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**UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION**  
Washington, D.C. 20549

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**FORM 6-K**

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**REPORT OF FOREIGN PRIVATE ISSUER  
PURSUANT TO RULE 13a-16 OR 15d-16  
UNDER THE SECURITIES EXCHANGE ACT OF 1934**

For the Month of December 2020

Commission File Number: 001-38547

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**Autolus Therapeutics plc**  
(Translation of registrant's name into English)

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Forest House  
58 Wood Lane  
White City  
London W12 7RZ  
United Kingdom  
(Address of principal executive office)

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Indicate by check mark whether the registrant files or will file annual reports under cover of Form 20-F or Form 40-F:

☒ Form 20-F      ☐ Form 40-F

Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101(b)(1): ☐

Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101(b)(7): ☐

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**ASH Press Releases**

On December 5, 2020, Autolus Therapeutics plc (the “Company”) issued a press release announcing the presentation of updated data from its ongoing Phase 1 clinical trial of AUTO1 in adult acute lymphoblastic leukemia (ALL) at the 62<sup>nd</sup> American Society of Hematology (“ASH”) Annual Meeting, being held December 5-8, 2020. A copy of the press release is furnished as Exhibit 99.1 attached hereto and is incorporated by reference herein.

Additionally, on December 7, 2020, the Company issued a press release announcing the presentation of additional data from its ALEXANDER trial, a Phase 1/2 clinical trial in relapsed/refractory diffuse large B cell lymphoma (DLBCL), at the 62<sup>nd</sup> ASH Annual Meeting. A copy of the press release is furnished as Exhibit 99.2 attached hereto and is incorporated by reference herein.

During a conference call and webcast scheduled to be held at 4:00 pm ET/9:00 pm GMT on December 7, 2020, the Company management will discuss the data presented by the Company at the 62<sup>nd</sup> ASH Annual Meeting. The slide presentation for the conference call and webcast is furnished as Exhibit 99.3 hereto and is incorporated by reference herein.

*The information contained in this “ASH Press Releases” section of the Report on Form 6-K, the press releases furnished as Exhibits 99.1 and 99.2 and the presentation furnished as Exhibit 99.3, shall not be deemed “filed” for the purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the “Exchange Act”), and is not incorporated by reference into any of the Company’s filings under the Securities Act of 1933, as amended, or the Exchange Act, whether made before or after the date hereof, except as shall be expressly set forth by specific reference in any such filing.*

**Business Update**

The Company recently updated its business information as follows:

**AUTO1 Phase 1 Clinical Trial in Adult ALL (ALLCAR19 Trial)**

The Company announced updated data from its Phase 1b/2 clinical trial of AUTO1 for the treatment of adult ALL. As of the data cut-off date of November 12, 2020, 19 patients with r/r ALL had received at least one dose of AUTO1. One additional patient was dosed, who died due to infectious complications assessed as unrelated to AUTO1. It was observed in the trial that AUTO1 was well tolerated, with no patients experiencing Grade 3 or higher cytokine release syndrome (CRS). Across all 20 patients, three patients, all of whom had high leukemia burden (>50% blasts), experienced Grade 3 neurotoxicity (NT) that resolved swiftly with steroids.

Of the 19 patients evaluable for efficacy in the trial, 16 (84%) patients achieved minimum residual disease (MRD)-negative complete response (CR) at one month. Most notably, the durability of remissions is highly encouraging. Across all treated patients, event free survival (EFS) at six and 12 months is 69% and 52%, respectively. Median EFS and overall survival (OS) has not been reached at a median follow up of 16.9 months (range up to 30.5 months). The EFS and OS data are preliminary considering the small number of patients.

Due to the impact on the trial from the ongoing COVID-19 pandemic, the Company now expects to report the final Phase 1 data from this trial in 2022. The Company is also evaluating the development of AUTO1 for the treatment of primary central nervous system lymphoma, with a potential study start in the first quarter of 2021.

**AUTO3 - DLBCL (ALEXANDER Trial)**

The Company announced updated data from its ALEXANDER trial, a Phase 1/2 clinical trial in relapsed/refractory DLBCL. As of the data cut-off date of October 30, 2020, 49 patients in the ALEXANDER trial have been treated and were evaluable for safety. It was observed in the trial that AUTO3 was well tolerated, with low rates of CRS and NT reported. Across all 49 patients, one case of Grade 3 CRS with primary infusion was observed, and three cases of NT have been reported, with two patients experiencing Grade 3 or higher NT. None of the patients achieving a CR experienced any NT and all cases of NT reported have been atypical in nature and seen in a setting with disease progression and confounding factors. No prophylactic measures of any kind have been used to manage patients in the trial.

The majority of patients receiving AUTO3 in the outpatient setting did not require hospital admission. Those patients who were admitted to the hospital were easily managed, with no patients requiring intensive care unit care. The profile of AUTO3 has the potential to support administration in an outpatient setting.

Across all dose levels, 43 patients were evaluable for efficacy in the trial, with an objective response rate (ORR) of 65% and a CR rate of 51%. Of the 29 evaluable patients receiving the recommended Phase 2 dose (doses of greater than  $150 \times 10^6$  CAR T cells) and pre-conditioning with pembrolizumab at Day -1, the ORR was 66% and the CR rate was 55%. A subsequent analysis of the data suggested a superior response rate at higher dose levels, with 15 evaluable patients treated at  $450 \times 10^6$  cells achieving an ORR of 87% and a CRR of 73%.

Across all cohorts in the trial, 73% of patients achieving a CR were without disease progression at a median follow up of 4 months (1 – 24 months). Of note, none of the five patients who achieved a CR in the cohort receiving three doses of pembrolizumab had disease progression as of the data cut-off date.

*This information in this "Business Update" section of the Report on Form 6-K shall be deemed to be incorporated by reference into the Company's registration statement on Form F-3 (File No. 333-232690) and registration statement on Form S-8 (File No. 333-226457) (including any prospectuses forming a part of such registration statements) and to be a part thereof from the date on which this report is filed, to the extent not superseded by documents or reports subsequently filed or furnished.*

#### **Special Note Regarding Forward-Looking Statements**

This Report on Form 6-K contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in the Report that do not relate to matters of historical fact should be considered forward-looking statements, including, without limitation, statements regarding the safety, therapeutic potential and commercial opportunity of AUTO1 and AUTO3 and the future clinical development of AUTO1 and AUTO3 including progress, expectations as to the reporting of data, conduct and timing. Such forward-looking statements are based on the Company's expectations and involve risks and uncertainties; consequently, actual results may differ materially from those expressed or implied in the statements due to a number of factors, including and other risks and uncertainties described in the Company's Annual Report on Form 20-F for the fiscal year ended December 31, 2019, as amended and its subsequent filings with the U.S. Securities and Exchange Commission. The Company makes no commitment to revise or update any forward-looking statements in order to reflect events or circumstances occurring or existing after the date of this report, except to the extent required by applicable law.

## EXHIBIT LIST

<u>Exhibit</u>	<u>Description</u>
99.1	<a href="#">Press Release dated December 5, 2020, "Autolus Therapeutics Presents compelling AUTO1 data from ALLCAR Phase 1 study in Adult Acute Lymphoblastic Leukemia (ALL) during the 62nd ASH Annual Meeting."</a>
99.2	<a href="#">Press Release dated December 7, 2020, "Autolus Therapeutics Presents Additional Data on AUTO3 in DLBCL during the 62nd ASH Annual Meeting."</a>
99.3	<a href="#">Slide presentation dated December 7, 2020.</a>



## SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

### Autolus Therapeutics plc

Date: December 7, 2020

By: /s/ Christian Itin

Name Christian Itin, Ph.D.

Title: Chief Executive Officer



**Autolus Therapeutics presents compelling AUTO1 data from ALLCAR Phase 1 study in Adult Acute Lymphoblastic Leukemia (ALL) during the 62nd ASH Annual Meeting**

Updated data from the ALLCAR study suggests AUTO1's potential for transformational activity in adult patients with r/r ALL

***Conference call and webcast to be held Monday, December 7, 2020  
at 4:00 pm ET / 9:00 pm GMT***

**LONDON, December 5, 2020** — Autolus Therapeutics plc (Nasdaq: AUTL), a clinical-stage biopharmaceutical company developing next-generation programmed T cell therapies, today announced new data highlighting progress on its AUTO1 program, the company's CAR T cell therapy being investigated in the ongoing ALLCAR Phase 1 study in relapsed / refractory adult B-Acute Lymphocytic Leukemia (ALL), during the American Society of Hematology (ASH) All-Virtual Annual Meeting, held between December 5-8, 2020.

As of the November 12, 2020 data cut-off date, 20 patients with r/r ALL had received AUTO1. AUTO1 was well tolerated, with no patients experiencing <sup>3</sup> Grade 3 cytokine release syndrome (CRS). Three patients (15%), all of whom had high leukemia burden (>50% blasts), experienced Grade 3 neurotoxicity (NT) that resolved swiftly with steroids.

Of the 19 patients evaluable for efficacy, 16 (84%) patients achieved minimum residual disease (MRD)-negative complete response (CR) at one month. Most notably, the durability of remissions is highly encouraging. Across all treated patients, event free survival (EFS) at six and 12 months is 69% and 52% respectively. Median EFS and overall survival (OS) has not been reached at a median follow up of 16.9 months (range up to 30.5 months).

"The high level of sustained CRs observed with AUTO1 in adult ALL, achieved without subsequent stem cell transplant, point to a potentially transformational treatment for adult ALL," said Dr. Claire Roddie, Consultant Hematologist, UCL Cancer Institute and University College London Hospital. "Despite high disease burden and despite this being a heavily pre-treated patient population on study, AUTO1 remains well tolerated. It's encouraging to also observe promising early activity and safety in indolent NHL."

