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Obsidian Therapeutics

Corporate Presentation

August 2026

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Obsidian Therapeutics: Novel Engineered TIL Cell Therapies

OBX-115:

Differentiated, Patient-centric TIL cell therapy

- Engineered with regulatable mbIL15; IL2-sparing
- Robust, proprietary scalable CMC process
- Favorable tolerability profile and lower treatment burden
- Fast Track & RMAT designations in advanced melanoma



Melanoma Ph 2: 67% ORR

YE 2027: Topline melanoma data from registration-enabling cohort



NSCLC Ph 1 Ongoing

1H 2027: Phase 1 NSCLC data

Team and resources to advance pipeline through clinical development

Strong TIL & oncology expertise

Preclinical development to expand cytoDRiVE platform into next-gen cellular therapies

\$350 million raised in oversubscribed PIPE to fund company into 2H 2028

NASDAQ: OBX



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IL2, interleukin 2; mbIL15, membrane-bound interleukin 15; NSCLC, non-small cell lung cancer; ORR, objective response rate; PIPE, private investment in public equity; RMAT, Regenerative Medicine Advanced Therapy; TIL, tumor-infiltrating lymphocytes.

Robust Executive Leadership with Deep TIL Expertise



**Madan Jagasia,
M.D., M.S.**
Chief Executive Officer



**Parameswaran Hari,
M.D., M.S.**
Chief Medical Officer



Julie Feder
Chief Financial
Officer



Dana Alexander
Chief Technical
Officer



Jennifer Peterson
Chief People
Officer



**Maria Fardis,
Ph.D., M.B.A.**
Board Chair

IOVANCE
BIOTHERAPEUTICS



IOVANCE
BIOTHERAPEUTICS



aura genzyme

VERASTEM
ONCOLOGY



sanofi

ThermoFisher
SCIENTIFIC

INARL

**INTRA
LINKS**

Monotype.

IOVANCE
BIOTHERAPEUTICS

FRAZIER
LIFE SCIENCES

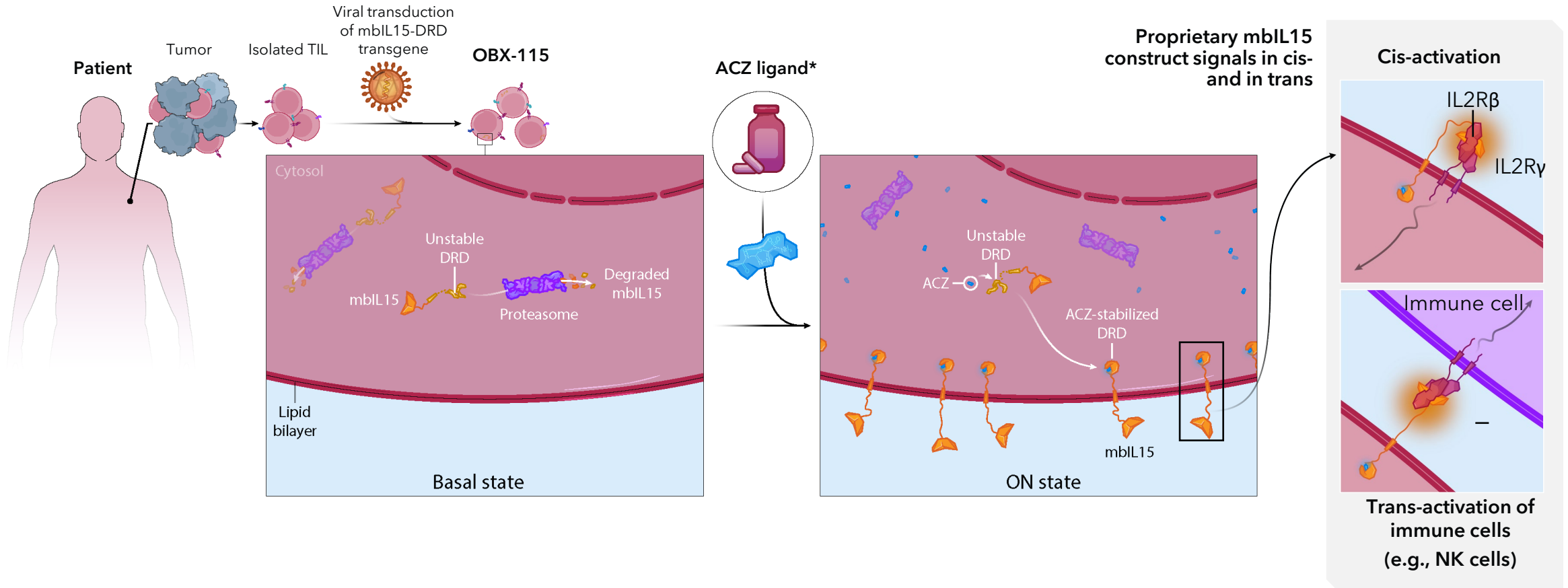
AirNexis Therapeutics



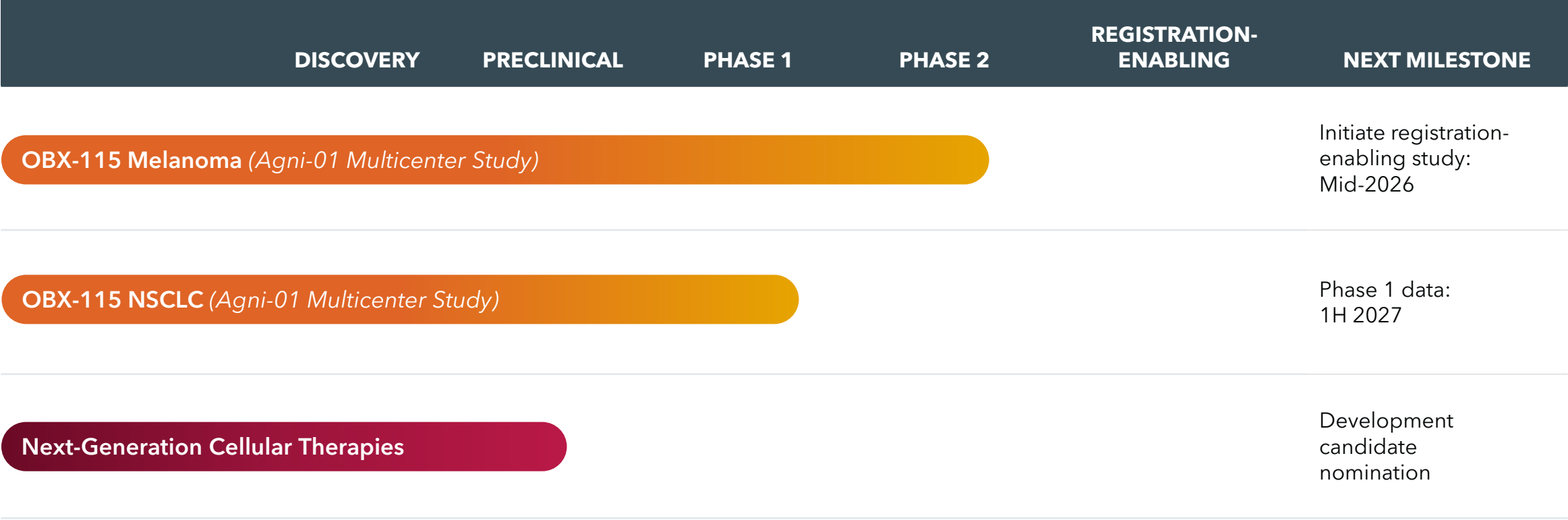
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TIL, tumor-infiltrating lymphocytes.

