Highlight Therapeutics announces positive preliminary results from Phase 2b study of BO-112 + anti-PD1 in confirmed anti-PD1 progressor melanoma patients at SITC

Breakthrough cancer treatment shows best-in-class potential to open up 2nd-line immunotherapy market to anti-PD1 resistant patients

- BO-112 demonstrates potential as best-in-class therapy to overcome anti-PD1 resistance in melanoma patients whose disease has progressed on prior anti-PD-1 treatment
- Primary endpoint met with a 27% Overall Response Rate (ORR), 8% Complete Responses (CR) & 65% Disease Control Rate (DCR) substantially exceeding current standard of care; further improvements anticipated over one year follow up
- Hard-to-treat mucosal melanoma patients achieved 66% ORR and 100% DCR
- Durable responses and manageable safety profile, with no patients discontinuing due to adverse events
- Preparation for pivotal trial based on FDA guidance underway; potential for use in multiple solid cancers resistant to anti-PD1 inhibitors, and with different anti-PD1 combinations

Madrid, Spain, 12 November, 2021 – Highlight Therapeutics, ("Highlight"), a clinical-stage biopharmaceutical company developing RNA-based therapies against cancer, today announced positive preliminary results of a Phase 2 study of intratumoral administration of BO-112 with pembrolizumab in patients with advanced melanoma whose disease had progressed on first-line anti-PD1-based therapy. BO-112 is a dsRNA agonist targeting anti-PD1 resistance, which has been successfully tested in several previous Phase 1b studies.

Initial results of the study were presented today (12th November) in a late-breaking session at The Society for Immunotherapy of Cancer (SITC) 36th Annual Meeting in Washington DC, Nov. 10–14, 2021. (LBA Poster Abstract (961): *Preliminary results of a phase 2 study of intratumoral administration of BO-112 with pembrolizumab in patients with advanced melanoma that have progressive disease on anti-PD-1-based therapy,* presented in the Poster Hall in Washington, D.C. and the virtual ePoster Hall beginning Friday, Nov. 12 at 7 a.m. EST).

"These are potentially game-changing results showing that BO-112 can rescue melanoma patients who have failed first-line immune-therapy with anti-PD1," ***said Dr Carlos Paya, Executive Chairman of Highlight Therapeutics****. "Anti-PD1 based immunotherapy has revolutionized oncology treatments, but only a fraction of patients initially respond and many of these patients progress thereafter. These initial Phase 2 results show that BO-112 combined with a leading PD1 inhibitor rescue around 65% of anti-PD1 failing patients, making many of them respond to the combined treatment. These much-anticipated outcomes demonstrate BO-112's potential as a best-in-class therapy for melanoma patients whose disease has progressed on prior anti-PD1 treatment, and we now look forward to further clinical studies, not only in melanoma but in other major tumor types in which anti-PD1 resistance is also an issue."*

Anti-PD1 therapies are valued at approximately $24 billion[1] and are used across most solid tumors but currently fewer than 20% of all cancer patients benefit from first-line anti-PD1 treatment. BO-112 in combination with anti-PD1 therapy is designed to resensitize tumors to anti-PD1 treatment through improved antigen presentation, enhanced T-cell infiltration and increased MHC-1 and PDL1 expression by the tumor itself.

"*This initial data is very encouraging and has the potential to change medical practice," said* ***Dr. Marisol Quintero, CEO of Highlight Therapeutics****. "The preliminary ORR of 27%, including 8% Complete Responses, already exceeds current standard of care, such as the use of anti-CTLA-4. Based on the mode of action and experience from previous BO-112 Phase 1 studies, additional follow-up of these patients is expected to deliver*

further improvements in ORR. We are also encouraged by the excellent safety profile, with no patients discontinuing the study due to adverse events. Highlight Therapeutics is in the planning stage of a pivotal Phase 3 trial, due to begin in 2022, and we look forward to opening discussions with potential partners to explore combinations with anti-PD1s."

Highlight Therapeutics and Merck, known as MSD outside the United States and Canada, conducted an open-label, single arm study to evaluate the efficacy & safety of intra-tumoral administration of BO-112 + pembrolizumab in mucosal, acral and cutaneous melanoma patients whose disease had progressed, confirmed by two consecutive CT scans. The study recruited 42 patients in France and Spain, with recruitment completed by August 24, 2021. Patients included those with high LDH levels, which are often associated with poor response rates and have been excluded from comparable clinical trials.

