



# Developing Next Generation Programmed T Cell Therapies

January 2022



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LEAD CLINICAL PROGRAM

obe-cel

For treatment of B-ALL and B-NHL

# Driving value with potential best-in-class adult ALL program

Multiple clinical data read-outs in 2022

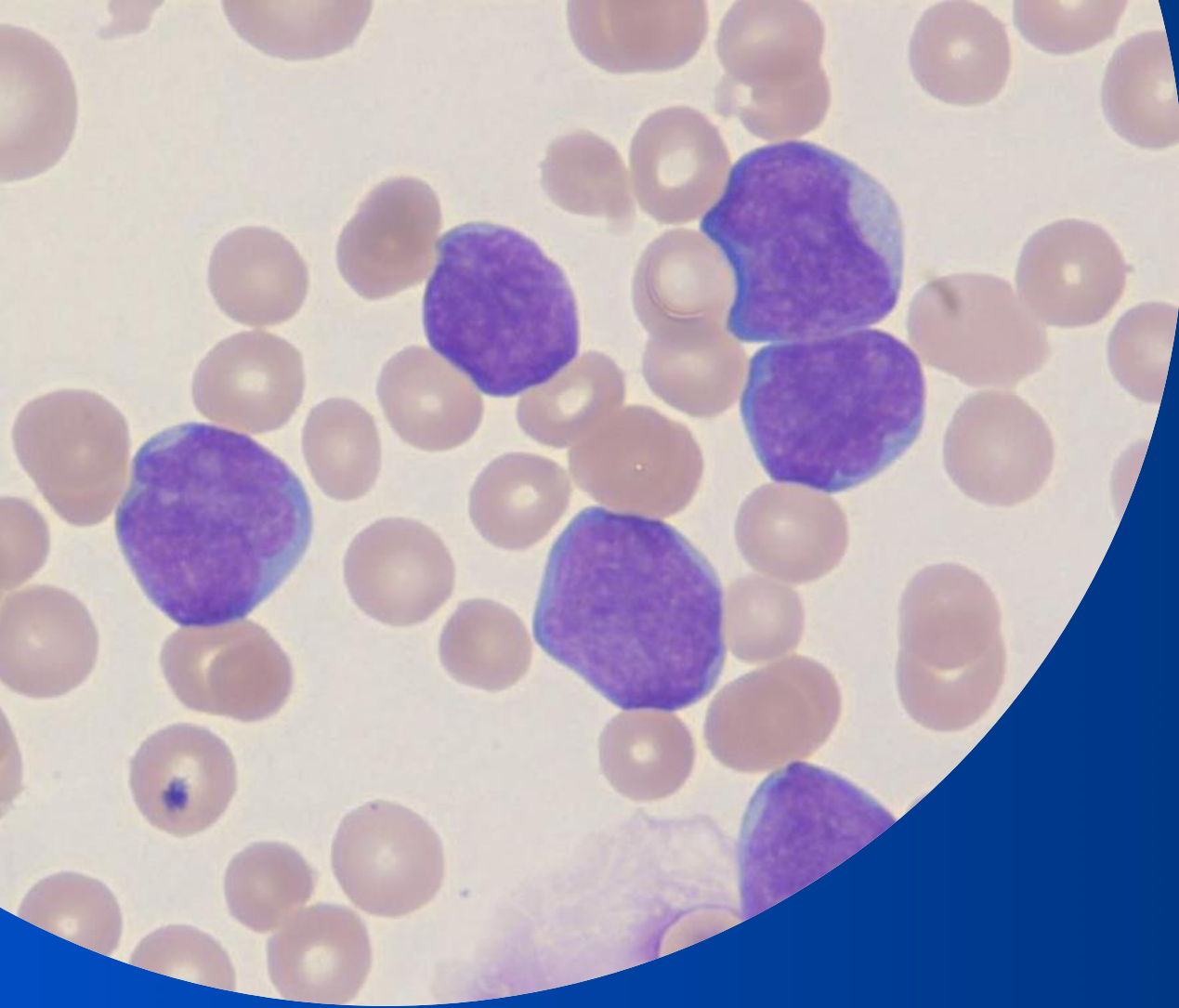
**Focused on delivering  
obe-cel, a potentially  
transformational treatment  
for Adult ALL**

Data for obe-cel (FELIX)  
trial in adult ALL expected  
in 2022

obe-cel data in B-NHL  
indications in H1 2022

Next generation  
AUTO1/22 data in  
pALL in H1 2022

- Additional value steps in T cell lymphoma and first solid tumor indication in 2022 and 2023
- Broad preclinical pipeline of next generation programs expected to transition to clinical stage in 2022
- Building on a scalable, fully enclosed manufacturing platform



# Adult Acute Lymphoblastic Leukemia

obe-cel — Potential as a standalone therapy

# High unmet need for adult ALL patients

Successful therapy requires high level of activity and sustained persistence paired with good tolerability

**ALL is a  
significant  
opportunity**

Up to **8,400**<sup>1</sup> new cases of adult ALL diagnosed yearly worldwide

Estimated R/R patients in US & EU **3,000** addressable patient population in last line setting

## HIGH UNMET MEDICAL NEED

- Combination chemotherapy enables 90% of adult ALL patients to experience CR, but only 30% to 40% will achieve long-term remission
- Median overall survival is < 1 year in r/r adult ALL
- Only redirected T cell therapies for adult patients are blinatumomab and brexucabtagene autoleucel
- CAR T therapies are highly active, but require subsequent allograft to achieve durability
- Patients are generally more fragile with co-morbidities, yet CAR T toxicities in this setting have been notable with high incidences of severe CRS and cases of fatal neurotoxicity
- Opportunity to expand the addressable patient population in earlier lines of therapy

Obe-cel granted Orphan Drug designation by FDA for B-ALL, Prime designation in R/R B-ALL by EMA And ILAP designation by MHRA in Adult R/R B-ALL

