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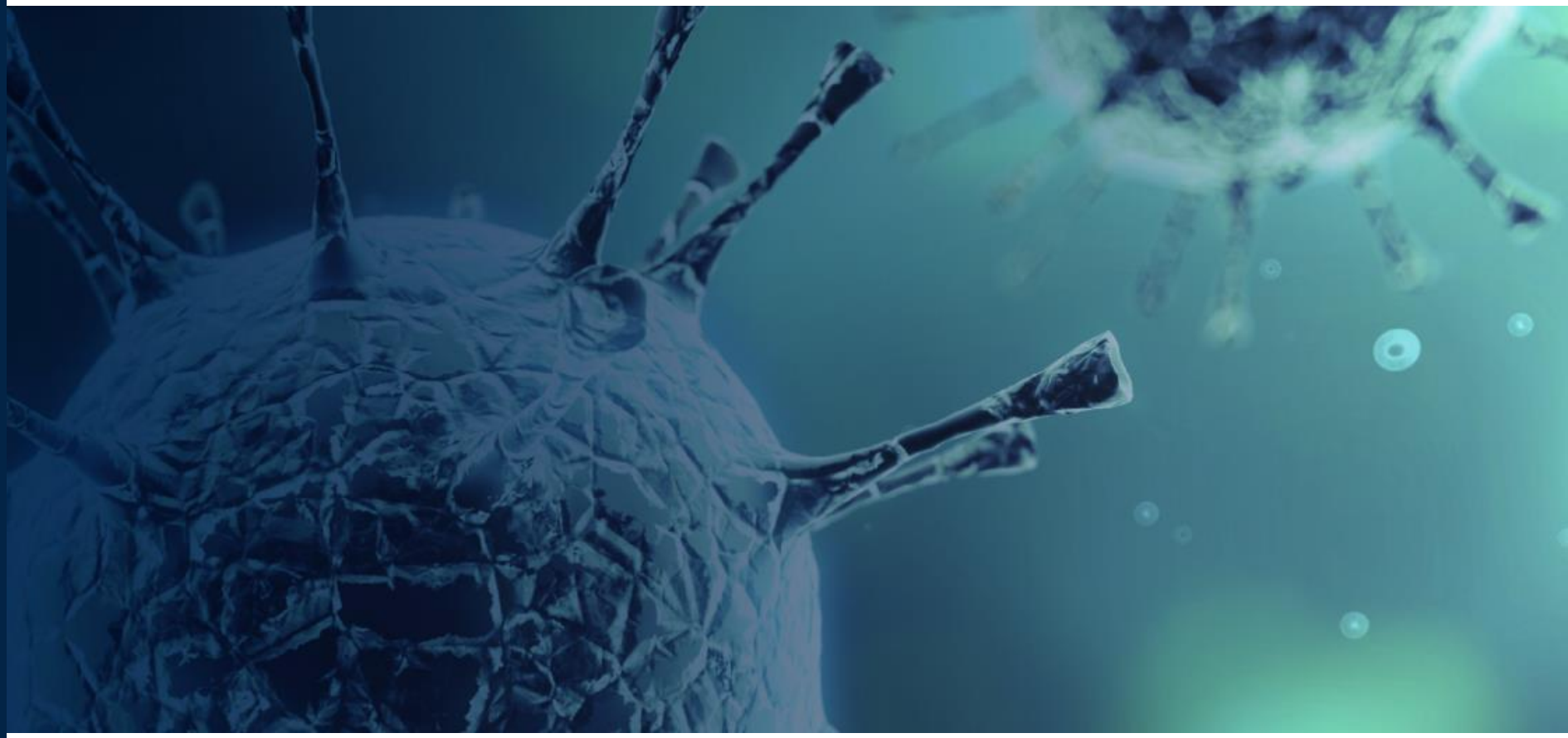
Nasdaq: AUTL



ASH 2019 Review: Next Generation Programmed T Cell Therapies

December 9, 2019

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Agenda for today

1. Welcome and Introduction
2. Data Review
3. Q&A

Data Review

Dr. Christian Itin
Chairman and CEO

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
- 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
- No CAR T therapy currently approved in adult ALL
- Only approved redirected T cell therapy is blinatumomab
- AUTO1 granted FDA orphan drug designation for ALL

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

AUTO1 is designed for long term persistence and reduced high-grade CRS

Unmet need in adult ALL patients

- Generally more fragile, more co-morbidities, and less likely to tolerate toxicity
- Durable benefit in adult ALL will require long term pressure on the leukemia
- Often higher tumor burden in the bone marrow, increasing risk of toxicities

