IO BIOTECH

OUR GOAL:

Establish our T-win® immune-modulating cancer vaccines as the potential backbone of therapy for multiple cancer types

Nasdaq: IOBT

Corporate Overview

May 2023

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Forward Looking Statements

Certain information contained in this presentation includes "forward-looking statements", within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, related to our business plan, clinical trials and regulatory submissions. We may, in some cases, use terms such as "may," "should," "would," "expects," "plans," "anticipates," "could," "intends," "target," "projects," "contemplates," "believes," "estimates," "predicts," "potential" or "continue" or other words that convey uncertainty of the future events or outcomes to identify these forward-looking statements. Our forward-looking statements are based on current beliefs and expectations of our management team that involve risks, potential changes in circumstances, assumptions, and uncertainties. Any or all of the forward-looking statements may turn out to be wrong or be affected by inaccurate assumptions we might make or by known or unknown risks and uncertainties. These forward-looking statements are subject to risks and uncertainties including risks related to the execution of our business plan, success and timing of our clinical trials or other studies and the other risks set forth in our filings with the U.S. Securities and Exchange Commission. For all these reasons, actual results and developments could be materially different from those expressed in or implied by our forward-looking statements. You are cautioned not to place undue reliance on these forward-looking statements, which are made only as of the date of this presentation. We undertake no obligation to publicly update such forward-looking statements to reflect subsequent events or circumstances.

"*Cancer Vaccines: the next immunotherapy frontier*"

nature cancer

REVIEW ARTICLE

https://doi.org/10.1038/s43018-022-00418-6

Check for updates

Cancer vaccines: the next immunotherapy frontier

Matthew J. Lin[1,2,3,4], Judit Svensson-Arvelund[1,2,3,5], Gabrielle S. Lubitz[1,2,3], Aurélien Marabelle[6], Ignacio Melero[7], Brian D. Brown[2] and Joshua D. Brody[1,2,3] ✉

After several decades, therapeutic cancer vaccines now show signs of efficacy and potential to help patients resistant to other standard-of-care immunotherapies, but they have yet to realize their full potential and expand the oncologic armamentarium. Here, we classify cancer vaccines by what is known of the included antigens, which tumors express those antigens and where the antigens colocalize with antigen-presenting cells, thus delineating predefined vaccines (shared or personalized) and anonymous vaccines (ex vivo or in situ). To expedite clinical development, we highlight the need for accurate immune monitoring of early trials to acknowledge failures and advance the most promising vaccines.

NATIONAL GEOGRAPHIC

Cancer vaccines are showing promise. Here's how they work.

The immediate goal is to create vaccines that destroy cancer cells—but some scientists are also testing vaccines that might prevent someone from developing cancer.

BY PRIYANKA RUNWAL

PUBLISHED 22 DEC 2022, 09:52 GMT

Seminal discovery of T cells that provide immunity against immune suppressive molecules (e.g., IDO1, PDL1).

T-win Vaccine Platform:

Pioneered first immune modulating therapy directed against cells (Tregs & TAMs) in the TME expressing immune-suppressive proteins (currently in Ph3)

Direct killing of immune suppressive cells (IDO1 & PDL1), including both tumor cells and genetically stable cells in the TME, demonstrated in Ph1/2

Modulation of the TME into a more pro-inflammatory, anti-tumor environment by eradicating IDO and PD-L1 positive Tregs and TAMs

T-win® IO102-IO103 vaccine has potential to significantly improve current treatment paradigm

1. Lin et al. *Nature Cancer* 3, 911-926 (2022)
2. Runwal P. National Geographic, published 22 Dec 2022

Growth Trajectory Supported by Significant Clinical Milestone Momentum

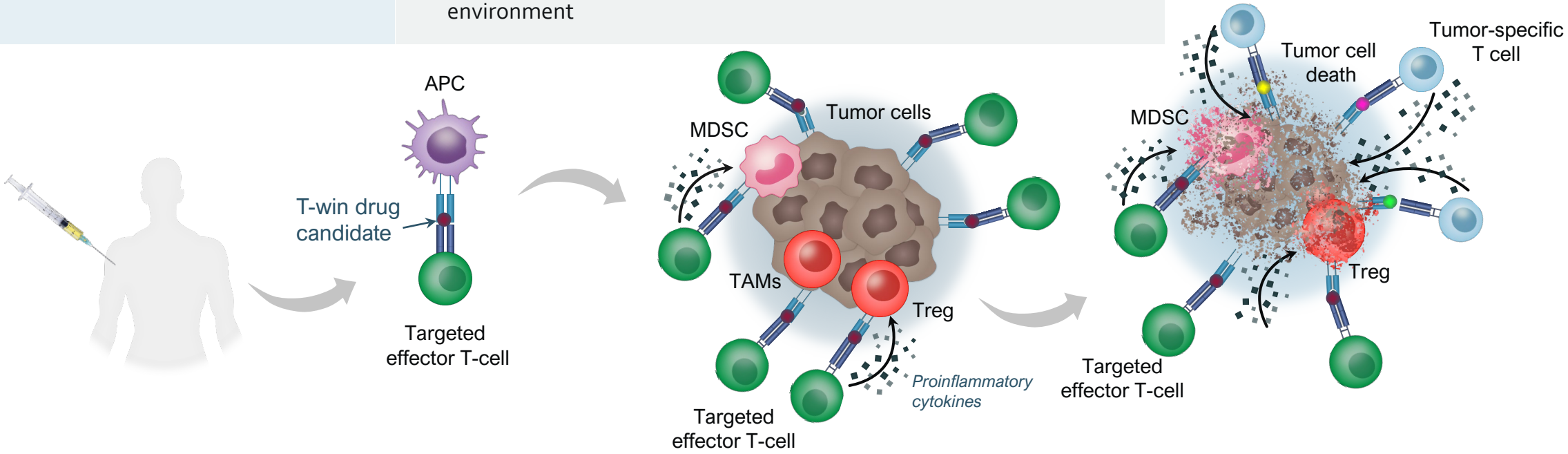
Industry Pioneers	• First immune-modulating cancer vaccine designed to target the TME, currently in Phase 3 clinical development • T-win® MOA designed to stimulate pre-existing T cells against both tumors *and* immune suppressive cells in the TME • Infiltrating T cells modulate the TME into an anti-tumor pro-inflammatory environment
Shifting the Paradigm	• 1st line melanoma combo with nivolumab: 80% ORR, 50% CR and 25.5 months median PFS* (n=30); durable results with favorable safety profile shown in Ph1/2 • Current SOC ~45%-58% ORR and ~7-12 months PFS • Breakthrough Therapy Designation (BTD) for melanoma granted by FDA based on Phase 1/2 data for IO102-IO103
Potential for US Market Entry in 2025	• Phase 3 global multi-center pivotal trial evaluating combination with pembrolizumab in 1st line advanced melanoma; completion of enrollment expected by year-end 2023; protocol calls for interim analysis of ORR one year after 225 patients have been randomized; potential submission of BLA for accelerated approval based on interim analysis • Potential efficacy and safety profiles may lead to T-win vaccine becoming a backbone of future combination therapy
Multiple Upside Opportunities in Other Solid Tumors	• Phase 2 basket trial enrolling patients across three cohorts (lung, head and neck, and bladder cancer) • Encouraging data from nine evaluable lung patients reported January 2023 • Early-stage pipeline targeting additional immune suppressive mechanisms
Poised for growth	• Nasdaq listing (IPO) in Nov. 2021 • Cash: ~$128.6 M (3-31-22 – preliminary and unaudited); runway through 3Q2024 • Continue organizational development in Denmark and United States

* January 23 update: One patient was re-evaluated and did not have "real progression" but instead pseudo progression.

