



# Fourth Quarter Financial Results and Operational Progress

March 2022



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# Agenda

- Welcome and Introduction: Dr. Lucinda Crabtree, SVP, Finance
- Operational Highlights: Dr. Christian Itin, CEO
- Financial Results: Andrew J. Oakley, CFO
- Upcoming Milestones and Conclusion: Dr. Christian Itin, CEO
- Q&A: Dr. Christian Itin, Andrew J. Oakley and Dr. Lucinda Crabtree



# Pipeline and Corporate Highlights

## Key operational updates – fourth quarter 2021

Continued progress on building a leading ALL company with Blackstone collaboration providing up to \$250 million financing

- Obe-cel shows highly consistent and best in class efficacy and safety profile across three B-ALL phase 1 studies in patients with a wide range of age, disease burden and prior therapies
- Strategic collaboration and financing agreement with Blackstone Life Sciences (NYSE: BX) providing up to \$250 million in equity and product financing
- Planning approval granted to build the Company's new manufacturing facility in Stevenage, UK
- Strengthened the Board with new appointments
  - John H. Johnson - Non-Executive Chairman
  - Dr. William D. Young - Non-Executive Director
- Post period, Lucinda Crabtree Ph.D. to replace Andrew Oakley as CFO on his retirement on 31 March 2022

# 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

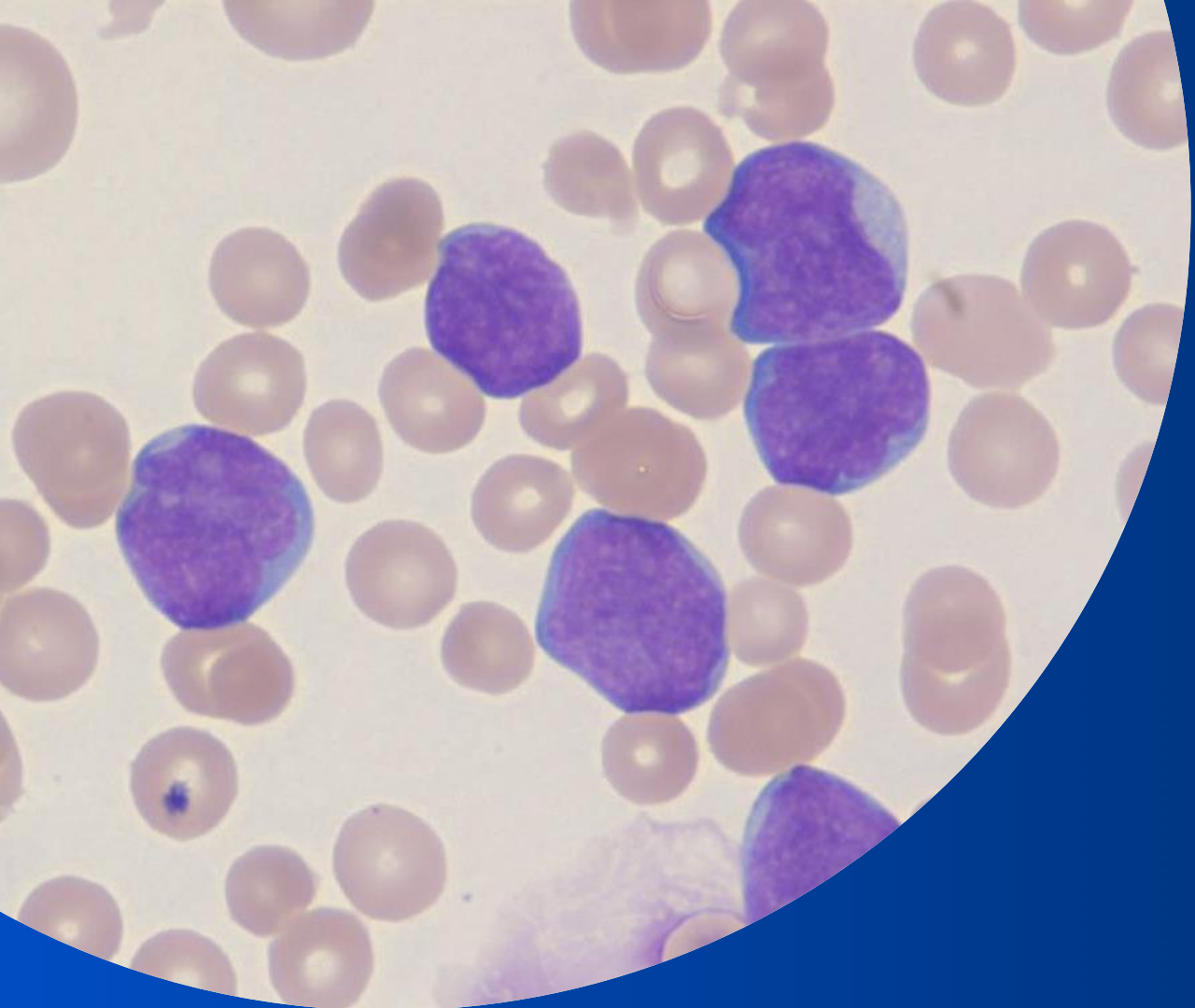
# Program updates – fourth quarter 2021

FELIX study progressing, Phase 1b data consistent with ALLCAR19, data in 2022

- Obe-cel in relapsed / refractory (r/r) adult ALL – Data at ASH in December 2021
  - Data from the FELIX Phase 1b portion show a favorable safety and efficacy profile consistent with ALLCAR19 study in adult r/r B-ALL
  - Duration of response from the ALLCAR19 study remains highly encouraging with morphological EFS for obe-cel of 46% at 24 months with a median follow-up of 29.3 months and patients approaching up to 42 months of durability
- Obe-cel in r/r B-NHL – ALLCAR19 extension - Data at ASH in December 2021\*
  - Favorable safety profile in B-NHL and CLL with no ICANS or severe Grade  $\geq 3$  CRS, consistent with safety profile observed in r/r B-ALL
  - Out of 14 patients evaluable for efficacy, 100% ORR and 13/13 B-NHL (100%) in complete metabolic response
  - Long term persistence of obe-cel demonstrated by qPCR
- AUTO1/22 in pediatric ALL – Positive translational pre-clinical data at ASH in December 2021\*\*
  - All 6 patients showed engraftment of single and double CAR positive populations, pointing to early CAR T cell persistence
- AUTO4 in Peripheral T Cell Lymphoma
  - Phase 1 clinical trial is progressing through dose escalation

