



## Disclaimer

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therefrom. This presentation does not imply an offering of Securities. This presentation may contain forward-looking statements within the meaning of applicable securities regulations. All statements other than statements of historical facts are forward-looking statements. In some cases, forward-looking statements may be identified by the use of words such as "anticipate," "believe," "plan," "estimate," "expect," "intend," "may," "will," "would," "could," "should," "might," "potential," or "continue" and variations or similar expressions. Readers should not unduly rely on these forward-looking statements, which are not a guarantee of future performance. There can be no assurance that forward-looking statements will prove to be accurate, as all such forward-looking state-

ments involve known and unknown risks, uncertainties and other factors which may cause actual results or future events to differ materially from the forward-looking statements. Such risks include, but may not be limited to: general economic and business conditions; technology changes; competition; changes in strategy or development plans; governmental regulations and the ability or failure to comply with governmental regulations; the timing of anticipated results; and other factors referenced in the Company's business materials and prospectuses.



## Free Writing Prospectus

Kiromic Bioharma, Inc. ("we" or "us") has filed a registration statement (including a preliminary prospectus) (the "Registration Statement") with the Securities and Exchange Commission (the "SEC") on Form S-1/A (SEC File No. 333-238153) for the offering to which this presentation relates.

Such registration statement has not yet become effective. Shares of our common stock may not be sold, nor may offers to buy be accepted, prior to the time the registration statement becomes effective. Before you invest, you should read the preliminary prospectus and other documents we file with the SEC for more complete information about our company and this offering.

You should read the prospectus in the Registration Statement and other documents that we have filed with the SEC for more complete information about us.

You may access these documents for free by visiting EDGAR on the SEC web site at

[www.sec.gov](http://www.sec.gov) or by contacting Thinkequity, a Division of Fordham Financial Mgmt., Inc.,

17 State Street, 22nd Floor, New York, NY 10004, by telephone at (877) 436-3673 or by email at [prospectus@think-equity.com](mailto:prospectus@think-equity.com).



## Offering Summary

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<b>Proposed Aggregate Offering</b>	\$25,000,000
<b>Price Range</b>	\$12.00 -14.00 per share
<b>Proposed Symbol</b>	KRBP (NASDAQ Capital Markets)
<b>Shares Offered</b>	1,923,100 Shares
<b>Pre-IPO Common Shares</b>	6,083,000 Shares as converted (07/06/2020)
<b>Post-IPO Common Shares</b>	8,006,100 Shares
<b>Use of Proceeds</b>	Advancing clinical development of PD-1, Iso-Mesothelin, our lead CAR-iNKT for the treatment of solid tumors, R&D working capital, general corporate
<b>Sole Book Runner</b>	ThinkEquity, a division of Fordham Financial Management, Inc.

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# Management

**CEO**  
Director

**Maurizio Chiriva-Internati, PhD**  
Mr. Chiriva-Internati is an associate professor at MD Anderson Cancer Center. He has spent the past 28 years studying cancer targets and is the founder of Kiromic Artificial Intelligence Neural Network. He has published +160 articles (+peer reviews) on cancer targeting and on the use of AI to expedite the search for these targets. He holds PhD in immunology (U of Nottingham), PhD in morphological science (Milan), and a Certificate in Artificial Intelligence - M.I.T.

**CSIO**  
Director

**Gianluca Rotino Chief Strategy, Innovation Officer**  
Mr. Rotino held CEO and Chairman roles in several Italian companies specializing in high-tech, and corporate consulting. He also worked at law firms in Milan where he specialized in M&A, intellectual property prosecution and corporate law. He holds a business development degree and bachelor of science (electronics) - EBD Academy in London, and completed the drug discovery, develop. and commercialization - U.C. San Diego.

**CFO**  
**COO**  
Director

**Tony Tontat**  
Mr. Tontat brings to Kiromic over 2 decades of business experience from public (NASDAQ: SRNE, NK) and privately held biotech. He had been healthcare analysts at specialist healthcare investment funds in New York, and Connecticut. He was also an investment banker at HSBC Securities in their New York, London, and Paris offices. Bachelor of Arts in Economics - Harvard University.

**CMO**

**Scott Dalhbeck, MD, PharmD**  
Dr. Dalhbeck was a radiation oncologist and was an adjunct professor of internal medicine, pathology, and urology at Texas Tech. He has also patented, manufactured, and commercialized IP and has more than a decade of experience in medical and oncology commerce. He holds an MD - Texas Health Science Center, and a PharmD - U of Nebraska. His residency was at Kaiser Permanente of Los Angeles.



## Diamond AI

Artificial Intelligence Neural Network  
for Target Selection

We are connecting the dots in cancer research by using AI and machine learning to connect silos of informations and arrive at cancer targets which will be more effective vs. classic development, saving man-years and billions in development dollars.



## Non-Viral Genome edit and delivery

Our single-cut gene edits carry a lower mutagenesis risk vs. classic double-cut gene edits.

Our CAR receptors will also have higher safety with an on-demand cut-off switch vs. classic CAR therapies with no off-switch.

# Kiromic at a Glance

Revolutionizing Next-Gen Allogenic CAR Therapy for Solid Tumors



## Gamma Delta T-cell Immune Cell Type

Our CAR Therapy will be using off-the-shelf Gamma-Delta T-cells and will have a higher yield and significantly lower yield variability vs. classic CAR-T therapies.

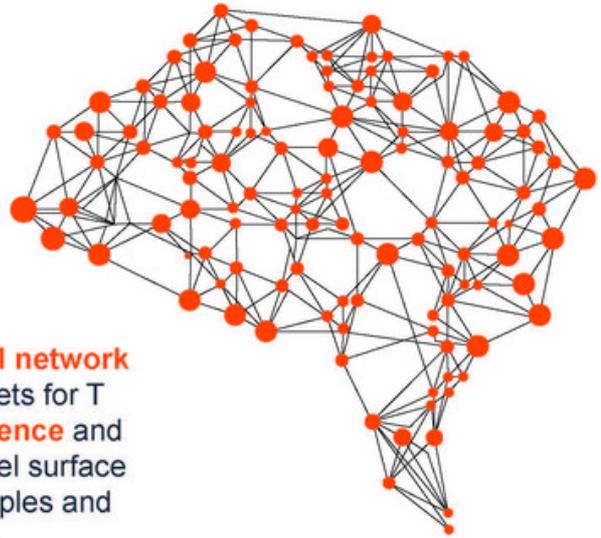


Solid Tumor

## Micro Tumor Environment

Our CAR Therapies will be able to access the micro tumor environment due to our PD-1 check-point inhibitor vs. classic CAR-T therapies.

