

## Gaining momentum.

Annual General Meeting November 2021

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## At the 2020 AGM we said:

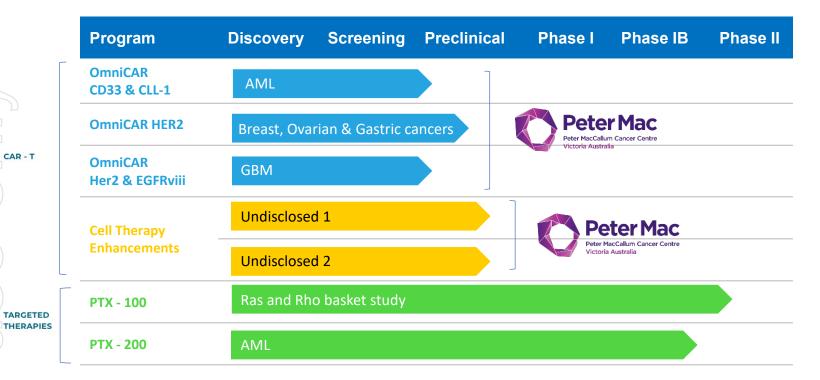


## A YEAR OF TRANSFORMATION

Annual General Meeting November 2020

## **Innovative Pipeline in Personalised Medicine**







# Key achievements during another productive year



- Strategic review of OmniCAR to identify three highly differentiated internal programs
  - AML

**Cell Therapies** 

- Her2+ solid tumours
- GBM
- Initiation and progress of these OmniCAR programs
- Manufacturing and testing of key OmniCAR components
  - Successful demonstration of unique OmniCAR features
  - CAR-T agreement with Peter Mac
- Transitioned Cell Therapy Enhancement program to Peter Mac



## **Targeted Therapies**

- Progression of PTX-200 in AML
- Completion of PTX-100 Phase 1b basket trial
  - Excellent safety profile
  - Encouraging data in area of unmet need
- Manufacturing PTX-100
- Investigating IST opportunities

## **Operations**

- Building world class capabilities
  - Bolstering PTX team in areas including:
    - cell therapy
  - immunology
  - biologic engineering
  - clinical operations
  - PTX & Peter Mac: a very productive and cohesive relationship
  - Full time post docs at Peter Mac together with Professor Phil Darcy
  - Significant business development interest



**Rebecca Lim, PhD** Director of Scientific Affairs



Leanne West Director of Clinical Affairs and Operations

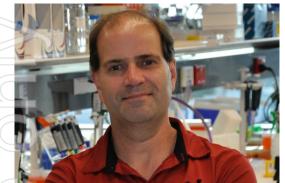




Daniel A. Shelly, PhD, MBA VP – Business Development & Alliances

## Assembling a world class Scientific Advisory Board





#### **Professor Phil Darcy**

Eminent CAR-T expert



#### Professor H. Miles Prince, AM

Internationally renowned haematologist

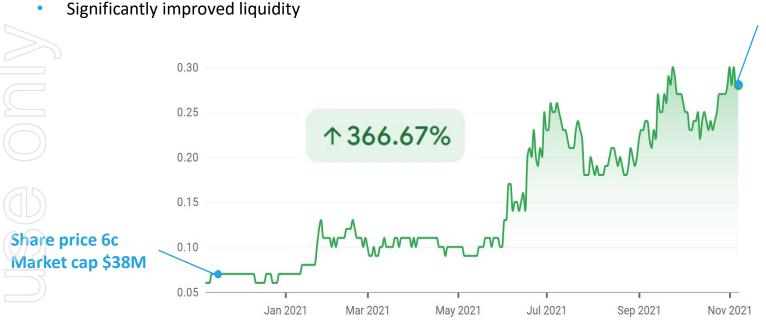


#### Professor Don O'Rourke, MD

Neurosurgeon & brain cancer key opinion leader

## Achievements becoming reflected in company valuation

• PTX one the best performing biotech stocks on ASX this year





## **Overcoming challenges**



#### COVID-19

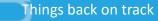


- No specific and material disruptions, but impossible to escape its impact
- US disruptions in 2021
  - AML recruitment