\*As of the cut-off date of October 15, 2021      \*\*As of the cut-off date of October 21, 2021

<sup>(1)</sup>Roddie et al. "Durable responses and low toxicity after fast off-rate CD19 CAR-T therapy in adults with relapsed/refractory B-ALL." DOI: 10.1200/JCO.21.00917 *Journal of Clinical Oncology* - published online before print August 31, 2021



# 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 adult patients are generally more fragile with co-morbidities and experience high incidences of severe CRS and 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 ≥ 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)

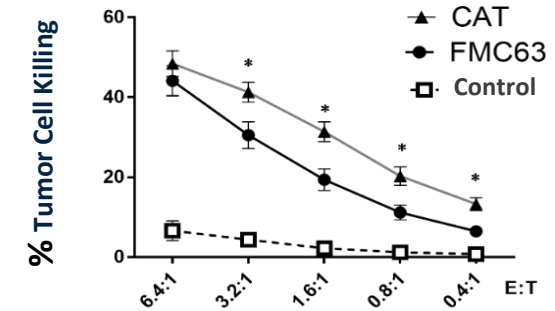
The estimates of EFS/PFS are read from the KM curves. The efficacy data in ZUMA-3 are based on the modified ITT population while the blinatumomab and inotuzumab data are based on the ITT population.

# obe-cel has a unique mechanism of action

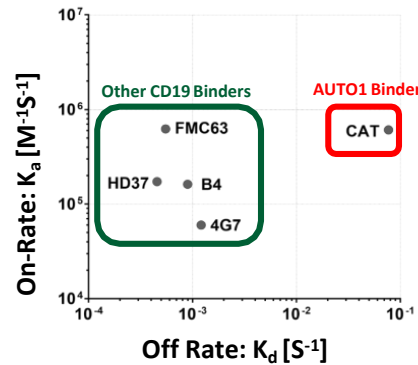
Fast off rate supports physiological engagement of target cells and avoids over-activation and exhaustion of CART cells

- obe-cel is designed to improve potency and persistence while reducing immunological toxicity
- Obe-cel (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