The preliminary analysis shows:

- Primary endpoint (ORR by independent reviewer) has been met
- With a median follow up of three months, there is a clear clinical benefit in patients with confirmed anti-PD1-resistant melanoma, with a 27% ORR and a 65% DCR, superior to 2nd line Standard of Care in stage III/IV melanoma of ~8% (continuing with anti-PD1 Ab) or 13% (second line ipilimumab).
- Three hard-to-treat mucosal melanoma patients have achieved an ORR of 66% and DCR of 100%
- High baseline LDH levels (>3xULN) predict progressive disease
- Responses and SD are durable
- Study treatment has a manageable safety profile, with no patients discontinuing due to adverse events

Next steps in the development of BO-112 include:

- Initiation of a pivotal Phase 3 study in 2nd-line melanoma is planned in 2022 following discussions with regulatory agencies in the US and Europe
- Highlight Therapeutics has initiated strategic partnerships discussions with anti-PD1 companies interested in enhancing their anti-PD1 market potential
- Initial data from a sponsor-initiated Phase 1B trial by UCLA evaluating BO-112 + pembrolizumab in anti-PD1 resistant hepatocellular carcinoma currently recruiting patients is expected in 2022

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1. *IQVIA Global Oncology Report 2020*

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Notes to editors

About Highlight Therapeutics

Highlight Therapeutics, formerly known as Bioncotech Therapeutics, is a private, clinical-stage company dedicated to unlocking the full potential of immuno-oncology. Our lead drug candidate BO-112 is a best-in-class RNA-based therapy which has been demonstrated to initiate a powerful immune response, leveraging a unique multi-target approach to turn 'cold' tumors 'hot' and therefore visible to the immune system. It has the potential to rescue patients who are resistant to current checkpoint inhibitor therapy, a very large market opportunity. BO-112 is currently being investigated in a range of clinical trials as a monotherapy and in combination with checkpoint inhibitors. In addition to in-house research, Highlight Therapeutics has a number of external collaborators, including Merck & Co and UCLA.

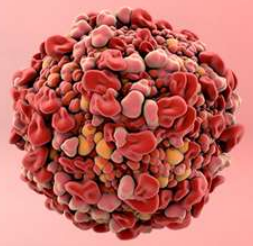
For more information, please visit www.highlighttherapeutics.com

HIGHLIGHT THERAPEUTICS

Unlocking the potential of immuno-oncology

Overcoming anti-PD1 resistance
to create best-in-class immunotherapy

2021



Highlight's mission is to re-sensitize tumors to anti-PD1 inhibitors in multiple solid tumors

~80% of patients do not respond to first line immunotherapy treatment

There are no approved 2nd line treatments for patients who do not respond, patients often turn to clinical trials

BO-112 has demonstrated potential as best-in-class 2nd line treatment in combination with anti-PD1s

Data driven opportunity to dramatically improve treatment and lead the market in 2nd line anti-PD1 market

