



# Developing Next Generation Programmed T Cell Therapies

December 2023



# Disclaimer

These slides contain 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 Autolus' development of the obe-cel program; the profile and potential application of obe-cel in additional disease settings; the future clinical development, efficacy, safety and therapeutic potential of the Company's product candidates, including progress, expectations as to the reporting of data, conduct and timing and potential future clinical activity and milestones; expectations regarding the initiation, design and reporting of data from clinical trials; expectations regarding the regulatory approval process for any product candidates; the benefits of the collaboration between Autolus and Blackstone, including the potential and timing to receive milestone payments and pay royalties under the terms of the strategic collaboration; the Company's current and future manufacturing capabilities; and the Company's anticipated cash runway. 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 COVID-19 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 7, 2023, 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 presentation is as of the date of the release, and Autolus 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.

# Building a leading CAR T company developing transformational therapies for cancer and autoimmune diseases

Established excellence in R&D and Manufacturing; scaling company toward commercialization



## Obe-cel potentially best in class CAR T for r/r adult ALL

- FELIX pivotal trial showed high ORR, encouraging EFS and favourable tolerability with low levels of high-grade CRS and ICANS
- BLA submitted to FDA
- EMA submission planned for 1H 2024



## Pipeline expansion strategy

- Expand obe-cel opportunity in B cell malignancies, autoimmune diseases & life cycle strategy
  - SLE
  - B-NHL indications
  - Bi-specific therapies (CD19 /CD22; CD19/BCMA)
- Expand to additional indications with novel CAR T therapies, alone or with partners



## Scalable manufacturing and in-house facility

- Demonstrated reliable clinical trial supply (96% target dose reached in FELIX pivotal study)
- New commercial cell manufacturing facility in qualification stage; planned annual capacity 2,000+ batches
- Vein-to-delivery time at launch of ~16 days



## Strategic collaborations

- Established technology collaborations with Moderna, BMS and Cabaletta
- Longstanding academic collaboration with University College London
- Partnering opportunities on pipeline programs and platform technology



## Strong cash position

- Cash \$256.4M (Q3 2023)
- Runway into 2025
- Enables execution on current strategy through approval of obe-cel



**LEAD CLINICAL PROGRAM**

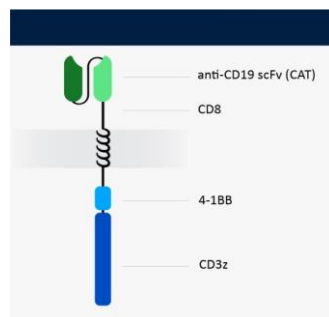
## Obe-cel

A standalone, potentially best-in-class  
CD19 CAR T cell therapy candidate

# Obe-cel has a unique mechanism of action

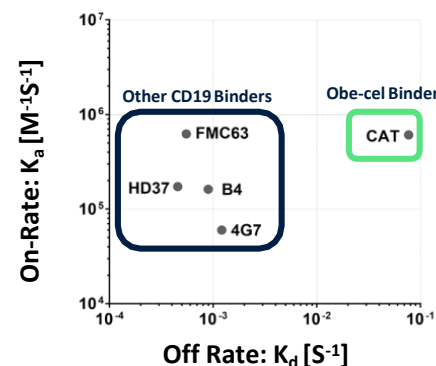
Designed for increased activity and reduced toxicity

## Differentiated CD19 binder



CD19 binder with fast off-rate

## Fast off-rate



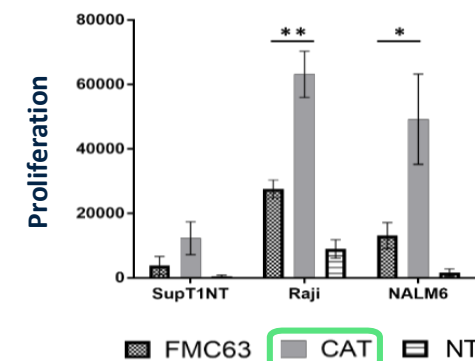
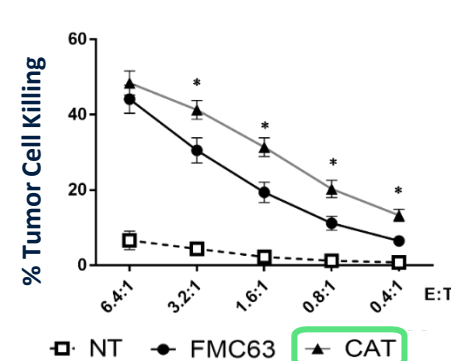
Shorter half-life of interaction compared to binders used in approved products

- obe-cel = 9.8 seconds
- Kymriah® = 21 minutes

## Potential for improved potency, reduced toxicity


- Avoids over-activation of CAR T cells → Reduced toxicities
- Increases CAR T peak expansion → Improved persistence
- Avoids exhaustion of CAR T-cells → Improved engraftment  
Improved persistence

## Enhanced cytotoxicity and proliferation




# FELIX data at ASCO and EHA 2023

## Trial design and patient baseline characteristics



**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

84% of enrolled patients were infused with obe-cel

Enrolled: N = 112

Infused: N = 94

Discontinued:

- Death
- Manufacturing related
- Adverse event
- Physician decision

n=18  
11  
5  
1  
1

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

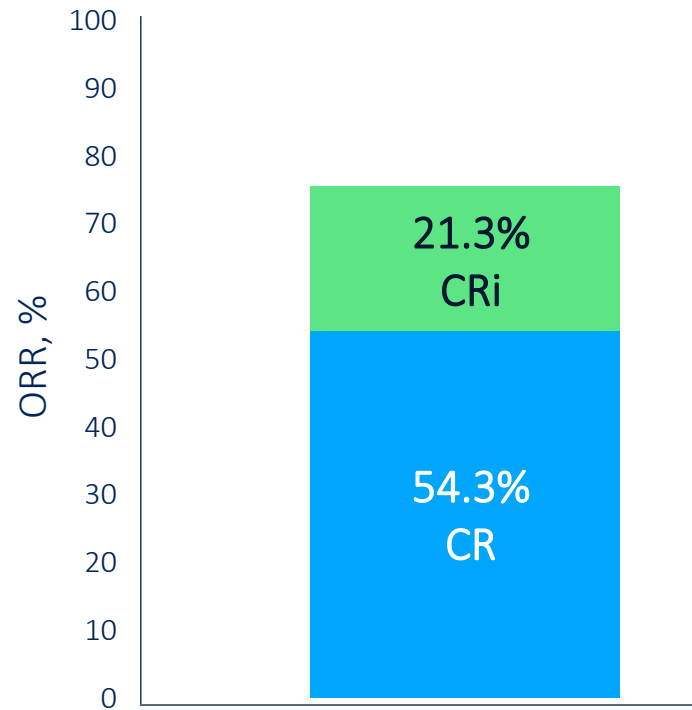
Baseline Characteristics	Total infused (N = 94)
Age years, median (range)	50 (20–81)
Gender male/female, n	47/47
Philadelphia chromosome-positive, n (%)	25 (26.6)
Prior therapies, median (range)	2 (1–6)
≥3 prior lines, n (%)	29 (30.9)
Refractory to last prior line of therapy, n (%)	50 (53.2)
Prior allogeneic SCT, n (%)	36 (38.3)
Prior blinatumomab, n (%)	33 (35.1)
Prior inotuzumab, n (%)	30 (31.9)
Prior blinatumomab and inotuzumab, n (%)	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)

\* 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: disease response per IRRC assessment

