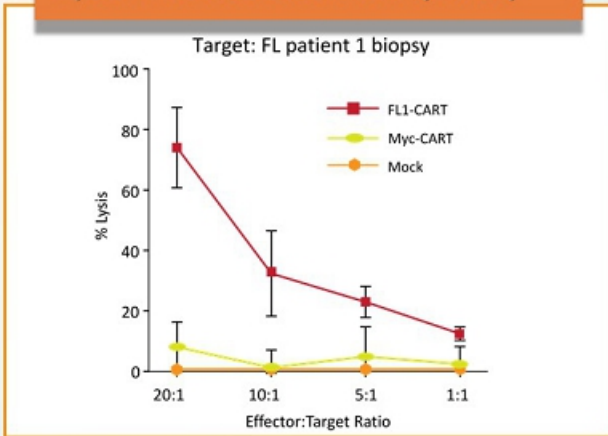
Raji Cells (Raji-FL1, Raji-FL2 and Raji-FL3) Expressing BCRs from the Respective FL Lymphomas Were Lysed by Activated Human CD8+ T Cells Bearing a Corresponding Cyclopeptide-CAR Construct



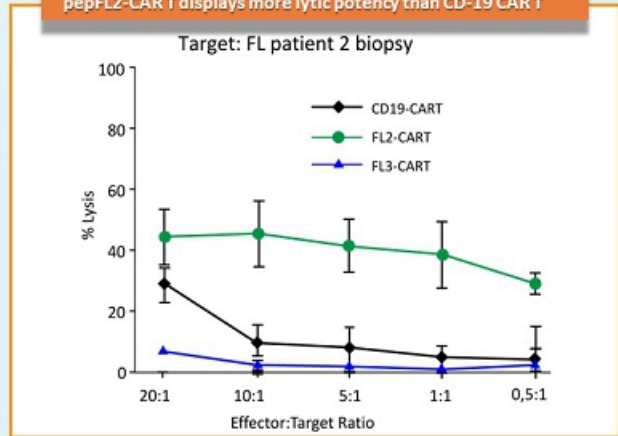
# Induction of CTL in *Ex Vivo* Biopsy Material

## XCART Proof-of-Mechanism: Patient Specificity

pepFL1-CAR T cells specifically lysed cells from pt-FL1  
Myc-CAR T and Mock CAR T control cells: No lytic activity



pepFL2-CAR T cells specifically lysed cells from pt-FL2  
pepFL3-CAR T showed no lytic activity vs. pt-FL2  
pepFL2-CAR T displays more lytic potency than CD-19 CAR T

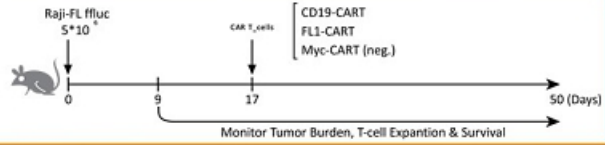




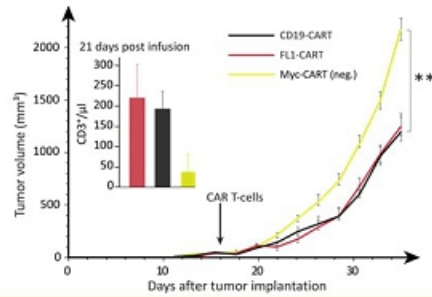
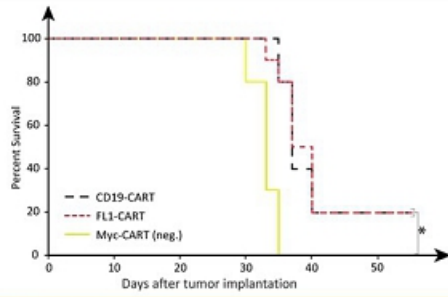
# pepFL1-CAR T in *In Vivo* Tumor Model of Raji-FL1 Cell Line

## XCART Proof-of-Mechanism: Efficacy and Selectivity

NOD SCID (CB17-Prkdc<sup>scid</sup>/NcrCr) mice were engrafted subcutaneously with  $5 \times 10^6$  Raji-FL1 cells (Raji cells expressing the malignant BCR of Patient pt-FL1)

