

There's a new way to kill tumors

by eradicating the immune suppressive nature of the TME

IO Biotech is a Phase 3 company leading the way



August 2022

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.

Investment Highlights

Differentiated Platform – T-win®

- Proprietary T-win® designed to activate pre-existing T cells
- MOA stimulates pre-existing T cells against both tumors *and* immunosuppressive cells in the TME
- Infiltrating T cells modulate the TME into an anti-tumor proinflammatory environment

Strong Phase 1/2 Data for IO102-IO103

- 1st line melanoma combo with nivolumab: 73.3% ORR and 25.3 months median PFS* (n=30)
- Current SOC ~45-58% ORR and ~7-12 months PFS
- Breakthrough Therapy Designation (BTD) granted based on Phase 1/2 data

Phase 3 in 1st Line Advanced Melanoma

- Phase 3 initiated: FPI May 2022; enrollment ongoing for global multi-site trial
- Combination with pembrolizumab in 1st line advanced melanoma
- Potential commercial positioning: durable efficacy with improved safety vs. nivolumab/ipilimumab

Multiple Upside Opportunities in Other Solid Tumors

- IO102-IO103 in other solid tumors such as head and neck cancer and lung cancer
- Early-stage pipeline targeting additional immunosuppressive mechanisms

Strong Cash Position

- Nasdaq listing (IPO) in Nov. 2021
- Cash: ~\$170M (6-30-22)
- Sufficient runway into mid 2024

Experienced Leadership

Mai-Britt Zocca, PhD

President and CEO



- 20 years industry and oncology drug development experience
- PhD in medicine (Immuno-Oncology)
- Serial life sciences entrepreneur, corporate strategy, financing and management, board member

Eva Ehrnrooth, MD PhD

Chief Medical Officer



- 20+ years in oncology & drug development
- Board certified clinical oncologist with a PhD in molecular oncology
- Successfully led multiple phase 3 oncology programs across multiple solid tumor indications leading to global registration

Muhammad Al-Hajj, PhD

Chief Scientific Officer



- 18+ years in oncology drug discovery
- PhD in molecular genetics with postdoctoral training in cancer and stem cell biology
- Leadership in oncology and immunotherapy translational sciences within pharma and biotech

Ideally Positioned in the Evolving Melanoma Landscape

Benefit-Risk Ratio

- Only P3 competitor in the desired “quadrant”
 - High PFS, high ORR, low AE’s

In Phase 3

- First mover advantage with targets of IO102-IO103

Broad Applicability

- Consistent efficacy across melanoma subgroups
- Potential for use among patients regardless of PD-L1 expression

Competitive Advantages

Triple therapy – Strong position to be considered in a potential new paradigm

BEMPEG learnings – Ratio of PD-L1 positive/negative patients can be an important determinant of efficacy

Opdualag learnings (Nivo-LAG-3) – Effect only in a subset of patients (PD-L1 low)

Pipeline Overview

Program	Line of therapy/ indication	Pre-clinical	Phase 1	Phase 2	Phase 3	Anticipated Next Milestone
Candidate: IO102–IO103 Targets: IDO, PD-L1	First Line Advanced Melanoma	Melanoma ⁽¹⁾				<ul style="list-style-type: none"> Continue enrolling Phase 3
	First Line Solid Tumors⁽²⁾	<ul style="list-style-type: none"> Lung (NSCLC)⁽⁴⁾ Head & Neck (SCCHN)⁽⁴⁾ Bladder (UBC)⁽⁴⁾ 				<ul style="list-style-type: none"> Continue enrolling Phase 2 “basket” trial Initial data in 2H 2022 in one indication Additional data in 2023
	Neo-adjuvant / Adjuvant Solid Tumors⁽²⁾	<ul style="list-style-type: none"> Melanoma Head & Neck (SCCHN)⁽⁴⁾ Indication TBD 				<ul style="list-style-type: none"> Initiate Phase 2 “basket” trial in one indication in 2023
Candidate: IO112 Target: Arginase 1	Solid Tumors	Indications TBD ⁽³⁾ IO102-IO103-IO112				<ul style="list-style-type: none"> File IND for IO112 in 2023

1. In combination with pembrolizumab

2. In combination with an anti-PD-1 monoclonal antibody therapy

3. Expected to be developed in combination with third party drugs or biologics

4. NSCLC = non-small cell lung cancer, UBC = urothelial bladder cancer, SCCHN = squamous cell carcinoma of the head and neck



T-win® Platform:

Novel Approach to Modulate the
Immune System to Treat Multiple
Solid Tumor Types



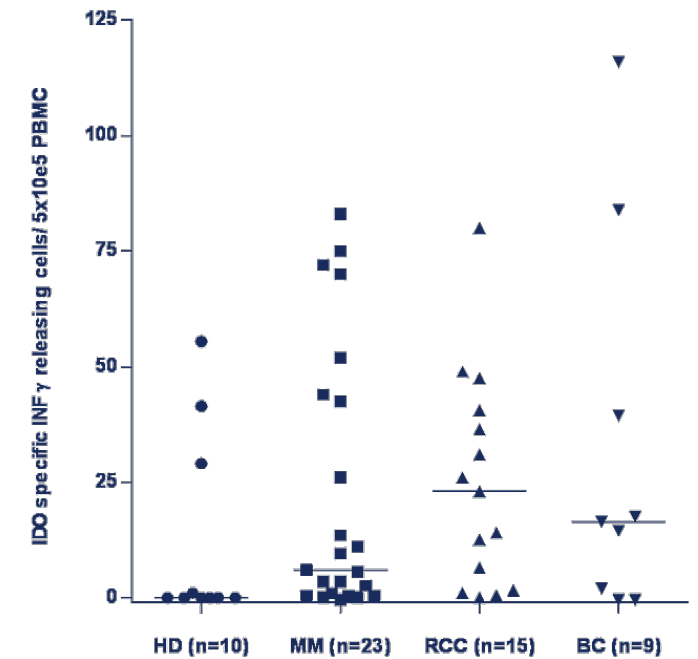
T-win Approach: Activate and Expand Pre-existing T Cells to Remodel the Tumor Microenvironment (TME)

Seminal discovery of pre-existing (intrinsic) T cells that provide immunity against immune suppressive molecules (e.g., IDO1) in healthy individuals and cancer patients.