## NOTES

1. SEER and EUCAN estimates (respectively) for US and EU epi



# Unmet medical need in r/r adult ALL despite approved agents

Current standard of care and recently approved agents in r/r adult ALL

	Standard of Care		Recently FDA approved
	Blincyto <sup>1</sup>	Besponsa <sup>2</sup>	Tecartus <sup>3</sup>
N	271	109	54
ORR (CR & CRi) (95% CI)	44% (38%, 50%)	81% (72%, 88%)	65% (51%, 77%)
EFS/PFS	31% @ 6m ~10% @ 18m	~45% @ 6m ~20% @ 18m	~65% @ 6m ~25% @ 18m
median DoR (95% CI)	7.3m (5.8, 9.9)	4.6m (3.9, 5.4)	13.6m (8.7, NE)
median OS (95% CI)	7.7m (5.6, 9.6)	7.7m (6.0, 9.2)	18.2m (15.9, NE)
CRS any Grade	14%	Not reported	92%
CRS $\geq$ Grade 3	5%	Not reported	26%
Neurotox any Grade	65%	Not reported	87%
Neurotox $\geq$ Grade 3	13%	Not reported	35%
Subsequent SCT post treatment	24%	41%	18%
Other notable observations	NA	14% Hepatic VoD	40% vasopressor use

1. Kantarjian et al., 2017/ USPI (product label) 2. Kantarjian et al., 2016/ USPI (product label) 3. Shah et al. Lancet 2021/ USPI (product label)

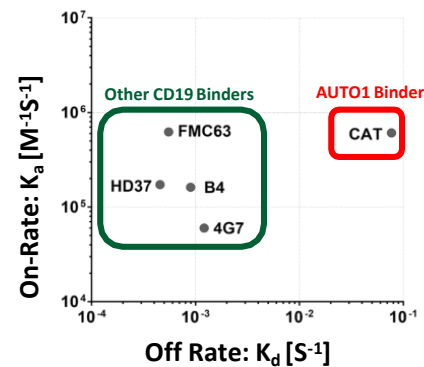
The estimates of EFS/PFS are read from the KM curves. The efficacy data in ZUMA-3 are based on the modified ITT population while the blinatumomab and inotuzumab data are based on the ITT population.

# obe-cel has a unique mechanism of action

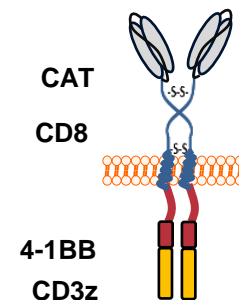
Fast off rate supports physiological engagement of target cells and avoids over-activation and exhaustion of CART cells

- AUTO1 is designed to improve potency and persistence while reducing immunological toxicity
- AUTO1 (CAT) binder with lower affinity for CD19
- Half-life of target interaction very short compared to Kymriah® (FMC63) binder:
  - AUTO1 = 9.8 seconds
  - Kymriah® = 21 minutes

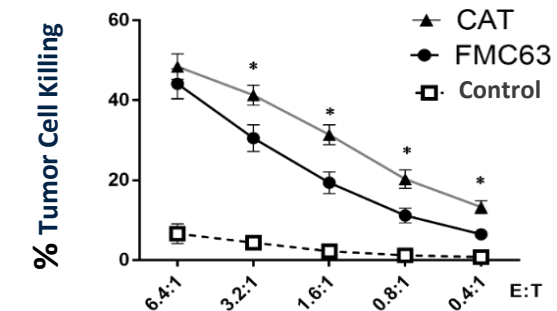
## Fast Off-Rate



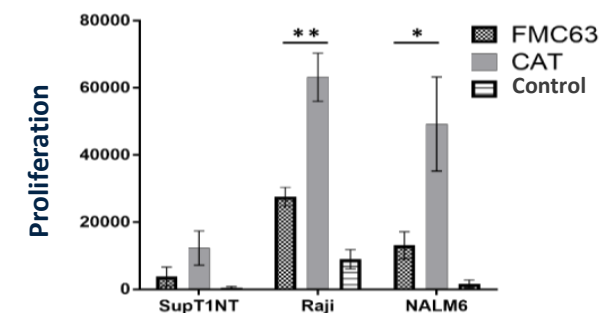
## Lentiviral Vector



## Enhanced Cytotoxicity



## Enhanced Proliferation





# obe-cel shows consistent safety and efficacy across ALL studies

Data from 3 studies across range of age groups and patient conditions

	CARPALL # <sup>1</sup> Peds ALL	ALLCAR19 # <sup>2</sup> Adult ALL	FELIX 1b # <sup>3</sup> Adult ALL
n	14	20	16
ORR (CR & CRI) (95% CI)	86% (57%, 98%)	85% (62%, 97%)	75% (48%, 93%)
CRS <sup>1</sup> ≥ Grade 3	0%	0%	0%
CRS <sup>1</sup> any grade	93%	55%	56%
Neurotox <sup>2</sup> ≥ Grade 3	7%	15%	6%
Neurotox <sup>2</sup> any Grade	50%	20%	13%
Median Age	9	42	42
Bone marrow blast >20% at LD	21%	60%	75%
Bone marrow blast <5% at LD	71%	35%	25%
Prior blinatumomab	7%	25%	56%

<sup>1</sup> CRS grading based on Lee et al (2014) for CARPALL and ALLCAR19, and ASTCT grading (Lee et al 2019) for FELIX

<sup>2</sup> Neurotoxicity grading based on CTCAE v4.03 for CARPALL and ALLCAR19, and ASTCT ICANS grading (Lee et al 2019) for FELIX

