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, including, but not limited to, statements regarding the capability of the XCART technology to expand the potential of CAR T cell therapy; the benefits of the acquisition of the XCART technology; the Company’s belief that our recent progress and momentum is not properly reflected in our current share price and that our catalytic shift in strategy with the differentiated CAR T platform technology will prove to be transformational for Xenetic; the expected results for XCART and the Company’s anticipated goals for its clinical developmental program seeking to confirm the early preclinical results, and demonstrating a more attractive safety profile than existing therapies; the Company’s plans to build off of the work of the XCART inventors; the Company’s plans to initially apply the XCART technology to develop cell-based therapeutics for the treatment of B-cell lymphomas and to leverage R&D efforts on the advancement of the XCART platform; the Company’s expectations regarding successfully achieving corporate, clinical and regulatory milestones and driving significant shareholder value both in near and long term; the Company’s potential to address an initial global market opportunity of over $5 billion annually; the Company’s belief that it has the potential to become a significant player in the dynamic CAR T oncology space; anticipated plans to leverage the XCART platform technology to innovate, develop and provide important new oncology therapeutics through regulatory approval and commercialization in areas of significant unmet medical need; the Company’s expectations regarding identifying multiple opportunities to collaborate with others in the CAR T field to maximize the potential and impact of XCART; the Company’s business development activities to explore partnerships utilizing its PolyXen delivery platform; the Company’s belief that PolyXen has potential utility in other molecule classes; the Company’s expectations regarding potential royalties resulting from the sublicense with Takeda commencing by the end of 2019; and the Company’s belief that it is currently in a much stronger financial position to execute on its strategic plan. Any forward-looking statements contained herein are based on current expectations, and are subject to a number of risks and uncertainties. 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) unexpected costs, charges or expenses resulting from the acquisition of the CAR T technology; (2) uncertainty of the expected financial performance of the Company following completion of the acquisition; (3) failure to realize the anticipated benefits of the acquisition; (4) the ability of the Company to implement its business strategy; and (5) 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. The foregoing list of important factors is not exclusive. 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.
Xenetic Investment Highlights

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

XCART Platform

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

1: Market Reports World. GLOBAL NON-HODGKIN LYMPHOMA THERAPEUTICS MARKET - SEGMENTED BY TYPE OF TREATMENT - GROWTH, TRENDS AND FORECASTS (2018 - 2023); BioPharm Insight Surveillance, Epidemiology, and End Results (SEER) 9 registries, National Cancer Institute, 2017
Experienced Management Team

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

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

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
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

Dr. Alexey Vinogradov, Director
Business Development Director and Operations Director at Cantreva LLC; Former General Manager at Togas Middle East LLC in Dubai, UAE
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
Expanding the Potential of CAR T Cell Therapy
CAR T Cell Therapy is Driving New Breakthroughs in the Treatment of Cancer

2 Approved CAR T Therapies

- KYMRIAH® (tisagenlecleucel) Suspension for IV Infusion
- YESCARTA® (axicabtagene ciloleucel) Suspension for IV Infusion

Advancing Development

- ~40 companies developing CAR T therapy
- >240 CAR T trials registered on clinicaltrials.gov

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

1: BioInformant, Database of CAR T-Cell Therapy Companies 2018
2: Cell 171, CD19 CAR T Cells, December 14, 2017
CAR T Value Indicators Suggest Potential Significant Upside

### Acquisitions

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<tr>
<th>Company</th>
<th>Lead Program</th>
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<td>Kite</td>
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### Licensing Agreements

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<td>Agenys</td>
<td>$80M upfront &amp; up to $185M per product</td>
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<tr>
<td>Johnson &amp; Johnson</td>
<td>agreement with Nanjing Legend</td>
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XCART Has the Potential to Transform CAR T Therapy

**XCART**

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

Alexey V. Stepanov¹, Oleg V. Markov², Ivan V. Chernikov², Danil V. Gladkikh², Hongkai Zhang³,⁴, Teresa Jones³, Alexandra V. Sen’kova⁵, Elena L. Chernolovskaya⁶, Marina A. Zenkova², Roman S. Kalinin¹, Marla P. Rubtsova⁷, Alexander N. Meleshko⁵, Dmitry D. Genkin⁷, Alexey A. Belogurov Jr.¹, Jia Xie⁸, Alexander G. Gabibov¹, Richard A. Lerner⁹

