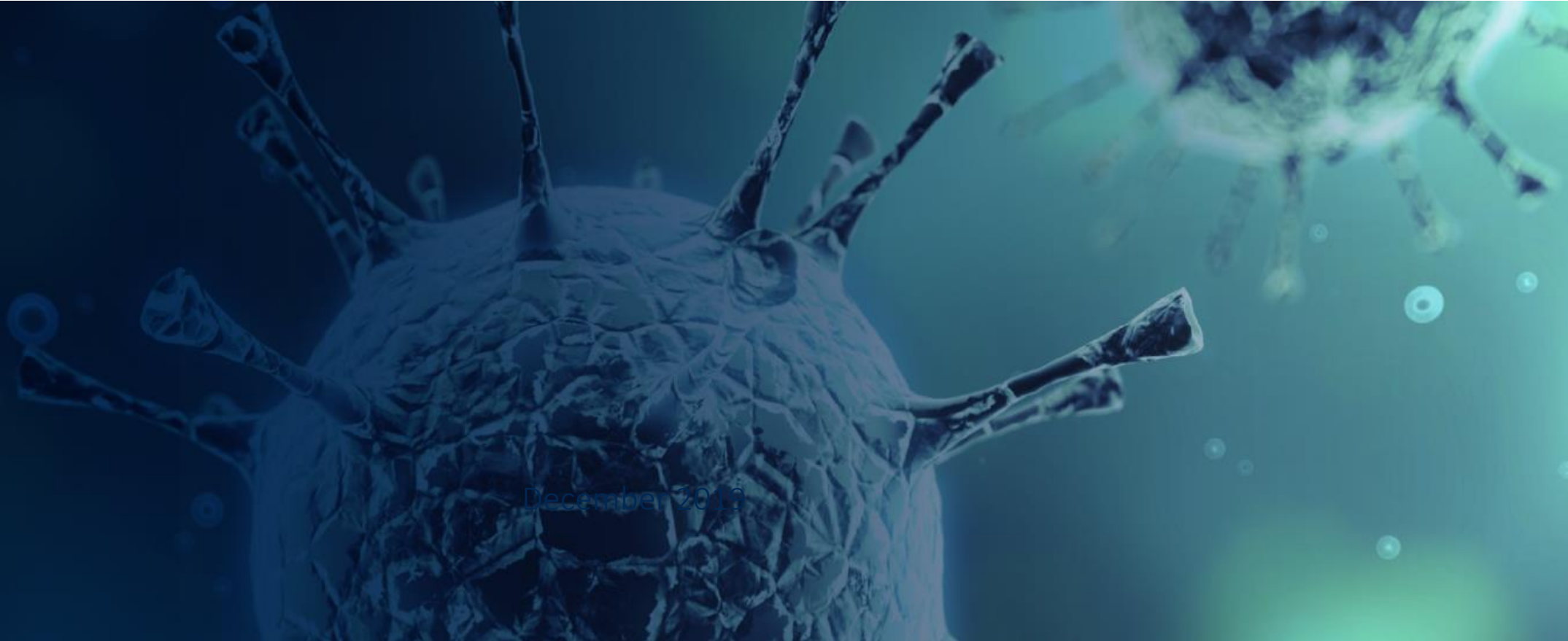


# Autolus

Nasdaq: AUTL



December 2019

Next Generation Programmed T Cell Therapies  
April 2020

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# Corporate strategy

## Short term value steps with best in class programs for ALL and DLBCL

- Focus on potentially best in class Acute Lymphoblastic Leukemia (ALL) and Diffuse Large B Cell Lymphoma (DLBCL) therapies with major value steps expected in 2020 / 2021
  - First pivotal study of adult ALL to complete in H1 2021 with approval targeted in 2022
  - Drive DLBCL program to POC and prepare for pivotal study
- Additional value steps in T cell lymphoma and first solid tumor indication
- Broad preclinical pipeline of next generation programs transitioning to clinical stage in 2020
- Broad proprietary cell programming technology
- Scalable, fully enclosed manufacturing platform

**Note on COVID-19:** Whilst the COVID-19 situation has had varying degrees of impact on the ability of clinical sites to operate normally; based on current expectations we anticipate the impact on most operations will be minimal

# Investment highlights

## Broad clinical-stage pipeline

- 4 product candidates
- 4 hematological indications
- 1 solid tumor program

## Multiple upcoming milestones

- AUTO1 long term follow up in aALL
- POC for AUTO3 in DLBCL
- POC for AUTO4 in PTCL

## Proprietary manufacturing process

- Fully enclosed, semi-automated
- Designed to be economical at commercial scale
- Expanding to new US/UK facilities

## Modular programming approach

- Enables rapid cycle of innovation
- 4 next gen programs to start Ph 1 in 2020
- Designed to address:
  - Targeting & control
  - Tumor defenses & microenvironment
  - GvHD & immune rejection (Allogeneic)
  - Manufacturing
- Portfolio of owned and in-licensed intellectual property; 93 patent families

## Strong Fundamentals

- \$210.6 million at December 31, 2019\*
- Worldwide rights retained for all programs
- Cash runway into 2022

# Broad pipeline of clinical programs

Designed to address limitations of current T cell therapies

Product	Indication	Target	Pre-clinical	Phase 1/2	Pivotal*
B Cell Malignancies					
AUTO1	Adult ALL	CD19	ALLCAR19		AUTO1-AL1
AUTO1	Pediatric ALL	CD19	CARPALL		
AUTO3	DLBCL	CD19 & CD22	ALEXANDER		
T Cell Lymphoma					
AUTO4	TRBC1+ Peripheral TCL (LibrA T1)	TRBC1	LibrA T1		
GD2+ Tumors					
AUTO6	Neuroblastoma	GD2	CRUK		



## **Adult Acute Lymphoblastic Leukemia**

**AUTO1 – tailored for adult ALL**

# No approved CAR T therapy for adult ALL patients

Severe toxicities of currently approved products have limited suitability in adult setting

- ALL is a significant opportunity
  - Up to 8,400\* new cases of adult ALL diagnosed yearly worldwide‡
  - Addressable patient population is projected at 3,000 patients US & EU
- 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 ALL
  - Only approved redirected T cell therapy approved for adults generally is blinatumomab
  - CAR T therapies are highly active, but no clear sense of durability without subsequent allograft
  - Patients are generally more fragile, more co-morbidities
  - Yet CAR T toxicities in this setting have been notable with high incidences of severe CRS and cases of fatal neurotoxicity

**FDA granted AUTO1 orphan drug designation for ALL**

# AUTO1: Key features

Designed for durability of responses without allo-transplant and reduced severe CRS

## Conventional CD19 CARs

- Approved and near approved CD19 CAR Ts use identical high affinity CD19 binder (FMC63)
- FMC63 has a fast on-rate and a very slow off rate
- Leads to over-activation, exhaustion and high-grade CRS and neurotoxicities