Led to T-win Drug Development Platform:

1. **Pioneered** first experimental immuno-modulating therapy directed against TME cells expressing immune-suppressive proteins
2. **Direct killing** of immunosuppressive cells, including both tumor cells and genetically stable cells in the TME
3. **Modulate the TME** into a more pro-inflammatory, anti-tumor environment

IDO-Specific T cells are Naturally Occuring¹



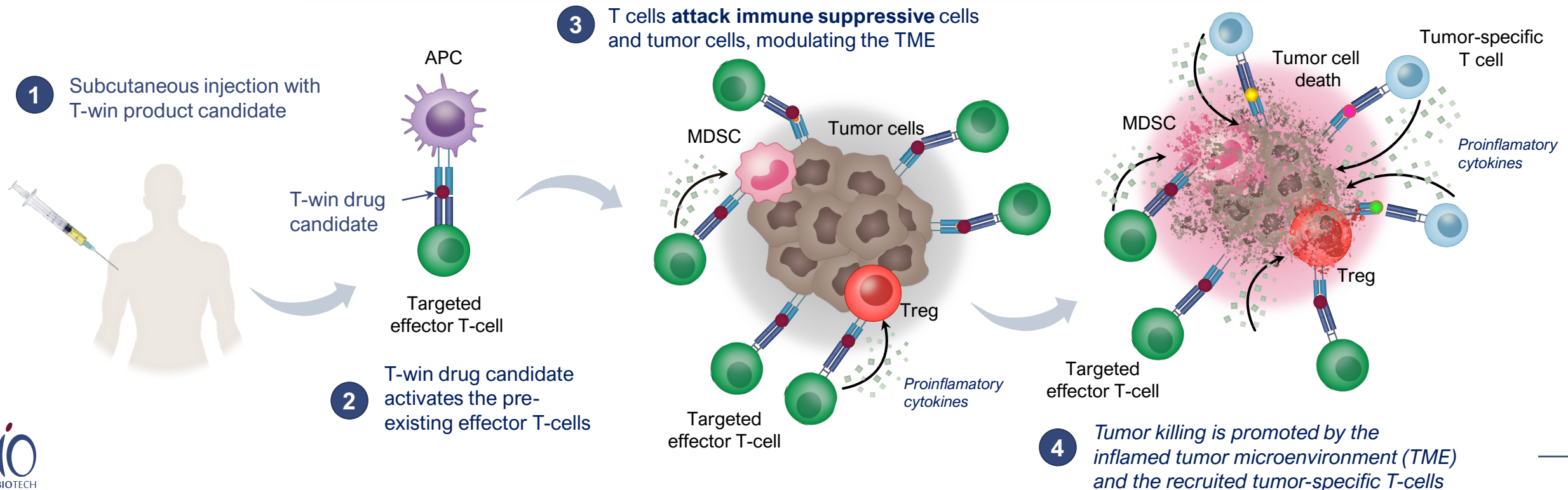
High frequency of T cells specific to IDO1 epitopes are found in various cancer patients and healthy individuals

HD = healthy donors
RCC = renal cell carcinoma

MM = multiple myeloma
BC = breast cancer

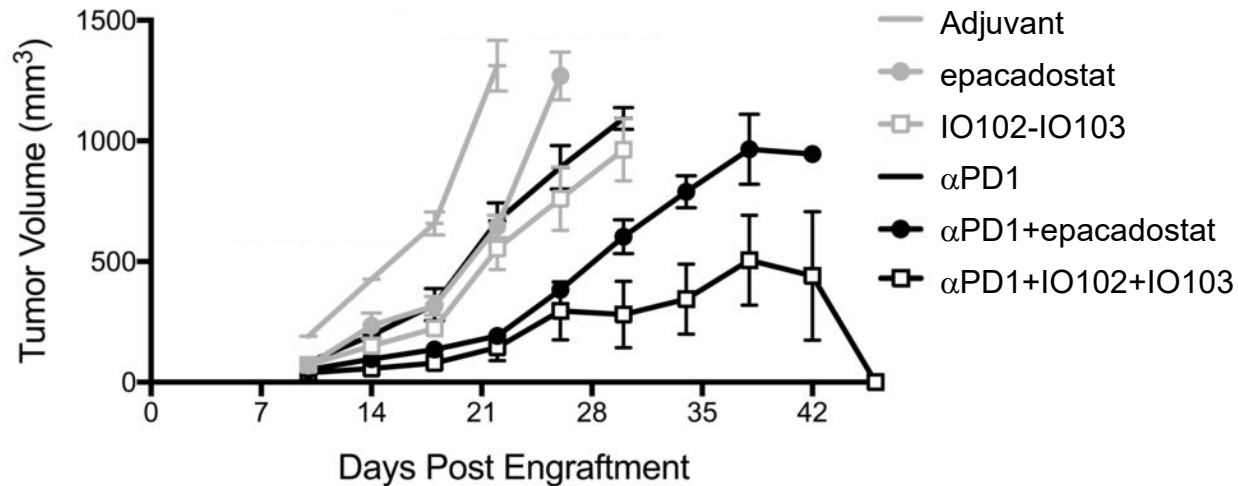
T-win Treatment Triggers Potent Immune Response Within TME