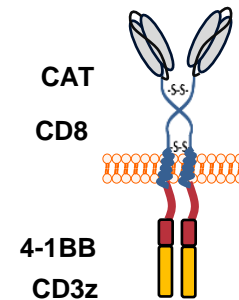
## Enhanced Cytotoxicity



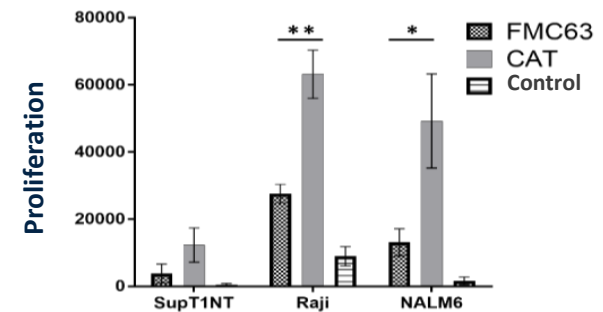
## Fast Off-Rate



## Lentiviral Vector



## Enhanced Proliferation



\*Ghorashian S, Pule MA, Amrolia P et al. *Nature Medicine* 2019

# obe-cel shows consistent clinical profile across three Phase 1 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

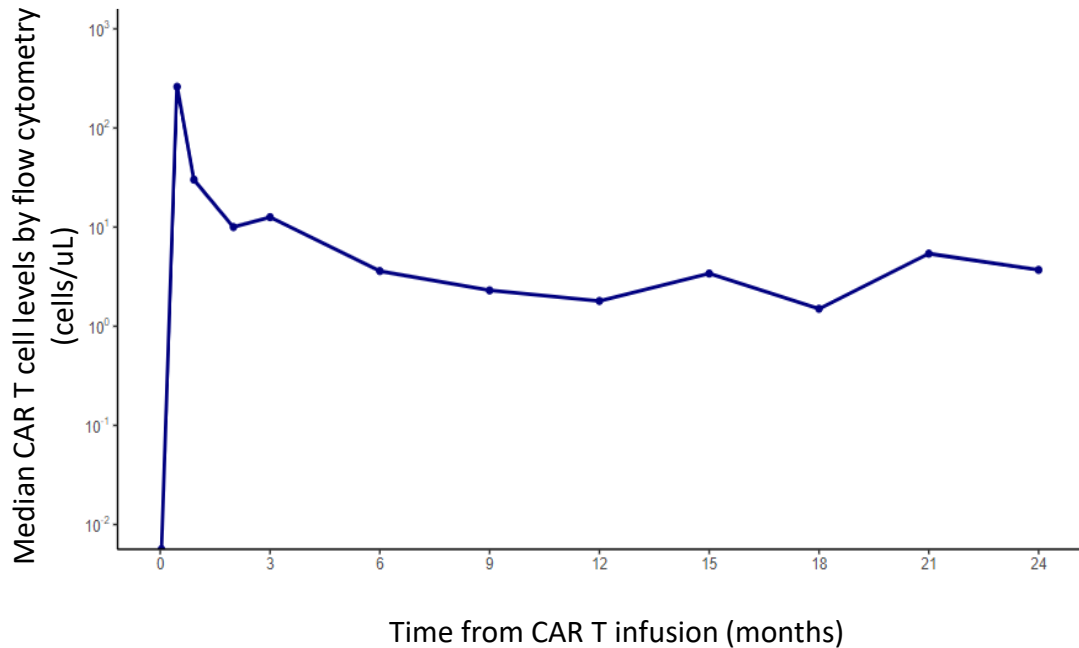
#2 Roddie et al. J Clin Oncol, 2021

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

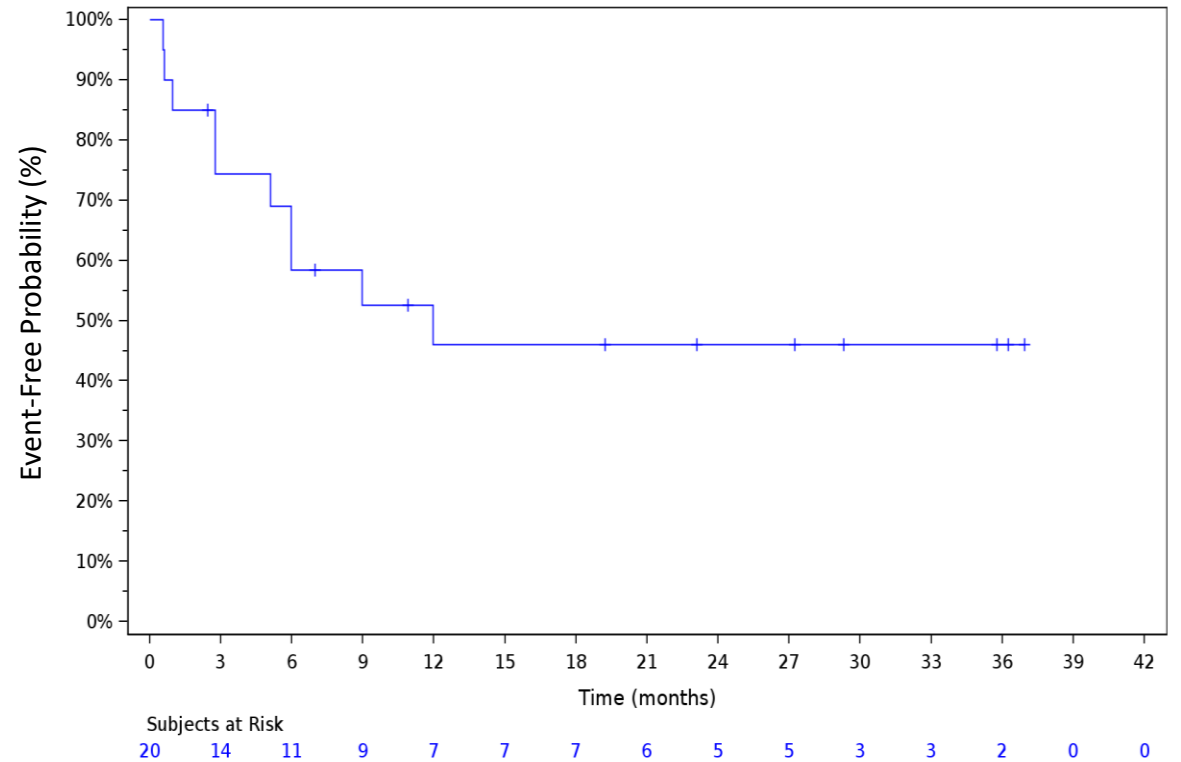
# obe-cel shows sustained event-free survival beyond 30 months

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

# 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 data in 2022  
and full data in H1 2023**

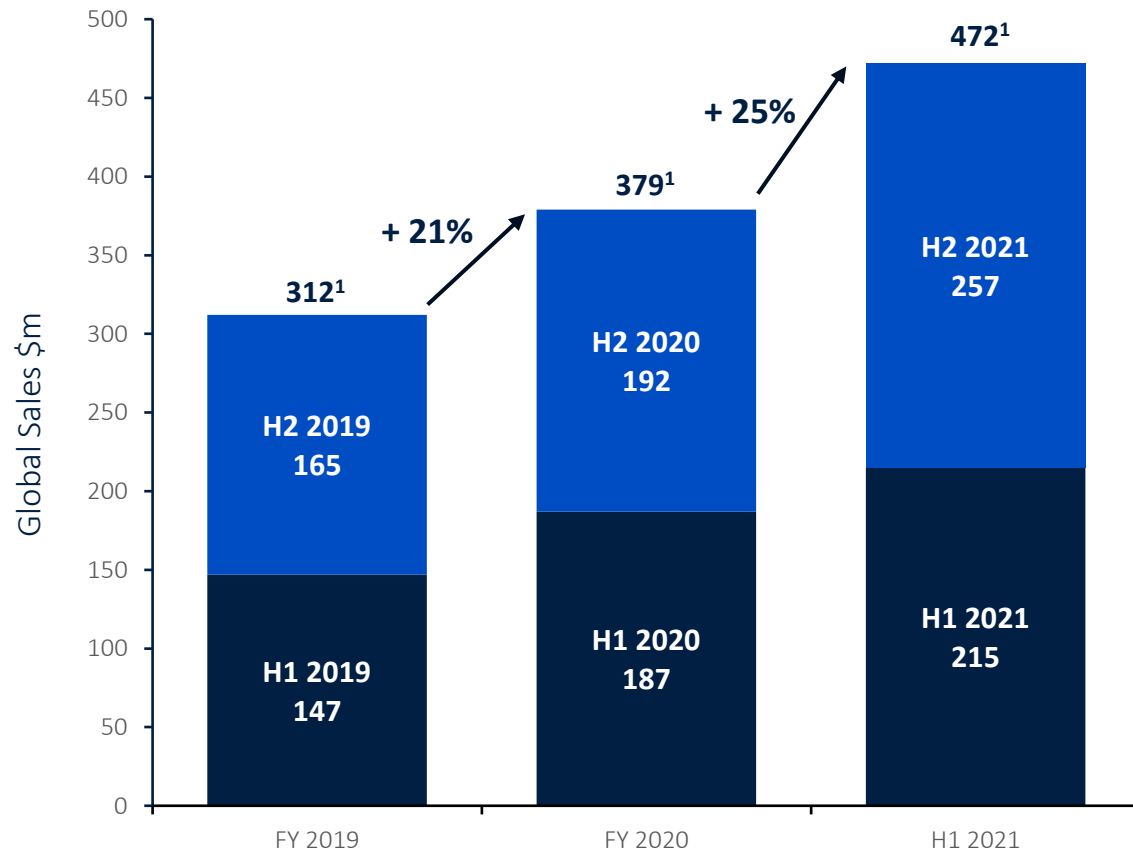
Phase 2 part of the FELIX study ongoing since mid 2021 with sites in UK, Spain and US

