

Autolus

# Developing Next Generation Programmed T Cell Therapies

May 2022



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# Autolus Overview

## Building a fully integrated CAR T company



### Best-in-class lead asset

- Lead product obe-cel potentially best-in-class for relapsed/refractory adult acute lymphoblastic leukemia (ALL)
- Phase 2 FELIX ALL initial data expected H2 22
- Updated exploratory data in NHL from Phase 1 studies expected in 2022



### Pipeline

- Pipeline built on modular innovation addressing cancers with limited treatment options
- AUTO1/22 in paediatric ALL
- AUTO4 /5 in T cell lymphoma
- AUTO6NG in neuroblastoma
- AUTO8 in multiple myeloma



### Scalable manufacturing

- In house cell manufacturing for clinical trial conduct
- Commercial fit-for-purpose cell manufacturing facility under construction with planned annual capacity of 2000 patient products



### Collaboration

- Collaboration with Blackstone Life Sciences to develop obe-cel in adult ALL
- Moderna granted exclusive license for binders to up to four IO targets
- Pipeline programs not partnered

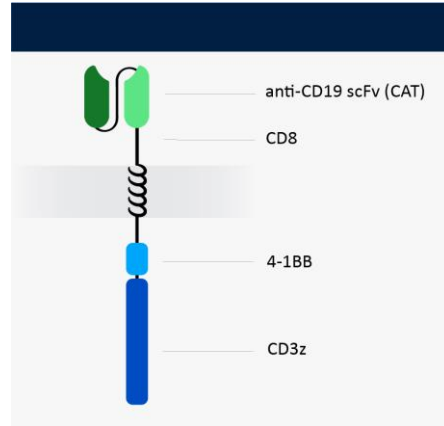


LEAD CLINICAL PROGRAM

obe-cel

A standalone, potentially best-in-class CD19 CAR T cell therapy

# obe-cel has a unique mechanism of action



CAT binder with lower affinity for CD19

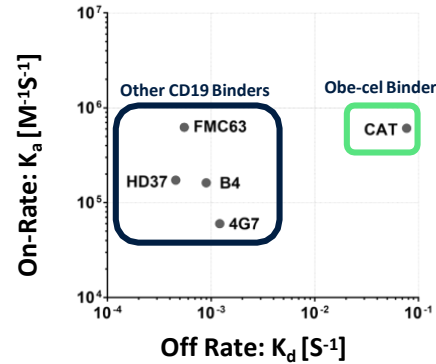
## Improved potency, reduced toxicity

Avoids over-activation of CAR T cells  
-> Reduced toxicities

Increased CAR T peak expansion  
-> Improved persistence

Avoids exhaustion of CAR T cells  
-> Improved engraftment  
-> Improved persistence

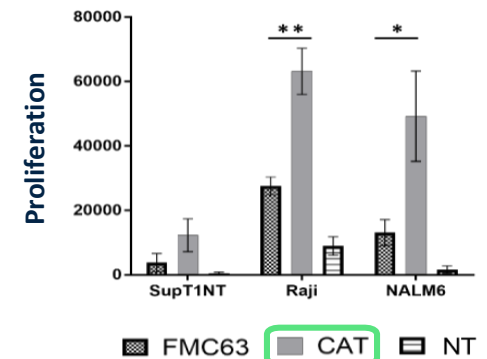
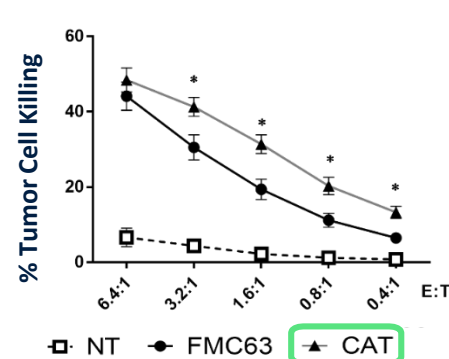
## Fast off-rate



obe-cel has lower CD19 affinity and shorter half-life of interaction compared to binders used in approved products

- obe-cel = 9.8 seconds
- Kymriah® = 21 minutes

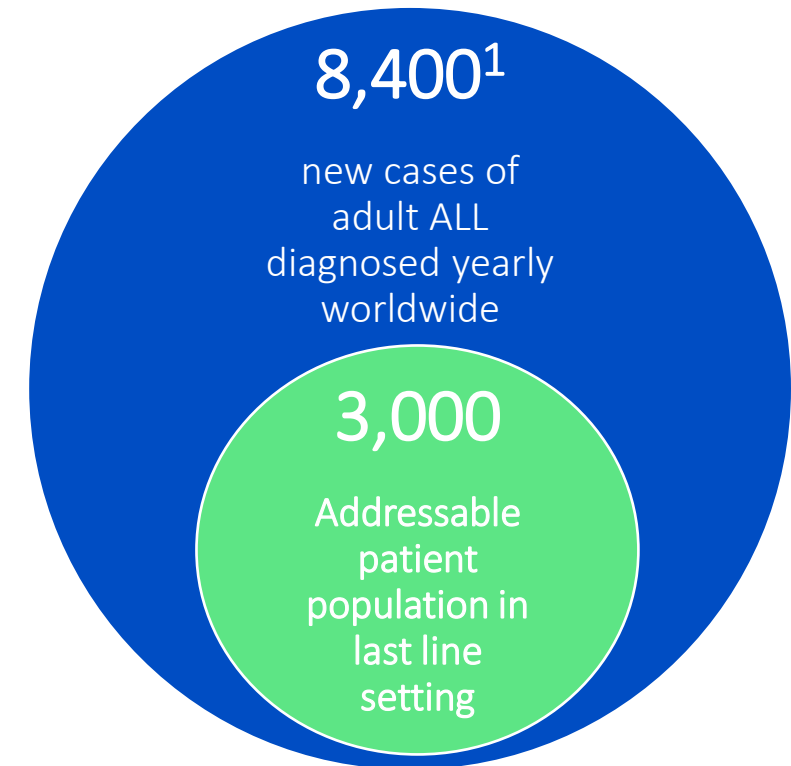
## Enhanced cytotoxicity and proliferation