Harnessing Regulatable mbIL15 to Enhance OBX-115



Our Pipeline



Current Approved Cell Therapy for 2L+ Melanoma Limited By Tolerability Profile



Available cell therapy option for 2L+ melanoma:

Non-engineered TIL cell therapy

Approved based on 31.5% ORR¹

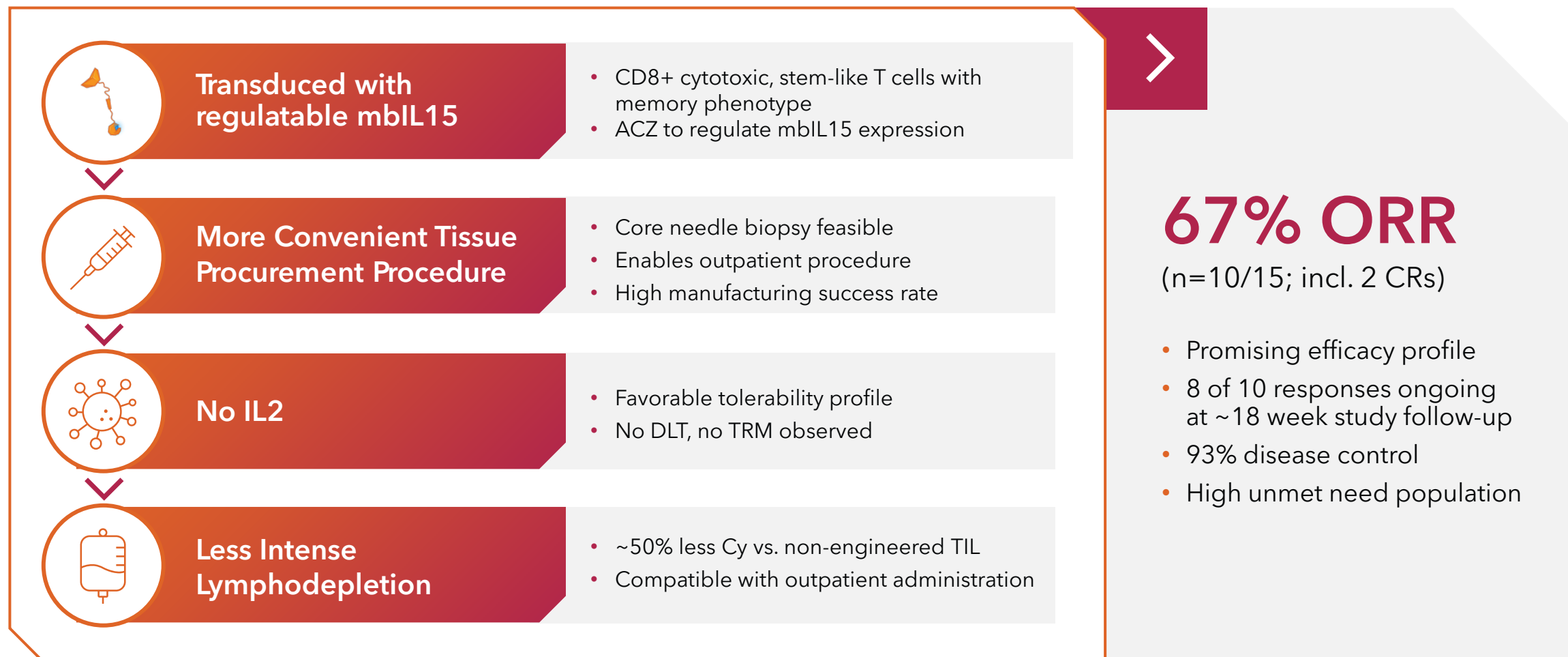


However, profile associated with tolerability and logistical challenges

- | | |
|--|--|
| ➤ High-dose IL2
IL2-dependent, terminally exhausted effector cells, severe AE's ¹ | ➤ Standard-dose LD
~4× more Cy vs approved CAR-T regimens |
| ➤ Black box warning
7.5% treatment-related mortality ¹ | ➤ Inpatient administration
23.6% ICU transfer ² , 17-day hospital stay ³ |
| ➤ Surgical excision required for tumor tissue procurement | ➤ High patient attrition (34%) ¹ post TTP |



Obsidian Leverages Regulatable mbIL15 to Deliver Patient-centric Cell Therapy in Melanoma



~\$3B+ Potential Addressable US Market Opportunity for OBX-115

2L+ Adult Patients with Advanced (Unresectable or Metastatic) Melanoma

~**10K**
patients¹

- ✓ Sufficient fitness & health performance
- ✓ Disease kinetics amenable to cell therapy
- ✓ Caregiver access / support

Cell Therapy Eligible

~**6K**
patients²

- ✓ OBX-115 maximizes cell therapy eligibility via no IL2, low-dose LD, and CNB TTP

OBX-115 Opportunity

~**5K**
patients²



IL2 Dependence Limits Addressable Market for Non-eng. TIL:

Eligibility for non-engineered TIL limited to 25% of 2L+ melanoma

Restricted to patients with adequate heart, liver, kidney function³



Potential for OBX-115 to Address Broadest Patient Population:

No IL2, low-dose LD, and core needle biopsy TTP expand eligibility to 50% of 2L+ melanoma