Current treatments

- Conventional CD19 CAR-Ts use identical high affinity CD19 binder (FMC63)
- A fast on-rate and a very slow off rate leads to over-activation and high-grade CRS

AUTO1

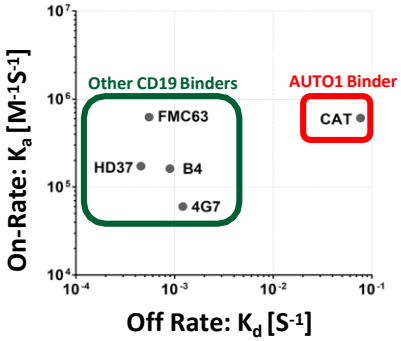
- Designed to reduce severe CRS (≥G3) through the introduction of a proprietary optimized CD19 CAR with a lower affinity and a fast off rate
- Engages efficiently with cancer cells, delivering a kill, but disengages rapidly like a normal T cell

AUTO1 shows enhanced activity vs FMC63 CARs

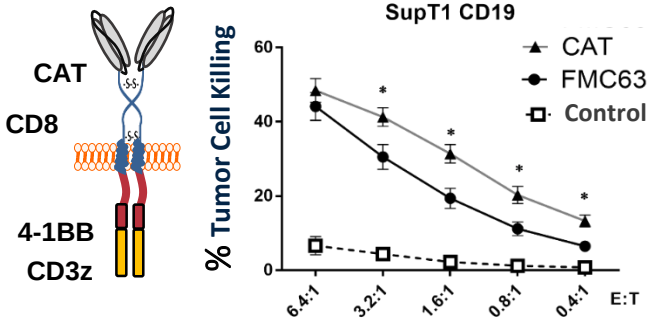
Preclinical data show higher potency and proliferation

- 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

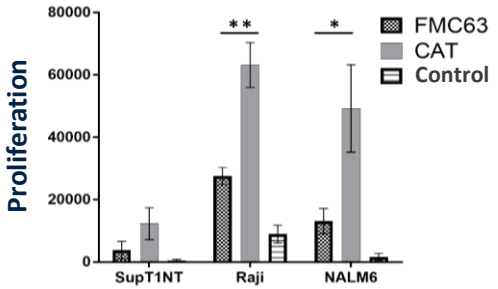
Fast Off-Rate



Enhanced Cytotoxicity



Enhanced Proliferation



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

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AUTO1 ALLCAR19: patient characteristics

High disease burden patients at risk for severe CRS

Baseline Characteristics	N=16 (%)
Median age, years (range)	35.5 (18-58)
Gender	10M/ 6F
Chromosomal/Molecular status	
• Ph+ (bcr-abl)	5 (31%)
• MLL	1 (6%)
• Other	6 (38%)
• Normal	3 (19%)
• Failed	1 (6%)
Prior lines of treatment	
• Median (range)	3 (2-6)
• **Prior Ino/Blina**	**10 (63%)**
• **Prior allo-HSCT**	**11 (69%)**
• Sibling/Haplo/VUD	2p/ 1p/ 8p

Leukemia Burden Prior To Lymphodepletion	N=16 (%)
Status at LD:	
• Primary refractory	4 (25%)
• 1st Relapse	0 (%)
• 2nd Relapse	8 (50%)
• > 2nd relapse	4 (25%)
Morphological disease	
• ≤ 5% blasts	5 (31%)
• 5 - 49% blasts	4(25%)
• **≥ 50% blasts**	**7 (44%)**
CNS status at registration	
• CNS 1	0 (0%)
• CNS II – III	0 (0%)
Other extranodal sites	3 (81%)

Ghorashian et al., (2019) ASH presentation

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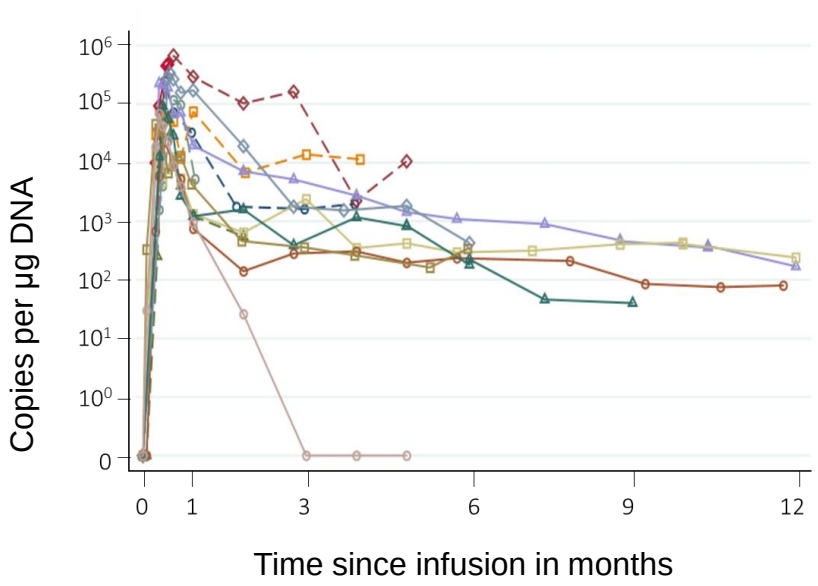
Robust AUTO1 expansion and persistence in Adult ALL patients support potential for sustained responses



