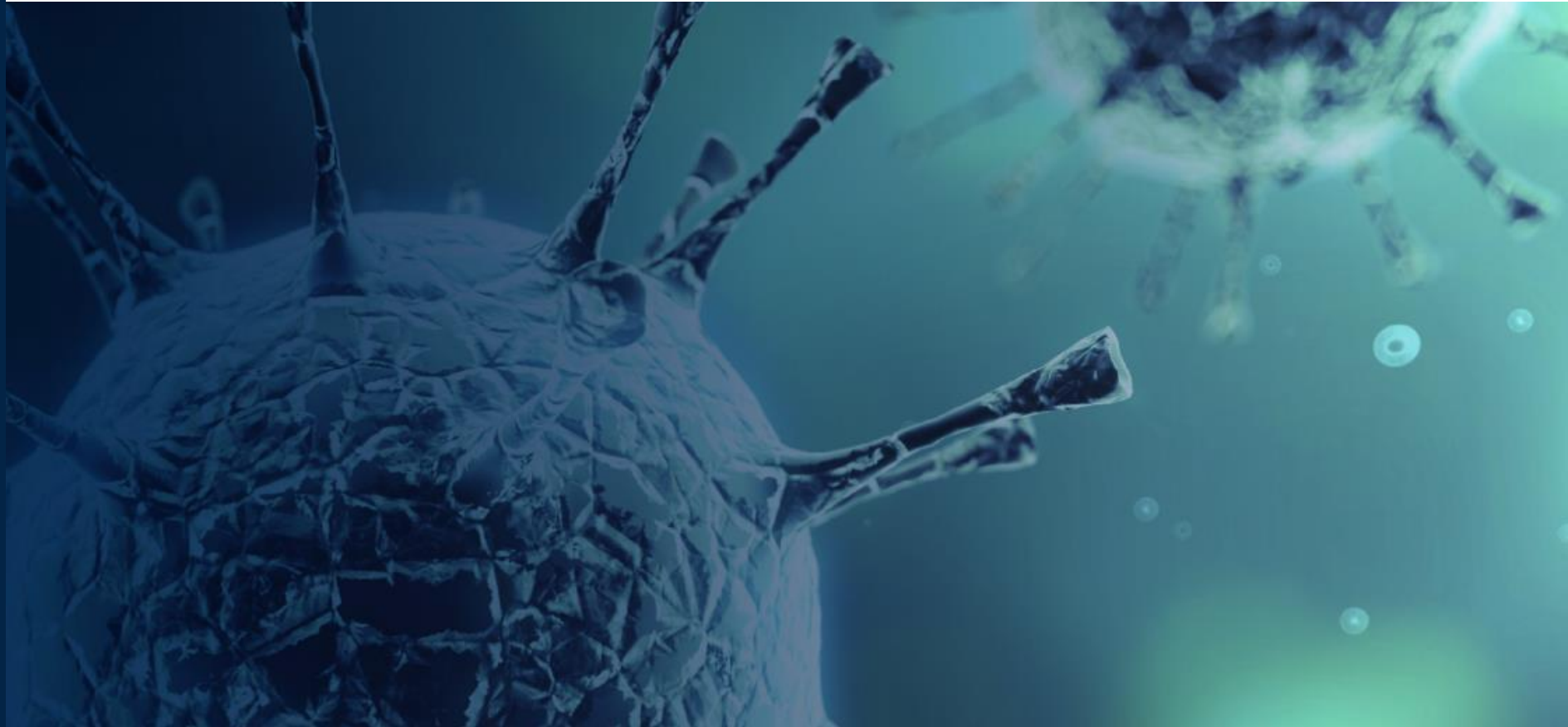




Nasdaq: AUTL



# Next Generation Programmed T Cell Therapies

September, 2019

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# Investment highlights

## **Broad clinical-stage pipeline**

- > 4 product candidates
- > 5 hematological indications
- > 1 solid tumor program

## **Multiple upcoming milestones**

- > Late and early stage clinical data from multiple programs

## **Proprietary manufacturing process**

- > Fully enclosed, semi-automated
- > Economical at commercial scale
- > Expanding to new US/UK facilities

## **Modular programming approach**

- > Enables rapid cycle of innovation
- > 4 next generation versions of lead programs
- > Designed to overcome tumor defenses

## **Broad technology base**

- > Portfolio of owned and in-licensed intellectual property; 85 patent families

## **Strong Fundamentals**

- > \$266 million at June 30, 2019
- > Worldwide rights retained for all programs
- > Cash runway into H2 2021

# Broad pipeline of clinical and NG programs

Product	Indication	Target	Preclinical	Phase 1/2	Phase 2/3
B Cell Malignancies					
AUTO1	Pediatric ALL	CD19	UCL - CARPALL		
AUTO1	Adult ALL	CD19	UCL – ALLCAR19		
AUTO1NG	ALL	CD19 & CD22			
AUTO3	DLBCL	CD19 & CD22	ALEXANDER		
AUTO3NG	DLBCL	CD19 & CD22			
Multiple Myeloma					
AUTO2NG	Multiple Myeloma	Undisclosed			
T Cell Lymphoma					
AUTO4	TRBC1+ Peripheral TCL (LibrA T1)	TRBC1	LibrA T1		
AUTO5	TRBC2+ Peripheral TCL	TRBC2			
GD2+ Tumors					
AUTO6	Neuroblastoma	GD2	CRUK		
AUTO6NG	Neuroblastoma; Melanoma; Osteosarcoma; SCLC	GD2			
Prostate Cancer					
AUTO7	Prostate Cancer	Undisclosed			

# Cancer cells defend against T Cells

- > Any aspiring cancer cell changes its internal programs, displays those changes on its surface and becomes a target for T cells
- > At time of first diagnosis, cancer cells have already acquired capability to defend against T cells
- > Mechanisms of defense are either driven by acquired mutations or use of common mechanisms of immune modulation, like checkpoint inhibition
- > Redirection of T cells is necessary but typically not sufficient for transformational clinical activity

# Each product candidate is designed to address a limitation of current T cell therapies

## B Cell Malignancies

- > **AUTO1** – Reduce high grade CRS\*, while achieving long persistence in acute leukemia
- > **AUTO1NG** – build on AUTO1 clinical experience and limit antigen driven escape by dual targeting
- > **AUTO3** – Limit antigen driven relapse by dual targeting and address checkpoint inhibition in DLBCL
- > **AUTO3NG** – Address 3 routes of escape

## Multiple Myeloma

- > **AUTO2NG** – Increase depth of initial response, counter tumor defense and increase CAR-T persistence