76% of infused patients achieved CR/CRi



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

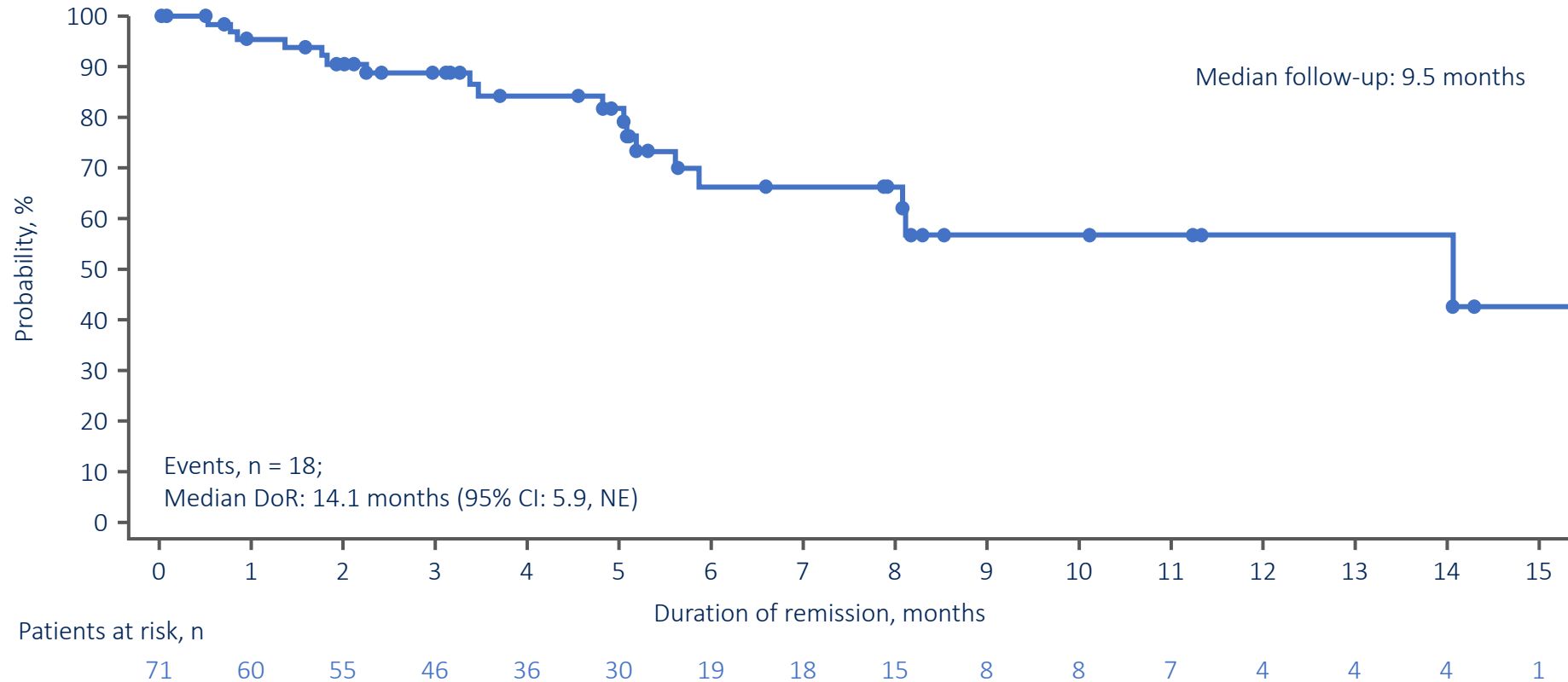
97% of responders with evaluable samples were MRD negative at  $10^{-4}$  level by flow cytometry

\*One-sided p-value from the exact test on  $H_0$ : ORR  $\leq 40\%$  vs  $H_1$ : 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



# FELIX: CRS and ICANS profile

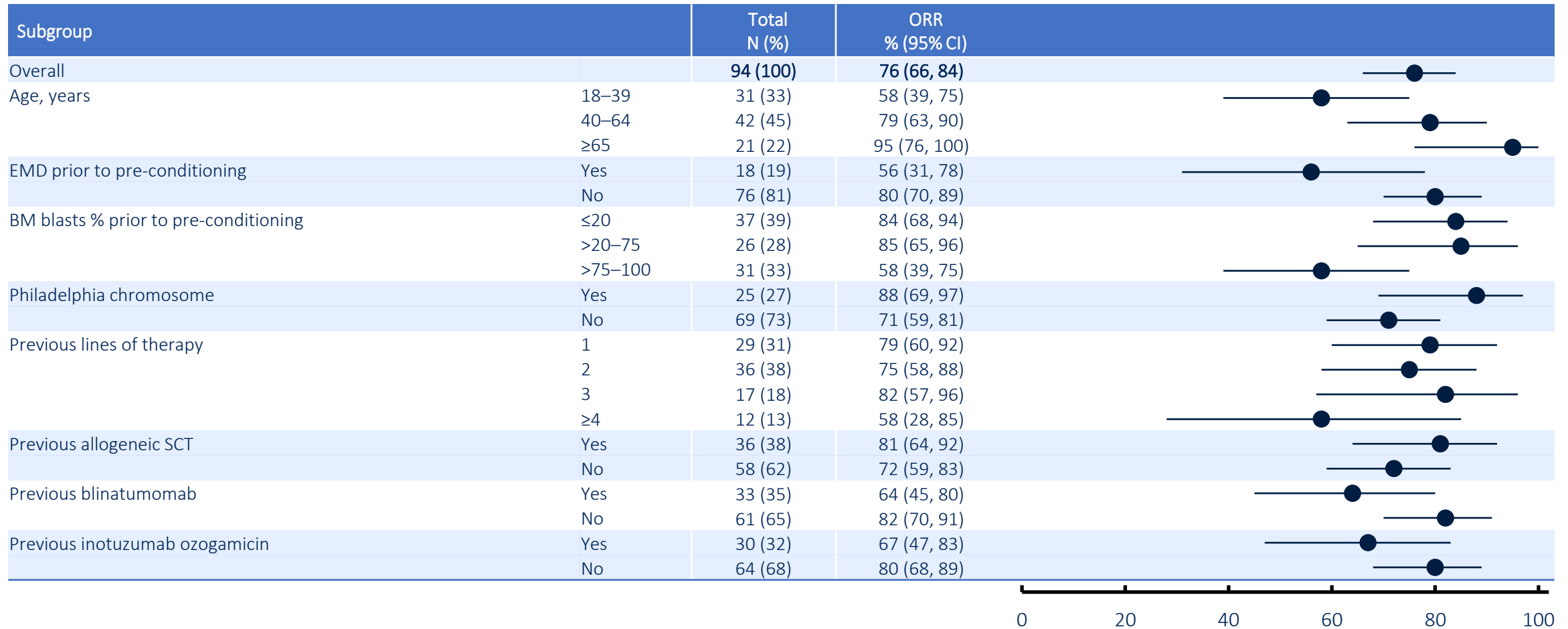
Low rates of Grade  $\geq 3$  CRS and/or ICANS were observed

	BM blasts $\leq 20\%$ 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 $\geq 3$ , n (%)	1 (2.7)	2 (3.5)	3 (3.2)
ICANS			
Any grade, n (%)	5 (13.5)	19 (33.3)	24 (25.5)
Grade $\geq 3$ , 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  $\geq 3$  ICANS were observed among patients with  $> 75\%$  BM blasts at pre-conditioning