PK analysis		
Parameters	AUTO1[1]	Kymriah[2]
Patient numbers	13	52
AUC (0 to 28) (copies/ug DNA)		
Geometric mean	634,719	342,732
Half life (days)		
Median	26.3	14.2
Maximum CAR T Level (copies/ug DNA)		
Geometric mean	111,239	47,988

1 Roddie et al., (2019) ASH presentation
2 Mueller et al., (2017) Blood

- Prolonged CAR T cell persistence was observed
  - 14 of 16 patients at last follow up

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Favorable safety profile, despite high disease burden and heavily pre-treated patients

- Grade 3 CRS was reported in 0/16 patients:
  - 7 (44%) patients had ≥ 50% BM blasts prior to LD (CRS 'high risk')
  - Tocilizumab used in 3/16 patients (19%)
  - 0/16 patients required admission to ICU for CRS

- Grade 3 CRES*was reported in 3/16 patients:
  - 2/3 cases resolved to G1 in <24h with steroids
  - 1/3 cases resolved to G1 in 72h with steroids
  - All three patients had more than 50% tumor burden

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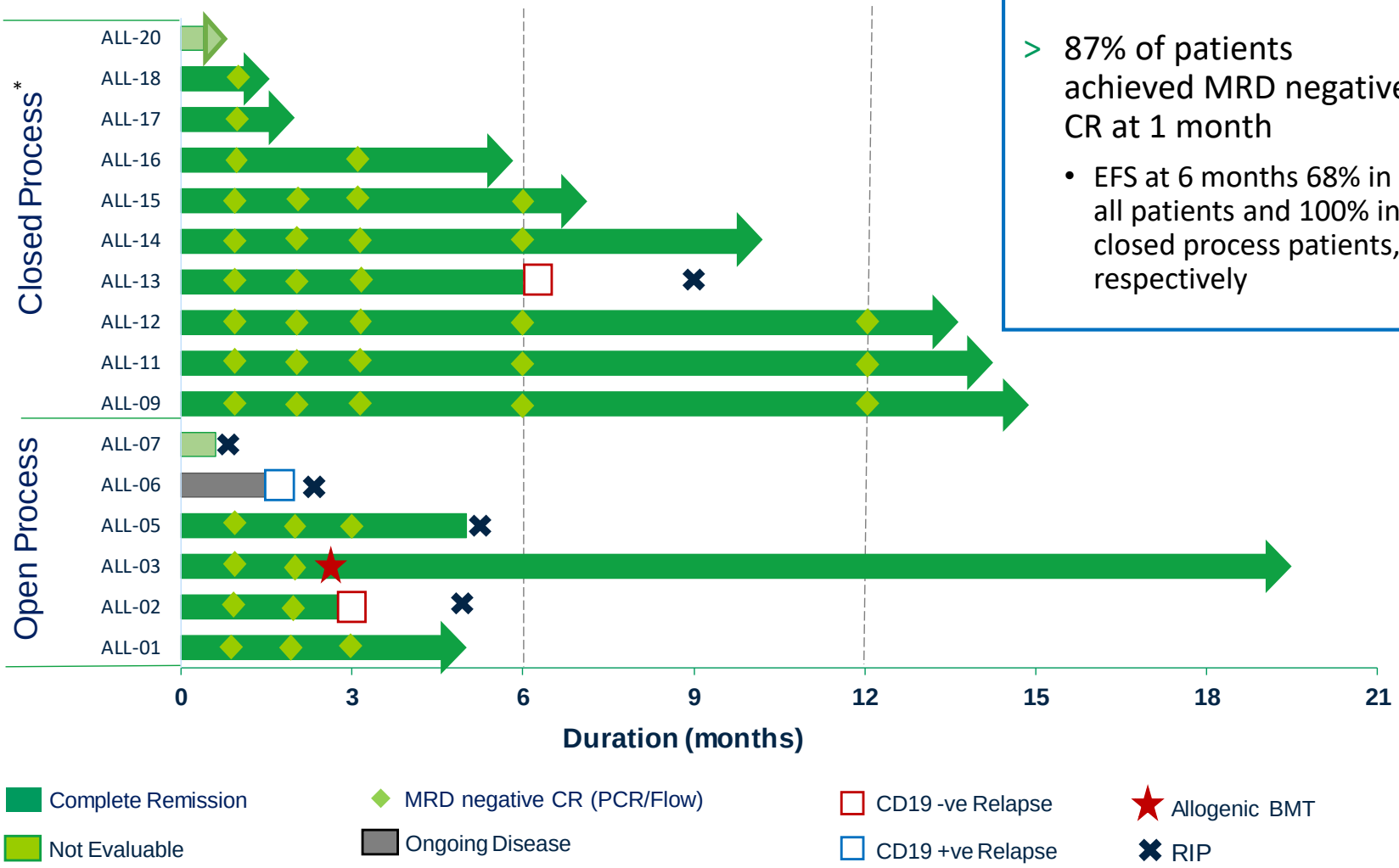
Roddie et al., (2019) ASH presentation
*CAR T cell-related encephalopathy syndrome