## T Cell Lymphoma

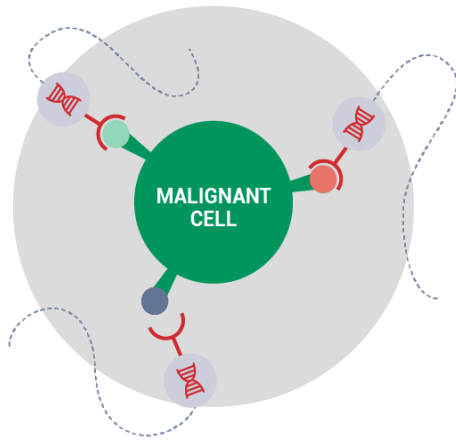
- > **AUTO4 / 5** – Unique targeting of T cell lymphoma while maintaining immunity

## Solid Tumors

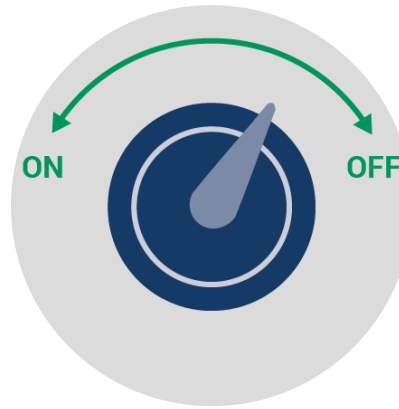
- > **AUTO6NG** – Target GD2+ tumors, increase persistence and address routes of escape
- > **AUTO7** – Target prostate cancer and address routes of escape

# Advanced T cell programming

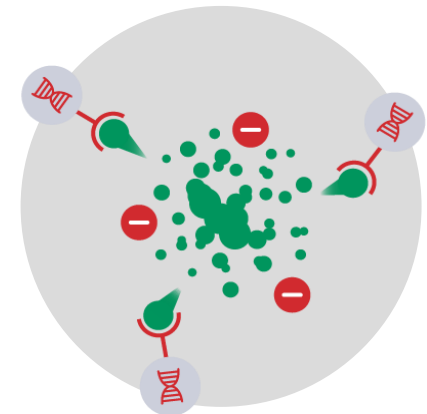
Driving modular innovation with a focus on changing T cell properties without inducing systemic toxicity



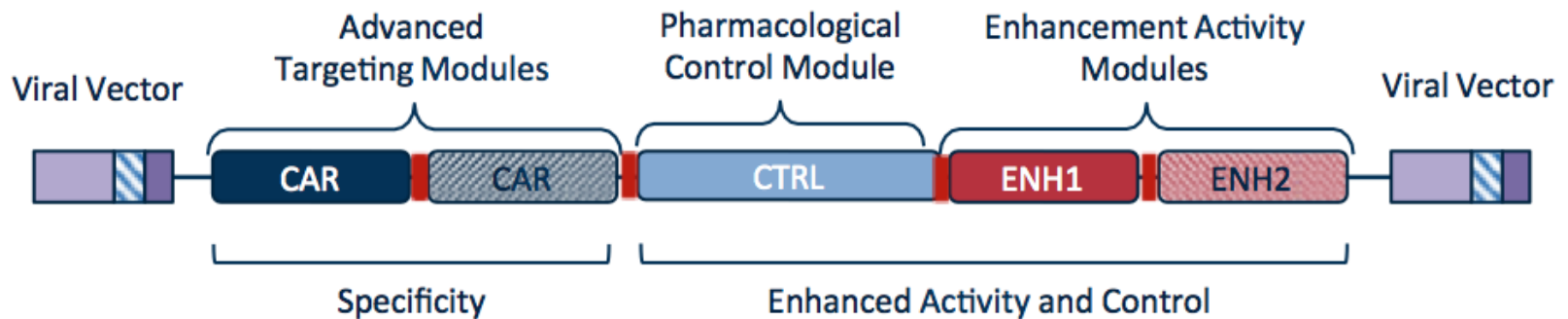
**Advanced targeting**



**Pharmacological Control**



**Enhanced Activity**



# Adult Acute Lymphoblastic Leukemia

Adult ALL is a significant commercial opportunity

- > Potential market size in adult ALL
  - Up to 8,400 new cases of adult ALL diagnosed yearly worldwide (incl. approx. 6,000 in US & EU5)
  - Addressable patient population is projected at 3,000 patients US & EU5
- > High unmet medical need
  - Combination chemotherapy enables 90% of adult ALL patients to experience CR, but approximately 50% will relapse
  - Median overall survival is < 1 year in r/r ALL
- > No CAR T therapy approved in ALL for adults > 25 years of age
- > Only approved redirected T cell therapy is Blincyto® (blinatumomab)



# AUTO1 designed to reduce high-grade CRS

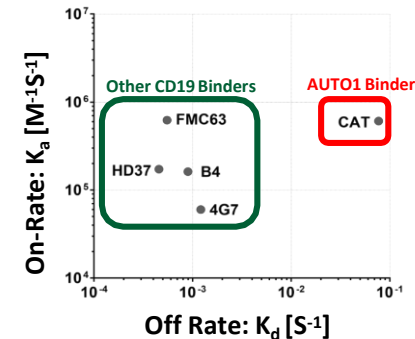
- > Adult ALL patients are generally more fragile, have more co-morbidities, and are less likely to tolerate toxicity compared to pediatric ALL patients
- > Adult ALL patients often have a higher tumor burden in the bone marrow, increasing the risk of adverse events
- > Conventional CD19 CAR Ts use an identical high affinity CD19 binder (FMC63), with a fast on-rate and a very slow off rate leading to over-activation and high-grade CRS
- > AUTO1 is designed to reduce severe ( $\geq$  Grade 3) CRS using an optimized CD19 CAR with a lower affinity and a fast off rate
  - Engages efficiently with cancer cells, delivering a kill, but disengages rapidly like a normal T cell

# AUTO1 shows enhanced activity vs FMC63 CARs

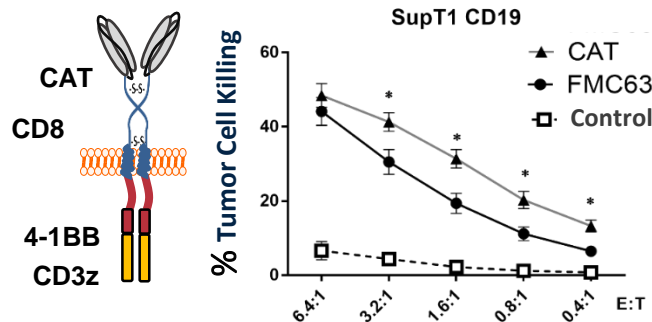
Preclinical data show higher potency and proliferation

