Autolus

Developing Next Generation Programmed T Cell Therapies

ASCO Analyst Call

June 2, 2023

Disclaimer

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Agenda

- Welcome and Introduction: Julia Wilson, Communications Consultant
- Opening Remarks: Dr. Christian Itin, CEO
- ASCO Data: Dr. Claire Roddie
- Building the obe-cel Opportunity and Next Steps: Dr. Christian Itin, CEO
- Q&A: Dr. Christian Itin and Dr. Claire Roddie

Building a fully integrated CAR T company

Expanding excellence in R&D and manufacturing to commercialization

Obe-cel met primary endpoint in pivotal study

- Lead product candidate obe-cel potentially best-in-class for relapsed/ refractory adult acute lymphoblastic leukemia (ALL)
- Pivotal Phase 2 trial in ALL met primary endpoint
- Attractive profile in B-NHL indications

Pipeline

- Pipeline built on modular innovation targeting cancers with limited treatment options

Scalable manufacturing

- In house cell manufacturing for clinical trial supply
- Commercial fit-for-purpose cell manufacturing facility running through validation process
- Planned annual capacity of at least 2,000 batches to service global demand in ALL

Collaboration

- Collaboration worth $250 million with Blackstone Life Sciences, of which $220M already received, to develop obe-cel in adult ALL
- Established technology collaborations with Moderna, BMS and Cabaletta
- Opportunity for partnering of pipeline programs

Strong cash position

- Blue chip investor base with recent fundraise adding $164M gross proceeds
- Q1 2023 cash position of $343.4M
- Strong cash position to deliver on current strategy through approval of obe-cel

FELIX trial results

ASCO 2023

SAFETY AND EFFICACY OF OBECABTAGENE-AUTOLEUCEL (OBE-CEL, AUTO1), A FAST-OFF RATE CD19 CAR, IN RELAPSED/REFRACTORY ADULT B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA (R/R B-ALL). TOP LINE RESULTS OF THE PIVOTAL FELIX STUDY

C. RODDIE, K.S. SANDHU, E. THOLOULI, P. SHAUGHNESSY, P. BARBA, M.N. GUERREIRO, D. YALLOP, M. ABEDI, S. CHAGANTI, A. GHOBADI, J. YARED, A. LOGAN, M.R. BISHOP, Y. ZHANG, W. BRUGGER, M. PULE, J.H. PARK, D.J. DEANGELO, E. JABBOUR, ON BEHALF OF THE FELIX INVESTIGATORS

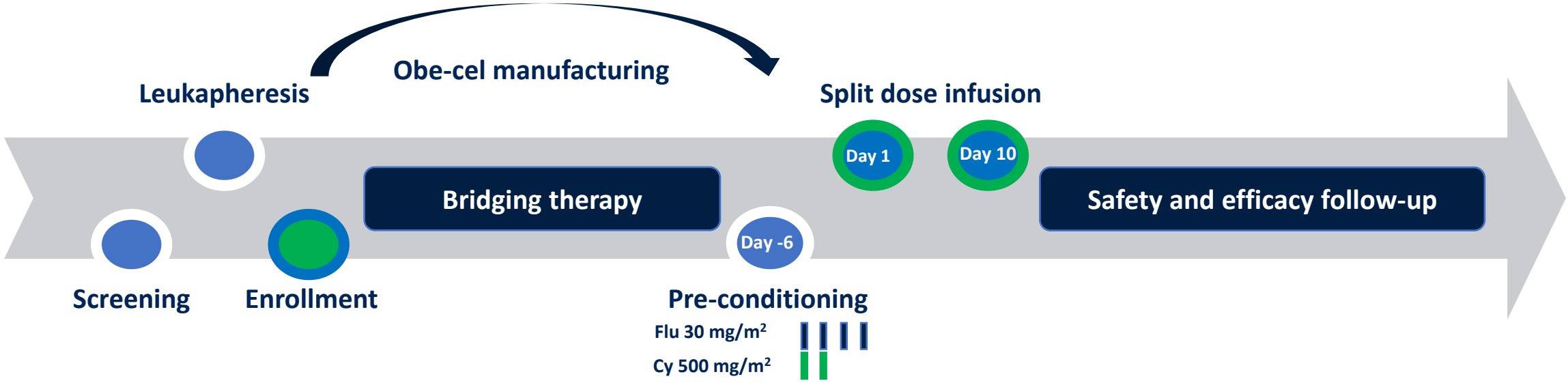
Background

- CD19 CAR-T therapy has revolutionized the field of R/R B-ALL[1]
- Obe-cel is an autologous CD19 CAR with a fast off-rate CD19 binding domain designed to mitigate safety concerns and improve persistence[2,3]
- The clinical activity of obe-cel has been tested in R/R pediatric[2] and adult B-ALL[3], and more recently in other B-cell malignancies (NCT02935257)[4]

We present results from adult patients with r/r B-ALL treated with obe-cel in the pivotal FELIX Phase II study (NCT04404660)

1 Pasvolsky O et al., Blood Adv 2023 [Epub ahead of print]; 2 Ghorashian S et al., Nat Med 2019;25(9):1408–14;
3 Roddie C et al., J Clin Oncol 2021;39(30):3352–63; 4 Roddie C et al., Blood 2022;140(Suppl 1):7452–3, ASH abstract

FELIX study: obe-cel for adults with r/r CD19+ B-ALL



Pre-conditioning

Tumor burden-adjusted split dosing to maximize the therapeutic index

Pre-conditioning	Tumor burden-adjusted split dosing to maximize the therapeutic index		
BM blasts ≤20%	100 x 10^6 CAR T cells	CRS Grade <2 No ICANS	310 x 10^6 CAR T cells
BM blasts >20%	10 x 10^6 CAR T cells		400 x 10^6 CAR T cells