- 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

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

Blincyto, current market leader, shows annual revenue growth of 25%

## 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 25%
- 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



# Stevenage Manufacturing Facility Update

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



- For commercial supply, Autolus new 72,000 square foot manufacturing facility in Stevenage, UK is currently under construction
- This new Stevenage facility will allow for GMP capacity for approx. 2,000 batches a year initially, with the option for further volume increases



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

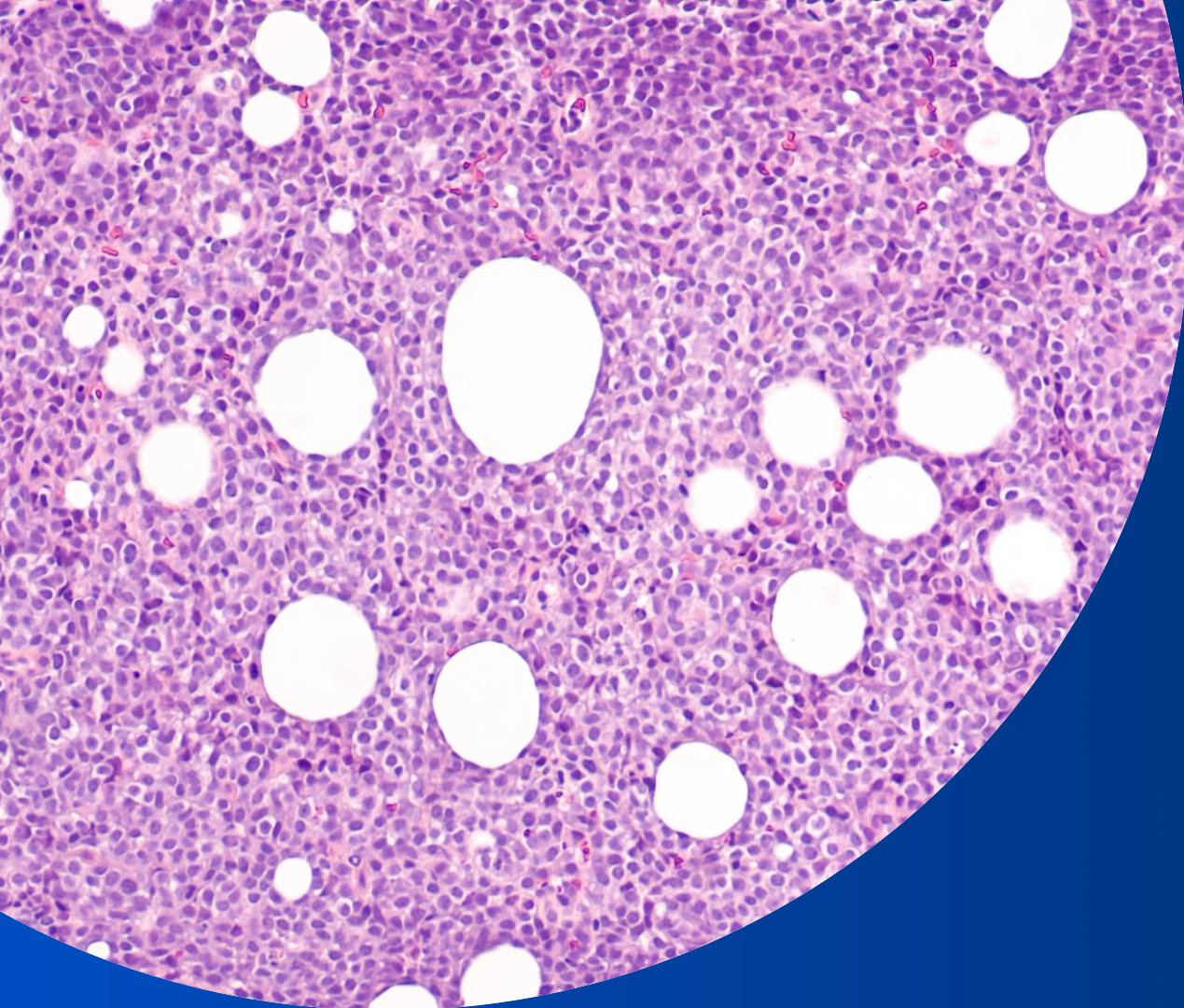
Evaluation of obe-cel activity in additional B-Cell malignancies to capitalize on potential market opportunity