- 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

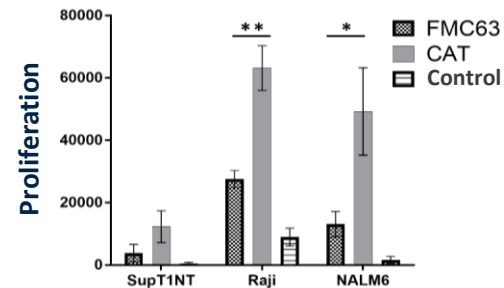
## Fast Off-Rate



## Enhanced Cytotoxicity



## Enhanced Proliferation

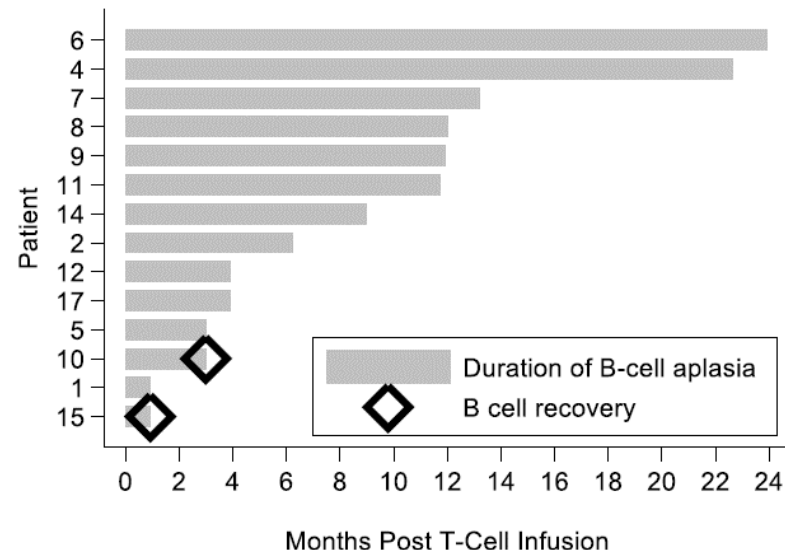
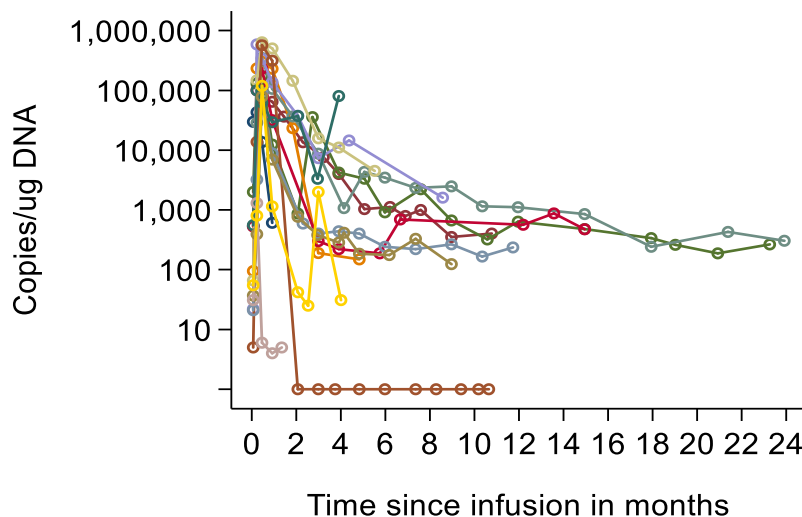


\*Similar binders are used in Yescarta® and JCAR-017

Amrolia, Persis J. et al. "Enhanced CAR T cell expansion and prolonged persistence in pediatric patients with ALL treated with a low-affinity CD19 CAR." *Nature Medicine*, September 2019.

# AUTO1 shows excellent expansion and persistence in pALL

AUTO1 expansion and persistence exceed Kymriah®



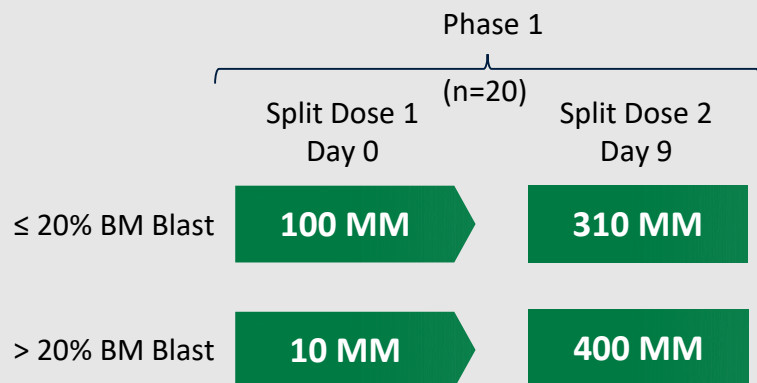
## > Enhanced Expansion:

- Peak expansion (Cmax) approximately 3 x higher than that reported for Kymriah®
- Area under the curve (day 0-28) 5 x higher than that reported for Kymriah®

## > Prolonged Persistence:

- Median half-life of AUTO1 cells (34 days) was more than 2 x longer than that reported for Kymriah® (14.2 days)
- At last follow-up, AUTO1 cells were detectable in 11/14 patients (79%) and correlated with ongoing B cell aplasia in these patients

# Adult ALL – AUTO1: Phase 1 trial is ongoing



CD19 CAR T Cells administered as fixed dose following Flu/Cy pre-conditioning

## Status

Initiated Phase 1 ALLCAR19 trial in Q1 2018

Phase 1 designed to assess safety in adult ALL; conducted in collaboration with UCL