94% of infused patients received both obe-cel infusions

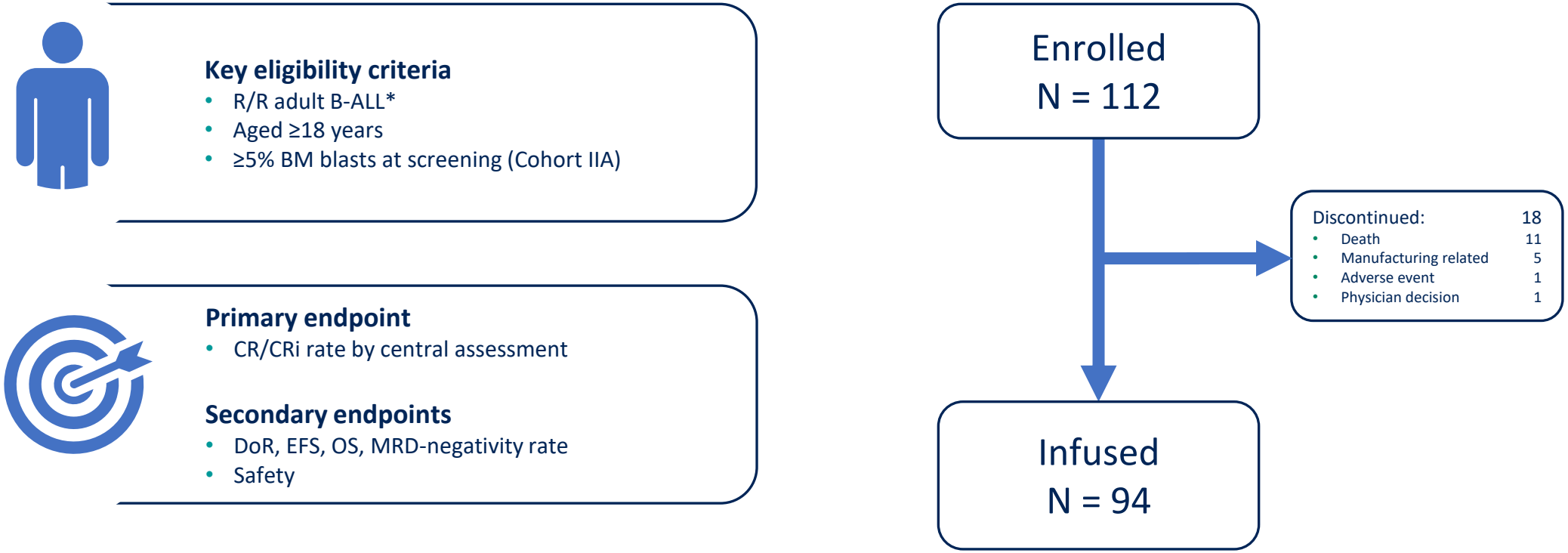
FELIX: eligibility, endpoints, and disposition

84% of enrolled patients were infused with obe-cel

Key eligibility criteria
- R/R adult B-ALL*
- Aged ≥18 years
- ≥5% BM blasts at screening (Cohort IIA)

Primary endpoint
- CR/CRi rate by central assessment

Secondary endpoints
- DoR, EFS, OS, MRD-negativity rate
- Safety



Median duration of follow-up: 9.5 months (1.9–19.0)

Data cut-off date: 16 March 2023

*** R/R B-ALL: Primary refractory; First relapse if first remission ≤12 months; R/R disease after ≥2 lines of systemic therapy; R/R disease after allogeneic transplant; R/R Philadelphia chromosome-positive ALL if intolerant to/failed two lines of any TKI or one line of second-generation TKI, or if TKI therapy is contraindicated**
Enrollment: all eligibility criteria met and the leukapheresate accepted for manufacturing

FELIX: baseline characteristics

Heavily pre-treated patients with high disease burden

	Total infused (N = 94)
Age years, median (range)	50 (20–81)
Gender male/female, n	47/47
Philadelphia chromosome-positive, n (%)	25 (26.6)
Prior therapies, median (range) ≥3 prior lines, n (%)	2 (1–6) 29 (30.9)
Refractory to last prior line of therapy, n (%)	50 (53.2)
Prior allogeneic SCT, n (%)	36 (38.3)
Prior blinatumomab, n (%) Prior inotuzumab, n (%) Prior blinatumomab and inotuzumab, n (%)	33 (35.1) 30 (31.9) 15 (16.0)
BM blasts % at screening, median (range)	49.5 (6–100)
BM blasts % at pre-conditioning, median (range)	41.1 (0–100)
Extramedullary disease at pre-conditioning, n (%)	18 (19.1)

