

Immunotherapy Revolution 2.0

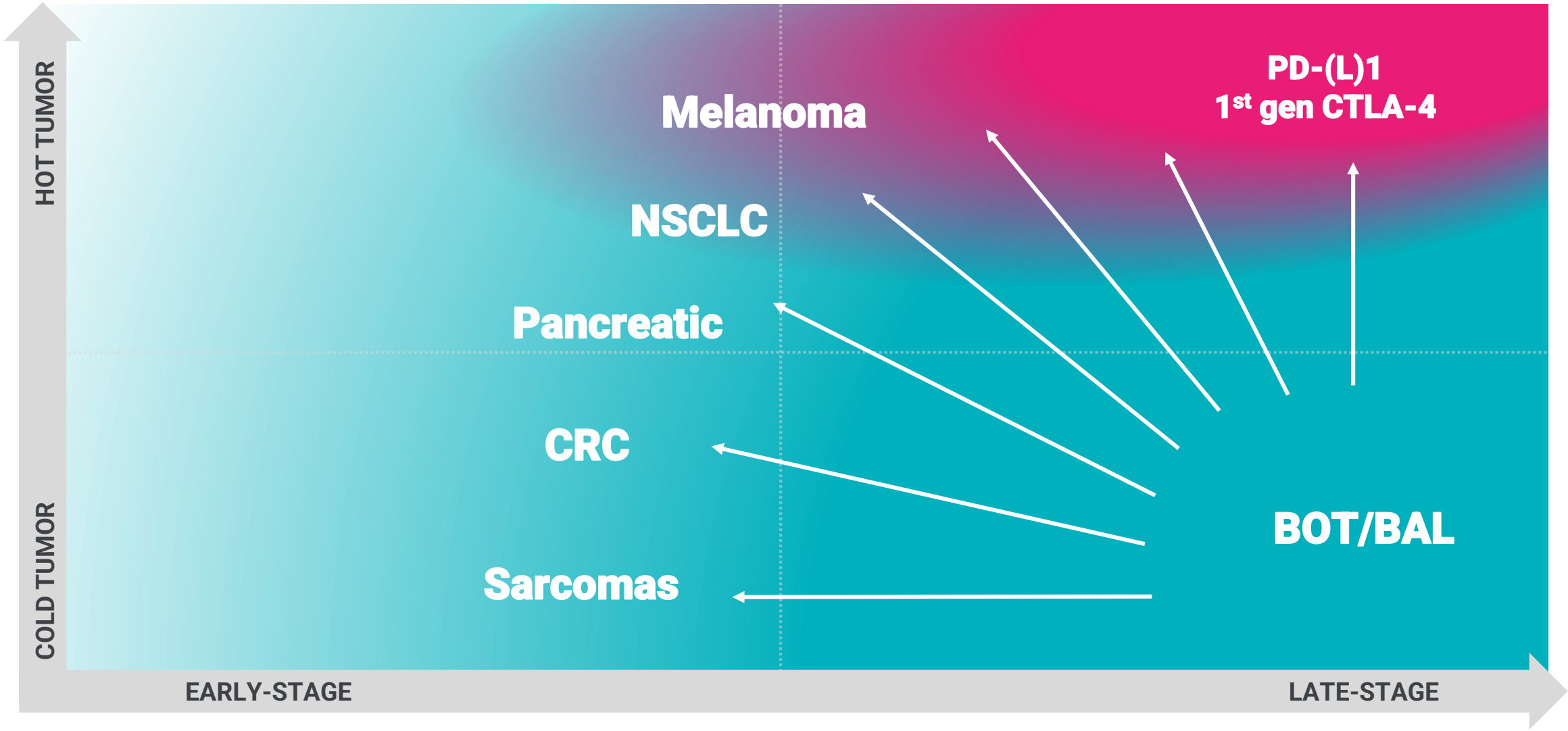
Agenus Corporate Event @ ESMO 2023

October 22, 2023

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BOT/BAL Potential

$48B
2022 IO market size [1]