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



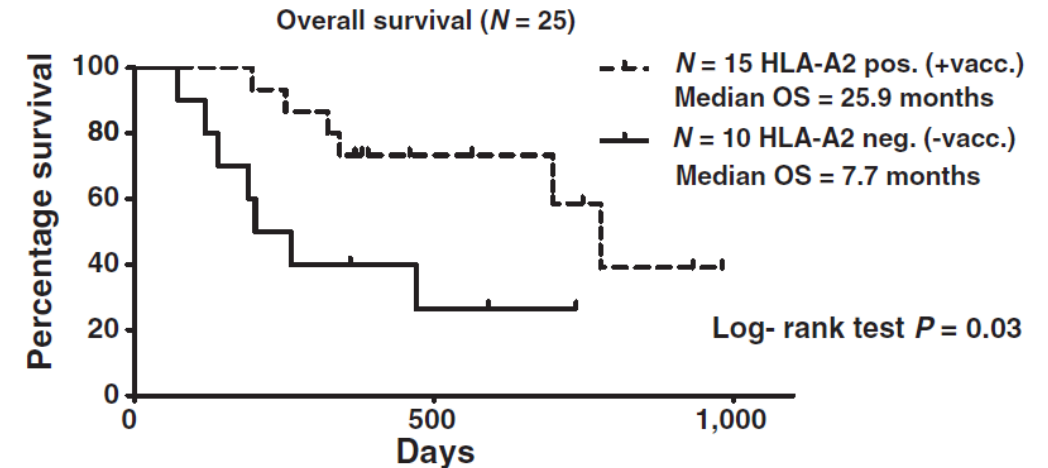
Differentiated MOA – IDO Example

Preclinical



- Synergistic and durable anti-tumor activity of IO102-IO103 treatment in combination with anti-PD-1 (CT26 model)
- In contrast, the combination with IDO small molecule inhibitor shows negligible synergy with no durable responses

Clinical



- T-win has demonstrated monotherapy activity, in contrast to IDO small molecule inhibitors
- First clinical POC data highlights the T-win differentiated MoA that leads to a better clinical outcome



IO102-IO103:

Activates pre-existing T cells targeting
IDO and PD-L1

Phase 3 trial for 1st line advanced
melanoma

Unresectable, Metastatic Melanoma is Serious and Life-Threatening

In 2021 in the U.S.:

106,000

Expected New
Melanoma Cases

&

7,200

Expected to Die
of Melanoma

**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 **5-year overall survival rate to about 52%**
but associated with considerable toxicity

Rationale Behind IO102-IO103 – MOA Now Clinically Validated

- **IO102** and **IO103** are peptides targeting highly immunogenic sequences of **IDO** and **PD-L1** respectively
- IDO and PD-L1 are often **dysregulated** and **over-expressed** in a wide range of solid tumors
 - Both inhibit the body's natural pro-inflammatory anti-tumor response within the TME
 - **IDO** overexpression is correlated with poor prognosis and reduced survival
 - **PD-L1** upregulation enables tumor cells to evade the immune system, and correlated with poor prognosis and aggressive disease
- A **dual targeting** approach that activates and expands T-cells to attack cells expressing IDO and PD-L1 is an attractive strategy to modulate the TME into a more pro-inflammatory and anti-tumor environment
- Successful outcomes in Phase 1/2 has now allowed progression into Phase 3 program

Phase 1/2 Trial in Metastatic anti-PD-1 Naïve Melanoma



TRIAL POPULATION:

- Measurable disease
- First-line metastatic melanoma
- Anti PD-1 / PD-L1 naïve
- Any PD-L1 and BRAF status
- N = 30

IO102 + IO103 plus nivolumab

- **Primary objective:** safety and feasibility, secondary objective immunogenicity and tertiary objective clinical efficacy
- IO102-IO103 (100 µg of each peptide) + montanide adjuvant (max. 15 treatments, up to 47 weeks)
- Nivolumab (3 mg/kg) q2w up to 2 years










Phase 1/2 Trial – Published in Nature Medicine December 2021

**nature
medicine**

ARTICLES

09 December 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 Klausen¹,
Cecilie Oelvang Madsen¹, Shamaila Munir Ahmed¹, Stine Emilie Weis-Banke ¹,
Morten Orebo Holmström¹, Helle Westergren Hendel³, Eva Ehrnrooth², Mai-Britt Zocca²,
Ayako Wakatsuki Pedersen², Mads Hald Andersen^{1,4} and Inge Marie Svane ¹ 

Phase 1/2 Trial: 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%)

