# Autolus

Full year Financial Results and Fourth Quarter Operational Progress



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### Agenda

- Welcome and Introduction: Julia Wilson, Communications Consultant
- Operational Highlights: Dr. Christian Itin, CEO
- Financial Results: Dr. Lucinda Crabtree, CFO
- Upcoming Milestones and Conclusion: Dr. Christian Itin, CEO
- Q&A: Dr. Christian Itin and Dr. Lucinda Crabtree

# Obe-cel and pipeline highlights – fourth quarter 2022

Continued progress against strategic and operational goals

#### obe-cel in relapsed / refractory (r/r) adult ALL

- FELIX pivotal Phase 2 trial met primary end point and confirmed the well manageable safety profile
- On track for FELIX data update from all patients treated at a clinical conference in mid-2023, and the filing for a Biologics License Application (BLA) to the US FDA is planned for the end of 2023
- ALLCAR19 Phase 1 data at ASH demonstrated that 35% of adult B-ALL patients remain in complete remission at a median follow up
  of 36 months without the need for additional anti-leukemia therapy

#### obe-cel in other indications

- ALLCAR19 extension study of obe-cel in r/r B-NHL data at ASH demonstrated the potentially best-in-class profile with continued high levels of clinical activity, and an encouraging tolerability profile across DLBCL, MCL, FL and CLL
- Next update for ALLCAR19 is planned for ASH 2023 with long term follow up
- CAROUSEL study of obe-cel in peripheral CNS Lymphoma is fully enrolled and data will be submitted for publication

#### Other pipeline updates

- CARPALL Phase 1 trial of AUTO1/22 in pediatric ALL data at ASH in Kymriah ineligible patients demonstrated a molecular CR rate
  of 83% of patients with no antigen negative relapses
- LibrA T1 Phase 1 trial of AUTO4 in Peripheral T Cell Lymphoma data at ASH demonstrated high metabolic CR rate
- MCARTY Phase 1 trial of AUTO8 in Multiple Myeloma continuing to enroll patients first data expected 2023
- Phase 1 trial of AUTO6NG in Neuroblastoma first patient expected to be dosed in 2023

### Operational highlights – fourth quarter 2022

Continued progress against strategic and operational goals

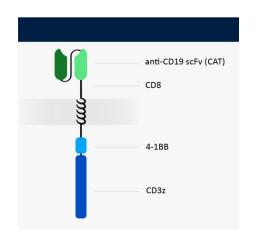
- Successful public offering raising c.\$164m gross proceeds
- Receipt of \$70m in milestones from Blackstone Life Sciences
  - \$35m on meeting the primary endpoint and confirming the favorable safety profile in the pivotal FELIX Phase 2 trial
  - \$35m on completion of planned activities supporting the performance and qualification of the obe-cel manufacturing process
- Three technology agreements announced
  - Bristol Myers Squibb access to the Company's proprietary RQR8 rituximab-induced safety switch
  - Moderna selected one of the proprietary binders to an undisclosed immuno-oncology target for the delivery of pioneering messenger RNA (mRNA) therapeutics
  - Cabaletta Bio, post period end access to the RQR8 safety switch for autoimmune disease
- Build of the commercial manufacturing facility in Stevenage, UK progressing on track with schedule
  - Phase 1 of build was completed on track for Good Manufacturing practice Operations commencing in H2 2023
  - Development work for CMC package on track, in preparation for potential submission of BLA by the end of the year
- Cash of \$382.8m at December 31, 2022, including restricted cash



# Che-cel

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

### Obe-cel has a unique mechanism of action



CD19 binder with fast off-rate

### Potential for improved potency, reduced toxicity

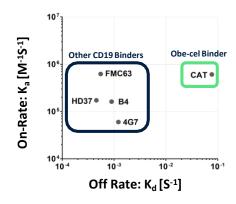
Avoided over-activation of CAR T cells
-> Reduced toxicities

