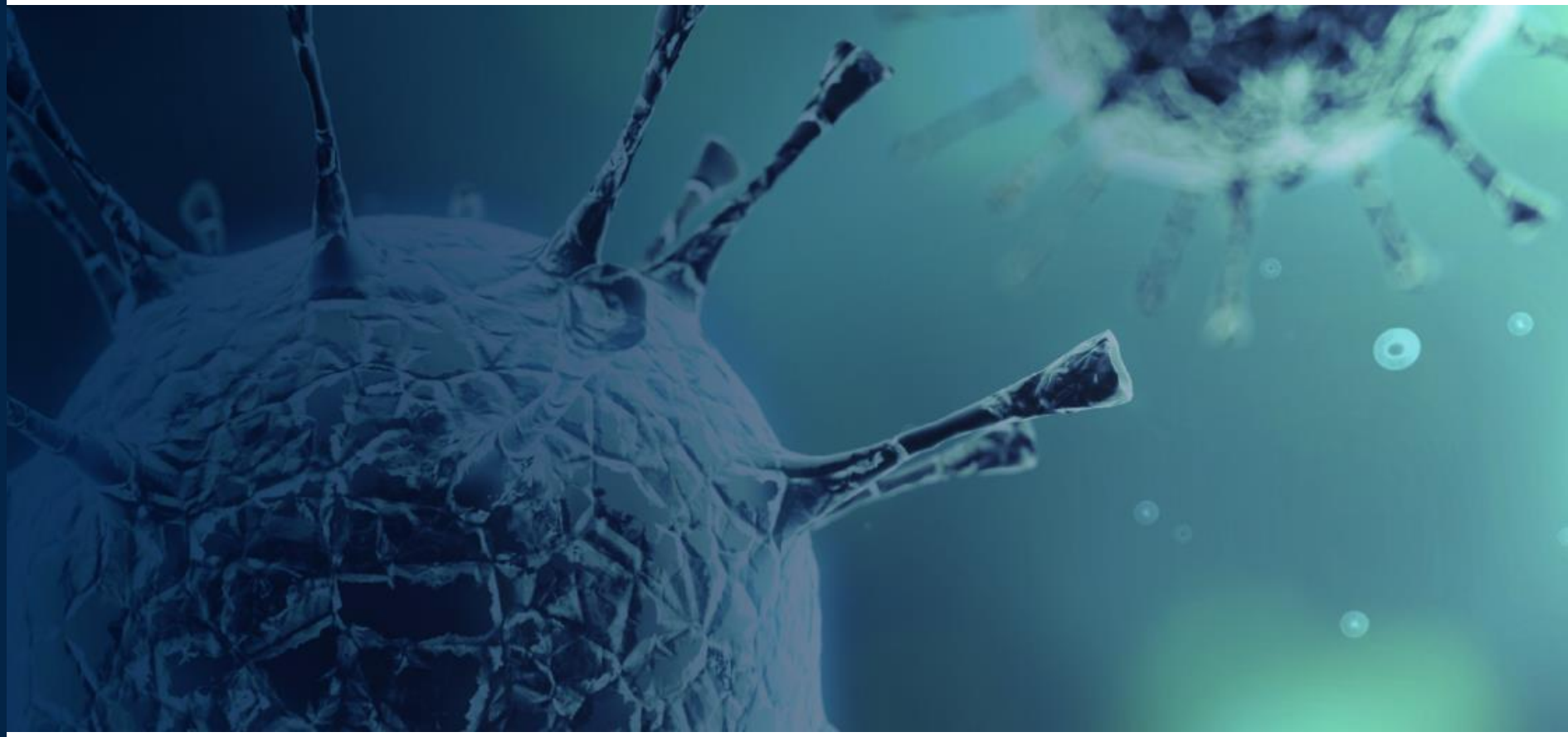
Autolus

Nasdaq: AUTL



Next-Generation Programmed T Cell Therapies

June, 2019

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Investment highlights

Broad clinical-stage pipeline

> 4 product candidates in 5 hematological indications

> 1 solid tumor program

Modular programming approach

> Enables rapid cycle of innovation

> 3 next generation versions of lead programs

Multiple upcoming milestones

> Expect to complete POC of 4 phase 1/2 clinical trials in hematological indications in 2019

Broad technology base

> Portfolio of owned and in-licensed intellectual property; 76 patent families

Proprietary manufacturing process

> Fully enclosed, semi-automated, economical

> Designed for scalability in connection with commercialization

> Expanding to new US/UK facilities

Strong Fundamentals

> $188 million at March 31, 2019

> Net proceeds of $109.0 million from April 2019 public offering, before estimated offering expenses

> Worldwide rights retained for all programs

> Cash runway into H2 2021

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

B Cell Malignancies:

>**AUTO1** – Reduce high grade CRS* for CD19 CAR-T approach
>**AUTO3** – Address antigen driven relapse by dual targeting
>**AUTO3NG** – Address three routes of escape

Multiple Myeloma:

>**AUTO2** – Address low antigen expression and antigen escape
>**AUTO2NG** - Address three routes of escape

T Cell Lymphoma:

>**AUTO4 / 5** - Target T cell lymphoma while maintaining immunity

Solid Tumors:

>**AUTO6NG** – Target GD2+ tumors without neurotoxicity/pain side effect
>**AUTO7** – Target prostate cancer and address routes of escape

*Cytokine Release Syndrome

AUTO1 designed to reduce high-grade CRS

CD19 CAR designed to disengage rapidly

- Most CD19 CAR T therapies show non-physiological interaction with target cells
- CAR T's cannot let go of target cell once granules are discharged
- Instead of minutes, engagement lasts for hours
- Extended engagement leads to overactivation of CAR T cells

- AUTO1 (CAT) designed for fast off-rate from CD19
- Half-life of target interaction very short compared to FMC63 (e.g. Kymriah®)[1] binder:
  - AUTO1 = 9.8 seconds
  - Kymriah = 21 minutes

AUTO1* Data Summary - 2018	
Patient Numbers	14
CRR (at 3 months)	86%
EFS (at 12 months)	46% (95% CI, 16 to 72)
CD19-neg relapse	83%
CRS ≥ Grade 3	0%
Neurotox ≥ Grade 3	7%
Tocilizumab use	No
Grade ≥ 4 Cytopenia > 1 month	57%

AUTO1 - one patient died due to a serious adverse event (sepsis)
*All data as of the November 16, 2018 data cut off

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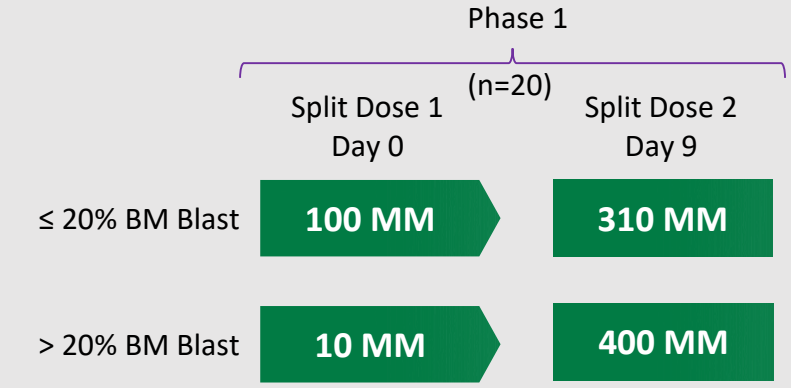
1. Similar binders are used in Yescarta and JCAR-017
2. Pule at al., Keystone Symposia: Emerging Cellular Therapies 2018