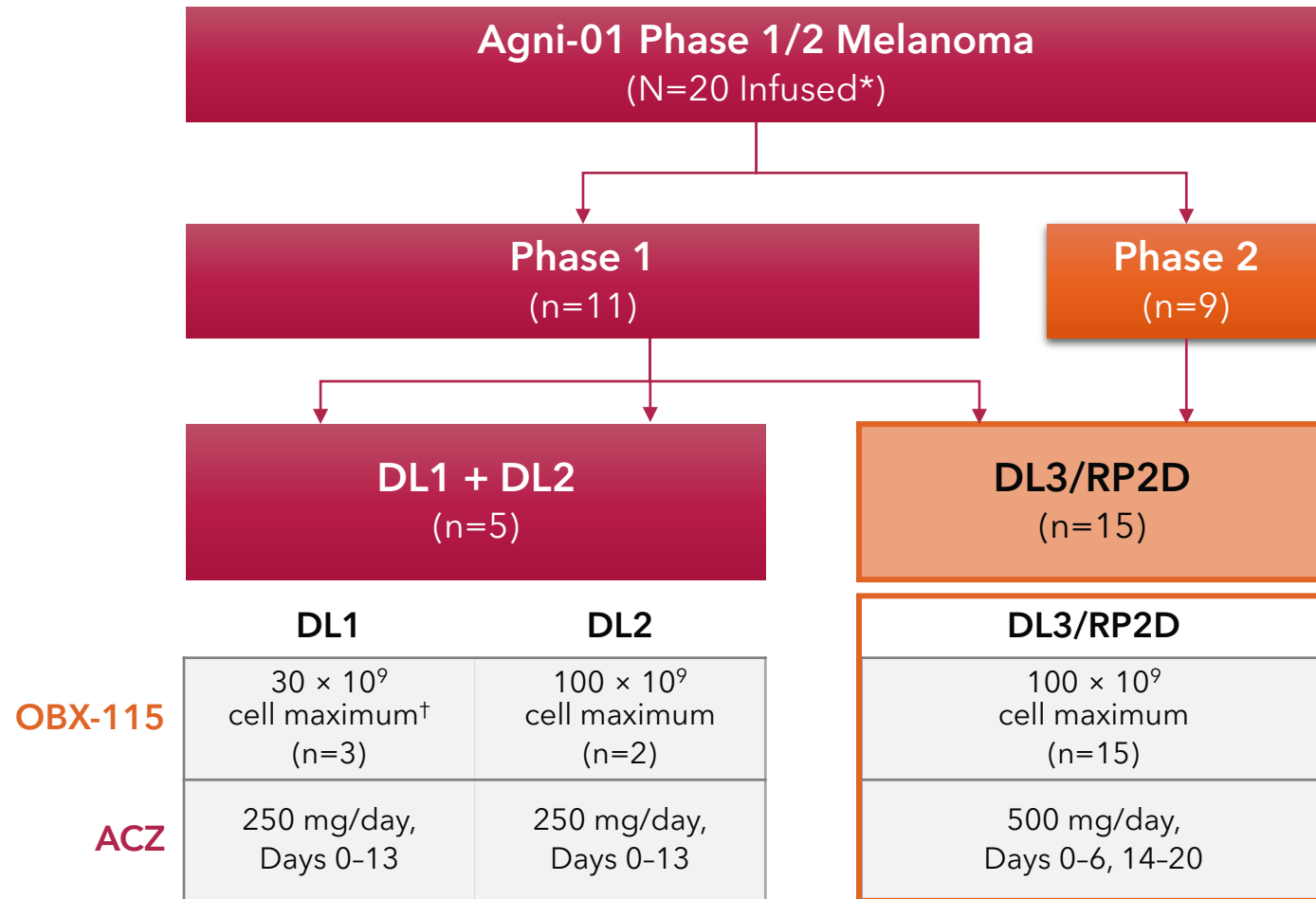
~\$3B+ addressable US market opportunity for OBX-115⁴ in melanoma



OBX-115 in Advanced Melanoma

Agni-01 Phase 1/2 Study Ongoing

Agni-01 Phase 1/2 Melanoma Patient Schema



At DL3/RP2D:

4 outpatient lymphodepletion

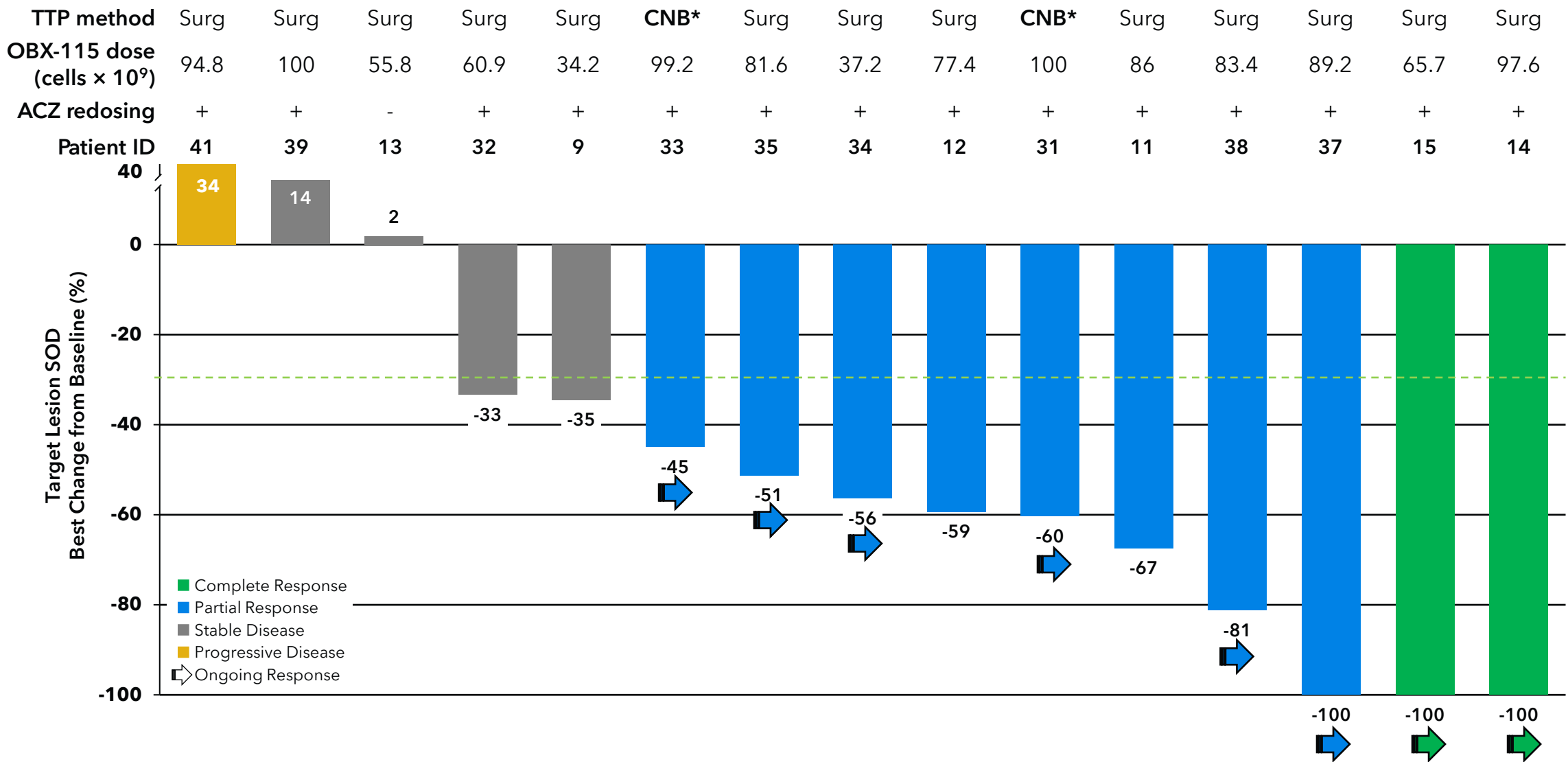
100% of ACZ redosing in outpatient setting[†]

Betof et al. ASCO 2026 (Abstract 9507). Data cutoff: 22 January 2026. *3 additional patients were enrolled and not infused: n=2 discontinued prior to treatment due to disease progression during DLT stagger phase; n=1 manufacturing failure.