T-Win® Vaccine Targets the Immune System

Vaccine designed to engage critical immune suppressive antigens (e.g. Tregs, TAMs, MDSCs)

T-win vaccine designed to target high value TME proteins	Induction of potent immune response within the TME to enhance killing of tumor cells:	Potential to overcome limitations of previous approaches
(e.g. IDO, PD-L1, arginase)	• Direct killing of target-expressing immunosuppressive cells in the TME • Modulation of the TME into a more pro-inflammatory, anti-tumor environment	

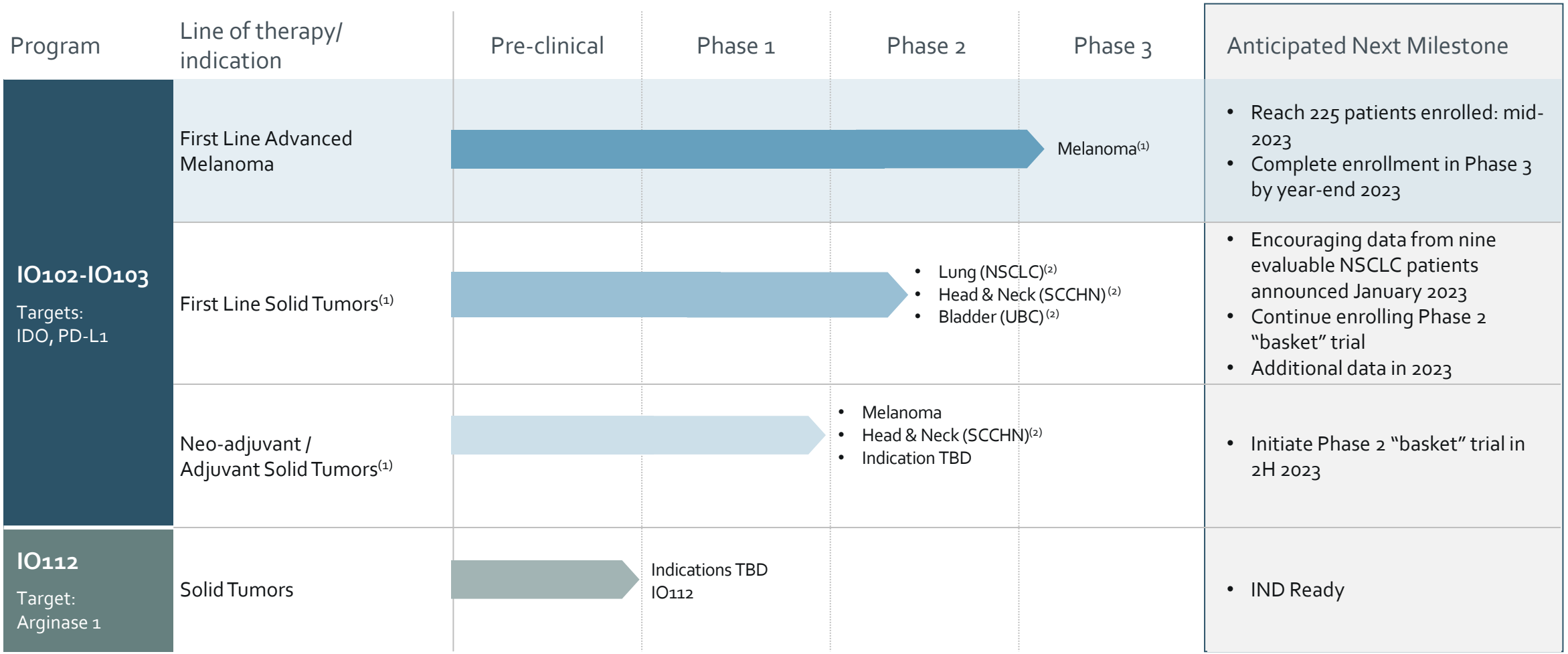


1. Subcutaneous injection with T-win vaccine
2. T-win vaccine activates T-cells
3. Vaccine activated T cells attack immune suppressive targeted antigen presenting cells
4. The inflamed TME becomes immune-permissive, enabling further tumor cell killing by the recruited tumor-specific T-cells

Kjeldsen *et al. Nat Med.* 2021;27:2212–2223. Erratum in: *Nat Med.* 2022;28(4):871

Translating our Science to Clinical Outcomes

Current Pipeline Overview



1. In combination with pembrolizumab
2. NSCLC = non-small cell lung cancer, SCCHN = squamous cell carcinoma of the head and neck, UBC = urothelial bladder cancer

IO Biotech's Clinical Strategy

Goal: Establish our T-win immune-modulating cancer vaccine as the backbone of therapy for multiple cancer types

FAST MARKET ENTRY

- **Melanoma 1L** in combination with pembrolizumab across PD-L1 & BRAF subtypes (potential accelerated approval under BTD) — IOB-013

MAXIMIZE within melanoma

- **Melanoma 1L** in combination with other CPI — MSKCC IIT
- **Earlier setting** in combination with pembrolizumab — IOB-032, KIEO IIT

EXPAND To other tumor types and LoT

- **NSCLC, SCCHN 1L** — IOB-022, IOB-032, HN1901, UCD IIT

IOB Market driver

REASONS TO BELIEVE

- ✓ Potential position in the "desired quadrant" of high efficacy and low toxicity
- ✓ Compelling ORR and CRR
- ✓ Strong data in key subgroups including elevated LDH, PD-L1+ and stage M1c
- ✓ Favorable survival with mOS still NR and 3-yr OS rate of 73%
- ✓ Favorable safety profile with Gr3/4 TRAEs of 17% pts

Melanoma By the Numbers

Unresectable / metastatic melanoma is serious and life-threatening

In 2023 in the U.S.*:

100,000
Expected New Melanoma Cases

8,000
Die each year

Stage IV melanoma patients (untreated) regardless of BRAF mutation status

37-39
months
Median OS

40-50%
5-Year OS

Anti-programmed death (PD)-1 antibodies (e.g. nivolumab and pembrolizumab) lead to a 5-year overall survival rate of

43-51%

Anti-cytotoxic T-lymphocyte associated antigen-4 (CTLA-4) antibody (i.e., ipilimumab) in combination with anti PD-1 antibody (nivolumab) can increase 6.5-year overall survival rate to about

49%...

...but associated with considerable toxicity:

59%

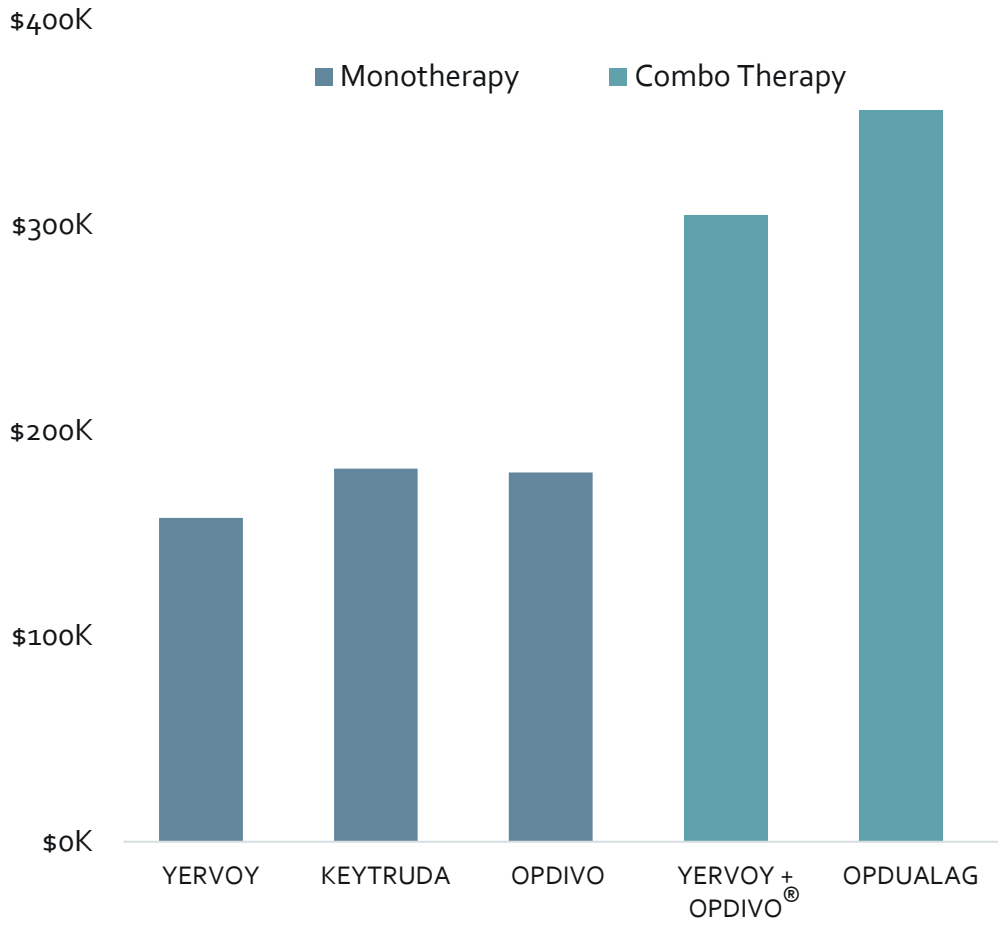
grade 3/4 TRAEs, highlighting the need for better tolerated combinations

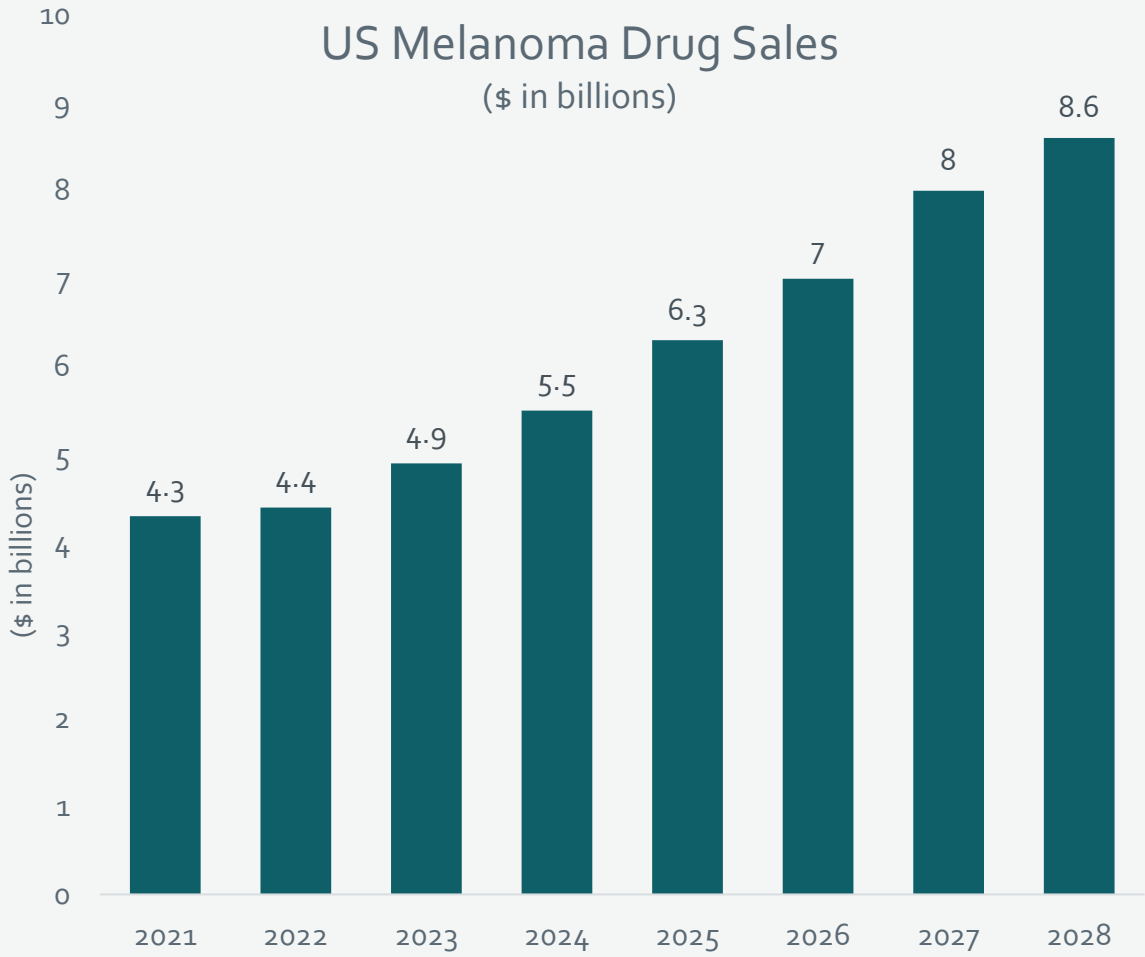
Larkin et al. *N Engl J Med.* 2019; 381(16):1535-1546; Robert 2019; Wolchock et al *ASCO* 2021 Abstract 9506; Wolchock et al. *J Clin Oncol* 2022: 40(2):127-137; * American Cancer Society website accessed 3/1/2023

US Melanoma Drug Pricing and Market – 10.6% CAGR 2021 - 2028

Combination therapy leading to significant market growth

US Melanoma Drug Pricing (annual WAC):





* Sources: Redbook, 5/9/2022; Evaluate Pharma 5/11/2023

Positioned for Leadership in the Evolving Melanoma Landscape

Our goal: Inducing meaningful tumor regression and establishing durable anti-tumor response while achieving a manageable tolerability profile for patients

Benefit-Risk Ratio

Io102-IO103 in the desired "quadrant"

- High PFS, high ORR, low AE's

In Phase 3

First mover advantage with IO102-IO103

Potential Competitive Advantages

Future combination therapy

- Strong potential to become backbone of future triple combination therapies
- No additional systemic toxicity observed in completed clinical trials
- Designed to be off-the-shelf vaccine

Potential broad applicability

- Consistent results across melanoma subgroups
- Applicability across tumor types and stages
- Potential for use across patients regardless of PD-L1 expression