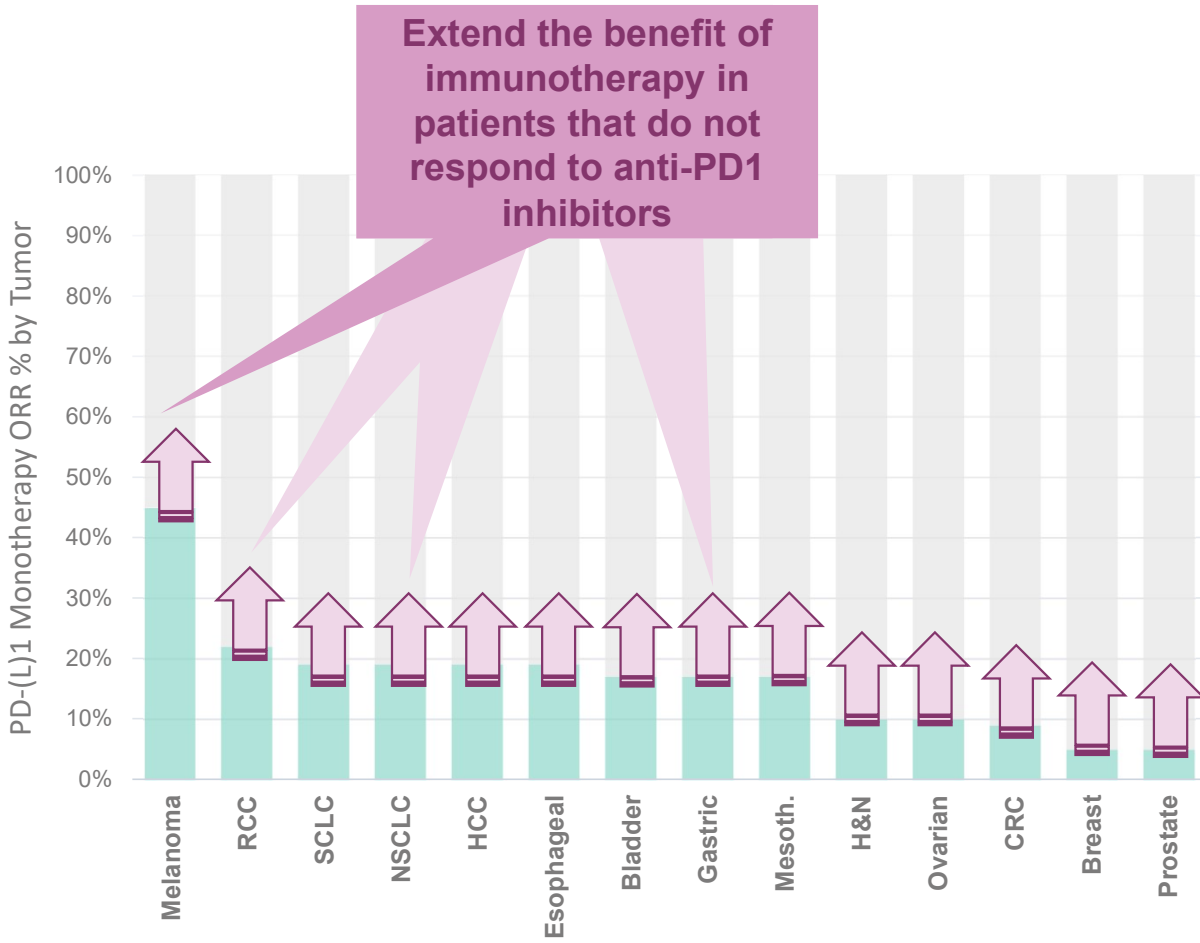
BO-112: Data-driven potential to treat the anti-PD1 resistance market

- BO-112 is a dsRNA agonist targeting anti-PD1 resistance successfully tested in several Phase 1b studies
- Phase 2 evaluating BO-112 + pembrolizumab in confirmed anti-PD1 progressor melanoma patients
- Targeting a best-in-class profile:
  - Overall Response Rate (ORR) > 25% and Disease Control Rate (DCR) > 50% (substantially superior to 2nd line Standard of Care in melanoma III/IV)
  - Durable & systemic responses in non-injected lesions > 12 months with a favorable safety profile
  - Potential for use in multiple solid cancers that are resistant to anti-PD1 inhibitors
- Opportunity
  - Expand the $24 billion anti-PD1 market to melanoma and other solid tumor patients resistant to anti-PD1 inhibitors
  - Targets include (melanoma, SCNHN, HCC, bladder, NSCLC, RCC)

BO-112 increases PDL1 expression and re-sensitizes tumors to anti-PD1 therapy

Our goal is to re-sensitize tumors to anti-PD1 inhibitors in multiple solid tumors