# obe-cel for adult Acute Lymphoblastic Leukemia (ALL): high unmet need

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

- Median overall survival is < 1 year in r/r adult ALL
- Combination chemotherapy enables 90% of adult ALL patients to experience Complete Response (CR)
  - Only 30% to 40% achieve long-term remission
- Current T cell therapies for adult patients are Blincyto® and Tecartus™
  - Therapies are highly active, but require subsequent allograft to achieve durability
  - Notable toxicity with high incidences of severe CRS and cases of fatal neurotoxicity
- Opportunity to expand the addressable patient population in earlier lines of therapy



## NOTES

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

# obe-cel is a potentially transformational therapy for adult ALL

Unique CAR T design drives differentiated product profile

- Unique mechanism of action built on a fast off-rate from CD19 target antigen
- High Overall Response Rate (ORR) across all patient populations evaluated<sup>1</sup>
- Sustained morphological Event Free Survival (EFS) of 46% with a median follow-up of 29.3 months<sup>2</sup>
- Long term CAR T persistence drives durability of effect
- Favorable safety profile:
  - No high-grade Cytokine Release Syndrome (CRS)
  - Limited immune effector cell-associated neurotoxicity syndrome (ICANS)

## obe-cel

**Orphan Drug designation** by  
FDA for B-ALL

**Orphan Medical Product  
designation** by EMA in ALL

**RMAT designation** by FDA  
in R/R B-ALL

**Prime designation** by EMA  
in R/R B-ALL

**ILAP designation** by MHRA in  
Adult R/R B-ALL

### NOTES

1. FELIX study
2. ALLCAR19 study

# obe-cel shows consistent clinical profile across three clinical studies

Data from 3 studies - range of ages and patient conditions

- obe-cel has a favourable safety profile with no high-grade CRS and limited ICANS

	CARPALL #1 Peds ALL	ALLCAR19 #2 Adult ALL	FELIX 1b #3 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

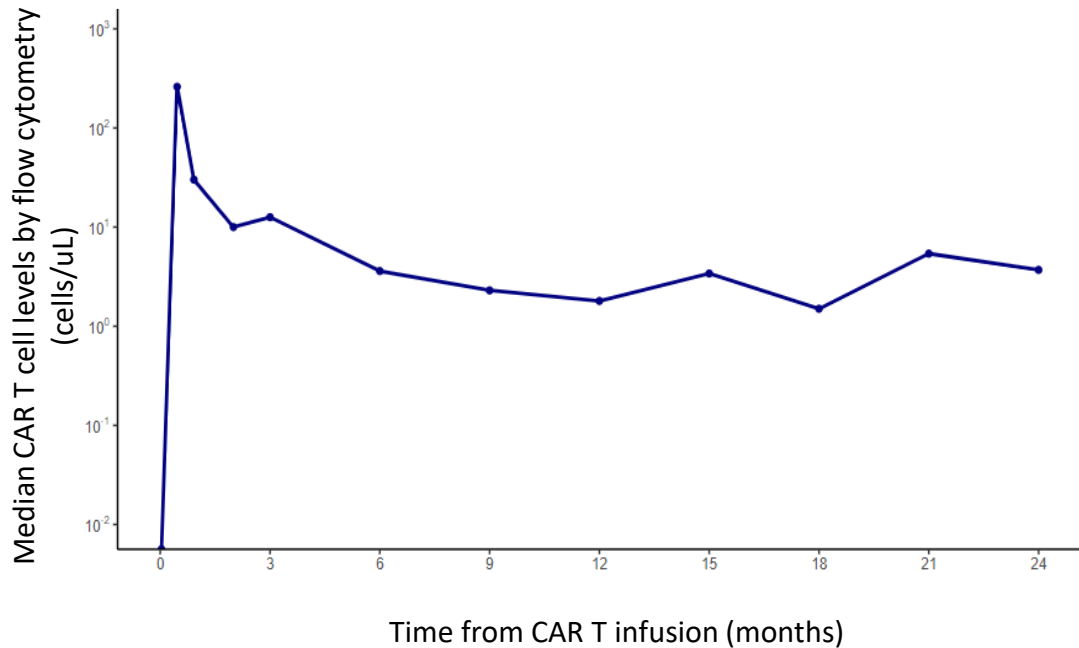
#3 Culshaw et al, ASH 2021, abstract #477



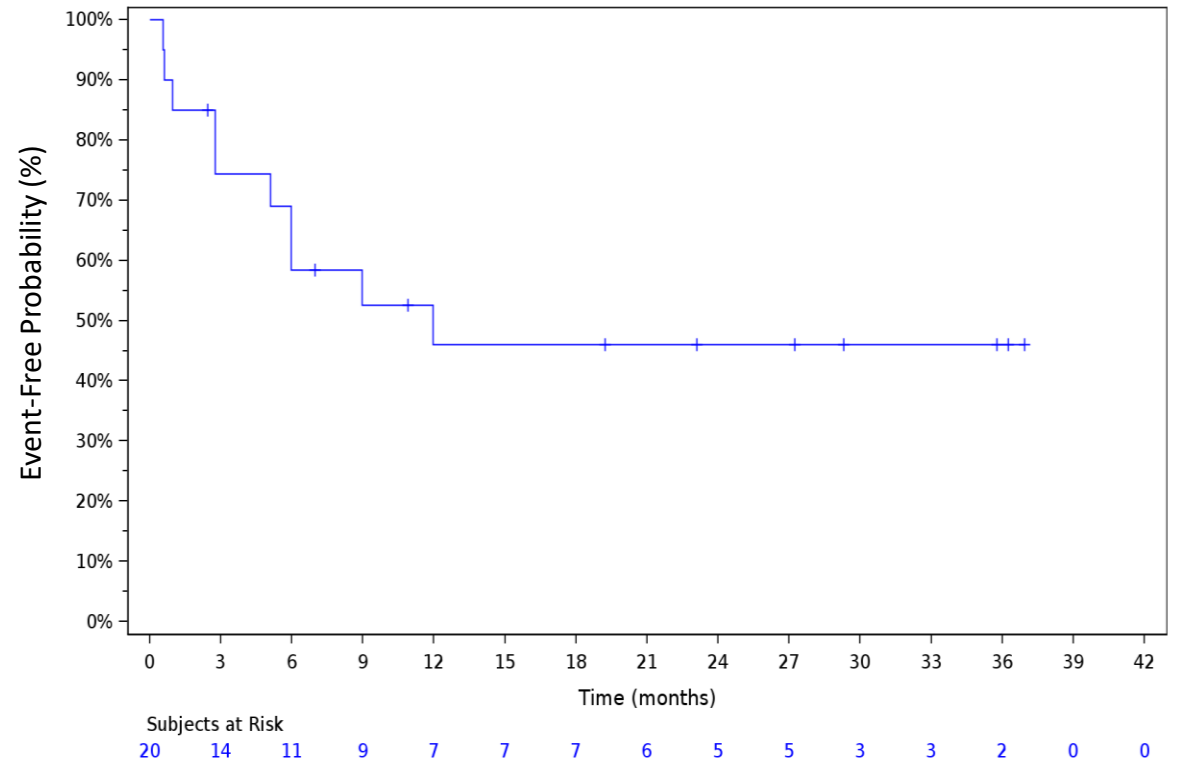
# obe-cel shows sustained event-free survival beyond 30 months