Phase 1 data on safety and preliminary efficacy data presented Q2 2019\*

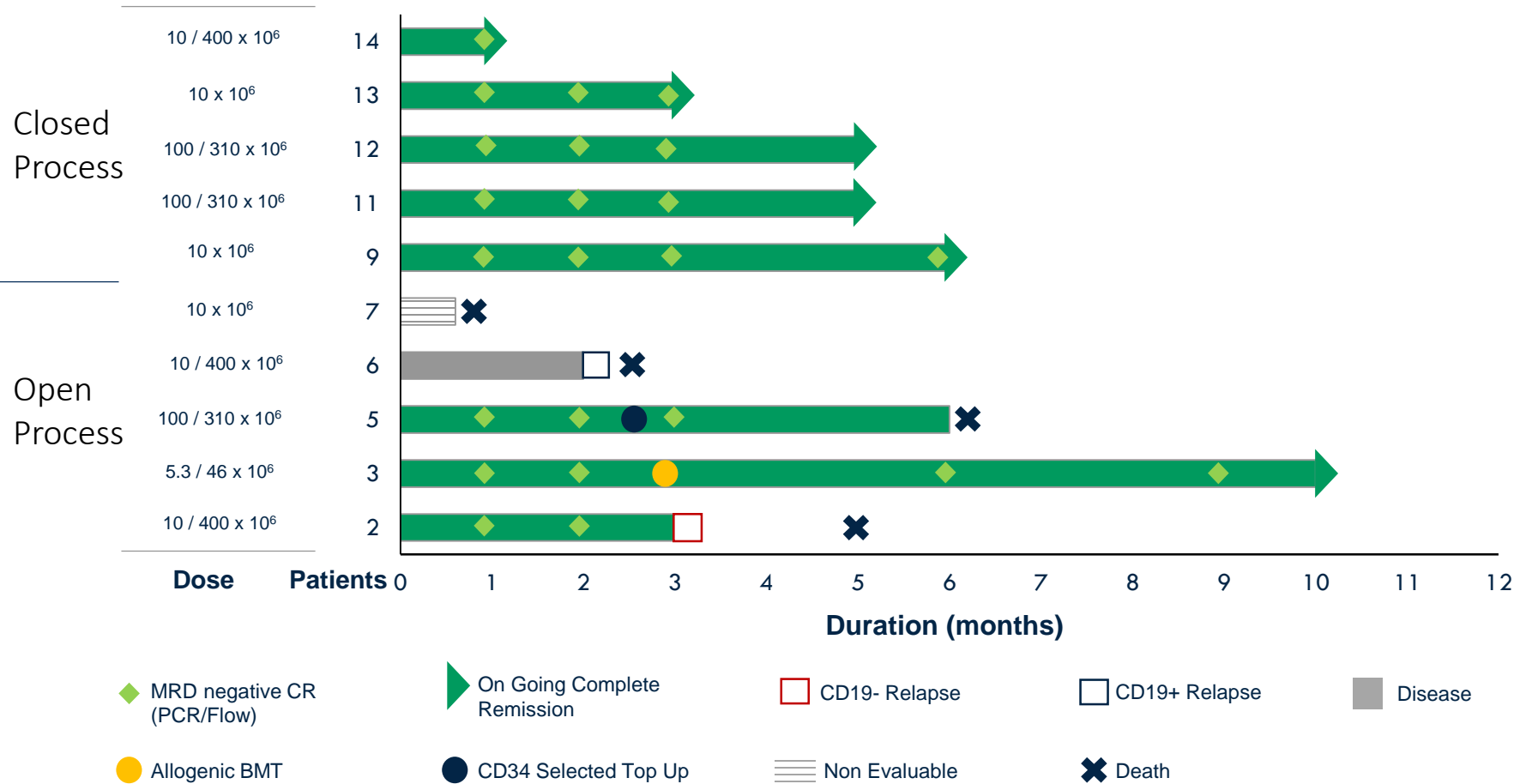
# AUTO1 in adult ALL: Favorable safety profile

Interim data from ALLCAR19 Phase 1 Study (N=10)

- > 5 patients had  $\geq 50\%$  BM blasts prior to lymphodepletion (CRS 'high risk')
- > Robust CAR T cell expansion and persistence
- > Zero patients  $\geq$  Grade 3 CRS (Lee criteria)
  - Only 2 patients with Grade 2 CRS
- > Neurotoxicity: 1 Grade 3 CRES\* (with rapid and complete resolution)
- > No patients admitted to ICU due to CRS

# AUTO1 in adult ALL: High level of efficacy

8/9 (88%)\* of evaluable patients at 1 month achieved molecular CR



MRD < 10<sup>-4</sup> by PCR or < 5 x 10<sup>-4</sup> based on limits of detection of assay

# Comparison of AUTO1 vs. Kymriah® and Blincyto®

AUTO1 – potential for best in class redirected T cell therapy in adult ALL

	Pediatric ALL		Adult ALL	
	<sup>1</sup> Kymriah® - pALL	<sup>2</sup> AUTO1 - pALL	<sup>3</sup> AUTO1 aALL	<sup>4</sup> Blincyto®
Patient Numbers	75	14	10	271
CR Rate	81%	86%	88%*	42%
EFS	EFS 12m: 50% (95% CI, 35 to 64)	EFS 12m: 46% (95% CI, 16 to 72)	tbd	EFS 6m: 31%
CRS ≥ Grade 3	47%	0%	0%	3%
Neurotox ≥ G3	13%	7%	10%	13%

\* In 8 of 9 evaluable patients at 1 month; 8 of 10 treated patients

1. Maude et al., NEJM 2018
2. Ghorashian et al., EU CAR T Cell Meeting 2019 and Amrolia, Persis J. et al. "Enhanced CAR T cell expansion and prolonged persistence in pediatric patients with ALL treated with a low-affinity CD19 CAR." *Nature Medicine*, September 2019.
3. Roddie et al., AACR 2019
4. Kantarjian et al., 2017

# AUTO1 in adult ALL - Summary and next steps

## First Autolus program to move to a registration trial

- > Favorable safety profile and high level of clinical activity
  - Data suggest AUTO1 may be twice as active as blinatumomab, with comparable safety profile
- > Phase 2 registration trial: planned start Q4 2019 (pending regulatory feedback)
  - Adult ALL patients in morphological relapse
  - Single arm study with approx. 70 patients
  - Clinical trial sites in US and Europe
- > Primary Endpoint is overall complete response rate (CR/CRi)
- > Secondary endpoints include:
  - MRD-negative CR
  - EFS at 6 months
- > Additional upcoming milestones:
  - Data update at ASH 2019
  - BLA filing targeted for H2 2021



# Pediatric ALL

## Assessing next steps

- > Pediatric ALL is most common cancer diagnosed in children. Patients respond well to first line therapy
  - Approx. 3,400 new cases diagnosed in the US every year\*
- > 10-20% of patients are relapsed/refractory, or approx. 1,000 patients US & EU5 combined
- > Kymriah® and Blincyto® are approved for r/r pALL

# Pediatric ALL

## AUTO3 data support dual antigen targeting hypothesis

- > AUTO3 molecular CRR and safety are comparable to AUTO1
- > AUTO1 primary cause of relapse was loss of antigen, which usually occurred within 6 months after AUTO1 infusion
- > Design premise for AUTO3 is to reduce antigen driven relapse using a dual targeting approach to CD19 and CD22
- > With AUTO3 one CD19 loss at relapse was observed at around 12 months
- > Recent updated data show good, but still less long-term persistence compared to AUTO1 and durability of effect may be inferior to AUTO1

# Pediatric ALL

Future focus will be on AUTO1/AUTO1NG

- > AUTO1 shows comparable clinical efficacy to Kymriah® with an improved safety profile, similar to Blincyto®
- > Development track in pediatric ALL will focus on AUTO1
  - Phase 1 data at ASH 2019
  - Pediatric program (PIP) with AUTO1
- > Development program includes dual-targeting AUTO1NG, which incorporates the CD19 CAR of AUTO1 and a novel CD22 CAR
  - Expect to present first preclinical data on novel CD22 CAR at ASH 2019
  - Initiate Phase 1 trial H2 2020 with interim Phase 1 data H1 2021

Mueller et al., (2018) Blood.