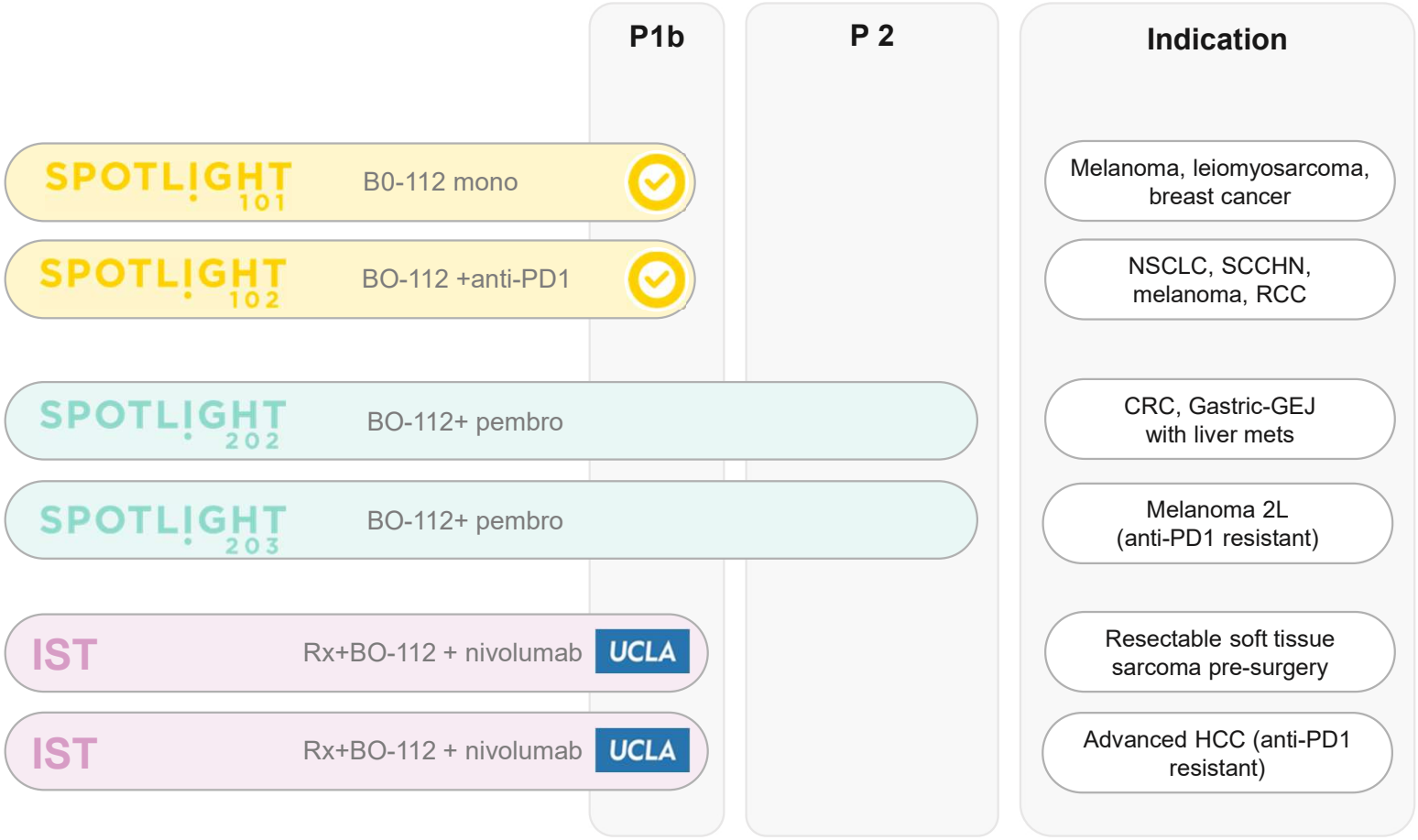
- Anti-PD(L) agents are valued at approximately ~$24 billion. Key drugs in this segment:
  - Keytruda (pembrolizumab)
  - Opdivo (nivolumab)
  - Tecentriq (atezolizumab)
  - Imfinzi (durvalumab)
- Only <20% of all cancer patients benefit from anti-PD1 1st line therapies
- BO-112 in combination with anti-PD1 can induce de novo sensitivity and/or reverse the secondary resistance to anti-PD1 1st line therapies. Its MOA:
  - Improved antigen presentation
  - Enhanced T-cell infiltration
  - Increased MHC-1 and PDL1 expression in tumor cells



Data assembled by Highlight Therapeutics

BO-112 development program in multiple solid tumors

SPOTLIGHT CLINICAL TRIALS



SPOTLIGHT 102: Phase 1b efficacy and safety confirmed across 4 tumor types

SPOTLIGHT 102

Study Period up to total of 1 year

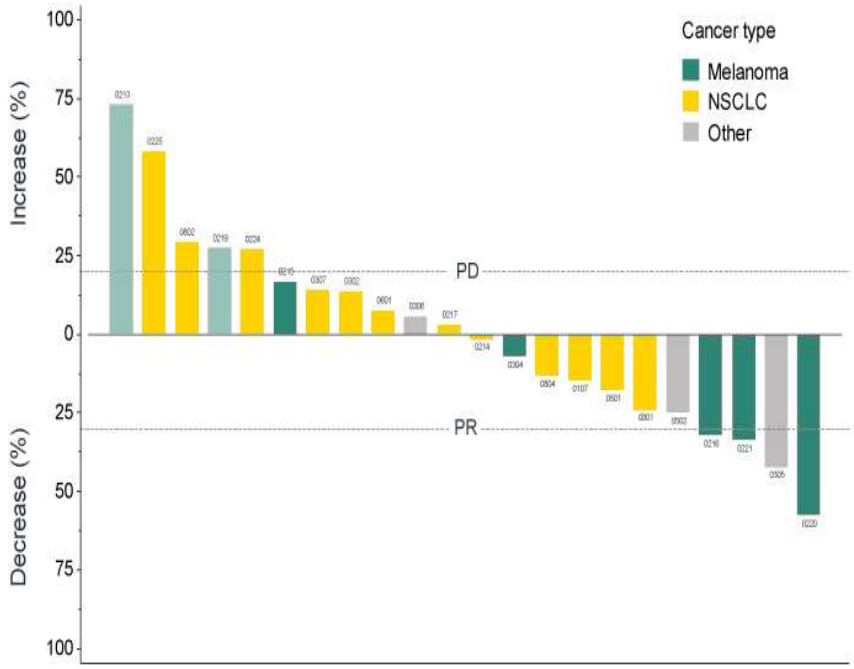
Nivolumab every 2 weeks or Prembrolizumab every 3 weeks