AUTO1 – Adult ALL: Phase 1 trial is ongoing at University College London (UCL)

AUTO1 has the potential to be significantly differentiated in adult ALL



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

- **Adult ALL Market size: 3,000* patients in US and EU5**
- Adult patients with ALL are more fragile and susceptible to adverse events than children with ALL
- No CAR-T therapy has been approved in adult ALL; only approved redirected T cell therapy is blinatumomab

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*Approximate addressable recurrent/refractory patient population

AUTO1 in adult ALL – initial safety data presented at AACR 2019

CRS (Lee Criteria)*	Neurotoxicity (CRES#)	≥ Grade 3 Cytopenia

• CRS (any) 3/10
• Grade 2 3/10
• ≥ Grade 3 CRS 0/10
• Tocilizumab use 2/10
	• CRES 2/10
	• Grade 2 1/10
	• Grade 3 1/10
		• ≥ Grade 3 Neutropenia
		  • Day -6: 4/10
		  • Day 28: 5/9
		• ≥ Grade 3 Thrombocytopenia
		  • Day -6: 5/10
		  • Day 28: 4/9

* One patient had G3 CRS by UPenn Criteria, per protocol assessment
# CAR-T-cell-related encephalopathy syndrome
Data as of March 18, 2019

> 5 patients had ≥ 50% BM blasts prior to LD (CRS 'high risk')

> Grade 3 CRES was in the context of extremely high CAR T-cell expansion (8627 CAR T-cells/uL) and resolved rapidly and completely

> Tocilizumab use (2/10)

> No patients were admitted to ICU due to cytokine release syndrome

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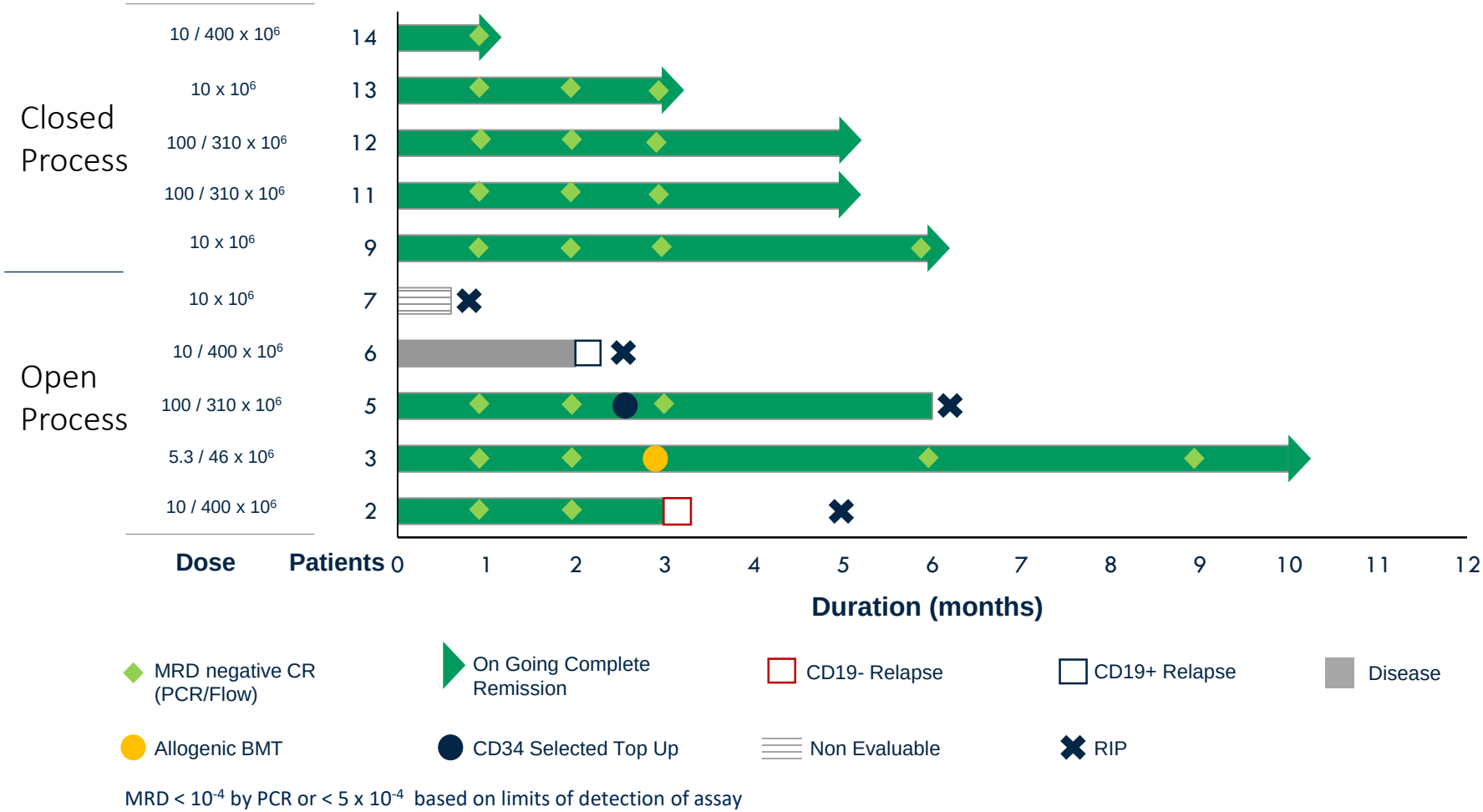
AUTO1 in adult ALL – Patient outcomes (n=10)

8/9 (88%) response-evaluable patients achieved molecular CR at 1 month



MRD < 10^{-4} by PCR or < 5×10^{-4} based on limits of detection of assay

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Key outcomes of CD19 CARs and BiTEs in ALL

AUTO1 – potential for best in class redirected T cell therapy in aALL

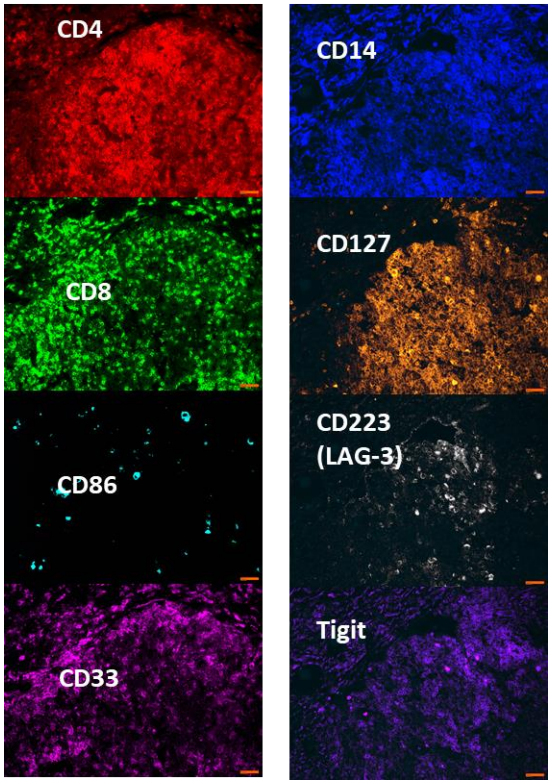
	Pediatric ALL		Adult ALL	
	[1]Kymriah-pALL	[2]AUTO1 - pALL	[3]AUTO1 aALL	[5]Blinatumomab
Patient Numbers	75	14	10	271
CR Rate	81%	86%	88%	42%
EFS	EFS 12m: 50% (95% CI, 35 to 64)	EFS 12m: 46% (95% CI, 16 to 72)	tbd	EFS 6m: 31%[6]
CRS ≥ Grade 3	47%	0%	0%*	3%
Neurotox ≥ Grade 3	13%	7%	11%	13%