"Adult ALL is a disease with high unmet need, whereby approximately 60% of patients relapse or are refractory to first line therapy," said Dr. Elias Jabbour, Professor of Leukemia at The University of Texas MD Anderson Cancer Center. "AUTO1 is a novel CD19 CAR T candidate with an impressive clinical profile. This profile has the potential to change standard of care as a curative therapy for r/r ALL."

Dr. Christian Itin, chairman and chief executive officer of Autolus, added “We are excited about the long-term remissions observed without a need for an additional stem cell transplant. Remarkably, this outstanding result was achieved with a well-tolerated safety profile in this fragile adult ALL population. We believe the unique characteristics of AUTO1, seen in the ALLCAR study, point to the potential for AUTO1 as a standalone and transformational therapy in t/r ALL. Our Phase 1b/2 pivotal study is under way, however, with the escalating COVID-19 pandemic, enrolment projections have had to be adjusted. We now expect to enroll patients throughout 2021 with a full data set in 2022.”

In addition to adult ALL, the ALLCAR study was extended to patients with indolent B cell Non-Hodgkin Lymphoma (NHL) (Cohort 1), high grade B-NHL (Cohort 2) and chronic lymphocytic leukemia (CLL) (Cohort 3). As of the data cut-off date of November 12, 2020, four patients in Cohort 1 had been infused with AUTO1. AUTO1 was well tolerated, with no patients experiencing <sup>3</sup> Grade 2 CRS and no patients experiencing NT of any grade. All four patients achieved a Complete Metabolic Response (CMR).

#### **Investor call on Monday December 7, 2020**

Management will host a conference call and webcast on Monday December 7, 2020 at 4:00 pm ET/9:00 pm GMT to discuss the ASH data. To listen to the webcast and view the accompanying slide presentation, please go to: <https://www.autolus.com/investor-relations/news-and-events/events>.

The call may also be accessed by dialing (866) 679-5407 for U.S. and Canada callers or (409) 217-8320 for international callers. Please reference conference ID 9188389. After the conference call, a replay will be available for one week. To access the replay, please dial (855) 859-2056 for U.S. and Canada callers or (404) 537-3406 for international callers. Please reference conference ID 9188389.

#### **About Autolus Therapeutics plc**

Autolus is a clinical-stage biopharmaceutical company developing next-generation, programmed T cell therapies for the treatment of cancer. Using a broad suite of proprietary and modular T cell programming technologies, the company is engineering precisely targeted, controlled and highly active T cell therapies that are designed to better recognize cancer cells, break down their defense mechanisms and eliminate these cells. Autolus has a pipeline of product candidates in development for the treatment of hematological malignancies and solid tumors. For more information please visit [www.autolus.com](http://www.autolus.com).

#### **About AUTO1**

AUTO1 is a CD19 CAR T cell investigational therapy designed to overcome the limitations in safety—while maintaining similar levels of efficacy—compared to current CD19 CAR T cell therapies. Designed to have a fast target binding off-rate to minimize excessive activation of the programmed T cells, AUTO1 may reduce toxicity and be less prone to T cell exhaustion, which could enhance persistence and improve the ability of the programmed T cells to engage in serial killing of target cancer cells. AUTO1 is currently being evaluated in two Phase 1 studies, one in pediatric ALL and one in adult ALL. The company has also now progressed the program to a potential pivotal study, AUTO1-AL1.

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**About AUTO1-AL1 pivotal study**

The AUTO1-AL1 study will enroll patients with relapsed / refractory ALL. The study will have a short Phase1b component prior to proceeding to a single arm Phase 2 study. The primary end point is overall response rate and the key secondary end points include duration of response, MRD negative CR rate and safety. The study will enroll approximately 100 patients across 30 of the leading academic and non-academic centers in the US, UK and Europe.

**Forward-Looking Statements**

This press release contains forward-looking statements within the meaning of the “safe harbor” provisions of the Private Securities Litigation Reform Act of 1995. Forward-looking statements are statements that are not historical facts, and in some cases can be identified by terms such as “may,” “will,” “could,” “expects,” “plans,” “anticipates,” and “believes.” These statements include, but are not limited to, statements regarding the efficacy, safety and therapeutic potential of AUTO3 and the future clinical development of AUTO3 including progress, expectations as to the reporting of data, conduct and timing. Any forward-looking statements are based on management’s current views and assumptions and involve risks and uncertainties that could cause actual results, performance or events to differ materially from those expressed or implied in such statements. These risks and uncertainties include, but are not limited to, the risks that Autolus’ preclinical or clinical programs do not advance or result in approved products on a timely or cost effective basis or at all; the results of early clinical trials are not always being predictive of future results; the cost, timing and results of clinical trials; that many product candidates do not become approved drugs on a timely or cost effective basis or at all; the ability to enroll patients in clinical trials; possible safety and efficacy concerns; and the impact of the ongoing COVID-19 pandemic on Autolus’ business. For a discussion of other risks and uncertainties, and other important factors, any of which could cause Autolus’ actual results to differ from those contained in the forward-looking statements, see the section titled “Risk Factors” in Autolus’ Annual Report on Form 20-F filed with the Securities and Exchange Commission on March 3, 2020, as amended, as well as discussions of potential risks, uncertainties, and other important factors in Autolus’ subsequent filings with the Securities and Exchange Commission. All information in this press release is as of the date of the release, and the company undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events, or otherwise, except as required by law.

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**Autolus Therapeutics presents additional data on AUTO3 in DLBCL during the 62nd ASH Annual Meeting**

AUTO3 continues to show a differentiated product profile supporting outpatient administration

***Conference call and webcast to be held Monday, December 7, 2020  
at 4:00 pm ET / 9:00 pm GMT***

**LONDON, December 7, 2020** — Autolus Therapeutics plc (Nasdaq: AUTL), a clinical-stage biopharmaceutical company developing next-generation programmed T cell therapies, today announced new data highlighting progress on AUTO3, the company's CD19 and CD22 dual targeting CAR T product candidate being investigated in the ALEXANDER study, a Phase 1/2 clinical study in relapsed/refractory diffuse large B cell lymphoma (DLBCL), during the American Society of Hematology (ASH) All-Virtual Annual Meeting, held between December 5-8, 2020.

As of the October 30, 2020 data cut-off date, 49 patients in the ALEXANDER study have been treated and were evaluable for safety. AUTO3 was observed to be well tolerated, with low rates of cytokine release syndrome (CRS) and neurotoxicity (NT). Across all 49 patients, there was only one case of Grade 3 CRS with primary infusion, and only three cases of NT were reported, with two being <sup>3</sup> Grade 3. None of the patients achieving a complete response (CR) experienced any NT and all cases of NT were seen in a setting of disease progression and with confounding factors. No prophylactic measures of any kind have been used to manage patients in this study.

The majority of patients receiving AUTO3 in the outpatient setting did not require hospital admission. Those patients admitted were easily managed, with no patients requiring ICU care. Combined with the overall favorable safety data across the Phase 1 study, the profile of AUTO3 supports administration in an outpatient setting.

Across all dose levels, 43 patients were evaluable for efficacy, with an objective response rate (ORR) of 65% and a CR rate of 51%. Of the 29 evaluable patients receiving the recommended Phase 2 dose (a dose of <sup>3</sup> 150 x 10<sup>6</sup> cells) and pre-conditioning with pembrolizumab at Day -1, the ORR was 66% and the CR rate was 55%. A subsequent analysis of these data suggested a superior response rate at higher dose levels, with 15 evaluable patients treated at 450 x 10<sup>6</sup> cells achieving an ORR of 87% and a CRR of 73%.

Across all cohorts in the study, 73% (16/22) of patients achieving a CR were without disease progression at a median follow up of 4 months (1 – 24 months). Of note, none of the five patients who achieved a CR in the cohort receiving three doses of pembrolizumab had disease progression.

“AUTO3 continues to have a tolerable and favorable safety profile when compared with approved CD19 CAR T therapies,” said Dr. Aravind Ramakrishnan, Medical Director, Adult Blood and Marrow Transplant, Texas Transplant Institute at the Sarah Cannon Blood Cancer Center at St. David’s South Austin Medical Center. “The complete response rate is high and the longest patient on the study is now over 2 years post treatment and remains in remission.”

Dr. Christian Itin, chairman and chief executive officer of Autolus, added “AUTO3 continues to show a high level of clinical activity across all dose levels and conditions evaluated in this expanded Phase 1 study. The favorable tolerability profile was confirmed in the outpatient cohort which supports the use of AUTO3 in an outpatient setting. This differentiated profile may widen the potential use of CAR T therapy in DLBCL. Based on these data, we are assessing a strategy that potentially optimizes the development path in r/r DLBCL and expect to update on next steps for AUTO3 in Q1 2021.”

#### **Investor call on Monday December 7, 2020**

Management will host a conference call and webcast today at 4:00 pm ET/9:00 pm GMT to discuss the ASH data. To listen to the webcast and view the accompanying slide presentation, please go to: <https://www.autolus.com/investor-relations/news-and-events/events>.

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#### **About Autolus Therapeutics plc**

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#### **About AUTO3**

AUTO3 is a programmed T cell therapy containing two independent chimeric antigen receptors targeting CD19 and CD22 that have each been independently optimized for single target activity. By simultaneously targeting two B cell antigens, AUTO3 is designed to minimize relapse due to single antigen loss in patients with B cell malignancies. AUTO3 is currently being tested in diffuse large B cell lymphoma in the ALEXANDER clinical study, including a 20-patient cohort to assess feasibility of treatment in an outpatient setting.