Increased CAR T peak expansion
-> Improved persistence

Avoided exhaustion of CAR T cells

- -> Improved engraftment
- -> Improved persistence

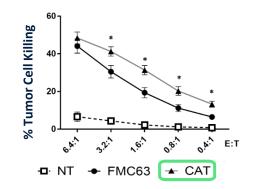
#### **Fast off-rate**

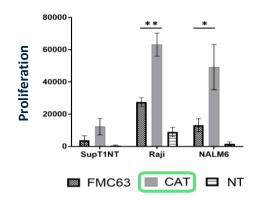


Obe-cel has a shorter half-life of interaction compared to binders used in approved products

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

#### **Enhanced cytotoxicity and proliferation**





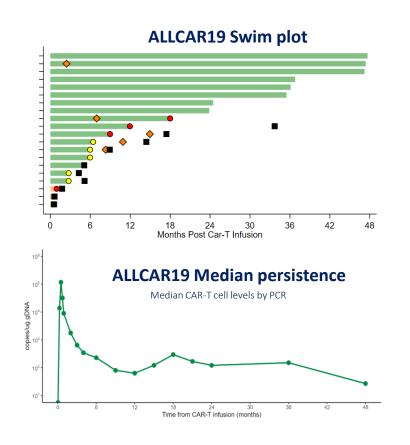
### Obe-cel is a potentially transformational therapy for adult ALL

Unique CAR T design to drive differentiated product profile

#### **Obe-cel – Key Properties**

- Target engagement with fast off-rate drives unique product properties
- High Overall Remission Rate (ORR) across all patient populations evaluated<sup>1,2</sup>
- 35% of patients with long-term remission, without any further therapy<sup>2</sup>
- All patients with long term remissions have long-term persisting CAR T cells<sup>2</sup>
- Well manageable safety profile

### Obe-cel – Key Data



#### **Regulatory Designations**

Orphan Drug designation by FDA for B-ALL

Orphan Medicinal 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

### **FELIX Phase 2 Study Overview**

Interim analysis completed Q4 2022 – met primary endpoint – next data readout expected mid 2023



Phase 2 has up to 100 relapsed/refractory adult ALL patients with morphological disease:

- 34 sites in US, UK and Spain
- Phase 1b run-in study completed
- Phase 2 study morphological cohort fully enrolled
- Phase 2 study interim analysis completed in Q4 2022 primary end point reached
- Phase 2 study data presentation planned for mid 2023

Patients with minimal residual disease (MRD) evaluated in separate study arm

**Primary** endpoint overall complete response rate (CR/CRi) Mid 2023 Data at medical conference Secondary endpoints include MRDnegative CR, **EFS and DoR** 

### FELIX Phase 2 Pivotal trial met primary endpoint

Positive data is a catalyst for the next stage of growth and preparation for commercialization

- Phase 2 pivotal FELIX study of obe-cel in r/r adult ALL has met its primary endpoint, based on an interim analysis of 50 patients with morphological disease, as verified by an IDMC
- The primary endpoint for the FELIX Phase 2 trial is the ORR, defined as CR and CRi
- Obe-cel demonstrated ORR of 70% in interim analysis of 50 patients with r/r ALL

- Encouraging tolerability data observed, with 3% ≥Grade 3
   Cytokine Release Syndrome (CRS) and 8% ≥Grade 3
   Immune effector cell-associated neurotoxicity syndrome
   (ICANS) in 92 patients evaluable for safety
- Screening completed for patients for entry into the morphological cohort
- Blackstone paid a development milestone of \$35 million,
   earlier than anticipated, at this interim analysis

### Obe-cel showed consistent clinical profile across three clinical studies

Data from 3 studies - range of ages and patient conditions

Obe-cel demonstrated a favourable tolerability profile: no high-grade CRS and limited ICANS

	CARPALL #1 Peds ALL	ALLCAR19 #2 Adult ALL	FELIX P1b <sup>#3</sup> Adult ALL	FELIX P2 Adult ALL
n	14	20	16	50 (92)*
ORR (CR & CRi) (95% CI)	86% (57%, 98%)	85% (62%, 97%)	75% (48%, 93%)	70%
CRS <sup>1</sup> ≥ Grade 3	0%	0%	0%	3%
CRS <sup>1</sup> any Grade	93%	55%	56%	ND
Neurotox <sup>2</sup> ≥ Grade 3	7%	15%	6%	8%
Neurotox <sup>2</sup> any Grade	50%	20%	13%	23%
Median Age	9	42	42	ND
Bone marrow blast >20% at LD	21%	60%	75%	ND
Bone marrow blast <5% at LD	71%	35%	25%	ND
Prior blinatumomab	7%	25%	56%	ND