Manufacturing and logistics bottlenecks





Pre-clinical work forged ahead despite Australian lockdowns

#### **Science and technical**



- New modality required bolstering inhouse expertise in new areas
- Matched by world-class SAB and Peter Mac collaboration
- Would novel experiments work in our hands? Even then, how long would it take?
- Outcomes: successful and rapid progress across programs

#### **Building OmniCAR awareness**



- One challenge of being "ahead of the curve" is educating stakeholders on cell therapy limitations and OmniCAR's capabilities
- Industry, clinicians, investors
- The more parties understand cell therapy, the more they appreciate the value of the platform!
- Playing the long game, and it is starting to pay off.





## **PTX-100**

FIRST IN CLASS RAS PATHWAY INHIBITOR

#### **PTX-100 PHASE 1B BASKET STUDY COMPLETED**



- Phase 1b PK/PD safety study
  - Focus on cancers prone to Ras and Rho mutations
- Basket trial of:
  - Gastric cancer
  - Pancreatic cancer
  - Colorectal cancer

- Myeloma
- T-cell lymphomas



Professor H. Miles Prince, AM Principal Investigator

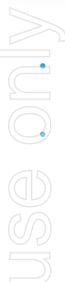


#### PTX-100 PHASE 1B SUMMARY



#### Prescient takes its PTX-100 trial to next level after Phase 1b success

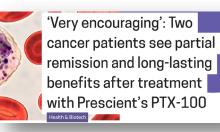
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#### **Excellent safety profile**

PTX-100 well tolerated up to and including 2,000 mg/m<sup>2</sup>

No SAEs related to PTX-100



## Prescient Therapeutics (ASX:PTX) expands trial of PTX-100

Health Care

#### **Early clinical activity**

- PRs in 2 patients with aggressive refractory TCL
- Expected PFS of <4 months on SoC</li>
  - r/r CTCL: **12 months** (19 cycles)
  - r/r PTCL: **17 months so far** (24 cycles, still on therapy)

### **PROGRESSING TO EXPANSION COHORT**

- 8 12 patients with r/r T cell lymphoma (esp PTCL)
  - Potential bridge to registration study
  - Focussing on sweet spot in an area of considerable unmet need
  - Shortest path to market
  - Awaiting delivery of drug product to Australia – US-wide manufacturing and logistics bottlenecks!
    - Working closely with manufacturer

#### **Case Study**

- pralatrexate (Folotyn<sup>®</sup>)
- Approved for PTCL
  - 5,600 cases/year in US
- US\$450,540 per patient, per year







## PTX-200 NOVEL AKT INHIBITION

### PHASE 1B TRIAL UNDERWAY: ACUTE MYELOID LEUKEMIA

- Building upon encouraging Phase 1 results with PTX-200 (monotherapy)
- PI Professor Jeff Lancet at Moffitt, with Dr Tara Lin at KUMC
  - 18 patients with cytarabine held constant at 200-400 mg/m<sup>2</sup> as continuous infusion
    - 3 CRs so far
  - Both sites were impacted by general COVID-19 disruptions in 2021, which impacted recruitment and correlative analysis
    - Currently screening second cohort at 45 mg/m<sup>2</sup>
    - Granted Orphan Drug Designation by US FDA









