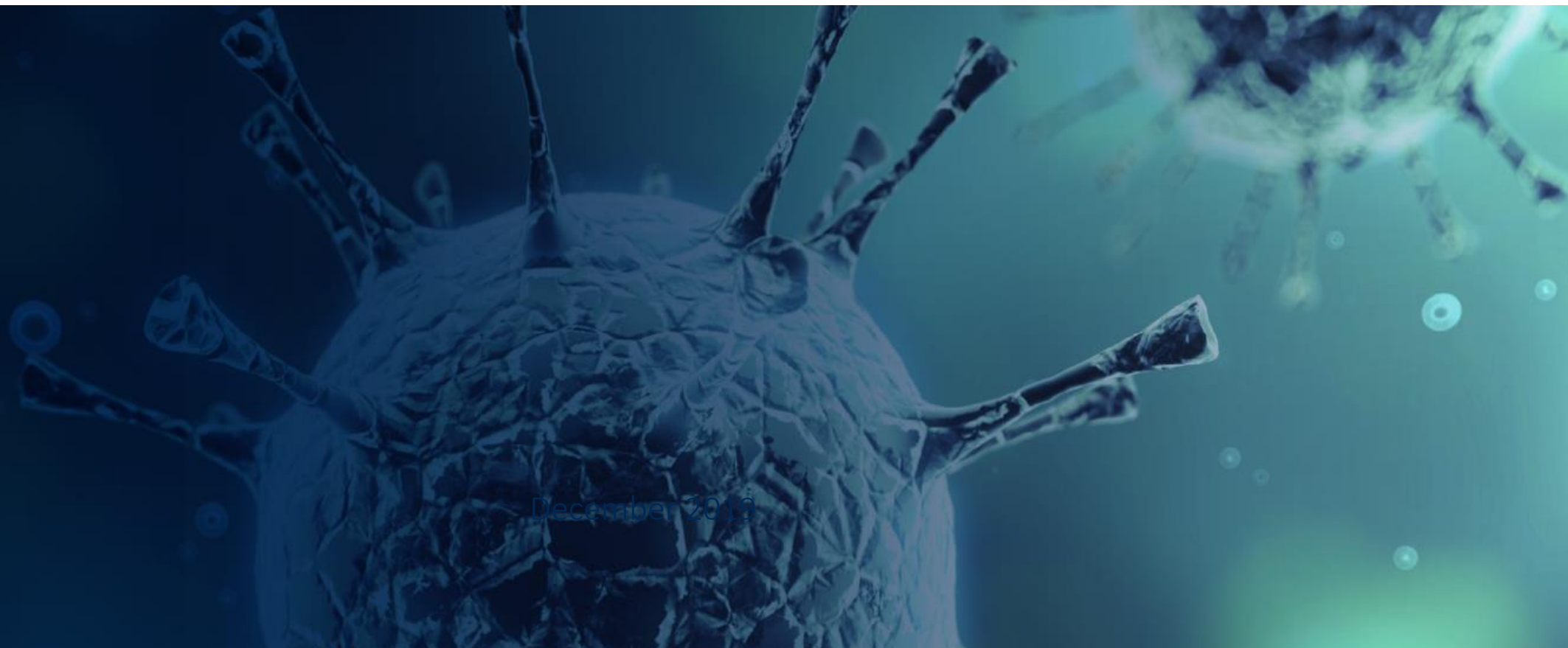


# Autolus

Nasdaq: AUTL



December 2019

EHA Data Update  
June 2020

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# Agenda

1. Welcome and Introduction: Dr. Christian Itin, Chairman and CEO
2. AUTO1 and AUTO3 Data Review: Dr. Nushmia Khokhar, VP, Head of Clinical Development
3. Adult ALL; Commercial Opportunity: Brent Rice, Vice President, Chief Commercial Officer, US
4. Summary & Next Steps: Dr Christian Itin
5. Q&A: Dr. Christian Itin, Andrew Oakley (CFO), Dr. Vijay Reddy (CMO), Dr. Nushmia Khokhar (Head of Clinical Development), Brent Rice (CCO, US)

# Welcome and introduction

*Dr. Christian Itin*

*Chairman and CEO*

# Broad expertise in CAR T therapy development and market access



## **Dr. Christian Itin**

*Chairman & CEO*

Previously CEO of Micromet; led development of Blincyto<sup>®</sup>, the first FDA-approved redirected T cell therapy



## **Dr. Nushmia Khokhar**

*VP, Head of Clinical Development*

Board certified oncologist, lead several successful registration trials within industry including global daratumumab program at Janssen Oncology



## **Dr. Vijay Peddareddigari**

*SVP, CMO*

Experienced oncologist and drug developer; MD Anderson, GSK and most recently J&J



## **Brent Rice**

*VP, Chief Commercial Officer, US*

25 years biotech/pharma experience; previously at Juno Therapeutics; 18 years at Amgen



## **Andrew Oakley**

*CFO*

17+ years experience as public company CFO in bio-pharma sector; more than 10 years at Actelion

# 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 ALL represents a significant opportunity

- ALL incidence and prevalence represents a significant market
  - 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
  - Relapsed refractory patients have a significant number of co-morbidities that have significantly limited utilization of CAR T therapies
- No CAR T therapy approved in adult ALL
- Only approved redirected T cell therapy is blinatumomab

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

# AUTO1: Key features

Designed for durable responses without allo-transplant and absence of 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

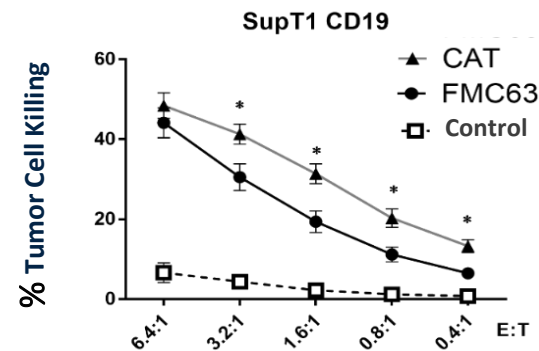
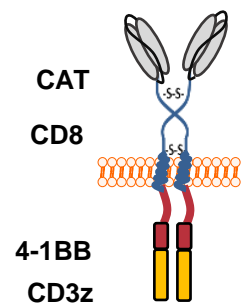
- AUTO1 has an optimized CD19 CAR with a lower (40x) affinity for CD19 and a fast off-rate\*
- Engages efficiently, delivers a kill, and disengages rapidly like a normal T cell
- Leads to enhanced activity and lower toxicities

# AUTO1 shows enhanced activity vs FMC63 CARs

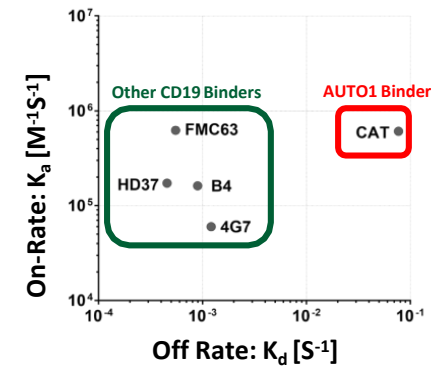
## Preclinical data show higher cytotoxicity and proliferation

