



Commitment to a Cure

Cellectis Clinical Update

December 2022

NASDAQ: CLLS

EURONEXT GROWTH: ALCLS.PA



Legal Notices

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All statements other than statements of present and historical facts regarding Collectis contained in this Presentation are forward-looking statements. You can identify certain forward-looking statements by words such as “anticipate,” “believe,” “can,” “could,” “estimate,” “expect,” “intend,” “is designed to,” “may,” “might,” “plan,” “potential,” “predict,” “objective,” “scheduled,” “should,” and “will,” or similar expressions (or the negative of these). Such forward-looking statements include, but are not limited to, statements regarding: the preliminary results for the AMELI-01 and BALLI-01 trials and the objectives of such trials, which remain ongoing; Collectis’ manufacturing capabilities and the scalability and cost thereof; the potential for profitable market access; Collectis’ expected cash runway and the projections taken into account therein; Collectis’ near term milestones and ability to achieve such expectations.

These forward-looking statements are subject to numerous risks and uncertainties, including with respect to the risk that initial, interim and preliminary data from clinical trials may change as more data becomes available, and that subsequent data may not bear out promising early results; the risk of disruptions or delays in our clinical trials as a result of failures by third-parties on whom we rely or arising out of regulatory inquiries or delays; the risk of manufacturing delays or problems; the risk associated with increased competition and/or adequate enrollment to support our clinical trials; and the various other risks associated with biopharmaceutical product candidate development, including those described under “Risk Factors” and “Special Note Regarding Forward-Looking Statements” in our Annual Report on Form 20-F filed with the Securities and Exchange Commission (the “SEC”) on March 3, 2022 and under “Risk Factors” in the subsequent reports that we file with the SEC. Actual results, performance or events may differ materially from those projected in any forward-looking statement. Except as required by law, we assume no obligation to update these forward-looking statements.

Legal Notices

References in this Presentation to Collectis' product candidates as "off-the-shelf" refers to the fact that our CAR T-cells are allogeneic, meaning they are derived from healthy donors rather than the patients themselves, which we believe allows for the development of cost-effective product candidates capable of being stored and distributed worldwide.

Caution should be exercised when interpreting preliminary results and results relating to a small number of patients or individually presented case studies — such results should not be viewed as predictive of future results.

Collectis at a Glance



4 Ongoing
Clinical Trials

40+ patients dosed in
Collectis-sponsored trials



**Global GMP
Facilities**

- Operational since 2021
- End-to-end manufacturing autonomy



Near-Term Clinical Catalyst

- UCART clinical data updates



\$103M

as of Sept 30, 2022

Expected Cash Runway
into 2024*

Diversified Partnerships with Industry Leaders



200+ patients dosed to date

- Potential revenues > **\$4B** in milestones + royalties
- **6 trials** sponsored by Collectis' licensed partners



- Cash position, includes cash, cash equivalent, financial assets and restricted cash
- Cash runway takes into account projected cash flow from operations, including payments Collectis expects to receive pursuant to strategic licensing agreements

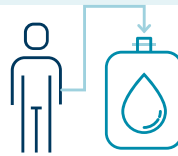
UCARTs are “Off-The-Shelf”

Scalable Manufacturing



Reduced cost
Scalable manufacturing:
1 batch = 100s of doses

Robustness



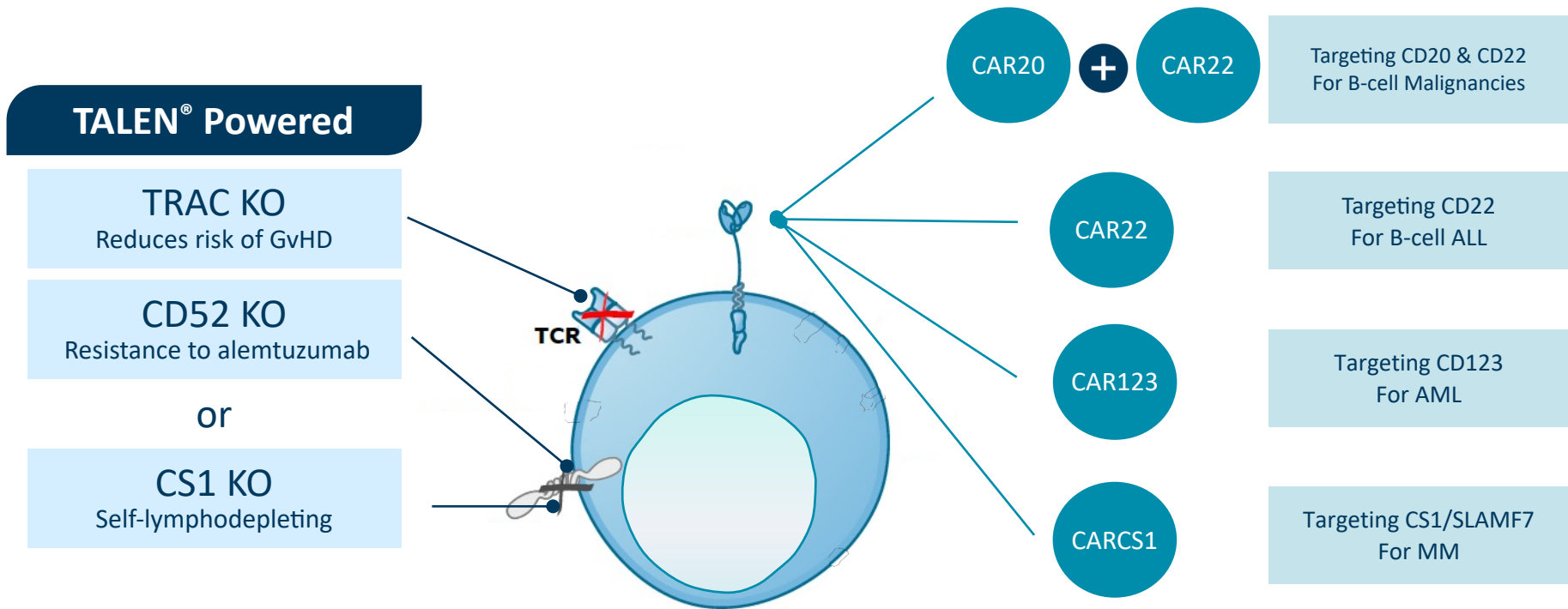
The goal is to provide
potency and consistency to
each patient