Potential to be well-positioned vs. recent combination market entrants

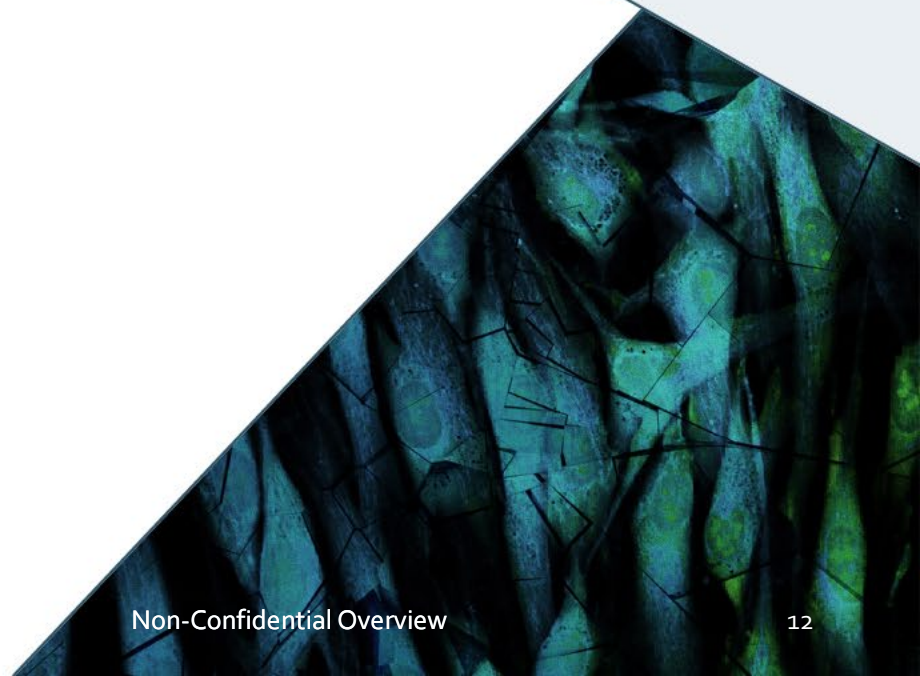
*Effect only in a subset of patients (PD-L1 low: < 1%)**

* Relativity 047 study data as reported

T-win® IO102-IO103 Immune-Modulating Cancer Vaccine

Phase 1/2 Clinical Trial

In collaboration with the Center for Cancer Immune Therapy



Compelling Phase 1/2 Data Published in *Nature Medicine*

Successful Outcomes Drive Continued Clinical Development

nature medicine

December 09, 2021

A phase 1/2 trial of an immune-modulatory vaccine against IDO/PD-L1 in combination with nivolumab in metastatic melanoma

Julie Westerlin Kjeldsen[1,5], Cathrine Lund Lorentzen[1,5], Evelina Martinenaite[1,2], Eva Ellebaek[1], Marco Donia[1], Rikke Boedker Holmstroem[1], Tobias Wirenfeldt Klausen[1], Cecilie Oelvang Madsen[1], Shamaila Munir Ahmed[1], Stine Emilie Weis-Banke[1], Morten Orebo Holmström[1], Helle Westergren Hendel[3], Eva Ehrnrooth[2], Mai-Britt Zocca[2], Ayako Wakatsuki Pedersen[2], Mads Hald Andersen[1,4] and Inge Marie Svane[1]✉

January 2023 Data Cut*

49.8
months median follow up

25.5
months mPFS

mOS
Not yet reached*

50%
CRR

80%
ORR

(as previously reported in Nature; RECIST1.1= 73.3% ORR)

* January 23 update: One patient was re-evaluated and did not have "real progression" but instead pseudo progression.

Lorentzen et al Long-term follow-up of anti-PD-1 naïve patients with metastatic melanoma treated with IDO/PD-L1 targeting peptide vaccine and nivolumab. JITC accepted for publication

Phase 1/2 Trial (MM1636) Baseline Demographics

Patient characteristics

Majority of patients had one or more poor prognostic factors:

- **43% PD-L1 negative**
- **60% M1c**
- **37% high LDH**

Baseline characteristics are largely similar to those in other trials

Patients	n = 30
Age (years)	
Mean (range)	70 (46-85)
Sex	
Female	14 (47%)
Male	16 (53%)
ECOG Performance status	
0	26 (87%)
1	4 (13%)
PD-L1 status	
Positive (≥1%)	17 (57%)
Negative (< 1%)	13 (43%)
BRAF status (%)	
Mutant (V600E, V600K)	11 (37%)
Wild-Type or non-V600 mutation	19 (63%)

Patients	n = 30
Stage (8th edition JACC) (%)	
M1a	6 (20%)
M1b	6 (20%)
M1c	18 (60%)
LDH (%)	
Normal	19 (63%)
Elevated > ULN	11 (37%)
Liver metastases (%)	
Yes	10 (33%)
No	20 (67%)
Number of metastatic sites	
1	7 (23%)
2-3	17 (57%)
> 3	6 (20%)

Kjeldsen *et al. Nat Med.* 2021;27:2212–2223.

Compelling ORR and CRR

Data externally confirmed

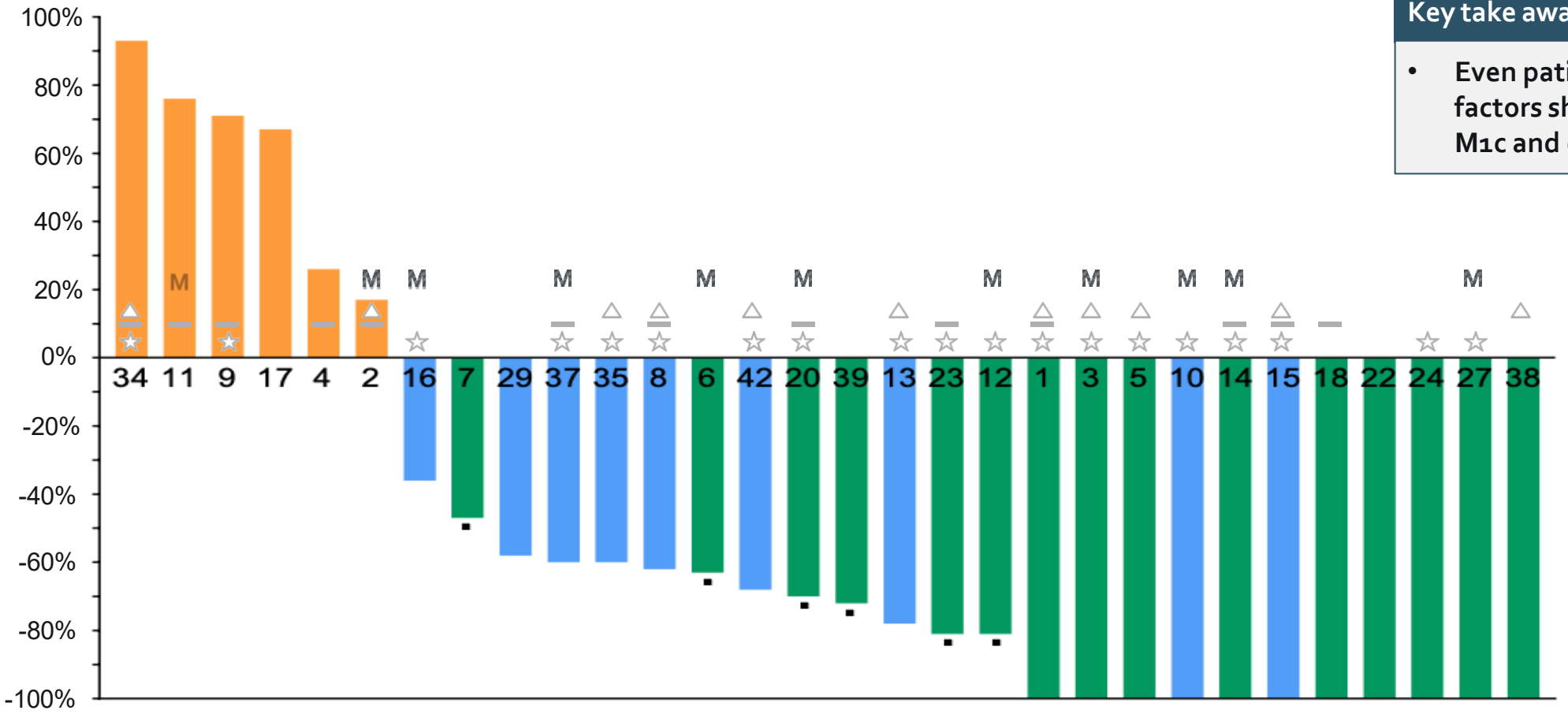
ORR and CRR
externally confirmed with
subsequent blinded review