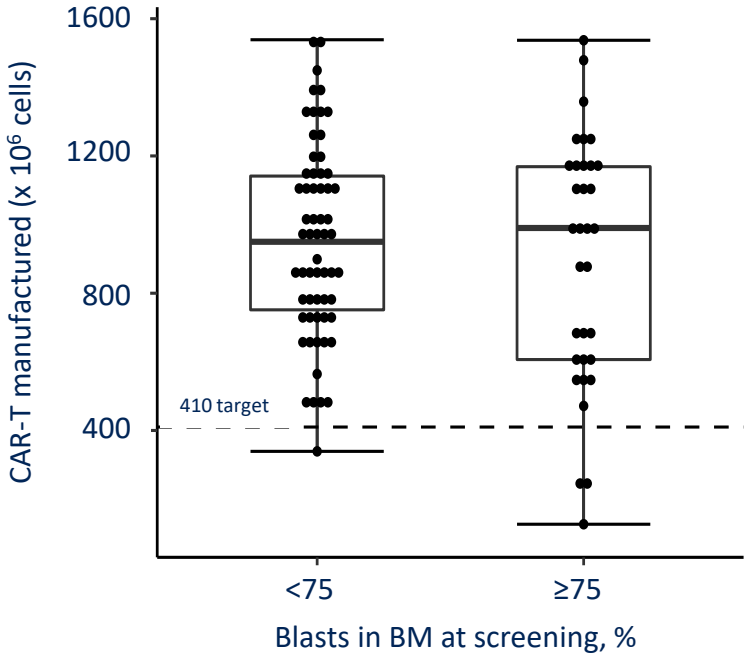
FELIX: obe-cel manufacturing

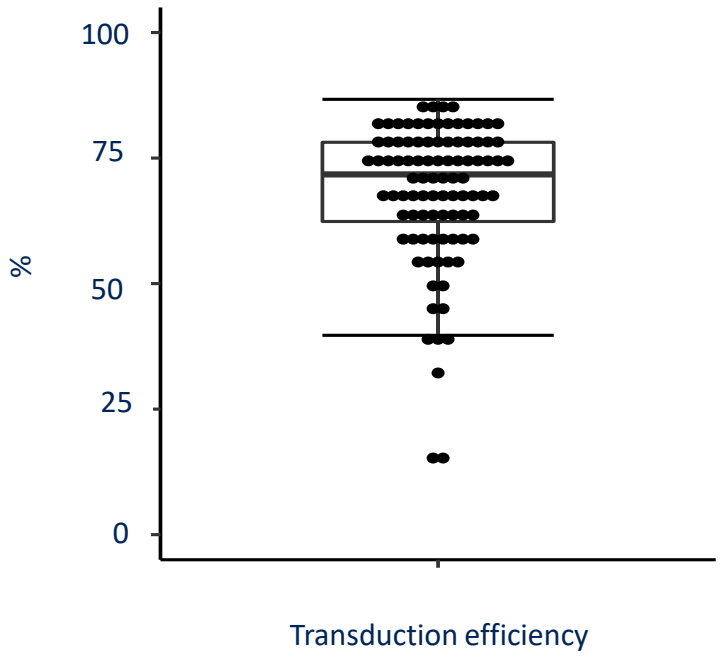
Manufacturing quality and logistics were reliable and consistent