High level of response and durability

10/15 (67%) evaluable patients remain disease-free[1]



- 87% of patients achieved MRD negative CR at 1 month
  - EFS at 6 months 68% in all patients and 100% in closed process patients, respectively

Roddie et al., (2019) ASH presentation

[1]Median 11 months follow up (range 0.5 – 21m)

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

Data cutoff 25-Nov-2019, Evaluable = All patients with at least M1 follow-up or RIP prior to Month 1.

*Commercial manufacturing process

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Adult ALL clinical data

AUTO1 may be best-in-class, redirected T cell therapy in ALL

		[2]AUTO1	
	[1]Blincyto	All patients	Closed Process[3]
Patient Numbers	271	16	9
CR Rate	42%	87%	100%
EFS 6m	31%	68%	100%
CRS ≥ Grade 3	3%	0%	0%
Neurotox ≥ Grade 3	13%	19%*	12%*

* All three patients had > 50% tumor burden

[1]Kantarjian et al., 2017
[2]Roddie et al., ASH 2019 presentation
[3]Commerical manufacturing process

Although the Company believes these observations from the CARPALL and ALLCAR trials are promising, no definitive conclusions regarding safety or effectiveness can be drawn between these trials and the others shown given the investigational stage of AUTO1, the small study size, differing study designs between the various trials, as well as other factors.

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AUTO1 in aALL - Potential for best-in-class profile

First Autolus program to move to late stage development

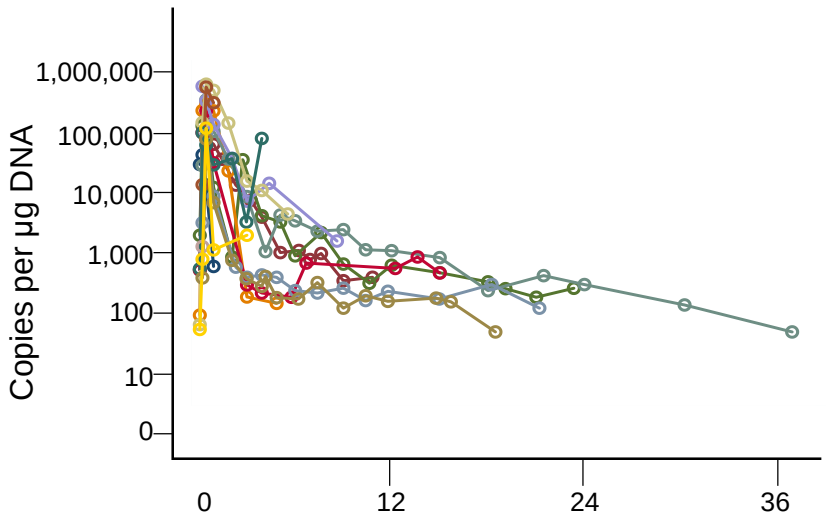
Well tolerated and high level of clinical activity

Study design

- CTA filed in UK in Nov, 2019 US IND to be filed in Q1 2020
- Single arm study
- 50 patients who have previously received blinatumomab or inotuzumab
- Primary endpoint: overall complete response rate (CR/CRi)
- Secondary endpoints include MRD-negative CR and EFS
- BLA filing targeted for H2 2021

AUTO1 pediatric data supports durable benefit in ALL

AUTO1 expansion and persistence exceed Kymriah® in pALL



PK analysis		
Parameters	AUTO1[1]	Kymriah[2]
Patient numbers	13	52
AUC (0 to 28), (copies/ug DNA)		
Geometric mean	2,617,042	342,731.8
Half life (days)		
Median	37.58	14.2
CAR T concentration at last follow-up (copies/ug DNA)		
Median	951.41	291.8

1 Ghorashian et al., (2019) ASH presentation
2 Mueller et al., (2017) Blood

- Enhanced AUTO1 Expansion:
  - Area under the curve 7.5 x higher than that reported for Kymriah®
  - Median half-life 2.5 x longer than that reported for Kymriah®

- Prolonged AUTO1 Persistence:
  - At last follow-up, AUTO1 cells were detectable in 11/14 patients (79%) and correlated with ongoing B cell aplasia in these patients.