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

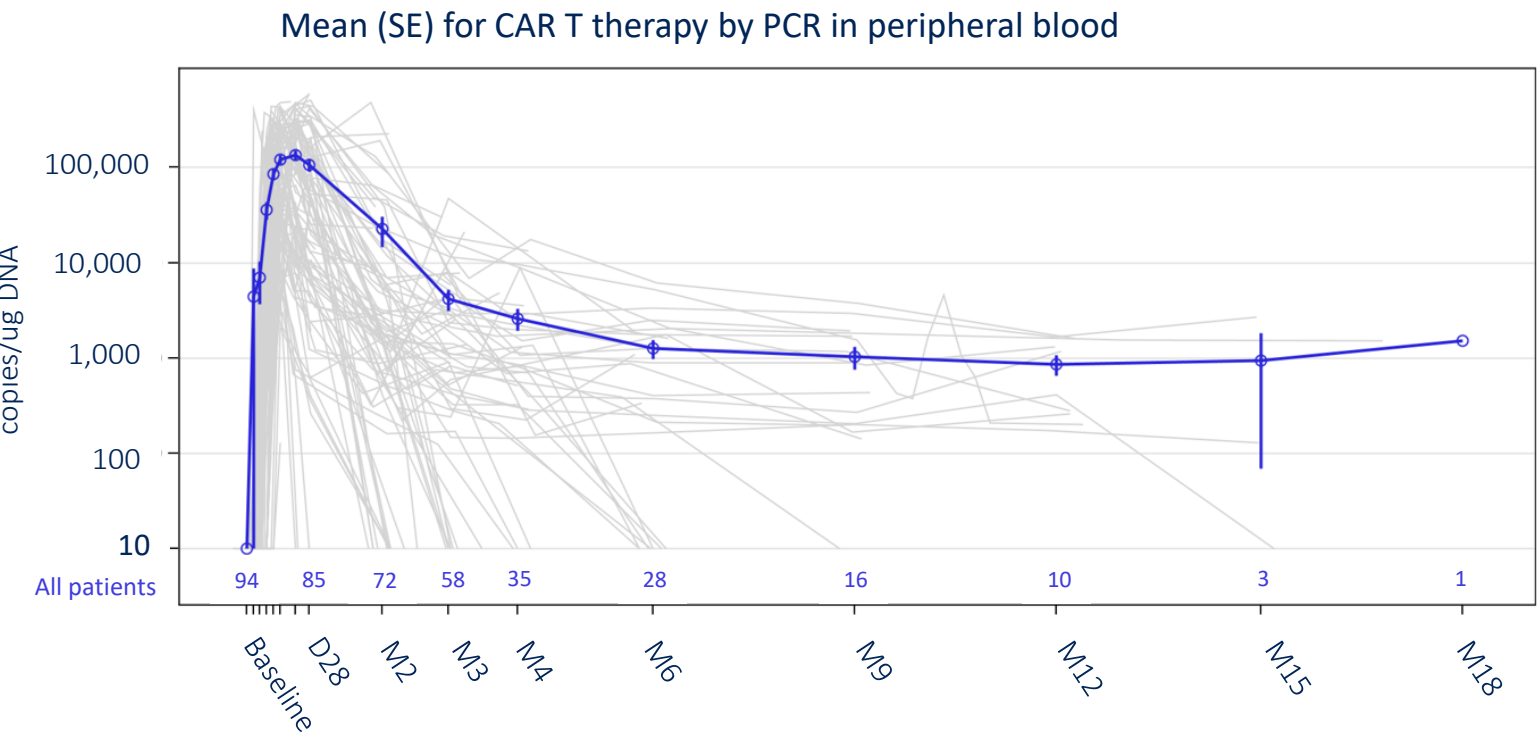
Benefits observed across all patient subgroups; high risk subgroups include EMD and high BM blasts at pre-conditioning



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

# FELIX: obe-cel expansion and persistence

CAR T cellular kinetics are consistent with the ALLCAR19 study<sup>1</sup>

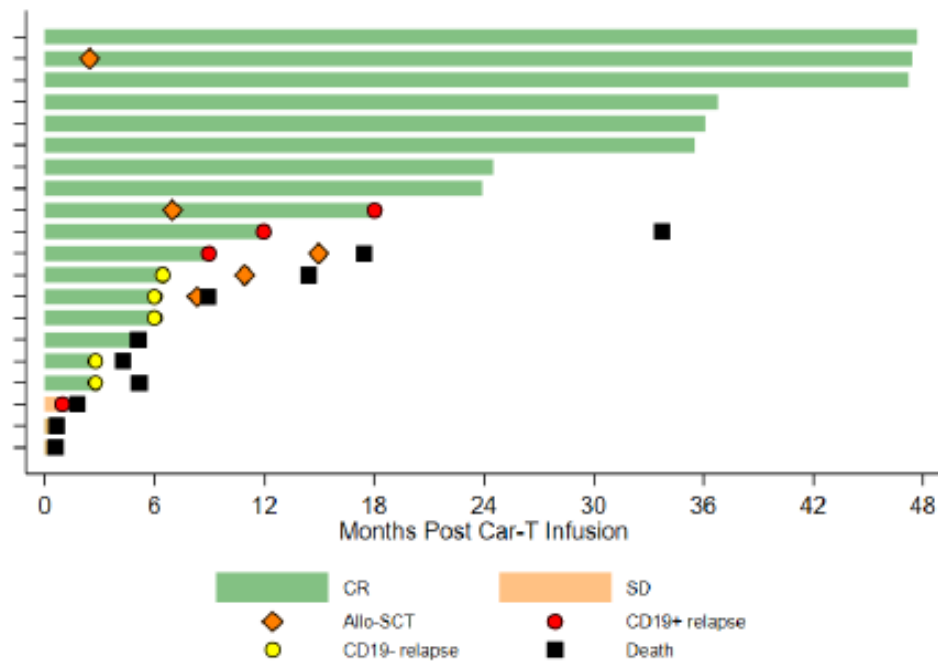


	FELIX (N = 94)	ALLCAR19 (N = 20)
$C_{max}$ , copies/ug Geo-Mean, CV%	114,982 (287.6)	127,152 (109.7)
$T_{max}$ , days Median, range	14 (2–55)	13 (7–21)
$AUC_{0-28d}$ , copies/ug×d Geo-Mean, CV%	1,139,380 (225.4)	1,251,802 (108.9)

# Obe-cel Phase 1 long term follow up demonstrates durable responses

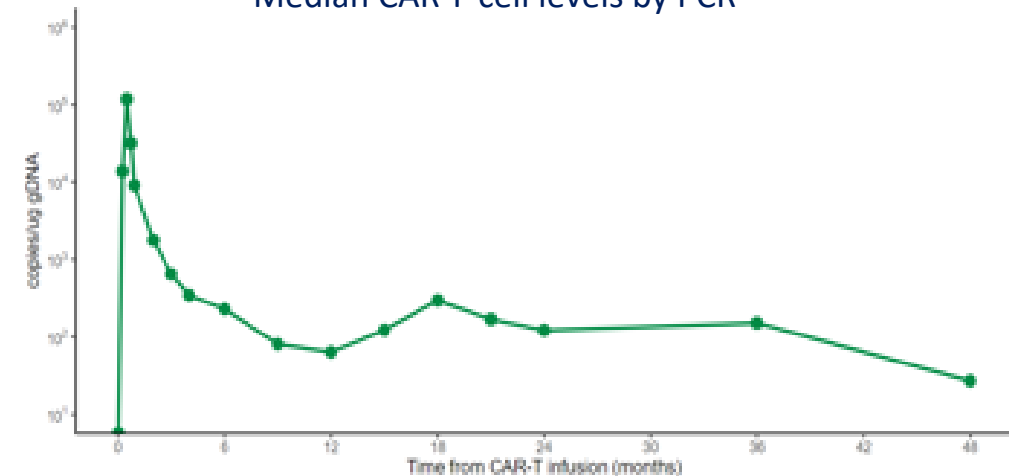
Long term follow up from Phase 1 ALLCAR19 study in r/r ALL of up to 4 years