Maude et al., (2014) NEJM.

Amrolia, Persis J. et al. "Enhanced CAR T cell expansion and prolonged persistence in pediatric patients with ALL treated with a low-affinity CD19 CAR." *Nature Medicine*, September 2019.

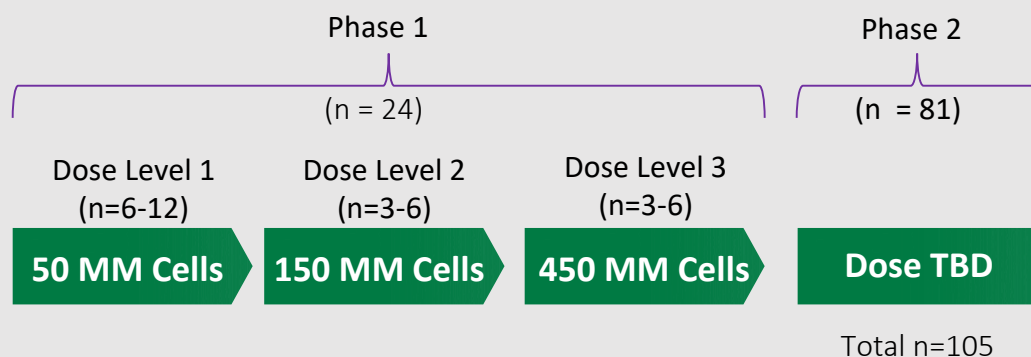
# Diffuse Large B Cell Lymphoma (DLBCL)

DLBCL is a large commercial opportunity

- > Potential market size in DLBCL
  - Approx. 24,000 patients diagnosed in the US every year\*
  - Addressable patient population projected at 10,000 patients for US & EU5 combined
  
- > Aggressive and rapidly advancing cancer
  - Most common type of Non-Hodgkin Lymphoma
  - High dose chemotherapy + monoclonal antibody (MAB) leads to remission in about 50-60% of patients
  
- > Two Approved CAR T products (Yescarta® and Kymriah®)
  - Yescarta® ongoing CR rate: 39%<sup>1</sup>
  - Kymriah® ongoing CR rate: 29%<sup>2</sup>

# AUTO3 in DLBCL\* - ALEXANDER study design and status

Potential to be best in class therapy in DLBCL by addressing antigen escape & PDL-1 mediated inhibition



CD19/22 CAR positive T cells administered as fixed dose following flu/cy pre-conditioning starting with the fourth patient. Three doses of consolidation therapy with pembrolizumab given 2 weeks after AUTO3 infusion

## Status<sup>#</sup>

Initiated Phase 1/2 ALEXANDER trial in Q3 2017

7 patients dosed to date

Anticipate completing Phase 1 dose escalation in H2 2019

# AUTO3 - ALEXANDER interim safety data presented at ASH 2018

Event	All Grade n (%)	Grade 3 n (%)	Grade 4 n (%)
CRS*	1 (14%)	0	0
Neurotoxicity	1 (14%)	1 (14%)	0

\*CRS grading as per Lee et al., *Blood* 2014

- > No dose limiting toxicities
- > No AUTO3 related deaths or Grade 5 adverse events
- > No pembrolizumab immune-related toxicities
- > No patient required ICU admission
- > Of the seven patients, seven had Grade 3-4 neutropenia; six had pyrexia, and six had decreased platelet count, of which five were Grade 3-4

**Preliminary data from the trial suggest AUTO3 at a dose of  $50 \times 10^6$  cells may have a manageable safety profile alone and in combination with pembrolizumab**

# AUTO3 – ALEXANDER initial clinical outcomes at ASH 2018 – clinical activity at initial dose level

Patient	Dose (no. of transduced CAR T-cells)	Pembrolizumab (Dosing days)	Best response*	Ongoing response
001	50 x 10 <sup>6</sup>	No	PD	
003	50 x 10 <sup>6</sup>	No	PR	PD at M3
006	50 x 10 <sup>6</sup>	No	CR	Ongoing CR at M6
007	50 x 10 <sup>6</sup>	Yes	CR	Ongoing CR at M3
008	50 x 10 <sup>6</sup>	Yes	PR	PD at M3
009	50 x 10 <sup>6</sup>	No	PD	
010	50 x 10 <sup>6</sup>	Yes	NE	

\* Response determined by PET scan based on Lugano criteria  
 PD, progressive disease; PR, partial response; CR, complete response; NE, not evaluable  
 Patient 010 NE, PET-negative disease after bridging chemotherapy and prior to AUTO3 infusion

- > Enrolment continues at higher doses of AUTO3
- > Phase 1 interim data at ASH 2019, with full Phase 1 data in H1 2020

# AUTO3 Next Generation

Designed for improved response rate & durability without external checkpoint inhibitor combination

dSHP2

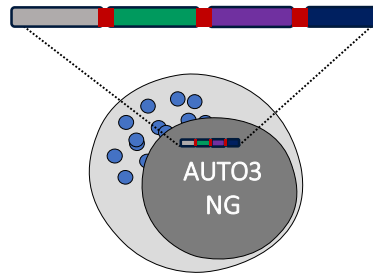
Truncated SHP2 to  
block multiple  
checkpoint  
pathways

dTGF $\beta$  Receptor

Truncated TGF $\beta$   
receptor to combat  
high levels of TGF $\beta$

CD19 CAR / CD22 CAR

Simultaneous targeting  
of CD19 and CD22  
designed to reduce  
relapse due to antigen  
loss