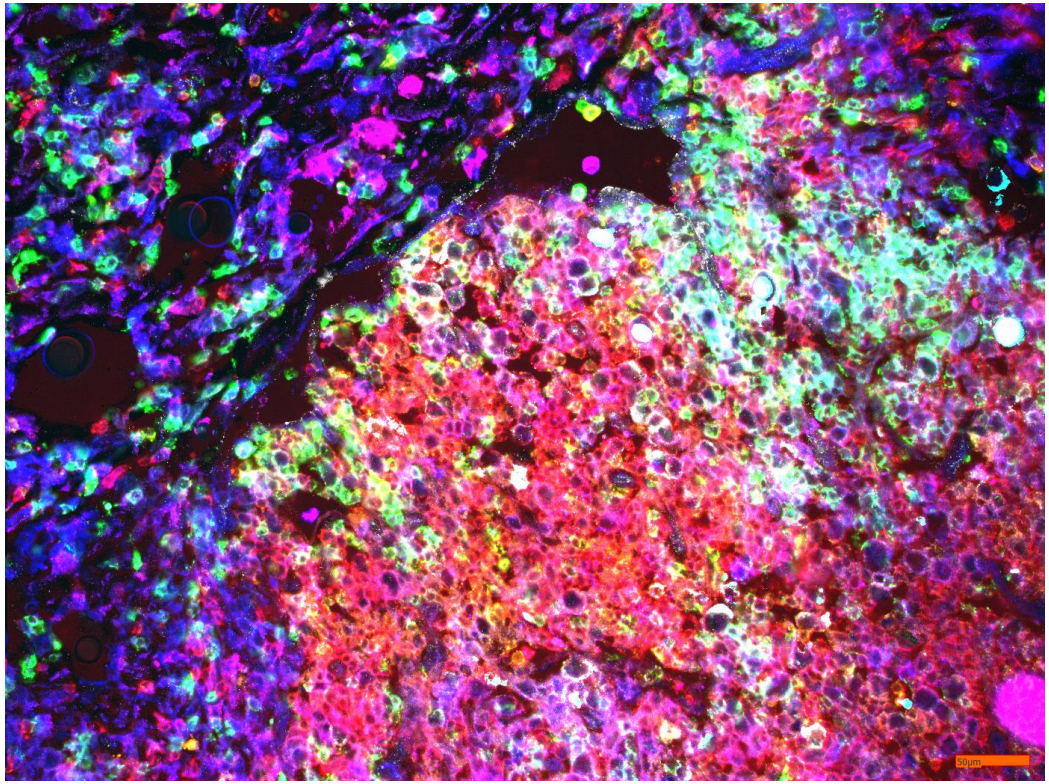
* One patient had G3 CRS by UPenn Criteria, per protocol assessment

1. Maude et al., NEJM 2018
2. Ghorashian et al., EU CAR T Cell Meeting 2019
3. Roddie et al., AACR 2019
4. Wierda et al., ASH 2018
5. Blinatumomab FDA label
6. Kantarjian et al., 2017

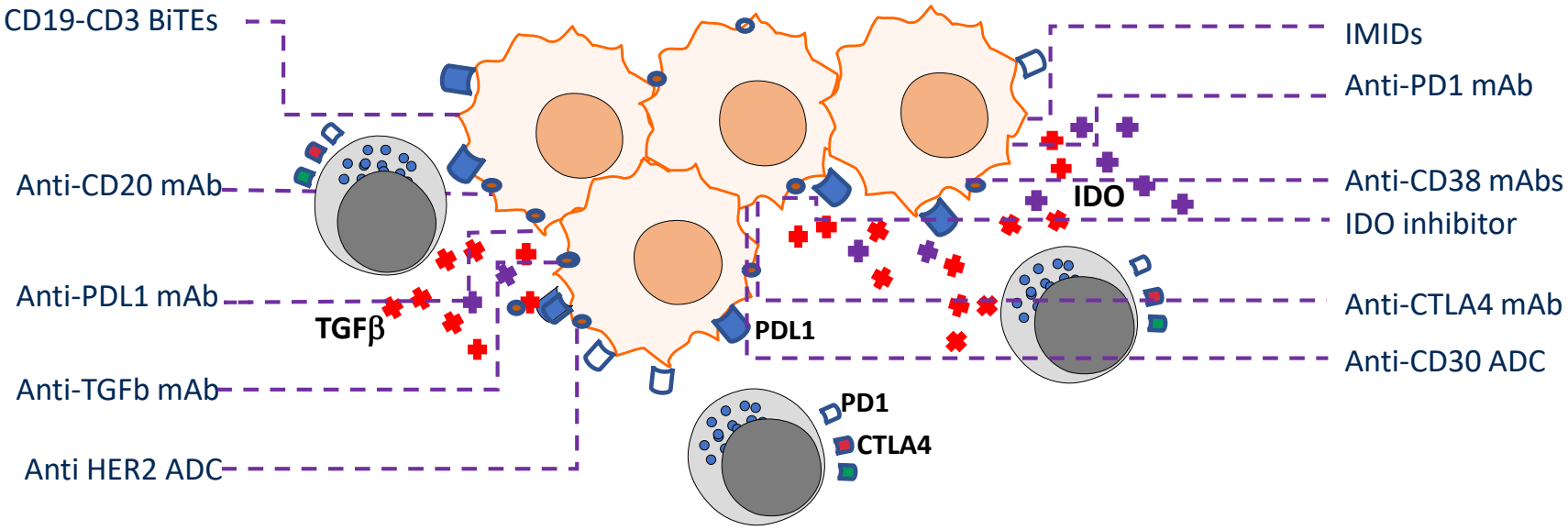
Complexity of tumor heterogeneity

Therapeutic approach has to adapt to complexity





Most traditional immunotherapies tackle one problem at a time



> Effects are systemic, which can lead to undesirable toxicities

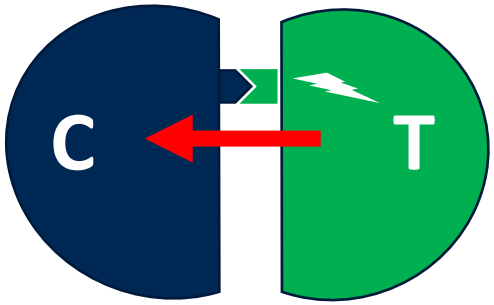
> Combinations are necessary, leading to development complexity and the potential for compounding toxicities