- 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

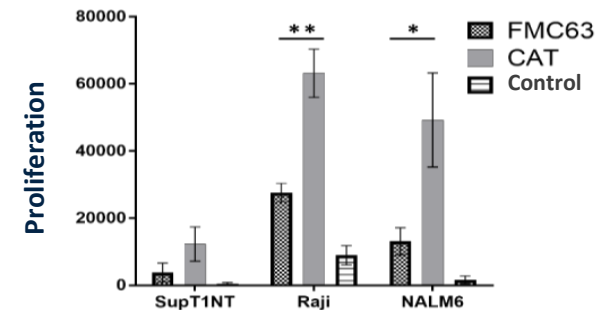
## Enhanced Cytotoxicity



## Fast Off-Rate



## Enhanced Proliferation



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

## Data Review

*Dr. Nushmia Khokhar*

*VP, Head of Clinical Development*



**Adult ALL**

**AUTO1 – tailored for ALL**

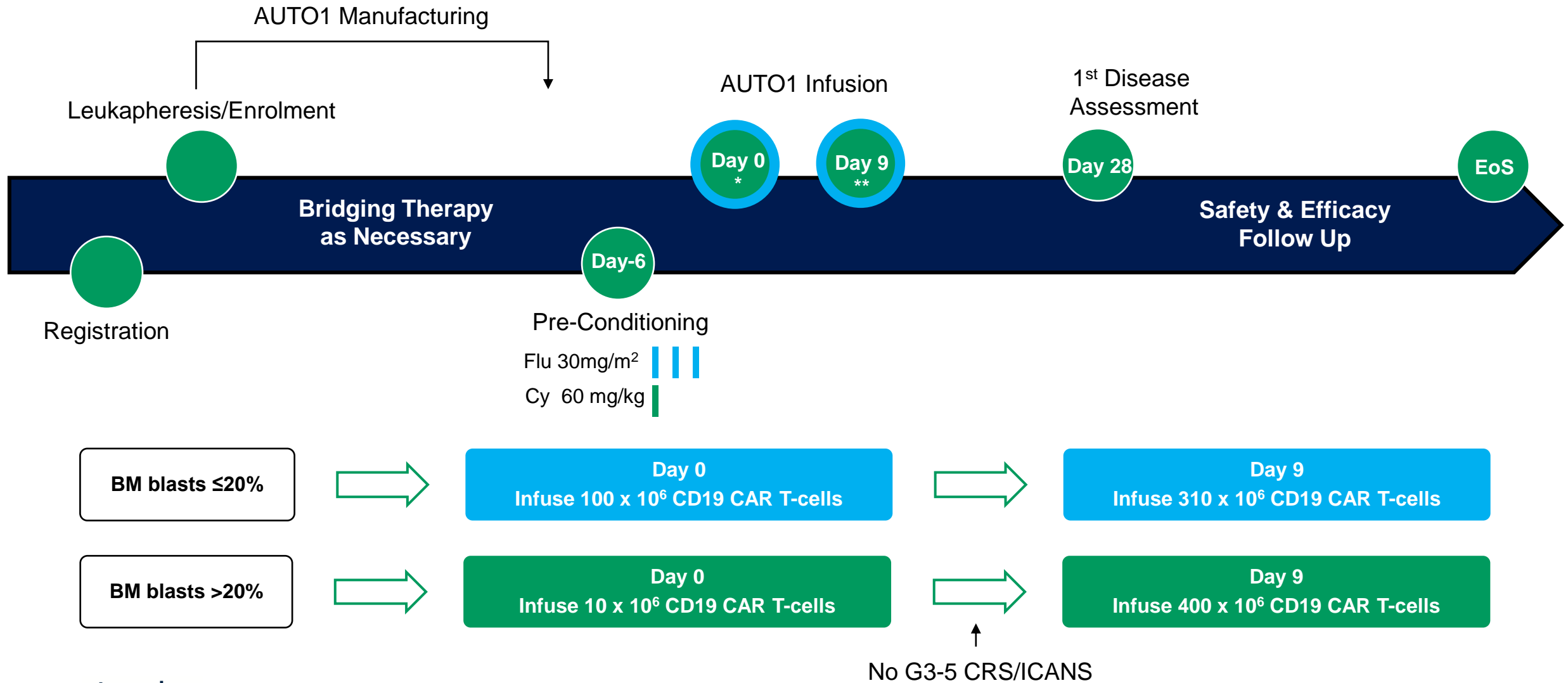
# Challenges and opportunity for curative therapy in adult r/r ALL

## AUTO1 designed to overcome the limitations of other CAR T therapies

- Adult ALL prognosis is poor; long-term remission rate limited to 30-40%
- Median overall survival is < 1 year in r/r ALL
- Only approved redirected T cell therapy approved for adults generally is blinatumomab
  - Bridge to allo-SCT, not a stand-alone curative option
- CAR T therapies are highly active, however toxicities have been notable with high incidence of CRS and cases of fatal neurotoxicity
- Developing safe and effective therapies have been challenging
  - Patients are generally more fragile, more co-morbidities
  - No clear sense of durability without subsequent allograft

**AUTO1 has the potential to be a curative therapy**

# ALLCAR19 Phase 1 study design



# Key eligibility criteria

## Inclusion criteria

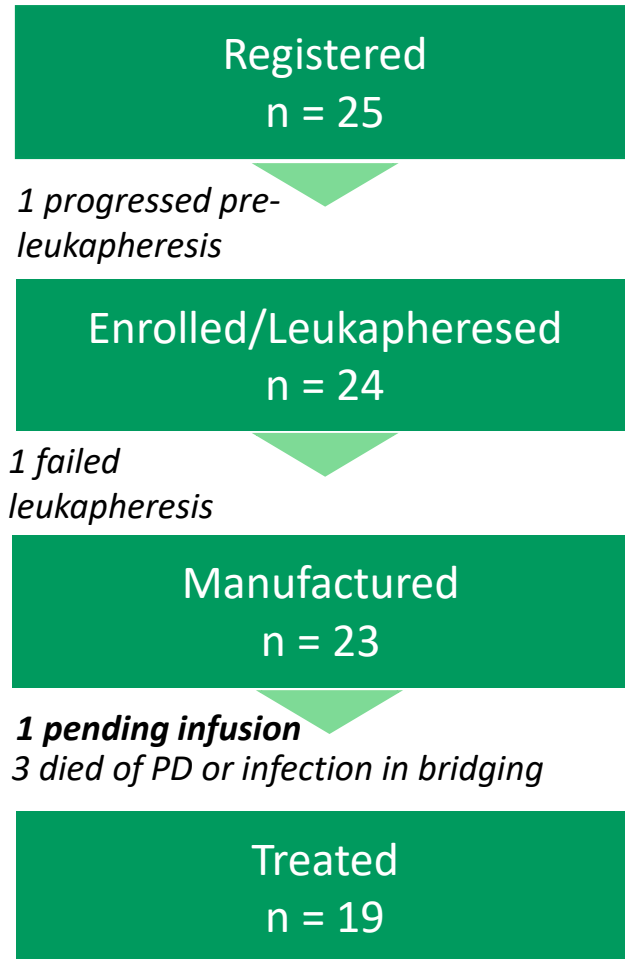
- Age 16 to 65 years
- High risk or relapsed histologically confirmed CD19+ B-ALL following standard therapy requiring salvage in whom alternative therapies are deemed inappropriate by their treating physician