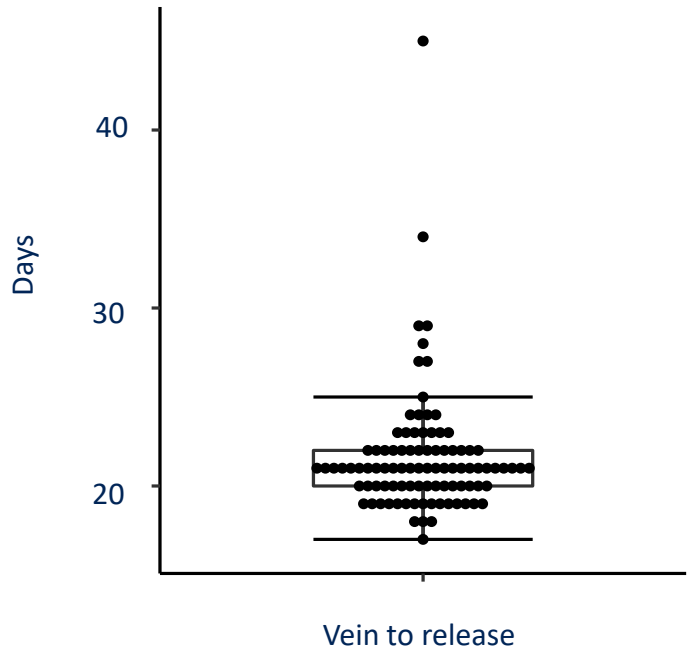
96% of products reached target dose

Median transduction efficiency of **72%**

Median **21 days** from vein to release

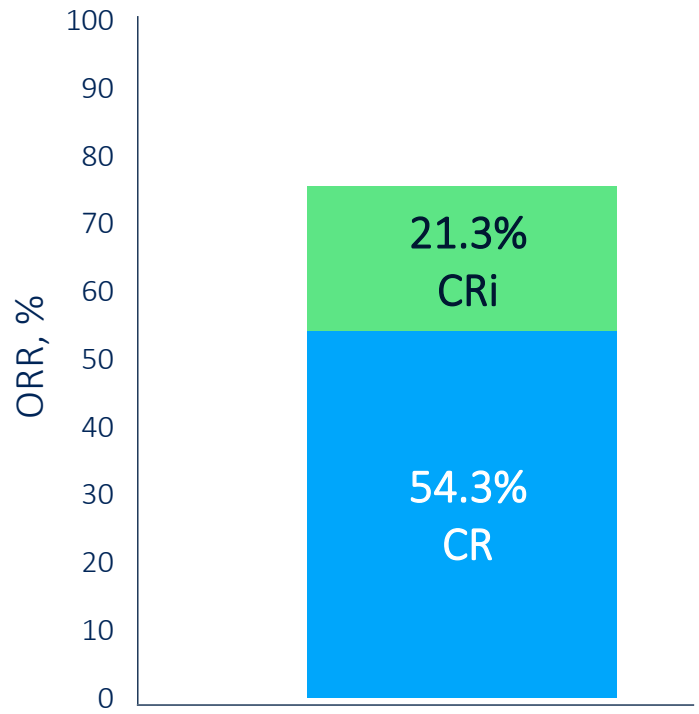






FELIX: disease response per IRRC assessment

76% of infused patients achieved CR/CRi



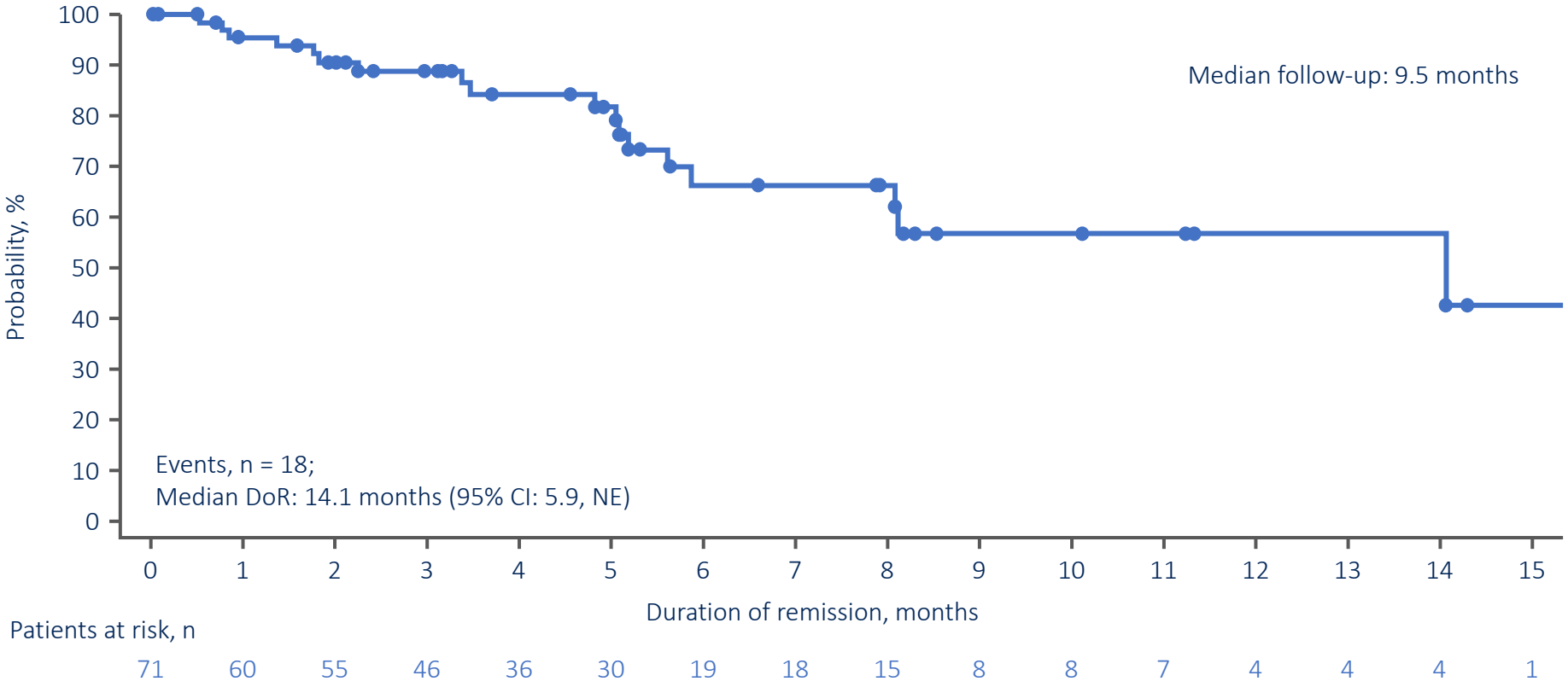
ORR: 76%
95% CI (66, 84)
p<0.0001*

97% of responders with evaluable samples were MRD negative at 10^{-4} level by flow cytometry

*One-sided p-value from the exact test on H0: ORR ≤40% vs H1: ORR >40%
CR, complete remission, CRi, CR with incomplete blood count recovery; IRRC, independent response review committee; MRD, minimal residual disease; ORR, overall remission rate

FELIX: duration of remission

61% responders in ongoing remission without subsequent anti-cancer therapies



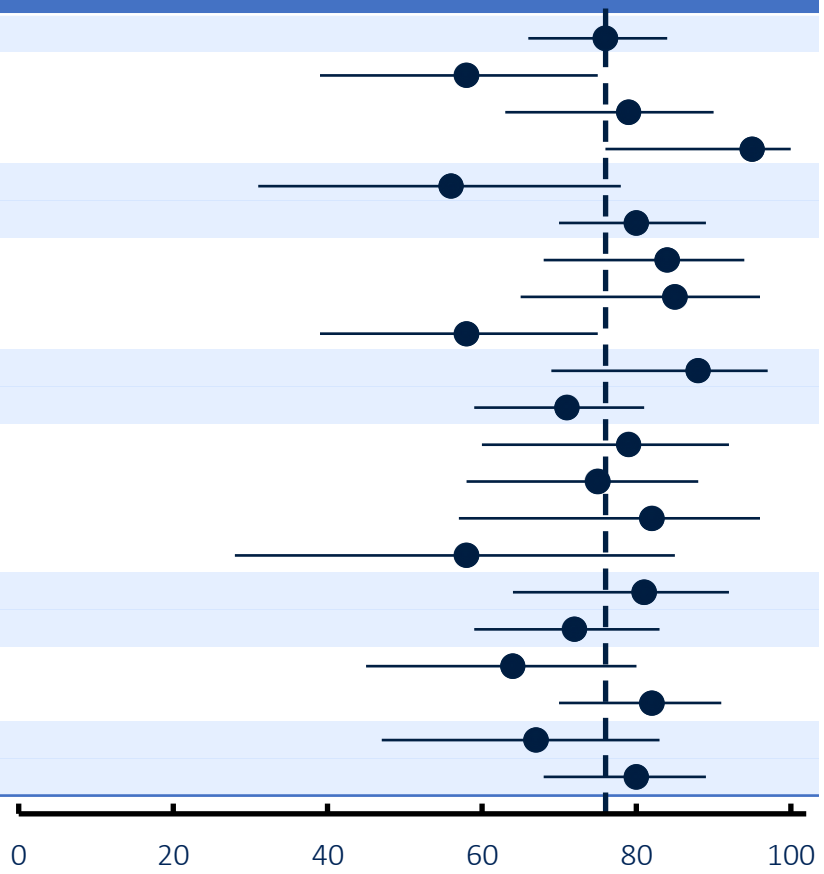
13% responders who proceeded to SCT while in remission were censored at the time of SCT