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Data is consistent between pediatric and adult cohorts

	CARPALL Cohort 1	ALL CAR All Patients	ALLCAR Closed Process*
Evaluable Patients	14	15	9
CR Rate	86%	87%	100%
EFS	6m: 71% (39% to 88%)	6m: 68% (33%, 87%)	6m: 100% (-,-)
CRS ≥ Grade 3	0%	0%	0%
Neurotox ≥ Grade 3	7%#	19% (3/16)	12% (1/9)

* Commercial manufacturing process
\# Considered unrelated to CAR T

CARPALL Highlights

- 12/14 (86%) patients in cohort 1 achieved molecular CR; in cohort 2, 7/7 (100%) patients treated using the closed process achieved molecular CR
- 6 /12 responding patients remain in molecular complete remission, first patients reaching 36 months
- 12 month EFS is 54%, no relapses observed after 12 months
- 5 of 6 relapsing patients had CD19 loss at time of relapse

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Diffuse Large B Cell Lymphoma (DLBCL)

DLBCL is a large commercial opportunity

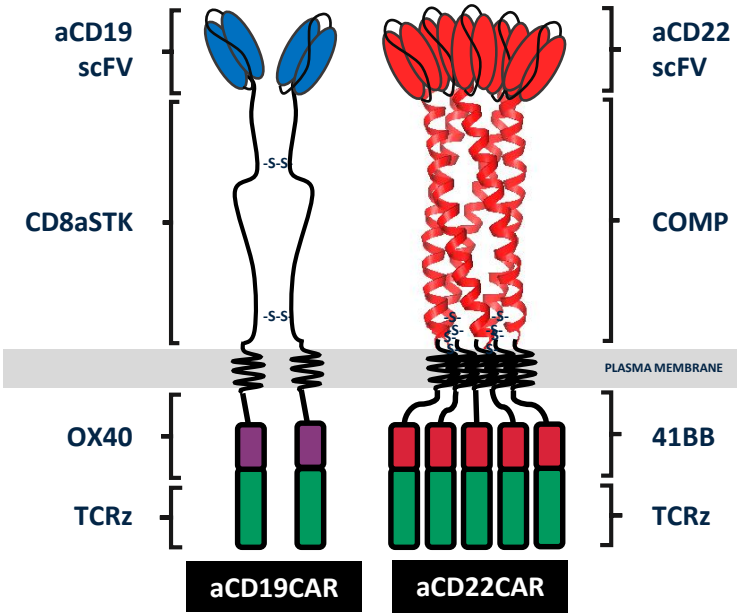
- Potential market size in DLBCL
  - Approx. 24,000 patients diagnosed in the US every year*
- Aggressive and rapidly advancing cancer
  - Most common type of Non-Hodgkin Lymphoma
  - High dose chemotherapy + mAb leads to remission in about 50-60% of patients
- Two approved CAR T products (Yescarta and Kymriah)

*Source: American Cancer Society

AUTO3: CD19 and CD22 targeting bicistronic CAR

Gamma-retroviral based vector with RD114 pseudotype

- Dual antigen targeting
- Two independent CARs delivered in single retroviral vector
- Humanized binders
- CD22 CAR with novel pentameric spacer
- OX40/41BB costimulatory domains designed to improve persistence
- Independently target CD19 or CD22