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

 B Cell Malignancies

\* Collaboration with UCL

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



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

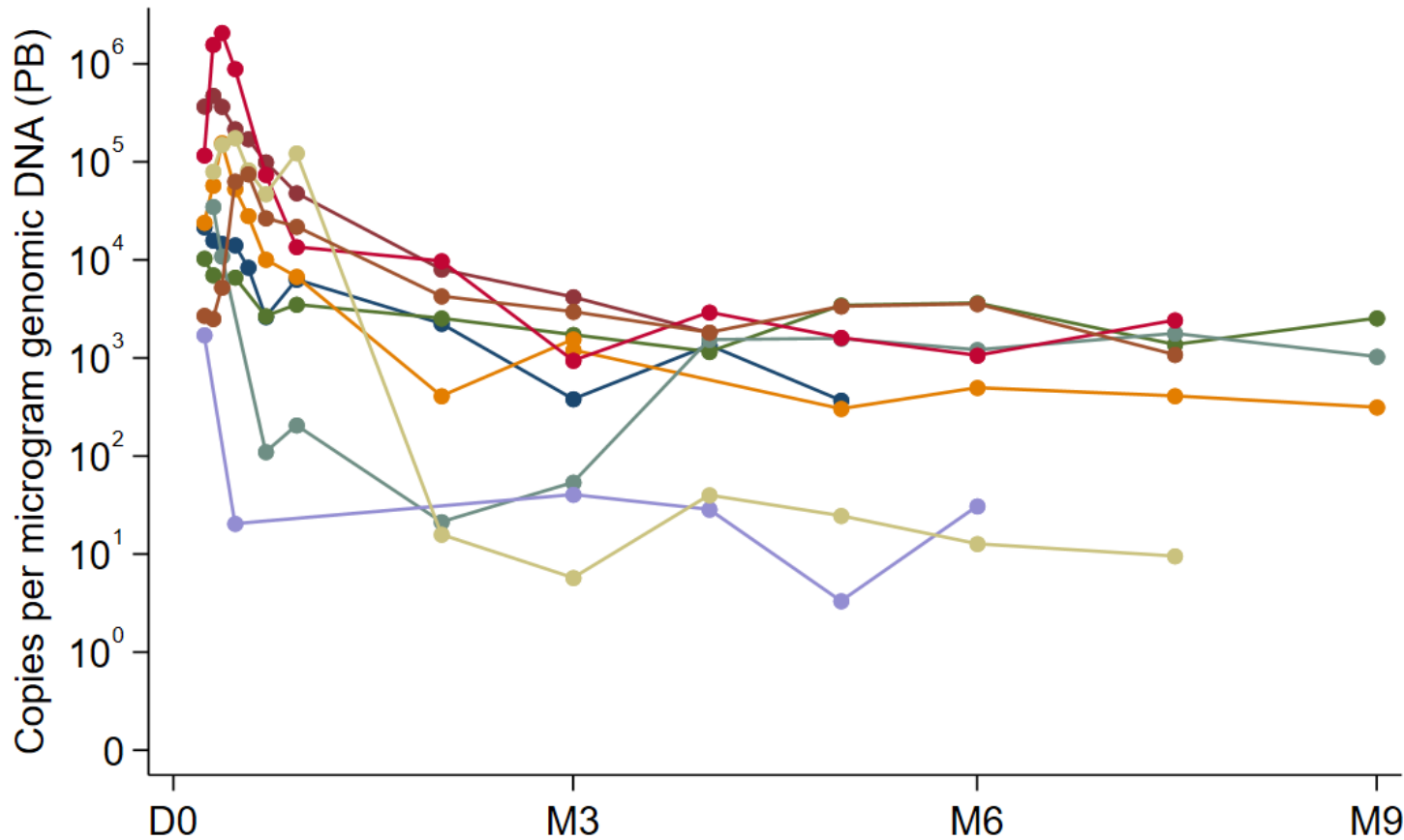
\*CRS grading by Lee et al 2018

Data cut: 15-OCT-2021

- 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

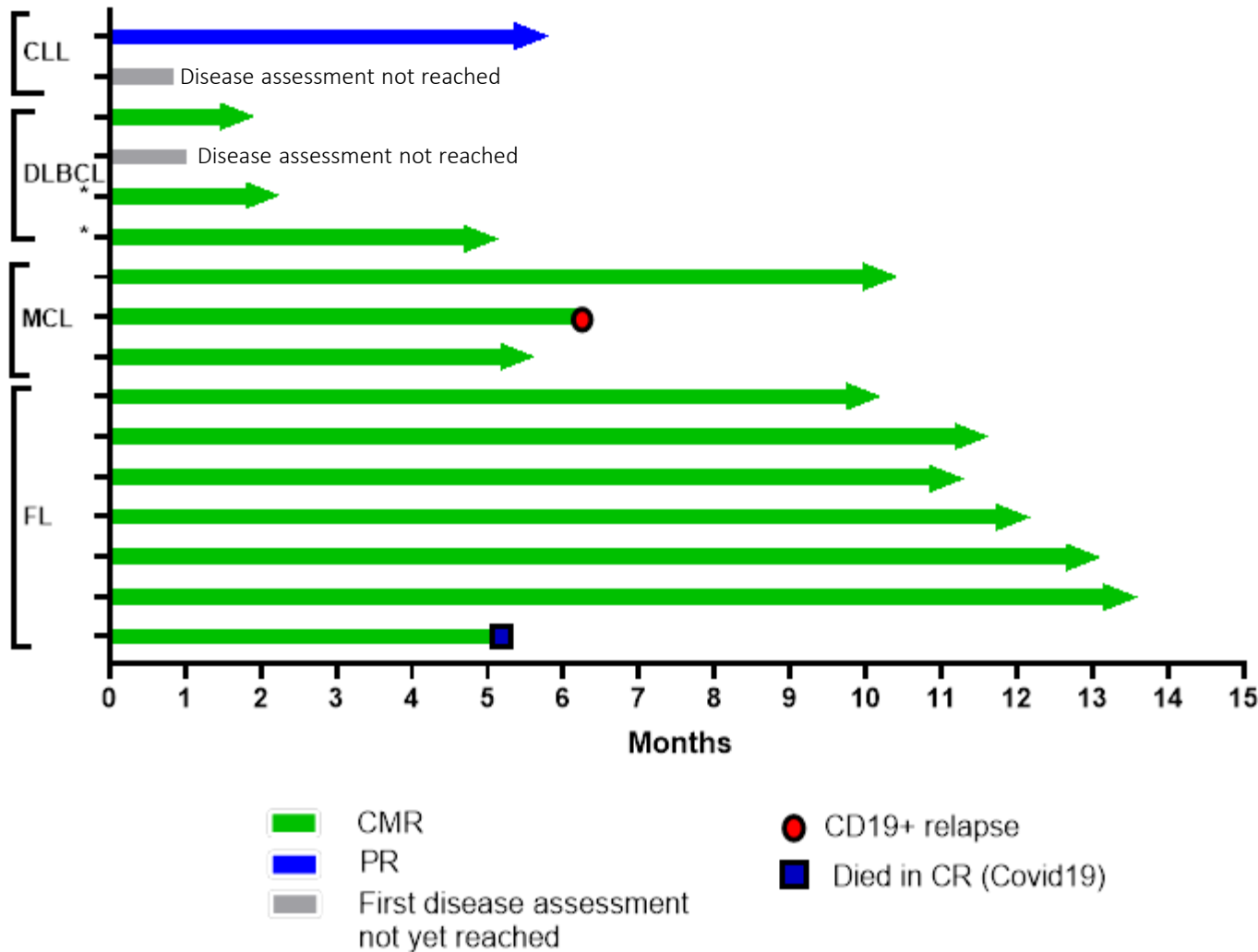


CAR, chimeric antigen receptor; VCN, vector copy number; qPCR, quantitative polymerase chain reaction, CV% , coefficient of variation

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



Data cut: 15-OCT-2021

DLBCL\* = transformed follicular lymphoma

	N (%)
<b>Follicular Lymphoma</b>	
CR + PR	7 (100%)
CR	7 (100%)
<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.)
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)