## AUTO1

- AUTO1 has an optimized CD19 CAR with a lower affinity and a fast off rate
- Engages efficiently, delivering a kill, disengages rapidly like a normal T cell
- Leads to enhanced activity and lower toxicities

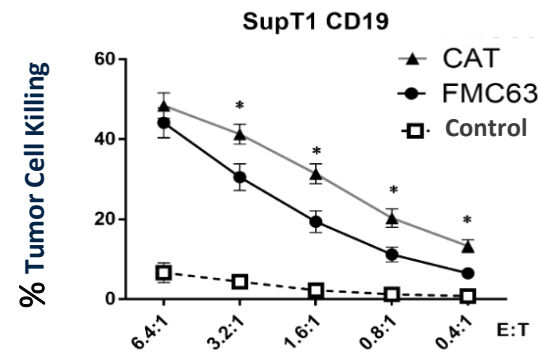
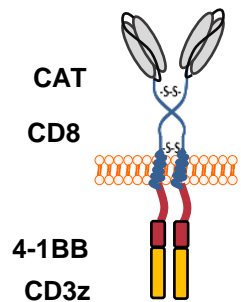


# AUTO1 shows enhanced activity vs FMC63 CARs

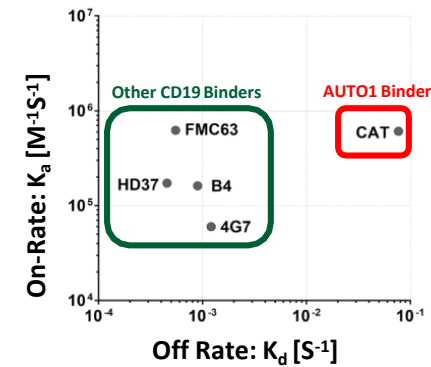
Preclinical data show higher cytotoxicity and proliferation

- AUTO1 is designed to reduce severe CRS ( $\geq G3$ ) through the introduction of a proprietary optimized CAT binder
- AUTO1 (CAT) binder with lower affinity for CD19
- Half-life of target interaction very short compared to Kymriah<sup>®</sup> (FMC63) binder\*:
  - AUTO1 = 9.8 seconds
  - Kymriah<sup>®</sup> = 21 minutes

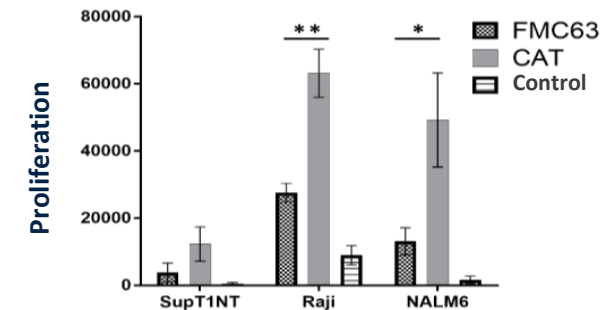
## Enhanced Cytotoxicity



## Fast Off-Rate



## Enhanced Proliferation



\*Similar binders are used in Yescarta<sup>®</sup> and JCAR-017  
Amrolia et al., (2019) Nature Medicine.

# AUTO1 may be best-in-class redirected T cell therapy

## Relapsed/refractory Adult ALL clinical data

		<sup>2</sup> AUTO1	
	<sup>1</sup> Blincyto	All patients	Closed Process <sup>3</sup>
Patient Numbers	271	16	9
CR Rate	42%	87% <sup>♦</sup>	100%
EFS 6m	31%	68% <sup>†</sup>	100%
CRS ≥ Grade 3	3%	0%	0%
Neurotox ≥ Grade 3	13%	19% <sup>‡</sup>	12% <sup>‡</sup>

<sup>♦</sup> 15 patients evaluable for efficacy with at least 4 weeks follow up or RIP prior to Month 1

<sup>†</sup> Based on Kaplan-Meier estimate in all patients infused with AUTO1

<sup>‡</sup> All three patients had > 50% tumor burden

Data cutoff 25-Nov-2019

<sup>1</sup>Kantarjian et al., 2017

<sup>2</sup>Roddie et al., ASH 2019 presentation

<sup>3</sup>Commercial manufacturing process

- AUTO1 preliminary data suggest manageable safety profile and a high level of clinical activity
- KTE-X19 CR Rate 68-84%, Grade ≥3 cytokine release syndrome (CRS) events occurred in 22-29% and neurologic events 11-38% of patients\*

Sources: Prevalence calculated using SEER and EUCAN and extrapolated using IMS; American Cancer Society

Gilbert et al., 2017 (SITC)

\*Shah et al, ASCO 2019

# AUTO1 is first Autolus program to move into a pivotal study

Pivotal study, AUTO1-AL1, in adult ALL:

- CTA approved by the MHRA in January 2020 and US IND accepted by the FDA in April 2020
- Short Phase1b run-in component prior to single arm Phase 2 study
- 100 relapsed / refractory adult ALL patients
- Primary endpoint: overall complete response rate (CR/CRi)
- Secondary endpoints include MRD-negative CR EFS and DoR
- BLA filing targeted for Q4 2021



## Diffuse Large B Cell Lymphoma

AUTO3 – tailored for DLBCL

# DLBCL is a large commercial opportunity

## AUTO3 addressable patients in DLBCL

- Potential market size in DLBCL
  - Approx. 24,000\* patients diagnosed in the US every year
- Aggressive and rapidly advancing cancer, survival outcomes remain poor
  - Most common type of Non-Hodgkin Lymphoma
  - High dose chemotherapy + mAb leads to remission in about 50-60% of patients
  - DLBCL patients who fail salvage regimens median overall survival 4.4m
- Two approved CAR T products (Yescarta® and Kymriah®)
- Initial AUTO3 positioning in DLBCL
  - High unmet need remains, despite highly active CD19 CARs in r/r DLBCL, given the responses are not durable and toxicity limits broad application

\*Autolus estimates

# Current status of CAR T Cell therapies in DLBCL

Two approved products (Yescarta® and Kymriah®) and one near to approval (JCAR017)

## Efficacy

- Despite high ORR (70-80%) and high best CRR (40-55%), only 29-37% patients achieve durable CRR in DLBCL<sup>1,2</sup>
- Approximately a third of CRs are lost over time
- Loss of CRs are caused by PD-L1 upregulation<sup>3</sup> which contributes to CAR T exhaustion and CD19 antigen loss<sup>4</sup>

## Safety

- High rates of severe cytokine release syndrome (13-22%) and severe neurotoxicity (12-28%)<sup>2,4</sup>
- Early onset and severity of toxicities requires intensive inpatient management

# Approach designed to address antigen escape & PDL-1 inhibition

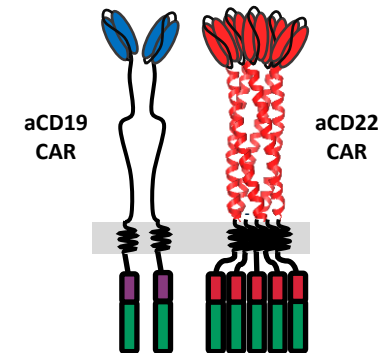
## AUTO3: CD19 and CD22 targeting bicistronic CAR