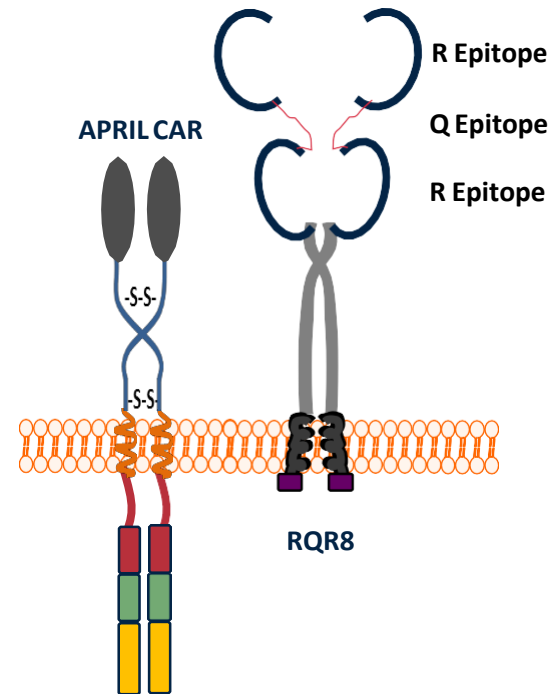
> Expect to initiate Phase 1 trial with AUTO3NG H1 2020



# AUTO2 and AUTO2NG

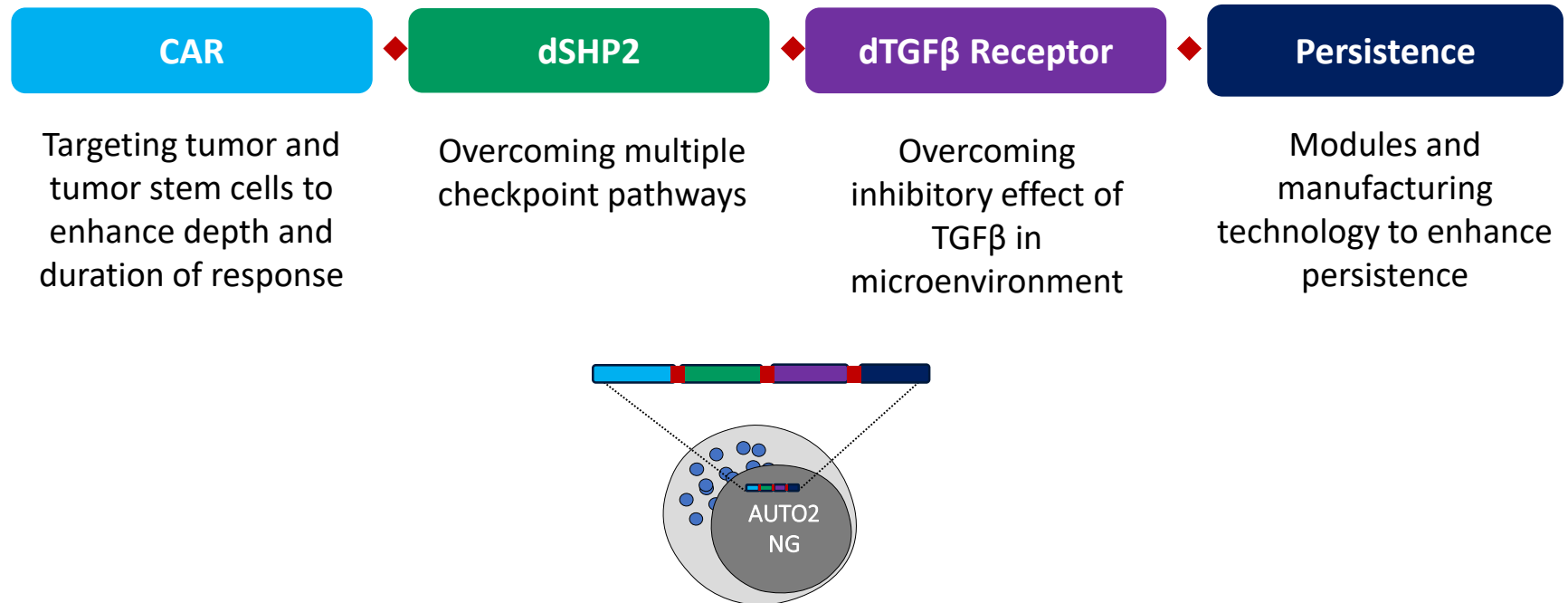
## Dual-targeting programmed T cell therapy for use in r/r multiple myeloma

- > Dual-targeting programmed T cell product candidate with human binder designed to:
  - Reduce risk of antigen escape
  - Overcome challenges of low antigen density
- > RQR8 safety switch designed to be triggered in the event of certain serious adverse events related to the T cell therapy



# AUTO2 and AUTO2NG

Potential to enhance depth of response and persistence and render therapy insensitive to tumor microenvironment

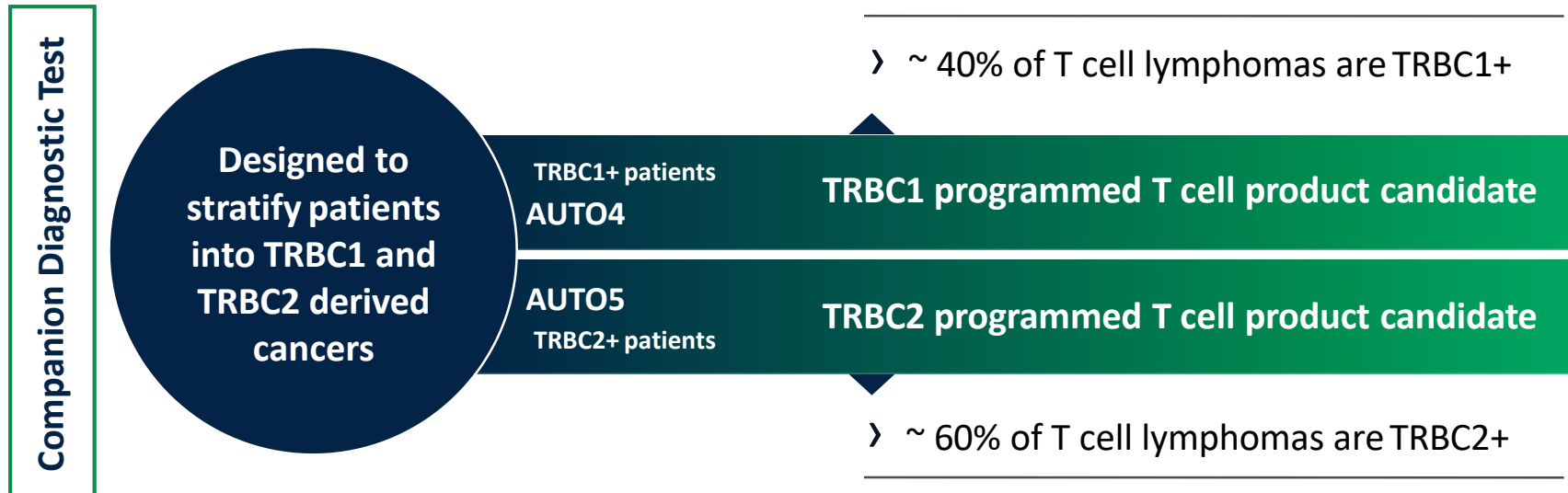


- > AUTO2 is not differentiated from more advanced competitor programs
- > Expect to present Phase 1 data at ASH 2019
- > Focus on moving next generation version into clinic in H1 2020