AUTO3: CD19 and CD22 targeting bicistronic CAR

Approach addresses antigen escape & PDL-1 mediated inhibition

Rationale

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

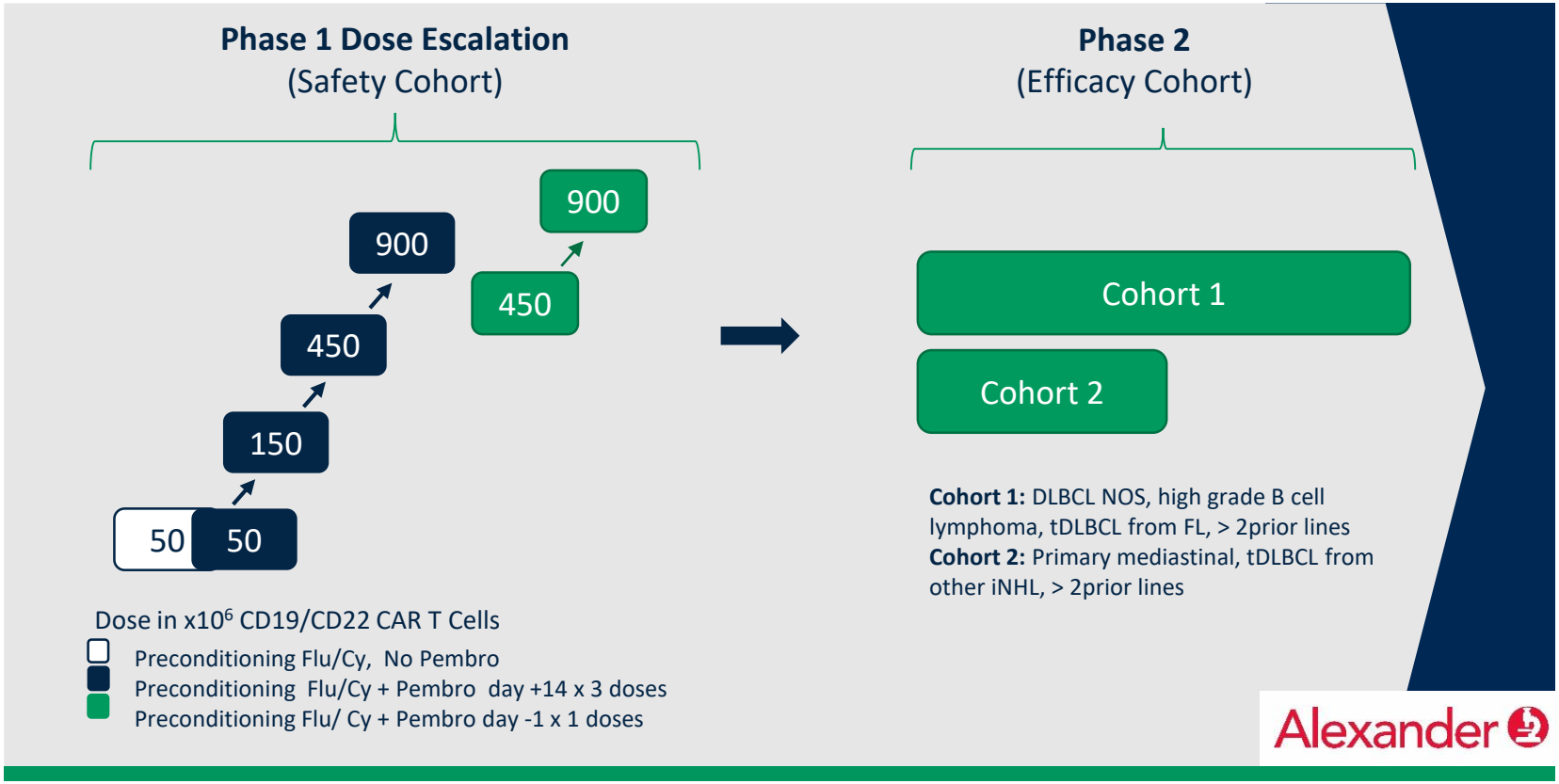
Hypothesis

- 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

[1]*Locke F et al Lancet Oncol 2019*
[2]*Schuster S et al NEJM 2019*
[3]*Neelapu S et al ASCO 2018*
[4]*Neelapu S et al NEJM 2017*

Alexander study design

AUTO3-DB1, single-arm, open-label, multi-center, Phase 1/2 Study



> Phase 1 – Rolling 6 design
> Phase 2 – Simon's 2-Stage optimal design

Patient population similar to other key trials

High risk population: all refractory, majority high IPI, majority stage IV

Baseline Patient Characteristics		N=16, Median
Age		55 (28-69)
Gender	Male, Female	10, 6
Histology	DLBCL - ABC - GCB - Non-GCB tDLBCL - FL - MZL	 4 4 2 5 1
Disease Stage	II III IV	2 4 10
Relapsed/ refractory	Refractory Relapsed Relapsed & Refractory	4 2 10

Baseline Patient Characteristics		N=16, Median
IPI	0-1 2 3-4	2 7 7
Number of Prior Therapy		3 (2-10)
Prior ASCT		3

ASCT: Autologous Stem Cell Transplant; tDLBCL: transformed DLBCL; IPI: International Prognostic Index; ABC: Activated B-Cell like; GCB: Germinal Center B Cell-like

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AUTO3: Adverse events of special interest