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

<sup>\*</sup> Efficacy analysis for FELIX 2 trial conducted in 50 patients whereas safety analysis conducted in 92 patients

<sup>#1</sup> Ghorashian et al. Nature Medicine 2019

<sup>#2</sup> Roddie et al. J Clin Oncol, 2021

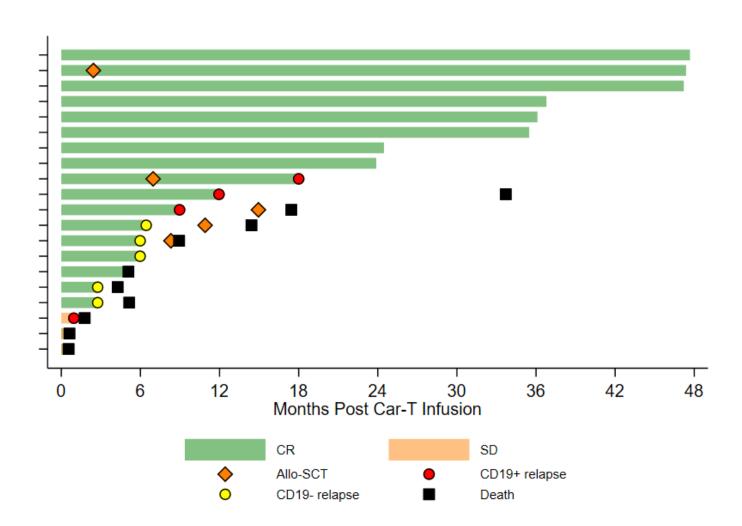
<sup>#3</sup> Culshaw et al, ASH 2021, abstract #477

# Obe-cel at ASH 2022 – B-ALL long term follow up from Ph1 ALLCAR19 trial

'Safety, Efficiency and Long-Term Follow-up of obe-cel, a Fast-Off Rate CD19 CAR in Relapsed/Refractory B-Cell Acute Lymphoblastic Leukaemia and Other B-Cell Malignancies'

#### **B-ALL** patients

- Of the 20 infused B-ALL patients, 8/20 (40%) are in ongoing CR at a median FU of 36 months (IQR 24-47) post obe-cel
- 7/8 (35%) maintain remission without any further therapy (including TKI)
- All patients with long term remissions have long term persisting CAR T cells



ALLCAR19 data cut: 2-NOV-2022

# New innovative options needed in r/r adult ALL despite approved agents

Current standard of care and recently approved agents in r/r adult ALL<sup>1</sup>

	STAND	RECENTLY APPROVED	
	Blincyto <sup>®2</sup> (blinatumomab)	Besponsa <sup>®3</sup> (inotuzumab ozogamicin)	Tecartus <sup>™4</sup> (brexucabtagene autoleucel)
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 <sup>5</sup>

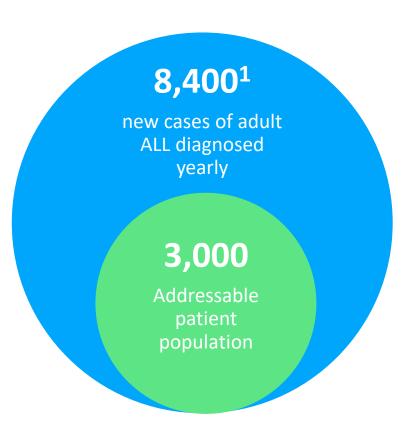
<sup>1.</sup> Data are not from head-to-head clinical testing and should not be viewed as comparative data

<sup>2.</sup> Kantarjian et al., 2017/ USPI (product label) 3. Kantarjian et al., 2016/ USPI (product label) 4. Shah et al. Lancet 2021/ USPI (product label) 5. Shah et al. ASCO 2021
The estimates of EFS/PFS are read from the KM curves. The efficacy data in ZUMA-3 evaluating brexucabtagene autoleucel are based on the modified ITT population while the blinatumomab and inotuzumab ozogamicin data are based on the ITT population