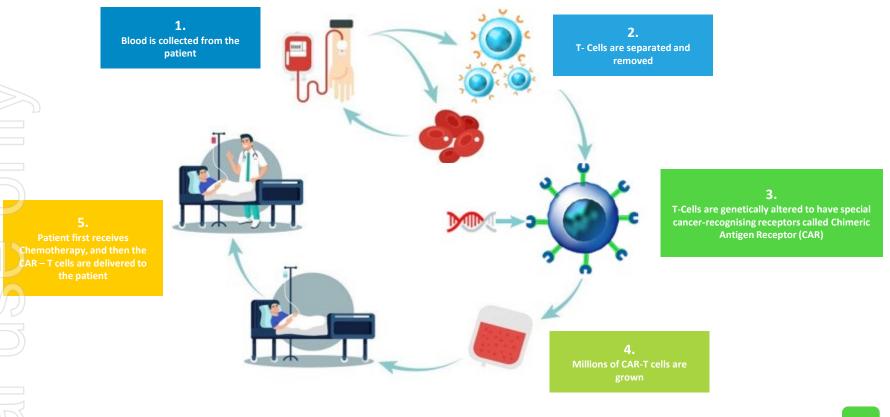




**Universal, Next Generation CAR-T** 

## How does the CAR-T process work?

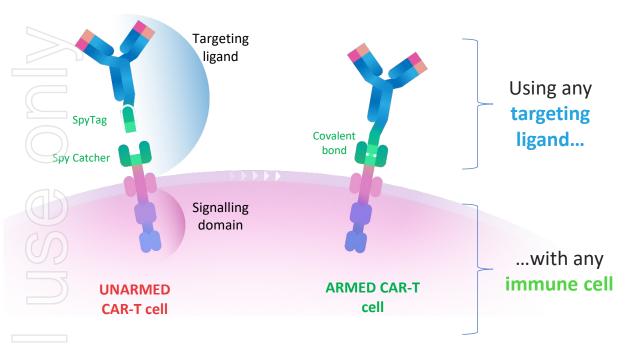




## **OmniCAR: flexible, modular CAR platform**













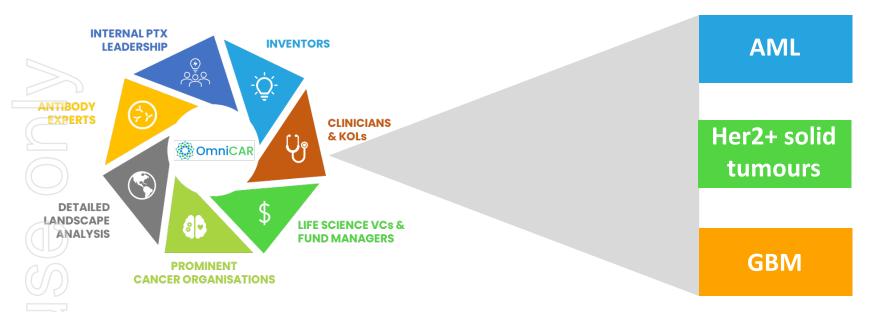
Associate Professor Daniel J. Powell, Jr Professor Andrew Tsourkas





# Thorough strategic review yielded 3 internal OmniCAR programs





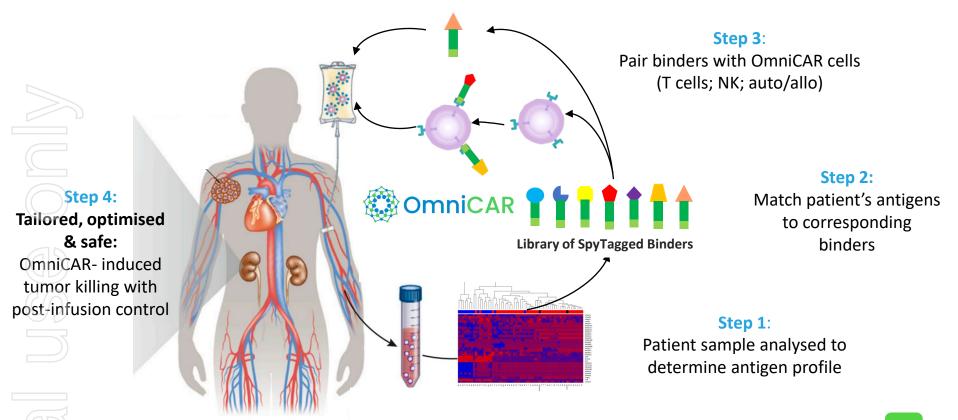
Prescient understands the landscape, challenges and opportunities