1. Global Data IO Market Report

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BOT/BAL and Standard of Care Clinical Readouts by Treatment Setting

Treatment Setting	Target Population *(current Standard of Care, or SOC)*	Overall Response Rate (ORR%)		Survival	
		SOC or Comparator	BOT or BOT/BAL	SOC median Overall Survival (mOS)	BOT or BOT/BAL
2/3L+ MSS CRC	MSS CRC Non-active Liver Mets *(regorafenib / lonsurf)*	2.8%	24%*	12.9 months	74% 12-month OS* mOS not reached
Neoadjuvant MSS CRC	MSS CRC *(surgery followed by radiation and/or chemo)*	29% (Ipi/Nivo)	67%	N/A	TBD
2L Pancreatic	Chemo-refractory Pancreatic *(gem-Abraxane)*	10-15%	1H 2024**	7-8 months	TBD
2L+ Melanoma	PD-1/CTLA-4 R/R Post-BRAF MEK *(various chemo regimens)*	<10%	2H 2024**	<12 months	TBD
2L+ NSCLC	PD(L)-1 or PD(L)-1 chemo R/R *(docetaxel)*	10-20%	56%	<14 months	TBD

*efficacy evaluable population; Sources: NCT02750514; Fisher et al. ASCO 2019; D'Angelo et al. Lancet Oncology 2018; Somaiah et al. Lancet Oncology 2022; NCT01928394; H.F. de Jesus et al. Therapeutic Advances in Medical Oncology 2020; Hinchcliff et al. Gyn Onc 2021, Garon EB et al. J Thorac Oncol. 2023; Zimmer et al. EJC 2017; Pires et al, Lancet Oncology 2021; SWOG 1616; Garon et al. Lancet Oncology 2014; Goldinger, et al. European Journal of Cancer 2022 Cohen et al ASCO 2023 1. Cerner – based on drug treated 7MM (US, France, Germany, Spain, Italy, UK, Japan) and Agenus analysis ; Chalabi M. ASCO 2022 (NICHE); Ho Ko, et al. Korean J Intern Med 2007; Note response rates in Neoadjuvant MSS CRC are Pathologic Responses as defined by 50% or more reduction in tumor volume; **expected timing

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Potential BLA Filings

Based on promising clinical signal across treatment settings

Treatment Setting	BOT/BAL Highlights	Development Plan	US + EU5 Patients[1]
2/3L+ MSS CRC NLM	**Data in >300 Patients** **Fast Track Designation Granted**	• U.S. and EU regulatory interactions ongoing • Planned BLA filing midyear 2024	13,000
2L Pancreatic	**Tumor and Biomarker Reduction in Majority of Patients**	• Anticipated 1H 2024 Phase 2 data update • Potential path to accelerated filing in 2025	22,000
2L+ Melanoma	**Confirmed Responses in PD-1/CTLA-4 Failures**	• Anticipated 2H 2024 Phase 2 data update • Potential path to accelerated filing in 2025	6,000
2L+ NSCLC	**Responses in PD-(L)1 Refractory Patients**	• Anticipated midyear 2024 data update	103,000
Neoadjuvant MSS CRC	**Significant Pathologic Responses**	• Evaluating study designs for potential registration	142,000
TOTAL			**286,000**

Source: 1. Cerner/Envisa 2022 Drug Treated Patients and CancerMpact Treatment Architecture

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CRC

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Colorectal Cancer (CRC): Growing Prevalence, High Unmet Neet



CRC is the 3rd most common cause of cancer mortality globally[1]

Despite advances in treatment of CRC, long term survival remains dismal[2,3]

- **3-year relative OS for patients with metastatic CRC is ~30-35%**
- **5-year relative OS for patients with metastatic CRC is ~15%**