Market Access



Immediately available to
eligible patients

Cellectis' UCART Candidate Platform



AMELI-01: UCART123

AMELI-01: Preliminary Results from A Phase I Trial of UCART123v1.2, an Anti-CD123 Allogeneic CAR-T Cell Product, in Adult Patients with Relapsed or Refractory (R/R) CD123+ Acute Myeloid Leukemia

David A. Sallman¹, Daniel J. DeAngelo², Naveen Pemmaraju³, Shira Dinner⁴, Saar Gill⁵, Rebecca Olin⁶, Eunice S. Wang⁷, Marina Konopleva³, Eileen Stark⁸, Ana Korngold⁸, Asifa Haider⁸, Kate Backhouse⁸, Carolyn Figliola⁸, Daniel J. Lee⁸, Kathryn Newhall⁸, Mark G. Frattini⁸, Carrie Brownstein⁸, Gail J. Roboz⁹

¹H. Lee Moffitt Cancer Center, ²Dana-Farber Cancer Institute, ³MD Anderson Cancer Center, ⁴Northwestern Medical Center, ⁵University of Pennsylvania Perelman School of Medicine, ⁶University of California San Francisco, ⁷Roswell Park Comprehensive Cancer Center, ⁸Collectis, Inc., and ⁹Weill Cornell Medical College

Background and Introduction

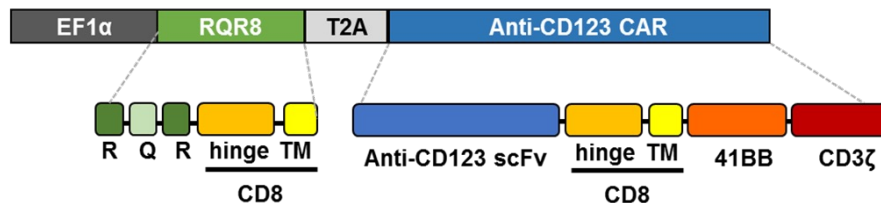
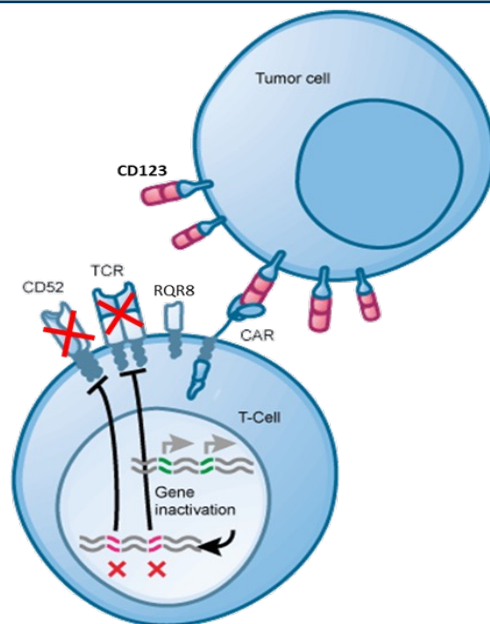
- It is estimated that 20,050 new cases and 11,540 deaths related to AML will occur in the US in 2022¹
- Outcomes for patients with R/R AML remain poor, with response rates <30% and an expected 5-year overall survival of <15%^{2,3}
- AMELI-01 (NCT03190278) is a phase I, open-label, dose-escalation trial evaluating the safety, tolerability, expansion, and preliminary activity of UCART123v1.2 given at escalating doses after LD with fludarabine and cyclophosphamide (FC) or FC with alemtuzumab (FCA) in patients with R/R CD123+ AML

¹ <https://www.cancer.org/cancer/acute-myeloid-leukemia/about/key-statistics.html>; ²Ganzel, C, et al. *Am J Hematol.* 2018; 93: 1074-1081; ³Döhner, H, et al. *Blood* 2017; 129 (4): 424–447.

UCART123v1.2: Allogeneic “Off-the-Shelf” T-cell Product

UCART123v1.2 (anti-CD123 scFv-41BB-CD3 ζ):

- CD123 is a validated therapeutic target in AML
- Genetically modified allogeneic T-cell product manufactured from non-HLA-matched healthy donor cells
- TRAC disrupted using TALEN[®] to eliminate TCR $\alpha\beta$ from the cell surface and reduce risk of GvHD
- CD52 disrupted using TALEN[®] to eliminate sensitivity to LD with alemtuzumab



AML, acute myeloid leukemia; CAR, chimeric antigen receptor; GvHD, graft-vs-host disease; HLA, human leukocyte antigen; LD, lymphodepletion; pts, patients; scFv, single-chain variable fragment; TCR, T-cell receptor; TRAC, T-cell receptor alpha constant; TALEN[®], Transcription Activator-Like Effector Nuclease.

AMELI-01 Study Design

Key inclusion criteria

- Relapsed or primary refractory AML ($\geq 5\%$ bone marrow blasts)
- Blasts expressing CD123
- PS of ≤ 1 and adequate organ function