Phase 1/2 Trial: Unprecedented ORR and CRR

Data externally confirmed

ORR and CRR externally confirmed with subsequent blinded review

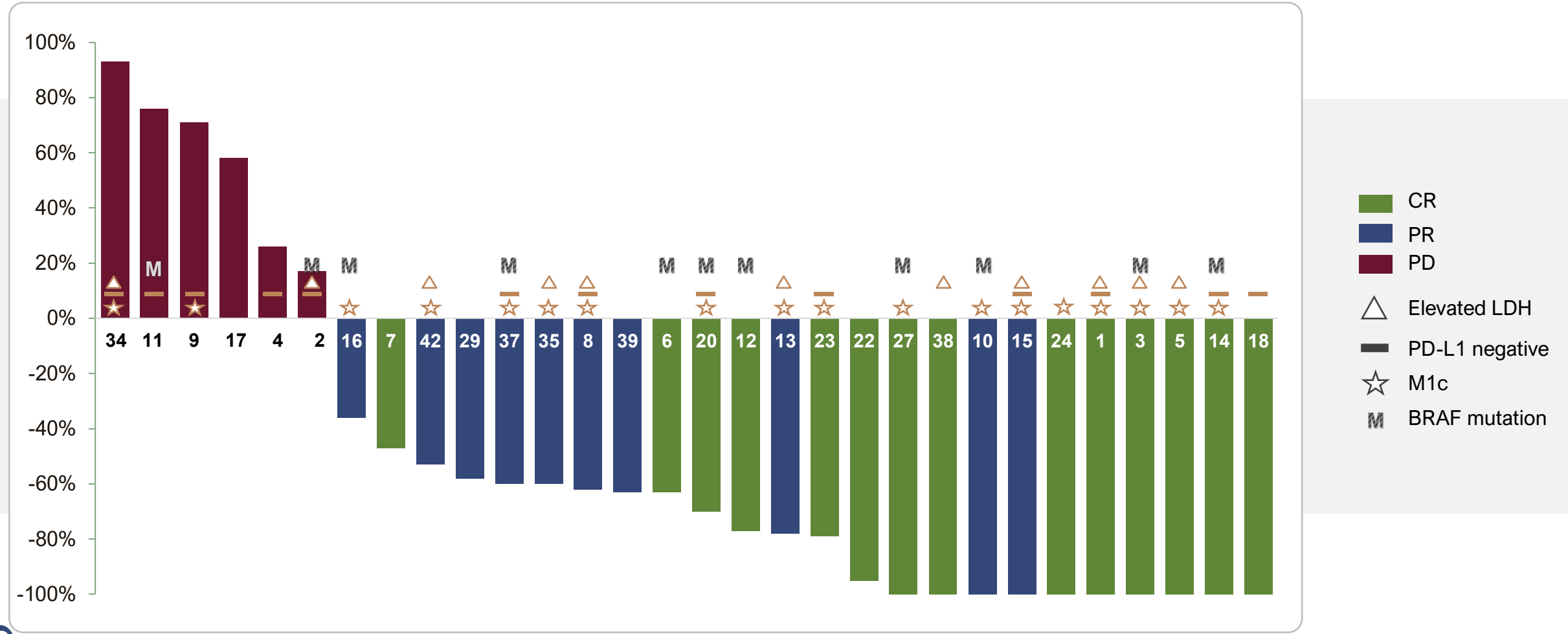
Best Overall Response	Investigator Review	
Responders – ORR*	24	80%
Best Overall Response Rate (RECIST 1.1**)	22	73.3%
Complete Response Rate	14	46.7%
Partial Response Rate	8	26.7%
SD	0	0%
PD	6	20%
Total	30	100%
ORR – PDL1 negative only (n = 13)	7	54%

- 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

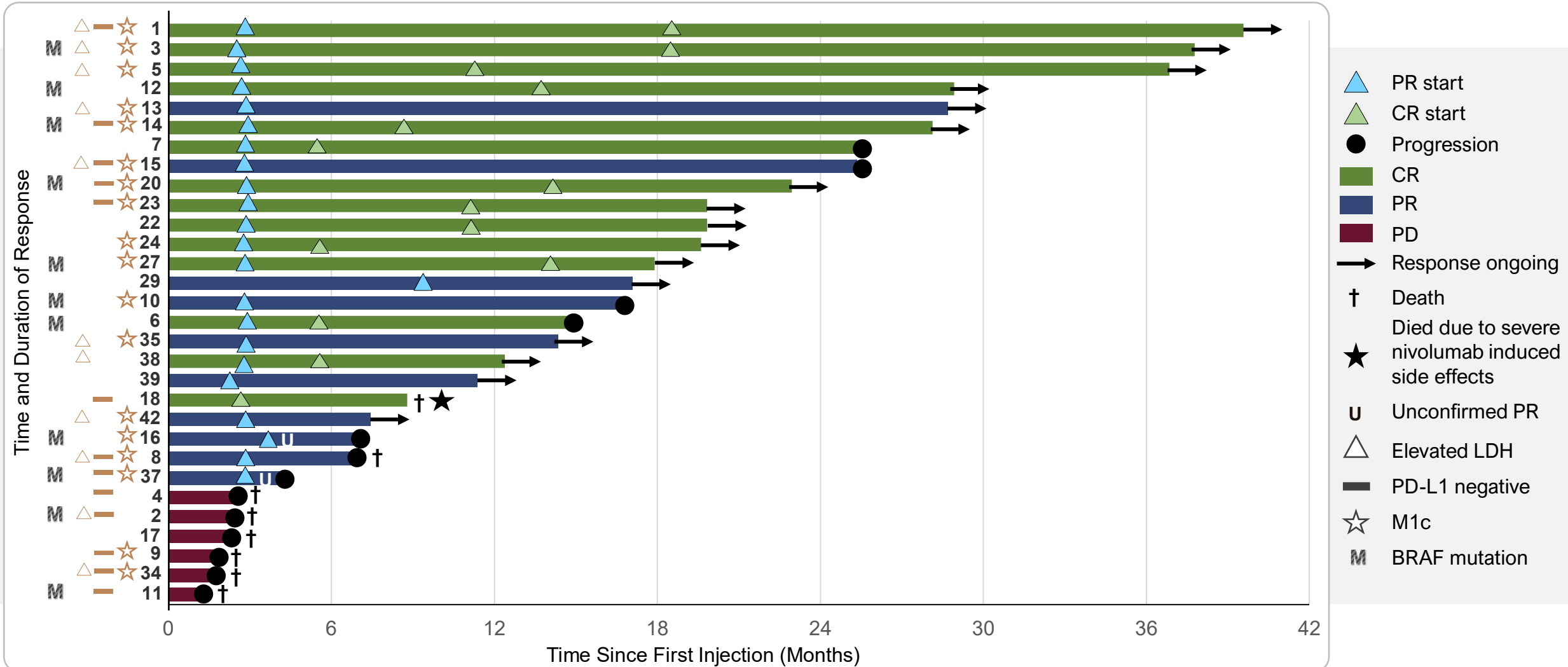
Phase 1/2: Change in Target Lesion Size by Patient