NE, not estimable

FELIX: subgroup analysis of CR/CRi (IRRC assessment)

High risk subgroups include EMD and high BM blasts at pre-conditioning

Subgroup		Total N (%)	ORR % (95% CI)
Overall		94 (100)	76 (66, 84)
Age, years	18–39	31 (33)	58 (39, 75)
	40–64	42 (45)	79 (63, 90)
	≥65	21 (22)	95 (76, 100)
EMD prior to pre-conditioning	Yes	18 (19)	56 (31, 78)
	No	76 (81)	80 (70, 89)
BM blasts % prior to pre-conditioning	≤20	37 (39)	84 (68, 94)
	>20–75	26 (28)	85 (65, 96)
	>75–100	31 (33)	58 (39, 75)
Philadelphia chromosome	Yes	25 (27)	88 (69, 97)
	No	69 (73)	71 (59, 81)
Previous lines of therapy	1	29 (31)	79 (60, 92)
	2	36 (38)	75 (58, 88)
	3	17 (18)	82 (57, 96)
	≥4	12 (13)	58 (28, 85)
Previous allogeneic SCT	Yes	36 (38)	81 (64, 92)
	No	58 (62)	72 (59, 83)
Previous blinatumomab	Yes	33 (35)	64 (45, 80)
	No	61 (65)	82 (70, 91)
Previous inotuzumab ozogamicin	Yes	30 (32)	67 (47, 83)
	No	64 (68)	80 (68, 89)



CR, complete remission; CRi, CR with incomplete blood count recovery; EMD, extramedullary disease; IRRC, independent response review committee; ORR, overall remission rate

FELIX: safety – CRS and ICANS

Low rates of Grade ≥3 CRS and/or ICANS were observed

	BM blasts ≤20% at pre-conditioning (N = 37)	BM blasts >20% at pre-conditioning (N = 57)	All infused patients (N = 94)
CRS			
Any grade, n (%)	24 (64.9)	47 (82.5)	71 (75.5)
Grade ≥3, n (%)	1 (2.7)	2 (3.5)	3 (3.2)
ICANS			
Any grade, n (%)	5 (13.5)	19 (33.3)	24 (25.5)
Grade ≥3, n (%)	1 (2.7)	6 (10.5)	7 (7.4)

- Tocilizumab and steroid was used to treat CRS in 53/94 (56%) and 16/94 (17%) patients, respectively
- 3/94 (3%) patients required vasopressor for treatment of CRS
- 6/7 (86%) Grade ≥3 ICANS were observed among patients with >75% BM blasts at pre-conditioning

CRS, cytokine release syndrome; ICANS, immune effector cell associated neurotoxicity syndrome

FELIX: safety – TEAEs

TEAEs that occurred in ≥20% of patients regardless of causality	All infused patients (N = 94)	
	Any grade, %	Grade ≥3, %
Patients with any TEAE	98.9	78.7
CRS	75.5	3.2
Neutropenia / neutrophil count decreased	39.4	36.2
Thrombocytopenia / platelet count decreased	28.7	25.5
Nausea	28.7	1.1
Pyrexia	27.7	1.1
Febrile neutropenia	25.5	25.5
Headache	25.5	0
ICANS	25.5	7.4
Diarrhea	24.5	0
Anemia	22.3	19.1
Hypotension	20.2	4.3

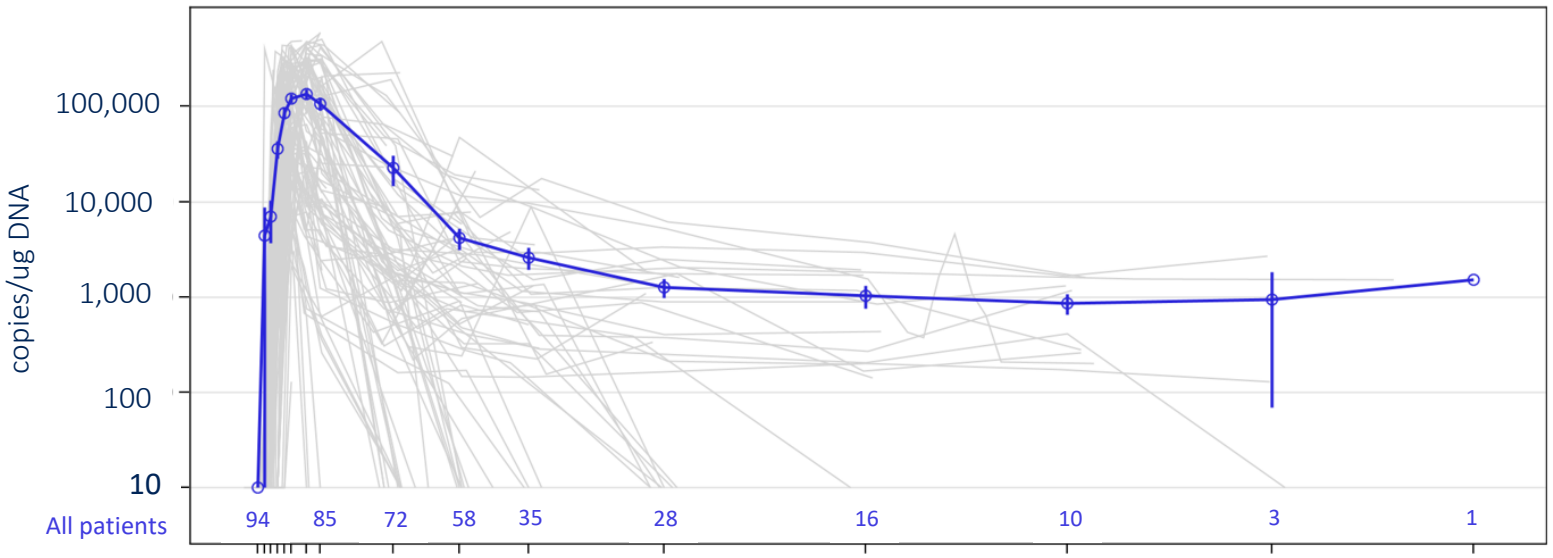
- The most common Grade ≥3 TEAEs were neutropenia (36.2%), thrombocytopenia (25.5%), febrile neutropenia (25.5%), and anemia (19.1%)
- 1/94 (1%) death considered obe-cel-related per investigator assessment (HLH and neutropenic sepsis)