### Over 8,000 new cases of adult ALL annually worldwide

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</li>
- 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 in for adult patients are Blincyto<sup>®</sup> and Tecartus<sup>TM 2</sup>
  - Both therapies are highly active, but frequently followed by subsequent treatments (e.g. alloSCT)
- Blincyto®: favourable safety profile, few patients experiencing severe CRS and ICANS, but limitations on convenience - continuous i.v. infusion during 4 week treatment cycles
- Tecartus™: more challenging to manage induces elevated levels of severe CRS, a high level of ICANS, and requires vasopressors for many patients
- Opportunity to expand the addressable patient population in earlier lines of therapy



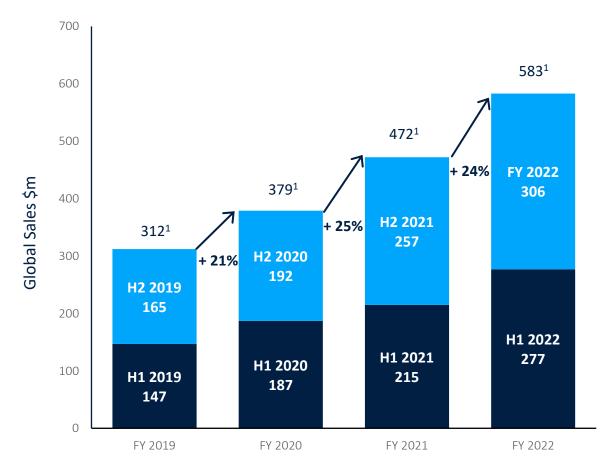
#### NOTES

- 1. SEER and EUCAN estimates (respectively) for US and EU
- 2. Currently approved in US only

# Obe-cel could launch into an expanding ALL market if approved

Blincyto<sup>®</sup>, current market leader, shows annual revenue growth of c.24%

### Reported Blincyto® sales¹



- Blincyto® sales price estimated to be \$207k² (for 2 cycles) supporting approx. >2,000 commercial adult ALL patients, growing at a rate of 24%
- Kymriah® is priced at \$508k in pediatric ALL. Breyanzi® is priced at \$447k in DLBCL³. Tecartus™ is priced at \$424k⁴ for adult ALL
- Breyanzi® and other CAR T cell therapies are expanding delivery center footprint
- Tecartus<sup>™</sup> is expected to establish CAR T use in adult ALL
- If approved obe-cel has the potential to be best-in-class curative therapy and expanding use beyond academic transplant centers

#### **NOTES**

- 1. As per Amgen quarterly SEC filings
- 2. https://www.cms.gov/medicare/medicare-part-b-drug-average-sales-price/2022-asp-drug-pricing-files
- 3. Bristol Myers finally wins FDA approval for cancer cell therapy | BioPharma Dive
- Komodo Health 2015 2020
- 4. Red Book pricing database https://www.ibm.com/products/micromedex-red-book/pricing

### Obe-cel next steps to commercialization

### Data and path to approval

- FELIX clinical data presentation planned for Q2 2023
- Filing of Biologics License Application (BLA) to U.S. Food and Drug Administration (FDA) planned for end of 2023
- Filings of EU and UK marketing authorization applications planned for 1H 2024

### **Manufacturing**

- Bespoke commercial manufacturing facility built in Stevenage UK
- Operational start up in 1H 2023 (qualification and validation)
- GMP license from MHRA planned for Q3 2023
- Facility has initial capacity to produce up to 2000 batches PA; sufficient for global demand in ALL

#### **Commercialization**

- Focus in 2023 on Medical affairs,
   HTA dossier compilation and center onboarding
- Focus in 2024 on launch preparation and execution
- Consider EU partner for launch

# Building the obe-cel opportunity

Deep value program with potentially broad applicability

### Obe-cel lifecycle outlook - NHL/CLL and Pediatric ALL - ASH 2022

High level of clinical activity with well manageable safety profile

- Clinical data supports differentiated product profile in Adult ALL, B-NHL (obe-cel) and Pediatric ALL (AUTO 1/22)
- Potential to drive adoption of obe-cel across B-cell malignancies