~1.9M

People diagnosed annually with CRC worldwide[1]

~380K

~20% of patients diagnosed have metastatic disease [2]

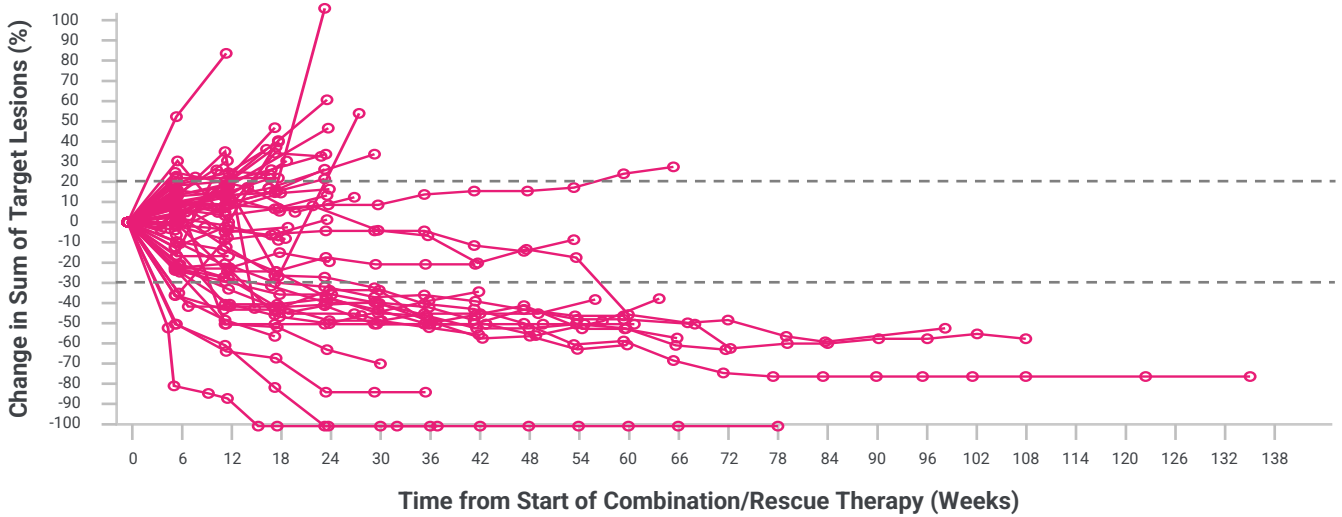
~360K

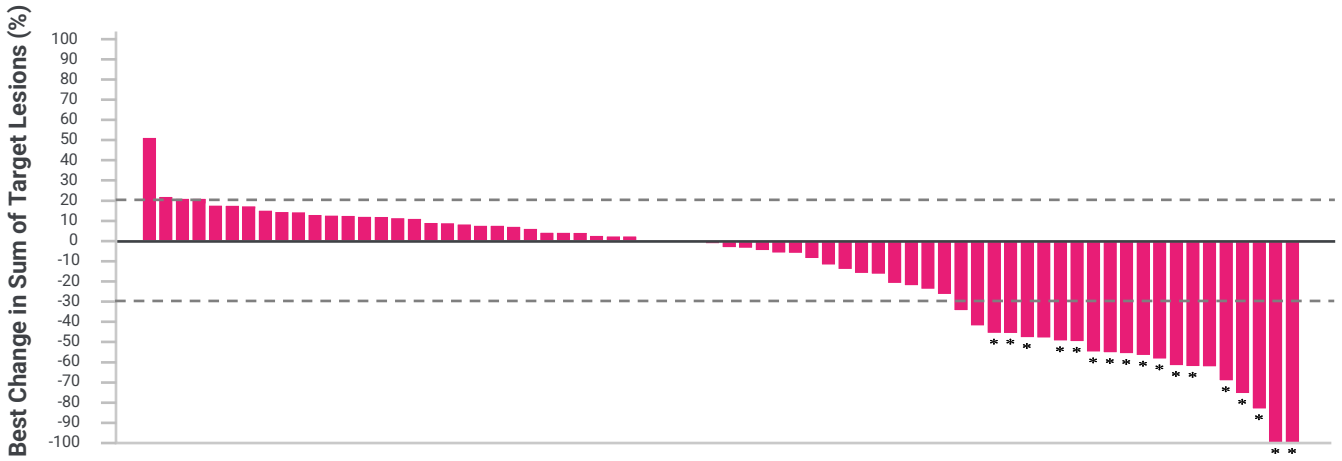
95%[4] of metastatic CRC patients have MSS CRC[3]