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%])

Data cut for ALLCAR19 study: 15-OCT-2021;  
 Patients were received SCT post obe-cel infusion are censored at date of SCT

# 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	44%	81%	65%
EFS/PFS	31% @ 6m ~10% @ 18m	~45% @ 6m ~20% @ 18m	~65% @ 6m ~25% @ 18m
median DoR	7.3m	4.6m	13.6m
median OS	7.7m	7.7m	18.2m
CRS ≥ Grade 3	5%	Not reported	26%
Neurotox any Grade	65%	Not reported	87%
Neurotox ≥ Grade 3	13%	Not reported	35%
Subsequent SCT post treatment	24%	41%	18%
Other notable observations	NA	14% Hepatic VoD	40% vasopressor use

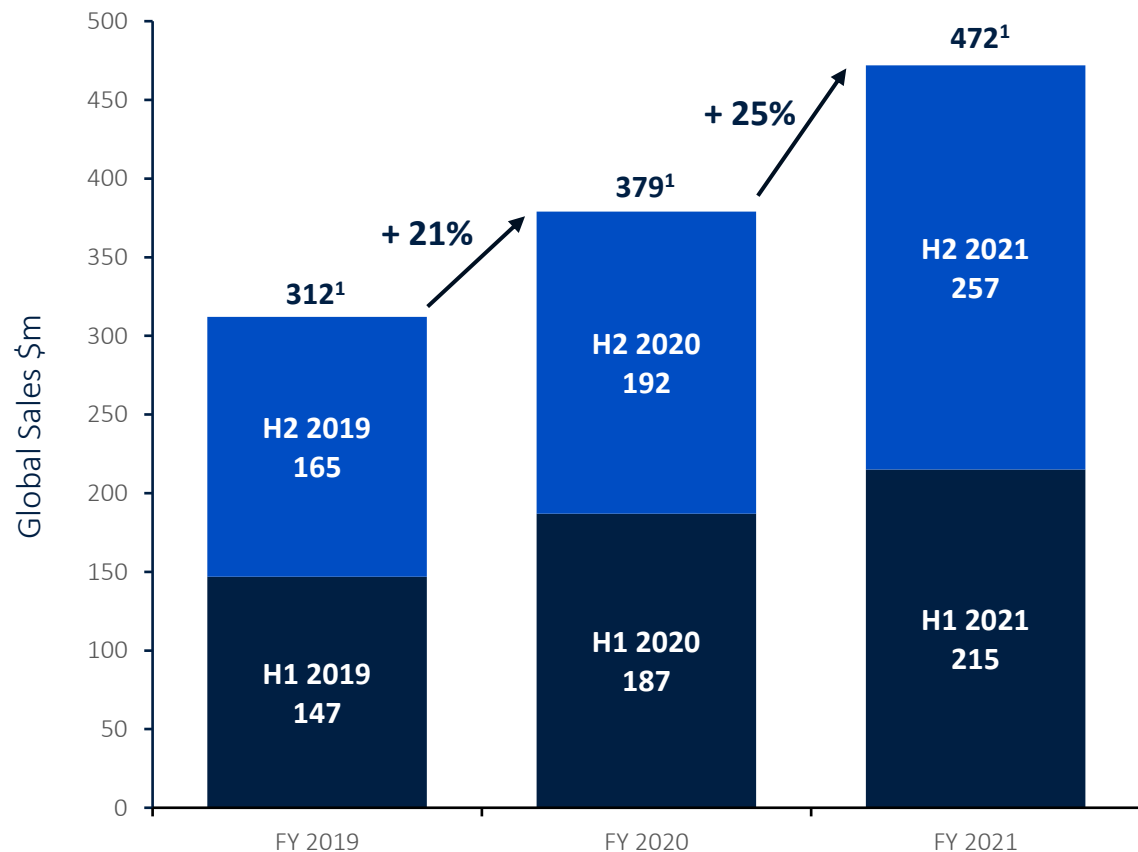
1. Kantarjian et al., 2017/ USPI (product label) 2. Kantarjian et al., 2016/ USPI (product label) 3. Shah et al. Lancet 2021/ USPI (product label)

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 could launch into an expanding ALL market

Blincyto<sup>®</sup>, current market leader, shows annual revenue growth of 25%

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



- Blincyto<sup>®</sup> sales price estimated to be \$178k<sup>3</sup> (for 2 cycles) supporting approx. >2,000 commercial adult ALL patients, growing at a rate of 25%
- Kymriah<sup>®</sup> is priced at \$475k in pediatric ALL. Breyanzi<sup>®</sup> is priced at \$410k in DLBCL<sup>4</sup>. Tecartus<sup>™</sup> is priced at \$399k for adult ALL.
- Breyanzi<sup>®</sup> and other CAR T cell therapies are expanding delivery center footprint
- Tecartus<sup>™</sup> 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

# Next steps: obe-cel initial data (FELIX) expected in H2 2022

obe-cel is the first Autolus program to move into a pivotal program: full data in H1 2023



Pivotal Phase 2 trial in adult ALL  
ongoing since mid 2021 with sites in  
UK, Spain and US

Up to 100 relapsed/refractory adult ALL patients  
Phase 1b run-in component, prior to single arm Phase 2 potential pivotal trial  
Pre-determined futility analysis passed in Q1 2022