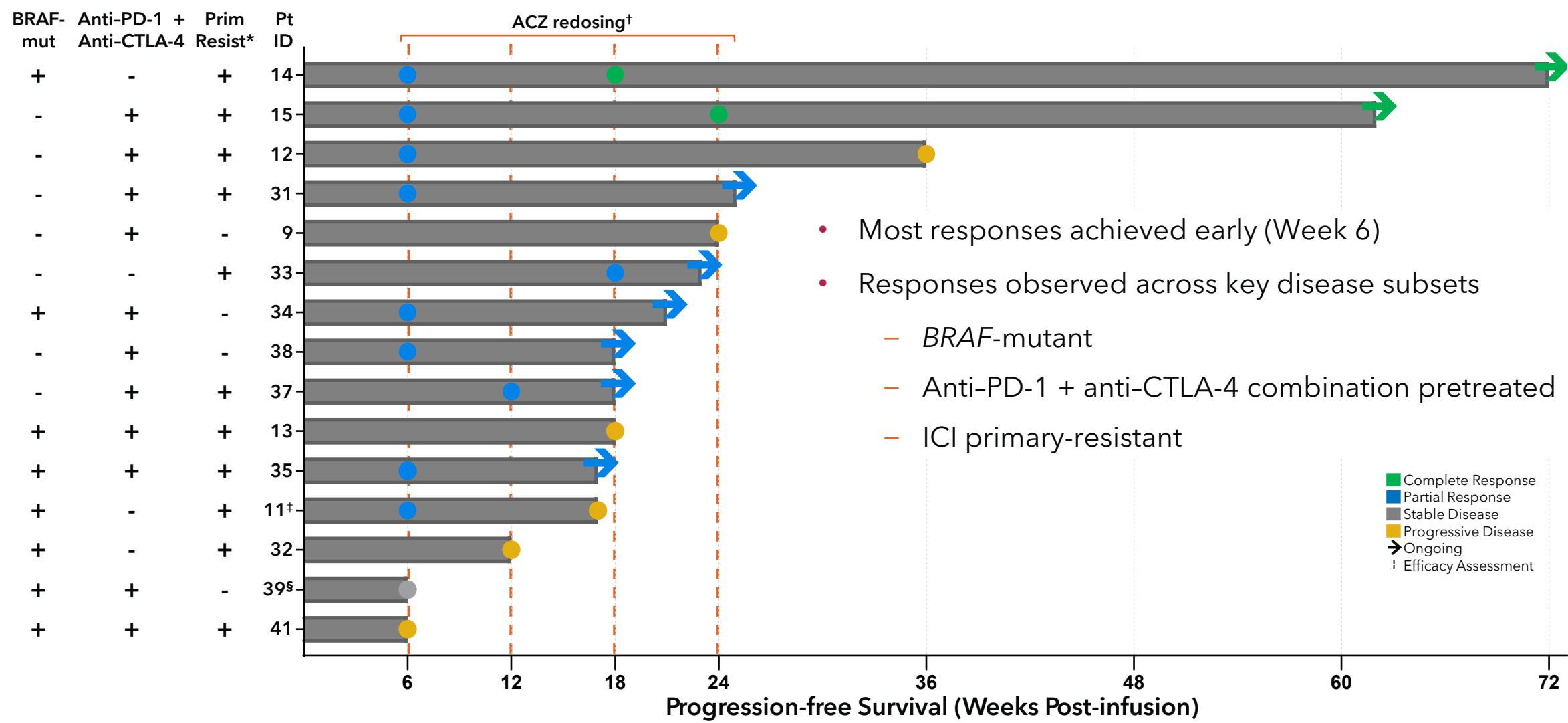
[†]Per-protocol maximum allowed infused cell dose.

ACZ, acetazolamide; D, Day; DL, dose level; RP2D, recommended phase 2 dose.

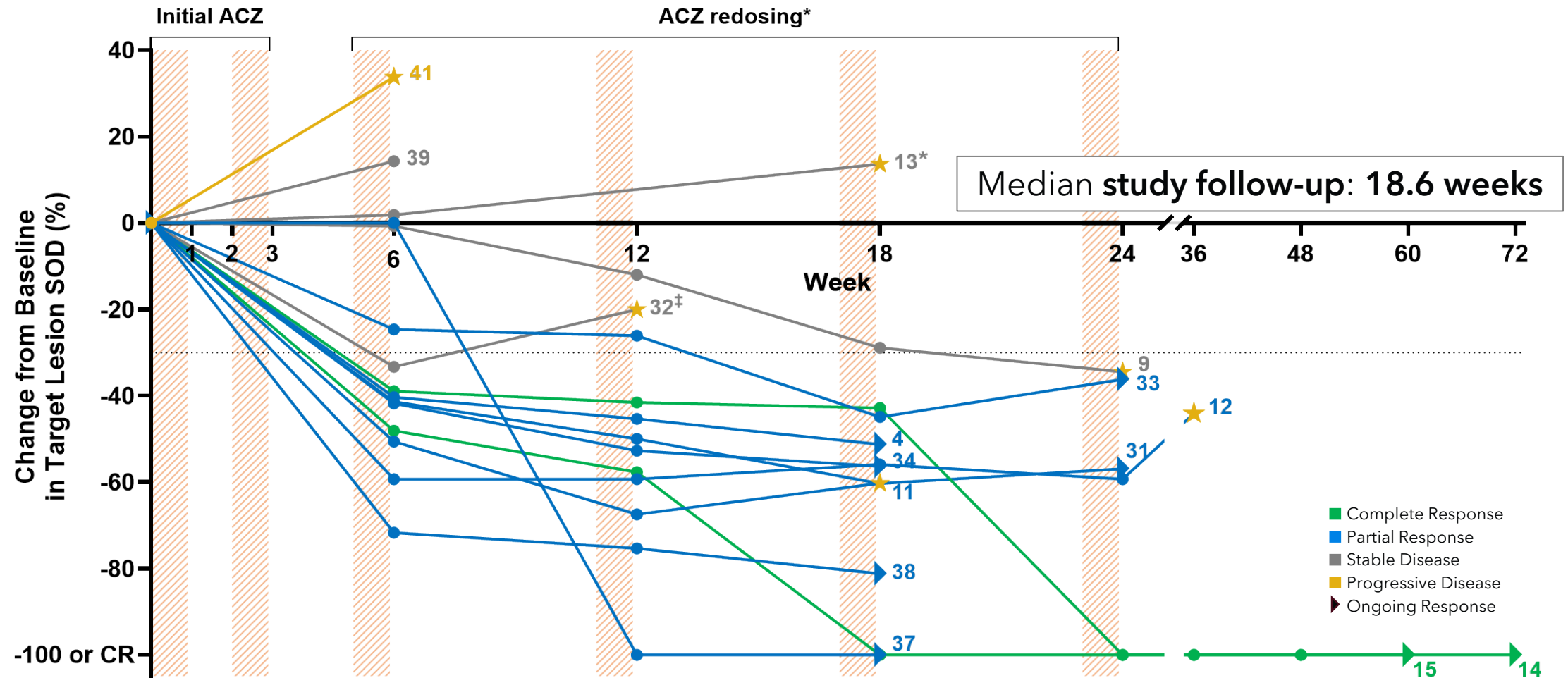
67% ORR, with SOD Reduction in 80% of Patients



Favorable Onset and Duration of Response



Deepening and Durable Responses



Data cut-off 22 Jan 2026.