## Exclusion criteria

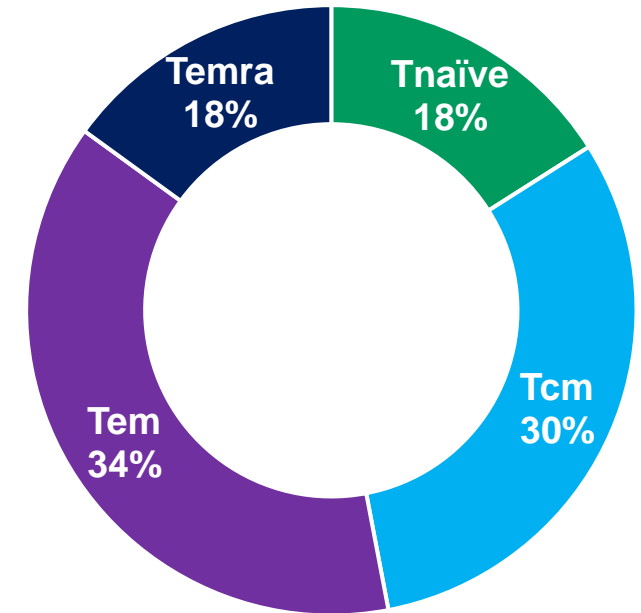
- CD19 negative disease
- Overt CNS involvement/isolated extramedullary disease
- Active hepatitis B, C or HIV infection
- Stem Cell Transplant patients only: no active GVHD
- Significant neurotoxicity following blinatumomab

**No exclusion for prior blinatumomab or inotuzumab ozogamicin**

# Product characteristics & feasibility



- 100% of successful leukaphereses resulted in released drug product
- Semi-automated closed manufacturing process was used in 17/23 products
- Advantages of closed process includes:
  - rapid, standardised manufacture
  - trend towards lower exhaustion markers
  - enrichment for Tcm and Tnaive CAR+ cells (48%)
- Mean transduction efficiency 65%
  - range 50 – 83%



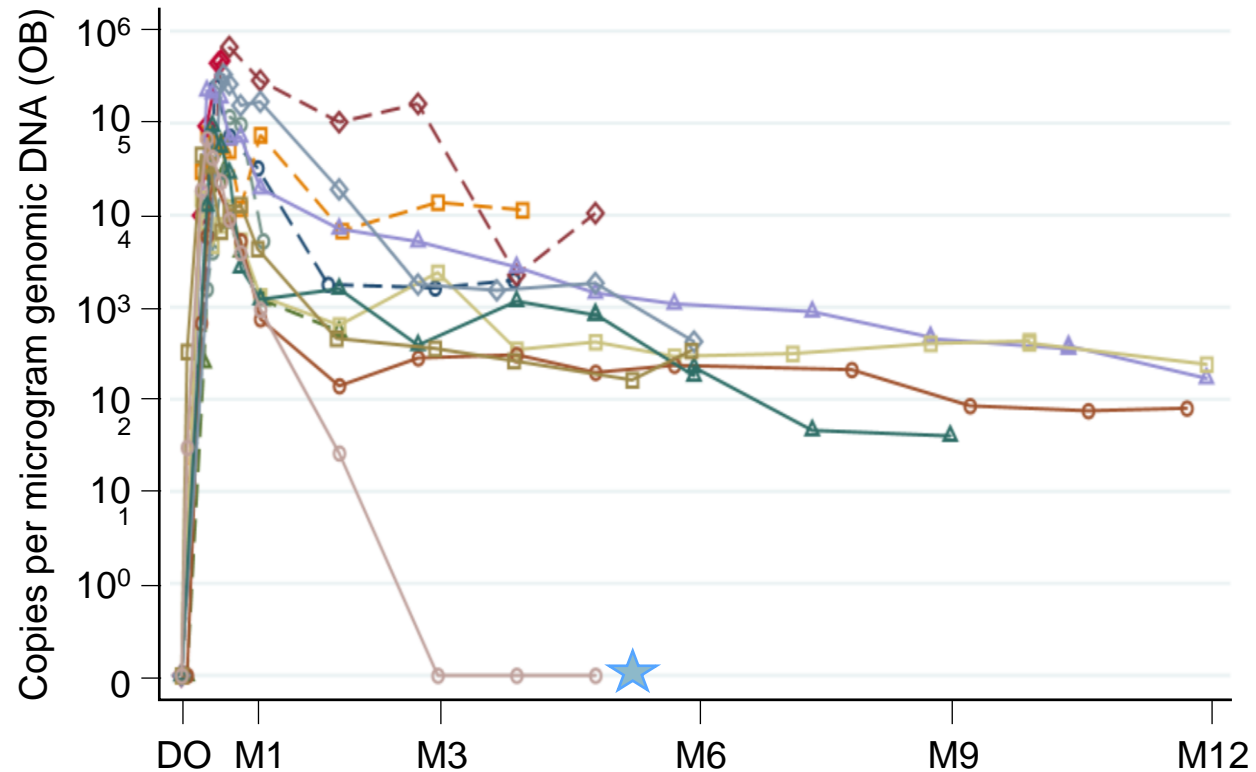
Tnaive – naïve T cells  
Tcm - naïve central memory T cells  
Tem - effector memory T cells  
Temra - effector memory RA T cells

# Patient characteristics: 19 patients treated

Baseline Characteristics	N=19 (%)	Leukemia Burden Prior to Lymphodepletion	N=19 (%)
Median age, years (range)	43 (18-62)	Status at LD:	
Gender	12M/7F	• Primary refractory	4 (21%)
Chromosomal/Molecular status		• 1 <sup>st</sup> Relapse	7 (37%)
• Ph+ (bcr-abl)	6 (32%)	• 2 <sup>nd</sup> Relapse	4 (21%)
• MLL	1 (5%)	• > 2 <sup>nd</sup> relapse	4 (21%)
• Other	7 (37%)	Morphological disease	
• Normal	4 (21%)	• ≤ 5% blasts	7 (37%)
• Failed	1 (5%)	• 5 - 49% blasts	4 (21%)
Prior lines of treatment		• <b>≥ 50% blasts</b>	<b>8 (42%)</b>
• Median (range)	3 (2-6)	CNS status at registration	
• <b>Prior Inotuzumab</b>	<b>9 (47%)</b>	• CNS 1	0 (0%)
• <b>Prior Blinatumomab</b>	<b>5 (26%)</b>	• CNS II – III	0 (0%)
• <b>Prior allo-HSCT</b>	<b>12 (63%)</b>	Other extranodal sites	3 (16%)
- sibling/haplo/VUD	3p/1p/8p		