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

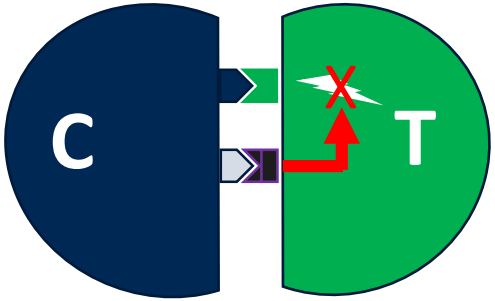
Cancer defense against T Cells

Defense at short range



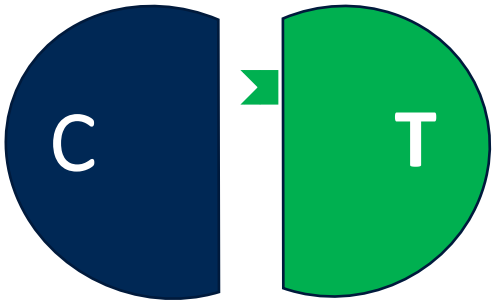
Perforin and granzymes turn on apoptosis

“Game Over”
NO ESCAPE



Checkpoints shut-off activated TCR or CAR

ESCAPE
even when recognized



By MHC loss, peptide processing defect, or antigen loss vs CAR T

ESCAPE
avoid recognition

C: Cancer Cell, **T**: T Cell

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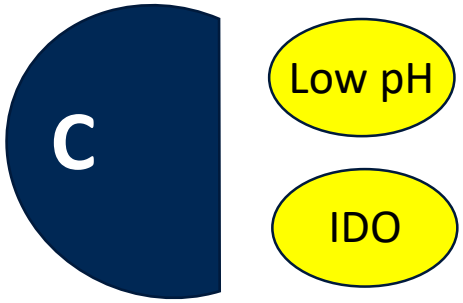
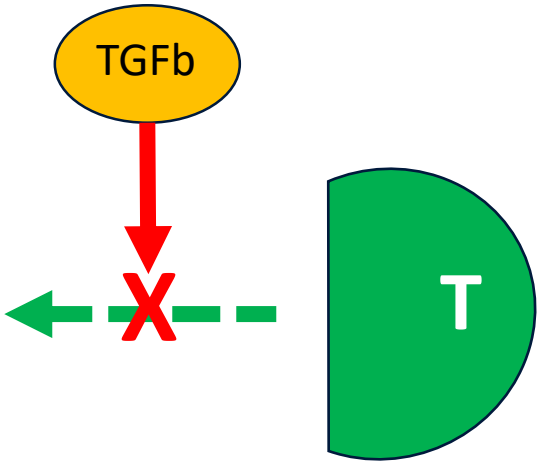
Cancer defense against T cells

Defense at a distance



Metabolic defense
e.g. IDO, low pH



Block migration, or
change T cell phenotype
e.g. TGFb, IL-10

Cancer cells can use multiple defense strategies

Breaking cancer defenses will require multiple approaches

> Standard pharmacological approaches will require a combination to multiple, systemically administered drugs
> Example of how to address defense mechanisms in a given tumor using pharmacological agents:

• Redirection of T cells:	T cell engager
• Family of checkpoints:	anti-PD1 or anti-PDL-1 anti-BTLA4 anti-CTLA4 anti-LAG3 etc.
• Block TGFb	anti-TGFb
• Change metabolic state:	e.g. IDO inhibitor

> All agents impact physiological pathways and have toxicities
> Combining agents drives systemic toxicity and require a complex development path

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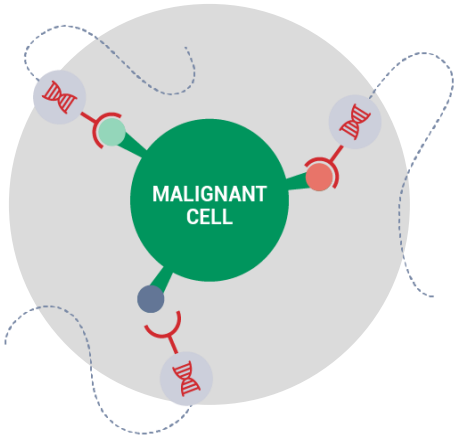
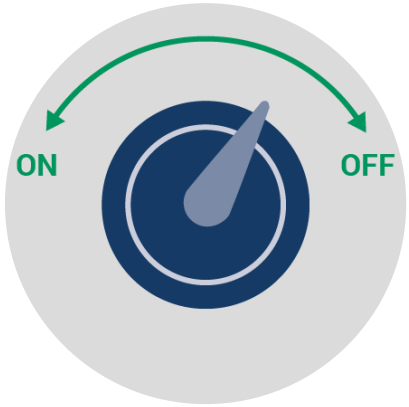
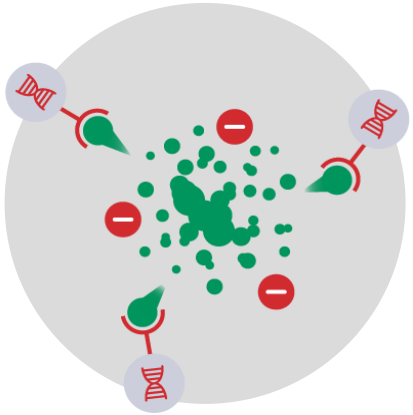
Advanced T cell programming

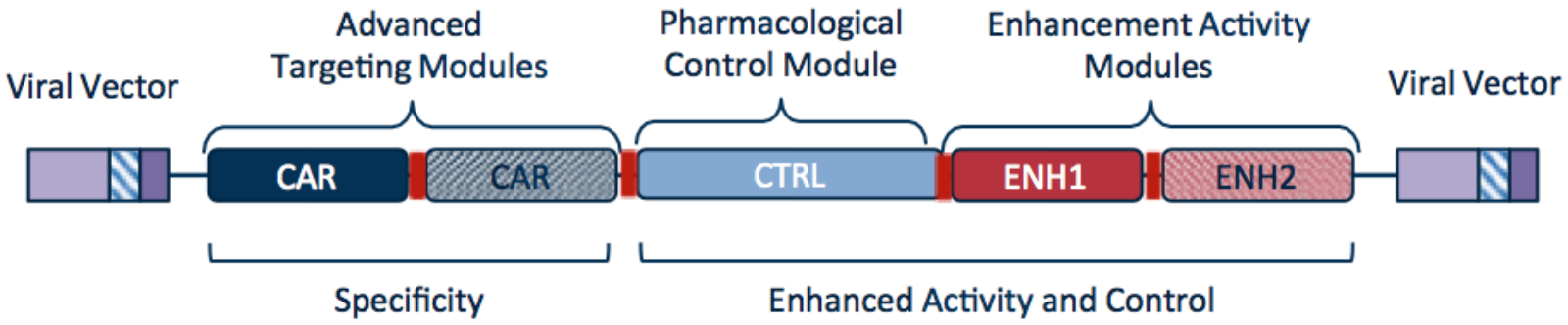
Driving modular innovation with a focus on changing T cell properties without inducing systemic toxicity







Advanced targeting | **Pharmacological Control** | **Enhanced Activity**



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Broad pipeline of clinical stage and next generation programs: five programs in clinical development

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		
AUTO3	Pediatric ALL	CD19 & CD22	AMELIA		
AUTO3	DLBCL	CD19 & CD22	ALEXANDER		
AUTO3 NG	B-Cell Malignancies	Undisclosed			
Multiple Myeloma					
AUTO2	Multiple Myeloma	BCMA & TACI			
AUTO2 NG	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		
AUTO6 NG	Neuroblastoma; Melanoma; Osteosarcoma; SCLC	Undisclosed			
Prostate Cancer					
AUTO7	Prostate Cancer	Undisclosed			