Manageable safety profile alone and in combination with pembrolizumab

	50 x10^6 AUTO3 no pem (n=4)	50 x10^6 AUTO3 D14 pem (n=3)	150 x10^6 AUTO3 D14 pem (n=4)	450 x10^6 AUTO3 D14 pem (n=4)	450 x10^6 AUTO3 D-1 pem (n=1)	Total (n=16)
All grades CRS	1	0	2	1	1	5 (31.3%)
≥ G3 CRS	0	0[1]	0	0	0	0
All grades NT	1	0	0	0	0	1 (6.3%)
≥ G3 NT	1	0	0	0	0	1 (6.3%)

[1] 1 patient who had no CRS with primary infusion, developed G3 CRS (severe hypoxia) with re-treatment 1 year later which happened in a setting of no CAR T expansion and significant disease burden in lung that had been treated with radiation

- With primary infusion
  - No grade 2 or higher CRS[2]
  - No ICU admission for CRS management
  - Only 1 patient received tociluzumab for CRS
- Only 1 case of grade 3 NT resolved quickly with steroids

[2] CRS grading as per Lee et al., *Blood* 2014

Ardeshna et al., ASH 2019

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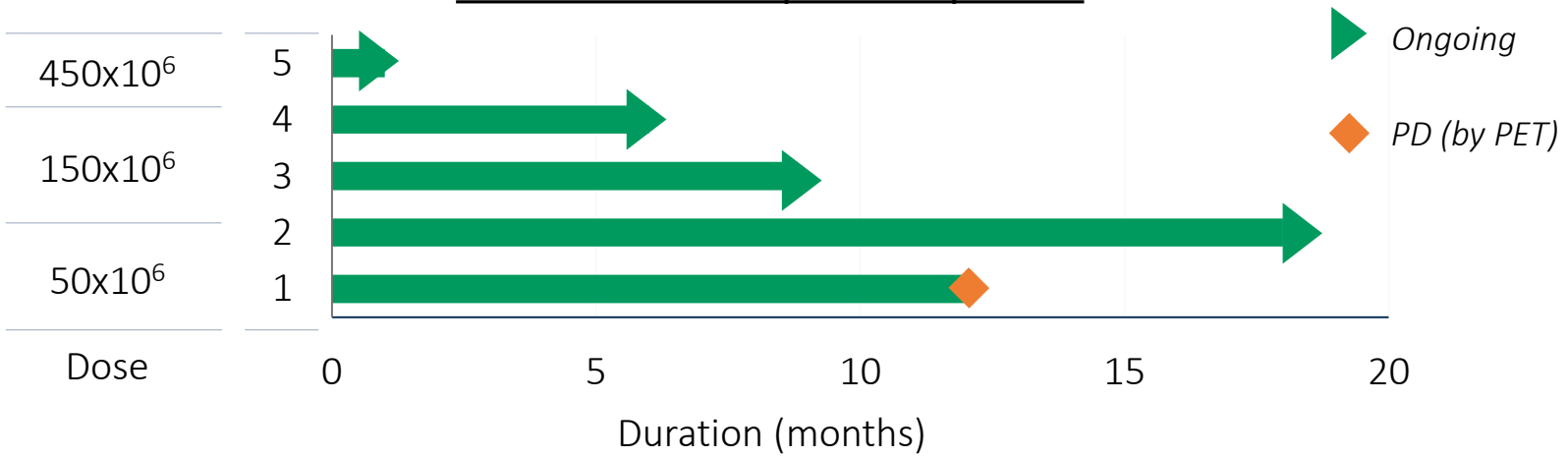
Preliminary efficacy of AUTO3 in DLBCL

Overview of responding patients

	50 x10^6 No Pem N=4	50 x10^6 D14 Pem N=3	150 x10^6 D14 Pem N=4	450 x10^6 D14 Pem N=4	450 x10^6 D-1 Pem N=1
CR	1	1	2	1	n/a
PR	1	1	0	1	n/a
NE	0	1	0	1	1

NE: Not Evaluable (too early)

Overview of complete responses



4 out of 5 (80%) CRs ongoing

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* Per Lugano criteria; CR: complete response; PR: partial response; NE: not evaluable; PD: progressive disease, Data for patients with 4 weeks efficacy follow-up

AUTO3 in DLBCL

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

- AUTO3 product was successfully made for all patients
  - Products manufactured at Cell and Gene Therapy Catapult at Stevenage in the UK for US and EU use
- 0% severe CRS and 1/14 (7%) severe NT with primary infusion
- 4/5 CRs ongoing
- Pembrolizumab on D-1 x single dose is being evaluated
- Decision for triggering Phase 2 initiation planned for mid 2020