#### **Forward-Looking Statements**

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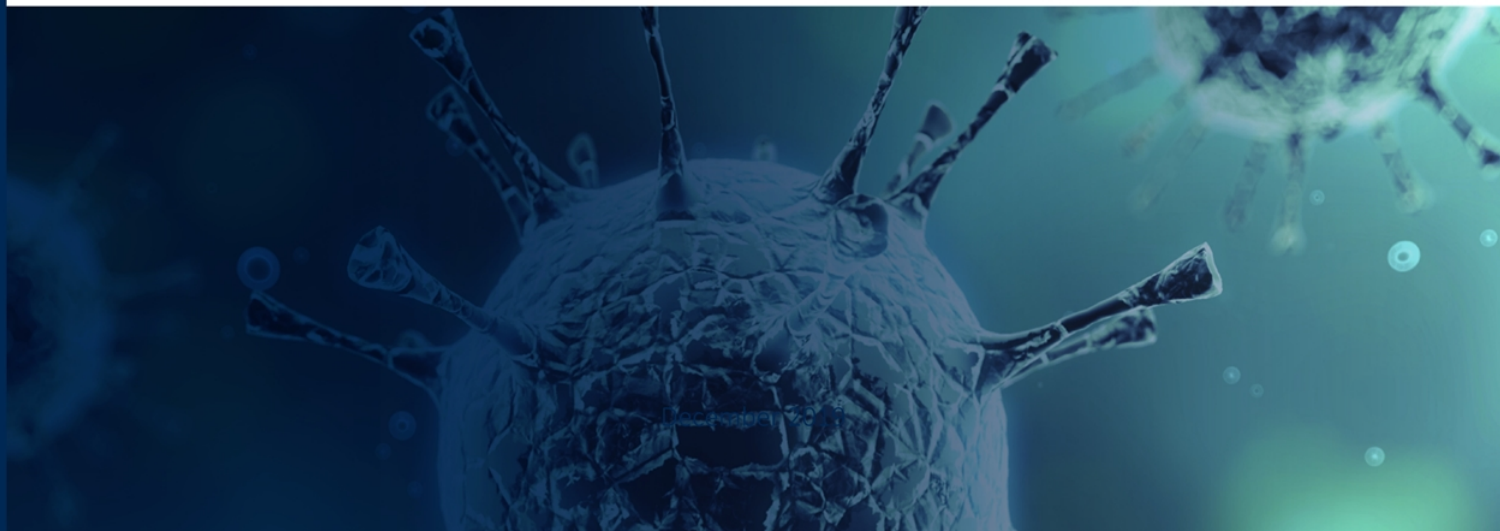
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AUTO1 and AUTO3 Data Update - ASH 2020  
December 2020



# Disclaimer

These slides and the accompanying oral presentation contain forward-looking statements within the meaning of the “safe harbor” provisions of The Private Securities Litigation Reform Act of 1995, including statements about the safety, therapeutic potential and commercial opportunity of AUTO1 and AUTO3 and the future clinical development of AUTO1 and AUTO3 including progress, expectations as to the reporting of data, conduct and timing; the Company's plans to develop and commercialize its other product candidates and next generation programs including statements regarding the timing of initiation, completion of enrollment and availability of data from the Company's current preclinical studies and clinical trials; the Company's commercialization, marketing and manufacturing capabilities and strategy; and the impact of the ongoing COVID-19 pandemic on the Company's operations and clinical trials. All statements other than statements of historical fact contained in this presentation, including statements regarding the Company's future results of operations and financial position, business strategy and plans and objectives of management for future operations, are forward-looking statements. In some cases, you can identify forward-looking statements by terms such as “may,” “should,” “expects,” “plans,” “anticipates,” “could,” “intends,” “target,” “projects,” “contemplates,” “believes,” “estimates,” “predicts,” “potential” or “continue” or the negative of these terms or other similar expressions. These statements involve known and unknown risks, uncertainties and other important factors that may cause the Company's actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. Factors that may cause actual results to differ materially from any future results expressed or implied by any forward-looking statements include the risks described in the “Risk Factors” section of the Company's Annual Report on Form 20-F for the year ended December 31, 2019, as amended, as well as those set forth from time to time in the Company's subsequent SEC filings, available at [www.sec.gov](http://www.sec.gov). All information contained herein is as of the date of the presentation, and the Company undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events, or otherwise, except as required by law. You should, therefore, not rely on these forward-looking statements as representing the Company's views as of any date subsequent to the date of this presentation.

Certain data in this presentation was obtained from various external sources. Such data speak only as of the date referenced in this presentation and neither the Company nor its affiliates, advisors or representatives make any representation as to the accuracy or completeness of that data or undertake to update such data after the date of this presentation. Such data involve risks and uncertainties and are subject to change based on various factors.

# Agenda

1. Welcome and Introduction: Dr. Christian Itin, Chairman and CEO
2. AUTO3 Data Review: Dr. Robert Chen, Executive Director, AUTO3 Program Lead
3. Commercial Opportunity in DLBCL : Brent Rice, Vice President, Chief Commercial Officer
4. AUTO1 Data Review: Dr. Nushmia Khokhar, Head of Clinical Development
5. Commercial Opportunity in Adult ALL: Brent Rice, Vice President, Chief Commercial Officer
6. Summary: Dr. Christian Itin, Chairman and CEO
7. Q&A: Dr. Christian Itin, Dr. Martin Pule (CSO), Andrew Oakley (CFO), Dr. Nushmia Khokhar, Dr. Robert Chen, Brent Rice

## 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®, the first FDA-approved redirected T cell therapy



### **Dr. Nushmia Khokhar**

*SVP, Head of Clinical Development*

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



### **Dr. Martin Pule**

*Founder & SVP, CSO*

Founder of Autolus; World leading expert in the development of CAR T cell therapies; Clinical senior lecturer & hon. consultant at UCL; Fulbright at Baylor



### **Dr. Robert Chen**

*Executive Director, Clinical Development*

Previously Associate Professor at City of Hope Medical Center and Associate Director of the Toni Stephenson Lymphoma Center. Authored 100+ peer reviewed publications and abstracts



### **Andrew Oakley**

*CFO*

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



### **Brent Rice**

*VP, Chief Commercial Officer*

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

# AUTO3 continues to show differentiated product profile

Data cut-off date October 30, 2020

- Safety data supports feasibility of outpatient administration
  - AUTO3 was observed to be well tolerated, with low rates of cytokine release syndrome (CRS) and neurotoxicity (NT) reported
  - No prophylactic measures of any kind have been used to manage patients in this study
  - Manageability in the outpatient cohort appears promising
- High complete response rates
  - CR rate was 55% for patients receiving  $\geq 150 \times 10^6$  cells and pre-conditioning with pembrolizumab at Day -1
  - Subsequent analysis indicates that at a dose of  $450 \times 10^6$  cells, CRR is 73%
  - 73% patients experiencing a CR, across all cohorts, were without disease progression (median follow up 4 months)
  - None of the five patients who achieved a CR in the cohort receiving three doses of pembrolizumab had disease progression
- We expect to update on next steps for AUTO3 in Q1 2021

# AUTO1 has potential for transformational outcomes in adult ALL

Data cut-off date November 12, 2020

- High level of sustained CRs, achieved without subsequent stem cell transplant
- Durability of remissions highly encouraging
  - Across all treated patients, event free survival (EFS) at six and 12 months is 69% and 52%, respectively
- AUTO1 remains well tolerated, despite patients having high disease burden and being heavily pre-treated
  - No patients experienced  $\geq$  Grade 3 cytokine release syndrome (CRS) as of data cut-off date
- Phase 1b/2 potential pivotal study underway, expect full data in 2022
  - Escalating COVID-19 pandemic is continuing to impact study conduct
- Adult ALL represents a sizeable market opportunity which requires limited commercial footprint

## Data Review

*Dr. Robert Chen*

*Executive Director, AUTO3 Program Lead*

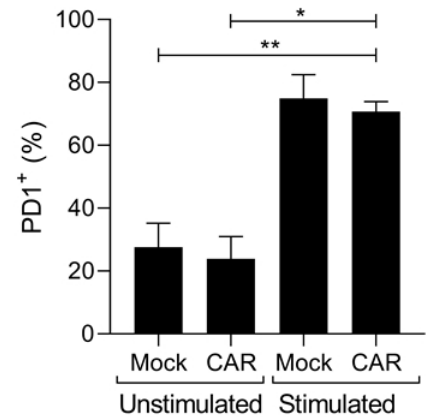
Phase 1/2 study of AUTO3, the first bicistronic chimeric antigen receptor (CAR) targeting CD19 and CD22, followed by an anti-PD1 in patients with relapsed/refractory (r/r) Diffuse Large B Cell Lymphoma (DLBCL): Results of Safety Cohorts of the ALEXANDER study\*

# Improving CAR T Cell Immunotherapy In DLBCL

## Dual targeting CAR & prevention of CAR T cell inhibition

- CD19 CARs are active in r/r DLBCL
- However unmet need remains with CD19 CAR T cell therapy
  - 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>
- Simultaneous targeting of CD19 and CD22 may reduce the probability of relapse due to antigen loss
- PD1/PDL1 mediated CAR T cell inhibition may be prevented by adding pembrolizumab to the preconditioning regimen