**H2 2022**  
Initial data

**Primary endpoint:**  
overall complete  
response rate  
(CR/Cri)

**H1 2023**  
Full data

**Secondary  
endpoints:** include  
MRD-negative CR,  
EFS and DoR



# Building obe-cel into a franchise

Deep value program with broad applicability

# Capitalising on the obe-cel profile in additional indications

Unique profile allows applicability in a broad range of indications

## Clinical data supports differentiated product profile

- High degree of activity and persistence -> drives long term outcomes
- Best-in-class safety profile -> will drive adoption of obe-cel in all clinical settings
- Initial NHL data is consistent with this profile

## Solid foundation for onward development

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

# B-cell Non-Hodgkin Lymphoma: Favorable tolerability profile reproduced

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

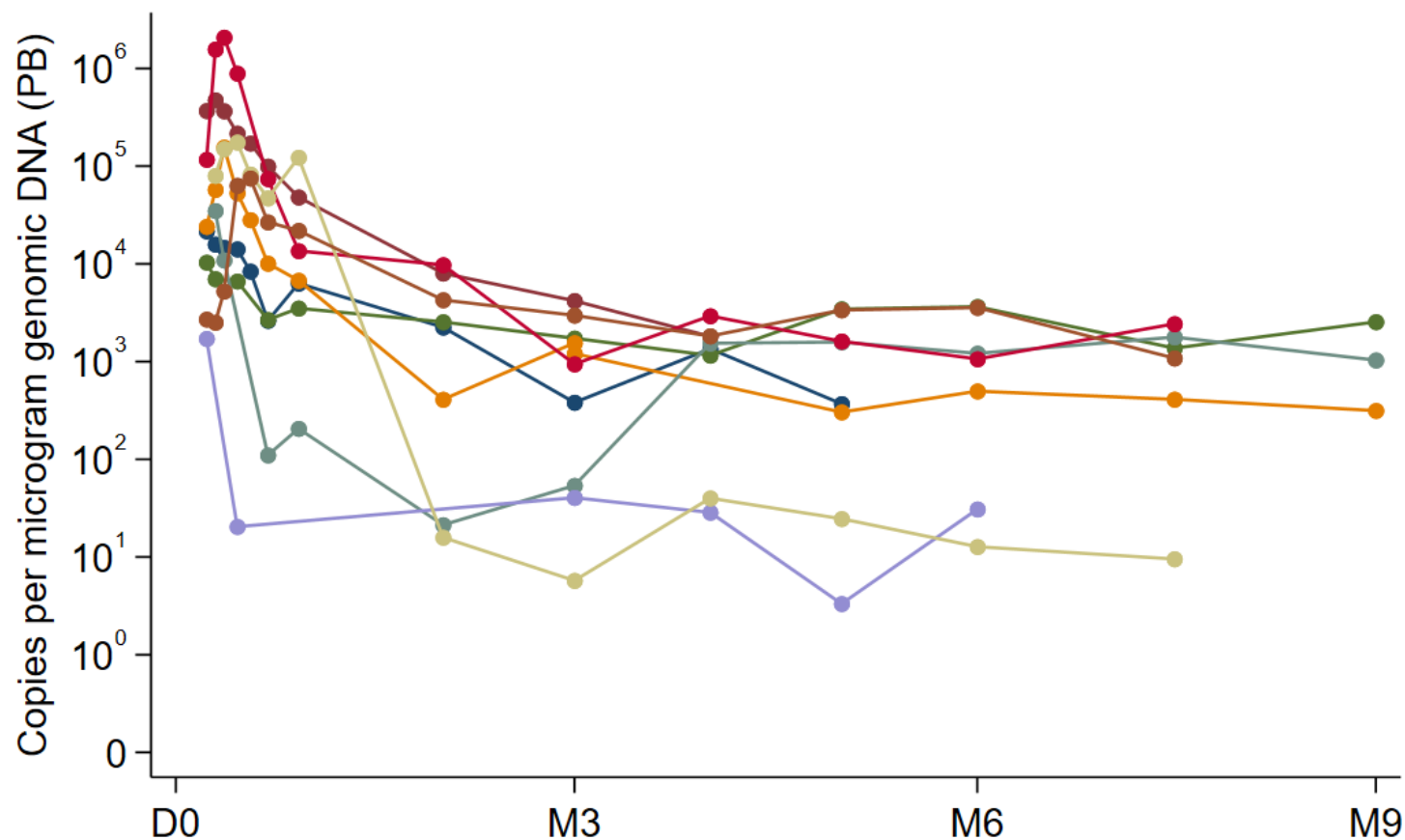
## Adverse Events of Special Interest

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
Event N = 16 patients	All Grades n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)

\*CRS grading by Lee et al 2018  
Data cut: 15-OCT-2021

# 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

Data cut: 15-OCT-2021

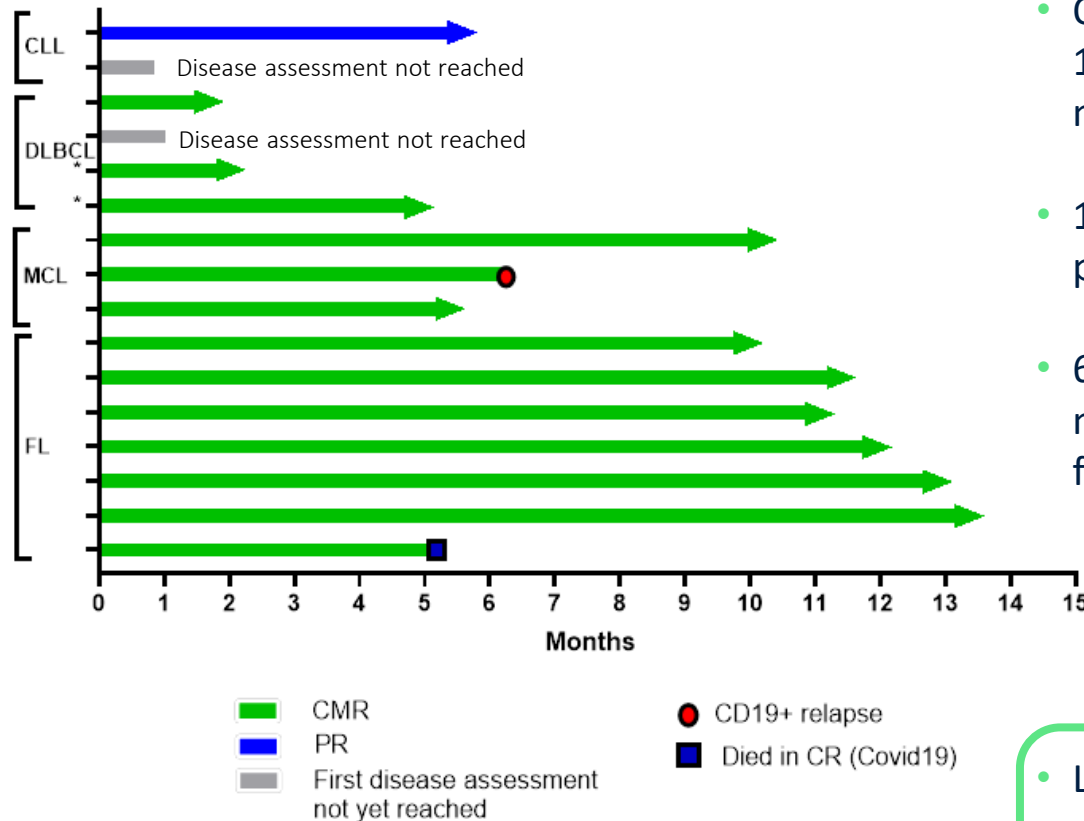
Cmax (CAR transgene per ug gDNA)	
n	9
Mean	336234
CV%	50.2%
Time to Cmax (Days)	
n	9
Median	9
Range	7-17
Time last measurable in Blood (Days)	
n	9
Median	228
Range	122-274