PD

Initial 12 weeks: 5 x BO-112 IT

Maintenance: 4 x BO-112 IT every 12 weeks

Dose of BO-112: 1mg



Melanoma (N=10) : 20% ORR (PR) & 50% DCR

RCC (N=1): 100% ORR (PR)

NSCLC (N=13) 46% DCR

SCCHN (N=4) : 50% DCR

NSCL: Non small cell carcinoma
RCC: Renal cell carcinoma
SCCHN: squamous cell carcinoma head and neck

Márquez-Rodas I, et al. Sci Transl Med. 2020 Oct

SPOTLIGHT 203 Phase 2: demonstrates potential for best-in-class in melanoma 2nd Line

Study design: - BO-112 + pembrolizumab in anti-PD1 resistant patients	• Open-label, single arm study to evaluate efficacy & safety of intra-tumoral administration of BO-112 + pembrolizumab in **confirmed progressors** (2 consecutive CT scans) • Indication: 2nd line metastatic melanoma (anti-PD1 progressors): mucosal, acral & cutaneous • 40 patients in France and Spain; Q1 2021 start; Q3 2021 completed
Endpoints	• Primary endpoint: ORR (Objective Response Rate) • Secondary endpoints: disease control rate (DCR), duration of response (DOR), progression-free survival (PFS), overall survival (OS), and iRECIST ORR, DCR, DOR and PFS • Regimen of BO-112 injections: QW 7W and then Q3W – **number of lesions (up to 8). Up to 2 mg**
Up to 2 year follow up	• Central independent review • Clinical collaboration with Merck: Highlight retains all product rights • Expected preliminary readouts November 2021

SPOTLIGHT 203

Study treatment up to total 2 years

PD *Pembrolizumab every 3 weeks +*

Initial 7 weeks: *Every week* BO-112 IT

Maintenance: BO-112 IT *every 3 weeks*

SPOTLIGHT 203 Phase 2: Unprecedented efficacy results to date

- All patients had confirmed progression per SITC on or within 12 weeks of stopping anti-PD1
- RECIST 1.1 objective response rate 27%
    - Response in 2/3 patients (67%) with mucosal melanoma
- Disease control rate 65% with majority of patients still on treatment
- Systemic tumor reduction (abscopal effect) in all responders (100%) with non-injected lesions (n=6)
- Responses observed in BRAF naïve and mutated patients
- Rapid PD in all 4 patients with LDH >3 x ULN (very high LDH levels)

SPOTLIGHT 203 Phase 2: Patient characteristics

	Total=42	
Sex	**N**	**%**
Male	25	59
Female	17	41
Age, median (min - max)	68	27 - 88
Type of melanoma	**N**	**%**
Acral	8	19
Cutaneous	31	74
Mucosal	3	7
***BRAF* status**	**N**	**%**
Mutated	6	14
Wild type	36	86
Previous treatment	**N**	**%**
Ipilimumab + nivolumab	6	14
Nivolumab monotherapy	15	36
Pembrolizumab monotherapy	18	43
Other anti-PD-1 combinations	3	7
Prior treatment line indication	**N**	**%**
Adjuvant	9	21
Advanced disease	33	79
Duration of previous treatment line (weeks) median (min - max)	30	6 - 128
Lactate dehydrogenase (LDH)	**N**	**%**
High (>ULN)	17	41
Normal	25	59