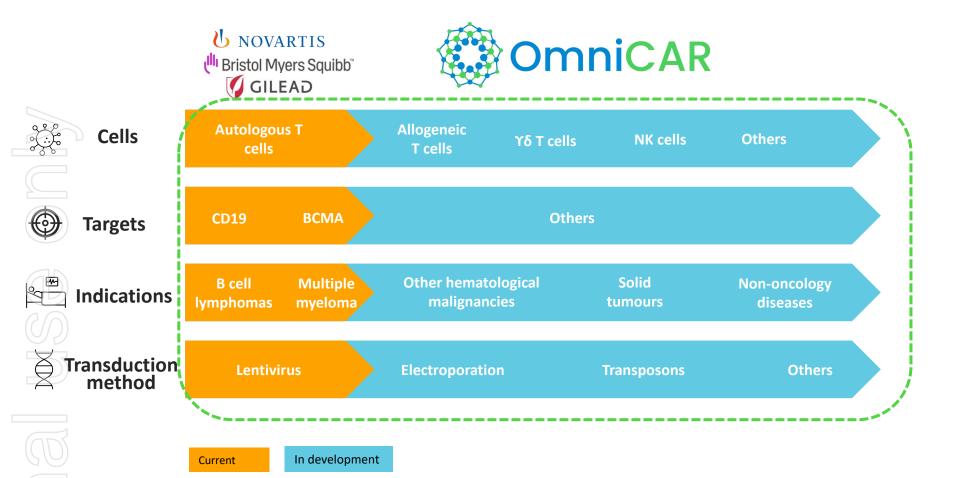
# What is the broader vision for cell therapy?

#### The future is efficient yet personalized: OmniCAR cells + "plug & play" binder library



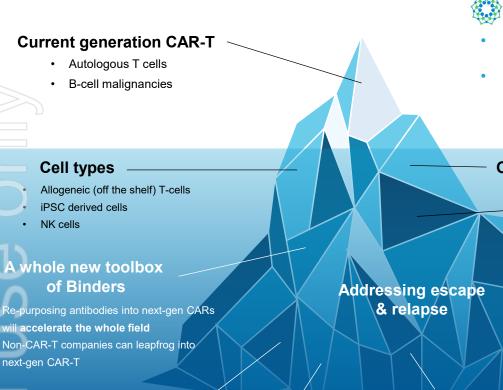


## Strategically positioned in a rapidly moving landscape for cell therapy



## With OmniCAR, this is just the start for CAR-T





Overcoming T-cell Exhaustion

**Companion diagnostics** 

## 

Adaptable and tailored CARs

- Seeking to enhance current generation CAR-Ts....
- ...& more significantly, help realise the broader potential of CAR-T, which is much bigger opportunity!

#### Other hematological malignancies

#### Solid tumours!!!

- Novel antigens & optimising antigen combinations
- Overcoming trafficking
- Tumor microenvironment

#### Safer CAR-T = more applications

- Safer and more controllable next-gen therapies will bring CAR-T to many more patients
- Opens opportunities beyond oncology

## **Business development**

- Extremely active business development activities, spearheaded by Dr Dan Shelly (US)
  - Different parties have different drivers
    - **Incumbent cell therapy players:** Top priorities are maximizing returns on their existing programs
    - **Emerging companies:** Believe the "second mouse will get the cheese"; looking for technologies to leapfrog competitors
    - **Companies with binders:** e.g. antibody companies. See OmniCAR as a way to add enter the cell Tx field and bolster their pipelines
    - OmniCAR can benefit all these groups!
  - Prescient is playing the long game for the <u>right</u> parties



#### **Considerations include:**



What is the party brining to the table, and how will it help us win?