#### ALLCAR19 - B-NHL and CLL

N		25
ORR		
	All patients	92%
	Follicular Lymphoma	100%
	Mantle Cell Lymphoma	100%
	DLBCL	88%
	CLL/SLL	80%
CRS ≥ Grade 3		0%
CRS any grade		56%
Neurotox/ICANS > Grade 3		0%
Neurotox/ICANS any Grade		4%

- Median Follow-Up time from infusion in NHL/CLL cohort: 12.9 months (IQR 7.4-18.0)
- High ORR, with long term persistence driving durable outcomes
- Favourable safety profile with low ICANS and no high grade CRS

#### CARPALL (AUTO1/22 cohort (n=12))

Molecular MRD neg CR/Cri by d30	10 (83%)
Disease progression	2
Relapse  Antigen negative relapse Emergence of molecular MRD CD19+/CD22+ relapse	0 3 2
CRS ≥ Grade 3	0
Neurotox/ ICANS > Grade 3	1 (8%)

- Patient population ineligible for commercial CAR T therapy
  - Including patients with CD19-ve disease and patients with isolated extramedullary disease
- Est. molecular CR rate for obe-cel in this patient group approx. 40%
- 1 year EFS 60% despite the high-risk patient cohort
- No antigen-ve relapse seen in responding patients
- At median FU 8.7 months, 5 of 10 responding patients were in MRD-ve CR (4-12 months)

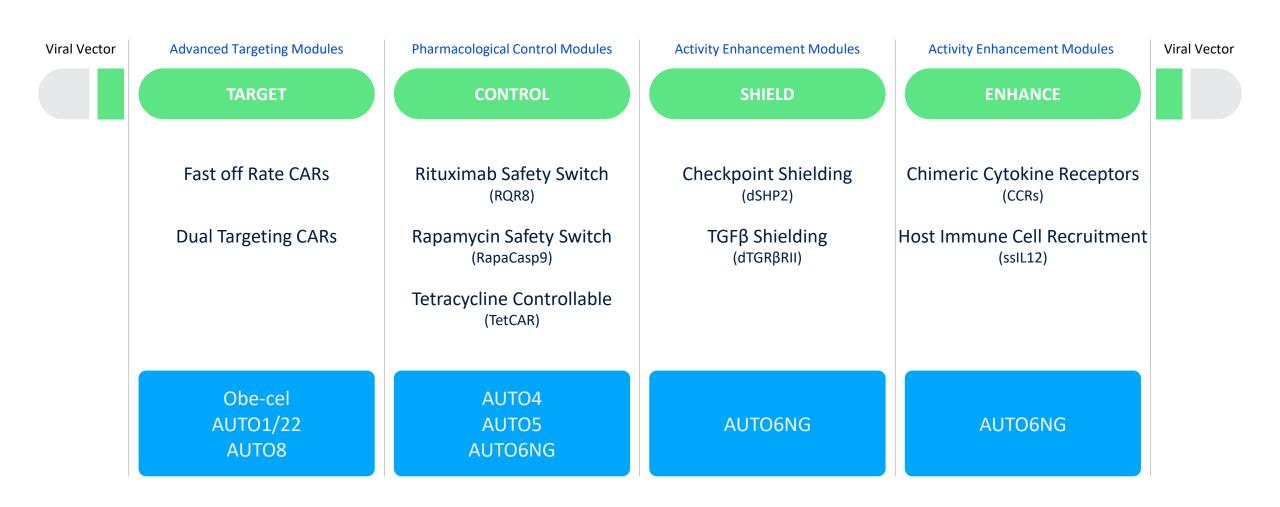
ALLCAR19 data cut: 2-NOV-2022 CARPALL data cut: 30-OCT-2022

# Pipeline

A broad portfolio of potential next generation modular T cell therapies

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

Advanced T cell programming



### Leveraging our industry leading technology platform via partnerships

### Technology partnerships

- Leveraging our modular programming technology to generate safer and more effective therapies
- Tumor targeting, pharmacological control and activity enhancement for cellular therapies
- Validating collaborations with leading pharma and biotech companies
- Potential for value creation through near term option exercise fees, milestone payments and royalties from net sales