SPOTLIGHT 203 Phase 2: Safety profile shows no Grade 5 adverse events

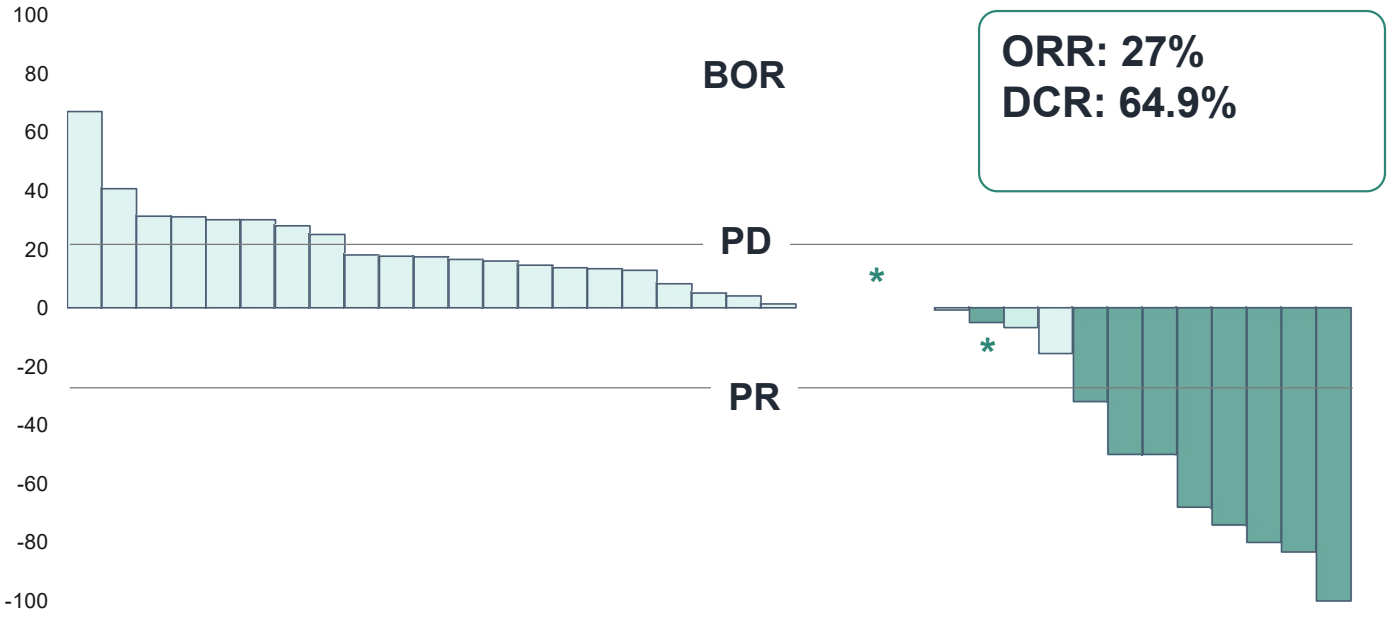
TEAEs related to BO-112 injection mostly grade 1 or 2 in severity

AE preferred term	Grade 1-2 n (%)	Grade 3-4* n (%)
Asthenia	21 (50)	0
Pyrexia	16 (38)	0
Diarrhoea	14 (33)	0
Vomiting	10 (24)	0
Chills	9 (21)	0
Nausea	9 (21)	0
Decreased appetite	6 (14)	0
Headache	6 (14)	0
Injection site pain/discomfort/haematoma/hypersensitivity	6 (14)	0
Arthralgia	5 (12)	0
Pruritus	5 (12)	0
Influenza-like illness	4 (10)	0
Back pain	4 (10)	0
Fatigue	3 (7)	0
Hypertension	3 (7)	0
Oedema peripheral	3 (7)	0
Temperature regulation disorder	2 (5)	0
Musculoskeletal pain	1 (2)	0
Neutropenia	1 (2)	0
Tumor haemorrhage	1 (2)	0
Infusion related reaction	0	1 (2)

*No grade 5 related AEs

SPOTLIGHT 203 Phase 2: 27% ORR in the whole population. 67% ORR in mucosal melanoma

Systemic tumor reduction observed in all responders suitable for assessment of abscopal effects