Best Overall Response	Nature Med 2021 February 2021 Data cut[1]		January 2023 Data cut[2]	
Responders – ORR*	**24**	**80%**	**24**	**80%**
Best Overall Response Rate (RECIST 1.1)**	**22**	**73.3%**	**22**	**73.3%**
Complete Response Rate	14	46.7%	**15**	**50%**
Partial Response Rate	8	26.7%	7	23.3%
Stable Disease	0	0%	0	0%
Progressive Disease	6	20%	6	20%
Total	**30**	**100%**	**30**	**100%**
Best ORR (confirmed) – PD-L1 negative (n = 13)	7	54%	7	54%

- *Ipi / Nivo ORR: 58% and CRR: 22% (Larkin 2019)*
- *Nivolumab or pembrolizumab ORR 45% - 46% (Larkin 2019 and Robert 2019)*

*Two of the 24 responding patients progressed before subsequent radiological confirmation; ** Radiologically confirmed at subsequent imaging
1. Kjeldsen *et al. Nat Med.* 2021;27:2212–2223. 2. January 2023 update

Change in Target Lesion Size by Patient

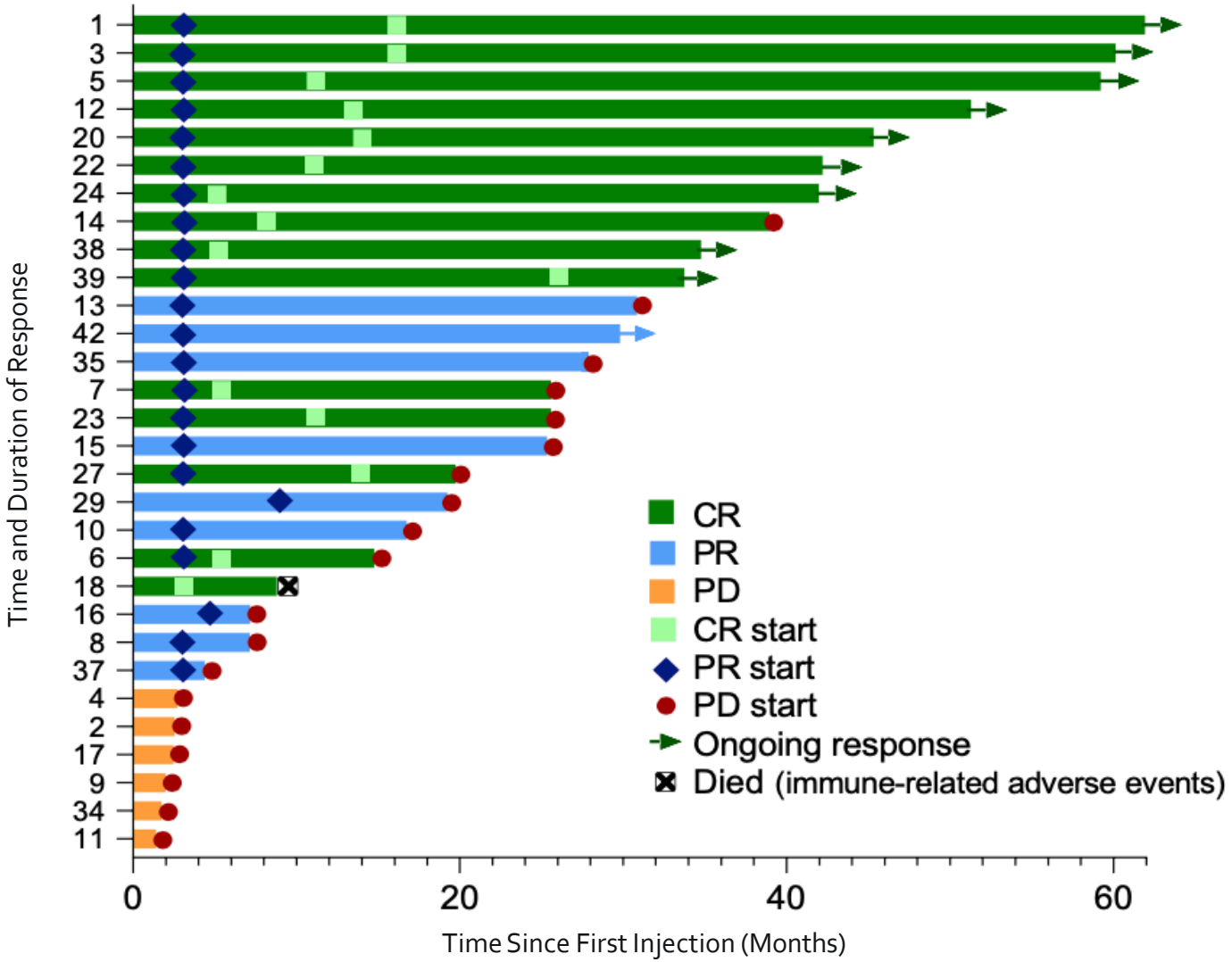


Key take away

- **Even patients with poor prognostic factors show clinical benefit (e.g. M1c and elevated LDH)**

CR, complete response; LDH, lactate dehydrogenase; PD, progressive disease; PD-L1, programmed death ligand 1; PR, partial response.
January 2023 update