### Activated T-cells Upregulate PD1



<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

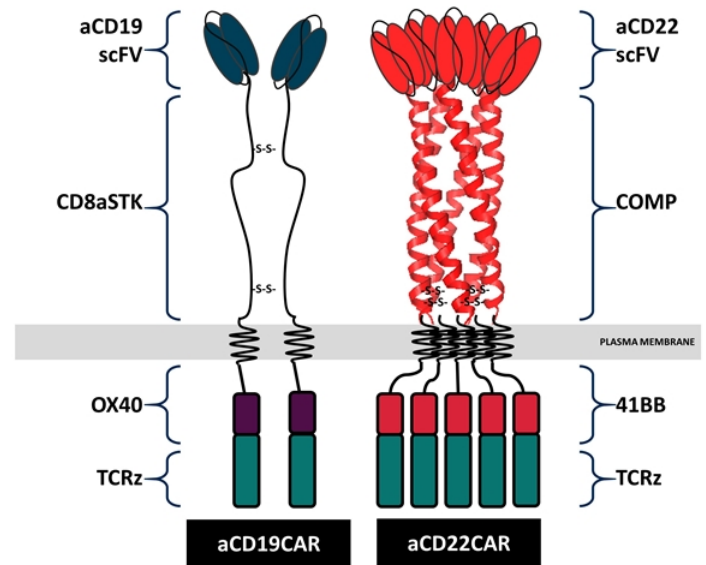
<sup>4</sup> Neelapu S et al NEJM 2017



# AUTO3: First CD19 and CD22 Targeting Bicistronic CAR

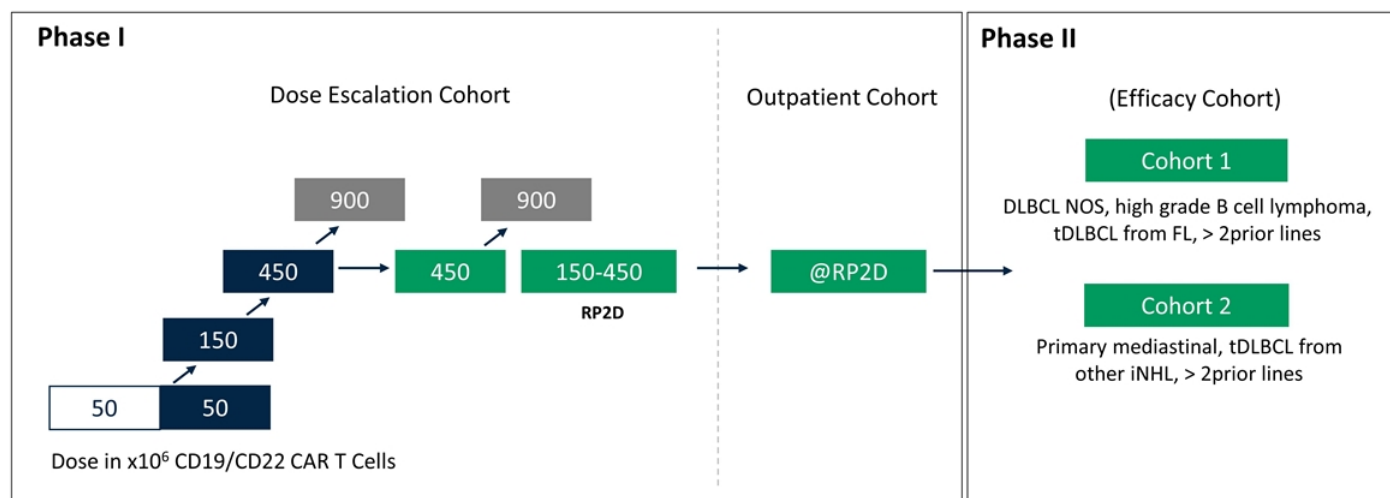
## Gamma Retroviral-Based Vector with RD114 Pseudotype

- 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 and CD22



# Alexander Study Design

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



Preconditioning: Flu/Cy	Flu/Cy + Pembro day 14 x 3 doses	Flu/Cy + Pembro day - 1 x 1 dose
----------------------------	-------------------------------------	-------------------------------------

## Phase 1 Outpatient Expansion Cohort

### Inclusion / Exclusion

- Subjects who do not have caregiver support (in line with institutional outpatient transplant guidelines) for outpatient/ambulatory care setting
- Subjects who are staying greater than 60 minutes (or whatever is permissible per institutional outpatient transplant guidelines) from the clinical trial site at the time of treatment

### Monitoring

- Monitored for at least 10 days in an outpatient/ambulatory care setting
- During the 10 days following AUTO3 infusion, monitored at a minimum every 2 to 3 days. Recommended for the patient to have a daily verbal communication with qualified nurse/medical personnel (phone call)

## Baseline Patient Characteristics: All Patients

Baseline Patient Characteristics		N=49
Age, median (min-max)		59 (27-83)
Gender, n	Male, Female	29, 20
Current Histology, n	DLBCL NOS	34 (69%)
	tDLBCL	11 (22%)
	High Grade B Cell Lymphoma	3 (6%)
	Primary Mediastinal Large B Cell Lymphoma	1 (2%)
Molecular Risk, n (%)	High Risk	27 (55%)
	- Triple HIT	-5
	- Double HIT	-14
	- Double Expressor	-8
	No High Risk	13 (27%)
Disease Stage, n (%)	Unknown/Not Done	9 (18%)
	II	4 (8%)
	III	10 (20%)
	IV	35 (71%)
Relapsed/Refractory, n (%)	Refractory	11 (22%)
	Relapsed	14 (29%)
	Relapsed and Refractory	24 (49%)
No. Prior Therapies, median (min-max)		3 (1-11)
Prior ASCT, n (%)		15 (31%)
SPD, median (min-max)		18.5 cm (2.1 – 260.8)

## Treatment Emergent Adverse Events $\geq 25\%$ and SAE $\geq 5\%$

AEs (Total N = 49)	All Grades n (%)	$\geq$ Grades 3 n (%)
Neutropenia	29 (59%)	28 (57%)
Anaemia	25 (51%)	20 (41%)
Thrombocytopenia	23 (47%)	18 (37%)
Cytokine release syndrome	17 (35%)	1 (2%)
Fever	13 (27%)	0
Infections	13 (27%)	8 (16%)

SAEs (Total N = 49)	All Grades n (%)	$\geq$ Grades 3 n (%)
Cytokine release syndrome	6 (12%)	1 (2%)
Fever	5 (10%)	0
Infections	4 (8%)	4 (8%)
Febrile neutropenia	3 (6%)	3 (6%)

- Majority of  $\geq$  Grade 3 AEs are haematological
- Two patients had death possibly related to AUTO3. One in the setting of disease progression and multiorgan failure and other due to infection in a patient with secondary HLH

## Safety by Cohort

	50 x10 <sup>6</sup> AUTO3 no pem (N=4)	50 x10 <sup>6</sup> AUTO3 D14 pem (N=3)	150-450 x10 <sup>6</sup> AUTO3 D14 pem (N=8)	150-450 x10 <sup>6</sup> AUTO3 D-1 pem Inpt (N=17)	150-450 x10 <sup>6</sup> AUTO3 D-1 pem Outpt (N=17)	Total (N=49)
<b>Safety</b>						
CRS All Grades	1	0	4	5	7	17 (35%)
CRS ≥ Grade 3	0	0*	0	0	1	1 (2%)
NTX All Grades	1	0	0	1	1	3 (6%)
NTX ≥ Grade 3	1	0	0	0	1	2 (4%)

\* 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

CRS grading as ASCT/ASBMT (Lee et al 2019)  
Data Cut-off Date: 30-Oct-2020

# Cytokine Release Syndrome (CRS)

## Low rates of CRS

	Total (N=49)	50 x 10 <sup>6</sup> AUTO3 (N=7)	150 x 10 <sup>6</sup> AUTO3 (N=16)	300 x 10 <sup>6</sup> AUTO3 (N=10)	450 x 10 <sup>6</sup> AUTO3 (N=16)
All Grades	17 (35%)	1 (14%)	4 (25%)	2 (20%)	10 (63%)
Grade 1	10 (20%)	1 (14%)	2 (13%)	2 (20%)	5 (31%)
Grade 2	6 (12%)	0	1 (6%)	0	5 (31%)
≥ Grade 3	1 (2%)	0*	1 (6%)	0	0

\* 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

- No prophylactic measures of any kind
- Median time to CRS 2 days (1-36), Median duration 3 days (1-19)
- Eight patients received tocilizumab (16%)
- No patients received steroids

## Neurotoxicity (NT/ICANS)

### Low rates of NT

	Total (N=49)	50 x 10 <sup>6</sup> AUTO3 (N=7)	150 x 10 <sup>6</sup> AUTO3 (N=16)	300 x 10 <sup>6</sup> AUTO3 (N=10)	450 x 10 <sup>6</sup> AUTO3 (N=16)
All Grades	3 (6%)	1 (14%)	2 (13%)	0	0
≥ Grade 3	2 (4%)	1 (14%)	1 (6%)	0	0

- No prophylactic measures of any kind
- No NT of any grade in patients that achieved CR
- All NT atypical in context of tumor progression with zero to minimal CAR T expansion in peripheral blood
  - **1st case of NT (G3):** Day 53. Duration 5 days (G2). The same symptoms of facial/muscle weakness occurred > 10 years ago without specific diagnosis. Resolved.
  - **2nd case of NT (G2):** Day 21. Duration 6 days. AMS\* associated with sepsis and narcotic. Resolved.
  - **3rd case of NT (G4):** Day 10. Encephalopathy associated with sepsis, hyponatremia, metabolic acidosis, and multiorgan failure. Patient died of disease progression and multiorgan failure



## Efficacy Data by Cohort

	50 x10 <sup>6</sup> AUTO3 no pem (N=4)	50 x10 <sup>6</sup> AUTO3 D14 pem (N=3)	150-450 x10 <sup>6</sup> AUTO3 D14 pem (N=8)	150-450 x10 <sup>6</sup> AUTO3 D-1 pem Inpt (N=17)	150-450 x10 <sup>6</sup> AUTO3 D-1 pem <b>Outpt</b> (N=17)	Total (N=49)
N Evaluable*	4	2	8	15	14	43
ORR (CR+PR)	2 (50%)	2 (100%)	5 (63%)	10 (67%)	9 (64%)	28 (65%)
CR	1 (25%)	1 (50%)	4 (50%)	9 (60%)	7 (50%)	22 (51%)
PR	1 (25%)	1 (50%)	1 (13%)	1 (7%)	2 (14%)	6 (14%)