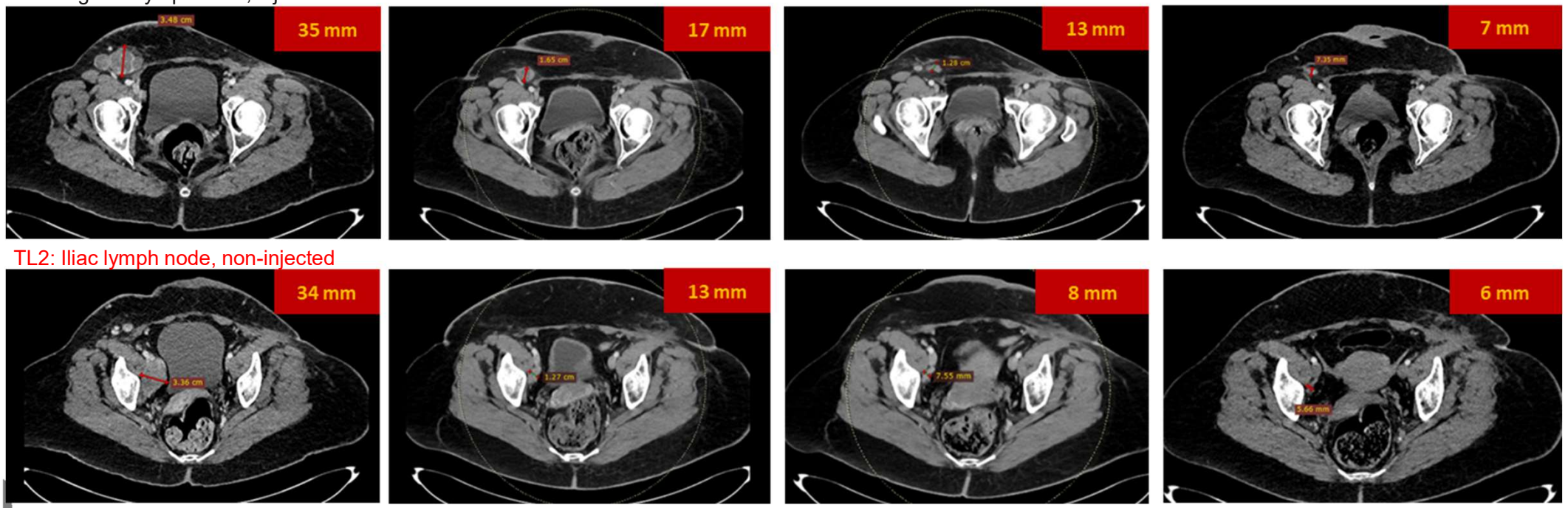
*pCR with RECIST SD

SPOTLIGHT 203 Phase 2: Continuous improvement seen in tumor mass over time

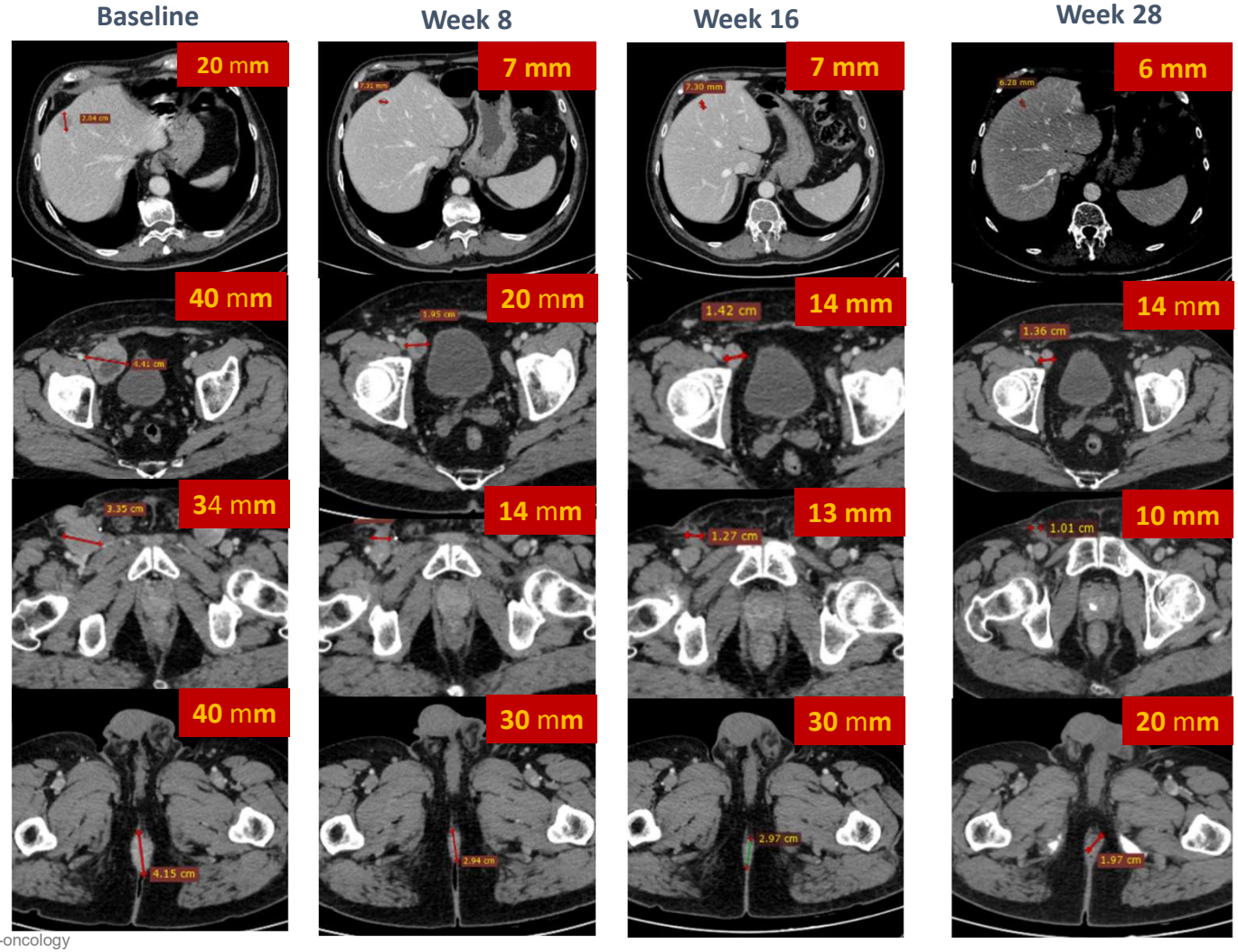
Mucosal melanoma in a 54 y/o female

Adjuvant nivolumab 12 months (Nov 2018) then nivolumab 16 weeks (July 2020) for advanced disease

	Baseline	Week 8	Week 16	Week 28
TL1: Inguinal lymph node, injected	35 mm	17 mm	13 mm	7 mm
TL2: Iliac lymph node, non-injected	34 mm	13 mm	8 mm	6 mm



SPOTLIGHT 203 Phase 2: Continuous reduction in multiple tumor mass over time



Mucosal melanoma in a 65 y/o female

First line pembrolizumab + peptidic vaccine for 14 weeks

SPOTLIGHT 203 Phase 2: Reduction of tumor by 80%

Cutaneous melanoma in a 71 y/o female

First line nivolumab for 36 weeks

SPOTLIGHT 301: Pivotal Phase 3 trial design

Flexibility on choice of anti-PD1	• Registration trial can be run with any anti-PD1 Ab • Accelerated approval potential based on ORR and DOR
Attractive target indication and label	• Treatment of melanoma with BO-112 & anti-PD1 1st line therapy that has progressed to prior anti-PD1 1st line treatment for unresectable malignant disease (stage III or IV) • Target regulatory approval date: **Q1 2025**
Melanoma efficacy trending superior to current standard of care	• **ORR:** Target > 25% (*vs.* ~8% for anti-PD1 1st line control; *vs.* ~13% for anti-CTLA4) • **DCR:** Target > 50% (*vs.* ~20% for anti-CTLA4) • **DOR:** Target > 12-18 months

Clear regulatory approval path to the first PD1 1st line resistant indication in melanoma
Positive data supports attractive life cycle in other tumors resistant to anti-PD1 1st line therapies