### Rationale

- CD19 CARs are highly active in r/r DLBCL
- Unmet need remains with CD19 CAR T Cell Therapy
  - Only 29-37% durable CRR in DLBCL<sup>1,2</sup>. The potential causes for relapse include:
    - PD-L1 upregulation<sup>3</sup> which contributes to CAR T exhaustion
    - CD19 antigen loss<sup>4</sup>
  - Rate of severe (grade  $\geq 3$ ) cytokine release syndrome (CRS 13-22%) and neurotoxicity (NT 12-28%)<sup>2,4</sup>

### Hypothesis

- Simultaneous targeting of CD19 and CD22 reducing the probability of antigen escape mechanism
- Prevent early PD1/PDL1 related CAR T cell exhaustion by adding pembrolizumab to the preconditioning regimen



<sup>1</sup>Locke F et al Lancet Oncol 2019

<sup>2</sup>Schuster S et al NEJM 2019

<sup>3</sup>Neelapu S et al ASCO 2018

<sup>4</sup>Neelapu S et al NEJM 2017

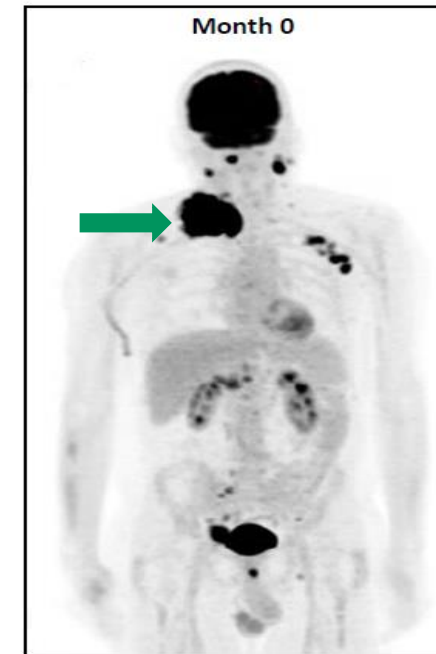
# Preliminary efficacy\* indication of dose response

## AUTO3 - DLBCL

	50 x 10 <sup>6</sup> No Pem (n=4)	50 x 10 <sup>6</sup> D14 Pem (n=3)	150 x 10 <sup>6</sup> D14 Pem (n=4)	450 x 10 <sup>6</sup> D14 Pem (n=4)	450 x 10 <sup>6</sup> D-1 Pem (n=3)
CR	1	1	2	2	2
PR	1	1	0	1	NA
NE	0	1	0	0	0
CRR	25%	33%	50%	50%	66%

- 450 million: ORR 5/7 (71%) and CR 4/7 (57%)

Pre-CAR T-cells



Post-CAR T-cells



**Dose:** 50 x 10<sup>6</sup>

**DLBCL:** ABC, Primary refractory & refractory to RCHOP/RICE/RESHAP

**No CRS or NT**

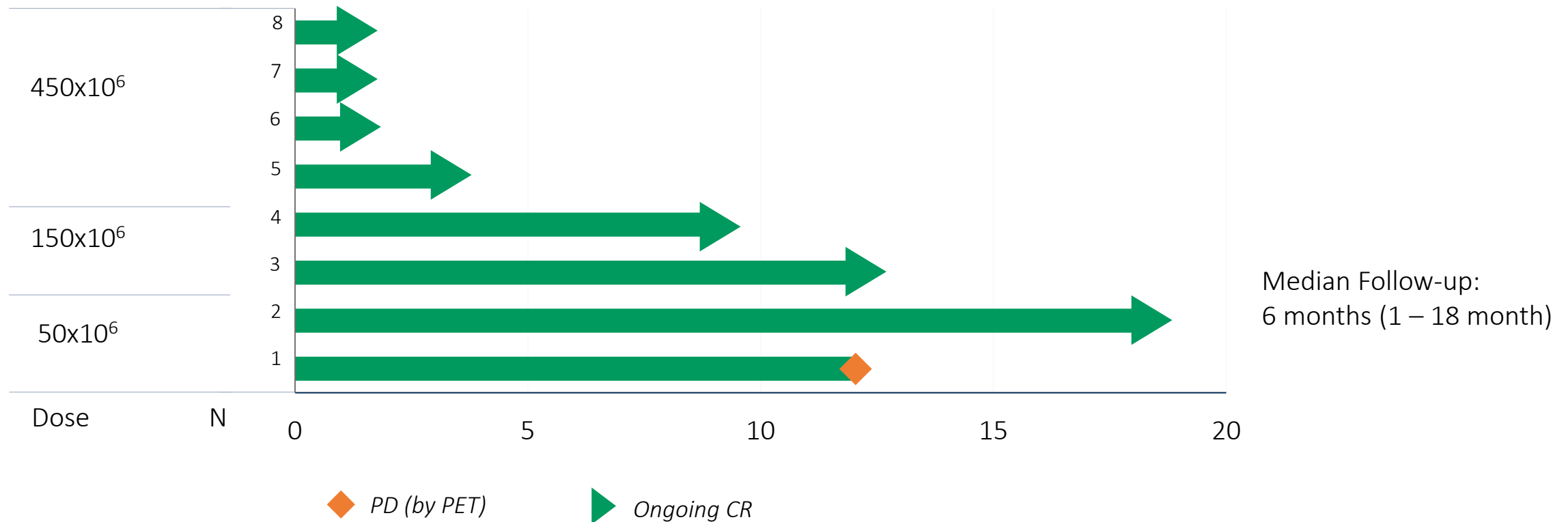
**CR duration 18 months+**

21 January 2020 data cut-off



# Early encouraging signs of durable complete responses

## Auto 3 - DLBCL



18 patients treated, 7 out of 8 (87%) CRs ongoing, 3 PRs not durable

7 of 7 (100%) CRs\* are ongoing in AUTO3+ Pembro cohorts at a median f/u of 3 months (1-18m)

21 January 2020 data cut-off

# Widespread adoption of CAR T products has been limited by toxicities

High rates and severity of toxicities require intensive management and inpatient care

	Yescarta <sup>#</sup>	Kymriah/ JCAR017 <sup>#</sup>	AUTO3
Best CRR	54%	40-53%	55%*
Ongoing CR rate	36% at 6m	29-35% at 6m	tbd
CRS ≥ grade 3	11%	2-23%	0%
NTX any grade	64%	21-30%	0%
NTX ≥ grade 3	28%	10-12%	0%
Toxicity management	Intensive		Minimal
Healthcare utilization	Inpatient Treatment		Outpatient Positioning

All CRs ongoing at a median f/u of 2 months (1-12 month)