Sources: 1. Biller LH et al. JAMA 2021. 2. Ciardiello F et al. CA Cancer J Clin. 2022. 3. Ciardiello F et al. CA Cancer J Clin. 2022. 4. CancerMPact® Treatment Architecture U.S., CRC 2021

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Updated Clinical Data in Refractory MSS CRC





2/3L+ MSS CRC with No Active Liver Mets *Efficacy Evaluable Population (n=70)*	
Confirmed ORR, % (95% CI)	**24%** (15%, 36%)
BOR, n (%)	
CR	1 (1%)
PR	16 (23%)
SD	39 (56%)
PD	14 (20%)
DCR (CR + PR + SD), % (95% CI)	**80%** (69%, 89%)
Responses ongoing	10 (59%)
Median follow-up, months (range)	12.3 (1.4 – 40.5)

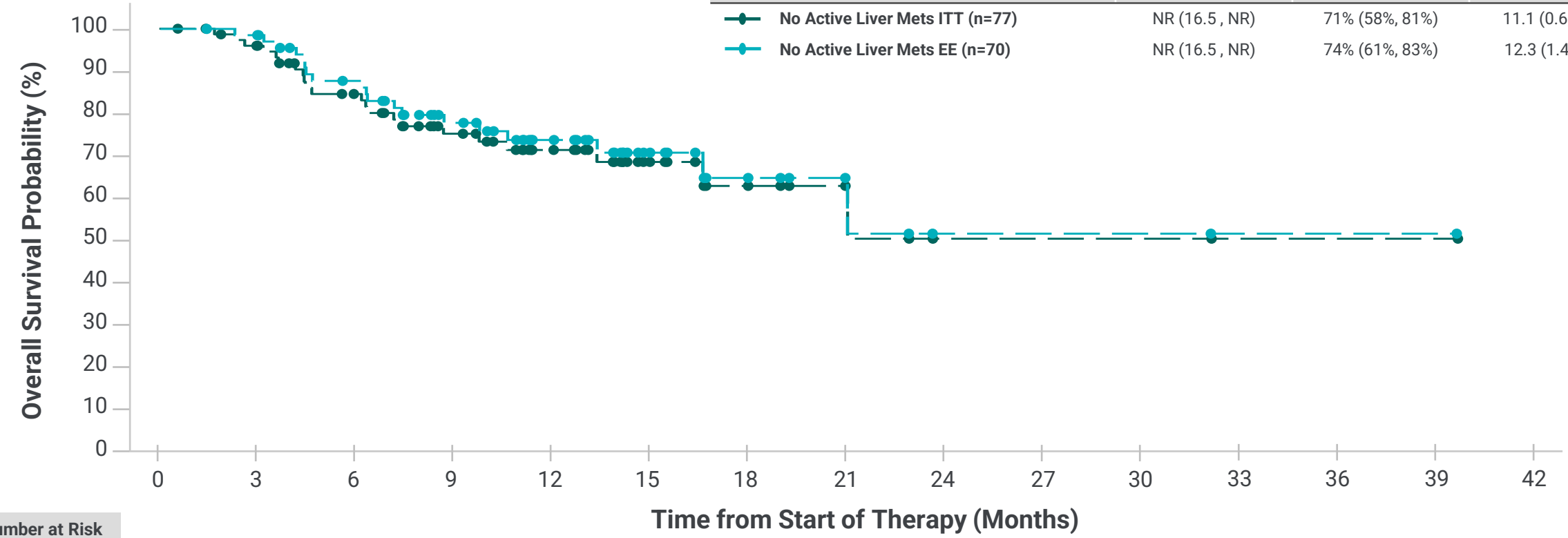
In the intent to treat (ITT) population with no active liver metastases (n=77), ORR was 22% and DCR was 73%