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

Long term persistence of obe-cel demonstrated by qPCR

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



- Out of 14 patients evaluable for efficacy, 100% ORR and 13/14 (93%) in complete metabolic response
- 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-term follow up and enrollment of additional patients ongoing, with update at European Hematology Congress (EHA), June 2022

- 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)

# AUTO1 in B-NHL, CLL/SLL: EHA abstract

## Data cut: 8 February 2022

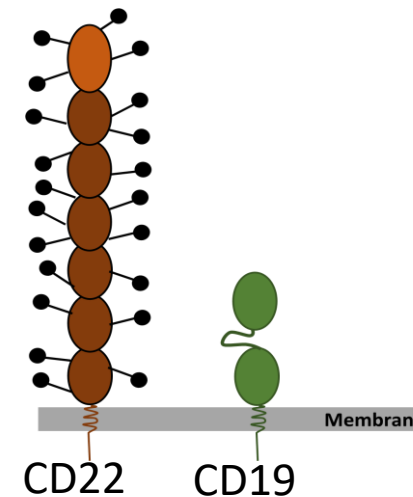
- 19 patients had been infused with AUTO1; 10 with low grade NHL, 6 with DLBCL, 3 with CLL
- Patients treated had received a median of 3 prior lines of treatment
- Grade 1 CRS was reported in 6/19 and Grade 2 CRS in 3/19
- No ICANS was observed in the B-NHL and CLL cohorts
- In the low grade-NHL and DCBCL cohorts, 10/10 and 4/5 evaluable patients respectively were in CMR post-treatment.
- Responses were ongoing in 9/10 low grade-NHL at 12 months and in 4/4 DLBCL at months 1,3,3 and 6.
- In the CLL cohort, 2/3 evaluable patients achieved MRD negative remission in the bone marrow with residual small volume lymph nodes by CT at 6 and 3 months of follow up respectively
- AUTO1 demonstrated a tolerable safety profile in patients with r/r B-NHL and CLL despite high disease burden. Early data shows excellent complete remission rates and excellent CAR engraftment/expansion

# AUTO1/22: Pediatric Acute Lymphoblastic Leukemia

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 is a next generation program that builds on obe-cel and adds a highly potent CD22 CAR, capable of targeting low levels of CD22
- AUTO1/22 is being evaluated in pediatric patients and data will be presented at EHA, June 2022