<sup>#</sup> CRS rates achieved with intensive management

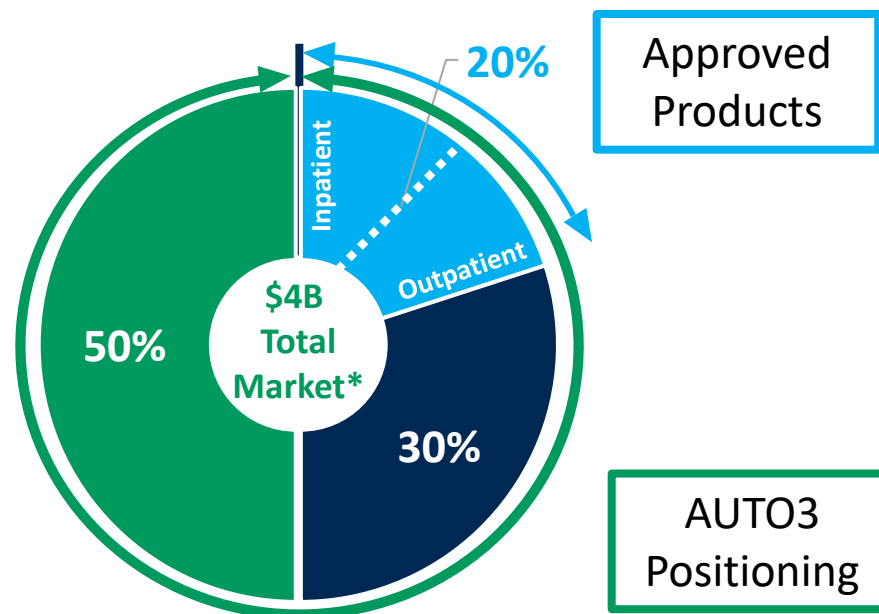
**AUTO3 has been designed to minimise loss of CRs with a safety profile suitable for all settings of care including outpatient therapy**

AUTO3: Jan 2020 Data cut (AUTO3 + Pembro ≥ 150 x10<sup>6</sup>)  
 Nellapu et al, 2017  
 Schuster et al., 2019  
 Abramson et al., 2019 (ASH)

# AUTO3 is designed to reach total addressable r/r DLBCL population

AUTO3 has the potential to be a true outpatient therapy

## US Site of Care Distribution 3L+ R/R DLBCL



- Academic Centers of Excellence
- Non-Academic Hospitals
- Oncology Clinics

Source: 2016 IMS & CMS patient claims data, \*Autolus approximate estimates

## Approved CD19 CAR T Products

- Patients receive approved products as inpatients in CoEs because of the high rate & severity of toxicities plus intensity of patient management
- Market opportunity limited to ~20% of patients

## AUTO3 Products

- Minimal tox management of AUTO3 should allow treatment across all settings of care
- Increased healthcare utilization of AUTO3 grows the addressable market and maximizes reimbursement options compared to approved products

# Early data encouraging – full read-out expected in mid-2020

## Sustained CRs and low toxicity to maximize the market via outpatient utilization

- AUTO3 product was successfully manufactured for all patients
  - Products manufactured at Cell and Gene Therapy Catapult at Stevenage in the UK for US and EU use
- No neurotoxicity or severe CRS\* in patients treated with AUTO3 at active dose levels
- Safety profile achieved without the need for intensive patient management suggesting suitability for outpatient and community administration
- Complete responses achieved without severe CRS, neurotoxicity or ICU care
- 7/8 CRs ongoing with a median follow up of 6 months (1-18 months)
- Pembrolizumab on D-1 x single dose is being evaluated further
- Decision for triggering Phase 2 initiation planned for mid-2020



T Cell Lymphoma

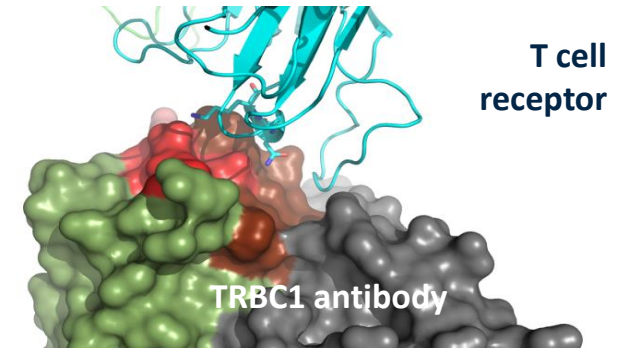
AUTO4 – tailored for T Cell Lymphoma

# Unique targeting of TRBC1 & TRBC2 opens new therapeutic approach

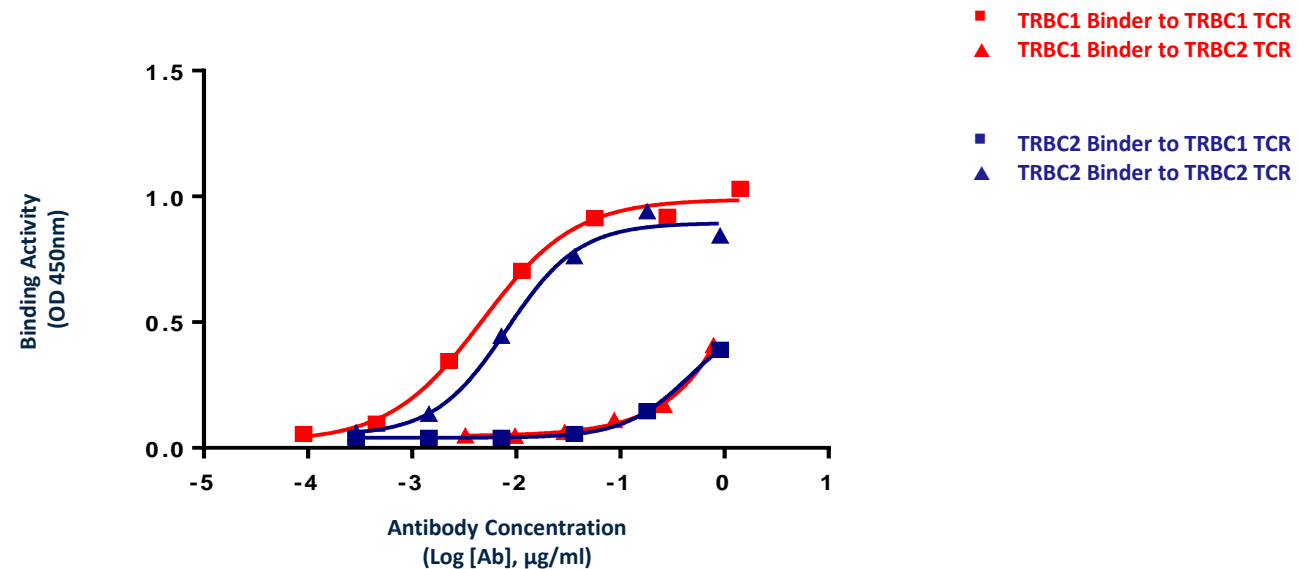
## AUTO4/5 in Peripheral T Cell Lymphoma