## 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 H1 2022

Pediatric ALL



# Autolus CAR T approach to treating pediatric ALL

CD19 negative antigen escape is a common cause of treatment failure

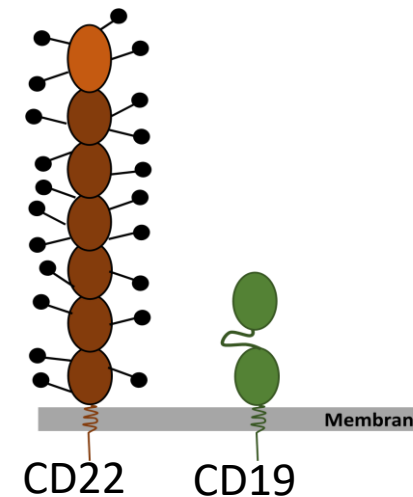
- obe-cel (AUTO1) in relapsed / refractory pediatric ALL is highly active and has a favourable safety profile - CARPALL study<sup>#1,2</sup>
- Medical need in pediatric ALL is to minimize rates of antigen-loss–driven relapses and improve long-term outcomes – points to need for a dual targeting CAR-T
- 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 is a next generation program that builds on obe-cel and adds a highly potent CD22 CAR, capable of targeting low levels of CD22

#1 NCT02443831

#2 Ghorashian et al., Nat Med 2019

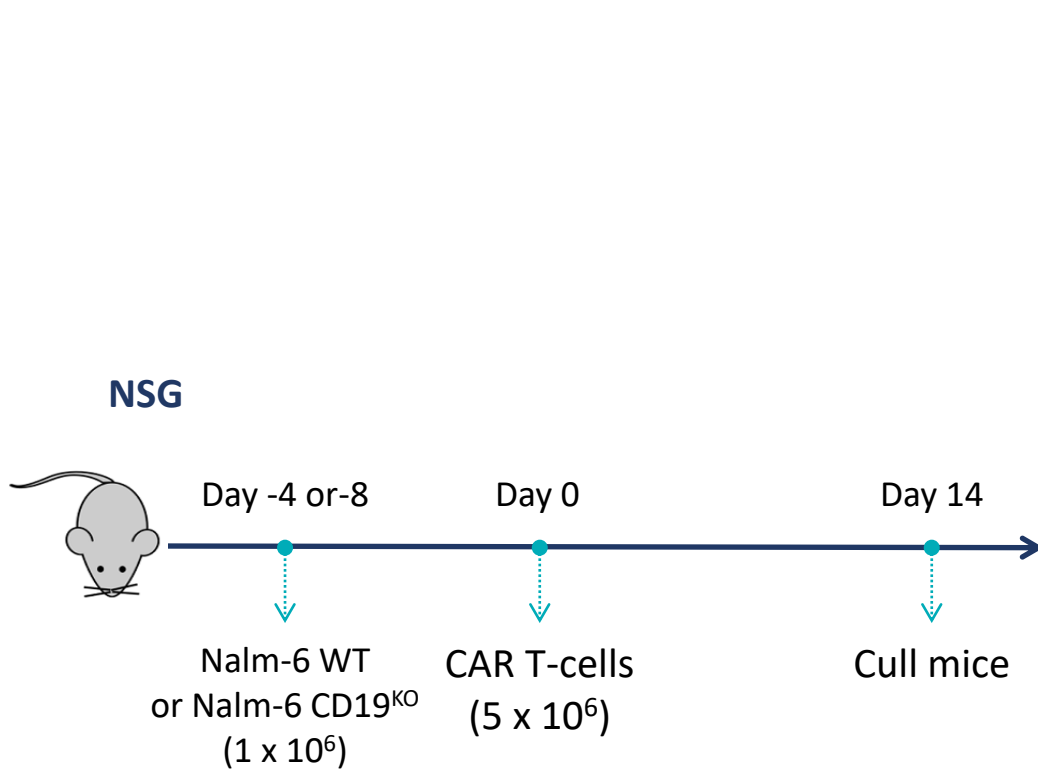
#3 Shah et al., JCO 2020, Spiegel et al., Nat Med 2021

	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%

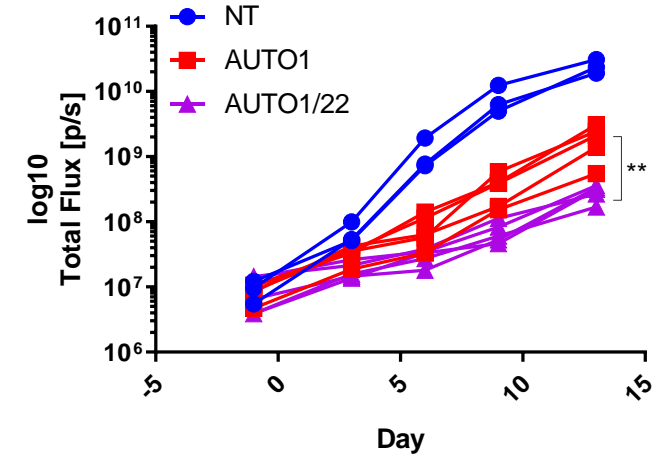
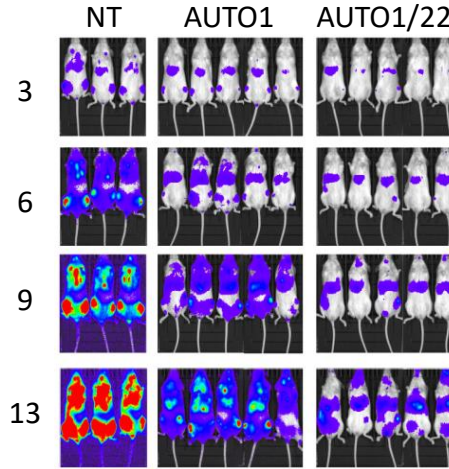