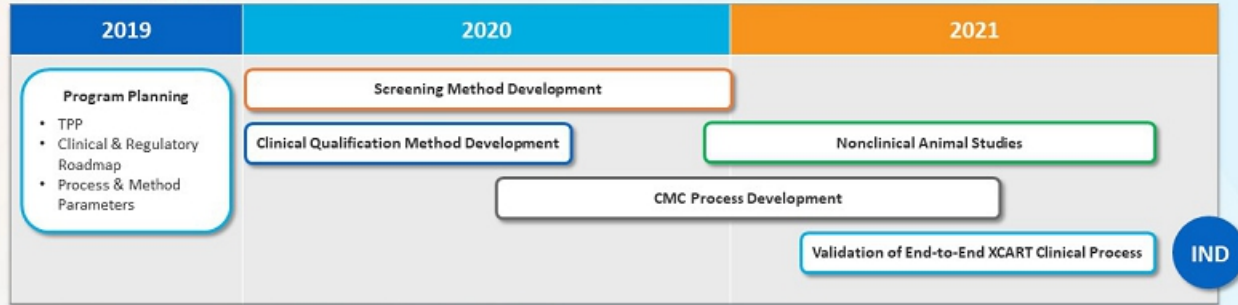


### pepFL1-CAR T and CD19 Showed Similar Effect



# XCART Development Program Driving Towards IND Filing

## Development Approach



## Program Strategy

Collaboration with Site & PI for IIT  
Offers Operational/Cost  
Efficiencies and Risk Mitigation

Early Engagement for Clinical Trial Conduct

Integration of Development and  
Clinical Manufacturing Capabilities

Accelerated Clinical  
Proof of Concept

## XCART is Differentiated from CD19 CAR T Therapies

### Tissue Specificity

- Recognizes only patient- and tumor-specific neoantigens
- Decreased antigen burden implies lower risk of CRS and Neurotoxicity

### Off-Tumor Toxicity

- No expectation of B-cell aplasia



### Tumor Antigen Escape

- Targets an antigen important to B-cell signaling and proliferation
- XCART therapy should not be susceptible to BCR antigen escape
- Could address the known issue of CD19 CAR T relapse

The graphic features a blue background with a large, stylized 'X' shape formed by overlapping diagonal bands of varying shades of blue. The text is positioned on the left side of the image.

# PolyXen™ PSA Technology Platform

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Enables Next Generation  
Biologic Drugs

# PolyXen: Next Generation Delivery Platform for Biologics

Polysialylation employs the biological polymer polysialic acid (PSA) to modulate the pharmacokinetic and pharmacodynamic profiles of protein drugs

## Key Features

- Retention of native protein conformation
- Non-immunogenic
- Biodegradable
- Fewer injections
- Improved protease stability
- Improved thermal stability
- Broad patent cover

## Broad Utility

- Clinically demonstrated to extend half-life of therapeutic proteins
- Applicable to franchise extensions as well as candidates in development
- Potential utility in other molecule classes such as peptides and small molecules



## License Agreement

- Exclusive License Agreement with Takeda in the field of coagulation disorders
- Granted right to Takeda to grant a nonexclusive sublicense to certain patents related to PolyXen
  - Received \$7.5 million upfront payment
  - Single digit royalties based on net sales
  - Royalty stream could commence by end of 2019
- One active development program

Seeking to build a pipeline of partnerships utilizing PolyXen

## Summary

- **Innovative XCART platform<sup>1</sup> addressing high-value oncology market**
- **PolyXen platform: next generation delivery for biologics**

### XCART Platform

**Lead Program Targeting \$5 Billion Initial Opportunity in B-Cell Non-Hodgkin Lymphoma**



- Proof-of-mechanism and preclinical evidence of target specificity

### PolyXen

#### Takeda Agreement



- Takeda granted a nonexclusive sublicense to certain patents
- Royalty stream could commence by end of 2019
- Active program with Takeda and potential for additional partnerships





Supplemental  
Information

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Enhancing lives with  
transformative therapies

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# Identification of Individualized BCR-Targeting CAR T Constructs

XCART Proof-of-Mechanism

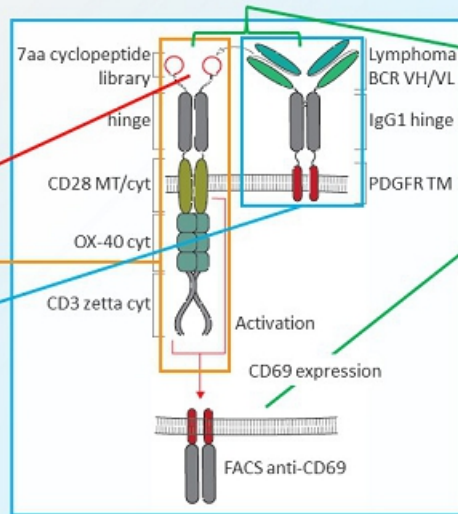
## Selection of cyclopeptide-CARs specific to a targeted BCR:

Library of immortal Jurkat human T lymphocytes were modified to simultaneously express:

Unique cyclopeptide in antigen-binding region of the CAR construct

CAR construct containing a cyclopeptide

Patient-derived lymphoma BCR fused to PDGFR membrane anchor



If the BCR interacts with a peptide from the cyclopeptide library, the signaling domains of the CAR trigger a T cell activation cascade