Classic CAR-T are limited to hematologic indications.



Diamond is a computational platform and a **neural network** that can identify new cancer immunological targets for T cells and B cells. Diamond is an **artificial intelligence** and **machine learning** approach that can identify novel surface tumor targets. It uses public and proprietary samples and can expand into the tumor target space.

## ADVANCING CAR through A.I.



Big Data Science

**Big Data Science**  
*meets*  
**Target Identification**



Manual Target Identification

dramatically compressing

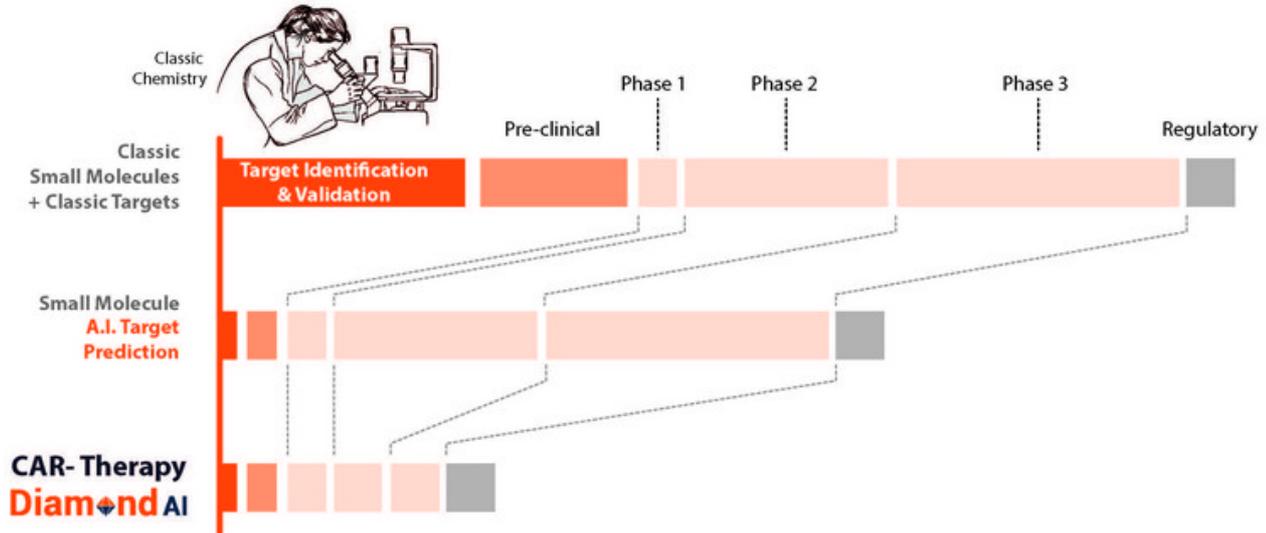
**Man-Years and Billions of Drug Development Dollars**