**ALLCAR19 Swim plot**



**ALLCAR19 Median persistence**

Median CAR T-cell levels by PCR



- Of the 20 infused B-ALL patients, 7/20 (35%) are in ongoing CR at a median FU of 36 months (IQR 24-47) post obe-cel
- All patients with long-term remissions have long-term persisting CAR T cells

## FELIX: conclusions

- **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
- **Very low rates of Grade  $\geq 3$  CRS (3.2%) and low rates of Grade  $\geq 3$  ICANS (7.4%)**
  - In total, obe-cel was evaluated in 94 patients with r/r B-ALL
  - 31% of patients had received  $\geq 3$  prior lines of therapy and 33% had  $>75\%$  marrow burden at infusion
- **Robust manufacturing process, with product released for 94% of leukapheresed patients**
  - 84% of enrolled patients received obe-cel
  - Median vein to release of 21 days
- **Excellent CAR T-cell engraftment**
  - $C_{\max}$  of 114,982 copies/ $\mu\text{g}$  DNA and  $T_{\max}$  at 14 days

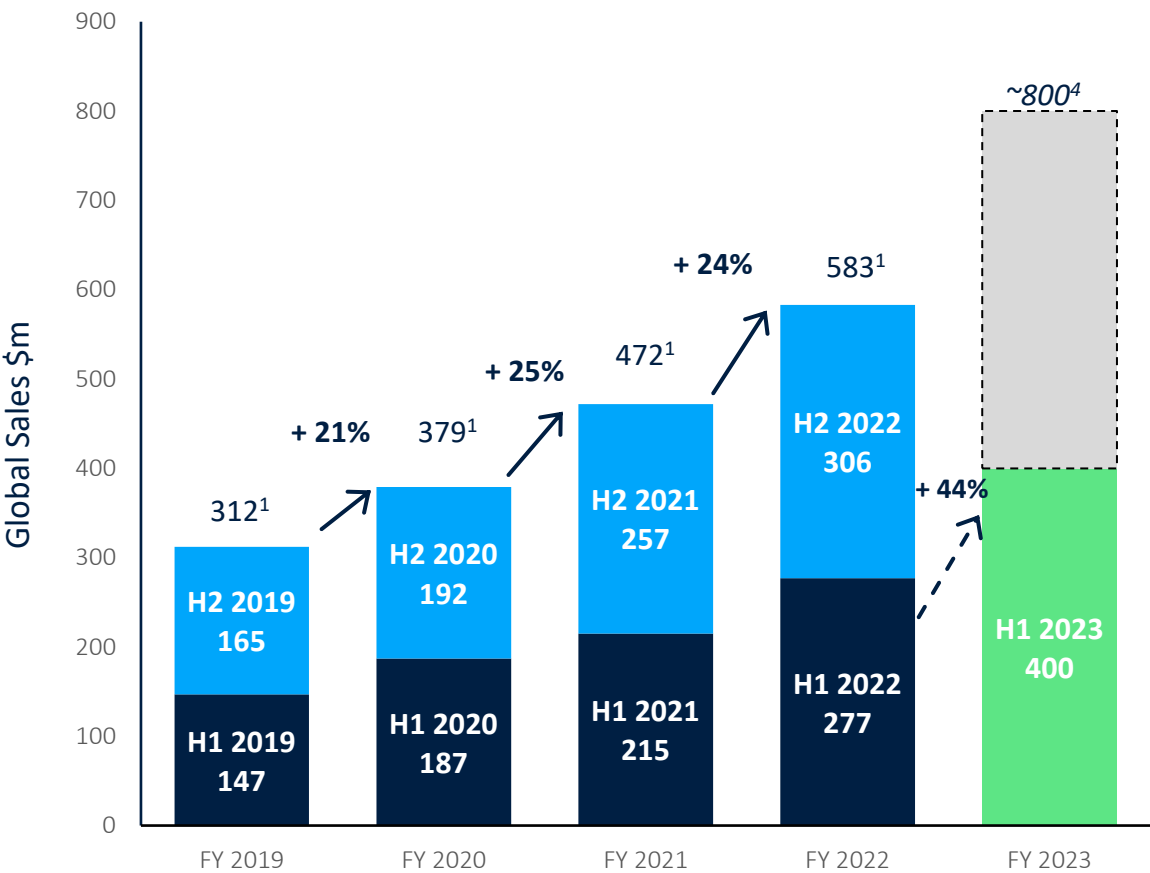


ALL: unmet need and market  
overview

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

Blincyto®, current market leader, sales increased 48% year-over-year to \$206 million for the second quarter 2023

## Reported Blincyto® sales<sup>1</sup>



- Blincyto® sales price estimated to be \$207k<sup>2</sup> (for 2 cycles) supporting approx. >2,000 commercial adult ALL patients. Sales increased 55% year-over-year to \$220 million for the third quarter 2023
- Kymriah® is priced at \$508k in pediatric ALL. Breyanzi® is priced at \$447k in DLBCL<sup>3</sup>. Tecartus™ is priced at \$424k<sup>3</sup> 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

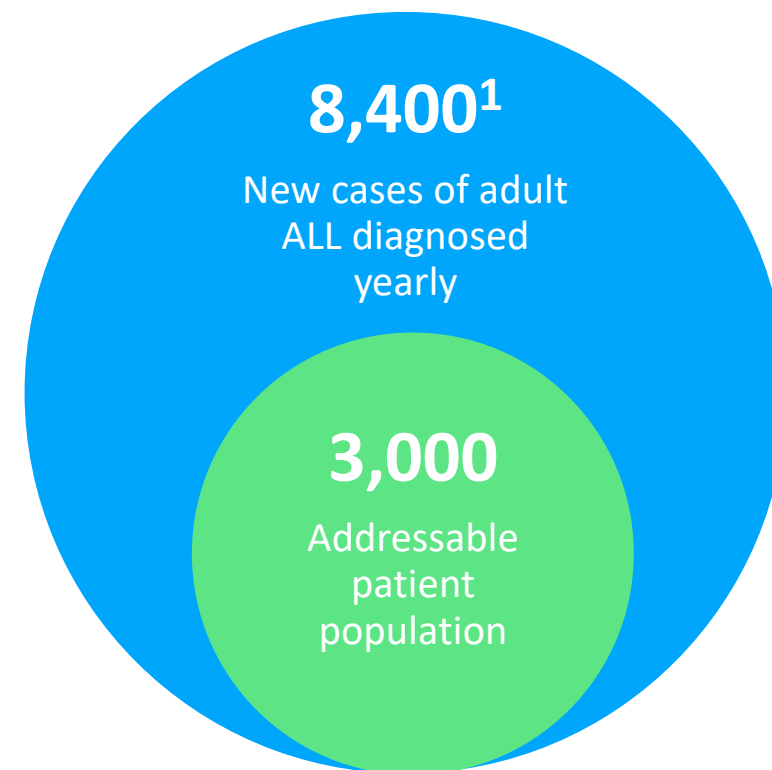
1. As per Amgen quarterly SEC filings
2. <https://www.cms.gov/medicare/medicare-part-b-drug-average-sales-price/2022-asp-drug-pricing-files>
3. Red Book pricing database <https://www.ibm.com/products/micromedex-red-book/pricing>
4. Autolus crude extrapolation from Q2 2023, based on sustaining growth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