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



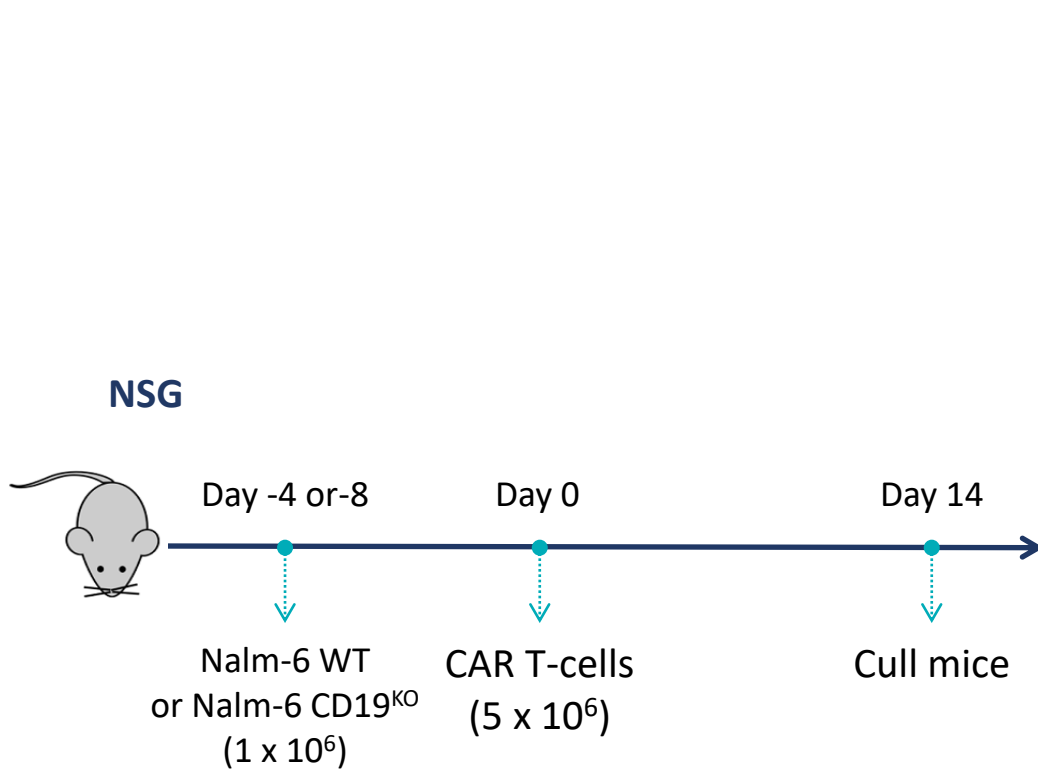
# AUTO1/22: EHA abstract

**Data cut: 8 February 2022**

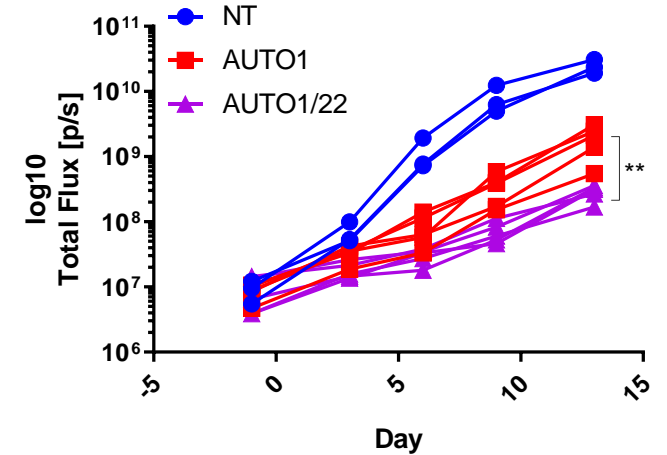
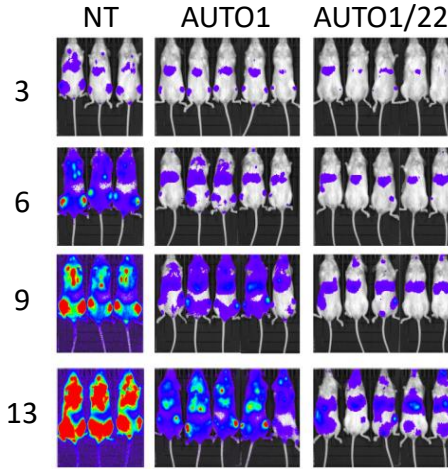
- 10 pediatric ALL patients have been treated with AUTO1/22 and 8 are evaluable with >1 month follow-up
- 5 of 8 patients had relapsed post allogeneic SCT
  - 4 had received prior Blincyto
  - 3 had relapsed after prior Kymriah
- CRS occurred in 7/8 patients (grade 1 n=2, grade 2 n=5), but severe CRS was not seen
- 7 of 8 evaluable patients achieved MRD negative CR at 1 month post infusion
- Overall, at a median follow up of 4.8 months, 5/8 patients remain in MRD negative CR at last follow up
- The study results demonstrate that dual CD19/22 targeting CAR T cells generated by co-transduction show an acceptable safety profile, with robust expansion/persistence and early efficacy in a heavily pre-treated cohort

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

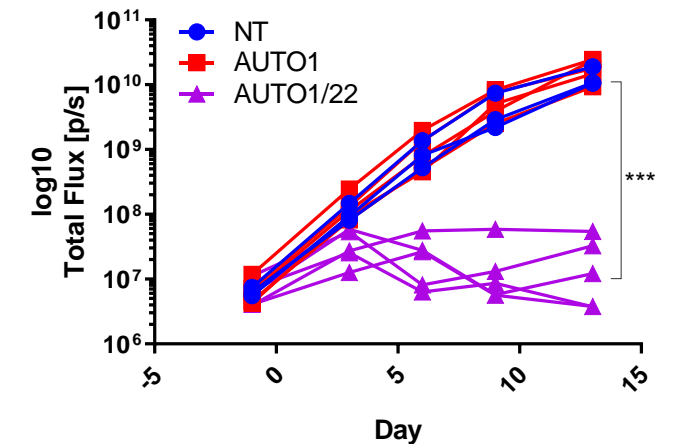
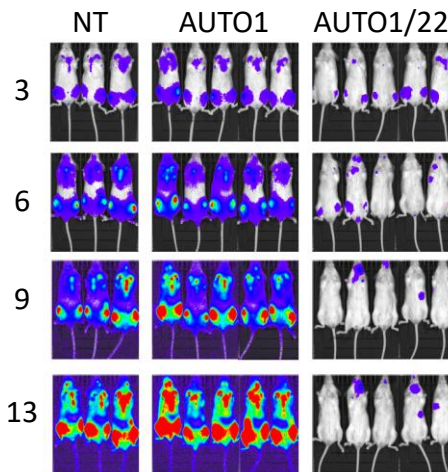
Dual targeting of CD19 and CD22 addresses CD19-negative target cells and enhances overall activity



## Nalm-6 WT



## Nalm-6 CD19<sup>KO</sup>



# AUTO1 in Primary CNS Lymphoma: EHA abstract

**Data cut: 14 February 2022**

- 6 patients with r/r PCNSL were enrolled where the median prior lines of treatment was 2
- 5 patients were infused with IV AUTO1 and 1 patient with intraventricular AUTO1
- Following CAR T infusion, grade 1 and 2 CRS affected 1 and 3 patients respectively and any grade ICANS was observed in 2 patients with 2 grade 3 events
- AUTO1 engraftment and response was evaluable in 4 patients at 1 month following iv infusion
- 2 of 4 patients had no measurable disease at 2 and 6 months of follow up respectively
- AUTO1 showed encouraging remission rates and excellent CAR T engraftment/expansion in the blood and CSF
- Intraventricular administration was well-tolerated and showed that AUTO1 has activity via that route in a patient who failed IV therapy

# Summary and next steps for obe-cel

## Building a franchise through broad applicability

- Favorable and consistent safety profile demonstrated in a number of indications
- Encouraging efficacy and duration in small patient numbers
- Longer-term follow up and enrolment of additional patients ongoing, with updates at European Hematology Congress (EHA), June 2022:
  - DLBCL and CLL – Phase 1 data (ALLCAR19 trial)
  - Primary CNS Lymphoma – Phase 1 data (CAROUSEL trial)
  - Pediatric ALL – Phase 1 data (CARPALL trial)