Primary objective

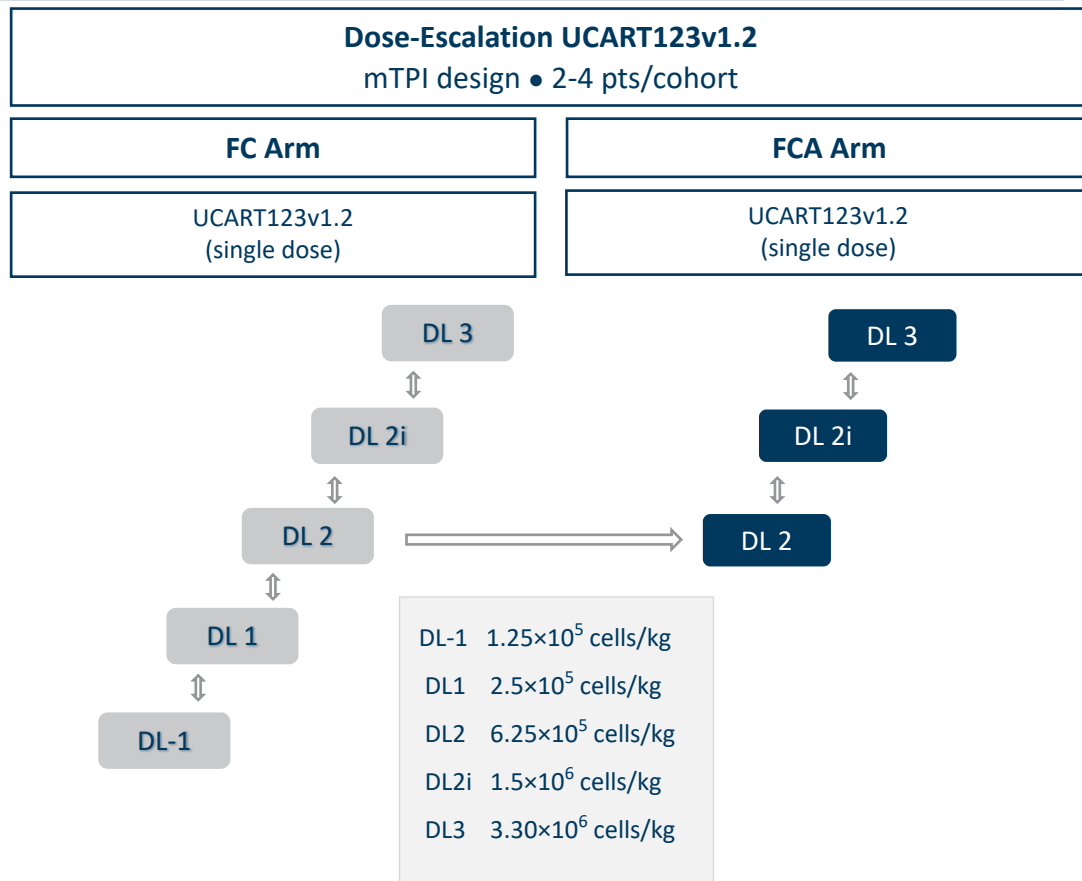
- Safety, tolerability, & MTD/RP2D of UCART123v1.2

Additional objectives

- Investigator-assessed response
- UCART123v1.2 expansion, trafficking, persistence in PB and BM
- Immune reconstitution

LD regimens:

- FC:** Fludarabine 30 mg/m² x 4d + Cyclophosphamide 750 mg/m² x 3d
- FCA:** Fludarabine 30 mg/m² x 4d + Cyclophosphamide 750 mg/m² x 3d + Alemtuzumab 12 mg/day x 4d



Baseline Characteristics

Characteristic	Total (N = 18*)
Age, median (range), years	57 (18-64)
Female, n (%)	8 (44)
ECOG PS 1, n (%)	17 (94)
ELN 2017 Classification, n (%)	
Adverse risk	14 (78)
Intermediate risk	3 (17)
Median baseline bone marrow blasts % (range)	37 (0-88)
Number of prior treatments, median (range)	4 (3-9)
Prior HSCT, n (%)	9 (50)
Cytogenetic and Molecular Abnormalities, n (%)	
TP53	6 (33)
FLT3-ITD	2 (11)
ASXL1	3 (17)
RUNX1	2 (11)
MECOM (EVI1)	2 (11)
MLL/KMT2A	1 (6)
Monosomal karyotype	3 (17)

*17 of the 18 pts who received LD with FC or FCA were treated with UCART123v1.2.

ECOG PS, Eastern Cooperative Oncology Group performance status; ELN, European Leukemia Net; FC, fludarabine + cyclophosphamide; FCA, FC + alemtuzumab; HSCT, hematopoietic stem cell transplantation; LD, lymphodepletion.

UCART123v1.2 - Related TEAEs (FC + FCA)

TEAE, n	FC		FCA		FC + FCA	
	FC Total [n=8] DL1=2; DL2=3; DL2i=2; DL3=1		FCA Total [n=9] DL2=8; DL2i=1		All patients N=17*	
	Any grade	Gr ≥3	Any grade	Gr ≥3	Any grade	Gr ≥3
CRS	8	2	9	2 ^o	17	4
HLH	1	1	1	0	2	1
ICANS	1	1	1	0	2	1
ALT increased	4	1	1	1	5	2
AST increased	4	1	1	1	5	1
Blood fibrinogen decreased	0	0	2	0	2	0
DIC	0	0	1	0	1	0
Confused state	1	0	1	0	2	0
Fatigue	2	0	0	0	2	0
Acute kidney injury	0	0	1	1	1	1
Bacterial infection	0	0	1	1	1	1
INR increased	0	0	1	1	1	1
Lymphocyte count decreased	0	0	1	1	1	1
Pulmonary edema	0	0	1	1	1	1
Sinus bradycardia	1	1	0	0	1	1
Vasogenic cerebral edema	1	1	0	0	1	1

DL, dose level; FC, fludarabine + cyclophosphamide; FCA, FC + alemtuzumab; GvHD, graft-vs-host disease; TEAE, treatment-emergent adverse event.; CRS, cytokine release syndrome; ALT, alanine aminotransferase; AST, aspartate aminotransferase; HLH, hemophagocytic lymphohistiocytosis; ICANS, immune effector cell associated neurotoxicity syndrome; DIS, disseminated intravascular coagulopathy; INR, international normalized ratio

*As of Oct. 10, 2022, 18 patients received LD, 17 received UCART123v1.2

^o 2 Grade 5 events (death) related to CRS

UCART123v1.2 - Serious TEAEs (All Cause – FC + FCA)