- 150-450 x 10<sup>6</sup>, Day -1 pem (N=29 evaluable): ORR 66%, CRR 55%

- \* Evaluable = PET positive disease prior to start of pre-conditioning and infused at least 28 days prior to data Cut-off date
- \* Response evaluation per Lugano 2014 criteria

ORR = Overall response rate; CR = Complete response; PR = Partial response; PD = Progressive disease

## Efficacy Data - Best Overall Responses

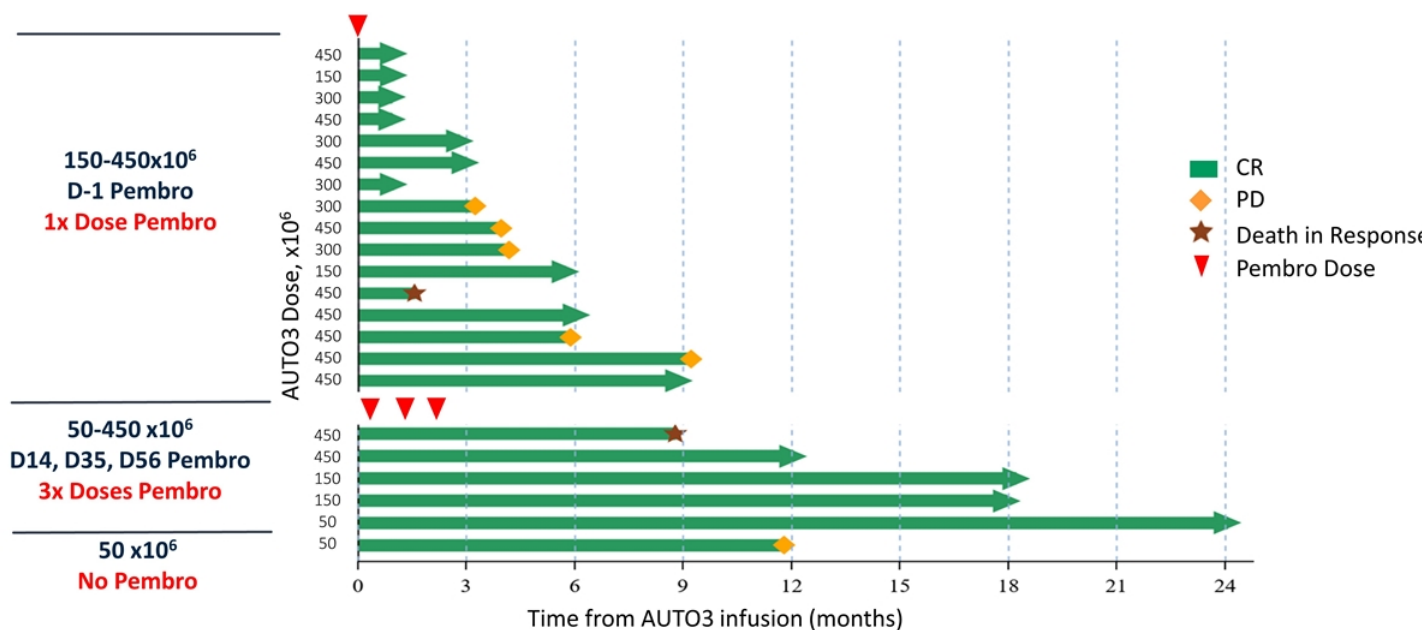
Complete responses observed at all doses

	Total (N=49)	50 x 10 <sup>6</sup> AUTO3 (N=7)	150 x 10 <sup>6</sup> AUTO3 (N=16)	300 x 10 <sup>6</sup> AUTO3 (N=10)	450 x 10 <sup>6</sup> AUTO3 (N=16)
N Evaluable*	43	6	13	9	15
ORR	28 (65%)	4 (67%)	4 (31%)	7 (78%)	13 (87%)
CR	22 (51%)	2 (33%)	4 (31%)	5 (56%)	11 (73%)
PR	6 (14%)	2 (33%)	0	2 (22%)	2 (13%)

- Across all doses CRR of 51% (n=43)
- Doses  $\geq 300 \times 10^6$ , CRR of 62% (n=26)
- Doses  $\geq 450 \times 10^6$ , CRR of 73% (n=15)

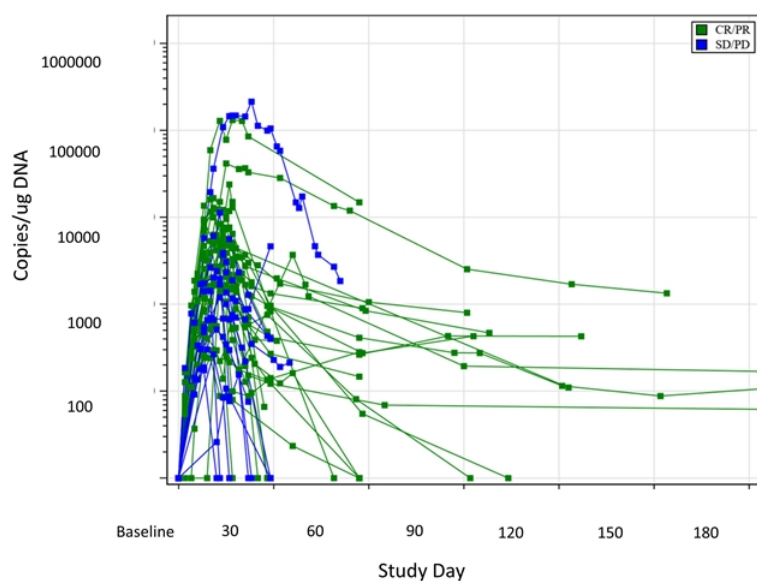
# Disease Assessment of CR Patients

16/22 (73%) without progression, median follow up of 4 months



# Cellular Kinetics by Best Overall Response

CR/PR are associated with higher expansion and longer persistence



	CR/PR (N=28)	SD/PD (N=13)
Tmax (days) median (range)	11 (7 – 35)	12 (7 – 28)
Cmax (copies/μg) Geo-mean (CV%)	6129 (175)	1841 (722)
AUC0-28 (copies/μg day) Geo-mean (CV%)	54419 (199)	13731 (1275)

- Ongoing CAR T persistency observed at ≥ 18 months

# AUTO3 Healthcare Utilizations in Outpatient Cohort

## Outpatient infusion of AUTO3 is feasible

	150-450 x10 <sup>6</sup> AUTO3 D-1 pem Outpt (N=17)
AUTO3 infusion inpatient	4
AUTO3 infusion outpatient	13
Admission post AUTO3	5 (38%)
ICU admission	0

- 5 patients received AUTO3 outpatient but admitted (due to FN and CRS)
- Median duration of hospitalisation was 5 days (range 1-9 days)

# Conclusions

## Phase I Cohorts, ALEXANDER study

- AUTO3 has a tolerable and best-in-class safety profile:
  - 35% CRS (2%  $\geq$  Grade 3 CRS) with primary infusion
  - 6% NT/ICANs\* (4%  $\geq$  Grade 3 NT/ICANs)
    - Patients that achieved CRs, where robust expansion was observed, no severe NT of any grade was seen
    - All three cases of NT in setting of disease progression, very minimal / undetectable CAR-T cells in peripheral blood and with confounding factors
- AUTO3 shows high rate of complete responses
  - Overall CRR of 51% (N=43)
  - Among patients receiving  $450 \times 10^6$  AUTO3, CRR of 73% (N=15)
  - Ongoing CR observed beyond 24 months
- Outpatient administration is feasible with low admission rate (38%)

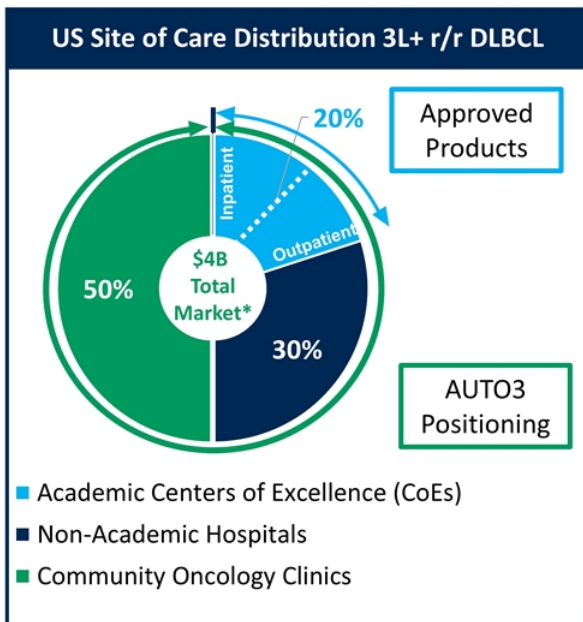
## Commercial Opportunity – DLBCL

*Brent Rice*

*Vice President, Chief Commercial Officer, US*

# Outpatient Cohort reinforces AUTO3 feasibility in Outpatient Setting

AUTO3 has the potential to be a true outpatient therapy



Source: US Retrospective Claims Analysis by Site of Distribution  
\*Autolus approximate estimates

Autolus

## 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

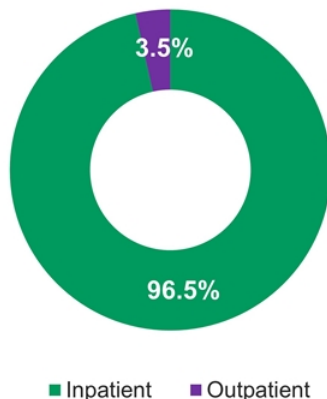
- Minimal toxicity management should allow treatment across all settings of care
- AUTO3 potentially grows the addressable market and maximizes reimbursement options compared to approved products
- >80% of 3L+ and 2L DLBCL patients treated outside of Academic CoEs