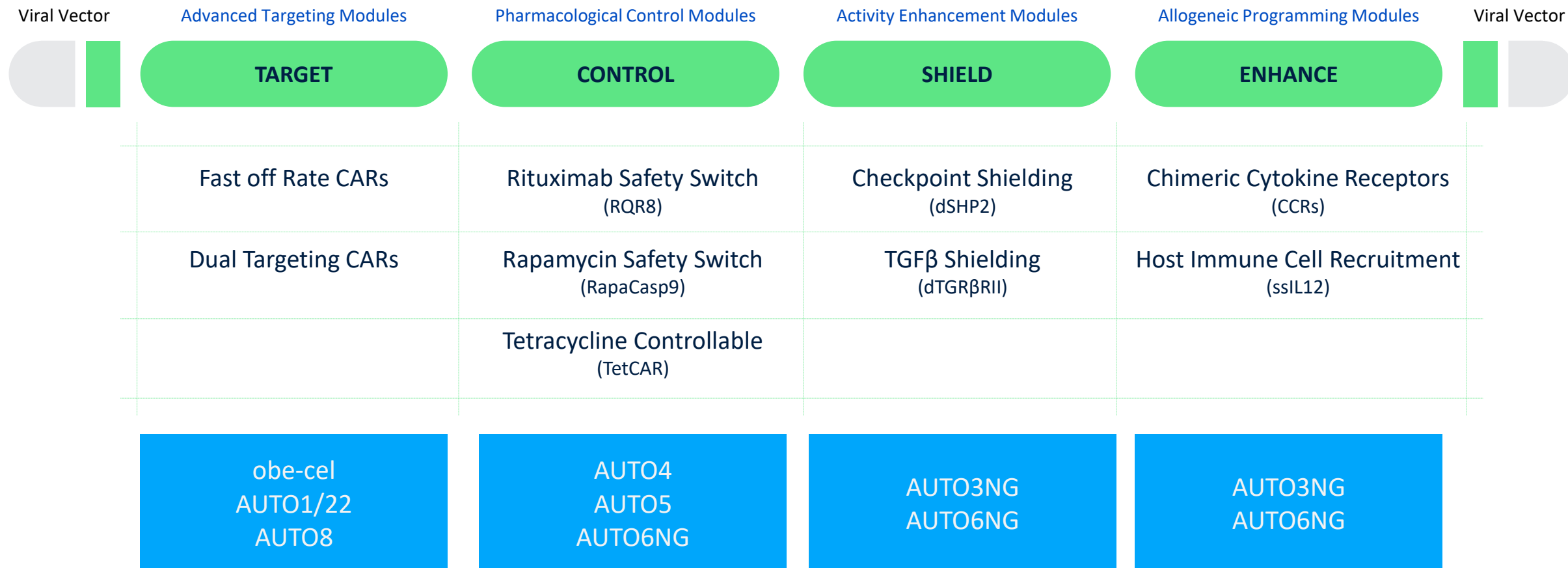
# Pipeline

A broad portfolio of next generation modular T cell therapies



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

## Advanced T cell programming



# Pipeline

Designed to address limitations of current T cell therapies

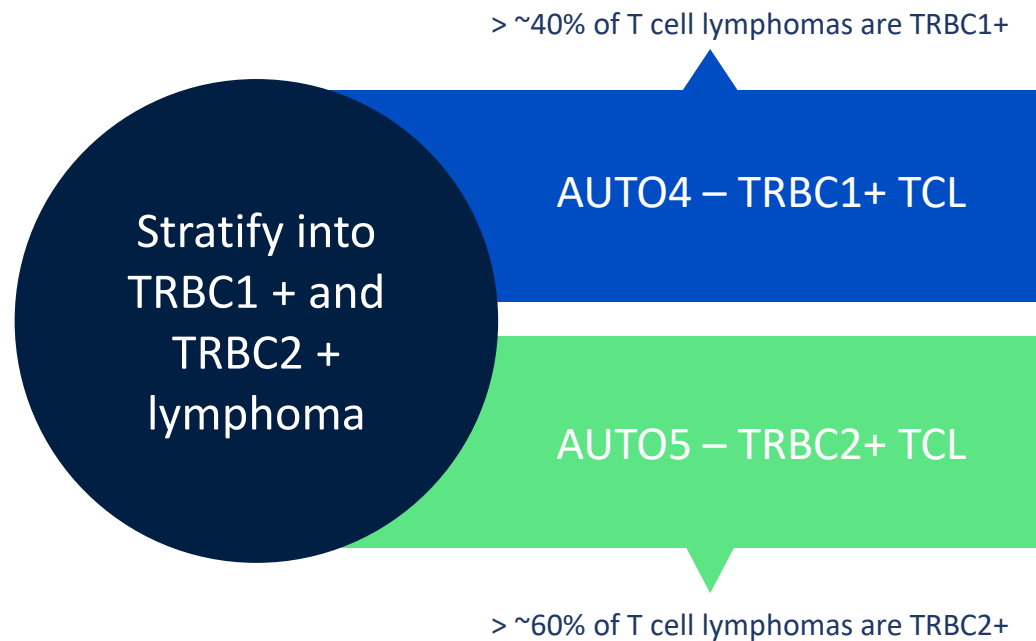
PRODUCT	INDICATION	TARGET	STUDY	PRE CLINICAL	PHASE 1	PHASE 2/ PIVOTAL	BLA
obe-cel	Adult ALL	CD19	FELIX				
obe-cel	B-NHL & CLL	CD19	ALLCAR19 Ext*				
obe-cel	Primary CNS Lymphoma	CD19	CAROUSEL*				
AUTO1/22	Pediatric ALL	CD19 & CD22	CARPALL*				
AUTO4	TRBC1+ Peripheral TCL	TRBC1	LibrA T1				
AUTO5	TRBC2+ Peripheral TCL	TRBC2					
AUTO6NG	Neuroblastoma; Other tumour types	GD2					
AUTO8	Multiple Myeloma	BCMA & CD19	MCARTY*				