CRS, cytokine release syndrome; HLH, hemophagocytic lymphohistiocytosis; ICANS, immune effector cell associated neurotoxicity syndrome; TEAE, treatment emergent adverse event

FELIX: obe-cel expansion and persistence

CAR T cellular kinetics are consistent with the ALLCAR19 study1

Mean (SE) for CAR-T therapy by PCR in peripheral blood



	FELIX (N = 94)	ALLCAR19 (N = 20)
C_{max}, copies/ug Geo-Mean, CV%	114,982 (287.6)	127,152 (109.7)
T_{max}, days Median, range	14 (2–55)	13 (7–21)
$AUC_{0–28d}$, copies/ug×d Geo-Mean, CV%	1,139,380 (225.4)	1,251,802 (108.9)

AUC, area under the curve; CV, coefficient of variation; Geo, geometric; PCR, polymerase chain reaction; SE, standard error

1Roddie C et al., J Clin Oncol 2021;39(30):3352–63

FELIX: conclusions

- Obe-cel infusion resulted in a CR/CRi rate of 76%, with 97% of responders becoming MRD negative
  - With a median of 9.5 months' follow-up, 61% of responders remain in remission
- Obe-cel infusion resulted in very low rates of Grade ≥3 CRS (3.2%) and low rates of Grade ≥3 ICANS (7.4%)
  - In total, obe-cel was evaluated in 94 patients with r/r B-ALL
  - 31% of patients had received ≥3 prior lines of therapy and 33% had >75% marrow burden at infusion
- Robust manufacturing process, with product released for 94% of leukapheresed patients and a median vein to delivery of 21 day
  - 84% of enrolled patients received obe-cel
- Excellent CAR T-cell engraftment with C_{max} of 114,982 copies/ug DNA and T_{max} at 14 days

Acknowledgments

- **The authors would like to acknowledge and thank:**
  - Patients, families, friends, and caregivers
  - Study investigators and coordinators
  - Healthcare staff at the study sites
  - Autolus Therapeutics

Christian Itin

Building the obe-cel opportunity and next steps

FELIX study suggests improved safety and efficacy profile vs SoC

Current standard of care for r/r adult ALL[1]

	STANDARD OF CARE		FELIX
	Blincyto®[2] (blinatumomab)	**Besponsa®[3] (inotuzumab ozogamicin)**	**Obe-cel (obecabtagene autoleucel)**
N	271	109	94
ORR	44%	81%	76% (64% on ITT)
median DoR	7.3m	4.6m	14.1m §
CRS ≥ Grade 3	26%	Not reported	3%
Neurotox any Grade	65%	NA	26%
Neurotox ≥ Grade 3	13%	NA	7%
Subsequent SCT post treatment	24%	41%	13%
Other notable observations	NA	14% Hepatic VoD	3% vasopressor use

§ Based on a median follow up of 9.5 months with a range of 1.9 to 19 months

1. Data are not from head-to-head clinical testing and should not be viewed as comparative data

2. Kantarjian et al., 2017/ USPI (product label) 3. Kantarjian et al., 2016/ USPI (product label) 4. Roddie et al. ASCO 2023
The estimates of EFS/PFS are read from the KM curves. The efficacy data for blinatumomab and inotuzumab ozogamicin data are based on the ITT population, FELIX on modified ITT

High grade ICANS are indicative of intensity of patient management

Relapsed/refractory ALL patients need therapies with high level of clinical activity and well manageable safety profile[1]

	Tecartus(R)		Obe-cel
	ZUMA-3[2]	ROCCO[3]	FELIX[4]
N	55	76	94
N >5% tumor burden at apheresis	55	52	94
ORR	71% (55% on ITT)	91% (64 of 70) (31% CR at apheresis)	76% (64% on ITT)
median DoR	13.6m	NA	14.1m §
CRS ≥ Grade 3/4	24%	6% (5/75)	3%
Neurotox any Grade	60%	59%	26%
Neurotox ≥ Grade 3/4	25%	39%* (29/76)	7%#
Subsequent SCT post treatment	18%	14%	13%
Other notable observations	40% vasopressor use [5]	NA	3% vasopressor use