Differences between TRBC1 and TRBC2 are small

		NK-KN 4/5	F-Y 36
TRBC1	1	EDLNKVFPPPEVAVFEPSEAEISHTQKATLVCLATGFFPDHVELSWWVNGK	
TRBC2	1	EDLNKVFPPPEVAVFEPSEAEISHTQKATLVCLATGFFPDHVELSWWVNGK	
TRBC1	51	EVHSGVSTDPPQLKEQPALNDSRYCLSSRLRVSAFWQNP RNHFRCQVQF	
TRBC2	51	EVHSGVSTDPPQLKEQPALNDSRYCLSSRLRVSAFWQNP RNHFRCQVQF	
TRBC1	101	YGLSENDEWTQDRAKPVTOIVSAEAWGRADCGFTSVSYQOGVLSAT	
TRBC2	101	YGLSENDEWTQDRAKPVTOIVSAEAWGRADCGFTSES YQOGVLSAT	
		V-E 135	



Antibody Binding Data

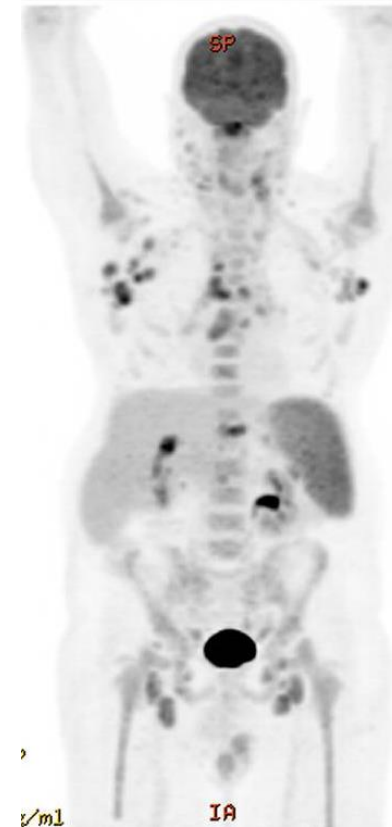


# Encouraging signal from AUTO4 treated patient

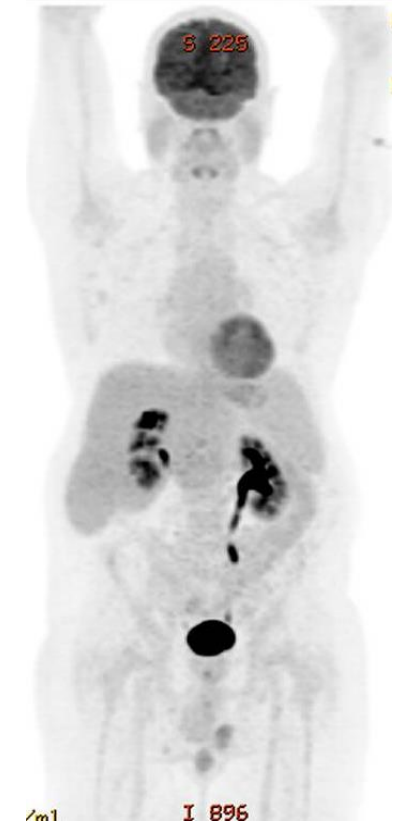
## Clinical outcome of patient 1

- 57 yr old with Angioimmunoblastic T cell lymphoma
- Past treatments include CHOP (CR) & IVE (refractory)
- AUTO4 Treatment
  - Treated with  $25 \times 10^6$  anti-TRBC1 CAR T cells
  - No expansion of CAR T cells was noted
  - No CRS or neurotoxicity or T-cell aplasia was noted
  - Initial PET/CT at one month showed Complete Metabolic Response but subsequently had progression on day 71

Baseline PET/CT scan  
Pre-AUTO4 treatment



Month 1 PET/CT scan













## Pipeline

A broad portfolio of next generation modular T cell therapies



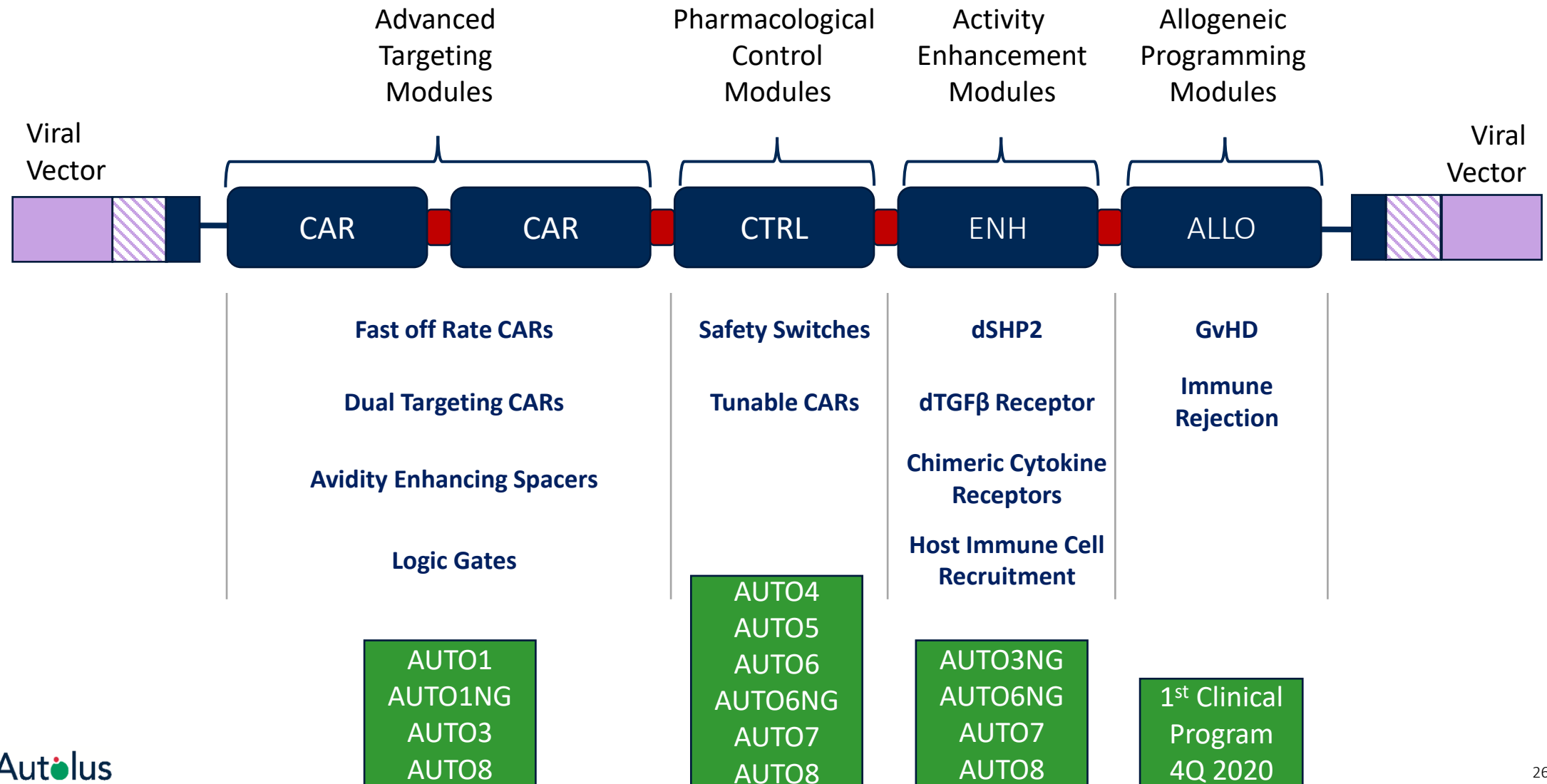
# Broad pipeline of next generation programs