Even patients with poor prognostic factors show clinical benefit



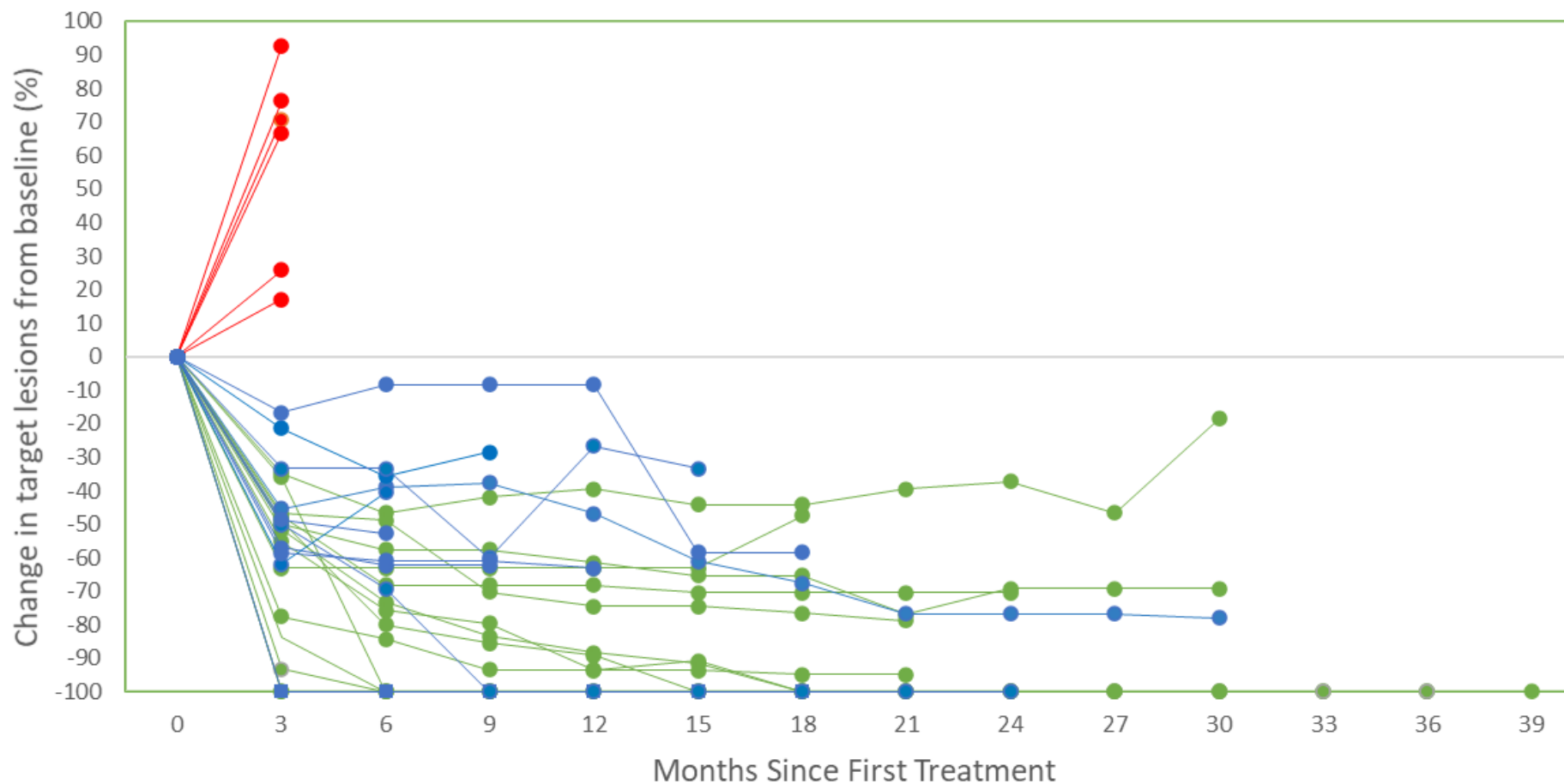
Phase 1/2: Rapid and Durable Responses

Median duration of response not yet reached



Updated February 2021

Phase 1/2: Deep and Durable Responses



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

Phase 1/2 vs. Contemporaneous Matched Historical Controls



- **Significantly higher ORR than matched historical controls – suggesting that the response observed with the combination therapy was unlikely to be due to patient selection bias**
- **Efficacy results in the matched historical cohort were comparable with Phase 3 benchmarks**

Comparison with contemporary anti PD-1 treated patients from the National Danish Metastatic Melanoma Database

938 anti PD-1 treated patients were extracted

218 patients were eligible for comparison and matching

60 patients were found to match

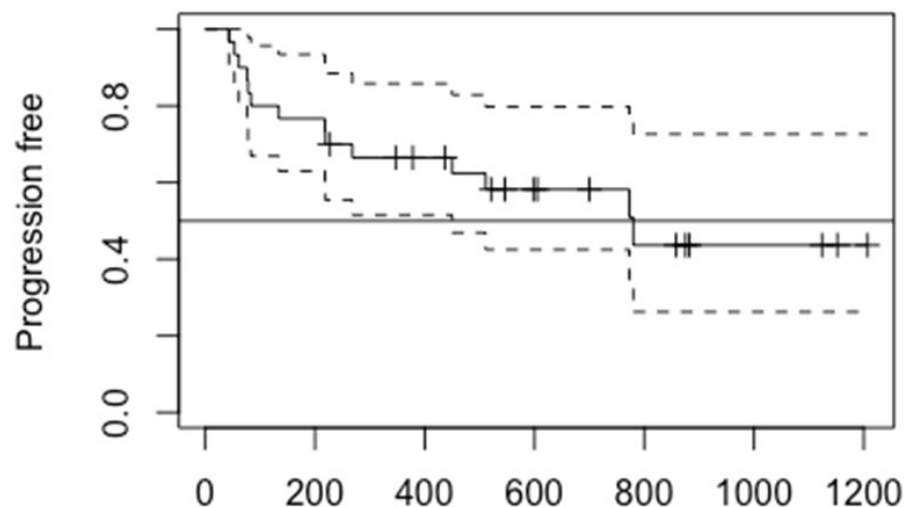
The ORR (79.3% vs. 41.7%) and CR (41.4% vs. 12%) - was significantly higher

BOR	Phase 1/2 % (95% CI) (Jan'20)	Matched dataset % (95% CI)
N	29	60
CR	41.4% (25% - 60%)	12% (6% - 22%)
ORR	79.3% (61% - 90%)	41.7 % (31% - 53.3%)