to develop a live drug

Artificial Intelligence Engine's

# Compression of Time & Costs

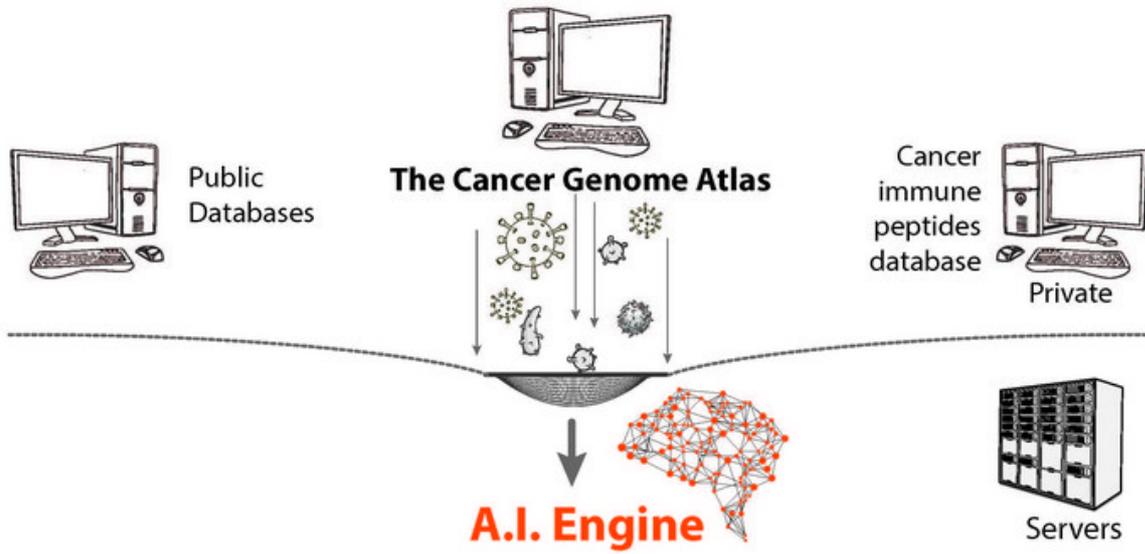
for live drug development



# Step 1



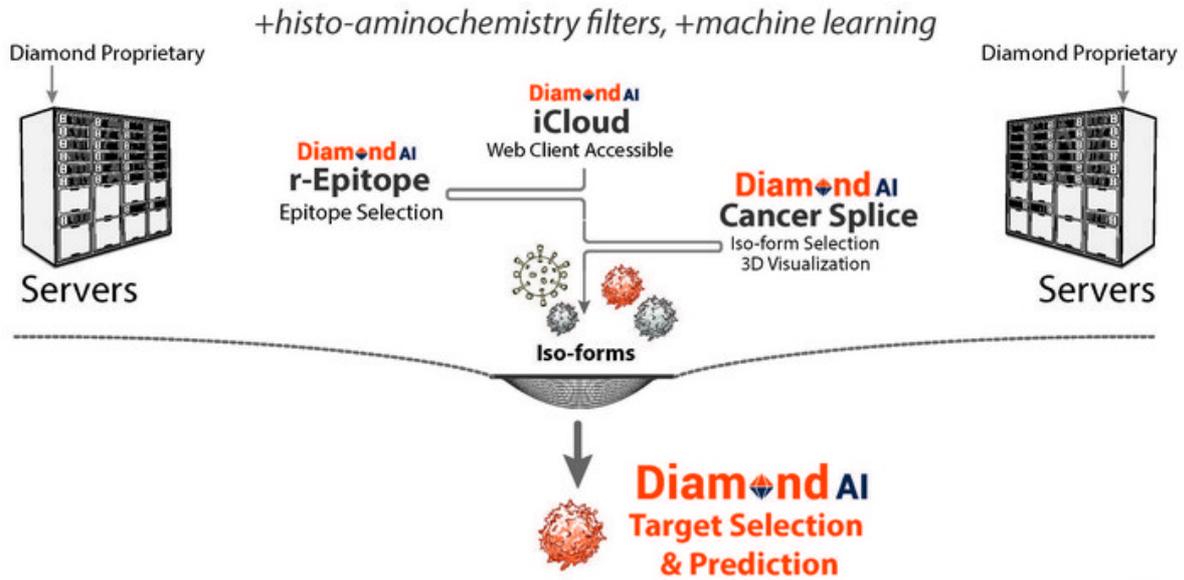
# Big Databases



# Step 2



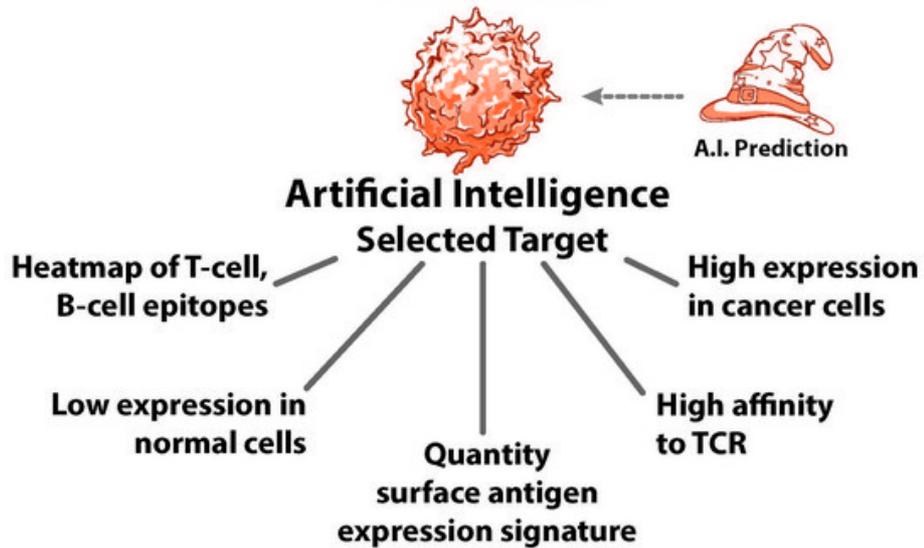
## Artificial Intelligence Engine



# Step 3

## Diamond AI

### Prediction



## Step 4



# Target Validation

*We rigorously validate all targets from our A.I. Prediction Engine  
Internal validations and then external validation*



### Wet Lab Validation

**MD ANDERSON  
CANCER CENTER**

*Baylor University*

*University of Rome*

*Humanitas Research Hospital (Milan)*



### Algorithm Validation



# Diamond AI Processes

non-exhaustive list of functions being applied by A.I. Engine

## Prioritizing T and B Cell Targets

Diamond generates a prioritized list of cancer immunological targets for T cells and B cells.

These targets can be used to create therapies such as antibody therapies, T cell therapies, T cell receptor therapies, CAR T cell therapies and vaccine therapies.

## Identify Highly Expressed Genes

Diamond's cognitive and deep learning capabilities extract information from our extensive digital library consisting of clinical studies, genomic and proteomic datasets.

Diamond harmonizes all the raw data and creates datasets which allows us to screen for cancer targets.

Diamond will identify and prioritize lists of genes (biomarkers, wild type, mutant, isoform, neoepitope, etc.) that are highly and specifically expressed in the disease of interest while providing its distribution and methylation status across the entire patient population.

It also maps out the exact portion of the gene that will elicit an immune response.

## Perform Meta Analysis

Diamond performs meta-analysis and convolution studies while standardizing and normalizing data across multiple and variable experimental platforms, then allows for the visualization of consistent and accurate results in a user-friendly fashion.

## Predict Isoform Targets

Cancer cells will down regulate or shed targets in order to avoid detection and destruction by T cells (the immune system).

These variations are known as isoforms.

CancerSplice also shows a box plot by tissue of expression of the isoform in normal cancer genome atlas tissues and a box plot of the matching isoform in genotype-tissue expression program normal data.

The sequence of amino acids that are specific for the selected cancer isoforms are then directly fed to Diamond's artificial neural capsule network for peptide design and prioritization.



# Diamond AI CancerSplice™

A key A.I. Engine

Target isoforms are protein variants of the same targets that occur during the normal processing of immature gene transcripts to the mature form.

Target isoforms include variations in their primary amino acid sequence that can change both the final folded form of the target plus their ability to be recognized by modified T cells (autologous/allogeneic) and other cells, such as NK or invariant NKT cells (often used in the allogeneic setting).