Designed to address limitations of current T cell therapies

Product	Indication	Target	Pre-clinical	Phase 1 Ready
B Cell Malignancies				
AUTO1NG	ALL	CD19 & CD22		H1 2020
AUTO3NG	DLBCL	CD19 & CD22		Life cycle mgmt
T Cell Lymphoma				
AUTO5	TRBC2+ Peripheral TCL	TRBC2		H1 2021
GD2+ Tumors				
AUTO6NG	Neuroblastoma; Melanoma; Osteosarcoma; SCLC	GD2		Q4 2020
Prostate Cancer				
AUTO7	Prostate Cancer	Undisclosed		H1 2021
Multiple Myeloma				
AUTO8	Multiple Myeloma	BCMA & CAR X		H2 2020

# A broad toolkit building on our core principles of modular innovation

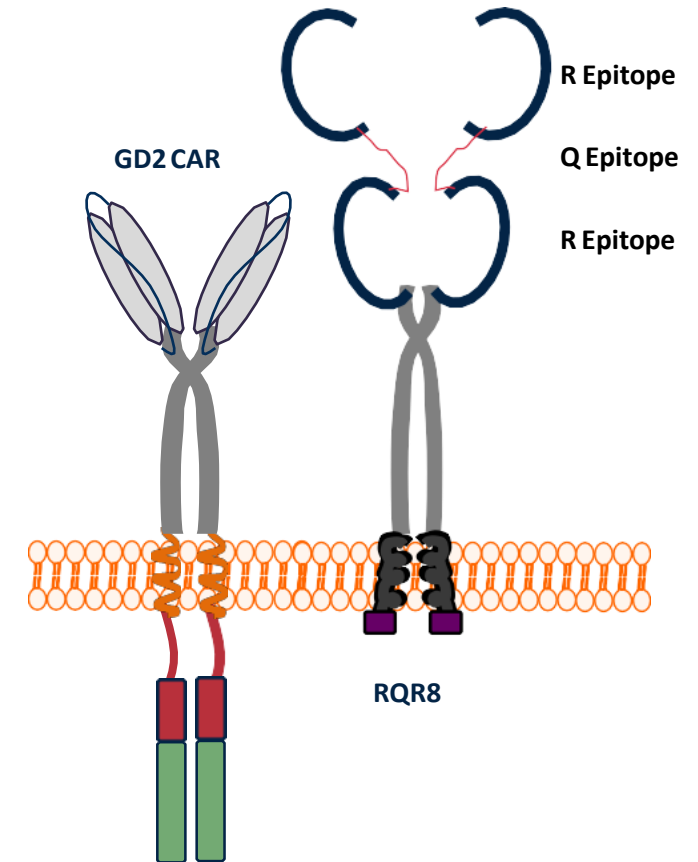
## Advanced T cell programming



# AUTO6 designed to drive anti-tumor activity without neurotoxicity

## AUTO6: GD2-targeted programmed T cell therapy

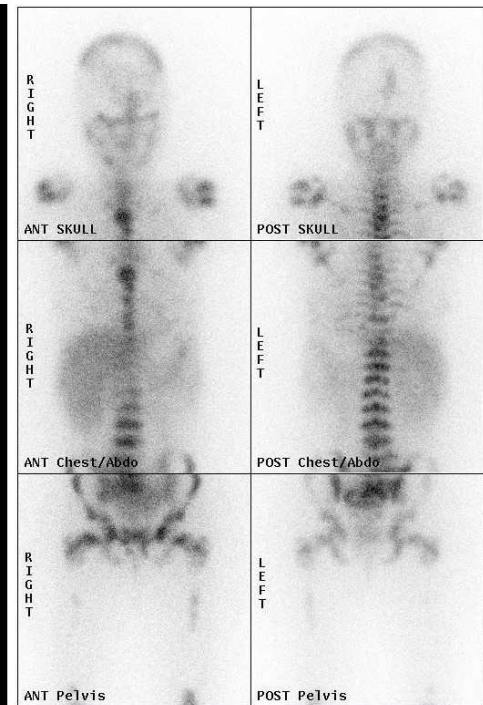
- Programmed T cell product candidate:
  - New binder to minimize on-target, off-tumor toxicity
  - Humanized binder to reduce immunogenicity
  - RQR8 safety switch
- Phase 1 clinical trial in r/r neuroblastoma conducted by CRUK\* in collaboration with UCL
- Autolus has exclusive worldwide rights to clinical data and patents



# Anti-tumor activity evident absent neurotoxicity

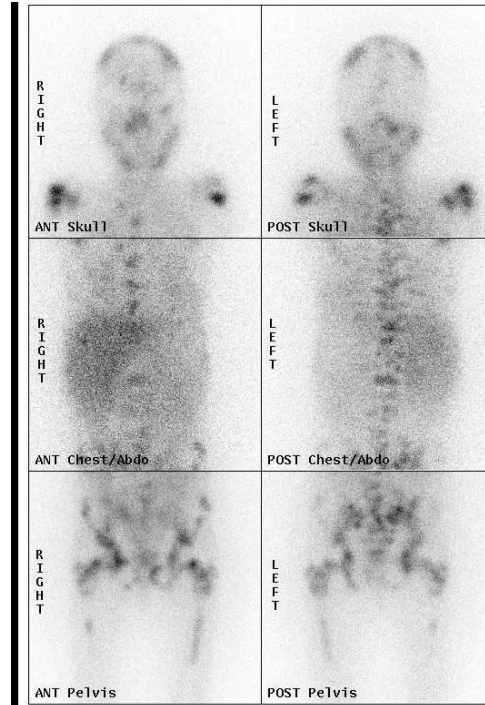
AUTO6 proof of principle presented at AACR 2018