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NG = Next Generation
SCLC = Small Cell Lung Cancer

Rationale for dual targeting CAR

Designed to reduce antigen-loss driven relapse

Rationale

> CD19 CARs are highly active in r/r pediatric ALL, with CR rates of 70–90%

> Event-free survival at 1 year is 45-50%[1-2]

> 40–65% of relapses are due to loss of CD19 antigen[2-3]

Hypothesis

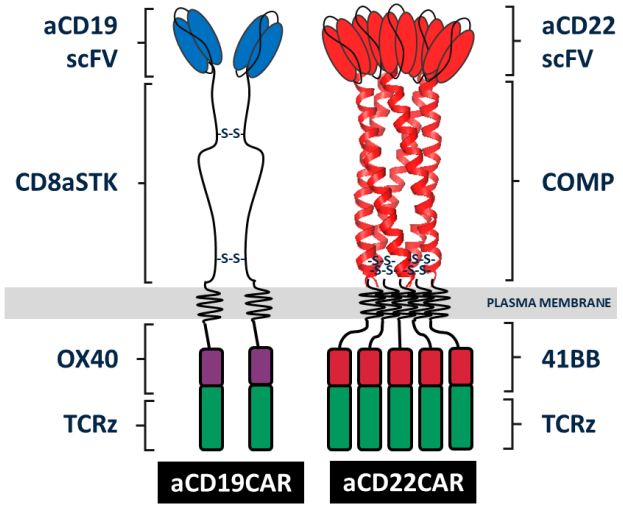
> Simultaneous targeting of CD19 and CD22 may prevent antigen loss

AUTO3: CD19 & CD22 targeting CAR T

> Humanized binders

> Two independent CARs delivered in single retroviral vector

> Independently target CD19 or CD22



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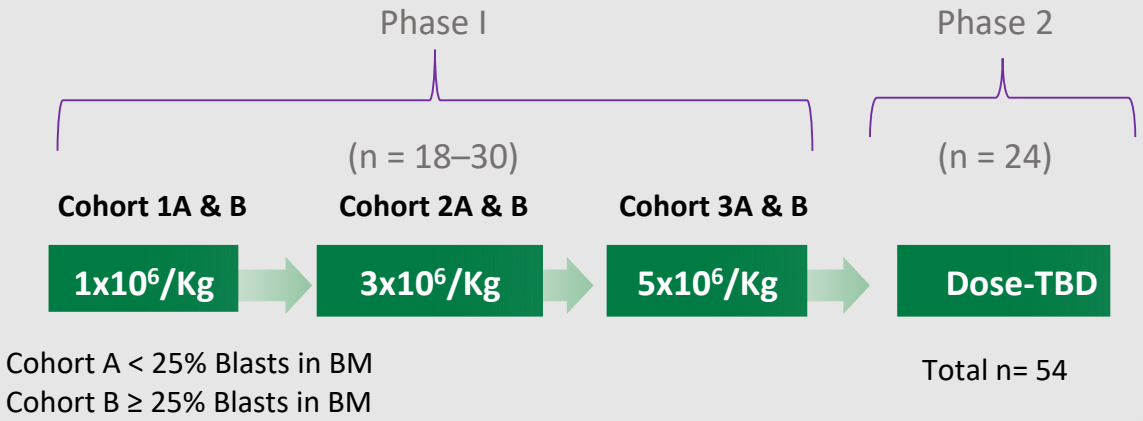
[1]Maude et al., N Engl J Med 2018;378; [2]Gardner et al., Blood 2016 128:219 ; [3]Grupp et al., Blood 2015 126:681

AUTO3 in Pediatric ALL - AMELIA study design and status

Potential to be best in class therapy in pALL by addressing antigen escape



Status*

Initiated Phase 1/2 AMELIA trial in Q3 2017

12 patients dosed to date*

Anticipate completing Phase 1 dose escalation and report final Phase 1 results in Q4 2019

*As of March 2019

> **Pediatric ALL Market size: 1,000* patients in US and EU5**

*Approximate addressable recurrent/refractory patient population

AUTO3 - AMELIA interim safety data presented at ASH 2018

N = 10 patients

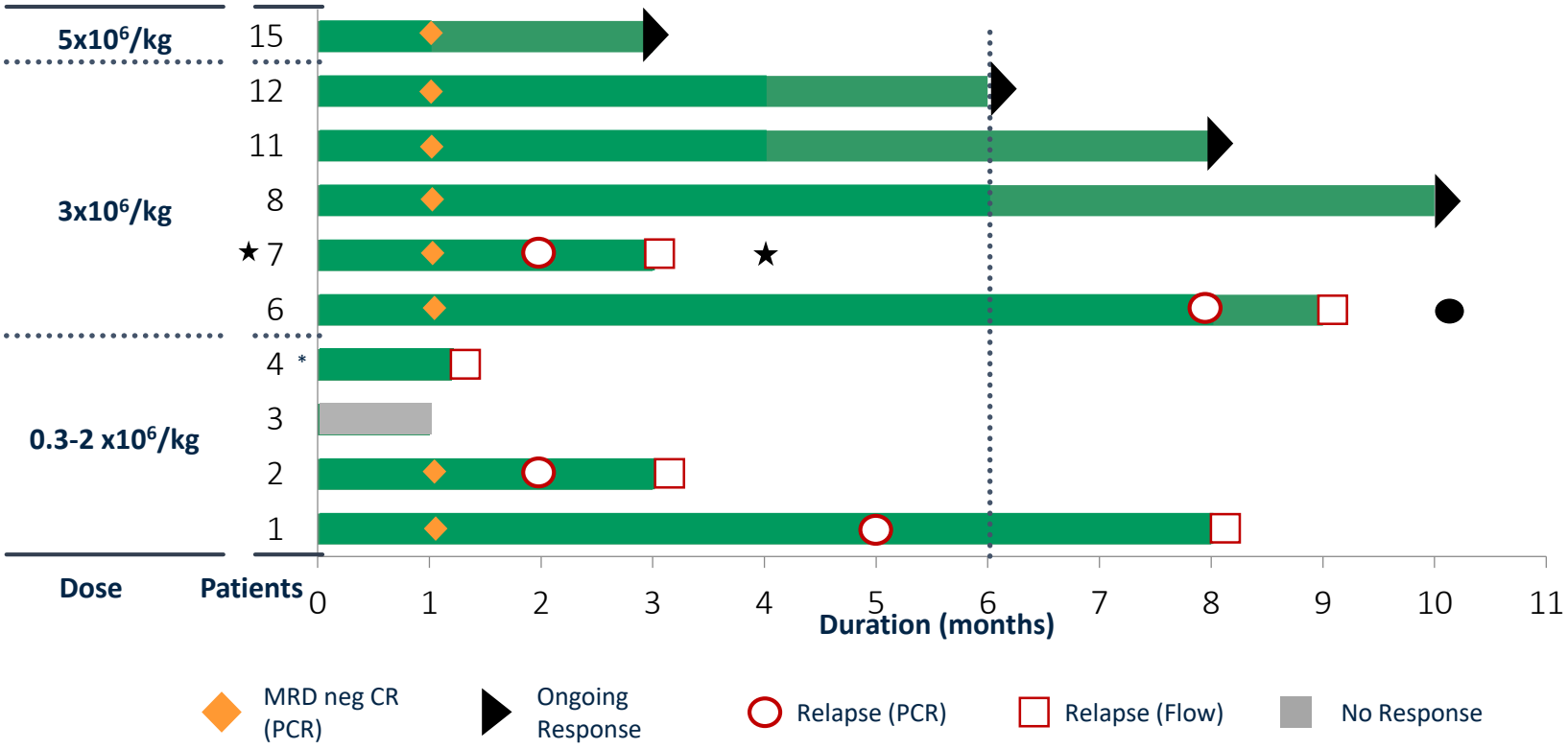
Severity	Neurotoxicity	CRS*
All grades	5 (50%)	7 (70%)
G1	4 (40%)	6 (60%)
G2	0 (0%)	1 (10%)
G3	1 (10%)	0 (0%)
G4	0 (0%)	0 (0%)