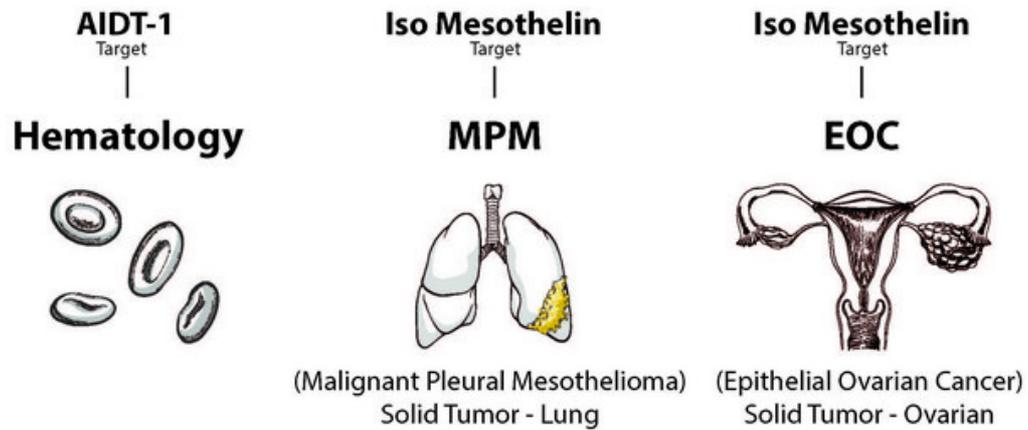
If they are the predominate form on the cell surface, these isoforms can make it impossible for T cells to outright bind the targets on cancer cells.

No binding or insufficient binding to the isoform results in no killing of cancer cells.

Our CancerSplice accurately predicts the most appropriate isoforms for T cells to bind and destroy cancer cells.

# Targets Which We Have Identified

How our identified targets are developed into therapies for live drugs to treat cancer



# Indications: By the Numbers



## Ovarian Cancer

**300,000**

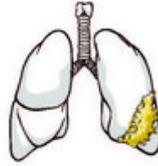
Worldwide number of patients  
American Cancer Society

**21,750**

2018 new cases in the USA  
American Cancer Society 2018

**\$1.2 BLN** in 2018

Grand View Research (July 2019)



## MPM - Lung Cancer

**43,000**

Worldwide number of patients  
American Cancer Society

**3,000**

Annually in the USA  
American Cancer Society 2018

**\$300 M** by 2025

Persistent Market Research, Jul 2017



## Hematological Cancers

**200,000**

Worldwide number of patients  
American Cancer Society

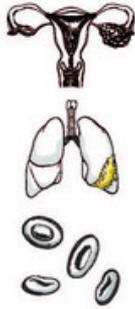
**30,000**

Annual Diagnosis in the USA  
American Cancer Society 2018

**\$4.6 BLN** by 2025

BIS Research, Nov 2019

# Our Pipeline



	In vitro validation	Pre clinical	IND	Phase 1	Phase 2	Phase 3
Alexis (γδ-T cells) Allogenic / Iso-Mesothelin EOC (Solid, Ovarian)						
Alexis (γδ-T cells) Allogenic / Iso-Mesothelin MPM /Pleural mets (Solid, Pleural)						
Alexis (γδ-T cells) Allogenic / AIDT-1 (Hematologic Indications)						
PD-1 check point inhibitor (Solid Tumors)						

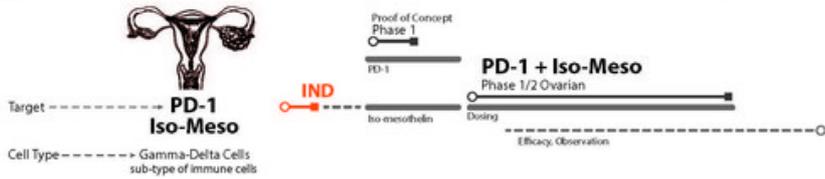
## PD-1 Check-Point Inhibition

A protein found on T cells (a type of immune cell) that helps keep the body's immune responses in check. When PD-1 is bound to another protein called PD-L1 (tumor), it helps keep T cells from killing other cells, including cancer cells. Some anticancer drugs, called immune checkpoint inhibitors, are used to block PD-1. When this protein is blocked, the "brakes" on the immune system are released and the ability of T cells to kill cancer cells is increased.

## Isoform Mesothelin

This is our lead target candidate which came out of our Artificial Intelligence Prediction Engine. Isoform targets are highly expressed on cancer cells while very lightly expressed on normal (healthy) cells.

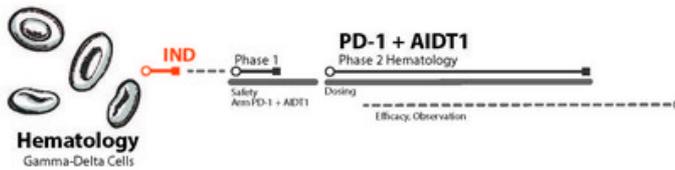
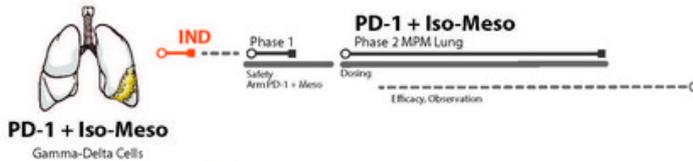
# Clinical Programs



## Solid Tumors: PD-1's Role

Classic CAR-T therapies are currently not being used in solid tumors. Solid tumors have PD-1s in their micro tumor environment. PD-1 put the "brakes" on T and NK Cells' killing of antigens (tumor cancer cells).

By inhibiting PD-1, our CAR Therapies will be able to access the micro tumor environment and kill solid tumor cancer cells which have eluded killing by classic CAR-T therapies.



# ADVANCING CAR through A.I.

Our Therapeutic Products

## Allogenic CAR

Immuno CAR-GD-T Therapy

in solid tumors

CAR = chimeric antigen receptors

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# Allogenic Engineered Immune Therapy