Source: Data cutoff of 26SEP2023
*Confirmed response (CR or PR)

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Updated Clinical Data in Refractory MSS CRC

	Median OS, Months (95% CI)	12-month OS, % (95% CI)	Median F/U, Months (Range)
No Active Liver Mets ITT (n=77)	NR (16.5 , NR)	71% (58%, 81%)	11.1 (0.6, 40.5)
No Active Liver Mets EE (n=70)	NR (16.5 , NR)	74% (61%, 83%)	12.3 (1.4 40.5)



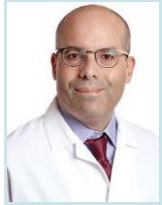
Number at Risk															
No Active Liver Mets ITT	77	69	56	42	29	15	8	4	2	2	2	1	1	1	0
No Active Liver Mets EE	70	66	48	42	29	15	8	4	2	2	2	1	1	1	0

Source: Agenus Data (26SEPT2023); NR = Not Reached

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Expansion into Earlier Treatment Lines in MSS CRC

Investigator sponsored studies support ongoing development and registrational strategy

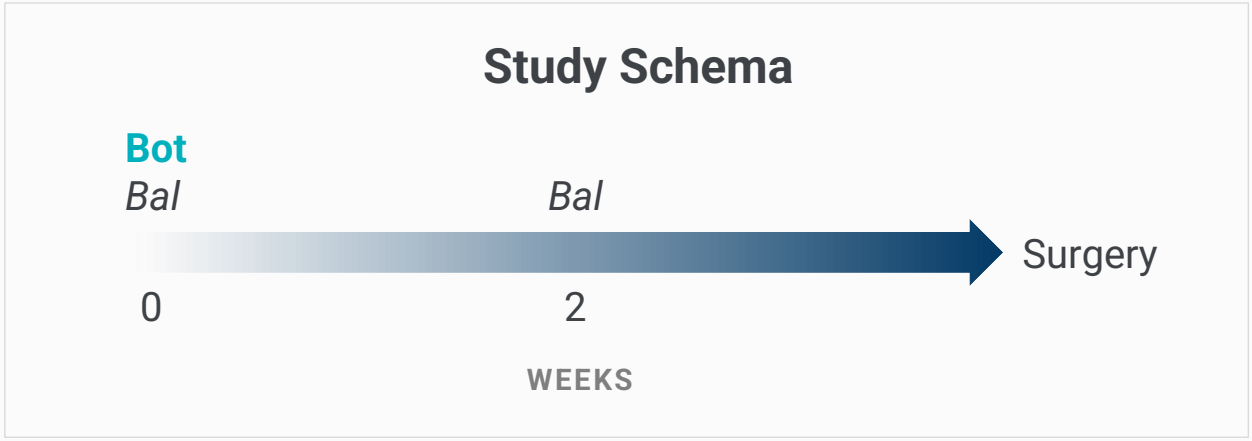
	IST / Disease Setting	Anticipated Data Readout
 City of Hope **Marwan Fakih, MD**	**1L MSS CRC** BOT/BAL + Bev + FOLFOX vs. Bev + FOLFOX	• 1H 2024
 Weill Cornell Medicine **Pashtoon Kasi, MD**	**Neoadjuvant MSS & MSI-H CRC** BOT/BAL pre-surgery	• 4Q 2023 pilot study; pilot study data submitted to 2024 medical meeting • 2Q 2024 expanded cohorts