Serious TEAE, n (%)	FC		FCA		FC + FCA	
	FC Total [n=8] DL1=2; DL2=3; DL2i=2; DL3=1		FCA Total [n=9] DL2=8; DL2i=1		Total patients N=17*	
	Any grade	Gr ≥3	Any grade	Gr ≥3	Any grade	Gr ≥3
CRS	3	2	2	2 ^o	5	4
ICANS	1	1	0	0	1	1
Pneumonia	1	1	1	1	2	2
Pneumonia fungal	2	2	0	0	2	2
Febrile neutropenia	0	0	1	1	1	1
Fungemia	0	0	1	1	1	1
Hemorrhage intracranial	0	0	1	1	1	1
Large intestinal hemorrhage	1	1	0	0	1	1
Pericardial effusion	1	1	0	0	1	1
Septic shock	1	1	0	0	1	1

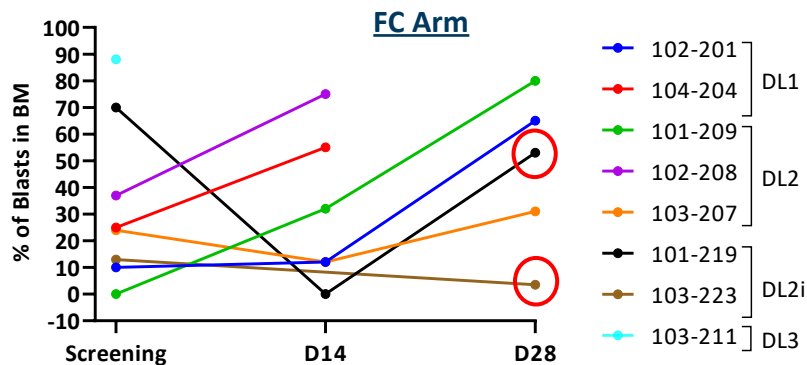
DL, dose level; FC, fludarabine + cyclophosphamide; FCA, FC + alemtuzumab; TEAE, treatment-emergent adverse event; CRS, cytokine release syndrome; ICANS, immune effector cell associated neurotoxicity syndrome

* As of Oct. 10, 2022, 18 patients received LD, 17 received UCART123v1.2

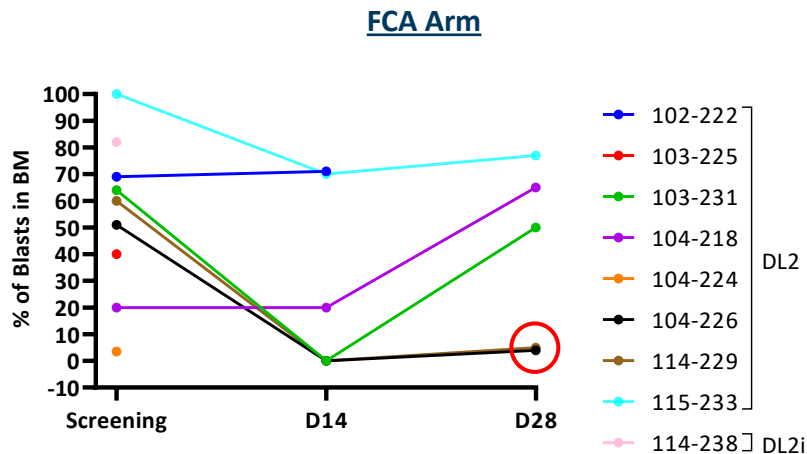
^o 2 Grade 5 events (death) related to CRS

No Difference In Infectious Complications With Alemtuzumab

Anti-Leukemic Activity Observed in 4/17 Patients



- FC arm
 - Patient **101-219** (DL2i): SD
 - Patient **103-223** (DL2i): MLFS

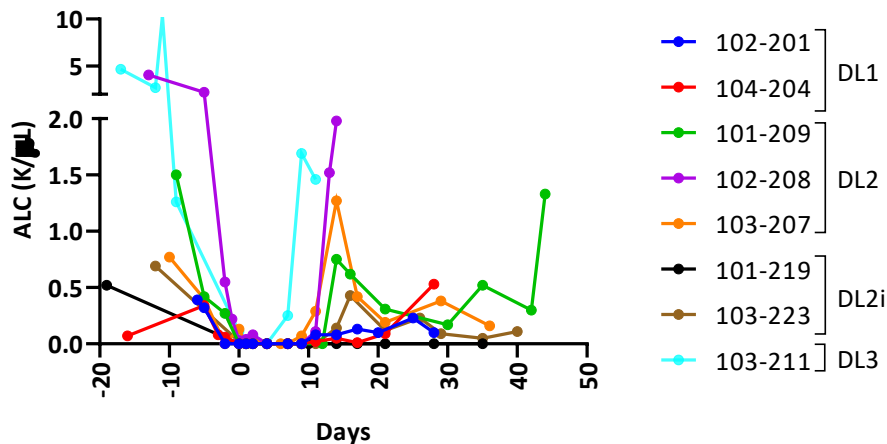


- FCA arm
 - Patient **114-229** (DL2): SD
 - Achieved greater than 90% BM blast reduction (60% to 5%) at D28
 - Patient **104-226** (DL2): MRD negative CR
 - Achieved CRi at D28 followed by MRD negative CR at D56

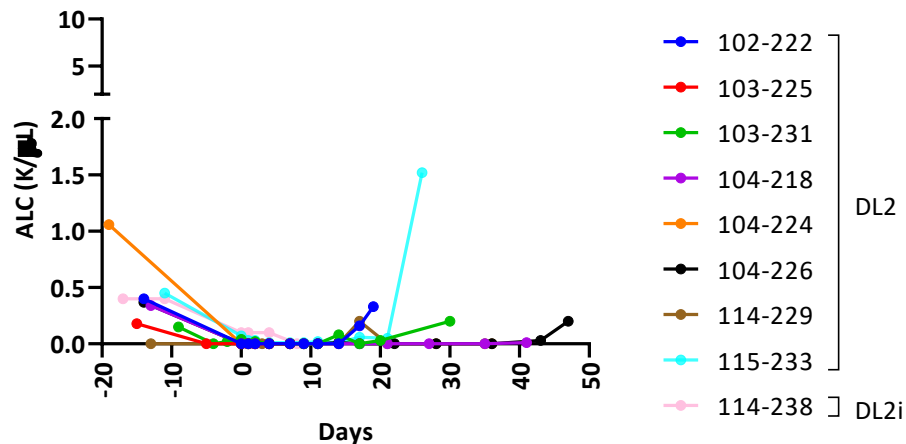
Addition of Alemtuzumab Results in Prolonged Lymphodepletion