# Addressing T cell lymphomas

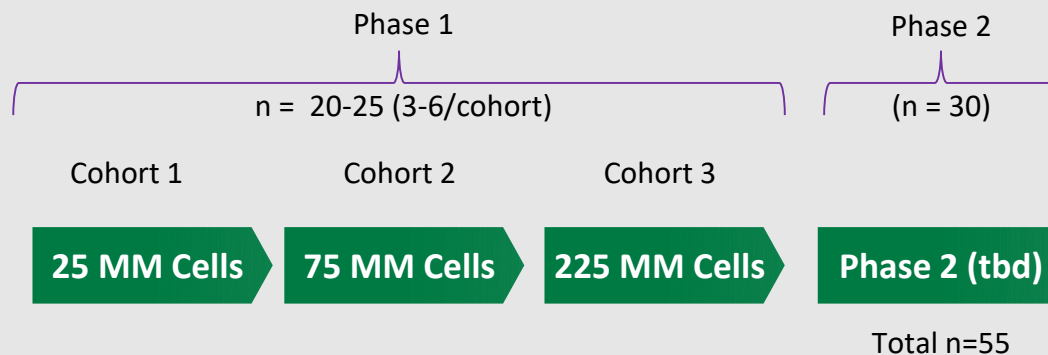
No standard of care after first relapse

Patient prognosis is poor



# AUTO4/5 in Peripheral T Cell Lymphoma – study design and status

Potential to be first in class therapies for T cell lymphoma designed to avoid severe immunosuppression typically associated with current treatments



TRBC1 CAR positive T Cells administered as Fixed Dose following Flu/Cy pre-conditioning

## Status

Initiated AUTO4 Phase 1/2 LibrA T1 trial in Q4 2018; first patient dosed

Expect initial dose ranging Phase 1 data in H2 2020

AUTO5 in preclinical development, will enter Ph 1/2 if POC established in LibrA T1

# AUTO6: GD2-targeted programmed T cell therapy

Designed to drive anti-tumor activity without inducing neurotoxicity

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## > Programmed T cell product candidate:

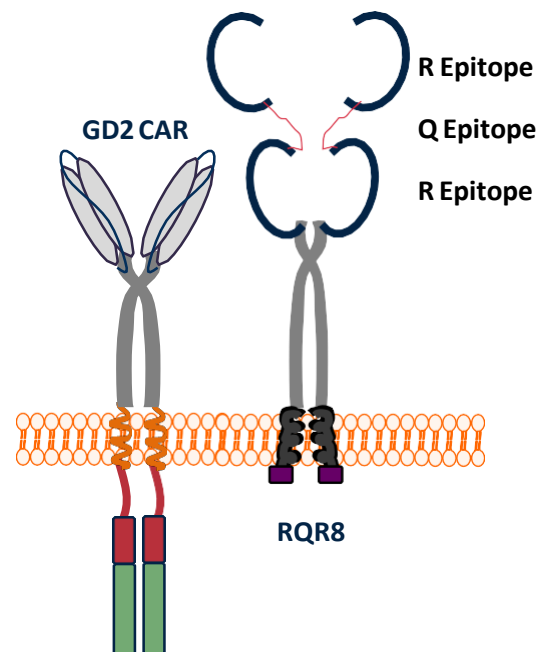
- New binder to minimize on-target, off-tumor toxicity
- Humanized binder to reduce immunogenicity
- RQR8 safety switch

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## > Phase 1 clinical trial in r/r neuroblastoma conducted by CRUK\* in collaboration with UCL

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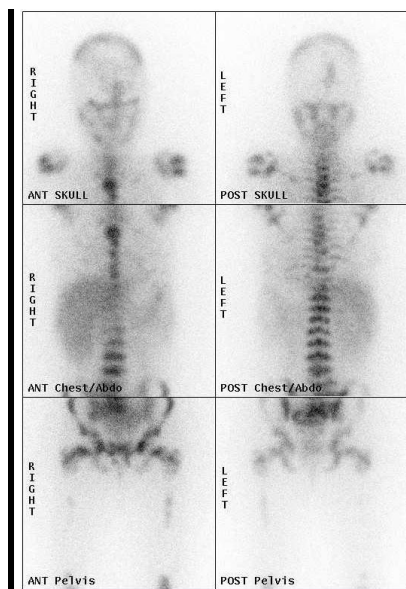
## > Autolus has exclusive worldwide rights to clinical data and patents



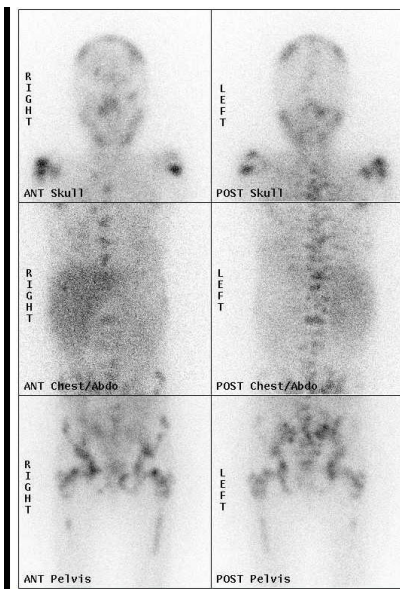
# AUTO6 proof of principle presented at AACR 2018