#1 Ghorashian et al. Nature Medicine 2019

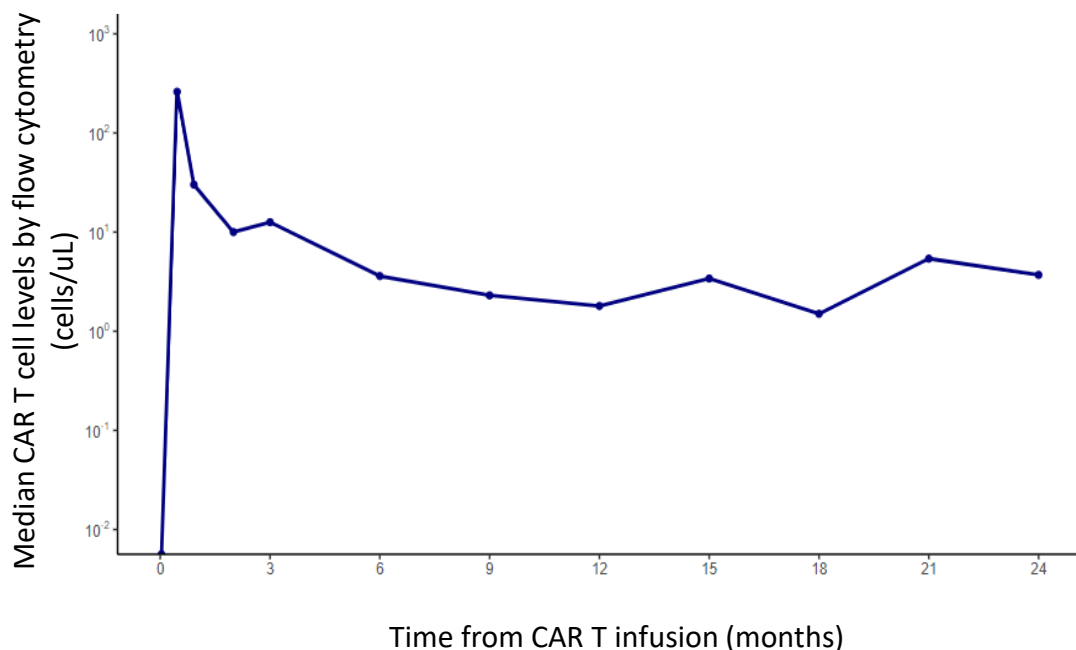
#2 Roddie et al. J Clin Oncol, 2021

#3 Culshaw et al, ASH 2021, abstract #477

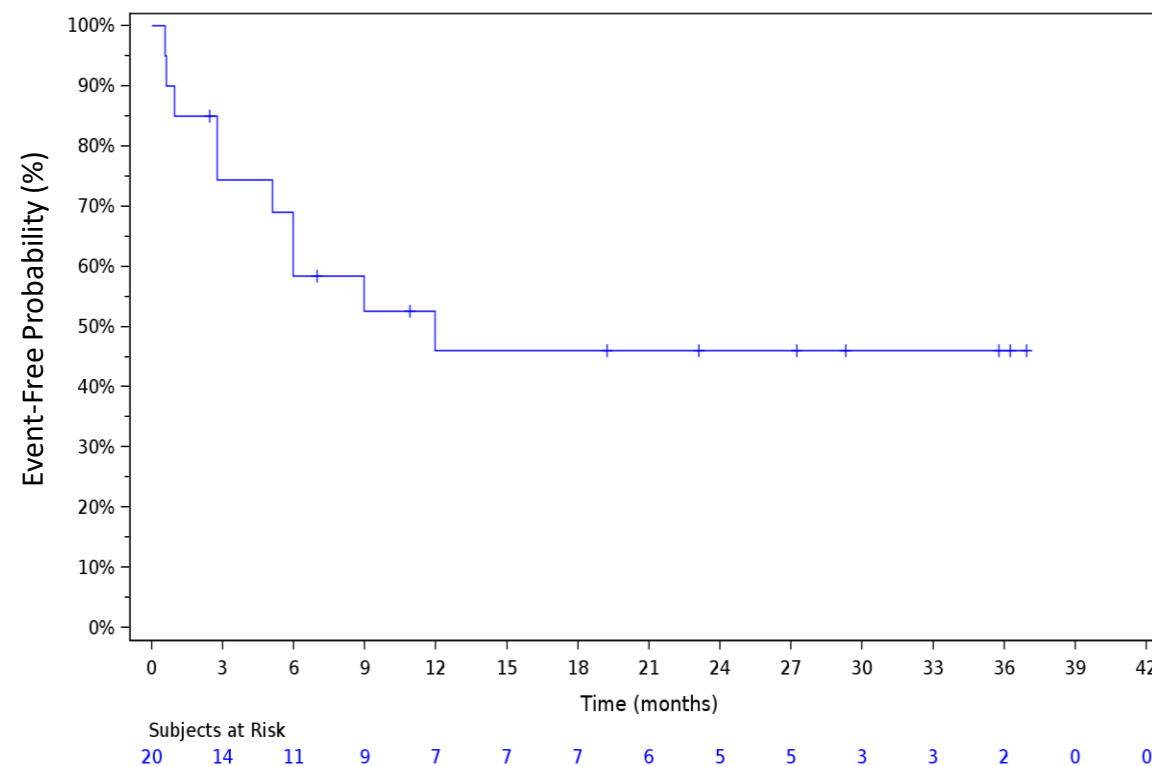
# obe-cel shows sustained event-free survival beyond 30 months

Long term CAR T persistence drives durability of effect

## Median CAR T cell levels in peripheral blood



## ALLCAR19 Event-Free Survival



**Median (range) follow-up time: 29.3 months (range 0.6 – 41.5)**

Median (95% CI) EFS: 12 months [2.8, NE]

EFS starting from Month 12 going forward: 46% (95% CI [23%, 67%])

# obe-cel has the potential for a transformational therapy in adult ALL

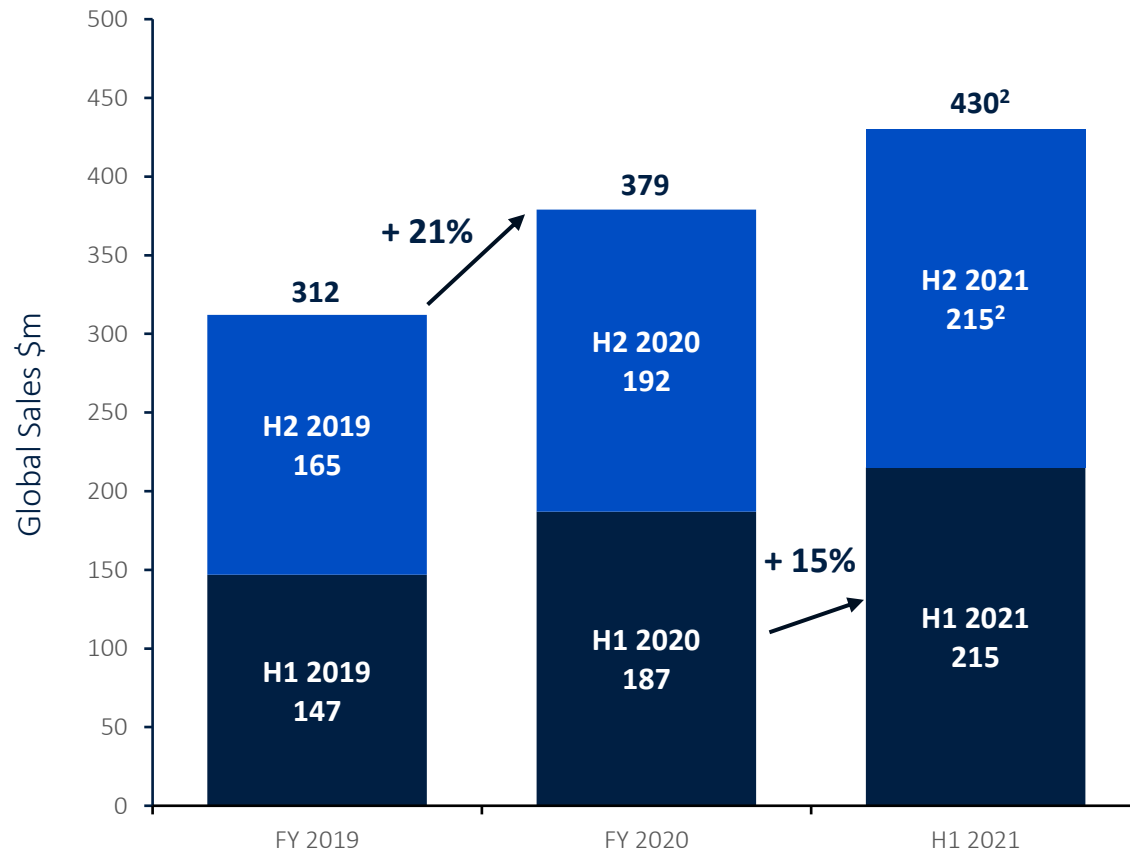
Unique CAR T design drives differentiated product profile