Rapid and Durable Responses



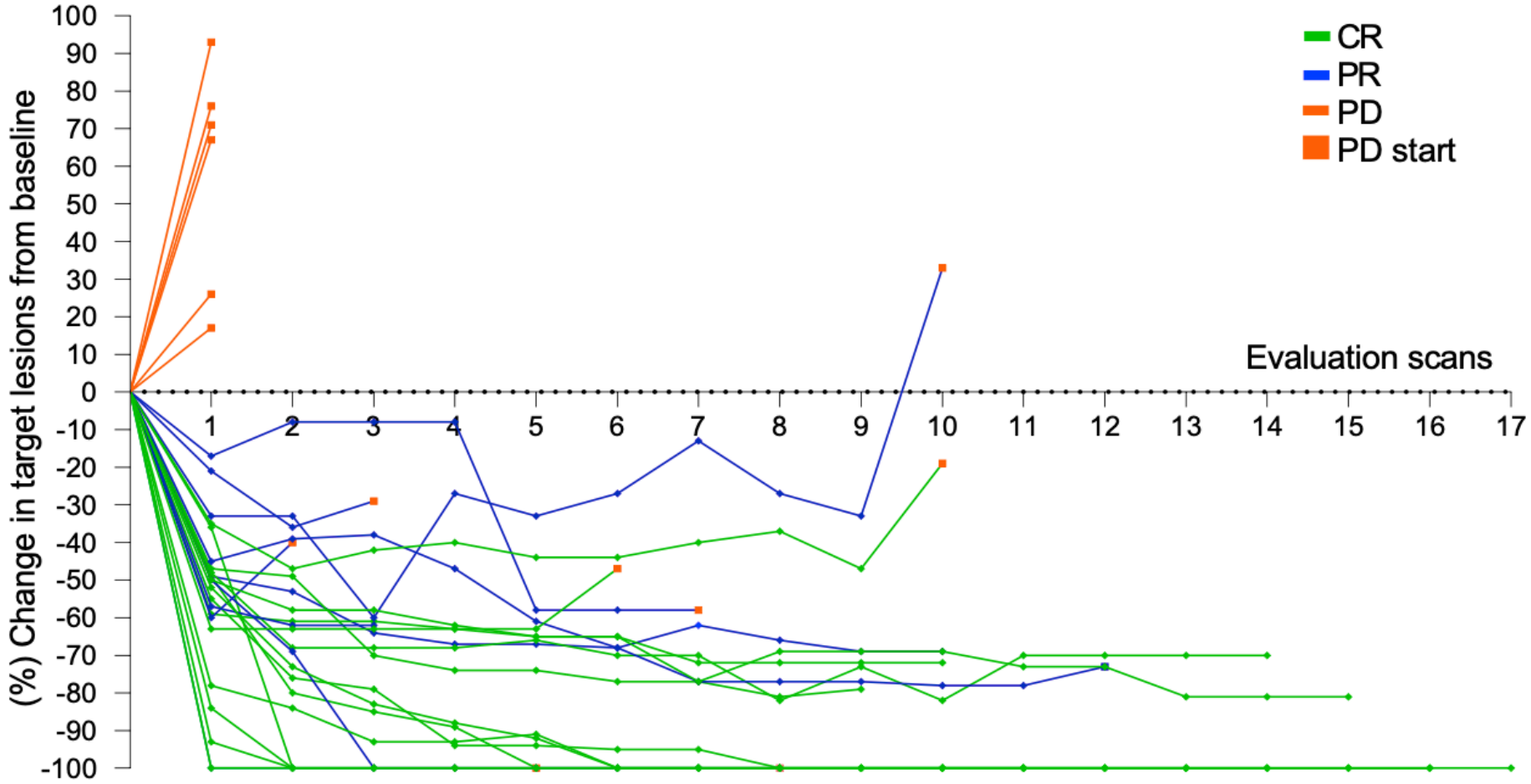
As of January 2023,
median duration of response was 27 months

Key take away

- **Early responses (12 weeks) and deepening of responses up to 18 months after treatment initiation**
- **Durable and deep (CR) responses in patients with poor prognostic factors**

CR, complete response; LDH, lactate dehydrogenase; PD, progressive disease; PD-L1, programmed death ligand 1; PR, partial response.
January 2023 update

Rapid, Deep and Durable Responses



Complete Response (CR) Partial Response (PR) Progressive Disease (PD)

Attractive Safety Profile

Potential to Become the Backbone of Combination Therapy

No increase in systemic AE's when combining IO102-IO103 with anti PD-1

High Grade (CTCAE 3-5) = 17%
Comparable with CM-066 (15%) and KN-006 (17%)

TRAEs Leading to Discontinuation = 17%
CM-066 (9%) and KN-006 (10%)

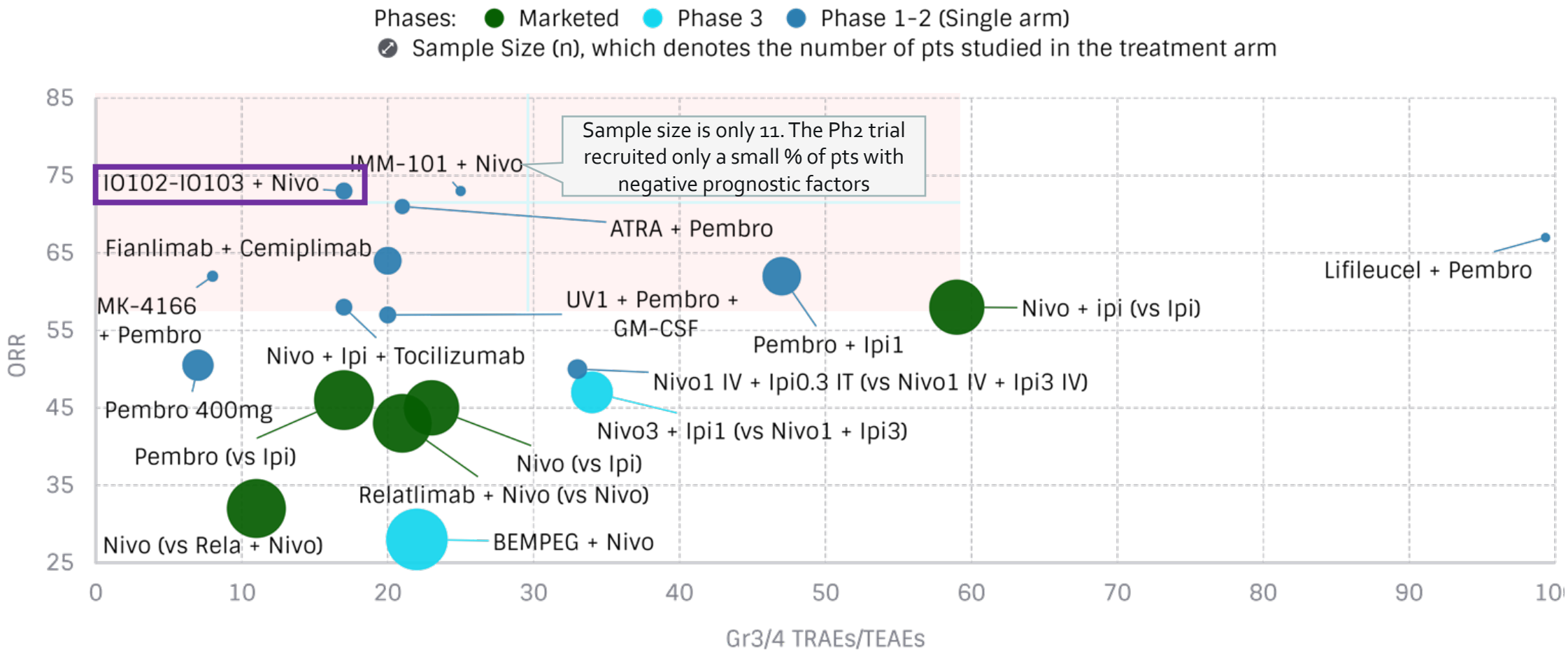
All the AEs leading to treatment discontinuation were considered by the investigator to be related to nivolumab. The rate of treatment-related adverse events leading to discontinuation of both nivolumab and IO102-IO103 was 17%.
77% of patients experienced local injection site reactions, most likely due to the Montanide adjuvant

Ipi/Nivo from Registrational Phase 3

High grade AEs occurred in **59%** and TRAEs led to **discontinuation** in **42%** of patients