## DLBCL: approved CAR T's are unable to penetrate outpatient setting

Creates significant opportunity for AUTO3 with potential to go where patients reside

Percentage of patients who currently receive a CAR T in outpatient or inpatient setting



- 97% of patients receive approved CAR Ts as inpatients in CoEs because of
  - the high rate and severity of toxicities and
  - the need for intensive patient management
- In the Outreach study\*, 63% of patients treated with liso-cel in an outpatient setting required hospitalization
- AUTO3 is designed to have best-in-class safety profile potentially best suited for outpatient use

## **AUTO3 continues to deliver on promise for patients in outpatient setting**

**Differentiated product profile has potential for access to full market opportunity**

- Across all lines of DLBCL the vast majority of patients are treated outside of COEs
- Going where patients are treated could eliminate the challenges involved in establishing referral networks
- Clinical profile and potential for flexible reimbursement has AUTO3 poised to penetrate outpatient setting
- AUTO3 positioned to fully reach addressable 2L and 3L+ patient opportunity

## Data Review

*Dr. Nushmia Khokhar*

*Head of Clinical Development*

ALLCAR19: Updated Data Using AUTO1, a Novel Fast-Off Rate CD19 CAR in Adult Relapsed/Refractory B-Acute Lymphoblastic Leukaemia\*

# Adult B-Acute Lymphoblastic Leukemia:

## Current standard of care

- Adult B-ALL prognosis is poor; long-term remission rates limited to 30-40%
  - 50% of all adult patients will relapse, with 5-year OS 7% (Fielding et al., 2007)
- Currently the only curative option for r/r ALL is allo-SCT in CR2, but <50% achieve CR2
- Blinatumomab and inotuzumab ozogamicin act as a bridge to allo-SCT (Topp et al. 2015; Kantarjian et al., 2019)
- CD19 CAR T can deliver excellent response rates but with considerable toxicity, particularly in elderly patients

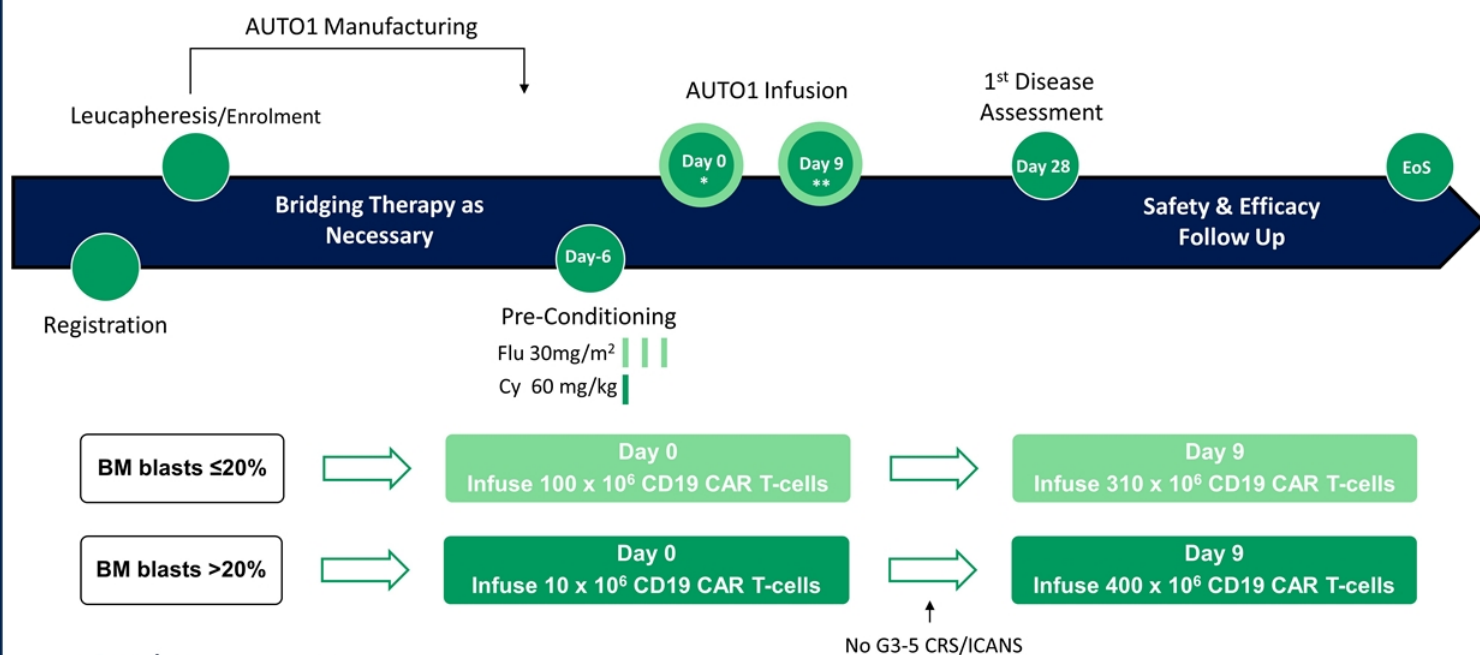
**Currently available CARs:** *high affinity CD19 binders*

**AUTO1:** *Lower affinity CD19 binder with fast off-rate\**

- Physiological T-cell activation
- Reduced toxicity
- Improved engraftment
- Potential long-term persistence, to deliver sustained responses

# ALLCAR19 Study Design

## B-ALL arm



## ALLCAR19 Study:

### Endpoints and eligibility

#### Primary Endpoints

- Grade 3-5 toxicity causally related to the ATIMP
- Feasibility of adequate leucapheresis & generation of AUTO1 CAR T-cells

#### Secondary Endpoints

- Depth of response at 1 and 3 months post ATIMP
- Persistence of CD19CAR T-cells in peripheral blood
- Incidence and duration of hypogammaglobulinaemia & B-cell aplasia
- Relapse rate, disease-free, overall survival, 1 & 2 years

#### Inclusion

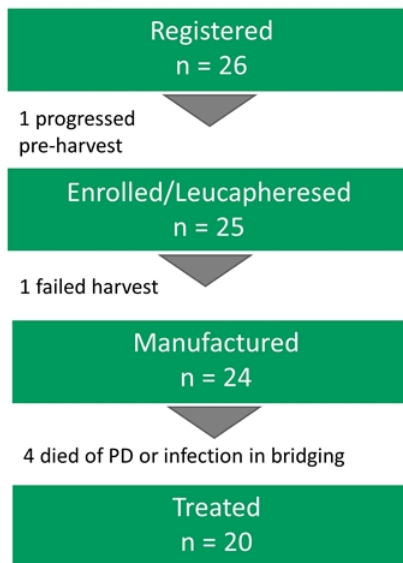
- Age 16 to 65 years
- High risk or relapsed histologically confirmed CD19+ B-ALL following standard therapy requiring salvage in whom alternative therapies are deemed inappropriate by their treating physician

#### Exclusion

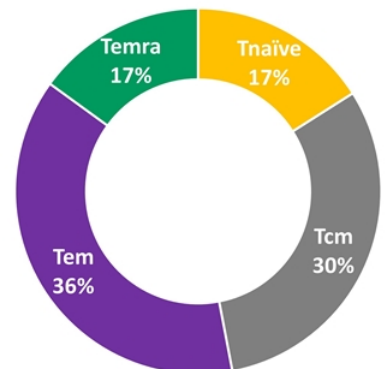
- CD19 negative disease
- Overt CNS involvement/isolated extramedullary disease
- Active hepatitis B, C or HIV infection
- Stem Cell Transplant patients only: no active GVHD
- Significant neurotoxicity following blinatumomab

# ALLCAR19 Manufacturing:

## Product characteristics & feasibility



- 100% of successful harvests result in a QP released product
- Semi-automated closed manufacturing process was used in 18/24 products
- Advantages of closed process includes:
  - rapid, standardised manufacture
  - trend towards lower exhaustion markers
  - enrichment for Tcm and Tnaive CAR+ cells (47%)
- Mean transduction efficiency 66.5%
  - Range 50-83%



## Patient Characteristics:

Treated (n=20)

Baseline Characteristics	N=20 (%)	Leukemia Burden Prior to Lymphodepletion	N=20 (%)
Median age, years (range)	43 (18-62)	Morphological disease	
Gender	13M/7F	• ≤ 5% blasts	7 (35%)
Chromosomal/Molecular status		• 5 - 49% blasts	4 (20%)
• Ph+ (bcr-abl)	6 (30%)	• <b>≥ 50% blasts</b>	<b>9 (45%)</b>
• MLL	1 (5%)	CNS status at registration	
• Other	8 (40%)	• CNS 1	0 (0%)
• Normal	4 (20%)	• CNS II – III	0 (0%)
• Failed	1 (5%)	Other extranodal sites	3 (16%)
Prior lines of treatment			
• Median (range)	3 (2-6)		
• <b>Prior Inotuzumab</b>	<b>10 (50%)</b>		
• <b>Prior Blinatumomab</b>	<b>5 (25%)</b>		
• <b>Prior allo-HSCT</b>	<b>13 (65%)</b>		
- sibling/haplo/VUD	4p/1p/8p		

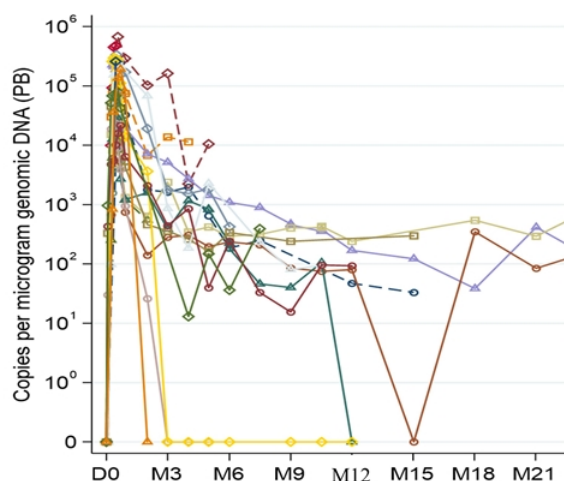
Autolus

20 patients have been infused (data cut off 12-Nov-2020)