- Moderna Tx
  - Access to propriety binders for the development of mRNA-based therapeutics for the treatment of cancer
- Bristol Myers Squibb
  - Access to the RQR8 safety switch for selected cell therapy programs for the treatment of cancer
- Cabaletta Bio
  - Access to the RQR8 safety switch for selected cell therapy programs for the treatment of autoimmune diseases

# Early-stage pipeline

Leveraging academic collaborations to generate opportunity for non-dilutive funding opportunities

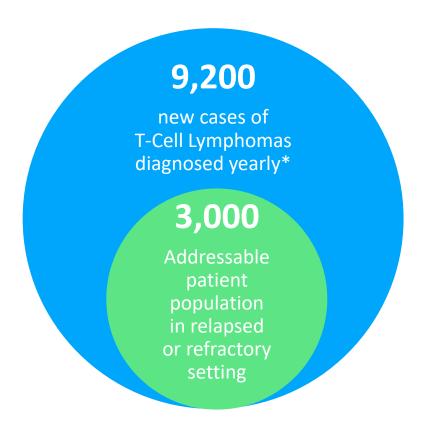
PRODUCT	INDICATION	TARGET	STUDY NAME	PHASE
AUTO4	TRBC1+ Peripheral TCL	TRBC1	LibrA T1	Phase 1
AUTO5	TRBC2+ Peripheral TCL	TRBC2		Preclinical
AUTO6NG	Neuroblastoma; Other tumor types	GD2		Preclinical
AUTO8	Multiple Myeloma	BCMA & CD19	MCARTY*	Phase 1
T-Cell Lymphoma	Solid Tumors Multiple Myeloma			* Collaboration with UCL

Next data readouts expected in 2023/2024

# AUTO4 and AUTO5 for Peripheral T-Cell Lymphoma

T-Cell Lymphoma is an aggressive disease with a very poor prognosis

- A large portion of T-Cell Lymphoma patients are refractory/relapse following first-line treatment (68%)<sup>1</sup>
- Standard of care is variable and often based on high-dose chemotherapy and stem cell transplants:
  - Median 5 yrs OS: 32%<sup>2</sup>
- Relapsed/refractory patients have a worse prognosis
- Median PFS approximately 3 months/ Median OS < 6 months<sup>1,3</sup>
- Brentuximab survival benefit restricted to CD30 positive ALCL subtype<sup>4</sup>
  - approx. 12% of total PTCL patient population<sup>4,5</sup>
- T cell lymphoma has not benefited from advances in immunotherapy
  - Pan T-cell depletion highly toxic; few/no tumor-specific antigen targets

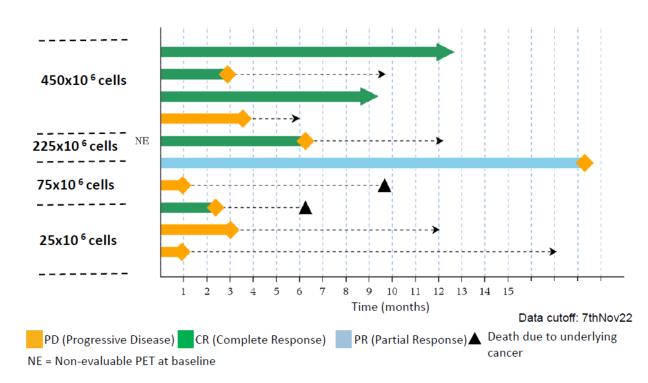


\*Japan, US and EU5 (2020 DRG Epidemiology Data)

### AUTO4 for Peripheral T-Cell Lymphoma: ASH 2022

Patients achieve durable metabolic complete responses

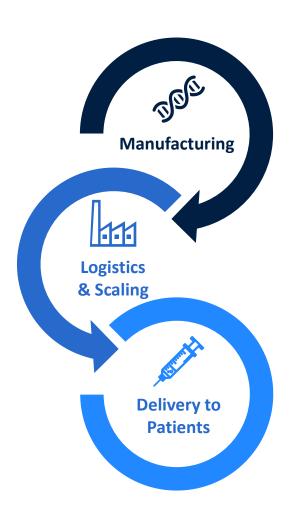
- AUTO4 treatment was well tolerated with no dose-limiting toxicities
- Ongoing responses at 9 and 12 months post-dosing at the highest dose tested (450x106) are encouraging
- No CAR T cell expansion was seen in peripheral blood but CAR
   T cells were detected in an on-treatment lymph node biopsy
- The study is ongoing, with additional patients due to be treated to define the recommended phase 2 dose