## Step 01: Fractionation



### Healthy Donor

Screening shows donor  
has healthy  
Gamma-Delta T cells



### Whole Blood



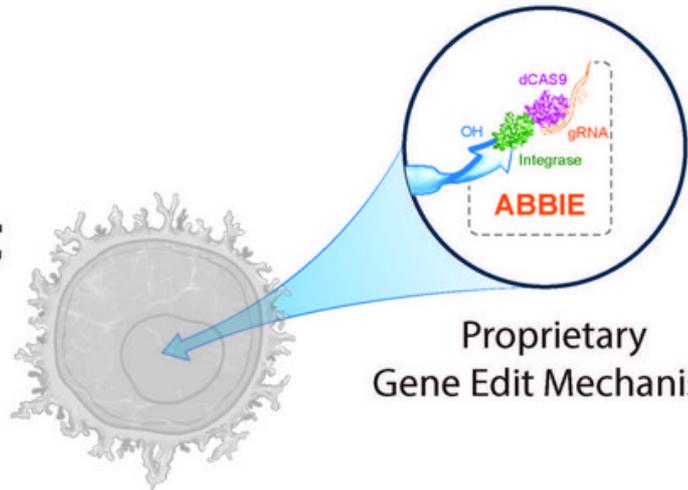
### Fractionation

Gamma-Delta T cells  
extracted

# Allogenic Engineered Immune Therapy

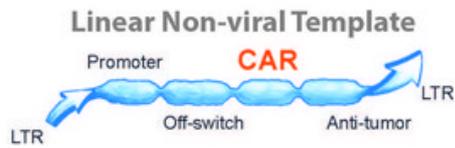
## Step 02: Genome Edit

### Genome Edit Gamma-Delta T cells

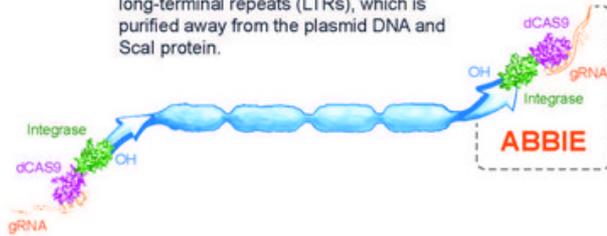


Proprietary  
Gene Edit Mechanism

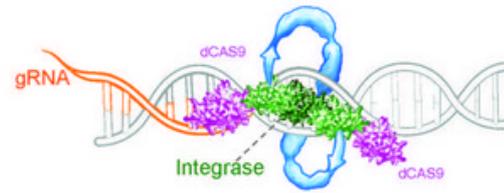
# ABBIE Gene Editing Technology



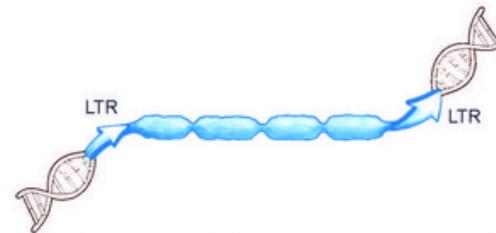
**Figure 1.** Our ABBIE gene-editing technology begins with the transgene template plasmid. Plasmid DNA is cut with restriction enzyme, *ScaI*, liberating the transgene template along with the retroviral-derived long-terminal repeats (LTRs), which is purified away from the plasmid DNA and *ScaI* protein.



**Figure 2.** The ABBIE integrase, derived from HIV, is added, which binds to the LTRs and exposes a reactive 3'-OH group on each end.



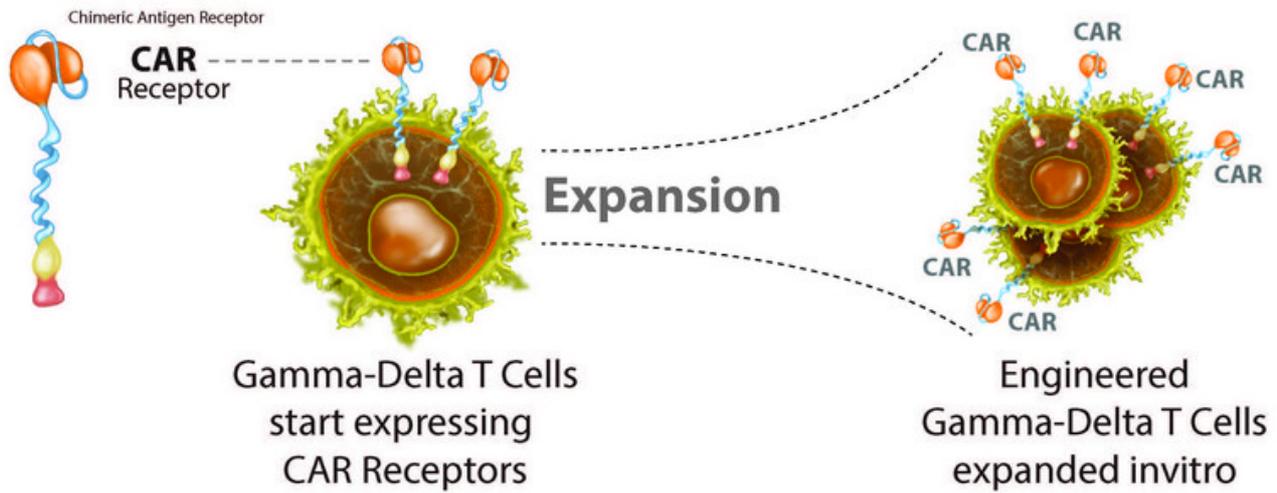
**Figure 3.** The guide RNA (gRNA) tethers ABBIE-bound template to the target site via DCas9, and Integrase helps to attach the exposed 3'OH groups to the target site on both strands without causing a dsDNA break.



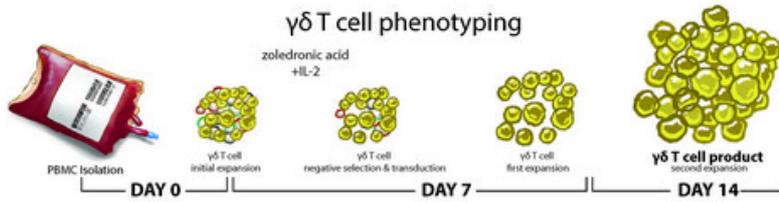
**Figure 4.** Following stable integration of the template into the target DNA locus, a short DNA duplication is present on each end.