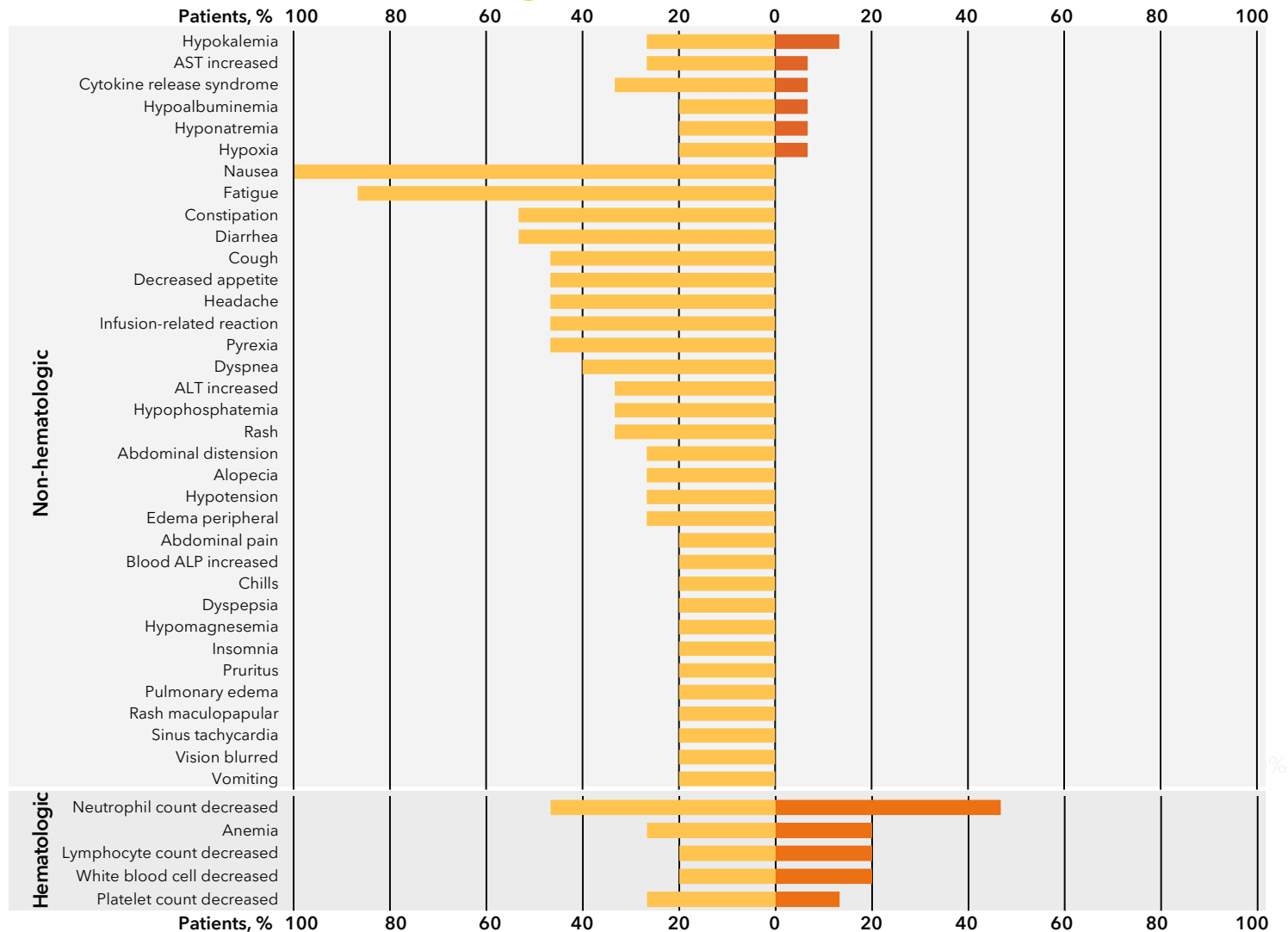
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Betof et al. ASCO 2026 (Abstract 9507). Data cutoff: 22 January 2026. *Patient 13 did not receive ACZ redosing. †Patient 32 had BRAF-refractory small-volume disease and a new satellite lesion at Week 12 that was biopsy-proven. ACZ, acetazolamide; CR, complete response; SOD, sum of diameters.

Favorable Safety & Tolerability Profile

TEAEs in $\geq 20\%$ of patients **All-grade**

Grade ≥ 3



- **Grade ≥ 3 non-hematologic toxicity was uncommon**
- **CRS** was reported for 5 patients (33%)
 - 1 event (7%) was Grade 3
- **Hematologic toxicity was favorable**
 - 1 event (7%) of febrile neutropenia (Grade 3)
- **No DLTs**
- **No ICANS**
- **No ICU transfer**

Data cut-off 22 Jan 2026.



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Betof et al. ASCO 2026 (Abstract 9507). Data cutoff: 22 January 2026. TEAE defined as any AE occurring after first dose of lymphodepletion, excluding AEs not related to OBX-115 or ACZ after Day 84.
ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CRS, cytokine release syndrome; DLT, dose-limiting toxicity; ICANS, immune effector cell-associated neurotoxicity syndrome; ICU, intensive care unit; TEAE, treatment-emergent adverse event.

Patients Had Difficult-to-treat Post-ICI Disease, With Majority Previously Exposed to Anti-PD-1 Combination

Baseline Patient and Disease Characteristics	OBX-115 (N=15)
Age, median (range), years	55 (41-78)
Sex, n (%)	
Female	6 (40.0)
ECOG PS, n (%)	
0	12 (80.0)
1	3 (20.0)
LDH >ULN, n (%)	6 (40.0)
Melanoma subtype, n (%)	
Cutaneous	9 (60.0)
Mucosal	3 (20.0)
Acral	3 (20.0)
Mutation status, n (%)	
BRAF V600-mutant	8 (53.3)
NRAS-mutant	3 (20.0)
Brain and/or liver lesions, n (%)	3 (20.0)
Target lesion SOD, mean (SD), mm	58.0 (14.2-213.0)

Treatment Characteristics	OBX-115 (N=15)
Lines of prior systemic therapy, median (range)*	2.0 (1-5)
Lines of prior ICI therapy	2.0 (1-5)
Prior systemic therapy, n (%)	15 (100.0)
Anti-PD-1 monotherapy only	1 (6.7)
Anti-PD-1 combination	14 (93.3)
Anti-PD-1 + anti-CTLA-4	11 (73.3)
Anti-PD-1 + anti-LAG3	8 (53.3)
BRAF ± MEK TKI	6/8 (75.0)
Primary-resistant (SITC criteria), n (%)	11/15 (73.3)
Anti-PD-1 ¹	5/9 (55.6)
Anti-PD-1 combination ²	8/14 (57.1)

- Patients had advanced and difficult-to-treat disease
- Disease progressed on several lines of standard-of-care therapies
 - **73% with prior anti-PD-1 + anti-CTLA-4 combination**
- Limited remaining treatment options

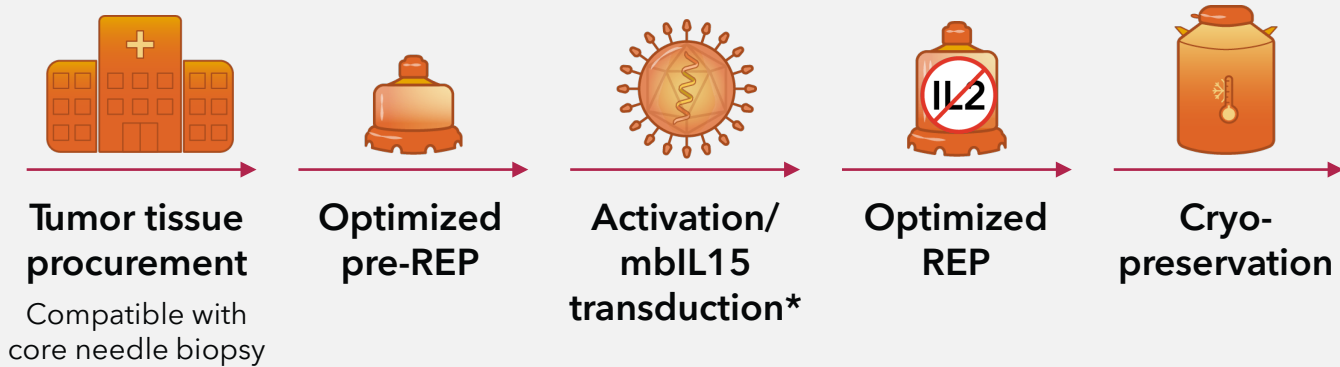
Betof et al. ASCO 2026 (Abstract 9507). Data cutoff: 22 January 2026. *Multiple prior lines were permitted.