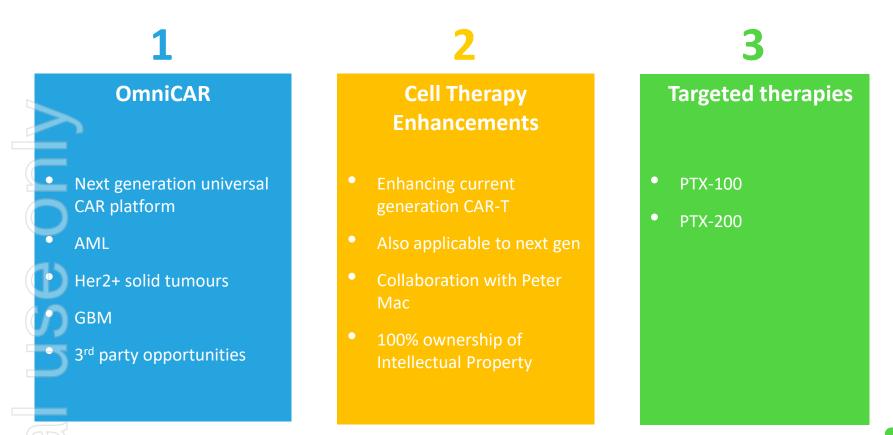
Balance between doing a deal and not jeopardising the bigger picture



# Summary

### Key building blocks to PTX Future Value





## In the next 12 months we will work towards:



- Ongoing business development
   activities
- Continuing to build awareness among investors, clinicians and corporates

- Announce further value-adding milestones for each OmniCAR program (several throughout 2022)
- Cell Therapy Enhancements come out of stealth mode (Q1/Q2 2022)
- Commence recruitment for PTX-100 expansion cohort in PTCL (Dec 2021) – awaiting drug delivery

PTX-100 expansion cohort read-out (~Q4 2022)

•

- Completion of enrolment in PTX-100 expansion cohort (Q2/3 2022)
  - Results for PTX-200 Ph1b AML trial (Q2 2022)
  - Dose escalation for PTX-200 Ph1b AML trial (Q1 2022)

\* Estimates only, given inherent uncertainty of biotech development



# Thank you!

ASX code: PTX

www.ptxtherapeutics.com



## Appendices

## **Key Challenges confronting the field of CAR-T**





#### Time and Cost

of delivering treatment



CAR-T can have serious safety concerns



#### Exhaustion

Targets

Finding targets that work;

Persistent stimulation of CAR-Immune cells leads to exhaustion

Antigen heterogeneity - esp. in solid tumours

#### **No Control**

Clinicians have no control of cells post infusion



#### Escape

Antigen loss leads to relapse

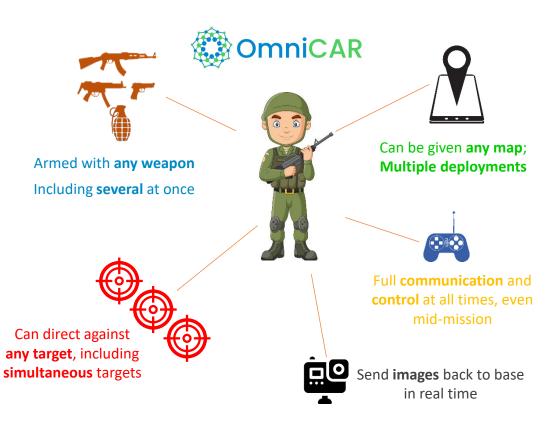
## **OmniCAR can do what conventional CAR-T cannot**



**Conventional CAR-T** 



- Soldier with only one map
- Single weapon
- Only trained to hit one target
- Incapable of redirection
- No communication or control in the field

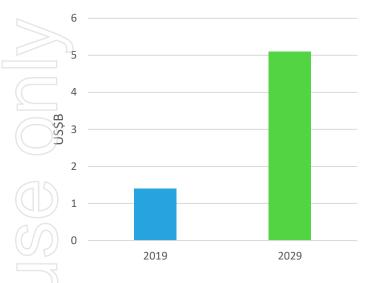




# CD33 & CLL-1 for AML

#### **Global AML market opportunity**





GlobalData; June 2020

#### AML Market Growth

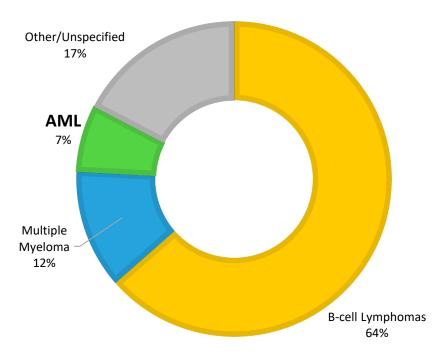
- AML market is expected to reach US\$5.1B in 2029
- CAGR of 13.6%
- Growth assumptions largely based on new targeted therapies
- Any CAR-T breakthrough in AML would grow this market further