Day 0



MIBG: iodine-123-meta-iodobenzylguanidine

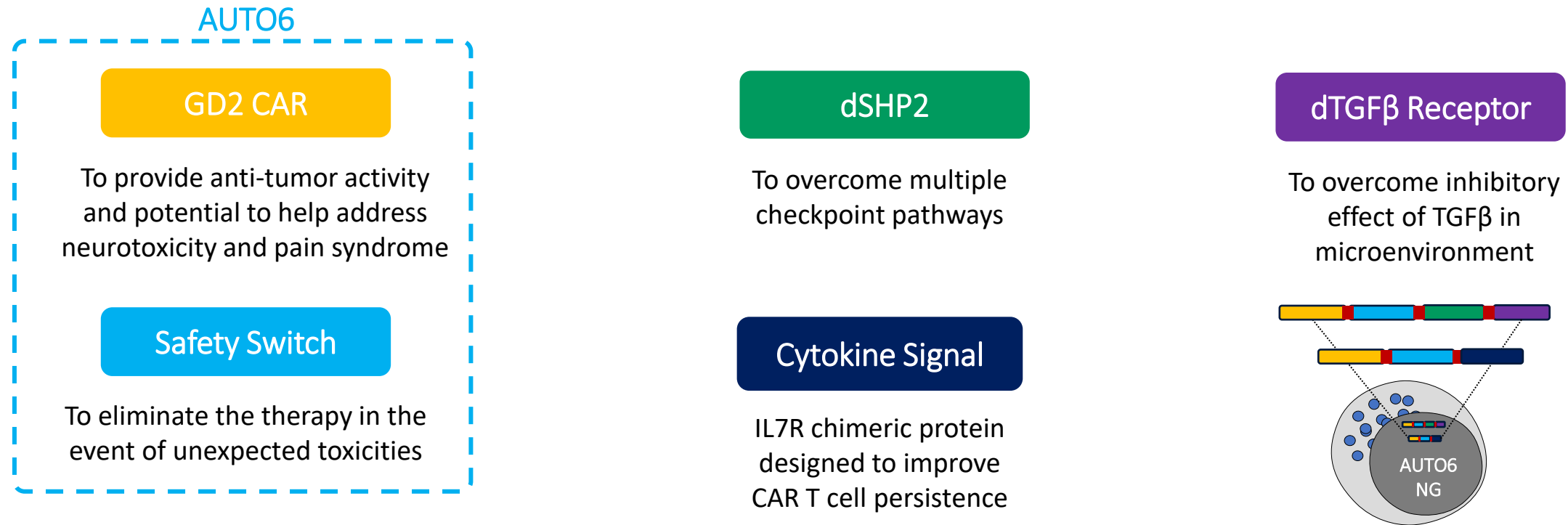
Day 28



- Significant decrease in disease hot spots by MIBG scan after therapy
- No DLTs and no neurotoxicity or pain syndrome observed
- First GD2 CAR reported to demonstrate CRS and tumor lysis syndrome in solid tumor setting
- AUTO6 next generation program in advanced pre-clinical development

# Modular approach enhances AUTO6NG for solid tumor environment

Next generation programs powered by a technology tool box

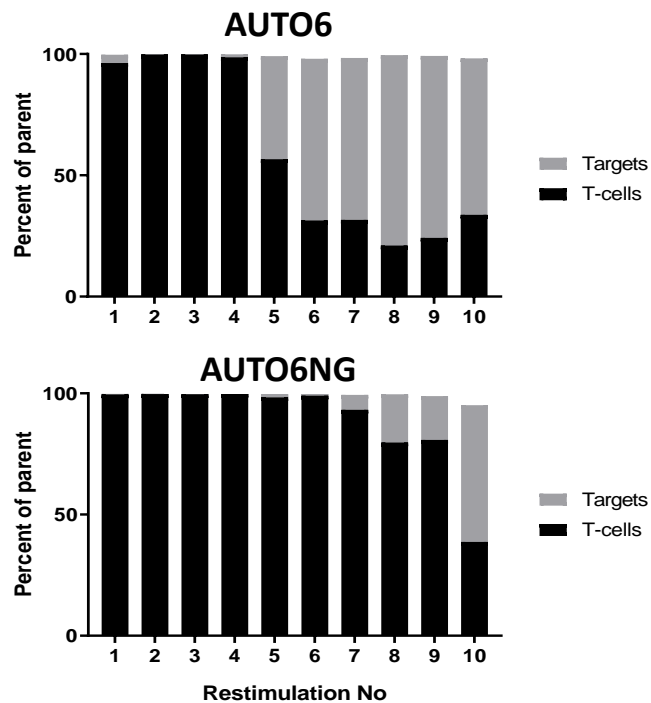


## AUTO6NG:

- Utilizes GD2 CAR from AUTO6, but further enhanced to address persistence, control and tumor defences
- Targeting neuroblastoma, osteosarcoma, melanoma and small cell lung cancer amongst others
- Plan to commence Phase 1 Q4 2020

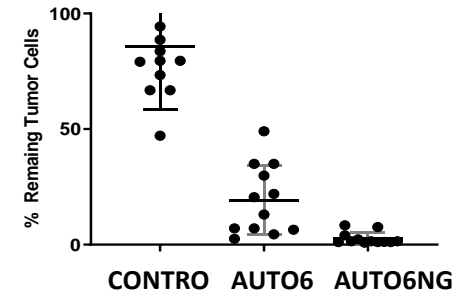
# AUTO6NG shows superior activity *in vitro*

## Enhanced Persistence



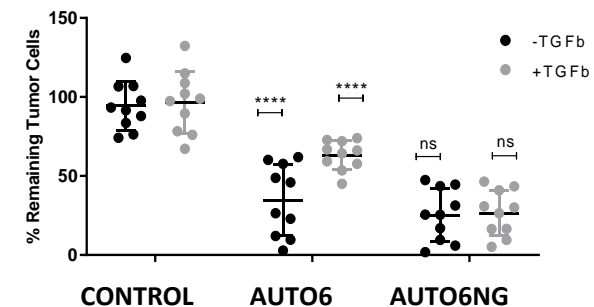
- Cytokine signal extends AUTO6NG activity through multiple rounds of restimulation

## Checkpoint Resistance



- dSHP2 enhances AUTO6NG activity against PDL1+ tumor cells.