1. Kluger HM et al. J Immunother Cancer 2020;8(1). 2. Kluger H et al. J Immunother Cancer 2023;11(3).

CTLA-4, cytotoxic T-lymphocyte antigen-4; ECOG PS, Eastern Cooperative Oncology Group performance status; ICI, immune checkpoint inhibitor; LAG3, lymphocyte activation gene 3; LDH, lactate dehydrogenase; PD-1, programmed cell death protein-1; SITC, Society for Immunotherapy of Cancer; SOD, sum of diameters; TKI, tyrosine kinase inhibitor; ULN, upper limit of normal.

Proprietary Manufacturing Process Enables Advantages in Phenotype, Yield, Process Control, and Procurement Method

Ex Vivo Manufacturing



Enhancements vs non-engineered TIL

- 4-1BB agonism in pre-REP
- iFeeder cells expressing IL21 and 4-1BBL
- ACZ (IL15)-driven expansion (no IL2)

Optimized product: median **>90%** CD8+; effector-memory phenotype, stem-like signature, minimally exhausted^{1,2}

High process control

Robust manufactured cell dose yield: median ~129B vs. 21.1B³ non-engineered TIL

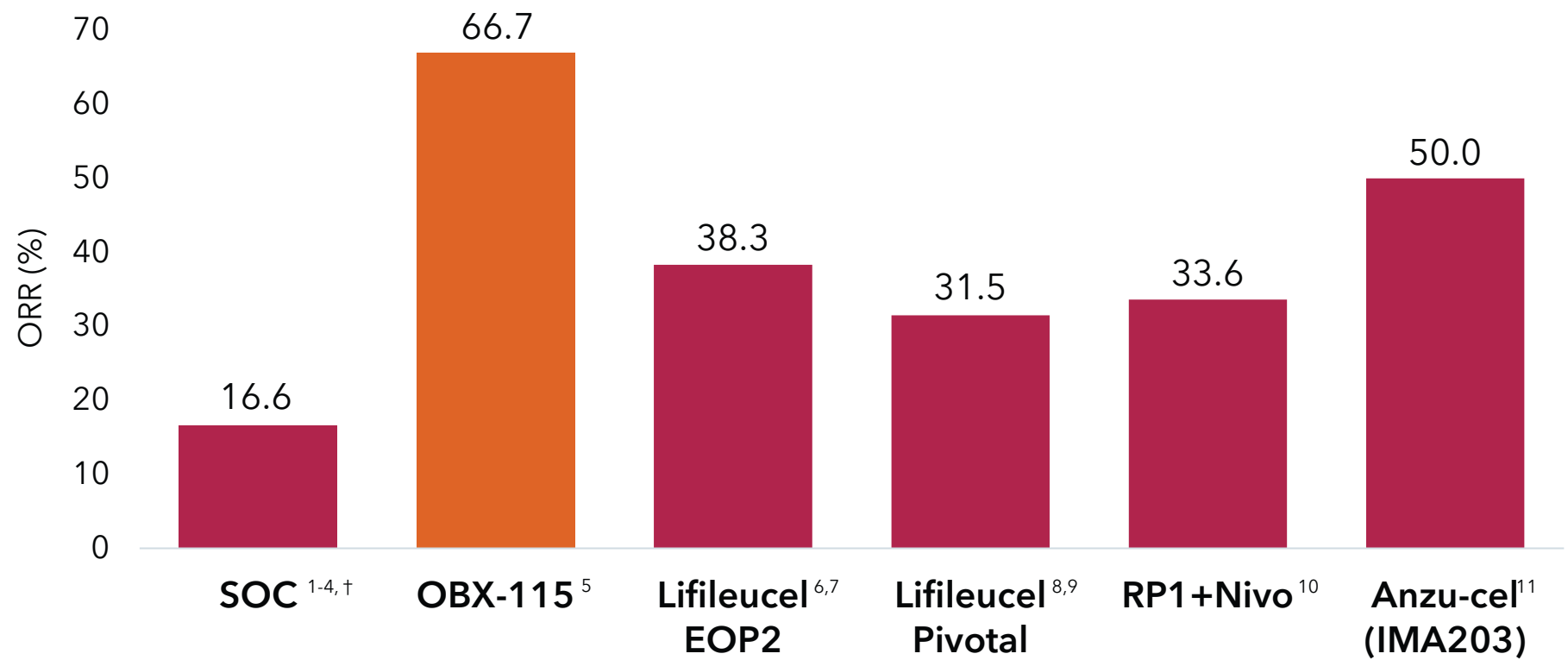
Core needle biopsy enabled for OBX-115 manufacturing

*Anti-CD3 Ab; retroviral vector.

1. Amaria RN et al. ASCO 2024 (Abstract 9515). 2. Amara RN et al. AACR 2024 (Poster CT176). 3. J. Journal for ImmunoTherapy of Cancer 2022;10:e005755.

ACZ, acetazolamide; CNB, core needle biopsy; IL2, interleukin 2; IL15, interleukin 15; IL21, interleukin 21; mbIL15, membrane-bound IL15; REP, rapid expansion protocol; TIL, tumor-infiltrating lymphocytes.

Encouraging Efficacy Profile in 2L+ Melanoma Across Modalities



	N	SOC ^{1-4, †}	OBX-115 ⁵	Lifileucel EOP2 ^{6,7}	Lifileucel Pivotal ^{8,9}	RP1+Nivo ¹⁰	Anzu-cel ¹¹ (IMA203)
Received anti-PD-1 + anti-CTLA-4 (or anti-LAG3) combination		971 ¹⁻⁴	15	47	73	140	14
Primary-resistant to ICI		12% ^{1,2}	93%	Not reported	58%	44%	71%
		~64% ¹	73%	Not reported	71%	66%	Not reported

Comparisons based on historical published data. No head-to-head studies have been conducted and cross-trial comparisons may not be reliable due to differences in molecule composition, trial design, and patient population and characteristics.

[†]SOC therapies include: Ipi+Nivo (ORR 28%),¹ Chemo (ORR 11%),² Rel+Nivo (ORR 12%),³ and ICI recycling (ORR 15.5%).⁴
1. VanderWalde A, Nat Med. 2023 Sep;29(9):2278-2285. 2. Goldinger SM Eur J Cancer 2022; 162:22-33. 3. Ascierto PA J Clin Oncol 2023;41(15):2724-2735. 4. Reschke R, J Dtsch Dermatol Ges. 2020; 18(5): 429-436. 5. Betof et al. ASCO 2026 (Abstract 9507). 6. Iovance Press Release. Oct 11, 2018. 7. Sarnaik A, SITC 2018 (Poster O22). 8. AMTAGVI (lifileucel) Prescribing Information. February 2024. 9. Chesney J. J Immunother Cancer 2022; 10:e005755. 10. Wise-Draper T. SITC 2025 (Abstract 1327). 11. Diwakar D ASCO 2026 (Abstract 9508).
CTLA-4, cytotoxic T-lymphocyte-associated protein 4; EOP2, end of phase 2; ICI, immune checkpoint inhibitors; LAG3, lymphocyte activation gene 3 protein; ORR, objective response rate; PD-1, programmed cell death protein-1; SOC, standard of care; Tx, therapy.