## Landscape for CAR-T in blood cancers







# For CAR-T to succeed in AML, it must overcome:





#### Safety

AML patients are especially ill with many unable to tolerate vigorous therapies like CAR-T



### **Rapidly Mutating Disease**

AML can mutate midtherapy, quickly rendering single CAR-Ts infective



### **Rapid Disease Progression**

Even if multiple current generation CAR-T therapies were available, resistant patients are likely to progress before subsequent therapies are manufactured for them

**OmniCAR is uniquely placed to address these CAR-T challenges in AML** 

## **OmniCAR CD33/CLL-1 for AML**

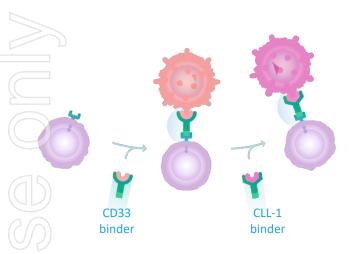


Targets	OmniCAR features	Comments
	<ul> <li>Titration (and ability to switch off/on) for improved safety &amp; tolerability</li> </ul>	<ul> <li>Validated targets</li> </ul>
CD33 + CLL-1	<ul> <li>Co-arming against CD33 &amp; CLL-1</li> </ul>	<ul> <li>Expressed on &gt;90% of AML blasts &amp; LSCs</li> </ul>
	<ul> <li>Sequential or simultaneous targeting</li> </ul>	
	<ul> <li>Ability to cease treatment to avoid neutropenia</li> </ul>	<ul> <li>Only 1 of 3 programs worldwide targeting CD33 &amp; CLL1</li> </ul>

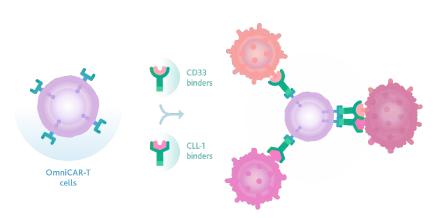
# **Unique OmniCAR flexibility important in AML**



Sequentially



## Simultaneously





## AML peer with CD33/CLL1 CAR-T



	Legend Biotech Corp	Prescient Therapeutics
Ticker	NASDAQ: LEGN	ASX: PTX
Market Cap	A\$8.2B	A\$174M
AML program	CD33 + CLL1	OmniCAR CD33 + CLL1
Generation	Current generation,	Next generation,
Generation	autologous	autologous
Stage of development	Phase 1	Discovery/Pre-clinical
Titratable for safety	×	$\checkmark$
Switch on/off	×	$\checkmark$
Persistent dosing without new cell product	×	$\checkmark$
Able to switch antigen targeting	×	$\checkmark$





Her2 for Ovarian, Breast & Gastric cancers

# **Key challenges for CAR-T in solid tumours**











**Targets** Limited targets that are cancer-specific Leads to on-target,

off-tumour effects

### Safety

Ability to titrate doses safely and switch off in the event of adverse events

### Trafficking

Inability of T-cells to reach tumour sites and penetrate physical barriers

#### TME

Overcoming an immunosuppressive Tumour Microenvironment once they get there

OmniCAR's features enable it to address these solid tumour challenges



# **Huge market opportunities for Her2+ cancers**



87,000
,
340,000
209,440

- Very large patient populations
- "Basket study" approach
- Patients failing Herceptin treatment would make excellent candidates

Luo, H et al, The prognostic value of HER2 in ovarian cancer: A meta-analysis of observational studies. PLoS ONE 13(1) 2018

Bang YJ, et al. Trastuzumab in combination with chemotherapy versus chemotherapy alone for treatment of HER2-positive advanced gastric or gastro-oesophageal junction cancer (ToGA): a phase 3, open-label, randomised controlled trial. *Lancet* 2010;376:687-97.