# Expansion and persistence support potential for sustained responses

## AUTO1 expansion and persistence by qPCR



ALLCAR19 qPCR PK all patients (n=14)	*Mueller 2017 (responders)	
<b>AUC D0-28</b> (Geometric Mean) (Copies/μg x days)	<b>716 769</b>	<b>342 732</b>
<b>Half life</b> (Median Days)	17 (Range 11-29)	14.2
<b>Max CAR T level</b> (Geometric Mean) (Copies/μg)	119 336	47 988
<b>T (Cmax)</b> (Median Days)	11 (Range 7-17)	

★ Developed a HAMA reaction to reject CAR

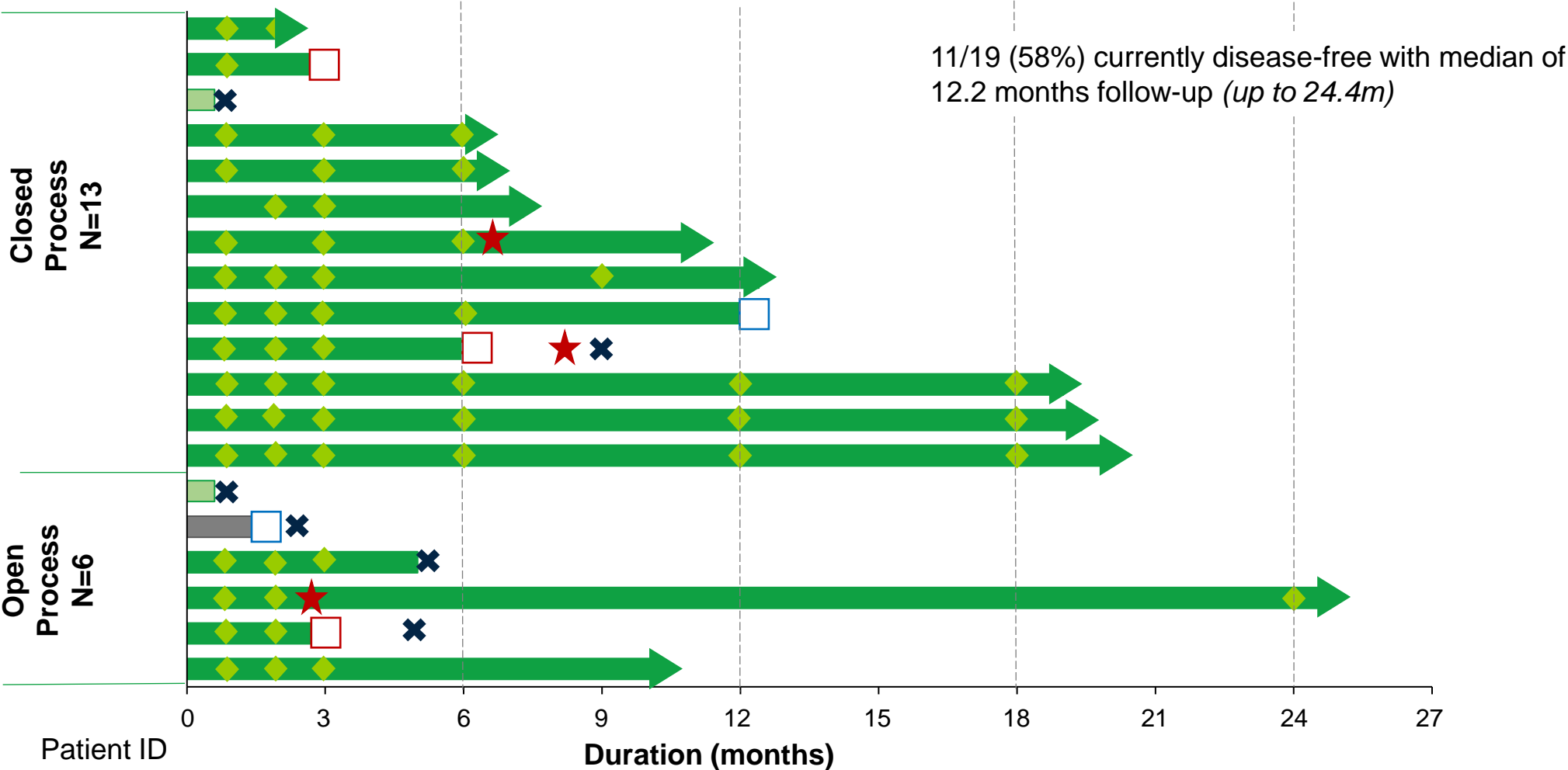
# Safety profile suited to adults with B-ALL

CRS (Lee Criteria)	Neurotoxicity (ICANS#)	≥ Grade 3 Cytopenia	Day -6	At Day 28
<ul style="list-style-type: none"> <li>CRS (any) in 9/19</li> <li>Grade 2 in 7/19</li> <li>≥ Grade 3 CRS in 0/19</li> </ul>	<ul style="list-style-type: none"> <li>ICANS (any) in 4/19</li> <li>Grade 2 in 1/19</li> <li>Grade 3 in 3/19</li> </ul>	<ul style="list-style-type: none"> <li>≥ Grade 3 Neutropenia</li> </ul>	7/19	8/17

- CRS
  - All patients who developed Grade 2 CRS had high burden B-ALL
  - Tocilizumab was used in 6/19 patients (32%)
- Neurotoxicity (ICANS)
  - ≥ Grade 2 ICANS was reported in 4/19 patients: all had ≥ 50% blasts; all cases were preceded by CRS
  - 3/4 cases resolved to G1 in <24h with steroids, 1/4 cases resolved to G1 in 72h with steroids
- ≥ Grade 3 neutropenia:
  - Pre-dated treatment in 7/19 patients
  - At Day 28, 8/17 evaluable patients had ≥ Grade 3 neutropenia with most resolving by Month 2/3
- 6/19 patients died on study:
  - 2/19 died from progressive B-ALL
  - 1/19 died post-progression from allo-transplant-related complications (VOD/sepsis)
  - 3/19 from infection: 2/3 before D28 (sepsis; invasive fungal); 1/3 at M6 in CR (MDR-pseudomonas in blood)