## TGF $\beta$ Resistance

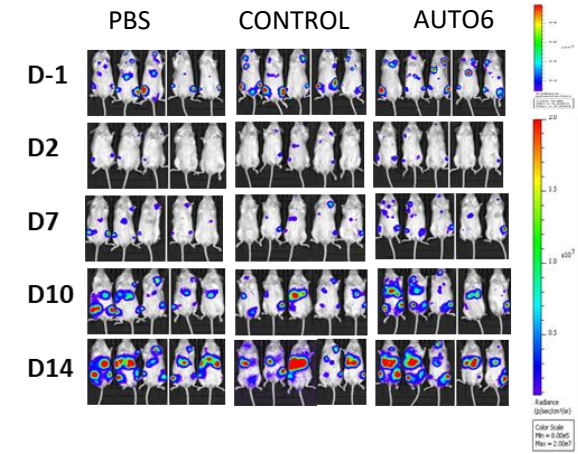
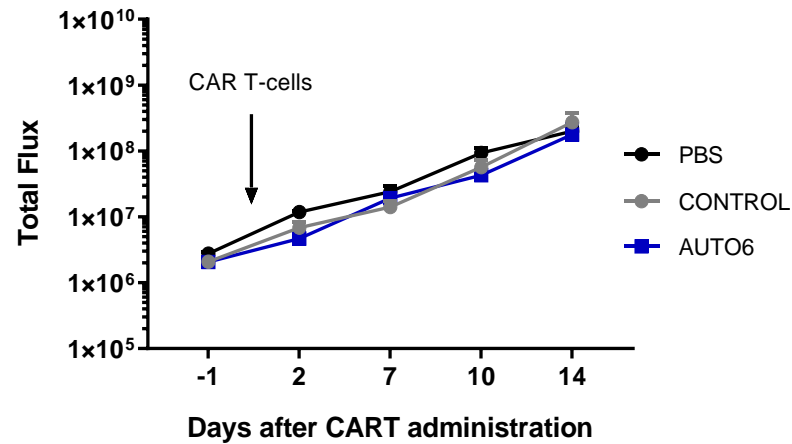


- dTGF $\beta$  Receptor enhances AUTO6NG activity in the presence of TGF $\beta$

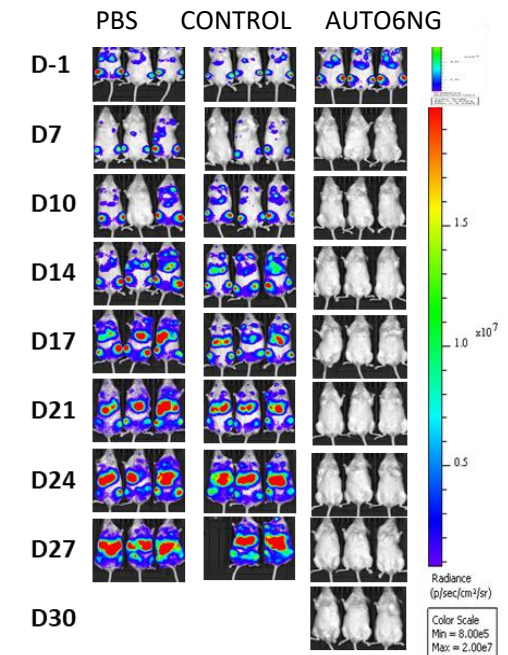
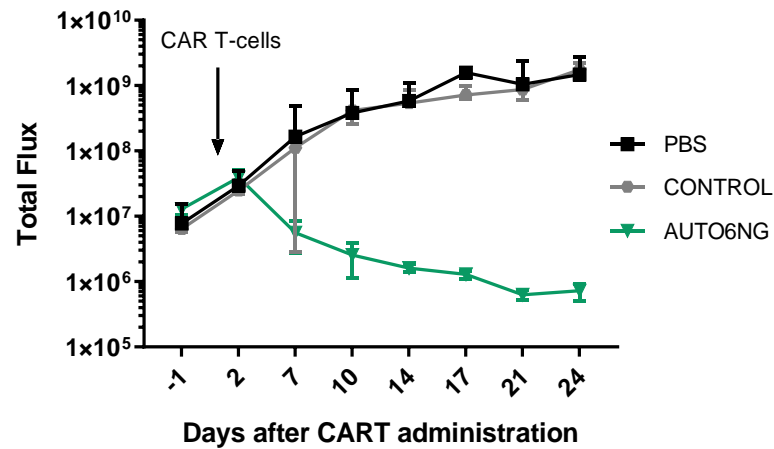
Achkova, D., et al SITC 2019 (abstract)

# AUTO6NG exhibits potent anti-tumor activity and extends survival in challenging *in vivo* model

AUTO6



AUTO6NG





# Economical & scalable product delivery platform

## Semi-automated and parallel processing

### Clinical supply & commercial launch

- Multiple samples to be processed within the same environment
- CGT Catapult (UK)
- Global clinical supply since Q3 2019



### Planned US commercial supply

- Collaboration with Alexandria Real Estate Partners (ARE)
- Fully scaled commercial site for cell process supply
- Planned capacity of 5,000 patients p.a.





# Multiple clinical data points expected through 2020

Product	Indication	Target	Event
B Cell Malignancies			
AUTO1	Adult ALL	CD19	<ul style="list-style-type: none"> <li>Ph 1 long-term follow up Q2 &amp; Q4 2020</li> <li>Ongoing recruitment and dose last patient H1 2021</li> </ul>
AUTO1NG	Pediatric ALL	CD19 & 22	<ul style="list-style-type: none"> <li>Ready to start Ph 1 H1 2020</li> </ul>
AUTO3	DLBCL	CD19 & 22	<ul style="list-style-type: none"> <li>Ph 1 data Q2 &amp; Q4 2020</li> <li>Decision on Ph 2 transition mid-2020</li> </ul>
AUTO3NG	DLBCL	CD19 & 22	<ul style="list-style-type: none"> <li>Ready to start Ph 1 H2 2020, life cycle mgmt</li> </ul>
Multiple Myeloma			
AUTO8	Multiple Myeloma	BCMA & CAR X	<ul style="list-style-type: none"> <li>Ready to start Ph 1 study H2 2020</li> </ul>
T Cell Lymphoma			
AUTO4	TRBC1+ Peripheral TCL	TRBC1	<ul style="list-style-type: none"> <li>Ph 1 interim data Q4 2020</li> </ul>
GD2+ Tumors			
AUTO6NG	Neuroblastoma; Melanoma; Osteosarcoma; SCLC	GD2	<ul style="list-style-type: none"> <li>Start Ph 1 Q4 2020</li> </ul>
Allogeneic Approach			
NA	NA	NA	<ul style="list-style-type: none"> <li>Start Ph 1 Q4 2020</li> </ul>

Pre-clinical data presentations at AACR II (June 2020)

# Autolus poised for value inflection in 2020

- AUTO1
  - Recruitment in UK & US in Autolus' first pivotal program in Adult ALL
  - FDA granted orphan drug designation for treatment of ALL
  - Opportunity for best in class CD19 CAR T
  - Pediatric ALL – moving forward with AUTO1/AUTO1NG
- AUTO3 – decision on Phase 2 transition targeted for mid-2020
  - Focus on DLBCL – potential to expand CAR T therapy beyond centers of excellence with safety profile manageable in out patient setting
  - AUTO3NG opportunity as next generation product
- Opportunity for additional value in 2020 from AUTO1NG, AUTO4, AUTO6NG and AUTO8
- Key data releases expected at upcoming medical conferences
  - H1 2020: Presentations targeted for AACR, ASCO and EHA
  - H2 2020: Presentations targeted for SITC and ASH
- Strong balance sheet with approx. \$286m\* in cash as of 31 Jan 2020

A microscopic image showing a large, textured, spherical virus-like particle with several long, thin, protruding spikes. The background is a soft-focus blue and green, with other smaller, similar structures visible in the distance.

**Thank you**