World Cancer Research Fund

<sup>-</sup> Shang AQ, et al. Relationship between HER2 and JAK/STAT-SOCS3 signaling pathway and clinicopathological features and prognosis of ovarian cancer. Cancer biology & therapy. 2017:1–9

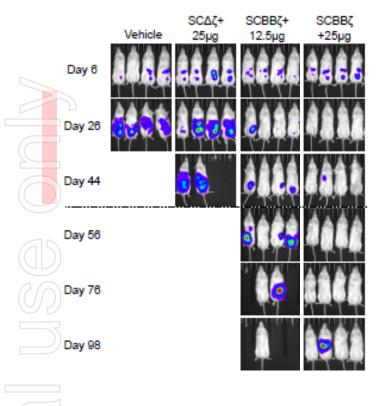
## **OmniCAR Her2 for Her2+ solid cancers**



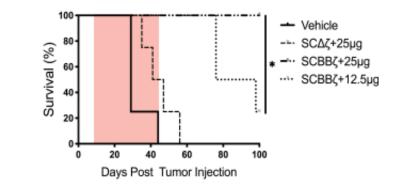
Her2• Titration for improved safety & tolerability• Validated targetHer2• Persistent binder dosing for improved efficacy and persistence• Large difference of antigen expression on tumor vs healthy tissue• TME and checkpoint enhancements• Most mature next-gen Her2 CAR-T program	Target	OmniCAR features	Comments
	Her2	<ul> <li>Persistent binder dosing for improved efficacy and persistence</li> </ul>	<ul> <li>Large difference of antigen expression on tumor vs healthy tissue</li> <li>Most mature next-gen Her2 CAR-T</li> </ul>

## **OmniCAR Her2:** durable, dose-dependent CAR-T activity





- Ovarian cancer model, using anti-Her2 OmniCAR
- Loading more binder results in **proportionate killing** of cancer...
- ...and proportionate survival
- Lasting effects even when cease dosing of binder



## **Notable Her2 CAR-T peers**



• Prescient the **most advanced next-generation CAR-T** program in Her2

>	Shenzhen Geno- Immune Medical Institute <sup>1</sup>	Tessa Therapeutcs <sup>2</sup>	Fate Therapeutics	Novartis <sup>3</sup>	Calibr	Xyphos	Prescient Therapeutics
Status	Hospital	Private Company	NASDAQ: FATE; Market cap A\$9.3B	Global pharma company	Research Institute	Acquired by Astellas 2019	ASX: PTX Market cap A\$174M
Indications	Breast cancer	Multiple cancers	Breast & other unspecified cancers	Ovarian cancer	Breast cancer	Solid cancers (unspecified)	Ovarian, Breast, Gastric
Generation	Current generation, autologous	Current generation + oncolytic virus	Current generation, autologous	Current generation, autologous	Next generation, autologous	Next generation, autologous	Next generation, autologous
Stage of development	Phase 2	Phase 1	Discovery	Discovery	Discovery	Discovery	Pre-clinical



1. Together with The Sixth Affiliated Hospital of Sun Yat-sen University

2. Together with Baylor College of Medicine





Her2 & EGFRviii for GBM

## **CAR-T challenges in GBM: single antigen targeting**



Limited effectiveness of CAR-Ts only targeting a single antigen in GBM

"A major limitation of a single-antigen targeting in GBM is the inherent heterogeneity and plasticity of the tumor cells, allowing some cells to **escape CAR-T** cell killing due to the **loss of the targeted antigen**..."