*ROCCO: All ICANS ≥ G3 appear to have occurred in patients with elevated tumor burden. 6 patients died with ICANS & infection.
§ FELIX median follow up of 9.5 months with a range of 1.9 to 19 months
# FELIX: 6 of 7 patients with ICANS ≥ G3 had more than 75% tumor burden at lymphodepletion

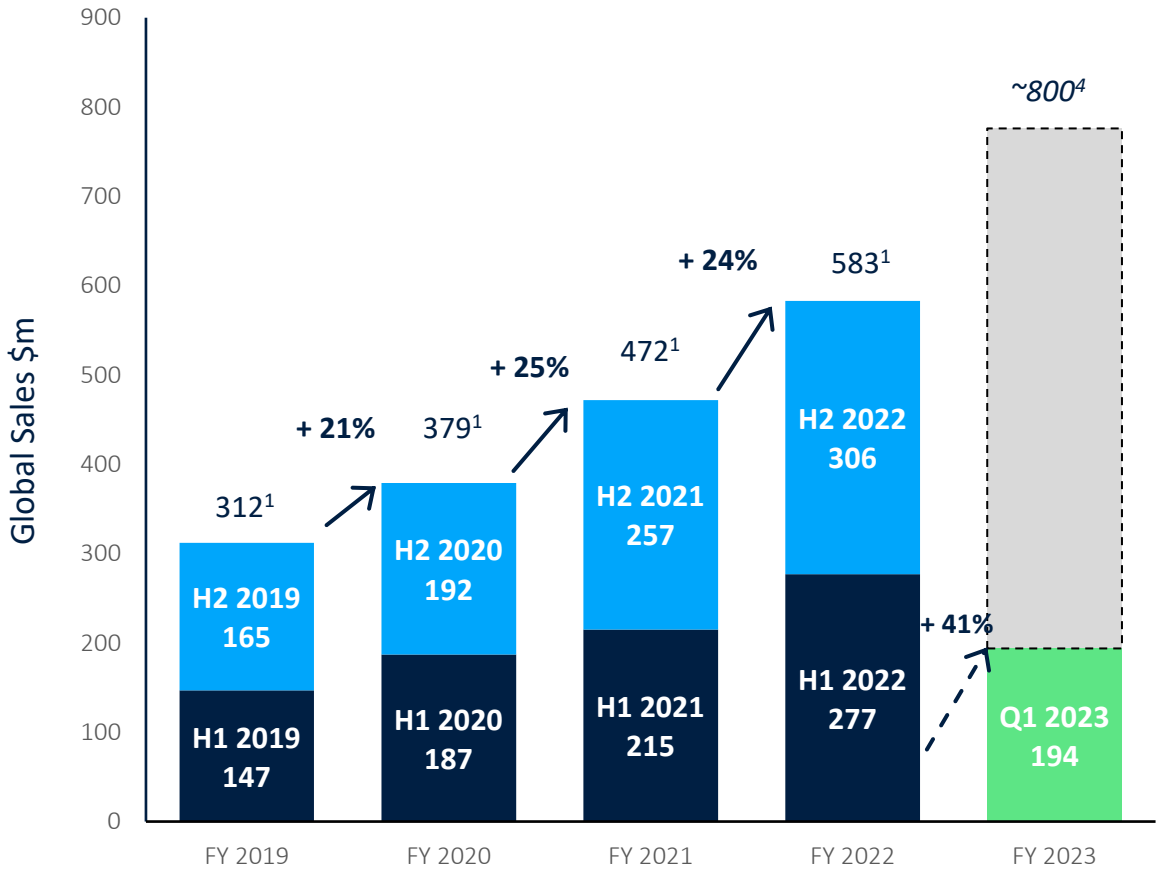
1. Data are not from head-to-head clinical testing and should not be viewed as comparative data

2. Shah et al. Lancet 2021 5. Shah et al. ASCO 2021 3. Roloff et al. ASCO 2023. 4. Roddie et al. ASCO 2023
The estimates of EFS/PFS are read from the KM curves. The efficacy data in ZUMA-3 evaluating brexucabtagene autoleucel and in FELIX for obe-cel are based on the modified ITT population

Obe-cel could launch into an expanding ALL market if approved

Blincyto®, current market leader, shows annual revenue growth of c.24% driven by well manageable safety profile

Reported Blincyto® sales[1]



- Blincyto® sales price estimated to be $207k[2] (for 2 cycles) supporting approx. >2,000 commercial adult ALL patients, growing at a rate of 24%
- Kymriah® is priced at $508k in pediatric ALL. Breyanzi® is priced at $447k in DLBCL[3]. Tecartus™ is priced at $424k[3] for adult ALL
- Breyanzi® and other CAR T cell therapies are expanding delivery center footprint
- Tecartus™ is expected to establish CAR T use in adult ALL
- If approved, obe-cel has the potential to be best-in-class curative therapy and expanding use beyond academic transplant centers

NOTES

1. As per Amgen quarterly SEC filings
2. https://www.cms.gov/medicare/medicare-part-b-drug-average-sales-price/2022-asp-drug-pricing-files
3. Red Book pricing database https://www.ibm.com/products/micromedex-red-book/pricing
4. Autolus crude extrapolation from Q1 2023, based on sustaining $194m for Q2, Q3, Q4 2023

Autolus

Manufacturing

Product supply

Critical success factors for a personalized cell therapy

- Reliable and timely delivery of every batch with consistent quality is critical for each patient

- Process
  - Manufacturing process to perform consistently with wide range of patient cell material
  - Turn around time to be consistently short
  - Product consistency and economies of scale require a certain level of automation

- People
  - Leadership to drive outcome
  - Highly trained and motivated work force - training center and program implemented
  - Culture of continuous improvement - need for operational excellence program

- Scale of operation
  - Capacity to match size of targeted patient population to avoid product shortages
  - Right size capacity to realize attractive COGS