# AUTO1/22: enhanced in vivo anti-tumor efficacy

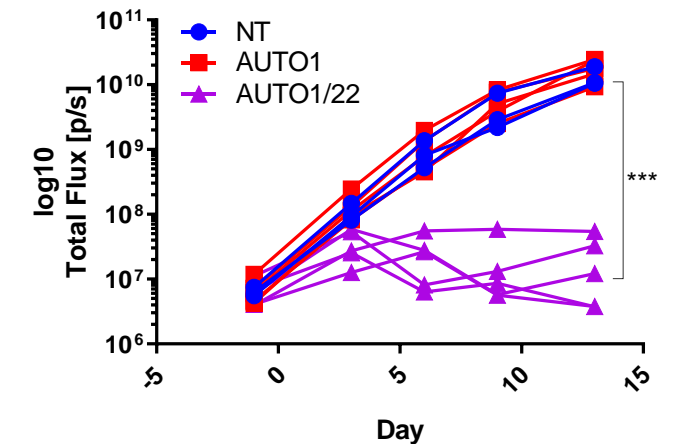
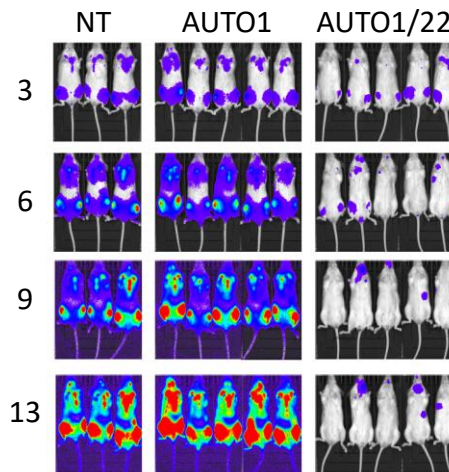
Dual targeting of CD19 and CD22 addresses CD19-negative target cells and enhances overall activity



## Nalm-6 WT



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



# AUTO1/22 – A dual targeting CAR T therapy

Currently being tested in pediatric ALL

- AUTO1/22 builds on excellent CD19 targeting of oxe-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 H1 2022

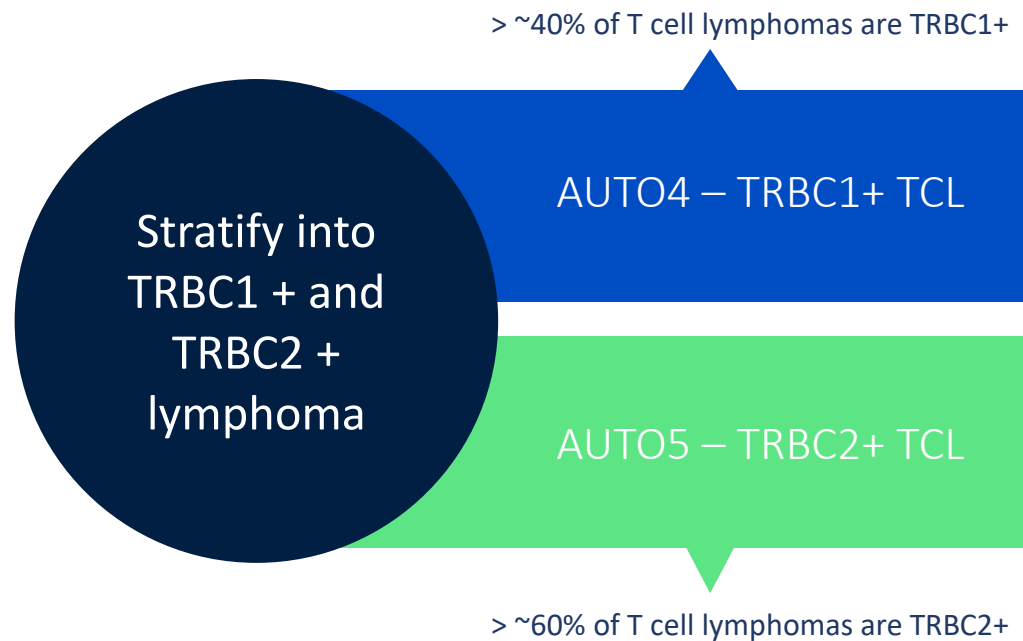
# Pipeline

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

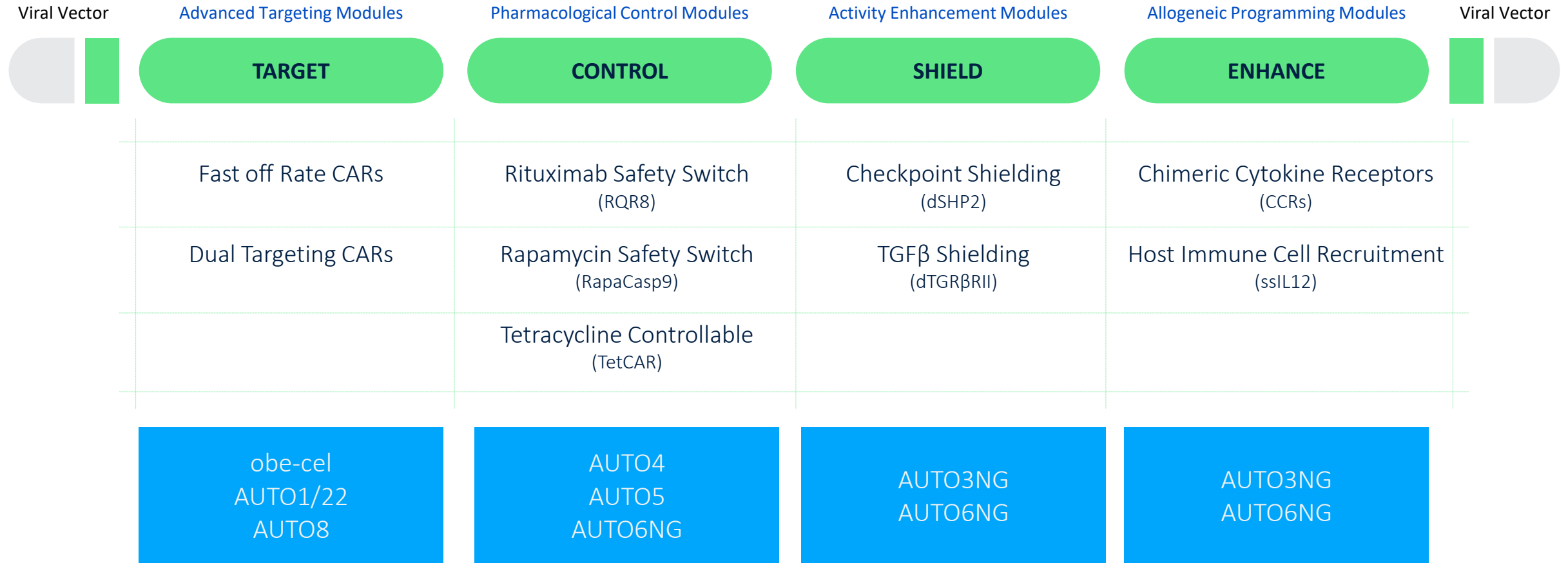
Three key elements to address T cell lymphomas:  
AUTO4, AUTO5 and a companion diagnostic test