# Over 8,000 new cases of adult ALL annually worldwide

Successful therapy requires high level of activity and sustained persistence paired with good tolerability

- Median overall survival is < 1 year in r/r adult ALL
- Combination chemotherapy enables 90% of adult ALL patients to experience Complete Response (CR)
  - Only 30% to 40% achieve long-term remission
- Current T cell therapies for adult patients are Blincyto® and Tecartus®
  - Both therapies are highly active, but frequently followed by subsequent treatments (e.g. alloSCT)
  - Blincyto®: favorable safety profile, few patients experiencing severe CRS and ICANS, but limitations on convenience - continuous i.v. infusion during 4-week treatment cycles
  - Tecartus® more challenging to manage - induces elevated levels of severe CRS, a high levels of severe ICANS, and requires vasopressors for many patients
- Opportunity to expand the addressable patient population in earlier lines of therapy



## NOTES

1. SEER and EUCAN estimates (respectively) for US and EU

# Critical drivers for market adoption

## PRODUCT PROFILE

### Durable and robust response

- CR/CRi rate of 76%, with 97% of responders becoming MRD negative<sup>1</sup>
- With a median of 9.5 months' follow-up, 61% of responders remain in remission<sup>1</sup>

### Predictable and manageable tolerability

- Very low rates of Grade  $\geq 3$  CRS (3.2%) and low rates of Grade  $\geq 3$  ICANS (7.4%)<sup>1</sup>



**Pivotal Phase 2  
trial in adult ALL**

## TREATMENT EXPERIENCE

### Timely & reliable product supply

- Quality product with low out-of-spec rates
- Timely delivery
  - Sufficient capacity and manufacturing slot access
  - Short vein-to-release times

### Best-in-class commercial systems and services integration

- Optimize relationship with accredited treatment centers

**Commercial Launch  
Readiness Plan**

1. Roddie et al., ASCO 2023, data cut-off date: March 16, 2023

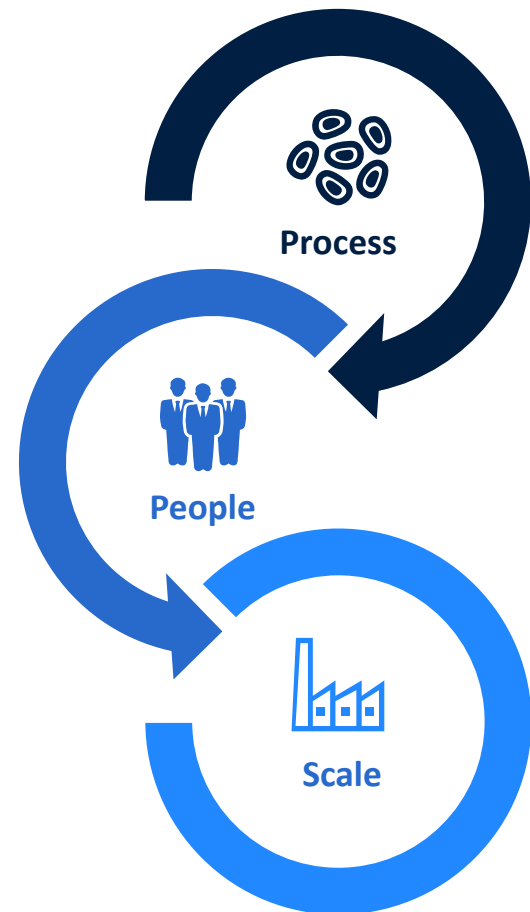


# Commercial Launch Readiness

# 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**



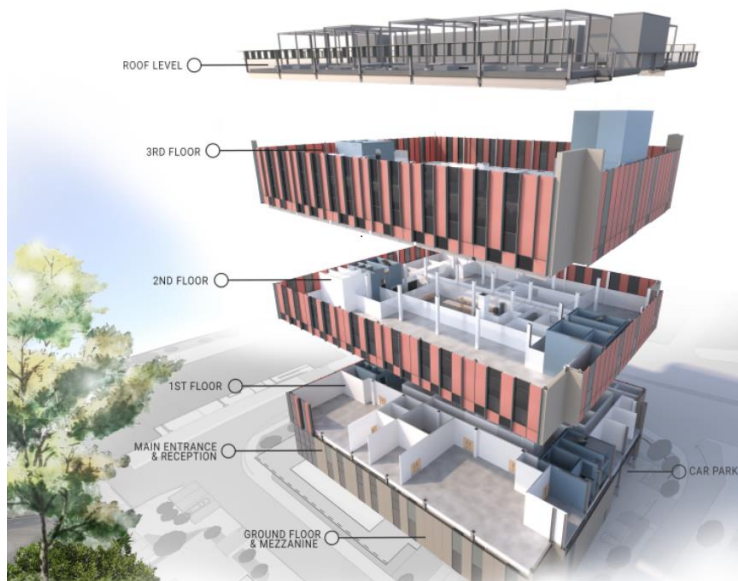
- Process
  - Consistent manufacturing process performance over a wide range of patient cell material
  - Consistently short turnaround time
  - A semiautomated production platform enabling product consistency and economies of scale
- People
  - Leadership to drive outcome
  - Highly trained and motivated work force - training center and program implemented
  - Culture of continuous improvement - continuing operational excellence program
- Scale of operation
  - Capacity to match demand
  - Right sized and scalable capacity to realize attractive COGS



# The Nucleus

State of the art design and operations established – validation completed

## Design



- ~70,000 sq ft facility
- Modular build using PAMs
- 70% built off-site
- 60% reduced build time
- BREEAM Excellent rating for sustainability

## Build



- Nov 8, 2021 ground breaking
- Nov 25, 2022 first clean room in operation
- Facility validation completed in 2H 2023

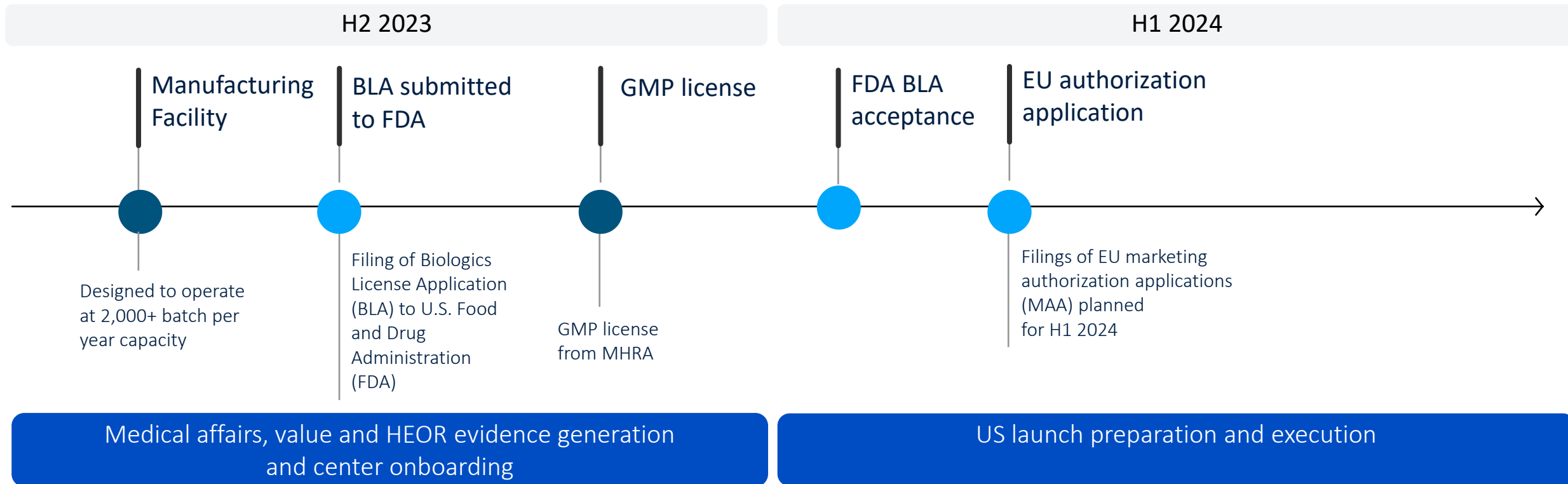
## Operations



- Dec 14, 2022 first Prodigy operational
- May 2023 capacity challenge
- Designed for 2,000+ batches per year
- Target vein to delivery time 16 days at launch