- Obe-cel has a unique mechanism of action built on a fast-off rate from CD19 target antigen
- Obe-cel has a high ORR across all patient populations evaluated
- Obe-cel shows a sustained morphological EFS of 46% with a median follow-up of 29.3 months
- Long term CAR T persistence drives durability of effect
- Obe-cel has a favorable safety profile with no high-grade CRS and limited ICANS

# obe-cel could potentially launch into an expanding ALL market

Blincyto, current market leader, revenues show annual growth of c.15-20%

## Reported Blincyto sales<sup>1</sup>



- Blincyto sales price estimated to be \$178k<sup>3</sup> (based on 2 cycles) supporting approx. 2,000 commercial adult ALL patients, growing at a rate of c.15-20%
- Kymriah is priced at \$475k in pediatric ALL. Breyanzi (lisocabtagene maraleucel) is priced at \$410k in DLBCL<sup>4</sup>. Tecartus is priced at \$399k for adult ALL.
- Breyanzi and other CAR T cell therapies are expanding delivery center footprint
- Tecartus (brexucabtagene autoleucel) is expected to establish CAR T use in adult ALL
- Obe-cel has the potential to be best in class curative therapy expanding use beyond academic transplant centers

### NOTES

1. As per Amgen quarterly SEC filings

2. H2 2021 is not yet reported, this is just an extrapolation based on H1 2021 reported sales

3. <https://www.medscape.com/viewarticle/836879>

4. Bristol Myers finally wins FDA approval for cancer cell therapy | BioPharma Dive

– Komodo Health 2015 – 2020

# FELIX Phase 2 study is under way with data expected in 2022

Obe-cel is the first Autolus program to move into a pivotal program

**Pivotal program,  
FELIX, in adult ALL  
enrolling with full data  
targeted in 2022**

CTA approved by the  
MHRA in January 2020  
and US IND has been  
open since April 2020

- Phase 1b run-in component, prior to single arm Phase 2 potential pivotal trial
- 100 relapsed/refractory adult ALL patients
- Primary endpoint: Overall Complete Response Rate (CR/CRi)
- Secondary endpoints: include MRD-negative CR EFS and DoR

# Unique profile of obe-cel offers potential across broader indications

Evaluation of obe-cel activity in additional B-Cell malignancies to capitalize on potential market opportunity

PRODUCT	INDICATION	TARGET	STUDY NAME	PHASE
obe-cel	Adult ALL	CD19	FELIX	Pivotal
obe-cel	B-NHL & CLL	CD19	ALLCAR19*	Phase 1
obe-cel	Primary CNS Lymphoma	CD19	CAROUSEL*	Phase 1
AUTO1/22	Pediatric ALL	CD19 & CD22	CARPALL*	Phase 1

 B Cell Malignancies

\* Collaboration with UCL

Opportunity to pursue in earlier lines of therapy and indications of Adult ALL



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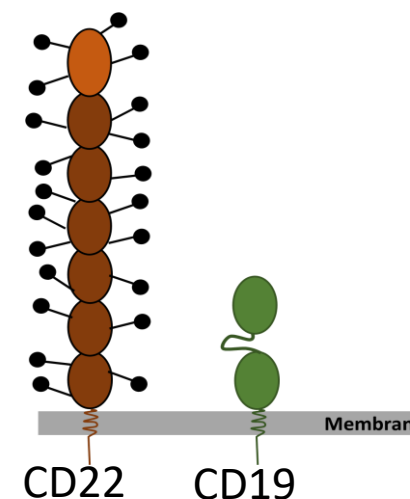
Pediatric ALL

# Autolus CAR T approach to treating pediatric ALL

CD19 negative antigen escape is a common cause of treatment failure

- obe-cel (AUTO1) in relapsed / refractory pediatric ALL is highly active and has a favourable safety profile - CARPALL study<sup>#1,2</sup>
- Medical need in pediatric ALL is to minimize rates of antigen-loss–driven relapses and improve long-term outcomes – points to need for a dual targeting CAR-T
- CD22 is challenging to target with a CAR as it is a rigid bulky molecule, expressed at a low density and can be downregulated further in response to CD22 targeting<sup>#3</sup>
- AUTO1/22 builds on obe-cel and adds a highly potent CD22 CAR, capable of targeting low levels of CD22

	CARPALL Study
n	14
CR Rate	86%
EFS 12m	52% (95% CI, 16% to 72%)
No. of CD19 negative relapses	5/6
CRS $\geq$ G3	0%
NTX $\geq$ G3	7%