Absolute Lymphocyte Counts

FC Arm

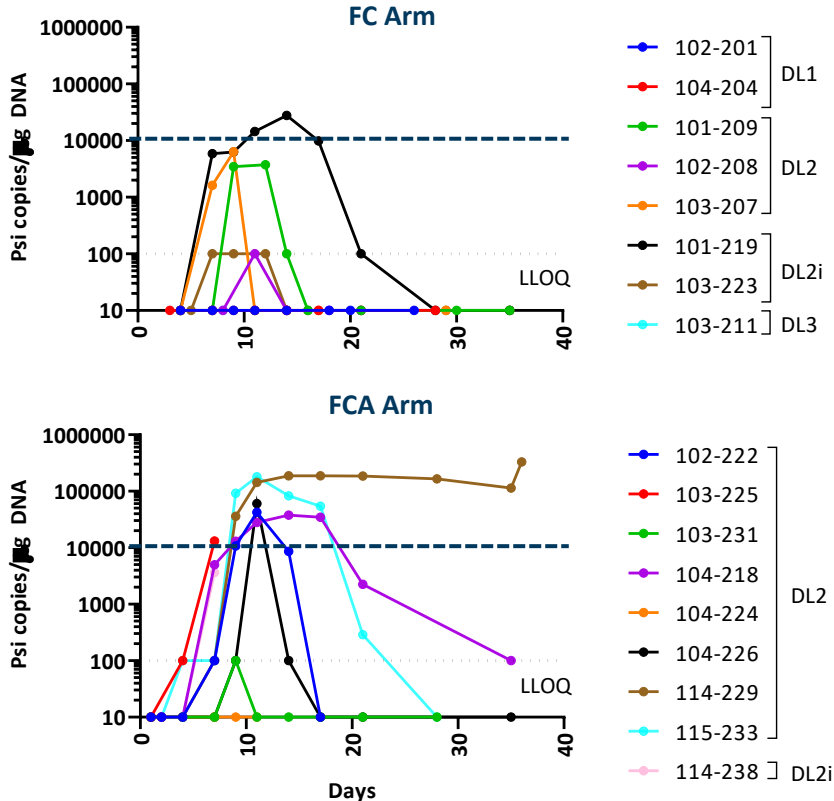


FCA Arm

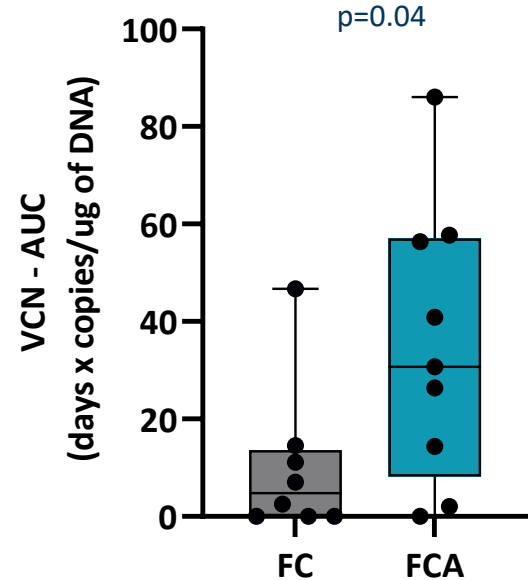


Addition of Alemtuzumab Results in Increased UCART123v1.2 Expansion

UCART123 Cell Expansion in WB by VCN

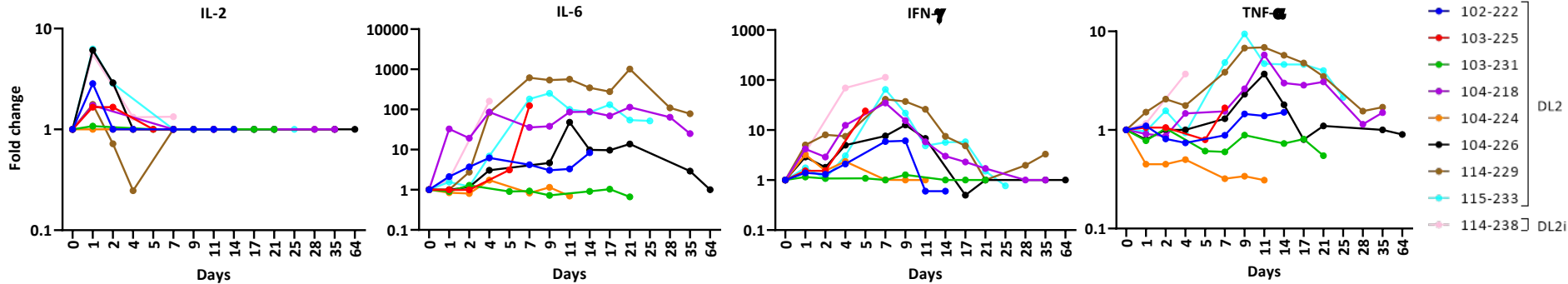


VCN AUC_(0-28days)