- No dose limiting toxicities, no ≥ Grade 3 CRS
- One Grade 3 encephalopathy at 0.3x106/kg dose, reported as unlikely related to AUTO3 and primarily attributed to intrathecal methotrexate
- Tocilizumab use 2 (20%), steroid use 0
- ICU admission for CRS management 0
- ≥ Grade 3 cytopenias lasting >30 days = 4⊕ (40%) patients
- No treatment related deaths

*CRS grading as per Lee et al., *Blood* 2014, ⊕ Includes an event reported after the data cut but prior to presentation of the data at ASH 2018; 3 patients with follow up data had recovery by month 2

13 Nov 2018 data cut presented at ASH 2018

AUTO3 – AMELIA interim efficacy data – ASH 2018 and data update March 2019



★ CD19 neg/pos disease due to prior CD19 CAR therapy, achieved MRD neg CR but poor engraftment resulted in recurrence of CD19 neg disease

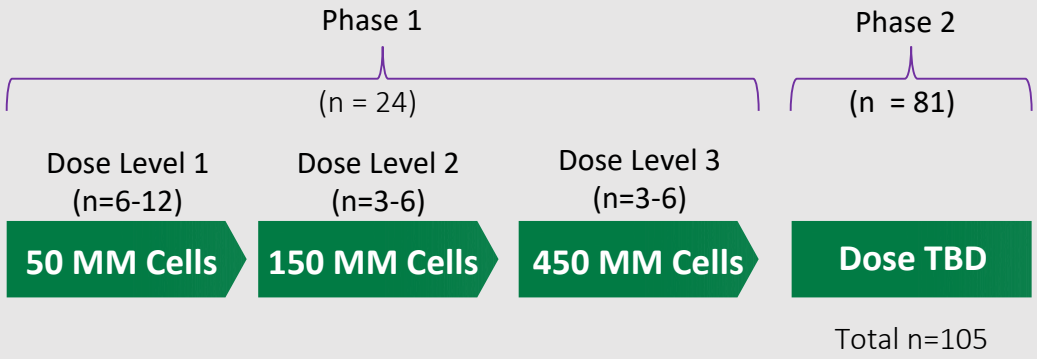
● CD19/CD22 positive relapse due to PD-L1 upregulation

*Patient 4 was MRD neg by flow at month 1, **MRD – minimum residual disease. Median duration of follow up 4.5 months

Feb 2019, data cut

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#

Initiated Phase 1/2 ALEXANDER trial in Q3 2017

7 patients dosed to date

Anticipate completing Phase 1 dose escalation in H2 2019

#All data as of October 2018

> **DLBCL Market size: 10,000** patients in US and EU5**

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*Diffuse large B cell lymphoma
**Approximate addressable recurrent/refractory patient population

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 x 10^6 cells may have a manageable safety profile alone and in combination with pembrolizumab

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All data as of October 2018
Presented at ASH 2018

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 10^6	No	PD	
003	50 x 10^6	No	PR	PD at M3
006	50 x 10^6	No	CR	Ongoing CR at M6
007	50 x 10^6	Yes	CR	Ongoing CR at M3
008	50 x 10^6	Yes	PR	PD at M3
009	50 x 10^6	No	PD	
010	50 x 10^6	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
> Next data update planned for ASH 2019

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All data as of October 2018
Presented at ASH 2018

AUTO3 Next Generation

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

dSHP2

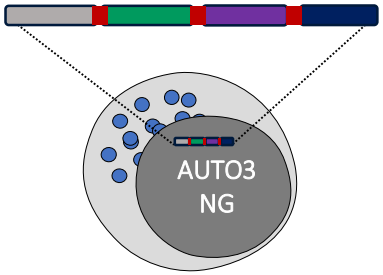
Truncated SHP2 to block multiple checkpoint pathways

dTGFβ Receptor

Truncated TGFβ receptor to combat high levels of TGFβ

CD19 CAR / CD22 CAR

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



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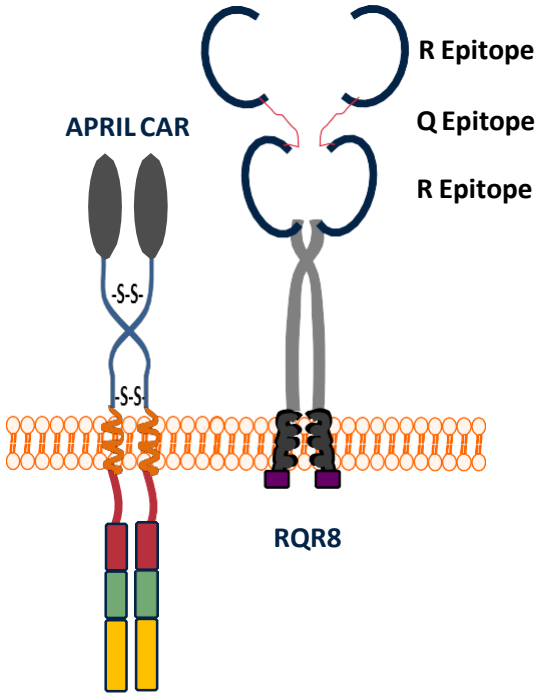
AUTO2 – dual-targeting programmed T cell therapy for use in r/r multiple myeloma

> 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



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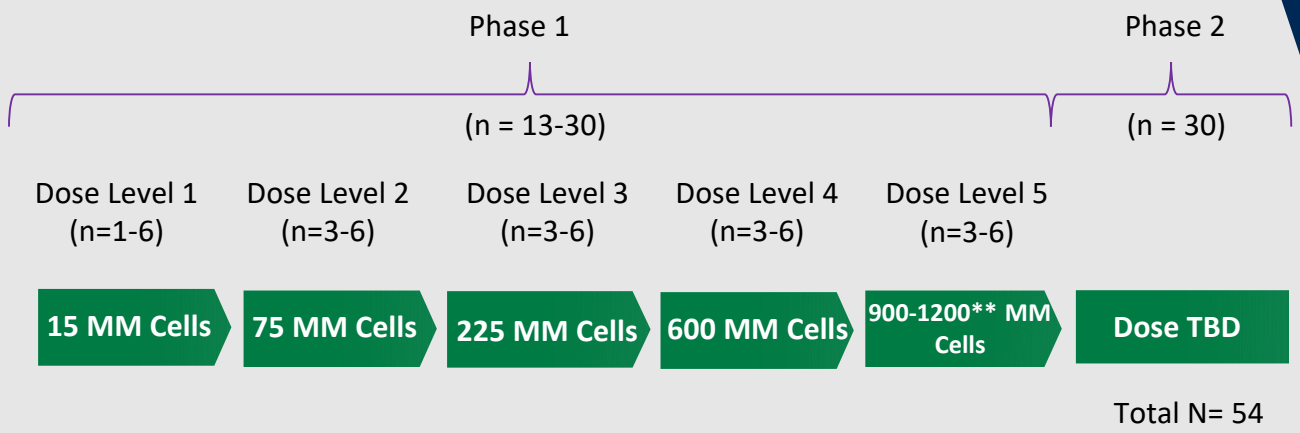
AUTO2 in Multiple Myeloma - study design and status