- 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

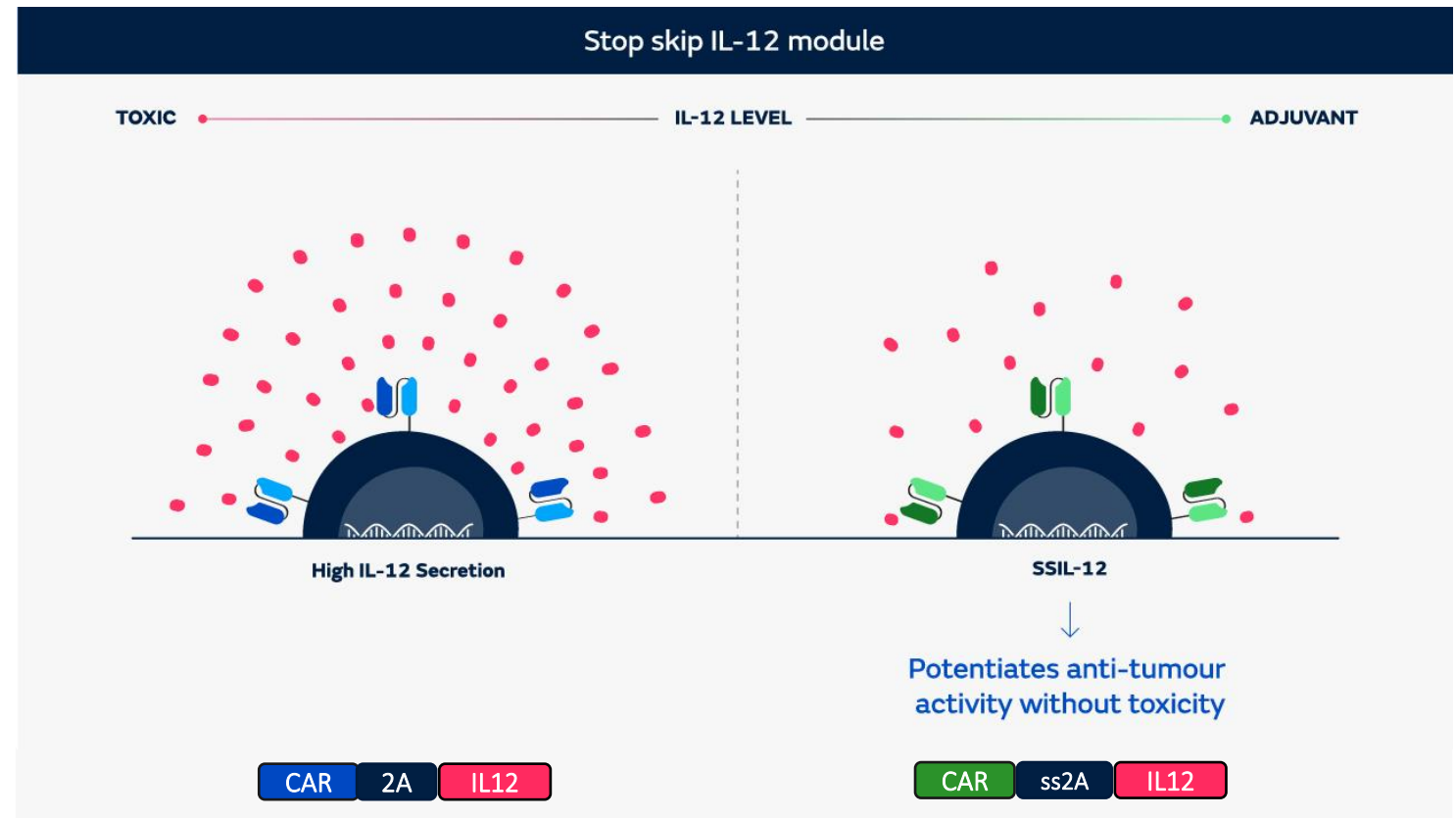
Advanced T cell programming



# SS-IL12 module maintains potent adjuvant activity with no toxicity

Module prevents toxicity by drastically reducing IL12 secretion

- IL-12 is a potent adjuvant that promotes a powerful anti-tumour response when combined with checkpoint inhibitors and adoptive T cell transfer<sup>1</sup>. However, IL-12 has been associated with systemic toxicity<sup>2</sup>
- Engineered version of the IL-12 (SS-IL12) has been designed to constrain expression while maintaining its adjuvant activity



# 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



# Financial Results

## Financial summary

USD m	FY 2021	FY 2020	Variance
Grant Income	0.8	1.5	(0.7)
License Income	1.5	0.2	1.3
R&D	(134.8)	(134.9)	0.1
G&A	(31.9)	(35.0)	3.1
Loss on disposal of leasehold improvements	(0.7)	-	(0.7)
Total Op Expense, Net	(165.0)	(168.1)	3.1
Interest Income	0.3	0.5	(0.2)
Other (Expense)/Income	(0.1)	1.4	(1.5)
Interest expense	(1.1)	-	(1.1)
Tax Benefit	23.9	24.2	(0.3)
Net Loss	(142.1)	(142.1)	-
USD m	FY 2021	FY 2020	Variance
Cash Balance	310.3	153.3	157.0

Cash runway into 2024, assuming all milestones received



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 with full data in H1 2023
- Evaluation in relapsed/refractory B-NHL and CLL ongoing, with next data update planned for European Hematology Association (EHA) Congress in H1 2022
- Evaluation in Primary CNS Lymphoma ongoing with initial data update planned for EHA in H1 2022

## AUTO1/22

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

## Pipeline

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

## Cash balance at December 31, 2021, \$310.3 million:

- Cash runway including project financing payments from Blackstone into 2024

Thank you