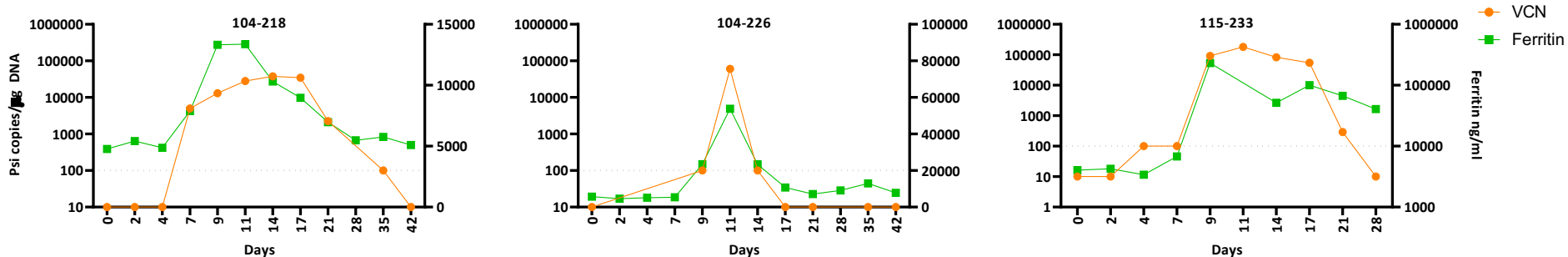


Cytokine Secretion and Ferritin Levels Correlated with UCART123v1.2 Cell Expansion

Cytokine Profile of All Patients from FCA Arm



Ferritin vs VCN in Select Patients from FCA Arm

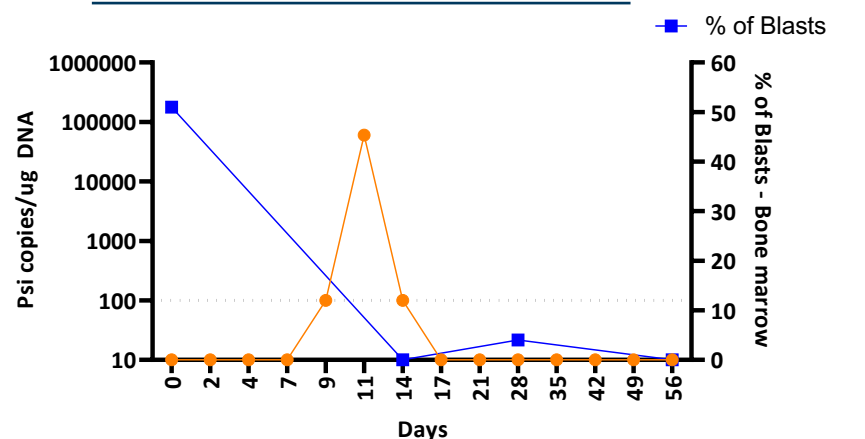


Patient 104-226 Achieved a Durable MRD Negative CR

Clinical Characteristics	
Age, Race, Sex	64 year old white female
ECOG PS	1
ELN 2017 Classification; WHO Classification	Adverse risk; AML with myelodysplasia-related changes
Cytogenetic and Molecular Abnormalities	45,XX,-7,t(10;12)(q24;p13)[5]; IDH1, EZH2
Number of prior treatments	5 - including allogeneic HSCT 2016
Past Medical History	MDS, 2011; Focal nodular hyperplasia of the liver, 2016

Response Summary	BM Biopsy Blast %	BM Aspirate Blast %	MRD	ELN Response
Screening Day -14	51%	Not done		
Day 14	0%	Not done		
Day 28	3.8%	4%	Pos 0.6%	CRi
Day 56	2.8%	0%	Neg	CR
Day 84	0%	0%	Neg	CR
FU 1, Day 181	2%	0%	Neg	CR
FU 2, Day 270	1%	0%	Neg	CR
FU 3, Day 365	0%	0%	Neg	CR