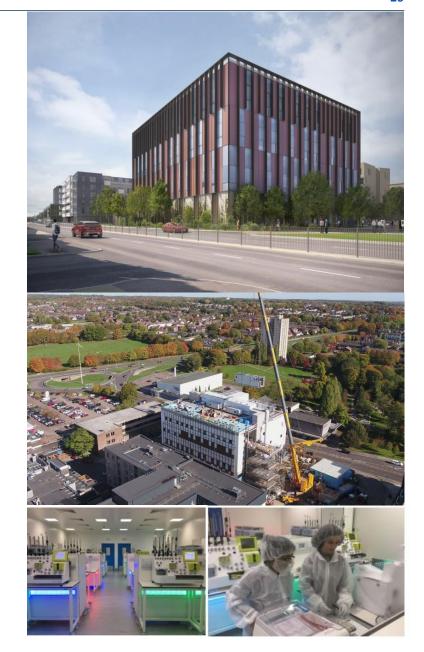
Manufacturing

### Commercial manufacturing facility on track

Building a fully integrated manufacturing and logistics platform



- Phase 1 of build project completed in Q4 2022 handover of first clean rooms to Autolus on Nov 25, 2022
- Equipment installations and qualification by Autolus on track for Good Manufacturing Practice (GMP) operations by H2 2023
- Tried and tested manufacturing process within an established regulatory framework
- Planned annual capacity of at least 2,000 batches per year to service global demand in ALL
- CMC package for submission to FDA progressing per plan



Financial Results

# Financial summary

Cash runway into 2025

USD	FY 2022 (\$ '000)	FY 2021 (\$ '000)	Variance (\$ '000)
Grant Income	166	823	(657)
License Income	6,194	1,507	4,687
R&D	(141,992)	(134,789)	(7,203)
G&A	(31,899)	(31,865)	(34)
Loss on disposal of leasehold improvements	(515)	(676)	161
Total Op Expense, Net	(168,046)	(165,000)	(3,046)
Interest Income	1,708	262	1,446
Other (expense) income, net	2,038	(145)	2,183
Interest expense	(8,905)	(1,105)	(7,800)
Tax Benefit	24,366	23,892	474
Net Loss after tax	(148,839)	(142,096)	(6,743)
USD	FY 2022 (\$ '000)	FY 2021 (\$ '000)	Variance (\$ '000)
Cash Balance (including restricted cash)	382,761	310,676	72,085

• Foreign currency: 48% of cash at 31 December 2022 held in GBP

Summary

### Autolus planned news flow

#### Obe-cel

- FELIX Phase 2 clinical data presentation planned for Q2 2023
- Biologics License Application (BLA)
   to U.S. Food and Drug
   Administration (FDA) by end of 2023
- Longer term follow up data planned for ASH 2023 and medical conferences in 1H 2024

### **Pipeline**

- Updates on AUTO1/22 and AUTO 4 planned for 2023
- Multiple academic clinical studies ongoing expected to generate additional news flow in 2023/2024
- Opportunity for news flow related to collaborations and technology licensing

### **Manufacturing**

- Qualification of Nucleus facility in H1 2023
- Commencement of GMP operations in H2 2023

### The Autolus opportunity

Building a fully integrated CAR T company - Expanding excellence in R&D and manufacturing to commercialization

- Obe-cel, a potentially best in class product candidate, met primary endpoint of ORR in adult patients with r/r ALL
- Planned BLA filing end of 2023
- Additional opportunity for obe-cel in B-NHL indications
- Highly valuable pipeline with potential broad applicability in cancers with limited treatment options

- Purpose-built commercial manufacturing facility ready for qualification and validation activities in 1H 2023 with an initial capacity of up to 2,000 batches per year, sufficient to serve global demand in ALL
- Strong technology foundation, validating collaborations with leading pharma and biotech companies – BMS, Moderna and Cabaletta Bio
- Strong cash position with \$382.8 million (December 31, 2022)

Autolus

Thank you