Potential to overcome challenges of low antigen density



APRIL CAR Positive T Cells administered as Fixed Dose following Flu/Cy pre-conditioning

Status*

Initiated Phase 1/2 APRIL trial in Q3 2017

8 patients dosed

Phase 1 portion of trial anticipated to be completed in Q4 2019

*All data as of October 20, 2018

**1200 dose is TBD subject to additional regulatory approvals in UK and NL

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AUTO2 Next Generation

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

CAR

Targeting tumor and tumor stem cells to enhance depth and duration of response

dSHP2

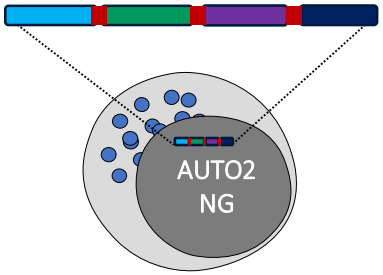
Overcoming multiple checkpoint pathways

dTGFβ Receptor

Overcoming inhibitory effect of TGFβ in microenvironment

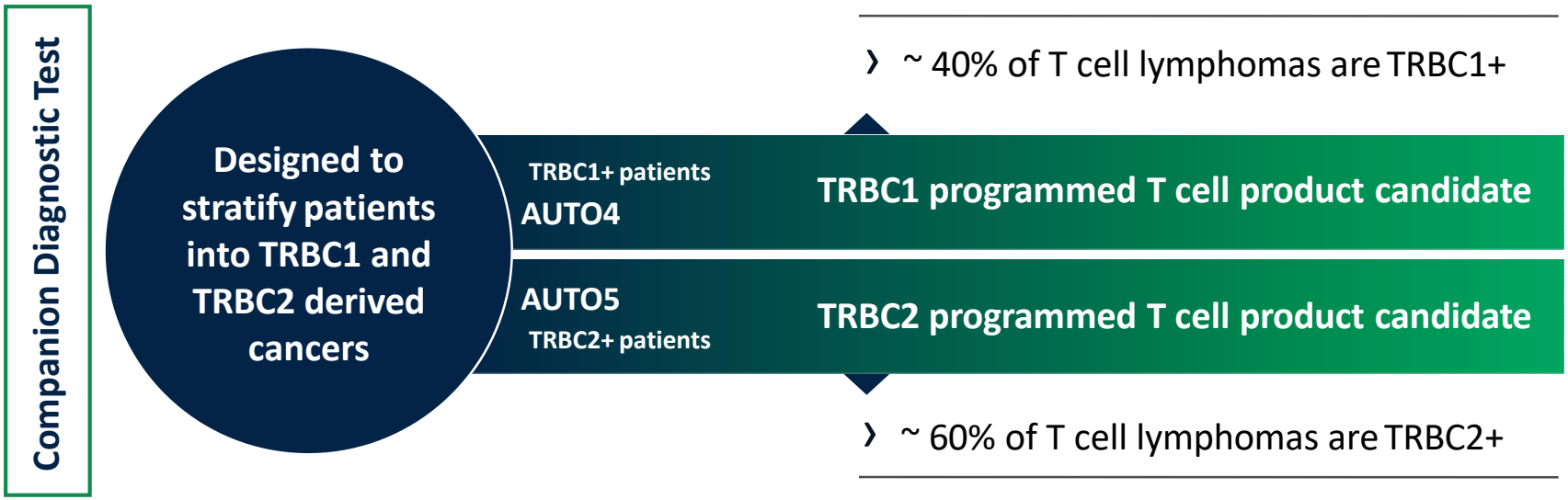
Persistence

Modules and manufacturing technology to enhance persistence



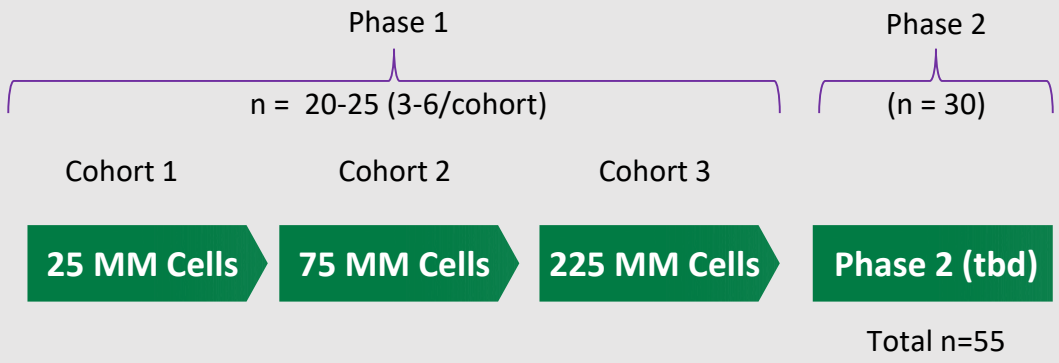
Addressing T cell lymphomas

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 LibrA T1 initial dose ranging Phase 1 data in Q4 2019

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

>T Cell Lymphoma (TRBC1 + TRBC2) Market size: 1,000* patients in US and EU5

*Approximate addressable recurrent/refractory patient population

AUTO6: GD2-targeted programmed T cell therapy

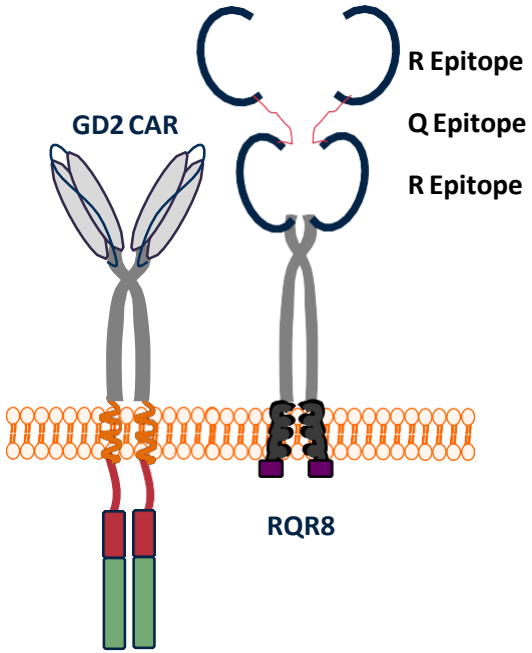
Designed to drive anti-tumor activity without inducing neurotoxicity