# Obe-cel steps to commercialization in r/r adult ALL

Roadmap to a 2024 commercial launch



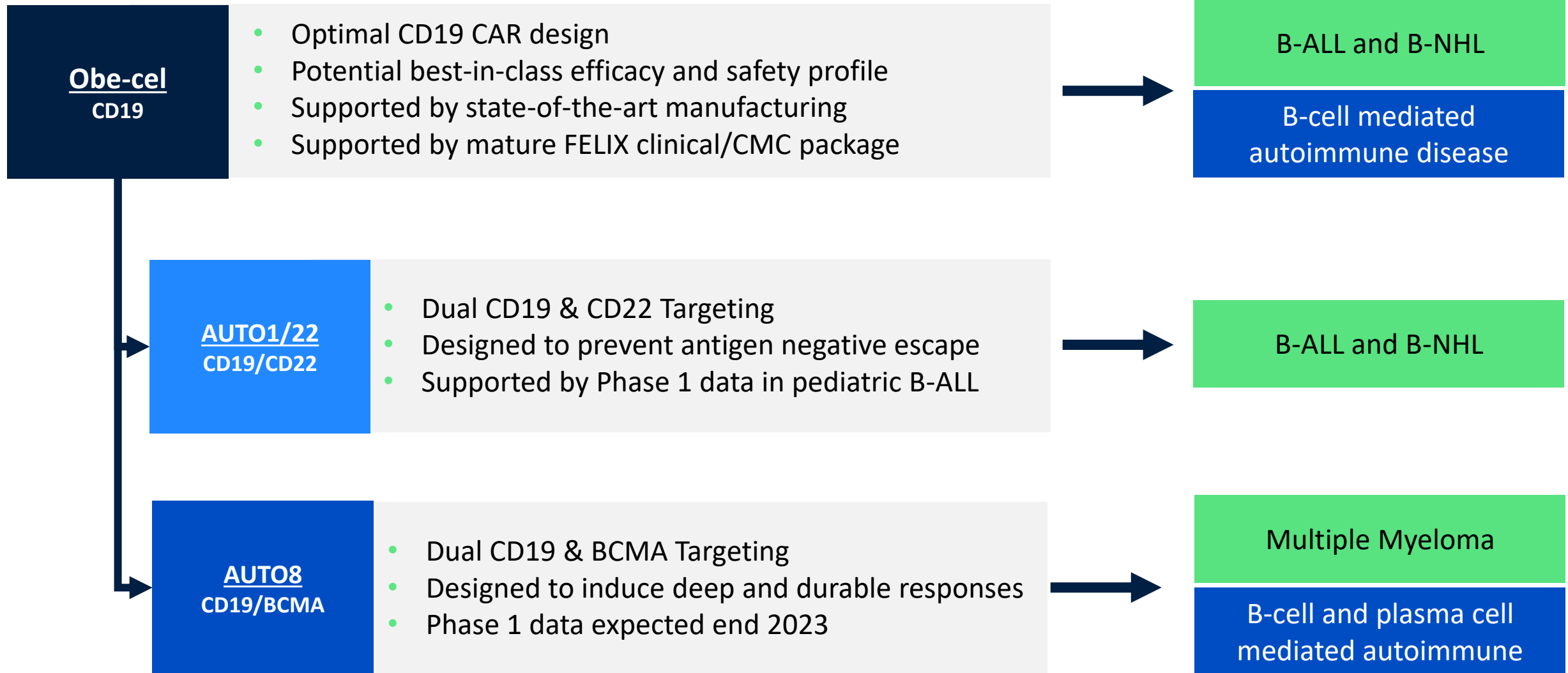
- Regulatory
- Manufacturing
- Commercialization

# Expanding the obe-cel opportunity

Deep value program with potentially broad applicability



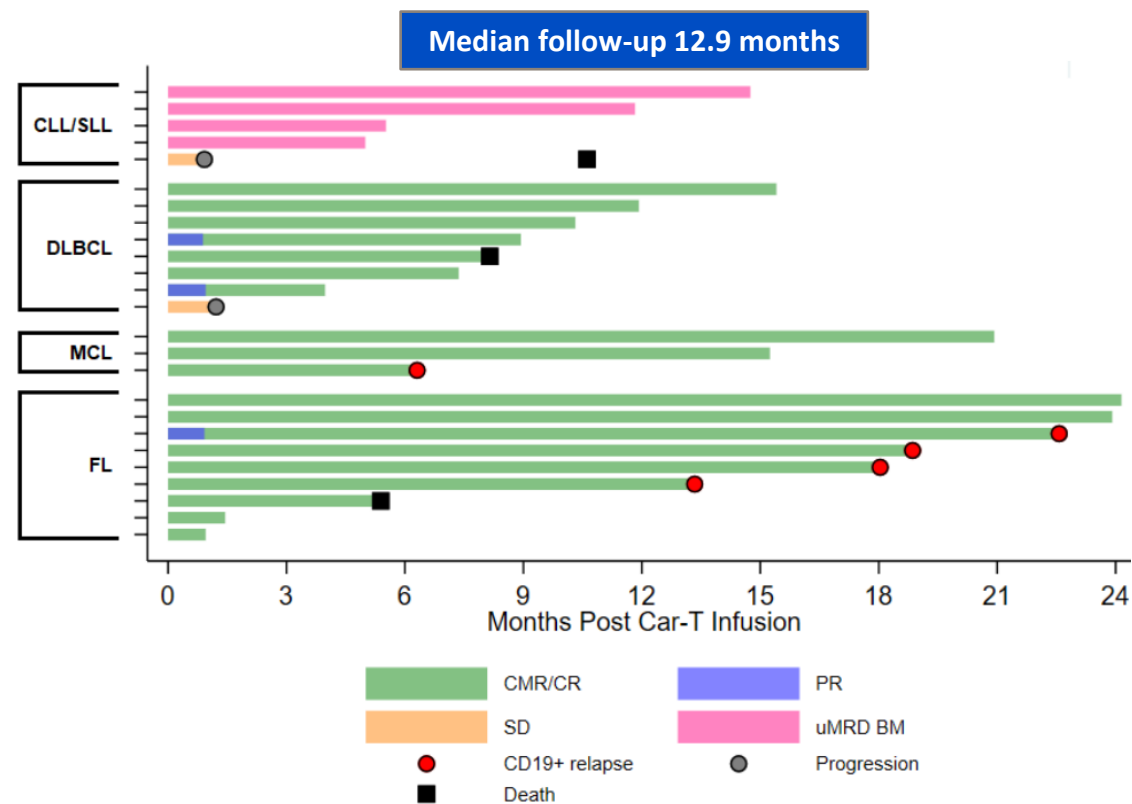
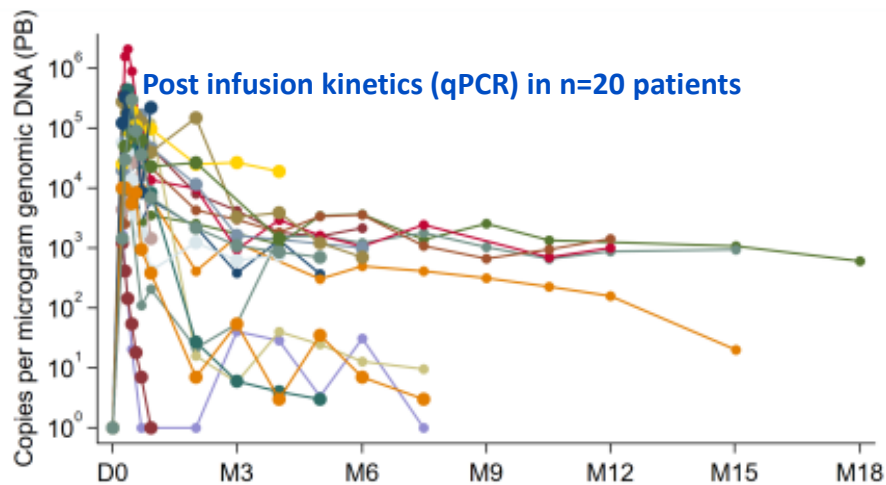
# The obe-cel product family and franchise opportunity