Phase 1/2: Median PFS of 25.3 Months and OS Not Reached

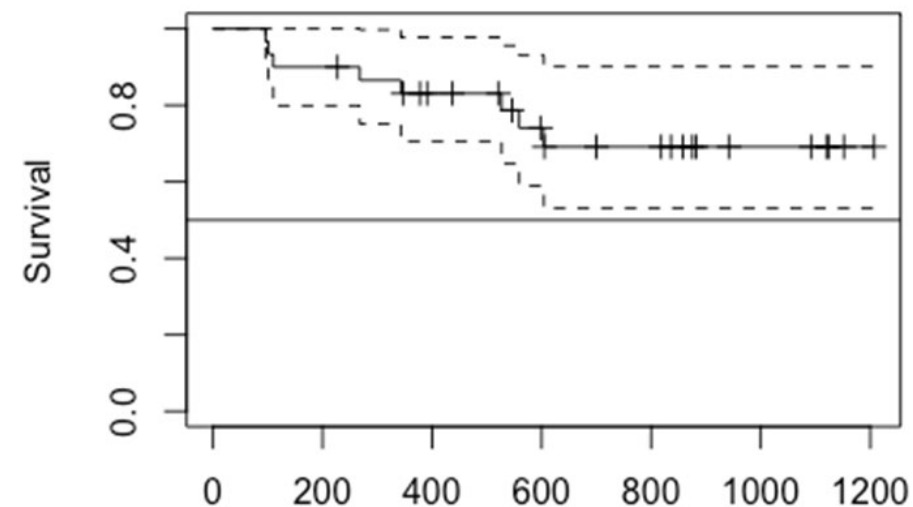


Progression Free Survival



- **mPFS = 780 days (25.6 months)**
- **Median duration of follow-up = 27.3 mo**

Overall Survival



- **mOS (N = 30) Not yet reached**

- Median PFS of 25.6 months in February 2021
- Median PFS of 25.3 months in June 2021
- Ipi / Nivo mPFS 12 months
- mOS Ipi / Nivo > 60.0 mo (95%CI, 38.2 to NR). mOS nivolumab = 36.9 mo (95% CI, 28.2 to 58.7)

Phase 1/2: Attractive Safety Profile

No AEs on top of anti PD-1 monotherapy

No increase in Grade 3+ 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%)

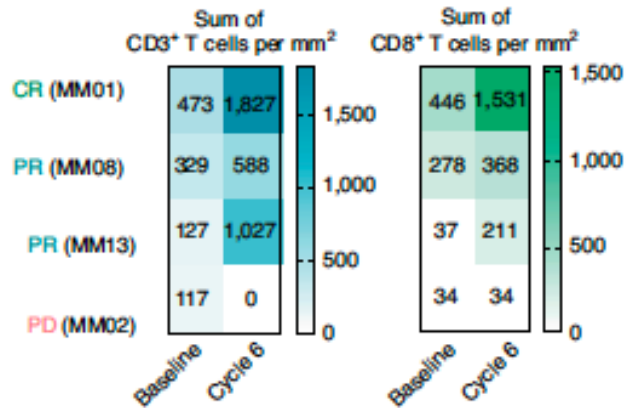
TRAEs Leading to Discontinuation = 17%

CM-066 (9%) and KN-006 (10%)

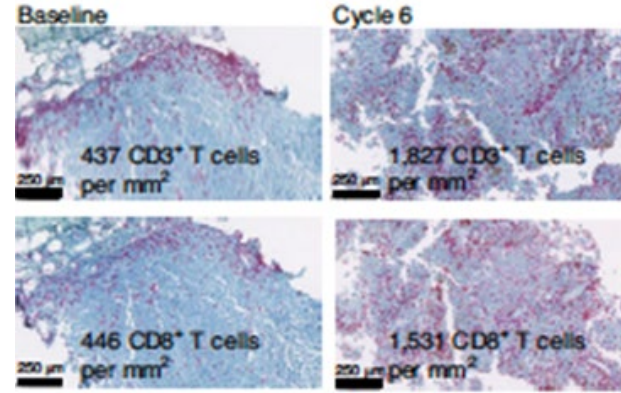
Ipi/Nivo from Registrational Phase 3

- **High grade AEs** occurred in **55%** and TRAEs led to **discontinuation** in **42%** of patients

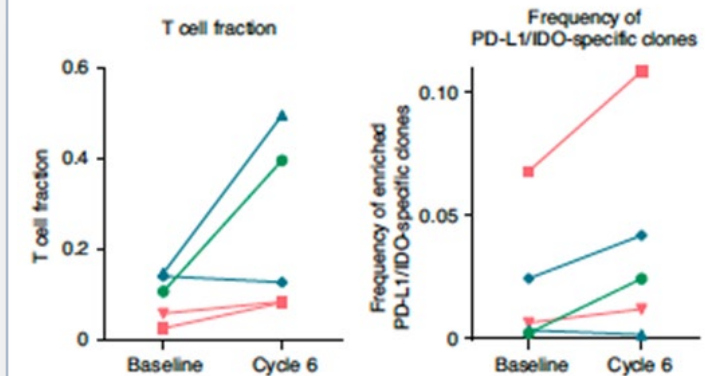
In Phase 1 / 2 Trial, MOA of IO102-IO103 and Nivolumab Worked as Anticipated (*Kjeldsen et al, NATURE Med 2021*)



Heat map of CD3+ & CD8+ T cells in paired biopsies pre and post treatment highlighting the **increase in infiltrating T cells into the tumor site post T-win treatment** as anticipated



An IHC example of the infiltration at the tumor site prior and after treatment showing clearly the extent of the T cell influx post T-win treatment (Pink)



TCR sequencing demonstrated that the T cell fraction at the tumor site post treatment was highly enriched in PDL-1 & IDO-specific clone