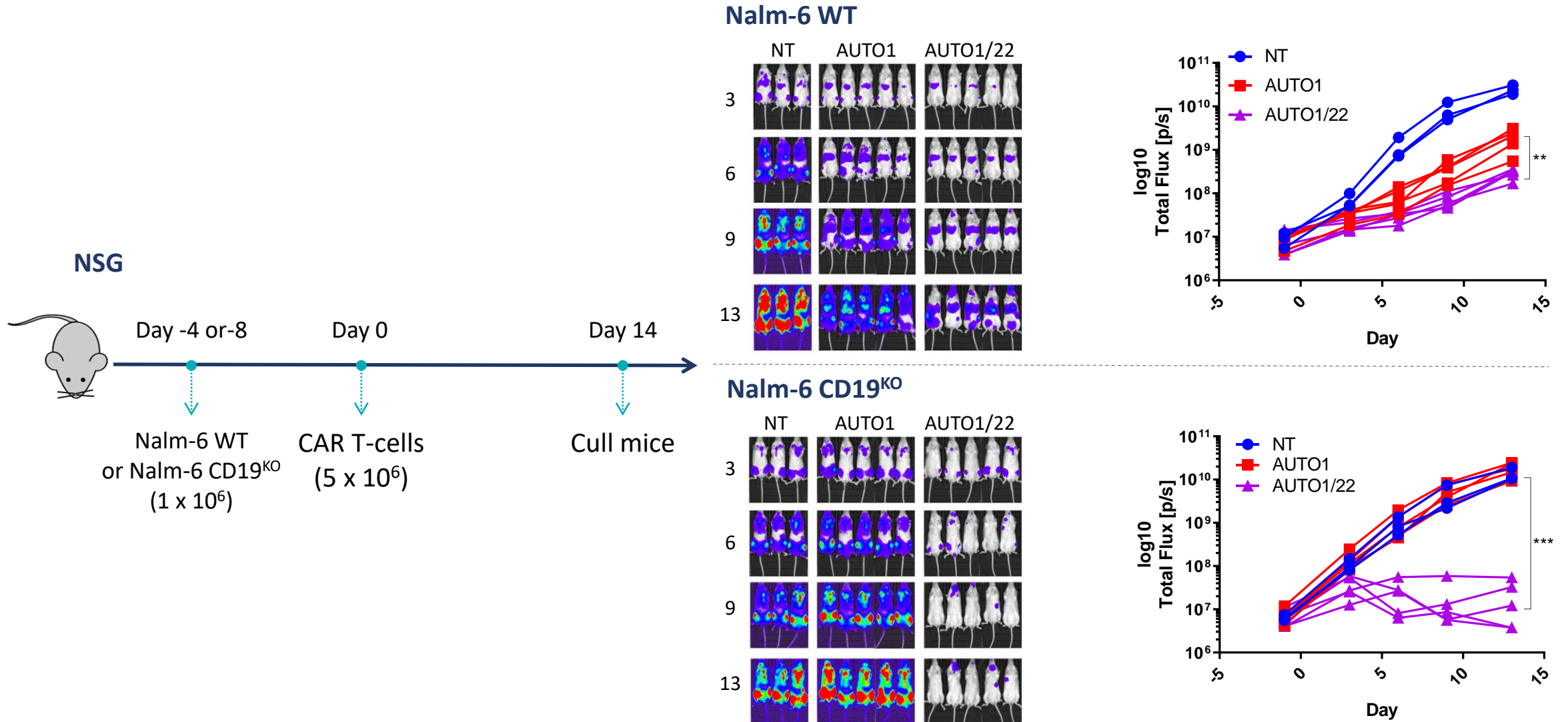
#1 NCT02443831

#2 Ghorashian et al., Nat Med 2019

#3 Shah et al., JCO 2020, Spiegel et al., Nat Med 2021

# AUTO1/22: enhanced in vivo anti-tumor efficacy

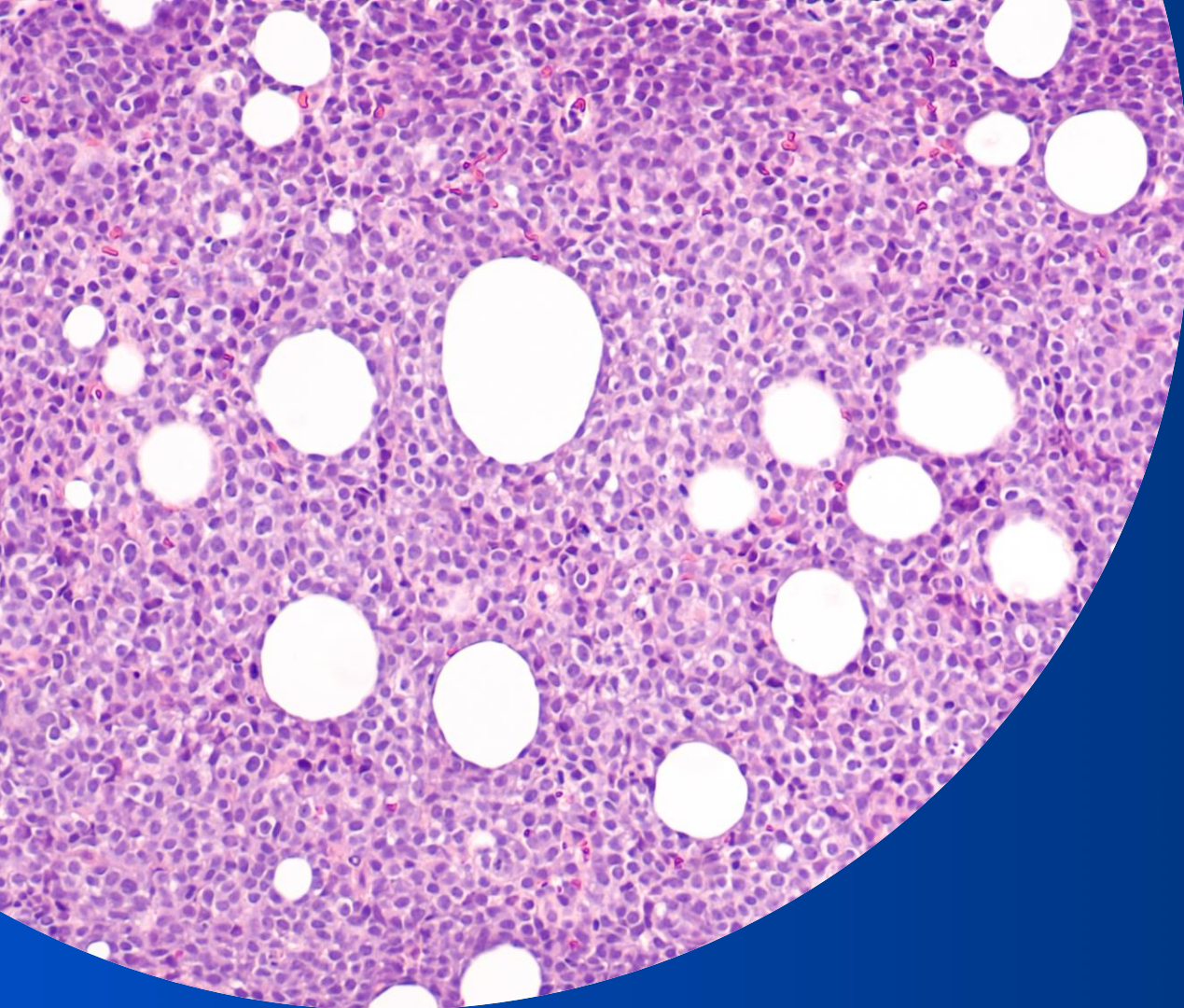
Dual targeting of CD19 and CD22 addresses CD19-negative target cells and enhances overall activity