Tumor burden vs VCN in Patient 104-226

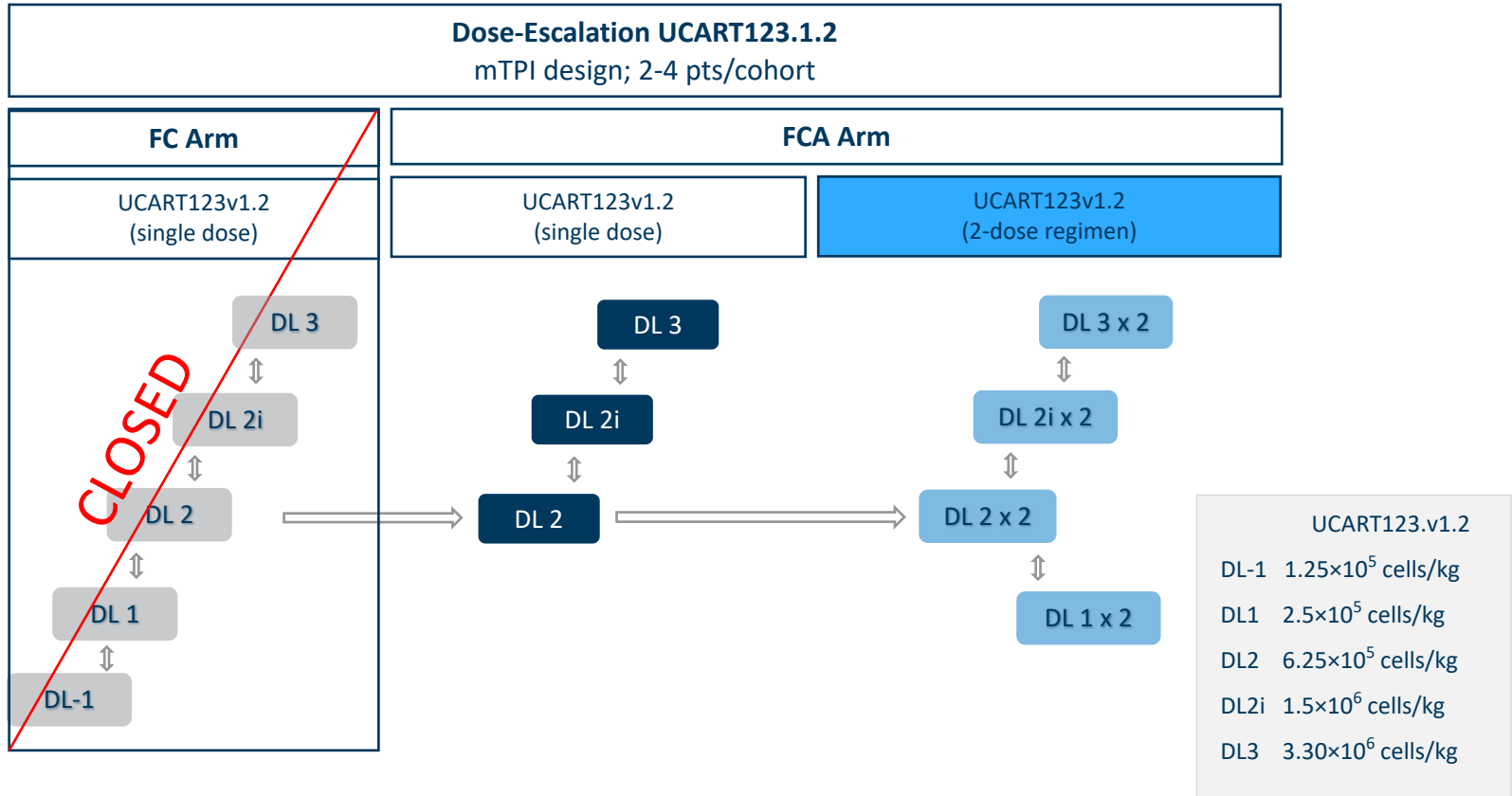


MDS myelodysplastic syndrome; HSCT Hemopoietic stem cell transplant; MRD minimal residual disease; CRi complete response with incomplete hematologic recovery; CR complete response

Translational Data From Patient 104-226 and Others Supports Use of a Two-Dose Regimen of UCART123v1.2

- UCART123v1.2 expansion correlates with reduction in tumor burden at DL2 (6.25×10^5 cells/kg) but at this dose, UCART123v1.2 cell function is not sufficient for sustained anti-leukemic activity in all patients
- A second dose would then be given to allow for additional UCART123v1.2 expansion and clinical activity after 10-14 days without the use of additional lymphodepletion
- The second peak of expansion in the setting of reduced disease burden should be safe and allow for clearance of residual disease
- The 2-dose regimen will initiate at DL2, a dose that has already been administered and cleared for safety as a single dose, and incorporate the use of prophylactic tocilizumab

AMELI-01 Amended Protocol with Two-Dose Regimen Design



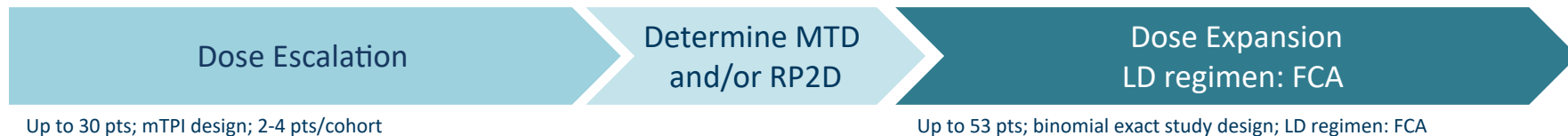
Conclusions

- Adding alemtuzumab to the FC regimen was associated with improved LD and significantly higher UCART123v1.2 cell expansion, which correlated with improved activity and cytokine profiles
 - One patient in the DL2 FCA arm achieved >90% blast reduction at Day 28
 - One patient in the DL2 FCA arm achieved a long term durable MRD negative CR (now past 12 months)
- Overall, these data support further study of UCART123v1.2 after FCA LD in pts with R/R AML
- Based on observed UCART123v1.2 expansion patterns and cytokine profiles, the study is enrolling patients in the FCA 2-dose regimen arm

BALLI-01: UCART22

UCART22 – BALLI-01 Trial Design

Phase I/IIa, Open Label Dose-escalation and Dose-expansion Study to Evaluate the Safety, Expansion, Persistence and Clinical Activity of UCART22 in Patients with Relapsed or Refractory CD22⁺ B-cell Acute Lymphoblastic Leukemia



Objectives	Key Eligibility Criteria	Dose Levels
<p>Primary/Secondary:</p> <ul style="list-style-type: none">Safety and tolerabilityMTD/RP2DResponse (Investigator assessed) <p>Exploratory</p> <ul style="list-style-type: none">UCART22 expansion and persistence, VCN and chimerism in WB and BMImmune reconstitution	<ul style="list-style-type: none">Patients aged 15 years to 70 yearsAdequate organ functionECOG PS ≤ 1B-ALL blast CD22 expression $\geq 70\%$Received ≥ 1 standard chemotherapy regimen and ≥ 1 salvage regimen	<ul style="list-style-type: none">DL-1 1×10^4 cells/kgDL1 1×10^5 cells/kgDL2 1×10^6 cells/kgDL2i 2.5×10^6 cells/kgDL3 5×10^6 cells/kg <p>F: 30 mg/m²/d x 4d; C: 1 g/m²/d x 3d; F: 30 mg/m²/d x 3d; C: 500 mg/m²/d x 3d; A: 20 mg x 3d</p>

NCT04150497

MTD: Maximum Tolerated Dose; RP2D: Recommended Phase 2 Dose; LD: Lymphodepletion; DL: Dose Level; F: Fludarabine; C: Cyclophosphamide; FC: Fludarabine + Cyclophosphamide;

FCA: Fludarabine + Cyclophosphamide + Alemtuzumab; NCCN: National Comprehensive Cancer Network; VCN: Viral Copy Number; WB: White Blood; BM: Bone Marrow;

ALL: Acute Lymphoblastic Leukemia

UCART22 Administration Shows Promising Safety Profile

Patient Characteristics (N=12)

Median age: 30 (20-61)

WHO classification:

- B-ALL with recurrent genetic abnormalities: 7 (58%);
- CRFL2 rearrangement: 4 (33%)

Median prior lines of therapy: 3 (2-6)

- Prior blinatumomab: 8 (73%)
- Prior inotuzumab: 5 (45%)
- Prior CD19 CART: 3 (27%)
- Prior HSCT: 3 (25%)

Safety: FCA Cohorts (N=6)

- 0** dose limiting toxicity
- 0** ICANS (immune effector cell associated neurotoxicity)
- 0** severe UCART22-related TEAEs (treatment emergent adverse events)
- 3** patients with mild to moderate CRS (cytokine release syndrome), Grade 1/2
- 1** patient with GII GvHD; skin only*