# Responses are durable without need for transplant

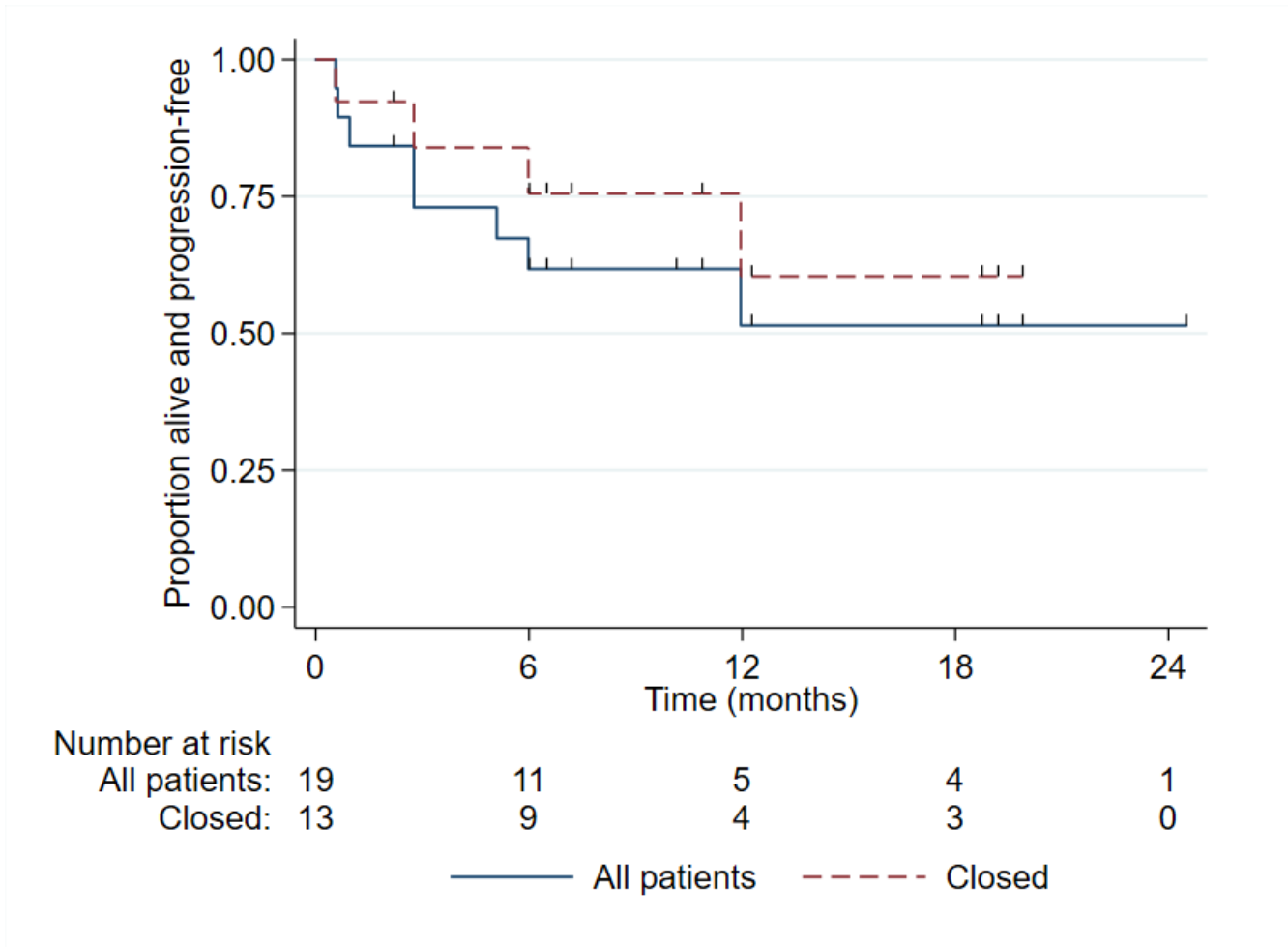
## MRD negative CRs ongoing past 18 months



- Complete Remission
- ◆ MRD negative CR (PCR/Flow)
- CD19 -ve Relapse
- ★ Allogenic BMT
- Not Evaluable
- Ongoing Disease
- CD19 +ve Relapse
- ✕ RIP

# High rate of CRs continue to be sustained

Encouraging duration of response with median EFS and OS not yet reached



	All patients Est [95% CI]	Closed process Est [95% CI]
<b>N *</b>	19	13
<b>ORR</b>	84%	92%
<b>MRD Neg CR</b>	84%	92%
<b>DOR</b>		
Median	Not reached	Not reached
6 month	73% [44%, 89%]	82% [45%, 95%]
<b>EFS</b>		
Median	Not reached	Not reached
6 months	62% [36%, 80%]	76% [42%, 91%]
<b>OS</b>		
Median	Not reached	Not reached
6 months	72% [45%, 87%]	92% [57%, 99%]

# AUTO1 potentially has a superior efficacy profile compared to standard of care

## Comparable and manageable safety profile

	<sup>1</sup> AUTO1		Standard of Care	
	All patients	Closed Process	<sup>2</sup> Blinatumumab	<sup>3</sup> Inotuzumab
Patient Numbers	19	13	271	218
CR Rate	84%	92%	44%	80.7%
EFS 6m	62%	76%	31%	mPFS 5m
CRS ≥ Grade 3	0%	0%	3%	0%
Neurotox ≥ Grade 3	16%*	15%*	13%	0%
Other notable toxicities				14% Hepatic VoD

- Approximately 50% of blinatumumab and inotuzumab patients received subsequent HSCT
- Veno-Occlusive Disease (VoD) during treatment and following subsequent HSCT, with the latter causing a higher post-HSCT non-relapse mortality rate, has limited inotuzumab uptake

\* Observed in patients with > 50% tumor burden

1. Roddie et al., EHA 2020
2. Kantarjian et al., 2017
3. Kantarjian et al., 2016

# AUTO1 has potential for best-in-class profile for efficacy and safety

	Competitor CAR T cell Therapies				
	<sup>1</sup> AUTO1	<sup>2</sup> Kymriah	<sup>3</sup> KTE-X19		<sup>4</sup> UCART19 <sup>\$</sup>
Patient Numbers	19	35	41		21
CR Rate	84% (92%#)	69% (90% <sup>@</sup> )	68% (84%##)		88%
EFS	62% (76%#) at 6 months	5.6 median (2.2m to 19.4m)	TBD		TBD
Allo-Transplant	10%	38%	Not known		78%
Tox Management	Normal	Normal	Normal	Intensive	Normal
CRS all Grade	47%	94%	100%	100%	94%
CRS ≥ Grade 3	0%	71% (17% G4/5)	29%	22%	16%
Neurotoxicity all Grade	21%	40%	93%	78%	33%
Neurotox ≥ Grade 3	16%*	6%	38%	11%	0%

# AUTO1 continues to show a unique and highly differentiated profile

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

- Manufacturing feasibility confirmed
  - 100% of leukaphereses resulted in successfully released drug product
- Tolerable safety profile
  - Despite high disease burden and patient population having received 2-6 prior lines of treatment
  - No Grade 3 CRS observed
  - Only 3/19 patients, all with high tumour burden, developed Grade 3 ICANS (rapid resolution with steroids)
- Robust expansion and prolonged CAR T persistence
- Potential best in class efficacy:
  - MRD negative CR achieved in 16/19 (84%) patients at 1 month (92% with closed process)
  - CR appears to be durable: 11/19 (58%) are currently disease-free at a median of 12.2 months
  - EFS at 6 months is 62% in all treated patients (76% in closed process patients)