Clinical Outcome Measures at ASCO

ASCO updates
First-line Setting/PD-1 naïve - Phase 3

Phase 3	Regimen	N	ORR (%)	mPFS (Months)	mOS (Months)	Gr3/4 TRAEs (%)	
	Nivo + Ipi; CHECKMATE-067	945	58%	11.5	72.1	59%	ASCO 2021
	Nivo3 + Ipi1; CheckMate 511	358	47%	10.2	NR (3-yr OS: 59.0%)	34%	ASCO 2021
	Pembro mono; KEYNOTE-006	549	46%	11.6	38.7	17%	
	Nivo mono; CHECKMATE-067	945	45%	6.9	36.9	24%	
	Relatlimab + Nivo; RELATIVITY-047	714	43%	10.2	NR (HR 0.80; p=0.059)	21%	ASCO Plenary'22
	Nivo mono; RELATIVITY-047	714	33%	4.6	34.1	1%	ASCO Plenary'22
	BEMPEG + Nivo; PIVOT-IO-001	781	NA (No significant benefit vs nivo mono)	5.0 (approximate [¶])	NA (No significant benefit vs nivo mono)	NA	Company PR

Abbreviations: 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; Pembro: Pembrolizumab; PR: Press release; TRAEs: Treatment related adverse events; [¶] mPFS of nivo mono (comparator) is 5.0 months and PFS HR is 1.09. Based on this, mPFS of BEMPEG + nivo is approximated at 5.0 months

Phase 3 Design and Registration Path in 1L Advanced Melanoma

Trial design and BLA submission strategy discussed and main features confirmed with FDA

- International randomized Phase 3 trial (N = 300)
- Trial name: IOB-013 / KN-D18
- Primary endpoint PFS (by independent review committee (IRC))
- Potential for accelerated approval under BTB, based on interim ORR (reviewed by IRC), supported by PR, CR, and descriptive PFS data
- Full approval could be based on PFS (reviewed by IRC) at the final analysis supported by data on OS
- ClinicalTrials.gov Identifier: NCT05155254



**Breakthrough Therapy
Designation Granted
December 2020**

1st Line Melanoma Pivotal Phase 3 Trial

IOB-013 / KN-D18 Currently Enrolling

Eligibility Criteria

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

Stratify

Stage (Low vs high risk)

BRAF (mut vs WT)

1:1

IO103-IO102 and
Pembrolizumab 200mg q3w
(N= 150)

Pembrolizumab 200mg q3w
(N= 150)

Endpoints

Primary endpoint:

- PFS by central review

Secondary endpoints:

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



IO102-IO103:

Expansion Opportunities

Additional solid tumors
In combination with PD-1

Clinical Development in 1-Line Metastatic NSCLC

Indication included in planned basket trial



Single epitope (IO102) + pembro

BASKET TRIAL



Dual epitope (IO102-IO103) + pembro

- Phase 1/2 clinical trial collaboration agreement with Merck & Co.
- Fully recruited – Safety data appears largely comparable in the experimental and control arms
- Readout prompted next development step → dual epitope in combination with pembrolizumab
- Basket trial with 3 cohorts (NSCLC, SCCHN and UBC)
- Ready to enrol in the first cohort (NSCLC)

Aim to replicate melanoma data

IO102-IO103 – Expansion Opportunities

- Multiple potential opportunities in various cancer settings with limited anti-PD-1 mAb efficacy or tolerability and toxicity concerns



**1st Line
Solid Tumors
Phase II Basket
(IOB-022/KN-D38)**

Lung (NSCLC)

Head & Neck (SCCHN)

Bladder (UBC)

**Neoadjuvant &
Adjuvant Solid Tumors
Phase II Basket
(IOB-032)**

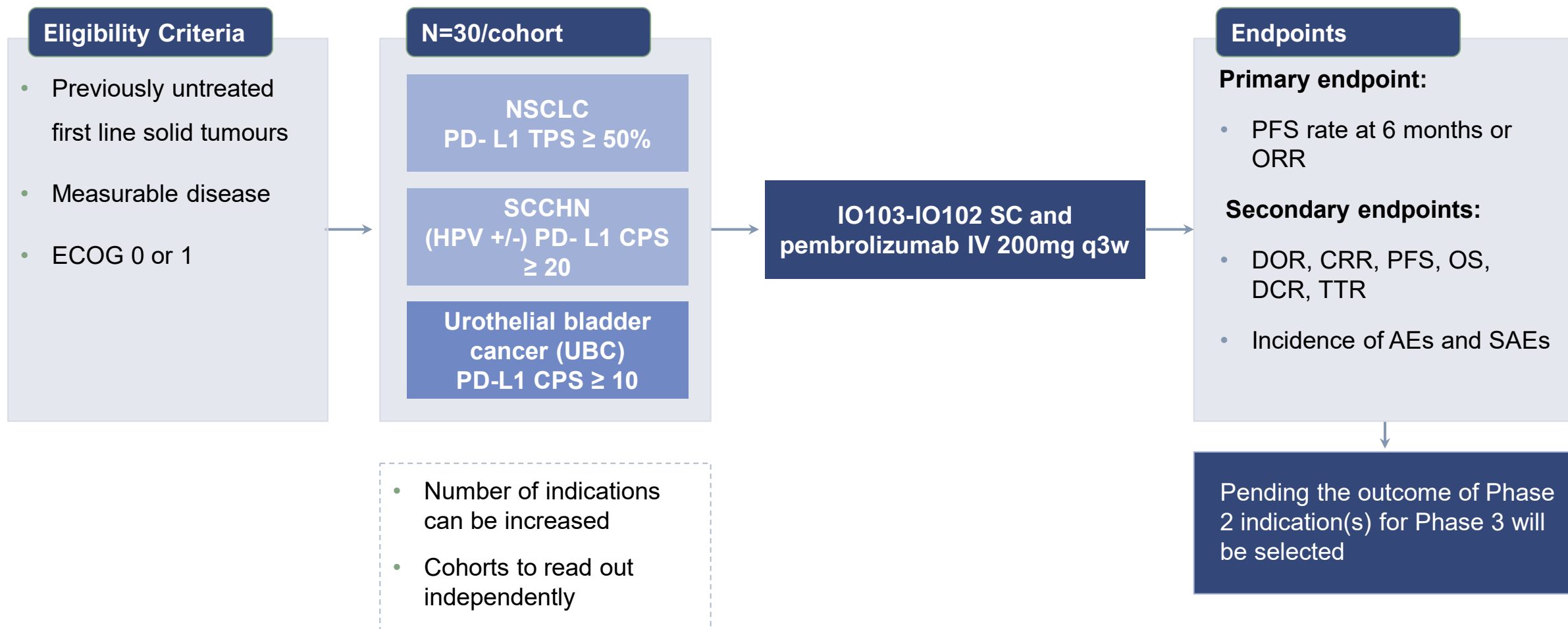
Melanoma

Head & Neck (SCCHN)