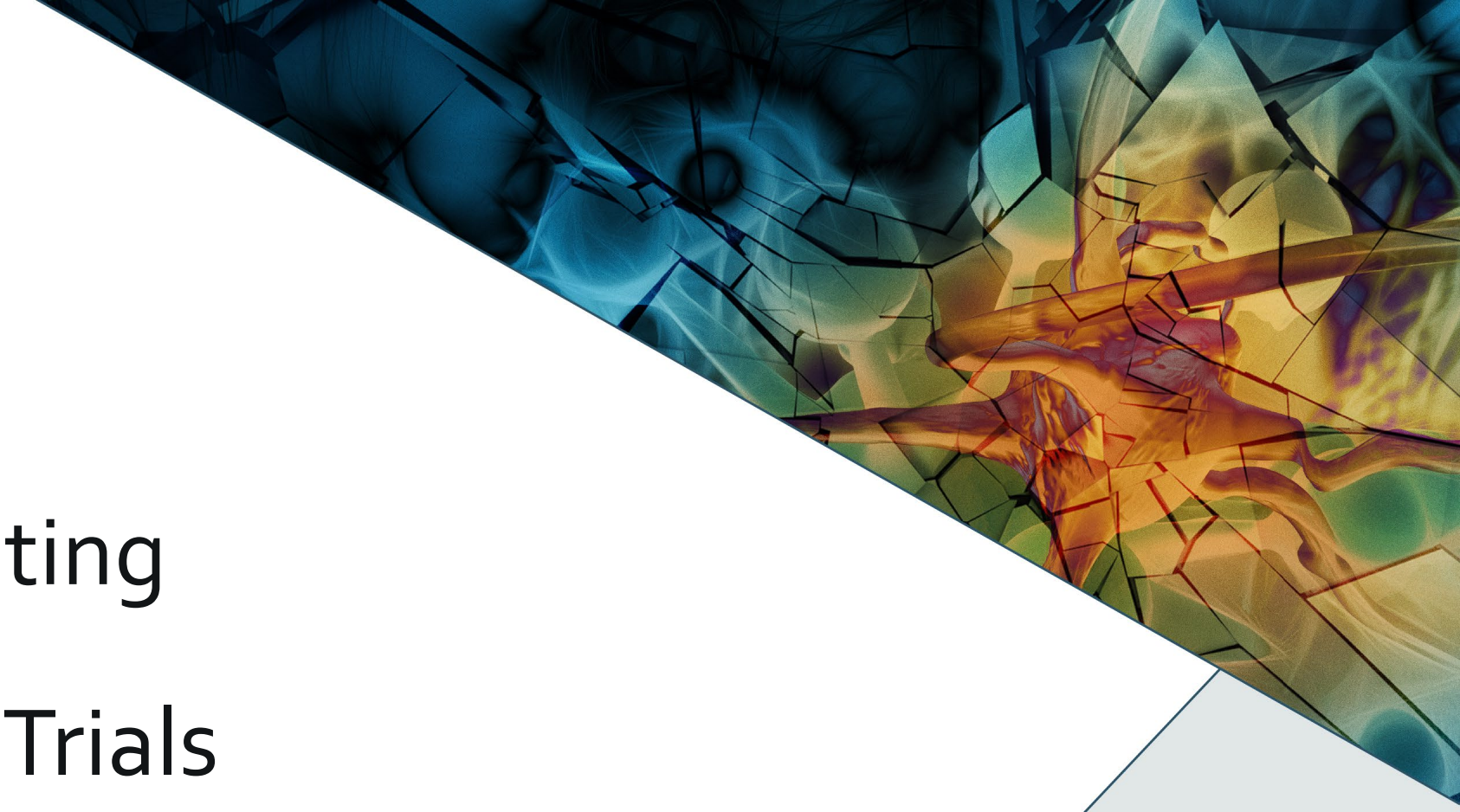
Kjeldsen *et al. Nat Med.* 2021;27:2212–2223; Larkin et al. *N Engl J Med.* 2019; 381(16):1535-1546; Robert 2019, Wolchock et al. *J Clin Oncol* 2022: 40(2):127-137

IO102-IO103 demonstrated compelling data with an ORR of 73% (CR: 50%) and Gr3/4 TRAEs of 17%



Abbreviations: ATRA: All-trans retinoic acid; Ipi: Ipilimumab; Ipio.3: Ipilimumab 0.3 mg/kg; Ipi1: Ipilimumab 1 mg/kg; Ipi3: Ipilimumab 3 mg/kg; IT: Intratumoral; IV: Intravenous; Nivo: Nivolumab; Nivo1: Nivolumab 1 mg/kg; Nivo3: Nivolumab 3 mg/kg; ORR: Objective response rate; Pembro: Pembrolizumab; Rela: Relatlimab; TEAE: Treatment emergent adverse events; TRAE: Treatment related adverse events

Notes: Molecules that do not have ORR, or Gr3/4 TRAEs/TEAEs data are not considered for this slide; Only the molecules targeting all-comers are considered for this slide to keep patient pool constant



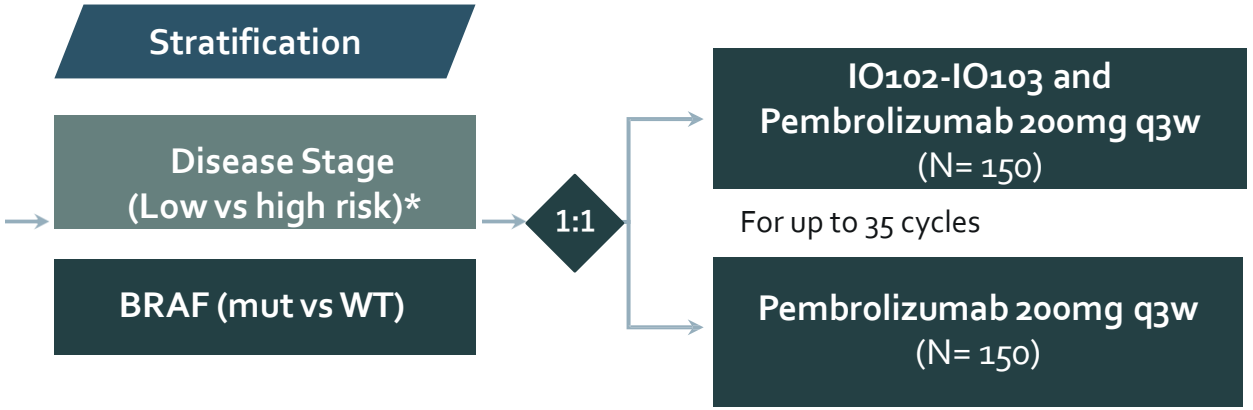
IO102-IO103 Immune-Modulating Cancer Vaccine: Ongoing Clinical Trials

Pivotal Phase 3 Trial Design in 1st Line Melanoma

IOB-013 / KN-D18 currently enrolling at ~100 active sites

Eligibility Criteria

- N=300
- Advanced melanoma
  - Unresectable Stage III
  - Metastatic Stage IV
- > 6 mo. after adj. neo- adjuvant anti-PD-1
- Measurable disease (RECIST 1.1)
- ECOG PS 0-1
- Stable CNS disease is allowed



Endpoints

Primary endpoint:

- PFS by central review

Secondary endpoints:

- ORR, DRR, CRR, OS, DoR, TTR, DCR
- Incidence of AEs and SAEs
- Quality of life
- Biomarkers in blood and tumor tissue will also be assessed

Interim analysis of ORR conducted one year after 225 patients have been randomized; Potential to file for accelerated approval based on interim analysis

*Stage IIID and IV M1a-b vs stage IV Mic-d

Phase 2 Solid Tumor Basket Trial

IOB-022 / KN-D38 currently enrolling

Eligibility Criteria

- N=up to 30 per cohort
- Previously untreated metastatic solid tumors
- No prior 1-line therapy
- Measurable disease
- ECOG PS 0 or 1

Cohorts[1]