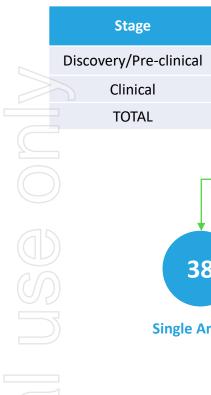
...**single antigen-targeting** CAR-T cells **fail to completely eradicate** brain tumors resulting in antigen negative **relapses**"

By contrast, CAR-Ts targeting multiple antigens have demonstrated anti tumor responses and more importantly prevented antigen escape in vivo

REVIEW	Open Acce
Chimeric antigen recept	or T-cell therapy
in glioblastoma: chargin	
Craig A. Land <sup>1</sup> , Phillip R. Musich <sup>1</sup> , Dalia Havdar <sup>1</sup> , Giedre	
Abstract	
Glioblastoma multiforme (GBM) is the most common mail	
impedes surgical eradication, resulting in early local recur agents lack permeability across the blood brain barrier (M	0), further reducing the efficacy of chemotherapy. Thus,
effective treatment against GBM requires tumor specific to recent advances in immunotherapy, genetically engineers	
ing a promising approach for treating cancer. By transduct associated antigen (TMA) recognition domain linked to the	ng Tlymphocytes with CAR constructs containing a tumo
may recognize a predefined TAA with high specificity in a	non-MHC restricted manner, and is independent of antige
processing. Active T cells can travel across the 888, providi ing. Here we review the CAR design and technical innovat	ions, the major targets that are in pre-clinical and clinical
development with a focus on GBM, and multiple strategie Keywords: Chimeric antigen receptors, CAR, T-cell therap	
	, and an a constant of the second state
Background Glioblastoma (GBM), WHO erade IV elioma, is the most	rates to about 50% of patients [4, 5]. During the su- period, genetically engineered T cell receptors (T)
devastating brain tumor in adults [1]. The intrinsic capa-	were explored to achieve robust T cell responses wh
bility of single tumor cells to invude normal brain tis- sue impedes surgical eradication, predictably resulting	ultimately led to the emergence of chimeric antip receptor (CAB) T-cell therapy [6, 7]. In 2017, CD19-C
in early local recurrence and death. Current treatment options for GBM include maximal surgical removal,	(tisagenlecleucel) became the first FDA-approved CAI cell therapy for treating patients with relapsed or refr
radiotherapy and chemotherapy. However, the overall	tory B cell acute lymphoblastic leukemia (ALL) [8].
survival rate has not changed significantly over the past decade.	The first ACT-based attempts for GRM therapy star about 40 years ago when several case reports showed t
Adoptive cell transfer (ACT) using autologous lym- phocytes for treating career started in 1988 with meta-	autologous leukocyte infusion into the resection cavit the time of tumor resection may improve patient's a
static melanoma patients [2]. While early trials reported	vival without tonicity [9-11]. However, these approach
an overall response in approximately 34% of patients [3], subsequent studies demonstrated that hyphodepletion	lacked specificity. To overcome this, genetic enginee T cells have been generated to specifically target be
price to ACT may significantly improve the response	tumor associated antigens (TAA) and have shapeoenising pre-clinical results. For GBM, interfeaking
Correspondence: aegligensieds	receptor alpha 2 (IL138a2) became the first CAR T-
Department of Biomedical Sciences, Quillen College of Medicine, East Tennesare State University Johnson City, TN XN14, USA	target tested in the clinic for its specific overexp sion in tumors but not in normal tissues [12]. Epider
full lot of author information is available at the end of the article	growth factor receptor variant III (EGFRsdII) [13], han
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## **Competitive landscape in CAR-T GBM**





Company data

# **# CAR-T programs** 25 16 41 38 3 **Single Antigen Multiple Antigens**

## OmniCAR 1 of only 3 targeting multiple antigens

- OmniCAR the only next gen CAR-T
- (The 2 other programs are at a not-for profit)





Targets	OmniCAR features	Comments
Her2 + EGFRviii	<ul> <li>Multivalent antigen targeting</li> <li>Persistent binder dosing for improved efficacy &amp; persistence</li> <li>Titration for improved safety</li> </ul>	<ul> <li>1 of 3 multiple antigen programs in the world</li> <li>Single antigen targeting is inadequate in GBM</li> </ul>