Activated T cells express CD69 and may be readily detected and isolated via FACS

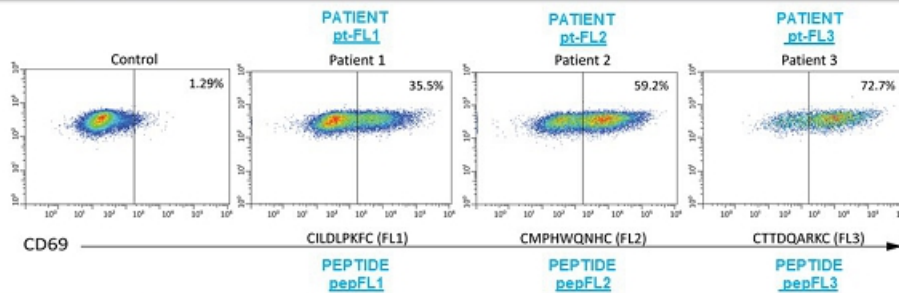
Selected BCR-specific "cyclopeptide-CAR" construct may be further used for transfection of patient T cells to target lymphomas

# Selection and Isolation of Individualized Cyclopeptide-CAR Fusion Constructs

XCART Proof-of-Mechanism: Workflow

- Patient-specific BCRs were cloned from malignant sections of lymph node biopsies in 3 Follicular Lymphoma (FL) patients
- Several rounds of selection resulted in discovery of three patient-specific, cyclopeptide-containing CAR constructs

Cyclopeptide-containing CAR constructs (pepFL1-CAR, pepFL2-CAR, pepFL3-CAR) are selective for respective patient-derived (pt-FL1, pt-FL2, pt-FL3) BCR scFvs

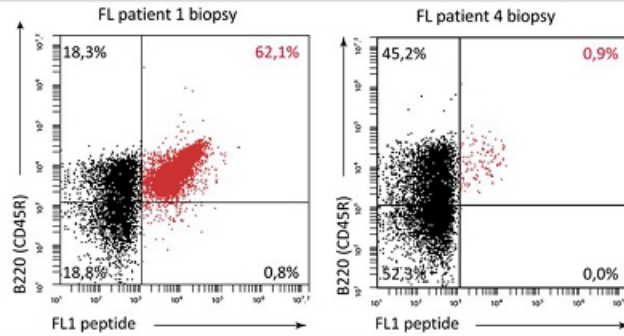


# Staining by pepFL1 Peptide Against pt-FL1 and pt-FL4 Ex-Vivo Samples

X-CART Proof-of-Mechanism: Patient and Target Specificity

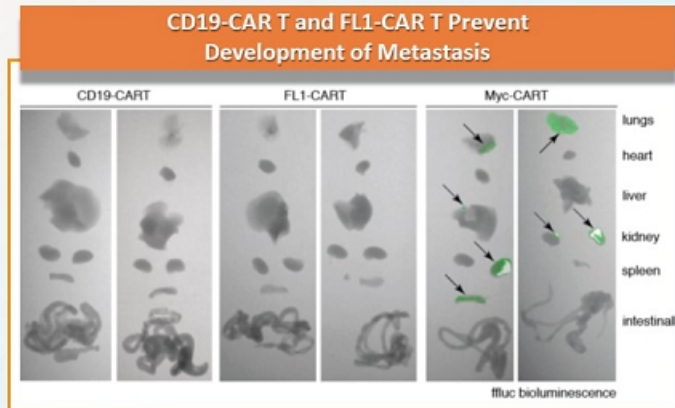
- More than 60% of cells in the biopsy sample are B-cells targeted by the FL1 peptide
- Cells from follicular lymphoma patient pt-FL4 were not significantly stained by the pepFL1 peptide

## BCR-Specific Peptides Selectively Stain Parental Cells from Corresponding Patient's Biopsy Material



## pepFL1-CAR T in *In Vivo* Metastasis Model

- Bioluminescent imaging of organ-specific metastasis Raji-FL1 cells detected by D-luciferin (i.p. injection)



Raji-FL1 cells (green) on Day 35 after tumor implantation in mice treated by CD19-CAR T, FL1-CAR T and Myc-CAR T

# pepFL1-CAR T Cells in Mouse Tumor Models of pt-FL1 Cells

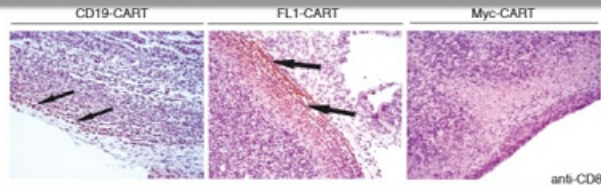
X-CART Proof-of-Mechanism: *In Vivo* PK

## Immunohistochemical Analysis:

CD19-CAR T and FL1-CAR T cells, but not Myc-CAR T cells, effectively invade the tumor

CAR T staining by human CD8-specific antibodies

Black arrows indicate CD19-CAR T, pepFL1-CAR T or Myc-CAR T infiltration into the tumor



## Flow Cytometry:

CAR-modified T cells persist in peripheral blood 21 days post infusion

pepFL1-CAR T and CD19-CAR T cells are present in significantly elevated amounts relative to Myc-CAR T cells