Sources: NCT05571293 ; NCT05627635

“Window of Opportunity” Neoadjuvant CRC Study Shows Promising Results

Treatment with BOT/BAL led to significant tumor reduction within four weeks; well tolerated

- BOT/BAL treatment with Standard of Care surgery
- Major tumor reductions observed within four weeks
- No safety signals or delayed surgery due to treatment



Topline results:

6/9 **(67%)**
patients with MSS CRC had pathologic responses of ≥50%

3/3 **(100%)**
patients with MSI-High CRC had major pathologic responses ≥90%

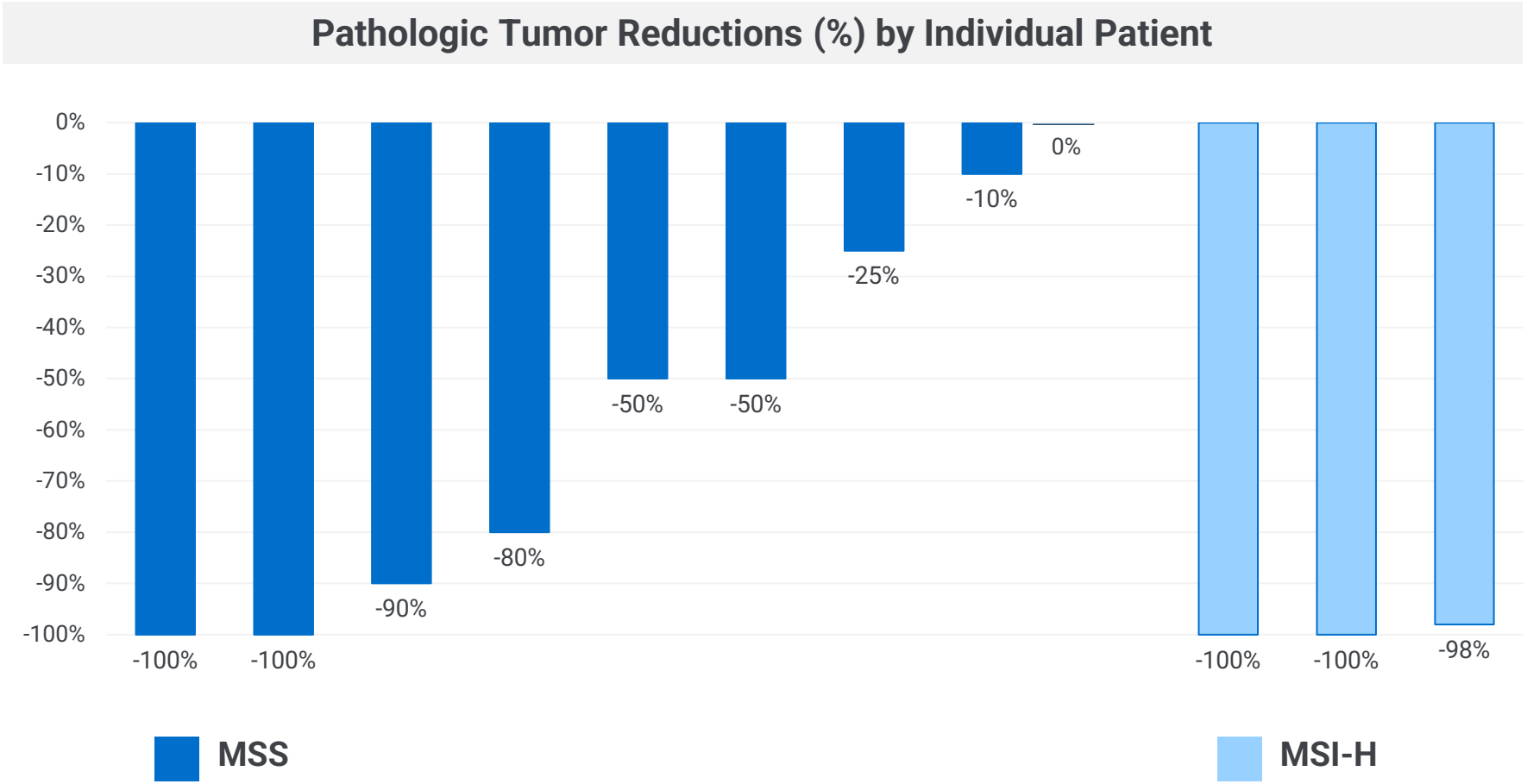
Robust immunogenic pathologic response (“inside-out” phenomenon)