**Preliminary data supports the development of AUTO1 as a stand-alone therapy**



**Diffuse Large B Cell Lymphoma**

AUTO3 – tailored for DLBCL

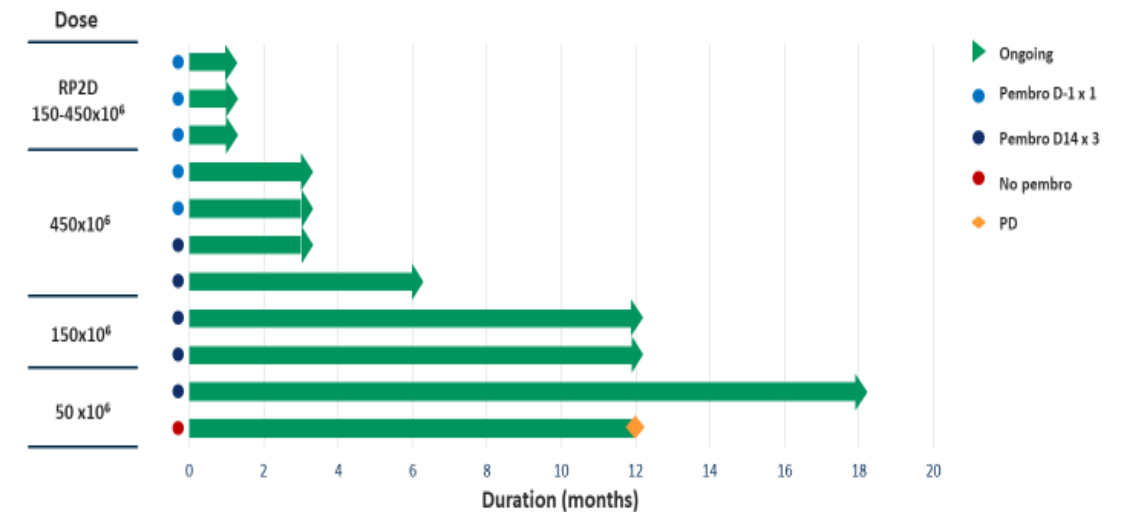
# AUTO3 has potential to access the full addressable DLBCL population

## Updated Alexander data suggests differentiated clinical profile

- ORR 75% and CRR 63% at dose  $\geq 150 \times 10^6$  cells with D-1 pembro
- All complete responses are ongoing at dose  $\geq 150 \times 10^6$  cells with pembro
- Outpatient expansion cohort is enrolling
- Potential for use in all settings of care
- RP2D range of 150 - 450  $\times 10^6$  cell dose with pembro D-1 selected
- Potential total market size of \$4-9bn

### Duration of Complete Responses

10 of 11 complete responses ongoing



At  $\geq 150 \times 10^6$  dose all complete responses are ongoing with a median follow up 3 months (range 1-12m)