# Allogenic Engineered Immune Therapy

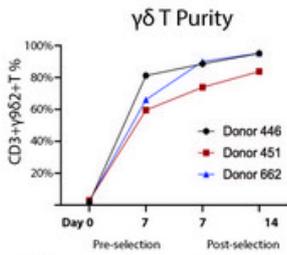
## Step 03: Gamma-Delta T Cells expanded invitro



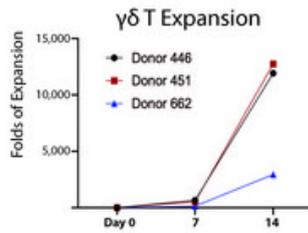
# How We Know: GD-T cell Expansion Works



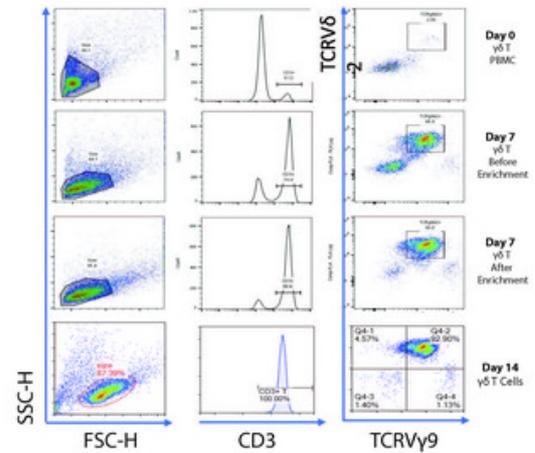
A large fold of expansion of highly pure  $\gamma\delta$  T cells during in vitro stimulation, culture, isolation and expansion process.



The percentage of CD3+ $\gamma$ 9+ $\delta$ 2+ T cells over 14-day culture.



The expansion fold of CD3+ $\gamma$ 9+ $\delta$ 2+ T cells with our method.



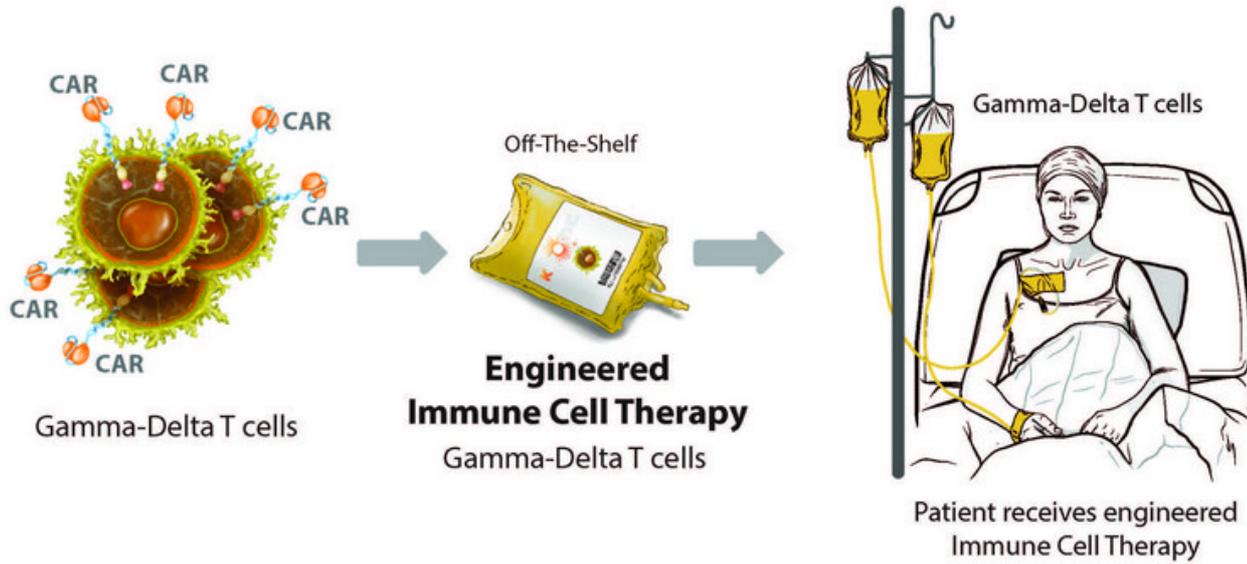
## CONCLUSION

Our method of  $\gamma\delta$  T expansion yield highest 12,000-fold expansion of  $\gamma\delta$  T cells, which is over 95% purity for positive for CD3,  $\gamma$ 9, and  $\delta$ 2.

This has potential to produce enough number  $\gamma\delta$  T for clinical use.

# Allogenic Engineered Immune Therapy

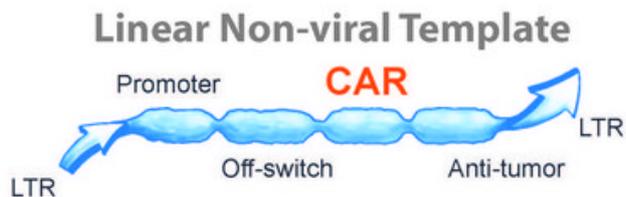
## Step 04: GD-T Cells infused into Patient



# Up-Armoring

Accessory proteins can “up-armor” cellular therapies

## Strategic choice of proteins to improve cellular function and neutralize anti-immune responses



- \* Activated signaling molecules chosen to enhance cell persistence by stimulating cytokine pathways
- \* Targeting the immunosuppressive “reactive” stroma can enable tumor targeting by therapeutic cells while increasing anti-tumor efficacy



# Switches



## ACTIVATION Switch

A rapidly deployed activation switch can provide a survival and proliferation signal to the therapeutic cells to enhance their efficacy and persistence in vivo.



## ATTENUATION Switch

A rapidly deployed attenuation switch can intercept activation signals transiently to minimize toxicity following successful anti-tumor interactions. Choice of two non-mutually exclusive Attenuation Switch approaches:

- (a) a protein-based switch that rapidly triggers attenuation of target cells in a dose-dependent fashion.
- (b) a small molecule-based approach to rapidly and reversibly attenuate cell signaling.



## SAFETY Switch

A rapidly deployed, protein-based safety switch can eliminate therapeutic cells in case of acute toxicity. The safety switch is designed to eliminate either:

- (a) essentially all active therapeutic cells.
- (b) only the most active cells, preserving a cohort of backup therapeutic cells for long-term control of residual relapsing tumor cells.

The Safety Switch will be co-expressed along with the bioactive chimeric activation receptor (CAR), the Activation Switch, and the Attenuation Switch.