# AUTO1 Pharmacokinetics:

## Expansion and persistence by qPCR



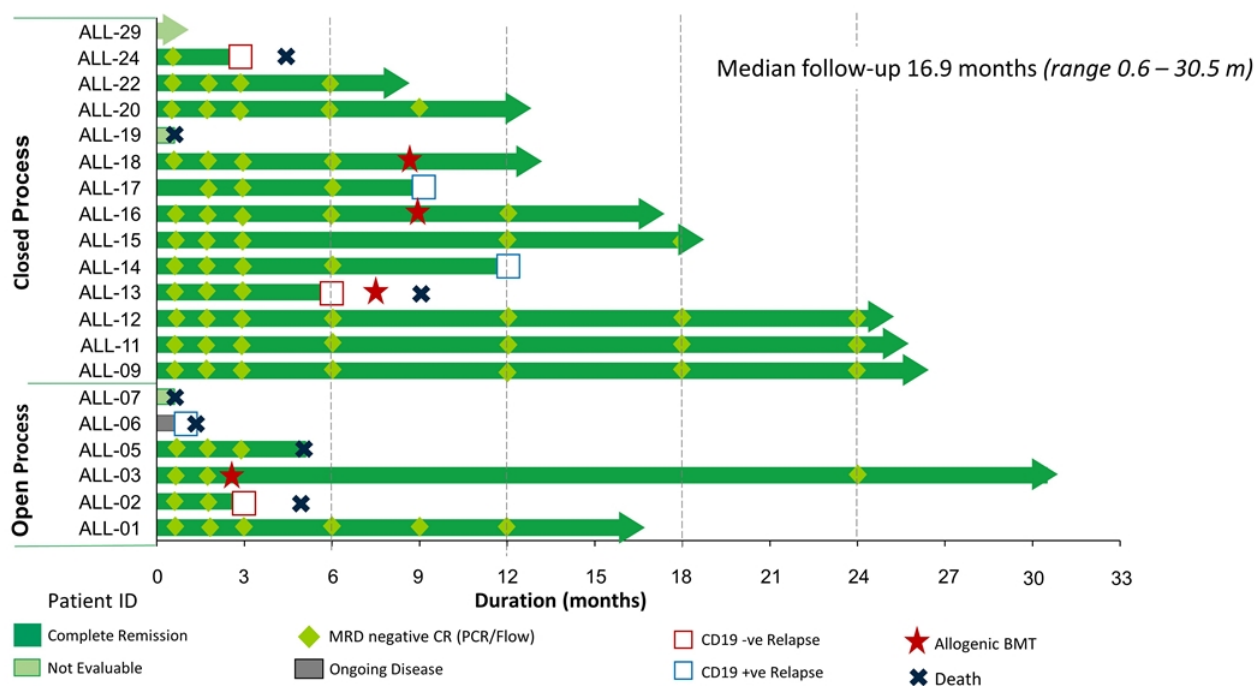
ALLCAR19 qPCR PK all patients (n = 19)	*Mueller 2017 (responders)	
<b>AUC DO-28</b> (Geometric Mean) (Copies/μg x days)	<b>750 320</b>	<b>342 732</b>
<b>Half life</b> (Median Days)	17 (Range 11-29)	14.2
<b>Max CART T Level</b> (Geometric Mean) (Copies/μg)	117 670	47 988
<b>T (Cmax)</b> (Median Days)	14 (Range 7-21)	

## Safety Profile

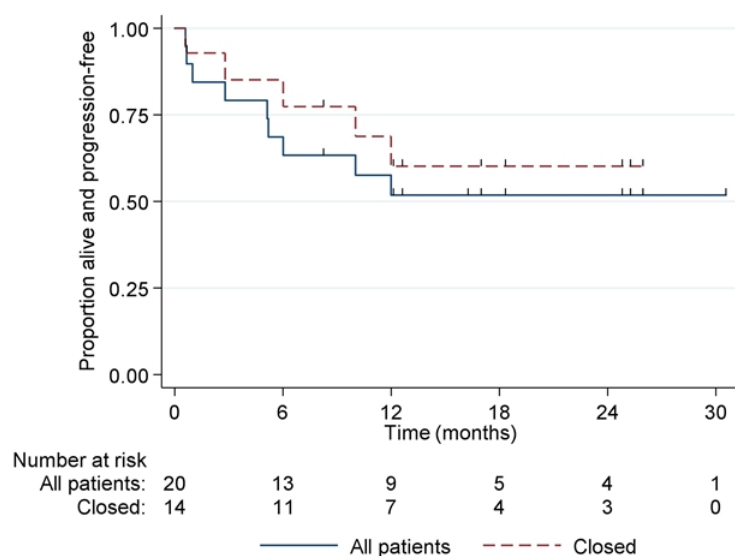
CRS (Lee Criteria)	Neurotoxicity (ICANS#)	≥ Grade 3 Cytopenia	Day -6	At Day 28
<ul style="list-style-type: none"> <li>CRS (any) in 10/20</li> <li>Grade 2 in 7/20</li> <li>≥ Grade 3 CRS in 0/20</li> </ul>	<ul style="list-style-type: none"> <li>ICANS (any) in 4/20</li> <li>Grade 2 in 1/20</li> <li>Grade 3 in 3/20</li> </ul>	<ul style="list-style-type: none"> <li>≥ Grade 3 Neutropenia</li> </ul>	7/20	8/17

- CRS
  - All patients who developed Grade 2 CRS had high burden B-ALL
  - Tocilizumab was used in 7/20 patients (35%)
- Neurotoxicity (ICANS)
  - ≥ Grade 2 ICANS was reported in 4/20 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 7/20 patients
  - At Day 28, 8/17 evaluable patients had ≥ Grade 3 neutropenia with most resolving by Month 2/3
- 7/20 patients died on study:
  - 2/20 died from progressive B-ALL
  - 1/20 died post-progression from allo-transplant-related complications (VOD/sepsis)
  - 4/20 from infection: 2/4 before D28 (sepsis; invasive fungal); 1/4 at M6 in CR (MDR-pseudomonas in blood); 1/4 at M3 of COVID-19

## Efficacy & Duration



# AUTO1: Efficacy Overview



		All patients Est [95% CI]	Closed process Est [95% CI]
	N *	19	13
	ORR	84%	92%
	MRD Neg CR	84%	92%
DOR	Median	Not reached	Not reached
	6 months	81% [52%, 94%]	83% [48%, 96%]
	12 months	68% [39%, 85%]	65% [31%, 85%]
EFS	Median	Not reached	Not reached
	6 months	69% [43%, 85%]	85% [52%, 96%]
	12 months	52% [28%, 71%]	60% [29%, 81%]
OS	Median	Not reached	Not reached
	6 months	68% [43%, 84%]	85% [51%, 96%]
	12 months	63% [37%, 80%]	76% [43%, 92%]

Autolus

N = All patients with at least M1 follow-up or RIP prior to Month 1.  
Event = death or morphological relapse.  
DOR, EFS and OS data are preliminary considering the small n

# ALLCAR19 Study:

Extending eligibility to Indolent NHL, HG-NHL and CLL

## Cohort 1: Indolent B-NHL (Dose = 200 million CD19 CAR T-cells)

- relapsed/refractory (r/r) Follicular Lymphoma
- r/r Mantle Cell Lymphoma
- r/r Marginal Zone Lymphoma
- $\geq 2$  prior lines of therapy including Rituximab and anthracycline

## Cohort 2: High grade B-NHL (Dose = 200 million CD19 CAR T-cells + Pembrolizumab)

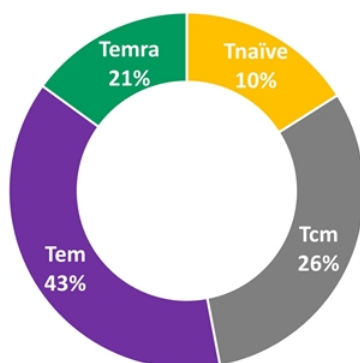
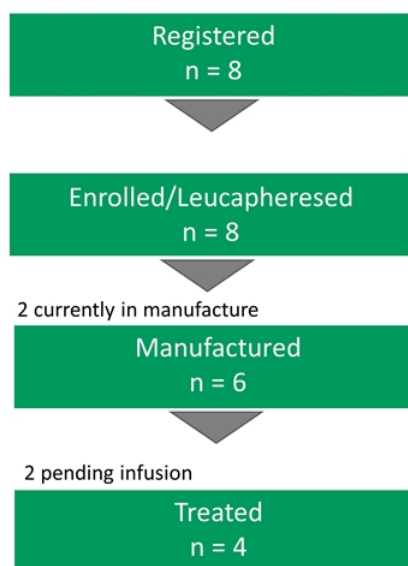
- r/r DLBCL, PMBCL, transformed FL
- not Richter's transformation
- $\geq 2$  prior lines of therapy including Rituximab and anthracycline

## Cohort 3: CLL/SLL (Dose = 230 million CD19 CAR T-cells/ split dose)

- r/r CLL/SLL
- $\geq 2$  prior lines of therapy including Ibrutinib/BTKi

# ALLCAR19 Study:

## Cohort 1: Indolent NHL- products and demographics



- N=6 products QP released
- Semi-automated, closed manufacturing
- Tcm/Tnaive CAR+ (36%)
- Transduction efficiency (mean 76%)