Sources: NCT05571293 ;Investigator sponsored trial, subject to change

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“Window of Opportunity” - Neoadjuvant CRC Study Shows Promising Results

Treatment with BOT/BAL led to significant tumor reduction within four weeks; well tolerated

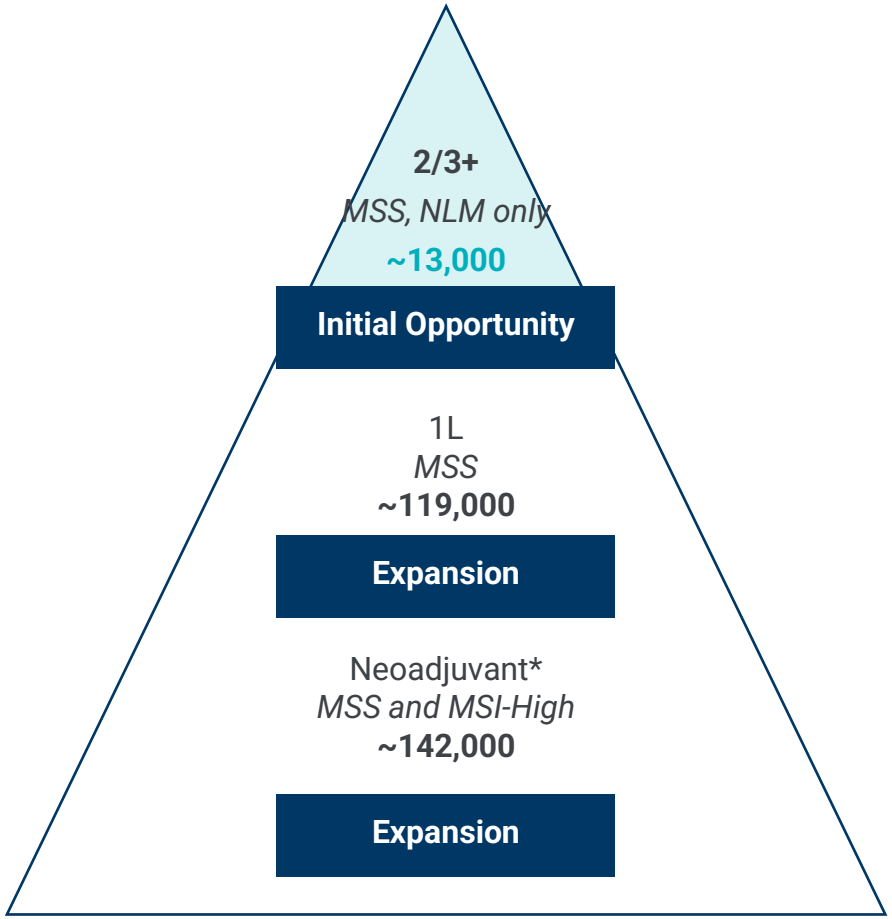


Sources: 1. NCT05571293; investigator sponsored study, subject to change

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BOT: Potential to Become a Backbone Therapy in CRC