# Use of Proceeds \$25M Raise

Net of offering expenses

## Clinical

\$5,600,000

Initiation of clinical trials for ALEXIS Isoform Mesothelin  
EOC and PD-1 product candidates

## IP

\$240,000

**R&D Working Capital & General Corporate**

\$16,100,000

# Comparables

## A.I. Targets + Small Molecules

**SCHRÖDINGER** **\$5.54 BLN**  
*IPO Feb 2020*

 **BLACK DIAMOND THERAPEUTICS** **\$1.13 BLN**  
*IPO Jan 2020*

 **bioXcel therapeutics** **\$1.22 BLN**  
*IPO Mar 2018*

 **Lantern Pharma** **\$76.8 M**  
*IPO Jun 2020*

## CART-T and CAR-NK

 **Fate THERAPEUTICS** **\$3.02 BLN**  
*Public*

**NEKT** **\$4.36 BLN**  
*Public*

 **Kite Pharma** **\$11.9 BLN**  
*Acquired*

 **JUNO THERAPEUTICS** **\$9.0 BLN**  
*Acquired*



# Cap Table

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Capitalization (07/13/2020)	
Common Stock	* 6,083,000
Option (WAEP \$11.84)	617,999
RSU (WAVG GDFV \$19.00)	709,334
Fully Diluted Common	7,410,332

\*Includes conversion of 21,822,301 Shares of Series A-1 Preferred Stock into 624,594 shares of common stock; 16,391,397 shares of Series B Preferred Stock into 469,136 shares of common stock

# Valuation

Valuation drivers are blended values from the following:

**Artificial Intelligence Predicted Targets**  
(vs. classic targets)

**CAR Therapies**  
(vs. classic small molecule)

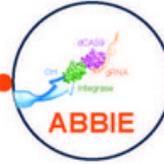
**CAR Allogenic (Gamma-Delta T cells)**  
(vs. classic CAR-T autologous)

**Solid Tumor (PD-1 checkpoint inhibition)**  
(vs. classic CAR-T liquid cancers)



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Artificial Intelligence Neural Network  
for Target Selection

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# Value Drivers

Revolutionizing Next-Gen Allogenic CAR Therapy for Solid Tumors

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**Gamma Delta T-cell**  
Immune Cell Type



Solid Tumor

**Micro Tumor Environment**

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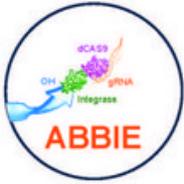


## THANK YOU

**7707 Fannin Street, Suite 140  
Houston, Texas 77054  
+1 (806) 368 - 6731**

**[ttontat@kiromic.com](mailto:ttontat@kiromic.com)**

# Intellectual Property



**Pending**

PCT/US2016/025426: CAS 9 Retroviral Integrase and CAS 9 Recombinase Systems for Targeted Incorporation of a DNA Sequence into a Genome of a Cell or Organism



**Granted**

9149441: Nanospheres Encapsulating Bioactive Material and Method for Formulation of Nanospheres

**Pending**

15/731,143: Platform for Identification of Tumor-Associated Cancer/Testis Antigens

PCT/US20/35183: Methods for Identifying and Using Diseases-Associated Antigens

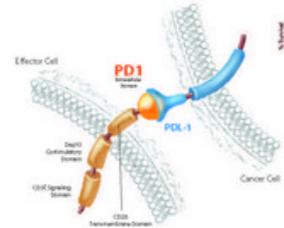
15/530,964: Anti-Human/Mouse Sperm Protein 17 (SP17) Antibody and Derivatives Thereof

PCT/US2017/022168: Compositions and Methods for Treating Cancers

15/932,396: CdS Quantum Dot-Chitosan-Anti-SP17 Nanohybrid as a Potential Cancer Biomarker

PCT/US2015/061703: Novel Nanoparticle—Based Vaccine Targeting Cancer/Testis Antigens (CTA) and its' Use in Solid and Hematological Malignancies

10004790: Nanospheres Encapsulating Bioactive Material and Method for Formulation of Nanospheres



**Pending**

PCT/US2018/052799: PD1-Specific Chimeric Antigen Receptor as an Immunotherapy

**Switch Technology  
Pending**

Provisional Patent Application No.: 63/039,364 - Tri Switch Technology for Multi-Dimensional Control of Cell Therapy

**Gamma-Delta T-cells  
Pending**

63/048,488. Mesothelin Isoform Binding Molecules and Uses Thereof



# Directors

Tony Tontat

Maurizio Chiriva-Internati, PhD

Gianluca Rotino

## *Independent*

### **Jerry Schneider, JD, MBA**

He currently serves on the board of directors and audit committee for Cognex, a provider of vision systems, software, sensors, and industrial barcode readers used in manufacturing automation since 2016. Cognex (CGNX) is publicly traded on the Nasdaq stock exchange. He serves on other for-profit and non-profit boards. Mr. Schneider received his Juris Doctor from Loyola Law School, and a B.S. in Accounting from the University of California at Berkeley. He has experience of being a "financial expert" appointed by the U.C. Regents which oversee the University of California's budget of over \$30M.

## *Independent*

### **Michael Nagel**

Mr. Nagel has served as a member of our board of directors since June 2020. He has over 30 years of sales and marketing experience in the medical device industry. Since 2012, Mr. Nagel has served as the President and CEO of Vomasit Innovations, Inc. which specializes in wireless microcurrent-generating technologies that are focused on regeneration, healing, and recovery. Previously, Mr. Nagel served as the Chief Commercial Officer of Neomend, a biomaterial company that developed ProGel, a PMA approved surgical sealant for lung surgery. From 1997 to 2005, Mr. Nagel also served as Co-Founder and Vice President of Worldwide Sales and Marketing at Vascular Solutions (VASC).

In addition to Mr. Nagel's executive experience, he also serves as a director for Franklin Mountain Medical, LLC an early stage company in the structural heart market. Mr. Nagel holds both a B.A. in Business and a M.B.A. from the University of St. Thomas.