*not confirmed by biopsy; in context of re-activation of prior allogeneic bone marrow donor stem cells

Data Source: ASH 2021 Conference Presentation

CRFL2: Cytokine Receptor-Like Factor 2 ; FCA: Fludarabine, Cyclophosphamide, Alemtuzumab ; ICANS: Immune effector Cell-Associated Neurotoxicity Syndrome ; TEAE: Treatment Emergent Adverse Event

CRS: Cytokine Release Syndrome ; GvHD: Graft versus Host Disease

N=11 for calculating patients with prior therapy

Patient 1

Age	34		
Sex	Male		
Prior Therapies	1: Induction: GRALL 2014 (Intensive chemotherapy) – Daunorubicin; vincristine; cyclophosphamide; L-asparaginase; mercaptopurine; methotrexate; etoposide; cytarabine; prednisone/dexamethasone 2: Salvage: Vincristine; HiDAC; vindesine; ifosfamide; thioguanine; PEG-asparaginase; mercaptopurine; methotrexate; daunorubicin; dexamethasone; followed by allogeneic HSCT (matched related donor) 3: Salvage: Vincristine; PEG-asparaginase; dexamethasone + venetoclax followed by autologous CD19 CART 4: Salvage: Venetoclax		
Cytogenetics at Screening	Very complex (>5 abnormalities): 46, XY, -1,+3,-4,-5,-6,+11,+14,-16,-17,+MAR[8]/46, XY[12]		
Molecular at Screening	IKZF1		
CRS	Days 3-8	Grade 1	
Best Response	MRD-negative CRi (currently Month 7)		

Patient 2

Age	24
Sex	Female
Prior Therapies	1: AALL1131 high-risk arm (Intensive chemotherapy) – Vincristine; daunorubicin; prednisone/dexamethasone; cyclophosphamide; cytarabine; mercaptopurine; PEG-asparaginase; methotrexate 2: Salvage: Vincristine; daunorubicin followed by autologous CD19 CART 3: Salvage: Liposomal vincristine + venetoclax followed by allogeneic HSCT (haploidentical donor)
Cytogenetics at Screening	46, XX, inv(3),inv(11)[2]/46, XX, t(1;10)(p10;p10)[1]/46, XX, +11[1]/46, XX, inv(11)[1]/46, XX[14]
Molecular at Screening	Unknown
CRS	None
Best Response	MRD-negative MLFS (until Day 84), now MRD-positive MLFS (currently Day 117)

Patient 3

Age	57		
Sex	Male		
Prior Therapies	1: Induction: Vincristine; daunorubicin; cyclophosphamide; PEG-asparaginase; prednisone + consolidation: blinatumomab ; cytarabine; methotrexate; vincristine; mercaptopurine; dexamethasone; followed by allogeneic HSCT (haploidentical donor) 2: Salvage: Vincristine + dexamethasone followed by autologous CD19 CART 3: Salvage: Vinblastine; cyclophosphamide + inotuzumab ozogamicin 4: Salvage: Vincristine + dexamethasone		
Cytogenetics at Screening	Normal		
Molecular at Screening	Normal		
CRS	Day 8	Grade 1	Tocilizumab x1
Best Response	MRD-negative CR (currently Day 71)		

Summary of UCART22 DL3 data

- Five subjects were dosed at DL3 (5×10^6 cells/kg) with UCART22 Process 1 (P1) using FCA LD:
 - No safety issues, no Grade 2 or higher CRS
 - 3 out of 5 clinical responses (60% ORR): 1 MRD neg. **CR**, 1 MRD neg. **CRi**, 1 **MLFS**
 - All 3 of the responders failed multiple lines of prior therapy including chemotherapy, CD19 directed autologous CAR T cell therapy, and allogeneic stem cell transplant. Additionally, 1 of the 3 failed prior blinatumomab and inotuzumab.

Next steps for BALLI-01

- Dosing started with UCART22 Process 2 (P2) made by Cellectis
- UCART22 P2 product candidate has shown a significantly higher potency *in vitro* than P1
- 1st subject dosing at DL2 (1×10^6 cells/kg)
- Next data set with P2 expected in 2023

SUMMARY

■ AMELI-01 (UCART123)

- Adding alemtuzumab to the FC lymphodepletion regimen was associated with improved LD and significantly higher UCART123v1.2 cell expansion, which correlated with improved activity
 - One patient in the DL2 FCA arm achieved >90% blast reduction at Day 28
 - One patient in the DL2 FCA arm achieved a long term durable MRD negative CR (now past 12 months)
- The study is enrolling patients in the FCA 2-dose regimen arm

■ BALLI-01 (UCART22)

- 3 out of 5 clinical responses (60% ORR) at DL3: 1 MRD neg. CR, 1 MRD neg. CRi, 1 MLFS
- UCART22 Process 2 (P2) made by Cellectis at the Raleigh facility is now being used in the clinical study.

Discover, Create, Develop, Produce and Test



New York, New York

Innovation, Clinical Development

~25,000 sq ft. facility

- ✓ Gene Editing platform – TALEN®
- ✓ I/O discovery platform
- ✓ Gene therapy discovery platform
- ✓ Clinical development



Paris, France

HQ, PD/AD, Starting Materials

~55,000 sq ft. facility

- ✓ Process & analytical development
- ✓ Raw materials manufacturing
- ✓ QC labs
- ✓ Warehouse
- ✓ Cryogenic Storage rooms



Raleigh, North Carolina

UCART – Clinical & potential for Commercial

~82,000 sq ft. facility

- ✓ Cell therapy GMP manufacturing
- ✓ QC labs
- ✓ Warehouse
- ✓ Cryogenic Storage rooms

Expected 2023 Milestones

UCART22 r/r B-ALL

Data update with
in-house
manufactured
product

UCART123 r/r AML

Data update with
2-dose regimen

UCARTCS1 r/r MM

Enroll DL1 with FC
lymphodepletion

UCART20x22 r/r NHL

1st in human data
update

Thank You

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