> 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



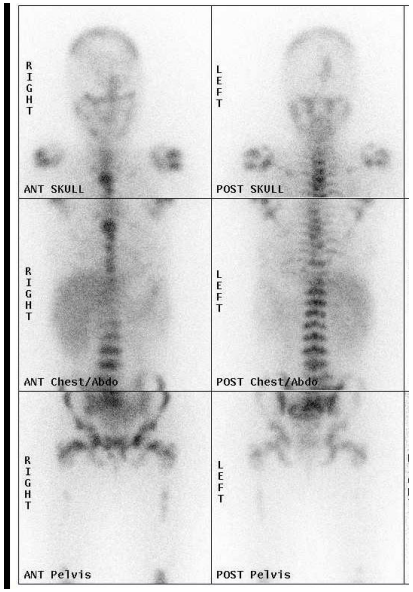
Autolus

*Cancer Research UK

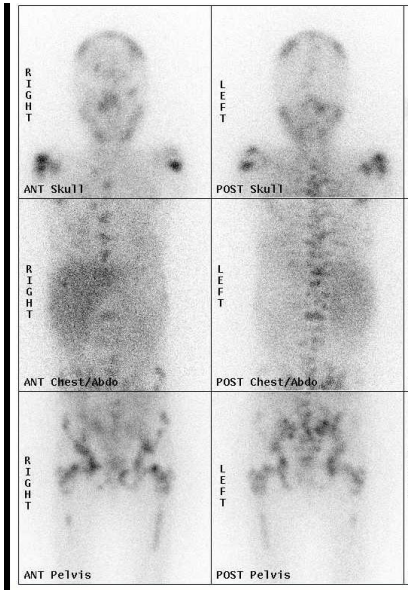
AUTO6 proof of principle presented at AACR 2018

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 next generation program in advanced pre-clinical development

Autolus

AUTO6 next generation T Cell therapy

Designed to overcome tumor defenses

GD2 CAR

Anti-tumor activity and no neurotoxicity or pain syndrome

Safety Switch

To eliminate the therapy in the event of unexpected toxicities

dSHP2

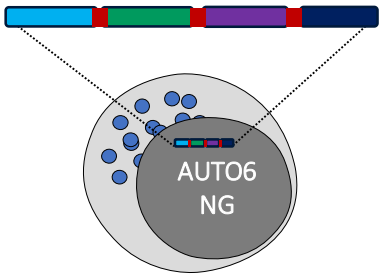
Overcoming multiple checkpoint pathways

dTGFβ Receptor

Overcoming inhibitory effect of TGFβ in microenvironment

Cytokine Signal

Increase persistence in a immunologically cold tumor



> Expected to initiate first Phase 1 in 2020
> 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

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)

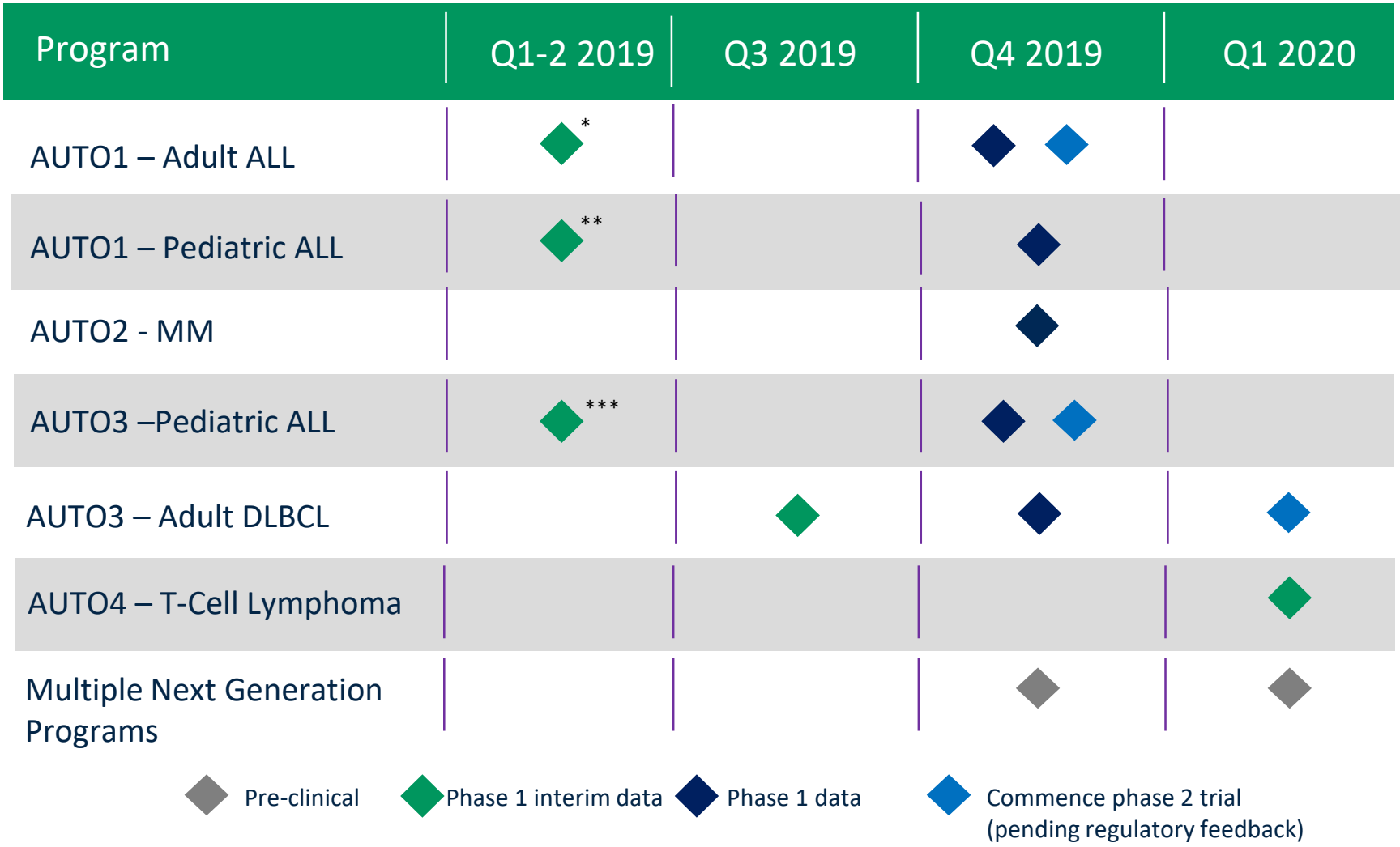
- Launch site for Cell Process and Vector Supply
- Design Complete
- Anticipated 2020
- Planned max capacity: 1000 p.a.

Autolus Commercial Facility (Rockville, MD, US)

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

Clinical newsflow expected through Q1 2020

Data could result in up to three Phase 2 trials within the next 12 months



* includes data presented at AACR Annual Meeting; April 2019
** includes data presented at EHA 1st European CAR T Meeting; Feb 2019
*** includes data presented at AUTL R&D Day Meeting; March 2019

Investment highlights

Broad clinical-stage pipeline

> 4 product candidates in 5 hematological indications

> 1 solid tumor program

Modular programming approach

> Enables rapid cycle of innovation

> 3 next generation versions of lead programs

Multiple upcoming milestones

> Expect to complete POC of 4 phase 1/2 clinical trials in hematological indications in 2019

Broad technology base

> Portfolio of owned and in-licensed intellectual property; 76 patent families

Proprietary manufacturing process

> Fully enclosed, semi-automated, economical

> Designed for scalability in connection with commercialization

> Expanding to new US/UK facilities

Strong Fundamentals

> $188 million at March 31, 2019

> Net proceeds of $109.0 million from April 2019 public offering, before estimated offering expenses

> Worldwide rights retained for all programs

> Cash runway into H2 2021

Thank you