Additional Indications

Phase 2 Basket Trial – 1L for Solid Tumors

IOB-022 / KN-D38 Open for Enrollment



Head and Neck Cancer – IO102-IO103 Development with Investigator Initiated Trials (IIT)

Rapid responses in the metastatic setting suggest opportunity in the neo-adjuvant setting (short-term trmt.)



Neo-adjuvant (IIT)

IO102-IO103

- Randomized Ph 2 umbrella trial
- Multiple sequential cohorts – single and dual-epitope
- Recruitment ongoing

Neo-adjuvant + adjuvant

IO102-IO103 plus anti-PD-1

- Ph 2 single arm trial
- Dual epitope + pembro followed by adjuvant therapy



**IN
PLANNING**

Clinical Development in Bladder Cancer – Tested in Two Settings

Muscle invasive bladder cancer included in basket trial

Muscle Invasive

- 0 Indication included in Ph 2 basket trial (IOB-022/KN-D38)
- 0 Protocol approved; ready to enroll



BASKET TRIAL

Non Muscle Invasive

- 0 Ph 1 single arm Investigator initiated trial
- 0 To inform our own development



IN PLANNING



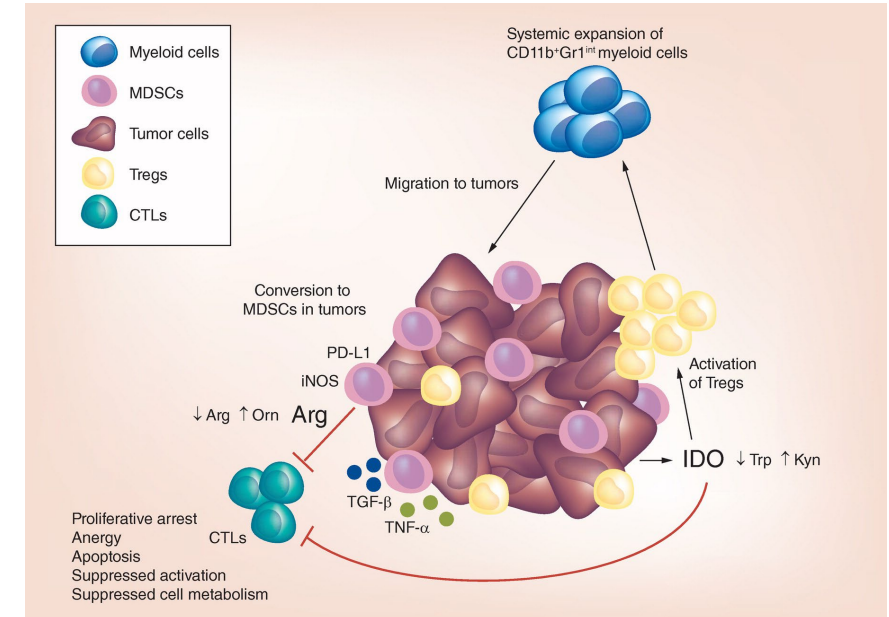
IO112:

Targeting Arginase 1
for Difficult to Treat Solid Tumors



Rationale Behind Arginase 1 Development

- Arginase 1 is an immunoregulatory enzyme that is de-regulated (overexpressed) in multiple tumors such as colorectal, breast, prostate, pancreatic and ovarian
- IO112 designed to activate T cells that specifically recognize epitopes derived from Arginase 1
- Pre-clinical results have shown a reduction of Arginase 1+ cells and an increased influx of T cells into the TME



Tryptophan- and arginine-degrading proteins (IDO & ARG1) cooperate to establish complex immunosuppressive networks in the TME. Direct killing of cells expressing either protein has the potential to disrupt these networks for therapeutic benefit

Clinical Studies for IO112

RECRUITING



Arginase monotherapy (IIT)*
Arg+ tumors



TRIAL IN
PLANNING

Multi epitope (IO102-IO103-IO112)
Arg+ tumors

Cash Runway into Mid 2024

- **Cash position:** ~\$170 million (as of 6-30-22)
- Phase 3 with dual epitope (IO102-IO103) in 1st line advanced melanoma
- Phase 2 basket trial with dual epitope in first line solid tumors
- Phase 2 basket trial with dual epitope in neoadjuvant / adjuvant solid tumors
- Phase 1/2 trial with multi-epitope (w. IO112) in 1st line, solid tumor
- Continue to build the organization in Denmark, UK and the US

Key Upcoming Data Readouts / Milestones

Multiple data readouts in 2022-2023 across indications

IO102-IO103 (PD-L1, IDO) - Dual Epitope			2022	2023
Phase 3	Melanoma	First-line advanced	<ul style="list-style-type: none"> First patient randomized/dosed – May 	-
Phase 2 Basket Trials	NSCLC SCCHN, UBC	First-line metastatic	<ul style="list-style-type: none"> First patient dosed – April Data in one indication 2H 	<ul style="list-style-type: none"> Data
	TBD	Neo-adjuvant / adjuvant		Initiate Phase 2 in one indication in 2023
IO112 (Arginase) – Multiple Epitope Combinations				
Phase 1/2	Solid tumors	-		File IND in 2023

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.



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