Alexander

No severe CRS or any grade NT at the Phase 2 dose range

# Commercial Opportunity in adult B-ALL

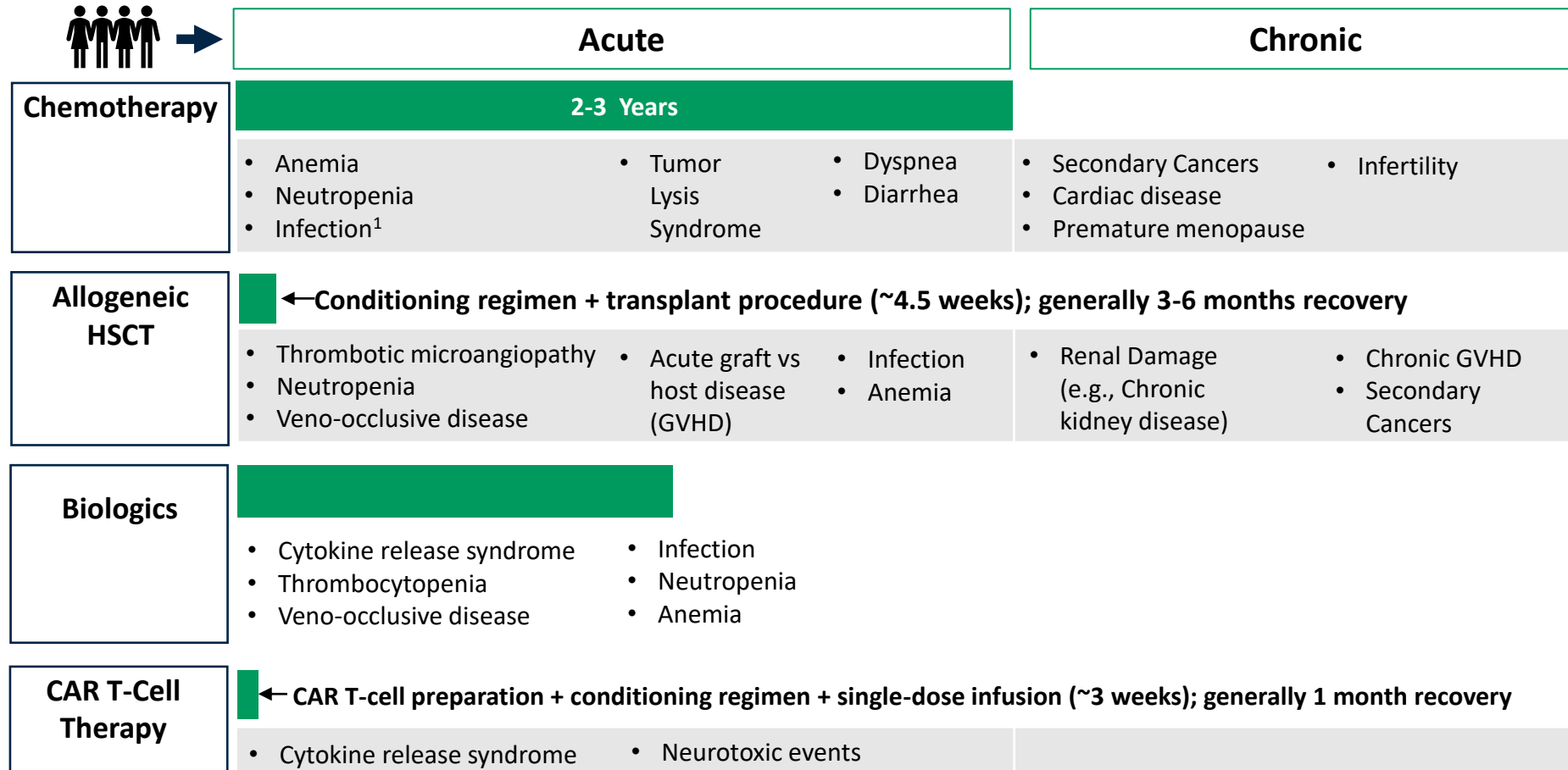
*Brent Rice*

*Vice President, Chief Commercial Officer, US*

# Adult ALL patients spend 2-3 years receiving treatment

## May expose adult ALL patients to negative acute and chronic clinical consequences

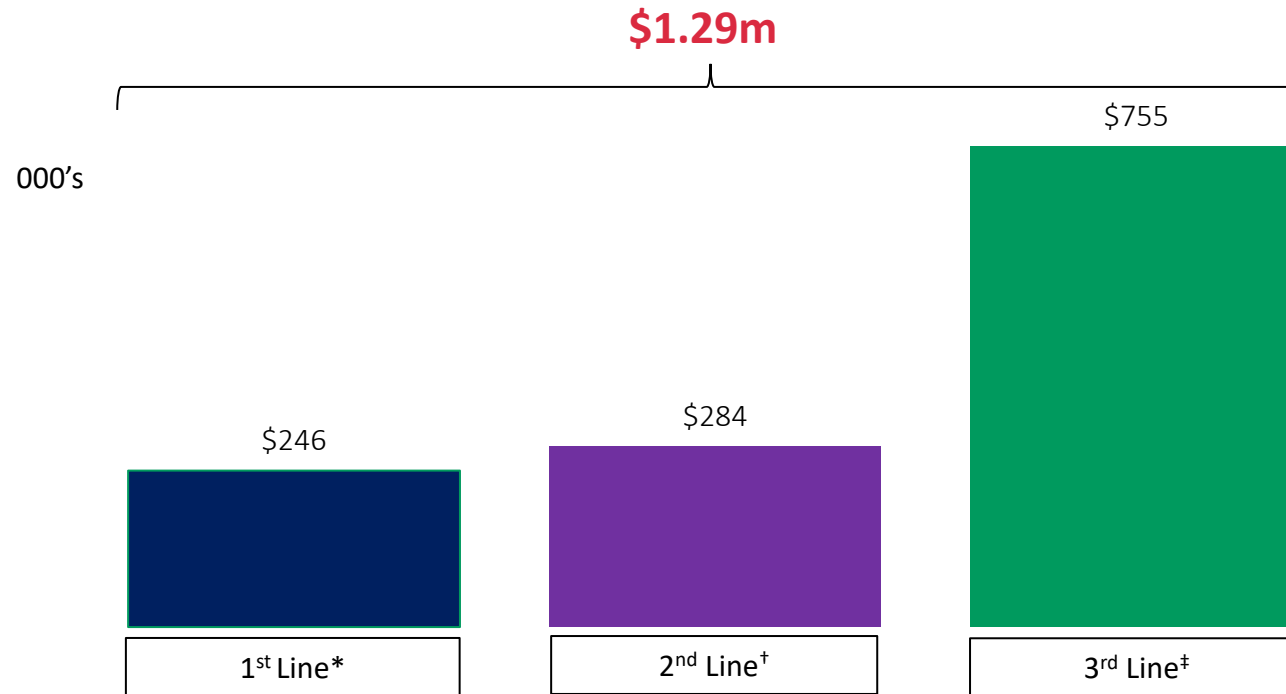
Current treatments are associated with significant effects, which can include, but are not limited to:



# Estimated ALL drug costs >\$1m for responding adults

## Excluding transplant

Estimated adult ALL drug acquisition costs by line of therapy



\* Modified hyper-CVAD + rituximab<sup>2</sup>

<sup>†</sup> Inotuzumab Ozogamicin (per product label)<sup>3</sup>

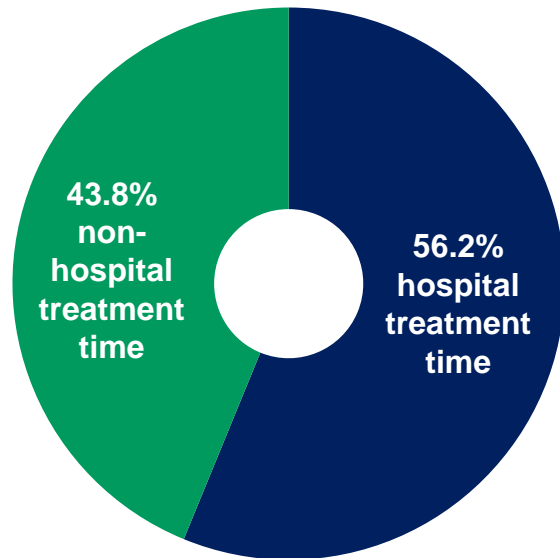
<sup>‡</sup> Blinatumomab (per product label)<sup>4</sup>

# Relapsed ALL patients spend > 50% treatment time in hospital

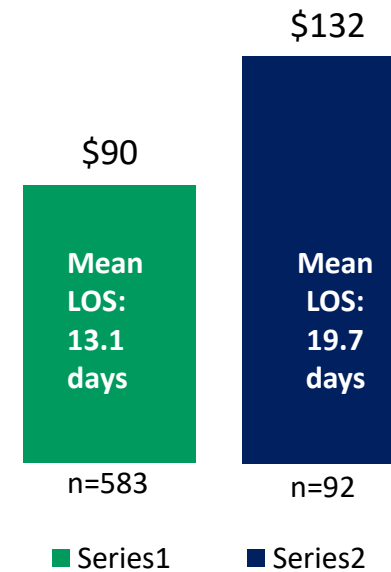
## Patients have repeated, prolonged, & costly hospitalizations

Chemotherapy administration is the primary reason for hospitalization (44.9%)<sup>1</sup>

Higher hospitalization costs for relapse ALL likely reflect greater salvage chemotherapy treatment expense<sup>1</sup>



Mean Hospitalization Cost (US, \$000's)<sup>1</sup>



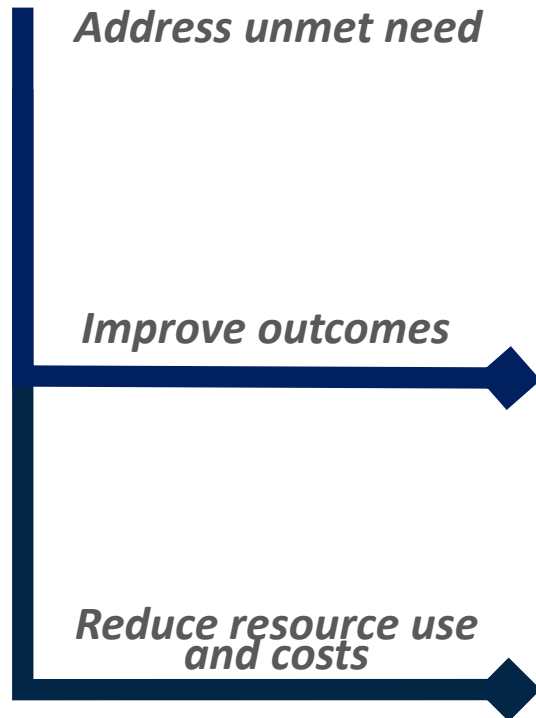
**2.8 Average number of hospitalizations during a mean treatment follow-up period following relapse of 80.2 days**

Population: Adults with Ph(-) relapsed B-precursor ALL receiving chemotherapy (Patient N=205; Hospitalization N=583)

Data Source: Truven Health MarketScan Commercial Claims and Encounter Database, April 2009-July 2014

# Unmet need in adult ALL has clinical and economic consequences

New innovations are essential to:



ALL represents a small population with a poor prognosis; limited treatment options exist