\*Collaboration with UCL

# AUTO4: 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 at EHA, June 2022

# AUTO4: EHA abstract

## Data cut: 9 February 2022

- 9 patients screened for r/r TRBC1+ peripheral T-cell lymphoma have been treated with AUTO4
- After lymphodepletion with Flu/Cy
  - 3 patients received 25 x 10<sup>6</sup> CAR T cells
  - 2 patients received 75 x 10<sup>6</sup> CAR T cells
  - 1 patient received 225 x 10<sup>6</sup> CAR T cells
  - 3 patients received 450 x 10<sup>6</sup> CAR T cells
- AUTO4 demonstrated a tolerable safety profile, with no patient experiencing any dose limiting toxicities, and no neurotoxicity/ICANS
  - Three patients experienced CRS (1 patient Grade 1, 1 patient Grade 2 and 1 patient Grade 3)
- Of the 9 patients treated, 5 patients had achieved complete metabolic responses (CMR) by PET-CT at Month 1, 1 patient remains with a PR 6 months post AUTO4 infusion, and 3 patients did not respond
- All 3 patients at the highest dose level achieved a CMR at Month 1



Manufacturing

# Manufacturing operations

First UK CAR T commercial facility expected to be ready for GMP operations in mid 2023

- Highly experienced team running manufacturing operations and supporting new facility build
- 70,000 ft<sup>2</sup> commercial facility under construction in Stevenage
  - Commercial Cell capacity of 2,000+ B/yr with option to increase
  - Vector capacity for clinical activities
  - In process and release QC - automation to drive V2D to < 20 Days
- The Stevenage facility supports retention of key staff and build of critical mass for US and EU expansion



# 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, priced at market
- Blackstone also committed to invest up to \$150 million in product financing to support obe-cel development and preparation for commercialization
  - \$50 million paid upon closing of the transaction
  - Remainder payable based on achievement of certain development and regulatory milestones
- Blackstone received a warrant to purchase up to \$24 million worth of Autolus ADSs at an exercise price premium to market
- Autolus to pay Blackstone a capped single digit royalty plus milestone payments based on net sales of obe-cel
- Transaction provides runway into 2024<sup>1</sup>

## NOTES

1. Assuming all milestones received



# Summary

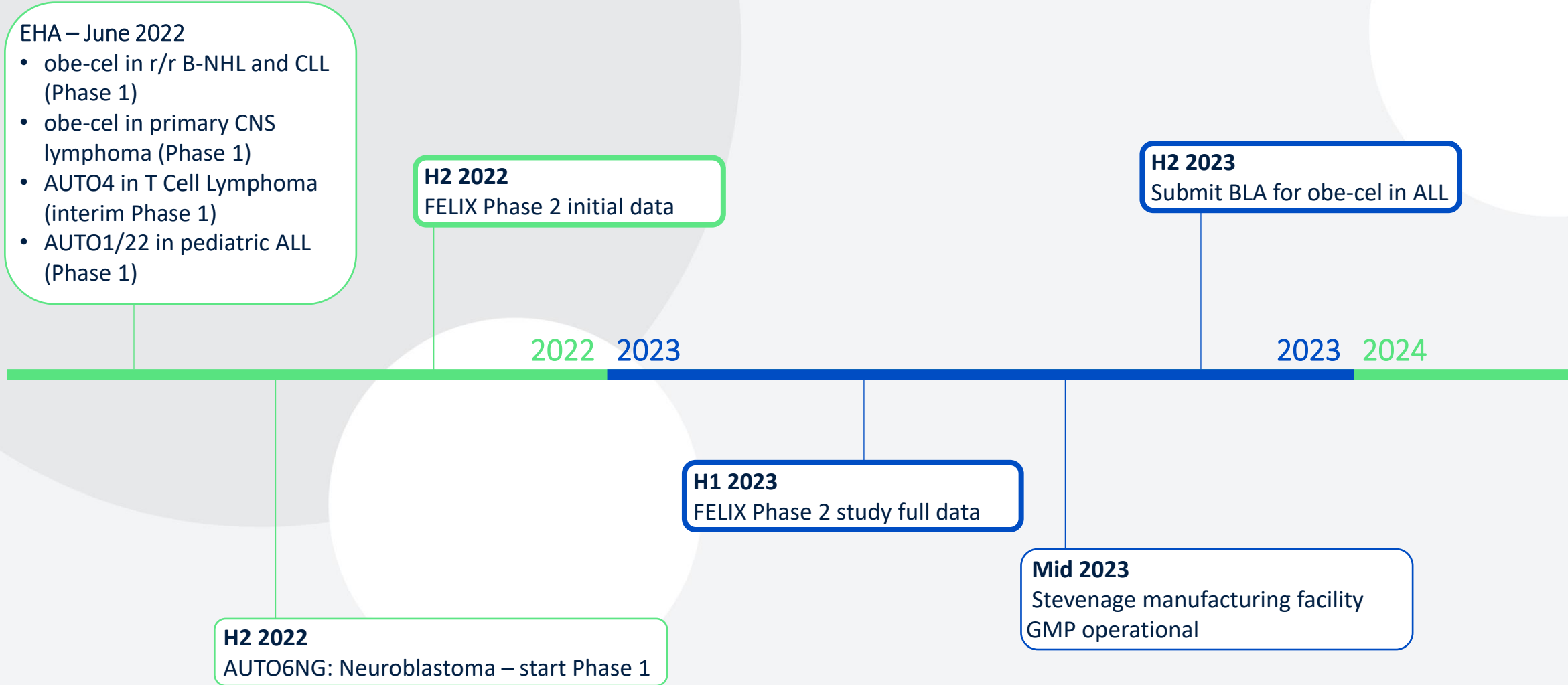
Multiple catalysts in H2 2022

# Autolus poised for potential value inflection

obe-cel pivotal data in adult ALL in 2022

- obe-cel
  - FELIX Phase 2 study in adult ALL ongoing; initial data expected in H2 2022 and full data in H1 2023
  - Evaluation in r/r B-NHL and CLL ongoing; next data update at the EHA Congress in June
  - Evaluation in Primary CNS Lymphoma ongoing; initial Phase 1 data (CAROUSEL study) at EHA in June
- AUTO1/22
  - AUTO1/22 Phase 1 (CARPALL) initial data in Pediatric ALL to be presented as an oral at EHA in June
  - Longer term follow-up data in H2 2022
- AUTO4 /AUTO5
  - AUTO4 Phase 1 (LibrA T1) initial data in Peripheral T cell lymphoma to be presented as an oral at EHA in June
- Pipeline transitioning to Phase 1 in 2022
  - AUTO8 Phase 1 study has started
  - AUTO6NG in Neuroblastoma – start Phase 1 H2 2022
- Cash balance at March 31, 2022, \$268.6 million

# Autolus key newsflow timeline



Thank you