# AUTO1/22 – A dual targeting CAR T therapy

Currently being tested in pediatric ALL

- AUTO1/22 builds on excellent CD19 targeting of obo-cel with its high activity and good safety profile and adds potent second CAR to target CD22
- AUTO1/22 eliminates target cells that express low density CD22 molecules
- AUTO1/22 is effective in in-vivo models of CD19 negative escape
- AUTO1/22 is being evaluated in pediatric patients and data will be presented in 2022



B-NHL

Obe-cel

# Favorable tolerability profile of obe-cel reproduced in B-NHL

No ICANS or severe CRS

AEs of Special Interest

Event N = 16 patients	All Grades n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)
CRS*	9 (56%)	6 (38%)	3 (19%)	0	0
ICANS	0	0	0	0	0

\*CRS grading by Lee et al 2018

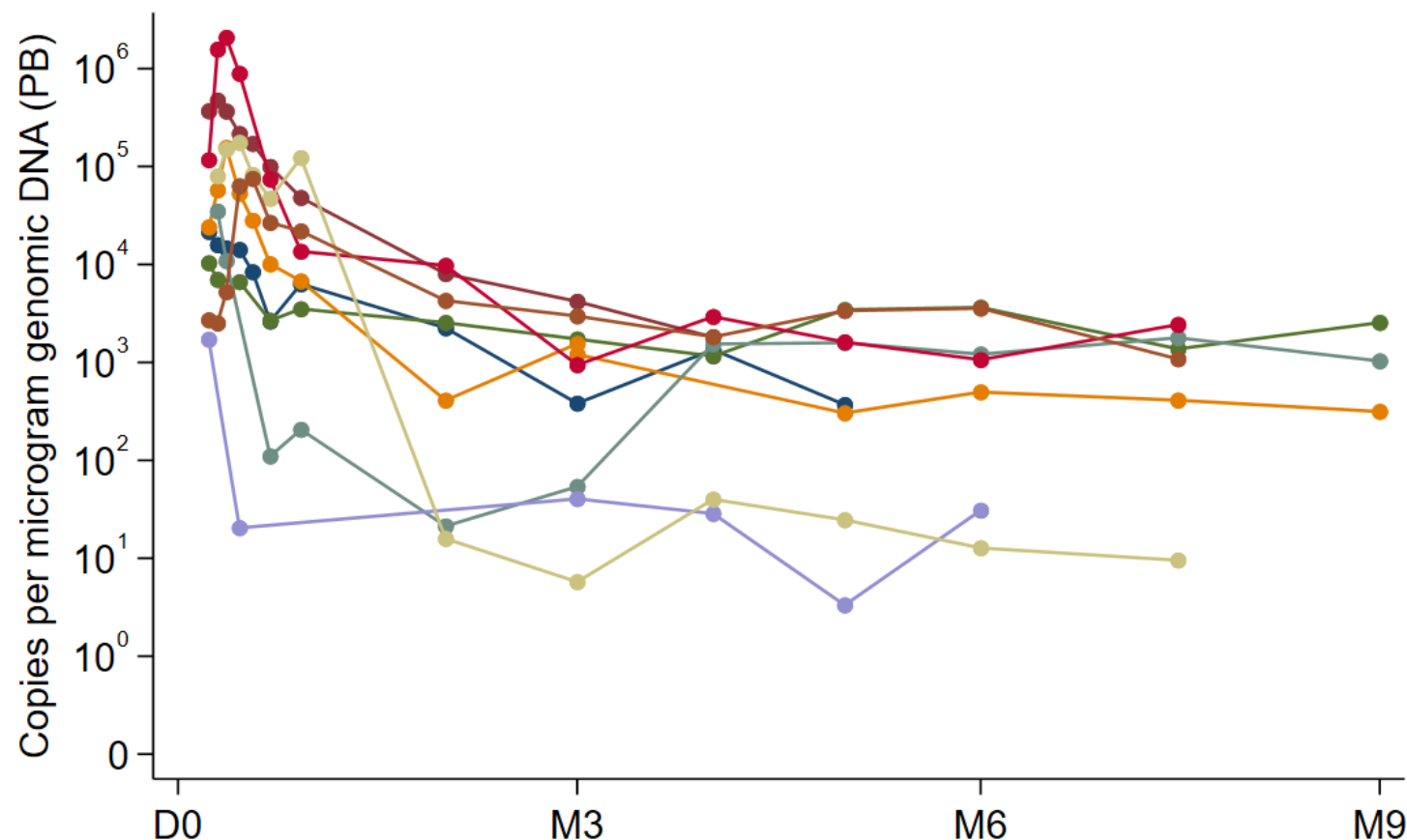
Data cut: 15-OCT-2021

- Consistent safety profile for obe-cel across indications tested
  - No ICANS
  - No high grade CRS



# obe-cel shows excellent T cell expansion and engraftment

ALLCAR19 – B-NHL Patients



CAR, chimeric antigen receptor; VCN, vector copy number; qPCR, quantitative polymerase chain reaction, CV% , coefficient of variation