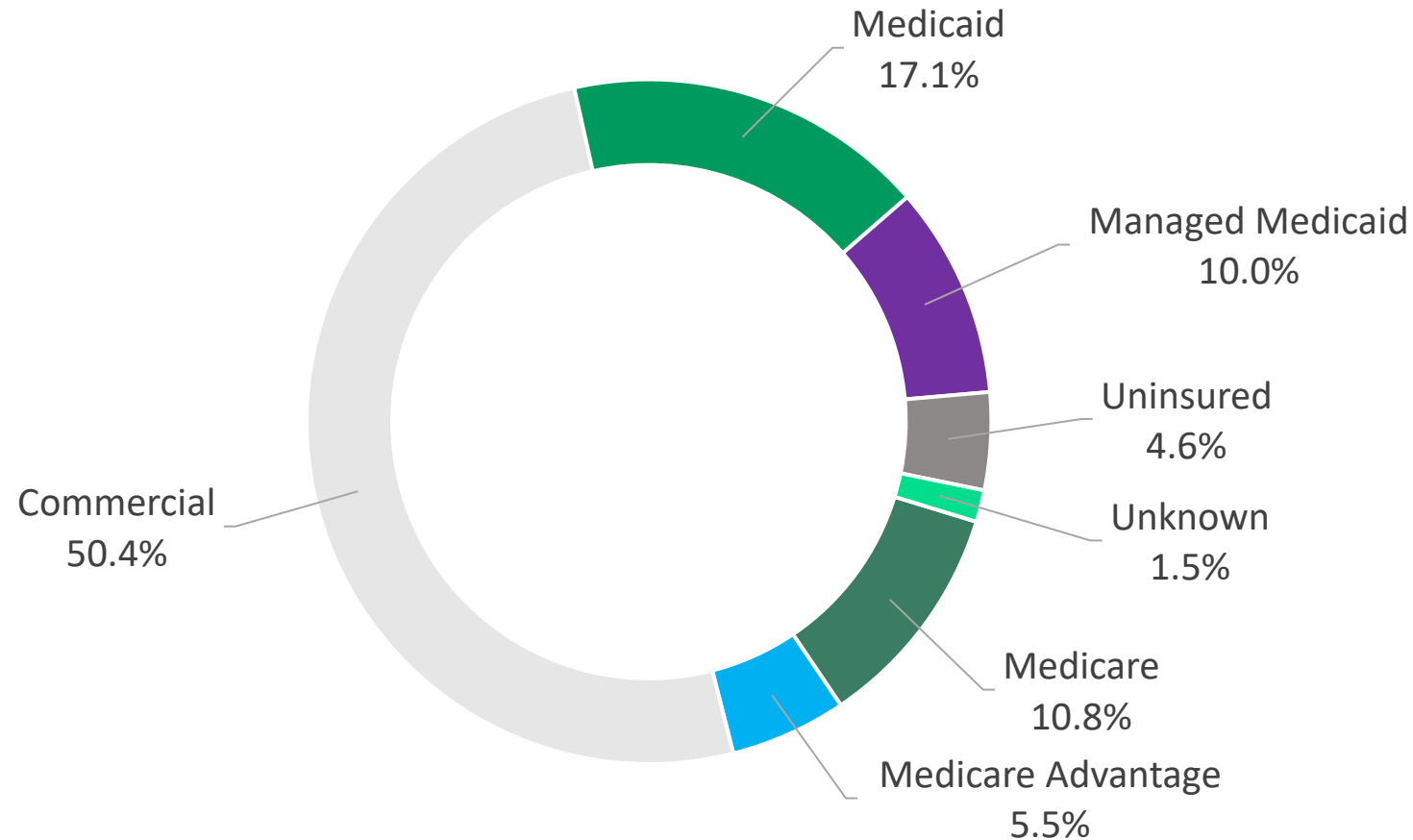
Survival and other clinical outcomes associated with adult ALL are poor; some treatments can worsen QOL



The economic burden of treatments and disease related costs in adult ALL is significant

# Adult ALL patients predominately covered by commercial insurance

## Minimal exposure to Medicare Part A



## Payor mix equates to favorable reimbursement landscape

# AUTO1 is designed for potential best-in-class efficacy and safety

- Potential best-in-class CD19 CAR designed for use as a stand-alone curative therapy
- Designed to provide potential best-in-class efficacy with high rates of durable complete responses
- Potential for best-in-class CAR T with more manageable safety profile
- Highly differentiated clinical profile with potential for hospital outpatient treatment in Academic and Non-Academic COEs
- Pivotal CAR T trial will inform select feasibility of outpatient administration

# AUTO1 has potential to reach full addressable adult ALL population

- Autologous CAR T therapies likely to be standard of care for adult ALL
- AUTO1 is clearly differentiated with a superior efficacy and manageable safety profile
- Adult ALL likely to have a more favorable reimbursement status given the high unmet medical need and patient mix
- Despite pediatric ALL having a higher incidence, most are cured; however only 30–40% of adult ALL patients will achieve long-term remission following induction chemotherapy<sup>1</sup>
- Adult ALL represents a significant opportunity with approx. 3000 eligible patients in US/EU5\*

## Summary and Next Steps

*Dr. Christian Itin*

*Chairman and CEO*

# AUTO1 is the 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
- Ph1b run-in component, prior to single arm Ph2 pivotal study
- 100 relapsed / refractory adult ALL patients
- Primary endpoint: overall complete response rate (CR/CRi)
- Secondary endpoints include MRD-negative CR EFS and DoR
- On track for full data by end 2021

# Autolus poised for value inflection in 2020

- AUTO1
  - Currently enrolling Autolus' first Phase 1b / 2 pivotal program in Adult ALL
  - Granted orphan drug designation by the FDA for treatment of ALL
  - Pediatric ALL – moving forward with AUTO1/AUTO1NG
- AUTO3
  - Outpatient treatment cohort started in Q2 2020
  - Confirmation of transition to pivotal stage in Q3 2020
  - Pivotal study could start early 2021
- Additional value inflection in 2020 from our preclinical solid tumor and hem-onc programs
- Key data releases expected at upcoming medical conferences
- Strong balance sheet with \$243.3m in cash as of March 31, 2020

# Multiple clinical data points expected through 2020

Product	Indication	Target	Event
<b>B Cell Malignancies</b>			
AUTO1	Adult ALL	CD19	<ul style="list-style-type: none"> <li>• Ph1 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>• Start Ph1 H2 2020</li> </ul>
AUTO3	DLBCL	CD19 & 22	<ul style="list-style-type: none"> <li>• Decision on Ph2 Q3 2020</li> <li>• Full Ph1 data H2 2020</li> </ul>
AUTO3NG	DLBCL	CD19 & 22	<ul style="list-style-type: none"> <li>• Ready to start Ph1 H2 2020, life cycle mgmt</li> </ul>
<b>Multiple Myeloma</b>			
AUTO8	Multiple Myeloma	BCMA & CAR X	<ul style="list-style-type: none"> <li>• Start Ph1 study H2 2020</li> </ul>
<b>T Cell Lymphoma</b>			
AUTO4	TRBC1+ Peripheral TCL	TRBC1	<ul style="list-style-type: none"> <li>• Ph1 interim data H1 2021</li> </ul>
<b>GD2+ Tumors</b>			
AUTO6NG	Neuroblastoma; Melanoma; Osteosarcoma; SCLC	GD2	<ul style="list-style-type: none"> <li>• Start Ph1 H1 2021</li> </ul>
<b>Allogeneic Approach</b>			
Undisclosed	Undisclosed	Undisclosed	<ul style="list-style-type: none"> <li>• Start Ph1 Q4 2020</li> </ul>

## Q&A

*Dr. Christian Itin (Chairman and CEO)*

*Andrew Oakley (CFO)*

*Dr. Vijay Reddy (CMO)*

*Dr. Nushmia Khokhar (VP, Clinical Development)*

*Brent Rice (VP, Chief Commercial Officer, US)*



**Thank you**