OBX-115 is Positioned Favorably vs Other Melanoma Cell Therapies

		OBX-115 <i>Agni-01 Ph 2 ongoing</i>	AMTAGVI <i>Approved</i>	ANZU-CEL <i>SUPRAME reg. trial ongoing</i>
Efficacy	ORR	67% ¹ (N=15)	31.5% ² (N=73)	50% ³ (N=14)
AE Profile Drivers	IL2-sparing	✓	✗	✗
	Low-dose LD	✓	✗	✓
	No TRM	✓	✗	✓
	No CRS Gr >3 or ICANS	✓	✗	✗
Treatment Burden	Outpatient-compatible	✓	✗	✓
	No ICU	✓	✗	?
	Material Procurement	CNB eligible	Surgical resection	Leukapheresis
Patient Eligibility	≥ 50% of 2L+ Mel.	✓	25% eligible; restricted to adequate heart, liver, kidney function ⁴	~30% eligible: restricted to cutaneous (~90%) ⁵ , LDH <2× ULN (~80%) ⁶ & HLA restricted (~40%) ⁷

Information for approved products based on FDA-approved labeling and publicly available data. Comparisons based on historical published data; no head-to-head studies have been conducted and cross-trial comparisons may not be reliable due to differences in molecule composition, trial design, and patient population and characteristics.

1. Betof et al. ASCO 2026 (Abstract 9507). 2. AMTAGVI (lifileucel) Prescribing Information. February 2024. 3. Diwakar D ASCO 2026 (Abstract 9508). 4. Due to high-dose IL2 and standard lymphodepletion regimen, restricted to patients with adequate heart, liver, kidney function (The Dedham Group KOL Market Research 2025). 5. Long GV et al. The Lancet. 2023; 402(10400):485-502. 6. Kocza K et al. Cancer Med. 2023 Feb;12(3):2427-2439. 7. Li X et al. Mol Oncol. 2021 Jul;15(7):1764-1782.
2L, second-line; AE, adverse event; CRS, cytokine release syndrome; DOR, duration of response; ICANS, immune effector cell-associated neurotoxicity syndrome; ICU, intensive care unit; IL2, interleukin 2; mDOR, median duration of response; NR, not reached; ORR, objective response rate; FDA, Food and Drug Administration; PDUFA, Prescription Drug User Fee Act; TRM, treatment-related mortality; Tx, therapy.

Advancing OBX-115 to Registration-enabling Study



FDA feedback

obtained on a **single-arm trial design** for accelerated approval (at Sponsor's risk)

For OBX-115 in patients with advanced melanoma progressing after ICI therapy



FDA alignment on:

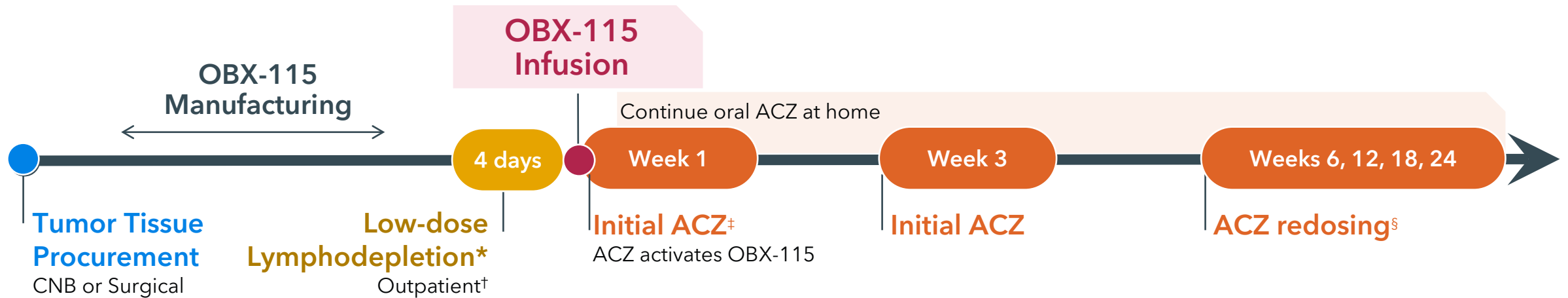
- Sufficiency of durable **ORR** as an endpoint that predicts clinical benefit
- **Sample size** for safety dataset
- No changes to proposed **eligibility criteria**
- Drug product **potency assay** development and qualification



Mid-2026: First patient enrolled in registration-enabling cohort of existing multi-center study

A **confirmatory study** will be underway at the time of BLA action

Agni-01 Melanoma Registration-enabling Study Design: Outpatient-compatible Regimen



Key Eligibility Criteria

- Post-ICI advanced melanoma
- ≤ 2 prior lines of systemic therapy
- BRAFi/MEKi therapy not mandated in BRAF-mut disease
- ≥1 lesion suitable for tumor tissue procurement
- ≥1 remaining lesion amenable to RECIST v1.1 response assessment

Primary Endpoints

- Blinded independent central reviewer (BICR)-assessed ORR

Key Secondary Endpoints

- DOR (BICR-assessed)
- and tolerability of the OBX-115 regimen
 - Incidence, severity, seriousness, relationship to study intervention, and characteristics of treatment-emergent adverse events (TEAEs)

NCT06060613. *Cy 750 mg/m² × 3 days and Flu 30 mg/m² × 4 days. † Outpatient or inpatient administration, at the discretion of the treating physician. ‡ Initial ACZ is administered once daily starting day of OBX-115 infusion for ≤14 days, split into two ≤7-day periods within 28 days (Day 0–6 or until ALC ≥5000 cells/μL whichever is earlier, and restarting between Day 14 and 21). § Additional ACZ dosing for ≤7 days at periodic intervals until Week 24, and upon progression when new anticancer therapy is not immediately warranted. ACZ, acetazolamide; BICR, blinded independent central review; CNB, core needle biopsy; Cy, cyclophosphamide; DOR, duration of response; Flu, fludarabine; ICI, immune checkpoint inhibitor; LD, lymphodepletion; ORR, objective response rate; RECIST, Response Evaluation Criteria in Solid Tumors; TTP, tumor tissue procurement.