## Cmax (CAR transgene per ug gDNA)

n	9
Mean	336234
CV%	50.2%

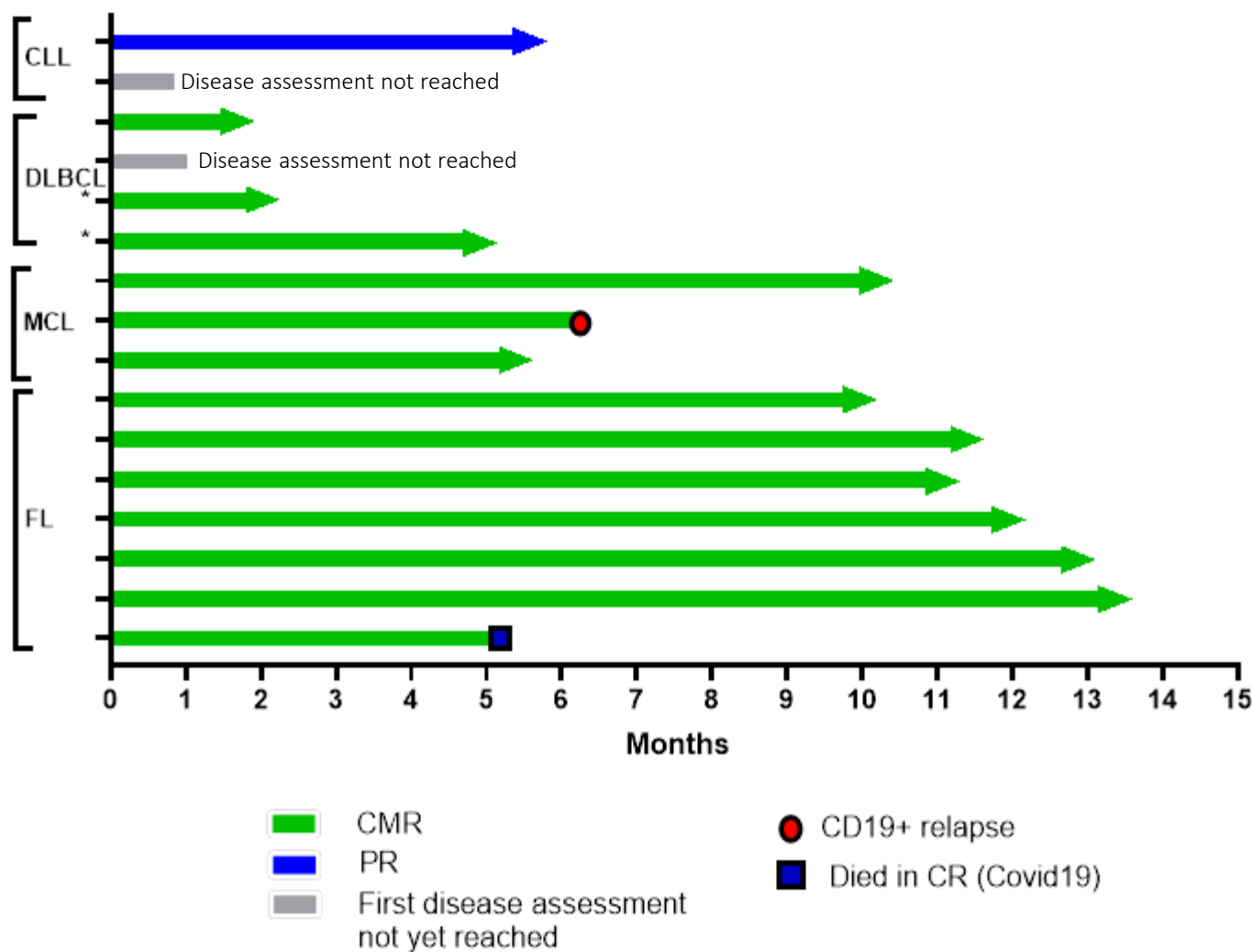
## Time to Cmax (Days)

n	9
Median	9
Range	7-17

## Time last measurable in Blood (Days)

n	9
Median	228
Range	122-274

# obe-cel shows encouraging efficacy and duration of response in NHL/CLL



	N (%)
Follicular Lymphoma	
CR + PR	7 (100%)
CR	7 (100%)
DLBCL	
CR + PR	3 (100%)
CR	3 (100%)
Pending	1
MCL	
CR + PR	3 (100%)
CR	3 (100%)
CLL/SLL	
CR + PR	1 PR (BM MRD-neg.)
Pending	1
Non-Response	0
Relapse	1 (MCL at 6 mos)

Median (Range) Follow-Up Time:

- FL/DLBCL: 11.8 Months (Range 2.0-14.2)
- MCL/CLL: 7.4 Months (Range 1.1-14.8)

Data cut: 15-OCT-2021  
DLBCL\* = transformed follicular lymphoma

## Summary and next steps for obe-cel in B-NHL

- Favorable safety profile in B-NHL with no ICANS or severe Grade  $\geq 3$  CRS events, consistent with safety profile observed in r/r B-ALL
- Out of 14 patients evaluable for efficacy, 100% ORR and 13/14 (93%) in complete metabolic response
- Long term persistence of obe-cel demonstrated by qPCR
- 15/16 patients are ongoing without disease progression
  - 6/7 FL patients in CR for more than 10 months (10-14 months), 1 patient died in CR from COVID
  - Longer follow-up and enrolment of additional DLBCL and CLL patients ongoing, further data planned for Q1 2022