AUTO3 AMELIA trial in pediatric ALL

Dual antigen targeting approach in pediatric ALL delivers well-tolerated safety

AEs of Special Interest

Event N=11 patients	All Grade n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)
CRS[1]	10 (91%)	9 (82%)	1 (9%)	0	0
Neurotoxicity	1 (9%)[2]	1 (9%)	0	0	0

[1]CRS grading by Lee et al 2014
[2]Neurotoxicity symptoms - Aphasia and headache

Safety Summary

Safety N=11 patients	n (%)
Number of subjects with at least one:	
-AE (any grade)	11 (100%)
-AE grade 3 & 4	11 (100%)
-AE grade 5	0
-SAE*	5 (45%)
-DLT AE	0
Number of deaths of any causality	2 (18%)

*SAEs reported as febrile neutropenia, neutropenia, thrombocytopenia, anemia, cellulitis and fever

- **No dose limiting toxicities**
- **No AUTO3-related deaths or Grade 5 adverse events**
- **No patient required ICU admission due to CRS**
- **Only one patient was treated with tocilizumab due to CRS**

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AUTO3 AMELIA trial in pediatric ALL

Data show role of dual antigen targeting in delivering high levels of complete molecular remission

N=10 patients
Median follow-up: 9.7 Months (1.8-18.0)

Outcomes	n (%)
CR/CRi[1]	9 (90%)
MRD negative (PCR) - HSCT[2]	8 (80%) 1
Non-Response	1 (10%)
Relapse[3]	5 (50%)

- **12 months EFS of 46%**
- **12 months overall survival of 100%**[4]
- **Median AUTO3 persistence of 170 days**

[#] The one additional patient who was previously treated with CAR T-cell therapy achieved MRD negativity after AUTO3 infusion and experienced morphological relapse approx. 4 months after treatment. This patient had a detectable CD19- and CD19+ mixed leukemic cell population at screening.
[1] Includes 1 patient with only one assessment as CR/CRi (without a confirmation of 4 weeks apart).
[2]One patient proceeded to hematopoietic stem cell transplantation (HSCT) after achieving complete molecular remission.
[3]Relapse is defined as morphological relapse (≥ 5% of blasts in blood or bone marrow or extramedullary disease, after achieving CR/CRi).
[4]The OS rate at 12 months is an estimate considering fewer patients at risk
Data cut-off date: 21th October 2019

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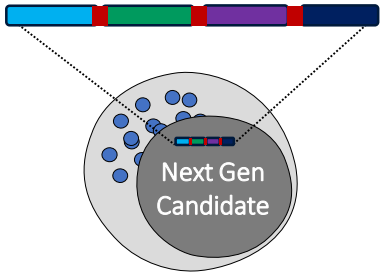
AUTO2 and AUTO 8 for r/r multiple myeloma

Transitioning focus to AUTO8

BCMA & CAR X	dSHP2	dTGFβ Receptor	Persistence
Targeting tumor and tumor stem cells to enhance depth and duration of response	Overcoming multiple checkpoint pathways	Overcoming inhibitory effect of TGFβ in microenvironment	Modules and manufacturing technology to enhance persistence



- Focus on moving next generation version (AUTO8) into clinic in H2 2020 with data expected H2 2021
  - Addresses need for increased persistence and tumor defense mechanisms
  - Incorporates additional programming modules
  - Study to be conducted in collaboration with University College London

Clinical newsflow expected through 2020

Product	Indication	Target	Event
B Cell Malignancies			
AUTO1	Pediatric ALL	CD19	• Ph 1 data 4Q 2019
AUTO1	Adult ALL	CD19	• Ph 1 (ALLCAR19) data 4Q 2019 • Start late stage program H1 2020
AUTO1NG	Pediatric ALL	CD19 & 22	• Start Ph 1 H1 2020
AUTO3	DLBCL	CD19 & 22	• Ph 1 interim data 4Q 2019 • Decision on Ph 2 transition mid 2020 • Ph 1 data H2 2020
AUTO3NG	DLBCL	CD19 & 22	• Start Ph 1 H2 2020
Multiple Myeloma			
AUTO8	Multiple Myeloma	BCMA & CAR X	• Start Ph 1 study H2 2020
T Cell Lymphoma			
AUTO4	TRBC1+ Peripheral TCL	TRBC1	• Ph 1 interim data H2 2020
GD2+ Tumors			
AUTO6NG	Neuroblastoma; Melanoma; Osteosarcoma; SCLC	GD2	• Start Ph 1 H2 2020

Additional updates on ALLCAR durability of response throughout the year

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Q&A

Dr. Christian Itin
Chairman and CEO

Thank you