OBX-115 in NSCLC

Agni-01 Phase 1/2 Study Ongoing

OBX-115 Potential to Deliver Improved Product Profile in NSCLC



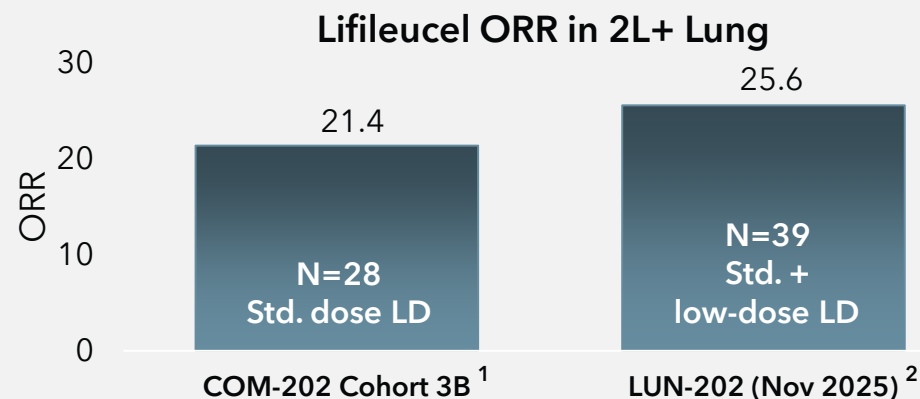
OBX-115: Potential to Improve NSCLC TPP & Expand Market Opportunity

- ✓ IL2-free regimen
- ✓ Low-dose LD
- ✓ Core needle biopsy compatible
- ✓ Tumor reduction signal (OBX-115 monotherapy) observed in early Phase 1 data

**NSCLC prevalence ~10× that of
advanced melanoma**



Lifileucel: Efficacy in 2L+ NSCLC, But Associated with Toxicity Risk



Proof of TIL efficacy & durability in Lung, however, concerning safety signals³:

- 12% died in first 30 days post-treatment
- G5 toxicity led to temporary clinical hold (2023)

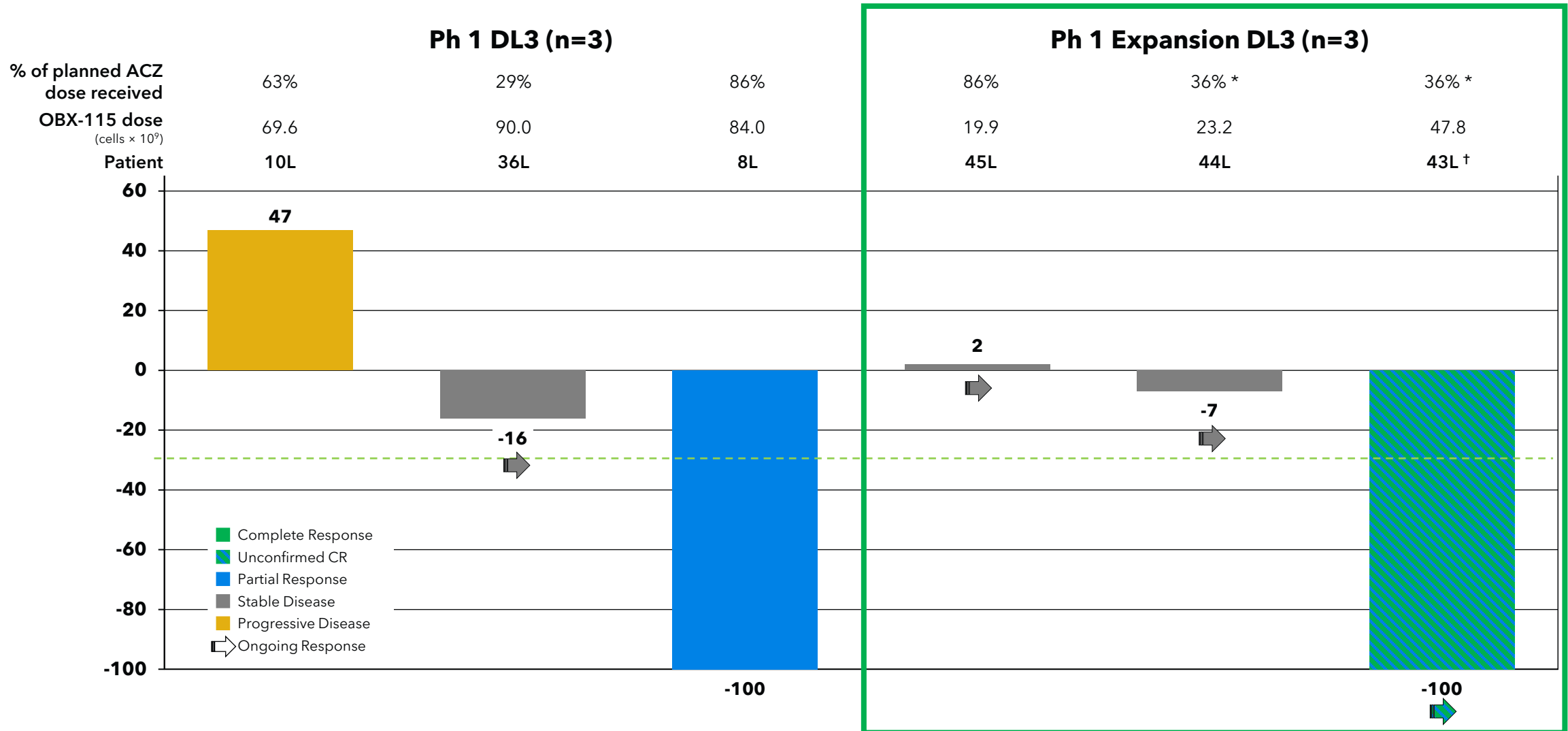


NSCLC Dose Escalation Leveraged Melanoma Experience; Dose Optimization at DL3 Ongoing

- ✓ Completed NSCLC dose escalation to get to DL3
- ✓ Exploring new intermediate cell dose cap (~60B) to maximize ACZ regimen
- ✓ Study enrollment ongoing

Infused Patients*		Melanoma		NSCLC
Dose Level		Phase 1 (N=11)	Phase 2 (N=9)	Phase 1 (N=10)
DL1	30B cell dose cap ACZ: 250 mg/day, Days 0-13 Planned 28-day cumulative dose: 3500 mg	3	0	1
DL2	100B cell dose cap ACZ: 250 mg/day, Days 0-13 Planned 28-day cumulative dose: 3500 mg	2	0	1
DL3	100B cell dose cap ACZ: 500 mg/day, Days 0-6, 14-20 Planned 28-day cumulative dose: 7000 mg	6	9	4*
	DL3 Expansion in NSCLC Intermediate cell dose cap (~60B) ACZ: 500 mg/day, Days 0-6, 14-20 Planned 28-day cumulative dose: 7000 mg + Extended ACZ redosing every other wk	0	0	4*

Encouraging Signal in NSCLC Patients Treated at 60B Cell Dose Cap



Data cut-off Jan 22, 2026.

*Both patients (43L and 44L) had ALC >5000 at Days 10-14 and Week 3 doses omitted. †Patient 43L Baseline ctDNA (160 ppm) was undetectable at D14 and D42.

ACZ, acetazolamide; CR, complete response; DL, dose level; NSCLC, non-small cell lung cancer; Ph, phase.

Expected Milestones Through 2027

Recent Achievements

- ✓ Positive Ph 2 data in Agni-01 melanoma multicenter study
- ✓ FDA clarity on Melanoma registrational pathway and potency assay
- ✓ Fast Track & RMAT designations in advanced melanoma
- ✓ NSCLC monotherapy response signal from early Ph 1 regimen optimization data

Anticipated Milestones



First patient enrolled in melanoma registration-enabling cohort **Mid-2026**

Melanoma top-line data **YE 2027**

NSCLC Phase 1 data **1H 2027**



Plan to Continue

Preclinical development and expand platform into next-gen cell therapies

Manufacturing and infrastructure investments to support future commercial scale



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Thank you