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.
Market Opportunity – Non-Hodgkin Lymphoma Therapeutics
Estimated 2018 US Incidence of NHL: 75,000¹

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)

- Of Refractory & Relapsed DLBCL have poor prognoses:²
  - ORR: 26% (7% CR)
  - Median OS: 6.3 months

Global Market for Non-Hodgkin Lymphoma³

<table>
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<tr>
<th>Year</th>
<th>2018</th>
<th>2019</th>
<th>2020</th>
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CAGR: 7.40%

Trends in NHL Incidence Rates, 1975-2014³

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

XCART Shown to be Effective in B-Cell Lymphoma

Engineered to target a patient- and tumor-specific neoantigen

**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

1. Patient Biopsy
2. CAR Library Screen
3. Characterize & Filter Candidates
4. Verification of CAR Construct for Clinical Use
5. Manufacturing & Release Testing
6. Patient Treatment
7. Clinical CAR T Production 14-21 days
8. XCART: 6 Month Process
# Unmet Need in Follicular Lymphoma (FL)

## FL Treatment Timeline

### First Line
- **POD > 2 yrs** (80%)
  - Treatment Decisions Based On:
    - Tumor burden
    - Other risk factors (e.g. FLIPI)
  - **POD < 2 yrs** (20%)
  - **XCART Opportunity**
    - \( \approx 3,000 \) patients/yr (US)

### Second Line(s)
- **R-CHOP**
- **R-mono**
- **R-CHOP Chemotherapy**
- **Targeted Agents**
- **Radioimmunotherapy**
- **High Dose Chemo / SCT**
- **CAR T**

### CAR T Relapse
- CD19 / CD19^+&

### Patients with FL have a 28-31% probability of high grade transformation at 10 years

### Diagnosis FL

### Time to first POD is an important prognostic indicator

### 5-year survival rate: 90%
- Median OS from first POD: >12 years

### 5-year survival rate: 50%
- Median OS from first POD: 5 years

### Addressable with 6-month XCART process

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

DLBCL Treatment Timeline

0 Month 12 Months 24 Months 36 Months 48 Months

Diagnosis DLBCL

First Line (R-CHOP)

Relapse

Primary Refractory

2nd Line Ablation/ BMT

(80%)

(20%)

50%

(50%) Xplant Ineligible

CAR T

Relapse/ Refractory

50%

NET ~70% (OS 5 yrs)

Addressable with 6-month XCART process

Patient-Level Analyses r/r DLBCL

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

- 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

• 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

**Target: FL patient 1 biopsy**

- FL1-CART
- Myc-CART
- Mock

**Target: FL patient 2 biopsy**

- CD19-CART
- FL2-CART
- FL3-CART
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>/NcrCrl) 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

- Monitor Tumor Burden, T-cell Expansion & Survival
Development Approach

<table>
<thead>
<tr>
<th>2019</th>
<th>2020</th>
<th>2021</th>
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<tr>
<td><strong>Program Planning</strong></td>
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<td>• TPP</td>
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<td>• Clinical &amp; Regulatory Roadmap</td>
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<td>• Process &amp; Method Parameters</td>
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<td><strong>IND</strong></td>
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<tr>
<td><strong>Validation of End-to-End XCART Clinical Process</strong></td>
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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
PolyXen™ PSA Technology Platform
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 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
Financial Snapshot
NASDAQ: XBIO

Market Cap

Shares Outstanding

Cash Balance

~$7.8M

~$14.4M

~5.5M

1: Based on September 5, 2019 closing price of $1.42 per share; 2: Includes 1.7 million of shares from exercise of warrants; 3: As of June 30, 2019 plus ~$13.4 million net proceeds received from July 2019 underwritten public offering.
Supplemental Information

Enhancing lives with transformative therapies
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.
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

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

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

**CD19-CAR T and FL1-CAR T Prevent Development of Metastasis**

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