BO-112: Data-driven potential to treat the anti-PD1 resistance market

Major opportunity in 2nd line melanoma as proof of concept for multiple cancers

- Potential best-in-class product for 2nd line immunotherapy treatment
  - Poor current Standard of Care
  - Targeting 25-30% ORR vs ~8% for 2nd line anti-PD1 1st line control & ~13% for 2nd line ipilimumab
- Ability to re-sensitize tumors to anti-PD1 therapy in several solid tumors supported by biomarkers and clinical activity
- Possibility of broad development in anti-PD1 1st line resistant populations opens up checkpoint inhibitor market & maximizes commercial potential
  - Phase 1 HCC trial in anti-PD1 resistant patients initiated by UCLA
- Regulatory flexibility to combine BO-112 with any anti-PD1, creating a leadership opportunity for an anti-PD1 in the treatment of anti-PD1 resistant patients

Next steps

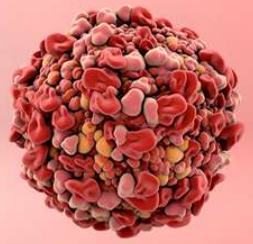
- Preliminary data from SPOTLIGHT 203 Phase 2 in anti-PD1 resistant melanoma presented at SITC 2021
- Patients continue to be followed for responses and DOR. Final results expected in mid 2022'
- Preparations to initiate registration trial in 2nd line melanoma in 2022
- Evaluating strategic partnership

~80% of patients do not respond to first line immunotherapy treatment

There are no approved 2nd line treatments for patients who do not respond, patients often turn to clinical trials

BO-112 has demonstrated potential as best-in-class 2nd line treatment in combination with anti-PD1s

Data driven opportunity to dramatically improve treatment and lead the market in 2nd line anti-PD1 market



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