## Patient 10: AUTO6 anti-tumor activity without inducing neurotoxicity

Day 0



Day 28

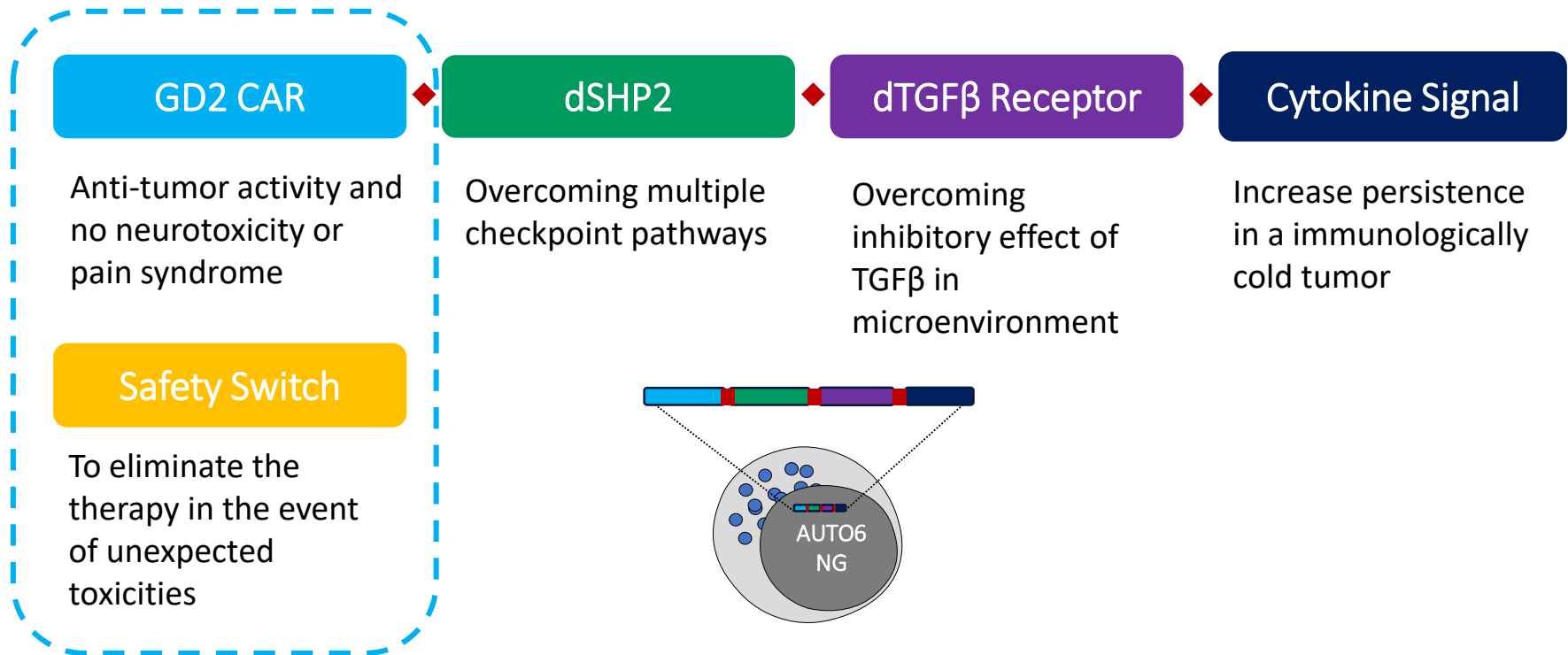


MIBG: iodine-123-meta-iodobenzylguanidine

- > Significant decrease in disease hot spots in patient 10 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 and AUTO6NG T Cell therapy

Designed to overcome tumor defenses



## > AUTO6NG:

- Utilizes the GD2 CAR from AUTO6
- Designed to address persistence, control and tumor defenses
- Target neuroblastoma, osteosarcoma, melanoma, small cell lung cancer and soft tissue sarcoma
- Expected to commence Phase 1 in H2 2020

# Economical & scalable product delivery platform

A key success factor for T cell innovators

Fully enclosed, semi-automated system for cell manufacturing

- > Designed to provide common platform suitable for all current product candidates
- > Designed for scalability in connection with commercialization
- > Long-term equipment and reagent supply agreement with Miltenyi Biotec



**Cell and Gene Therapy  
Catapult (Stevenage,  
UK)**

- Approved for GMP Clinical Supply
- Existing max capacity: 300 p.a. with option to expand to 500 in 2020



**Autolus Launch  
Facility - The GRiD  
(Enfield, UK)**

- Launch site for Cell Process and Vector Supply
- Design Complete
- Anticipated 2020
- Planned max capacity: 1000 p.a.



**Autolus Commercial  
Facility (Rockville,  
MD, US)**

- Fully scaled Commercial site for Cell Process Supply
- Lease agreed
- Anticipated 2021
- Planned max capacity: 5000 p.a.



# Multiple near term clinical data points expected

Product	Indication	Target	Catalyst
B Cell Malignancies			
AUTO1	Pediatric ALL	CD19	<ul style="list-style-type: none"> <li>Phase 1 data Q4 2019</li> </ul>
AUTO1	Adult ALL	CD19	<ul style="list-style-type: none"> <li>Phase 1 data Q4 2019</li> <li>Start Phase 2 end of 2019</li> </ul>
AUTO1NG	ALL	CD19 & CD22	<ul style="list-style-type: none"> <li>Start Phase 1 H2 2020</li> <li>Interim data H1 2021</li> </ul>
AUTO3	DLBCL	CD19 & CD22	<ul style="list-style-type: none"> <li>Phase 1 interim data Q4 2019</li> <li>Start Phase 2 mid 2020</li> </ul>
AUTO3NG	DLBCL	CD19 & CD22	<ul style="list-style-type: none"> <li>Start Phase 1 2020</li> </ul>
Multiple Myeloma			
AUTO2NG	Multiple Myeloma	Undisclosed	<ul style="list-style-type: none"> <li>Start Phase 1 H1 2020</li> </ul>
T Cell Lymphoma			
AUTO4	TRBC1+ Peripheral TCL (Libra T1)	TRBC1	<ul style="list-style-type: none"> <li>Phase 1 interim data 2020</li> </ul>
AUTO5	TRBC2+ Peripheral TCL	TRBC2	<ul style="list-style-type: none"> <li>Start Phase 1 H2 2020</li> </ul>
GD2+ Tumors			
AUTO6NG	Neuroblastoma; Melanoma; Osteosarcoma; SCLC	GD2	<ul style="list-style-type: none"> <li>Non-clinical data Q4 2019</li> <li>Start Phase 1 H2 2020</li> </ul>
Prostate Cancer			
AUTO7	Prostate Cancer	Undisclosed	<ul style="list-style-type: none"> <li>Start Phase 1 H1 2021</li> </ul>

# Investment highlights

## Broad clinical-stage pipeline

- > 4 product candidates
- > 5 hematological indications
- > 1 solid tumor program

## Multiple upcoming milestones

- > Late and early stage clinical data from multiple programs

## Proprietary manufacturing process

- > Fully enclosed, semi-automated
- > Economical at commercial scale
- > Expanding to new US/UK facilities

## Modular programming approach

- > Enables rapid cycle of innovation
- > 4 next generation versions of lead programs
- > Designed to overcome tumor defenses

## Broad technology base

- > Portfolio of owned and in-licensed intellectual property; 85 patent families

## Strong Fundamentals

- > \$266 million at June 30, 2019
- > Worldwide rights retained for all programs
- > Cash runway into H2 2021



**Thank you**