## *Independent*

### **Americo Cicchetti, PhD**

Dr. Cicchetti has served as a member of our board of directors since March 2020. Dr. Cicchetti has served as a Professor of Management at Università Cattolica del Sacro Cuore, Faculty of Economics, Rome since 2006. He is also currently the Director of the Graduate School of Health Economics and Management at Università Cattolica del Sacro Cuore. In addition to his academic experience, Dr. Cicchetti was a member of the Price and Reimbursement Committee of the Italian National Drug Agency from 2009-2015. He is a member of the European Network of Health Technology Assessment; Member of the Innovation Steering Group of the National HTA Program for Medical Devices (Ministry of Health, Italy); Member of the National Immunization Technical Advisory Group at the Ministry of Health, Italy since 2019; Member of the Health and Research Commission of the Rome Foundation since 2007; and a Member of the Board of Directors of the Health and Research Foundation since 2017.

Furthermore, Dr. Cicchetti is the Chief Executive Officer and Director for Molipharma, whose core business is the research and development of new drugs and diagnostics aimed at predicting, detecting and treating female oncological diseases. He also serves as an independent board member for Foundation Health and Research, and Leorda SICAF, a fixed capital investment company. He obtained his PhD in Management from University of Bologna, and his B.A. from University of Rome.

## *Independent*

### **Pietro Bersani, CPA**

Mr. Bersani has served as a member of our board of directors since June 2020. Since April 2020, Mr. Bersani is a Partner with B2B CFO Partners, LLC, which provides strategic management advisory services to owners of privately held companies. During October 2016 and July 2018, he served as the President, and Chief Executive Officer at K.P. Diamond Eagle, Inc., a consulting firm specialized in development of innovative commercial and private aviation business models. He also held the same positions at K.P. Diamond Eagle, Inc. between November 2019 and March 2020. He later served as a Senior Director within Alvarez & Marsal's Private Equity Performance Improvement Practice, LLP between August 2018 and October 2019. Prior to those professional experiences, Mr. Bersani served as the Chief Financial Officer of Fuel Systems Solutions, Inc. between April 2011 and October 2016.

Mr. Bersani is a Certified Public Accountant and is also a Certified Public Auditor and a Chartered Certified Accountant in Italy where he developed a significant knowledge of US GAAP and IFRS. Mr. Bersani earned a BA and MA in Business Economics from L. Bocconi University, Italy. Mr. Bersani was designated by certain holders of our Series B Preferred Stock. Except for the foregoing, there is no arrangement or understanding between any director or executive officer and any other person pursuant to which he was or is to be selected as a director.

## Artificial Intelligence Neural Network

# 162 Internal Publications



**Chiriva-Internati M**, Cobos E, Cannon MJ. Editorial: Prospects and Challenges for Immunotherapy of Ovarian Cancer-What Can We Learn from the Tumor Microenvironment? **International Reviews of Immunology**. 2011;30(2-3):67-70.



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Wachtel MS, Zhang Y, Xu T, **Chiriva-Internati M**, Frezza EE. Combined hepatocellular cholangiocarcinomas; analysis of a large database. **Clin Med Pathol** 1:43-7. 2008



Mirandola L, J Cannon M, Cobos E, Bernardini G, Jenkins MR, Kast WM, **Chiriva-Internati M**. Cancer testis antigens: novel biomarkers and targetable proteins for ovarian cancer. *Int Rev Immunol*. Apr-Jun;30(2-3):127-37. doi: 10.3109/08830185.2011.572504. 2011

Bumm K, Zheng M, Bailey C, Zhan F, **Chiriva-Internati M**, Eddlemon P, Terry J, Barlogie B, Shaughnessy JD Jr. CGO: utilizing and integrating gene expression microarray data in clinical research and data management. **Bioinformatics**. 2002 Feb;18(2):327-8. 2002

**Maurizio Chiriva-Internati**, Leonardo Mirandola, Franco Marincola, Gianluca Rotino, Jose A. Figueroa, Fabio Grizzi, and Robert Bresaller The Quest for the Next-Generation of Tumor Targets: Discovery and Prioritization in the Genomics Era. Springer, Published 2019 ( chapter for a book "immune-Oncology: Cellular and Translational Approaches" 2019

**Maurizio Chiriva-Internati** & Adrian Bot. New Era in Cancer Immunotherapy: Discovering Novel Targets and Reprogramming the Immune System. **International Reviews of Immunology**, 34:2, 101-103. 2015

Grizzi F, Gaetani P, Tancioni F, Di Ieva A, Bollati A, Baena R, Dioguardi N, and **Chiriva-Internati M**. From Discovery to the Clinical Application In Nervo System Neoplasia. In: Tumor Associated Antigens, 2004.

Figueroa AJ ,Pena C ,Mirandola L, , Reidy A , Payne D, Hosiuluck N, Suvorava N, Rahman LR , Whitlow AR ,Verma R , Cobos E and **Chiriva-Internati M**. "Therapeutic Monoclonal Antibodies and Their Targets" by Wiley Production\_Biosimilars of Monoclonal Antibodies: **A Practical Guide to Manufacturing, Preclinical and Clinical Development, First Edition**. Edited by Cheng Liu and K. John Morrow Jr. © 2017 John Wiley & Sons, Inc. Published 2017.

Grizzi F, Russo C, Portinaro N, Hermonat PL, **Chiriva-Internati M**. Complexity and cancer. **Gastroenterology**. 2004 Feb;126(2):630-1; author reply 631-2. PubMed PMID: 14765401.2004

## ABBIE: Non-Viral Genome Editing Mechanism

ABBIE is a novel gene-editing system for inserting therapeutic genes safely into the genome of a host cell.

ABBIE technology comprises two main components,

(i) a genome template (extracted from the ALEXIS plasmid), containing the therapeutic genes needed to retrain tumor-killing cells, and

(ii) the gene-editing machinery required to safely insert this template into the genome of the therapeutic cells.

The ABBIE protein accompanies the CAR-containing genome template as it passes through the cell membrane into the nucleus and guides the template-flanking sequences (the "glue") safely into the target genome.

Due to this targeting ability, ABBIE can also be used to remove unwanted, inhibitory genes. CAR expression on the Gamma-Delta T cells allows them to detect and destroy the antigen-expressing targeted cells.

The OFF switch permits fast shutdown in the event of an unexpected toxicity. Additional Anti-tumor factors can help neutralize the toxic tumor microenvironment.