# Obe-cel in B-NHL/CLL: High level clinical activity with durable outcomes

Long term persistence driving durable outcomes

ALLCAR19 – B-NHL and CLL		
N		25
ORR		
All patients		92%
Follicular Lymphoma		100%
Mantle Cell Lymphoma		100%
DLBCL		88%
CLL/SLL		80%

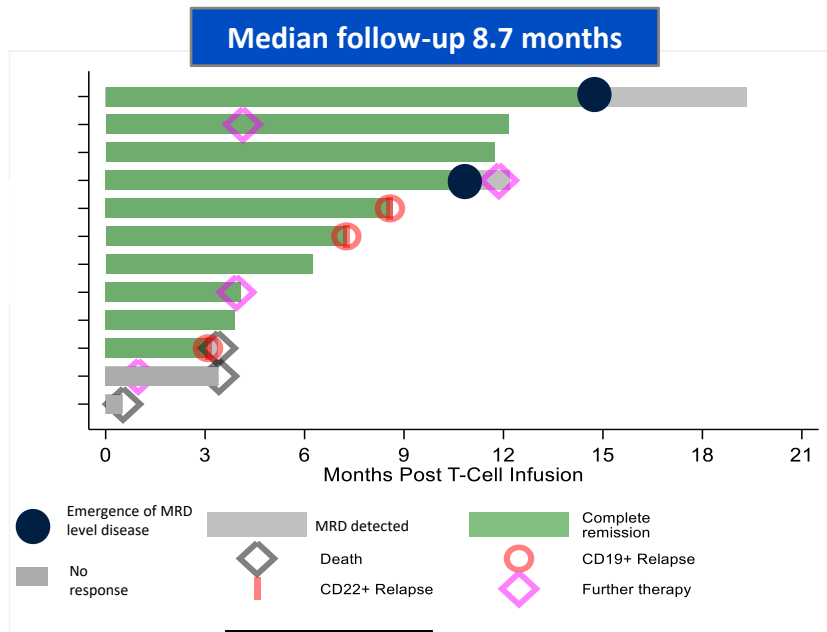


- No  $\geq$  grade 3 CRS and ICANS reported
- 2 deaths in remission from COVID19; 1 death from PD

# AUTO1/22 in pediatric ALL

No antigen negative relapse seen in responding patients

CARPALL Disease Response (n=12)	
Molecular MRD neg CR/Cri by d30	10 (83%)
Disease progression	2
Relapse	
Antigen negative relapse	0
CD19+/CD22+ relapse	5



- Favorable adverse event profile with no severe CRS
- Excellent CAR T expansion and very encouraging activity:
  - 83% MRD negative CR/CRI
  - Despite high-risk pts (4 Kymriah failures, 3 CD19neg disease, 3 non-CNS extramedullary disease)
- 2 of 3 patients who had CD19neg disease achieved CR/CRI demonstrating a response to the CD22 CAR
- 1-year EFS 60% despite the high-risk patient cohort
- At median FU 8.7 months, no cases of leukemic relapse or emergence of MRD related to antigen escape

# AUTO8: combining a sensitive BCMA CAR with the CD19 CAR from obe-cel

Designed to induce deep and durable responses

AUTO8

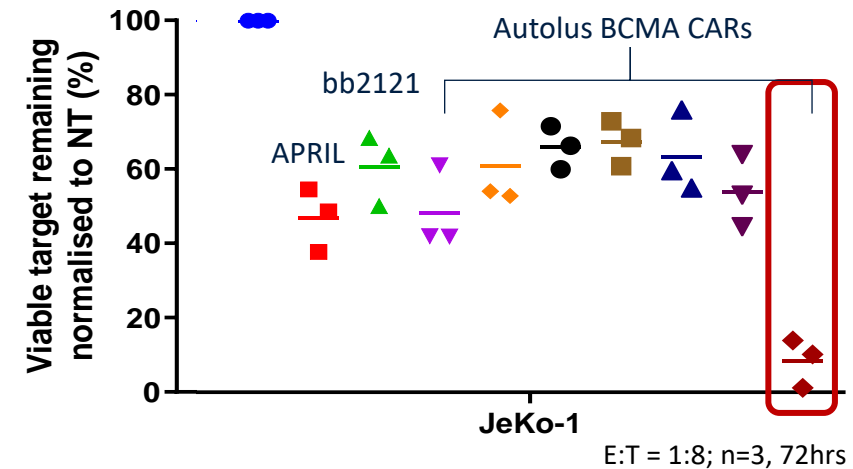
## BCMA CAR

Novel format CAR designed to be highly sensitive to low BCMA density found on malignant plasma cells

## CD19 CAR

Coupled to obe-cel to drive persistence and long-term durability of response, and to deplete CD19+ myeloma stem cell

## Screening for high sensitivity BCMA binders



## Phase 1 Design

Cohort 1: BCMA CAR

50MM

150MM

Cohort 2: BCMA CAR  
+ CD19CAR

50MM

150MM

Phase 1 study currently enrolling patients with  
first data expected end 2023

# Uniquely positioned to deliver CAR T therapy in autoimmune disease

## Obe-cel's potential advantages

Outstanding tolerability to drive physician and patient acceptability in rheumatology settings

Deep cut into the CD19+ B and plasma cell compartment to remove all autoreactive clones

Development of robust, economical and scalable manufacturing and commercial infrastructure

High treatment effect enables smaller clinical program and accelerated regulatory path to launch

## Supporting evidence

- ✓ Potential best-in-class risk/benefit profile in pivotal FELIX trial in adult ALL
- ✓ Low rates of high-grade CRS and ICANS across all patients

















- ✓ Demonstrated in B-ALL with very high rate of MRD negative complete remissions (97% of responders)

- ✓ Potential approved, commercial manufacturing facility in adult ALL with attractive cost of goods at launch for SLE
- ✓ Commercial systems and CAR T center services established with potential adult ALL launch