NSCLC
PD- L1 TPS ≥ 50%

SCCHN (HPV +/-)
PD- L1 CPS ≥ 20

UBC
PD-L1 CPS ≥ 10

IO102-IO103 and Pembrolizumab 200mg q3w

For up to 35 cycles

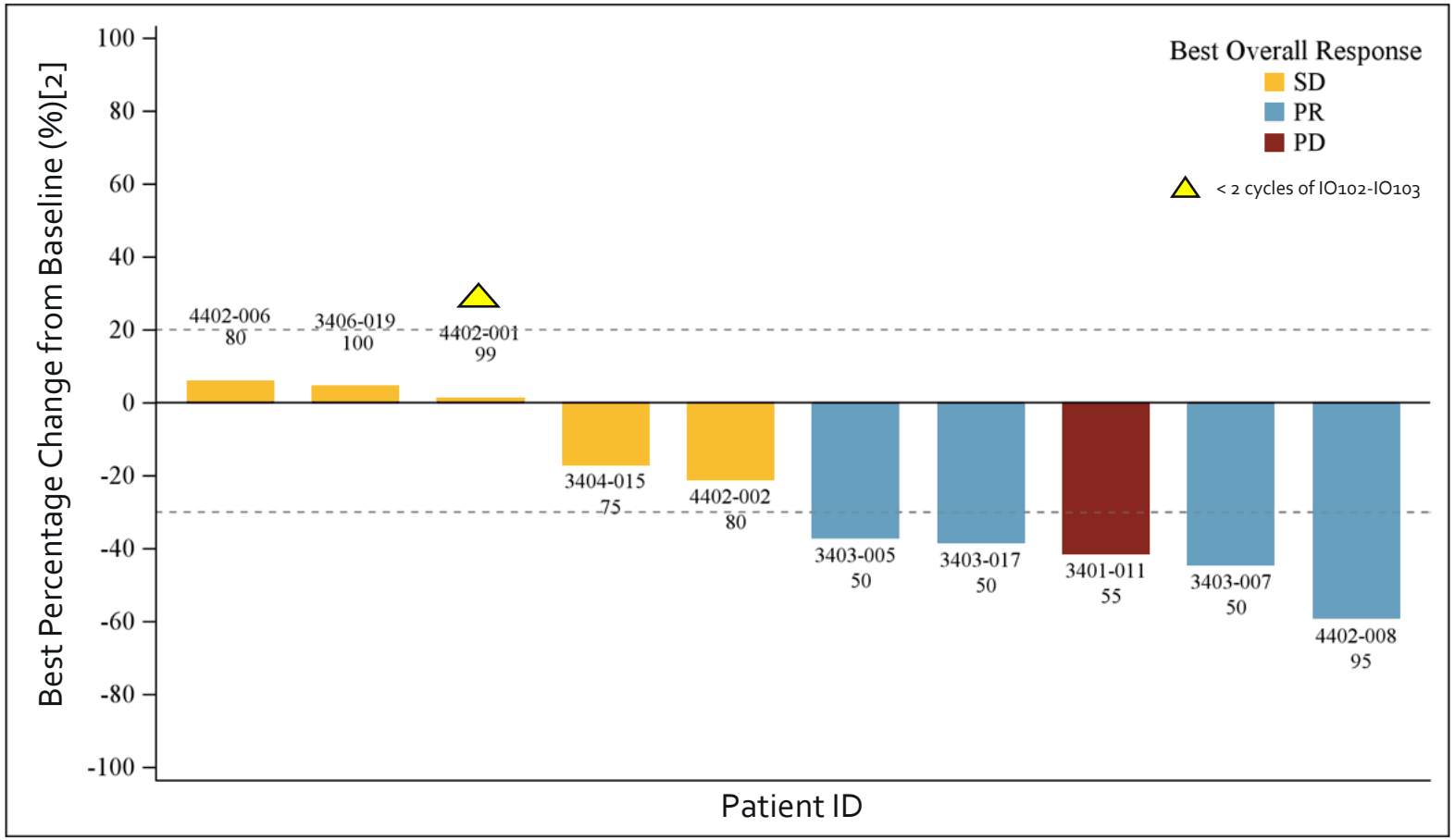
Endpoints

Primary endpoint:
- ORR

Secondary endpoints:
- PFS (RECIST1.1)
- DoR
- CR
- DCR
- OS
- Safety

Cohort A = Non-small cell lung cancer adenocarcinoma
Cohort B = Squamous cell carcinoma of the head and neck R/M disease
Cohort C = Urothelial bladder cancer ineligible for platinum-containing chemotherapy

IOB-022: Encouraging initial data NSCLC cohort



Key take away

- All patients have had one scan at 9 weeks post treatment
- To be considered efficacy evaluable, patients must have had at least 2 cycles of IO102-IO103
- Encouraging early data

NSCLC Clinical Benchmarks

NSCLC with PD-L1 ≥50% - First-line Setting

Phase 3

Regimen	N	ORR (%)	mPFS (Months)	mOS (Months)	Gr3/4 TRAEs (%)
Pembro + Carbo + Pacli/Nab-pacli; KEYNOTE-407	146	64%	8.0	**NR; HR: 0.68**	57%‡
Pembro + Peme + Cis/Carbo; KEYNOTE-189	202	62%	11.1	27.7	52%‡
Atezo + Carbo + Nab-pacli; IMpower131	91	62%	10.1	23.4	68%‡
Nivo + Ipi + Chemo; CHECKMATE-9LA	174	50%	7.5	18.9	48%‡
Cemiplimab mono; EMPOWER-Lung 1	710	47%	8.1	26.1	18%‡
Pembro mono; KEYNOTE-024¶	305	46%	7.7	26.3	31%
Nivo + Ipi; CHECKMATE-227	205	44%	6.7	21.2	33%‡
Pembro mono; KEYNOTE-042	599	39%	6.5	20.0	19%‡
Atezo mono; IMpower110	205	38%	8.1	20.2	13%
Atezo + Beva + Carbo + Pacli; IMPower150	350	**NA**	15.2	30.0	57%‡

Abbreviations: ¶ represents trials that exclusively enrolled pts with PD-L1≥50%; ‡ Gr3/4 TRAEs data from all enrolled pts; * Gr≥3 AEs; AEs: Adverse events; Atezo: Atezolizumab; Beva: Bevacizumab; Carbo: Carboplatin; Cis: Cisplatin; Gr: Grade; HR: Hazard ratio; Ipi: Ipilimumab; mOS: Median overall survival; mPFS: Median progression free survival; NA: Not available; Nivo: Nivolumab; NR: Not reached; ORR: Objective response rate; OS: Overall survival; Pacli: Paclitaxel; Pembro: Pembrolizumab; Peme: Pemetrexed; PFS: Progression free survival; TRAEs: Treatment related adverse events

Note: Ph3 trials that enrolled pts only in China have not been included here

Moving Forward

Recap and Upcoming Milestones

Multiple milestones in 2023 across indications

IO102-IO103 (PD-L1, IDO) - Dual Epitope			2022	Next Milestones
Phase 3	**Melanoma**	First-line advanced	First patient randomized/dosed – May	• Reach 225 patients enrolled: mid-2023 • Complete enrollment in Phase 3 by year-end 2023
Phase 2 Basket Trials	**NSCLC SCCHN, UBC**	First-line metastatic	First patient dosed – April	Additional Data
	Melanoma and SCCHN	Neo-adjuvant / adjuvant		Initiate Phase 2 in one indication in 2H2023
IO112 (Arginase)				
Phase 1/2	**Solid tumors**	-		IND Ready

These are not projections; they are targets/goals and are forward-looking, subject to significant business, economic, regulatory and competitive uncertainties and contingencies, many of which are beyond the control of the Company and its management, and are based upon assumptions with respect to future decisions, which are subject to change. Actual results will vary and those variations may be material. For discussion of some of the important factors that could cause these variations, please consult the "Risk Factors" section of the preliminary prospectus. Nothing in this presentation should be regarded as a representation by any person that these goals will be achieved and the Company undertakes no duty to update its goals.

Thank you

Contact: info@iobiotech.com

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