Baseline Characteristics	N=8 (%)
Median age, years (range)	57 (39 - 68)
Gender	6M/2F
Histological diagnoses	
• MCL	2 (25%)
• FL	6 (75%)
Disease Stage	
• Stage I/II	0 (0)
• Stage III/IV	8 (100%)
Prior lines of treatment	
• Median (range)	3 (2-4)
• Prior ASCT	4 (50%)
• Prior allo-HSCT	1 (12.5%)
- sibling/haplo/VUD	0p/0p/1p

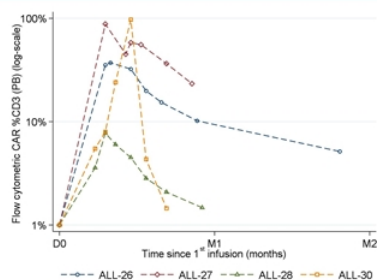
# ALLCAR19 Study:

## Cohort 1: Indolent NHL- toxicity, responses, engraftment

### Toxicity

	N = 4
CRS	
Any grade	3/4
≥ Grade 2	0/4
Neurotoxicity (ICANS)	
Any grade	0/4
≥ Grade 3 Neutropenia	
Day -6	0/4
Day 28	0/4

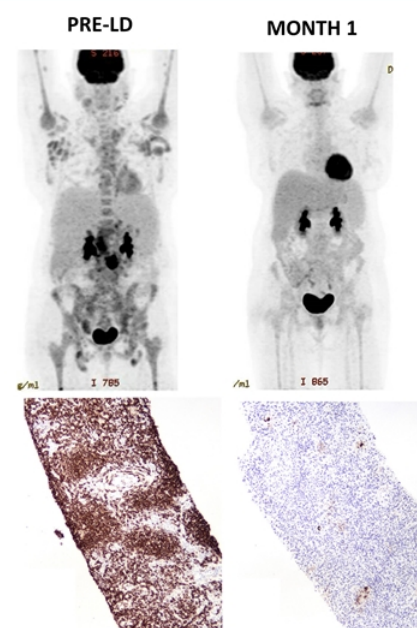
### Engraftment



Autolus

### Responses based on Lugano Criteria and IHC (CD20)

	N = 4
CMR	4/4
PR	0/4
SD	0/4
PD	0/4



Serial LN Biopsies, CD20 by IHC, Dr Teresa Marafioti, UCL

## AUTO1:

### Conclusions

- Tolerable Safety Profile was observed:
  - Despite high disease burden and despite heavily pre-treated patient population on study
    - No Grade 3 CRS was observed
    - Only 3/20 patients developed Grade 3 ICANS (rapid resolution with steroids)
- Robust expansion and prolonged CAR persistence was observed
- Efficacy in adult r/r ALL:
  - MRD negative CR was achieved in 16/19 (84%) patients at 1 month
  - EFS at 6 and 12 months is 69% and 52% respectively, in all treated patients
  - Responses are durable and ongoing CRs observed beyond 24 months, supporting the development of AUTO1 as a stand-alone therapy
- Promising early activity and safety has been observed in indolent NHL

**Global Phase Ib/II AUTO1 study in r/r ALL has started**



## Commercial Opportunity – Adult ALL

*Brent Rice*

*Vice President, Chief Commercial Officer, US*

## No approved CAR T therapy for adult ALL patients

### Transformative therapy needed to address high unmet need despite current SOC

- 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 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
- Opportunity to conduct further clinical study for second line treatment label increasing addressable patient population

### FDA granted AUTO1 orphan drug designation for ALL

## Key Features of a Successful Therapy for Adult ALL

	Adult ALL Challenge	Product Property	CAR T Feature
●	Fast proliferating disease	Very high level of anti-leukemic activity	Rapid CAR T mediated kill and high level of CAR T expansion
●	Almost stem cell like nature of leukemic cells	Sustain long term pressure on leukemia	Long CAR T persistence
●	Poor patient condition	Good tolerability	Minimize high grade CRS and NT

# AUTO1 holds promise for patients as potential Standalone Therapy

## A cross study comparison of AUTO1 vs Standard of Care

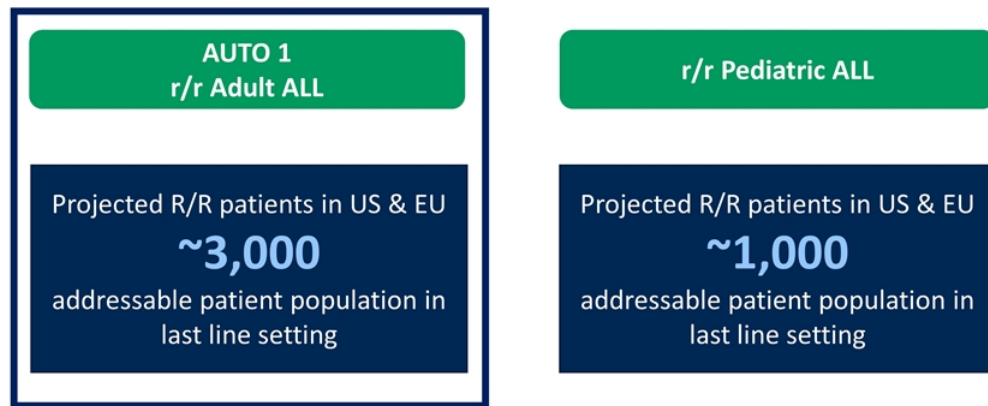
	<sup>1</sup> AUTO1	Standard of Care	
	All patients	<sup>2</sup> Blinatumumab	<sup>3</sup> Inotuzumab
Patient Numbers	19	271	218
CR Rate	84%	44%	80.7%
EFS 6m (EFS 12m)	69% (52%)	31%	mPFS 5m
CRS ≥ Grade 3 <sup>†</sup>	0%	3%	0%
Neurotox ≥ Grade 3 <sup>†</sup>	15%*	13%	0%
Other notable toxicities			14% Hepatic VoD

<sup>†</sup>20 patients evaluable for safety

- 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

## Adult ALL is a promising commercial opportunity with limited competition

R/R adult ALL is three times the size of r/r pediatric ALL



Additional potential for AUTO1 to move to 1<sup>st</sup> and 2<sup>nd</sup> lines

# Capitalizing on the unique profile of AUTO1 in Adult ALL

## Exploration of AUTO1 activity in additional B-Cell malignancies

PRODUCT	INDICATION	TARGET	Phase 1	Pivotal
AUTO1	Adult ALL	CD19	ALLCAR19	AUTO1-AL1
AUTO1	iNHL & CLL	CD19	ALLCAR19 ext.	
AUTO1	Primary CNS Lymphoma*	CD19	CAROUSEL	
AUTO1/22	Pediatric ALL	CD19 & CD22	CARPALL ext.	

\*Primary CNS lymphoma annual incidence approx. 1400 cases in the US . Reference: Keva Green; Jeffery P. Hogg <https://www.ncbi.nlm.nih.gov/books/NBK545145/>.

# AUTO1 is designed for potential Best-In-Class Efficacy and Safety

Novel construct for durable responses without allo-transplant and absence of severe CRS

- Novel CD19 CAR designed for use as a stand-alone curative therapy
- Potential transformative clinical profile with high rates of durable complete responses
- Highly differentiated clinical profile with potential for hospital outpatient treatment in Academic and Non-Academic Transplant Centers
- Differentiated product profile should open access to larger market opportunity, potential to reduce burden on healthcare resources and patients
- Opportunity to pursue in earlier lines of therapy and indications outside of adult ALL

## Summary and Next Steps

*Dr. Christian Itin*

*Chairman and CEO*



## Summary of AUTO1 and AUTO3 Clinical Programs

- AUTO1
  - High level of sustained CRs, durability of remissions highly encouraging
  - Well tolerated, despite high disease burden and heavy pre-treatment of the patients in this study
  - Currently enrolling Autolus' first Ph1b / 2 pivotal program with data planned in 2022
  - Adult ALL is an attractive commercial opportunity; initial target population is 3,000 patients in last line alone
  - ALLCAR study extension in iNHL and CLL ongoing
  - Opportunity to develop AUTO1 in Primary CNS Lymphoma, study start planned for Q1 2021
- AUTO3
  - AUTO3 continues to show a differentiated product profile supporting possible out-patient administration
  - Complete response rates are consistently high across all dose levels, data point to a potential to further improve on clinical outcome
  - Assessing a development strategy that potentially optimizes the development path in r/r DLBCL
  - Plan to update on next steps in Q1 2021

## Multiple clinical milestones planned through Q4 2020 / 2021

PRODUCT	INDICATION	TARGET	EVENT
AUTO1	Adult ALL	CD19	Ph1 long-term follow up, AL-1 data in 2022
AUTO1/22	Pediatric ALL	CD19 & CD22	Started Ph1 Q4 2020
AUTO1	PCNSL	CD19	Ph1 study start Q1 2021
AUTO3	DLBCL	CD19 & CD22	Ph1 long-term follow up, update on next steps
AUTO4	TRBC1+ Peripheral TCL	TRBC1	Ph1 interim data 2021
AUTO6NG	Neuroblastoma; Melanoma; Osteosarcoma; SCLC	GD2	Start Ph1 2021
AUTO7	Prostate Cancer	PSMA	Start Ph1 H1 2022
AUTO8	Multiple Myeloma	BCMA & CAR X	Start Ph1 study H1 2021
Allo Product	Undisclosed	Undisclosed	Start Ph1 H1 2021

Autolus  B Cell Malignancies  T Cell Lymphoma  Solid Tumors  Multiple Myeloma  Allogeneic Approach

## Q&A

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*Dr. Martin Pule (Founder and CSO)*

*Andrew Oakley (CFO)*

*Dr. Nushmia Khokhar (SVP, Head of Clinical Development)*

*Dr. Robert Chen (Executive Director, AUTO3 Program)*

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