- ✓ Treatment effect demonstrated in Erlangen proof-of concept
- ✓ Clinical safety data from ALLCAR19 and FELIX as well as potential commercial patient data to supplement SLE pivotal study

# Obe-cel ideally positioned as potential best in class and fastest to market

Could offer fastest and lowest risk cell therapy approach for B-cell mediated autoimmune diseases

	Established Tolerability Profile	Established Clinical Profile	Manufacturing Infrastructure	Commercial Infrastructure	Comment
<b>AUTOLUS</b> (obe-cel)					Potential best-in-class risk/benefit ratio. Established manufacturing and product delivery. ALL commercial infrastructure in place for SLE
<b>BIOTECH:</b> (new CAR T entrants)					Clinical profile not yet established. Likely use CDMO or local site for manufacturing with unfavorable cost implications
<b>PHARMA:</b> (new CAR T products)					New products under development. Will need to re-establish efficacy & safety profile and commercial manufacturing for autoimmune
<b>ALLOGENEIC</b>					Clinical profile not yet established






# Other pipeline programs and technologies

A broad portfolio of potential next generation modular T cell therapies



# Autolus pipeline

## Obe-cel product family

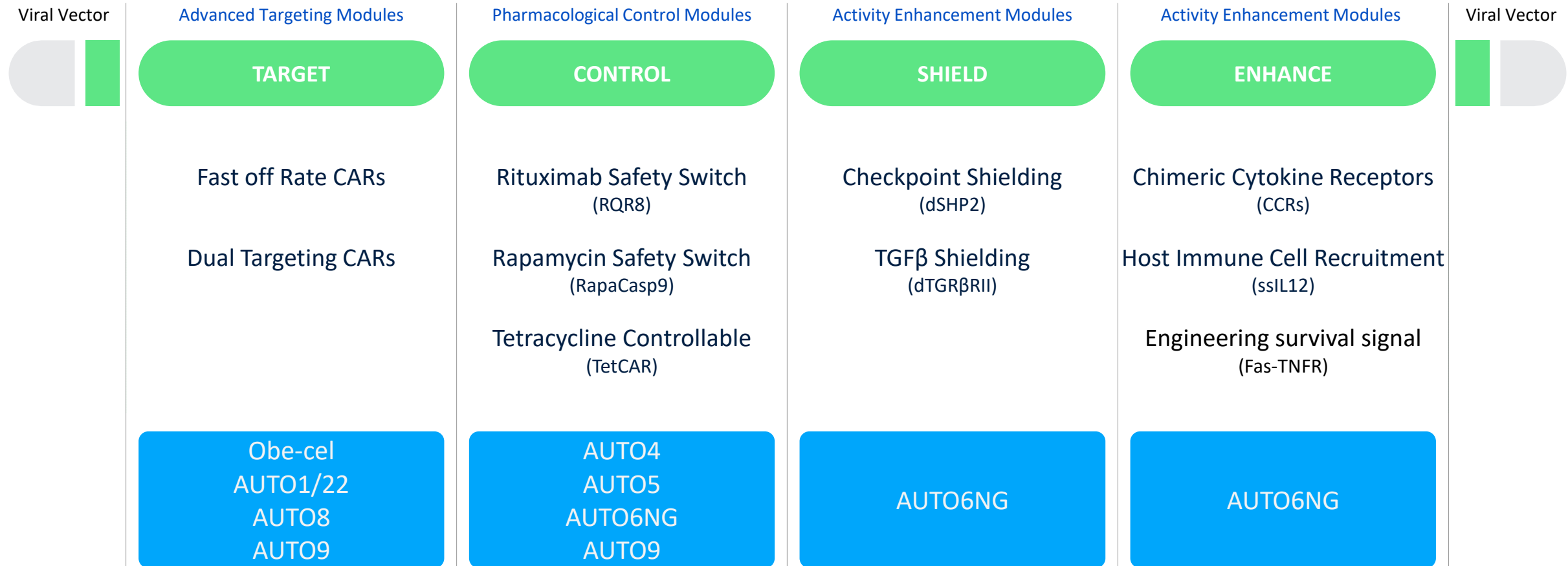
PRODUCT	INDICATION	TARGET	STUDY NAME	COLLABORATION	PHASE	UPCOMING CATALYST
Obe-cel	Adult B-ALL	CD19	FELIX		Pivotal	Q4 2023: FELIX data updates Q4 2023: BLA filing with FDA
Obe-cel	Systemic Lupus Erythematosus	CD19	TBD		Preclinical	Early 2024: Phase 1 initiation
Obe-cel	B-NHL and CLL	CD19	ALLCAR19		Phase 1	Data in peer reviewed journal
Obe-cel	PCNSL	CD19	CAROUSEL		Phase 1	Data in peer reviewed journal
Allogeneic obe-cel	B-Cell malignancies	CD19	KCAT19		Phase 1	First clinical data end of 2024
AUTO1/22	Pediatric ALL	CD19 & CD22	CARPALL		Phase1	Data in peer reviewed journal
AUTO8	Multiple Myeloma	CD19 & BCMA	MCARTY		Phase 1	Q4 2023: First clinical data

## Additional pipeline programs

AUTO4	TRBC1+ Peripheral TCL	TRBC1	LibrA T1		Phase 1	Data in peer reviewed journal
AUTO5	TRBC2+ Peripheral TCL	TRBC2	-		Preclinical	Preclinical data in peer reviewed journal
AUTO6NG	Neuroblastoma	GD2	MAGNETO		CTA submitted	Q4 2023: Phase 1 initiation
AUTO9	Acute Myeloid Leukemia	CD33, CD123 & CLL1	TBD		Preclinical	First clinical data in 2025

# A broad toolkit which is core to our strategy of modular innovation

## Advanced T cell programming



Underpinned by a broad and robust patent estate of more than 80 global patent families

# Leveraging our industry leading technology platform via partnerships

## Technology partnerships

Leveraging our modular programming technology to generate safer and more effective therapies

Tumor targeting, pharmacological control and activity enhancement for cellular therapies

Validating collaborations with leading pharma and biotech companies

Potential for value creation through near term option exercise fees, milestone payments and royalties from net sales

moderna

Access to proprietary binders for the development of mRNA-based therapeutics for the treatment of cancer

 Bristol Myers Squibb

Access to the RQR8 safety switch for selected cell therapy programs for the treatment of cancer

Cabaletta Bio®

Access to the RQR8 safety switch for selected cell therapy programs for the treatment of autoimmune diseases

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Upcoming news flow

## Autolus planned news flow

Anticipated Milestone or Data Catalysts	Timing
Obe-cel Biologics License Application (BLA) to FDA	<b>Complete</b>
Obe-cel FELIX data update at ASH	<b>December 2023</b>
AUTO8 update (MCARTY) at ASH	<b>December 2023</b>
AUTO6NG Phase 1 study start (MAGNETO)	<b>By end 2023</b>
Obe-cel in autoimmune disease – refractory SLE Phase 1 study start	<b>Early 2024</b>
Obe-cel 60-day FDA feedback on BLA submission	<b>January 2024</b>
Obe-cel Marketing Authorization Application (MAA) to EMA	<b>First half 2024</b>

# Summary

# Building a leading CAR T company developing transformational therapies for cancer and autoimmune diseases

Established excellence in R&D and Manufacturing; scaling company toward commercialization



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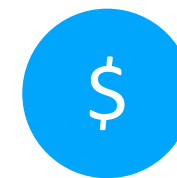
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- Cash \$256.4M (Q3 2023)
- Runway into 2025
- Enables execution on current strategy through approval of obe-cel



Thank you