Supply of FELIX study pressure tested all aspects of product delivery

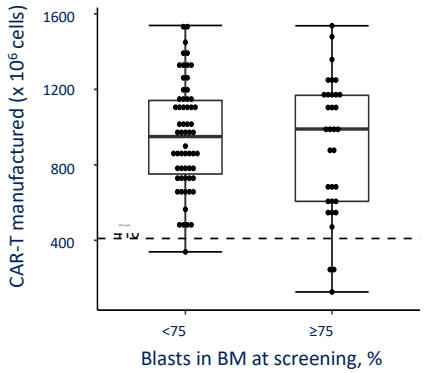
New approach to manufacturing – requires new thinking to be successful

- Semi-automated manufacturing process optimized to manage wide range of apheresis materials
- Finetuned in process controls and release analytics
- Training center set up to establish and maintain operating workforce
- 2 shifts / 7 days per week commercial manufacturing operations implemented
- Operational excellence program implemented to continuously optimize manufacturing operations and COGS
- Logistics operated for 24 US clinics during COVID restrictions and transatlantic flights as low as 5% of pre-pandemic levels

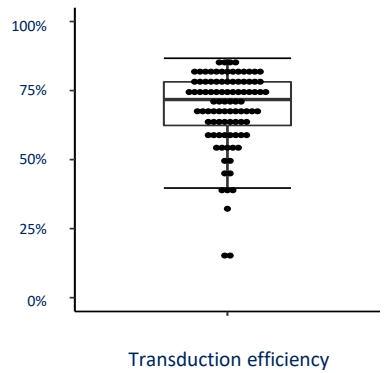
CliniMACS **Prodigy®**

Miltenyi Biotec

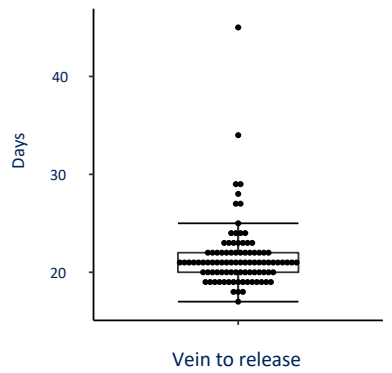
96% of products reached target dose



Median transduction efficiency of **72%**



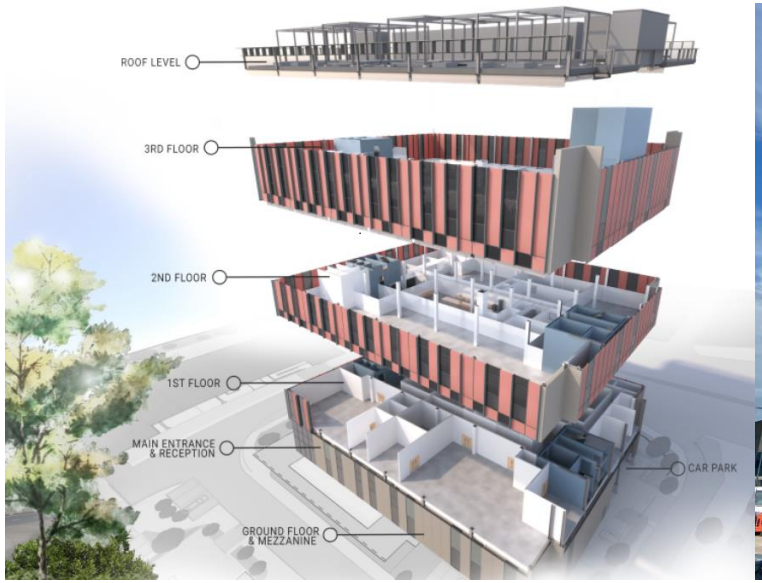
Median **21 days** from vein to release



Commercial manufacturing facility – The Nucleus

State of the art design and operations established – validation on track

Design



- Modular build using PAMs
- 70% built off-site
- Reduction of build time by 60%

Build

- Nov 8, 2021 ground breaking
- Nov 22, 2022 first clean room in operation

Operations

- Dec 14, 2022 first Prodigy machine operational
- May 2023 capacity challenge
- 2000+ batches per year capacity

Outlook on next steps

Obe-cel next steps to commercialization

Preparing for launch in 2024

Data and path to approval

- FELIX – clinical data presentations at ASCO and EHA
- Filing of Biologics License Application (BLA) to U.S. Food and Drug Administration (FDA) expected for end of 2023
- Filings of EU and UK marketing authorization applications planned for H1 2024

Manufacturing

- Complete full characterization of Nucleus facility
- GMP license from MHRA planned for 2H 2023
- Facility has initial capacity to produce up to 2,000 batches PA; sufficient for global demand in ALL

Commercialization

- Focus in 2023 on Medical affairs, value and HEOR evidence generation and center onboarding
- Focus in 2024 on launch preparation and execution

The Autolus opportunity

Building a fully integrated CAR T company - Expanding excellence in R&D and manufacturing to commercialization

- Obe-cel, a potentially best in class product candidate, met primary endpoint of ORR in adult patients with r/r ALL
- Planned BLA filing end of 2023
- Additional opportunity for obe-cel in B-NHL indications
- Highly valuable pipeline with potential broad applicability in cancers with limited treatment options

- Purpose-built commercial manufacturing facility ready for qualification and validation activities in 1H 2023 with an initial capacity of up to 2,000 batches per year, sufficient to serve global demand in ALL
- Strong technology foundation, validating collaborations with leading pharma and biotech companies – BMS, Moderna and Cabaletta Bio
- Strong cash position with $343.4 million (March 31, 2023)

Autolus

Thank you