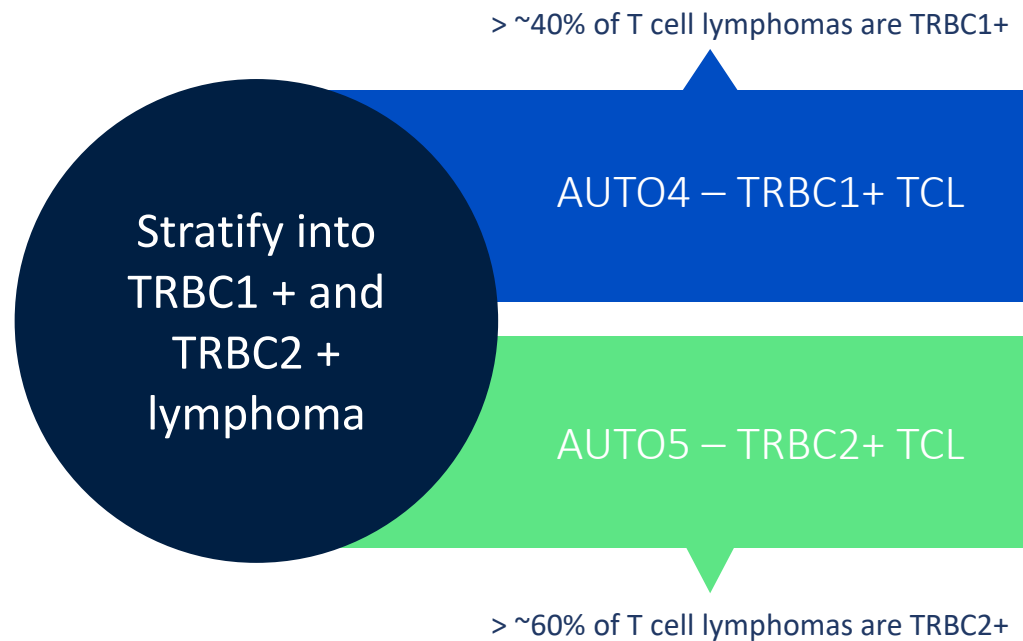
# Pipeline

A broad portfolio of next generation modular T cell therapies

# T Cell Lymphoma

No standard of care after first relapse and no T cell therapy approved

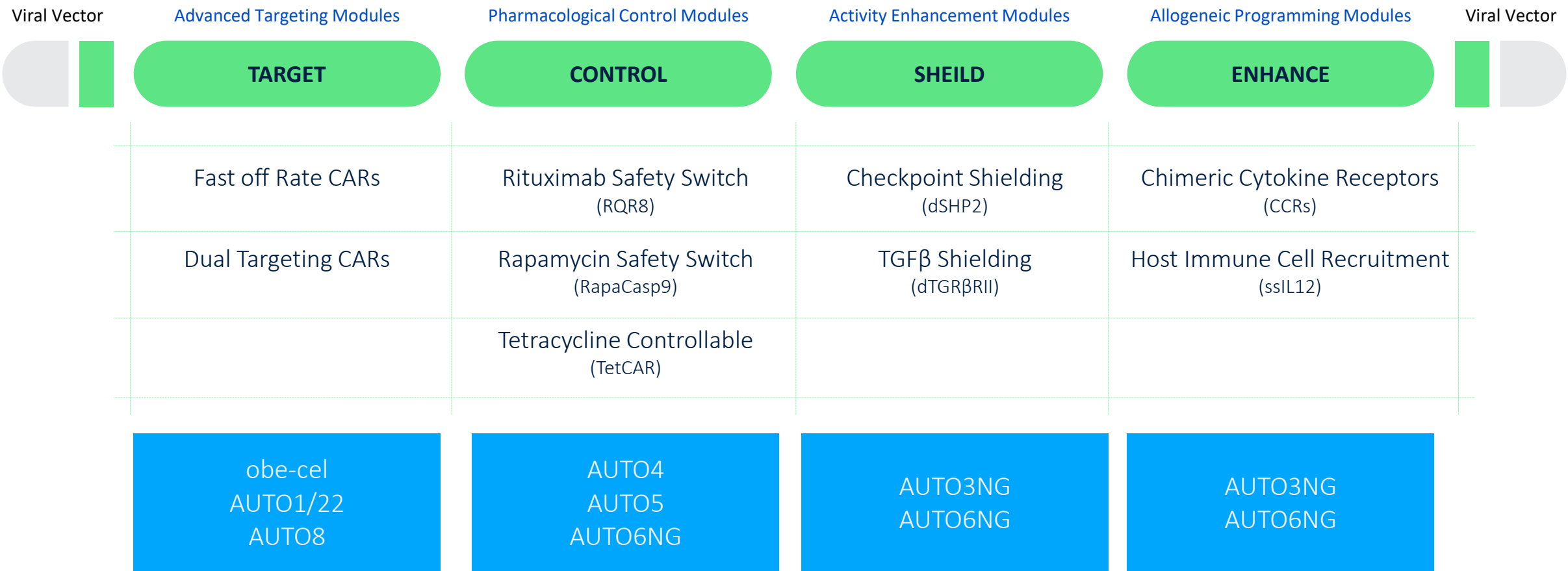
Three key elements to address T cell lymphomas:  
AUTO4, AUTO5 and a companion diagnostic test



- T cell lymphoma is an aggressive disease with a very poor prognosis for patients
- Median 5 yrs OS: 32%
- Standard of care is variable and often based on high-dose chemotherapy and stem cell transplants
- A large portion of T cell lymphoma patients are refractory to or relapsed following treatment with standard therapies
- T cell lymphomas have not, so far, benefited from advances in immunotherapeutic approaches
- AUTO4 Phase 1 interim data expected in H1 2022

# A broad toolkit which is core to our strategy of modular innovation

Advanced T cell programming





# Next generation programs

Designed to address limitations of current T cell therapies

PRODUCT	INDICATION	TARGET	STUDY NAME	PHASE
AUTO1/22	Pediatric ALL	CD19 & CD22	CARPALL*	Phase 1
AUTO4	TRBC1+ Peripheral TCL	TRBC1	LibrA T1	Phase 1/2
AUTO5	TRBC2+ Peripheral TCL	TRBC2		Preclinical
AUTO6NG	Neuroblastoma; Other tumor types	GD2		Preclinical
AUTO8	Multiple Myeloma	BCMA & CD19	MCARTY*	Phase 1

B Cell Malignancies

T-Cell Lymphoma

Solid Tumors

Multiple Myeloma

\* Collaboration with UCL



# Blackstone Collaboration

# Blackstone Life Sciences to invest up to \$250m to develop obe-cel in adult ALL

Investment of \$100m in equity and up to \$150 million in product financing

- Blackstone agreed to purchase \$100 million of Autolus' American Depositary Shares (ADS') in a private placement
- Blackstone also committed to invest up to \$150 million in product financing to support obe-cel development and commercialization
  - \$50 million payable upon closing of the transaction
  - Remainder payable based on achievement of certain development and regulatory milestones
- Blackstone will receive a warrant to purchase up to \$24 million worth of Autolus ADSs at an exercise price premium to market
- Autolus agreed to pay Blackstone a capped single digit royalty plus milestone payments based on worldwide net sales of obe-cel
- Fully funds development and filing of obe-cel in r/r adult ALL, as well as funding commercial and manufacturing infrastructure build
- Transaction strengthens balance sheet and provides runway into 2024<sup>1</sup>

## NOTES

1. Assuming all milestones received

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Next Steps

# Autolus poised for potential value inflection

obe-cel pivotal data in adult ALL in 2022

## obe-cel

- FELIX Phase 2 study in adult ALL data expected in 2022
- Evaluation in relapsed/refractory B-NHL and CLL ongoing, with next data update expected in H1 2022
- Evaluation in Primary CNS Lymphoma ongoing with initial data update expected in Q1 2022

## AUTO1/22

- Pediatric ALL – AUTO1/22 Phase initial 1 data expected in H1 2022 and longer follow-up data in H2 2022

## Pipeline

- AUTO4: Peripheral T cell lymphoma - interim phase 1 data expected in H1 2022
- AUTO6NG: Neuroblastoma – start phase 1 in H1 2022
- AUTO8: Multiple Myeloma – start phase 1 in H1 2022

## Cash balance at September 30, 2021, \$173.1 million:

- +\$25M R&D tax credit received in October 2021
- +\$150M from Blackstone in November 2021
- Cash runway including project financing payments from Blackstone into 2024

Thank you