US/EU5 - CRC Patients Treated Annually



2/3L+ MSS CRC

- >300 patients treated with BOT/BAL
  - ORR: 24%; 74% 12-month OS; mOS: not reached (n=70)
- Fast Track Designation granted by FDA in April 2023
- BLA filing planned midyear 2024

1L MSS CRC

- Planned Phase 3 study
- BOT/BAL + Bevacizumab + FOLFOX vs. Bevacizumab + FOLFOX
- IST ongoing @ City of Hope (NCT05627635) designed to evaluate tolerability with chemo

Neoadjuvant MSS CRC and MSI-H CRC

- Treatment with BOT/BAL pre-surgery
- IST ongoing @ Weill-Cornell in MSS & MSI-H CRC (NCT05571293)
- IST expanding; initial data at ESMO 2023 event; data readout expected in 2Q 2024

Sources: Cohen et al ASCO 2023; Cerner/Envisa 2022 Drug Treated Patients; CancerMpact Treatment Architecture
*stage II-III

Rapid Development Pathway for BOT/BAL in 2/3L+ MSS CRC

Registration Strategy

- No active liver mets (clinical marker)
- Filing planned for midyear 2024
- Population: ~380 patients with MSS CRC
  - Ph. 1b (n~150)
  - Randomized Ph. 2 (n~230); enrollment completed
- Efficacy based on ~175 patients at each dose level (1 & 2) with reference SOC chemo and synthetic control (supportive survival)
- Results (in efficacy evaluable no active liver mets subpopulation):
  - ORR ~24% (95% CI, 15%, 36%)
  - Median OS not reached (95% CI, 16.5, not reached)
  - 12-month OS% 74% (95% CI, 61%, 83%)

Regulatory Engagement

US

- Fast Track designation **granted**
- Dose optimization **completed**
- Pediatric study plan **completed**
- FDA alignment on Phase 1L study as a confirmatory study **in progress**
- **Planned submission Midyear 2024**

Europe

- National advice from Denmark and Spain **completed**
- Pediatric study plan **in progress**
- Scientific advice from EMA **in progress**
- **Planned submission to EMA in 1H 2025**

Case Study: Recent Precedence for Accelerated Approval in Advanced mCRC

- Tucatinib & trastuzumab for HER2-positive mCRC
- Approval January 2023
- Efficacy based on 86 patients with ≥1 dose tucatinib + trastuzumab

Results:
- ORR of 38.1% (95% CI, 27.7, 49.3)
- Median DOR of 12.4 months (95% CI, 8.5, 20.5)
- OS of 24.1 months (95% CI, 20.3, 36.7)

Go-To-Market Strategy

Experienced leadership team in place to deliver successful launch of BOT upon approval

Clinical Team with I/O Pioneers

- ✓ **KOL relationships across 40+ countries** facilitating scientific exchange
- ✓ **25+ podium & clinical presentations** at major medical conferences
- ✓ **PIs from the top cancer centers** (Dana Farber, City of Hope, Weill Cornell etc.)



Chief Medical Officer
Steven O'Day

YERVOY



VP, Clinical Development
Joseph Grossman

Beth Israel Deaconess

Extensive Medical Affairs Engagement

- ✓ **25+ FTEs with big pharma and biotech experience** (BMS, Amgen, BeiGene, Turning Point, Agios etc.)
- ✓ **Multiple KOL meetings at ASCO 2023** with major tertiary care research centers in US, EU, Japan and CIS
- ✓ **Extensive engagement** with globally-renowned GI & CRC oncologists as investigators on Phase 1 & 2 studies



Chief Regulatory Advisor
Shefali Agarwal

TESARO Epizyme



Chief Strategic Advisor
Todd Yancey

BeiGene AMGEN Genentech

Commercial Preparedness

- ✓ **Robust planning for commercial launch**
- ✓ Fully integrated **cGMP manufacturing capabilities underway**



Chief Commercial Officer
Robin Taylor

Genentech AstraZeneca Seagen



Chief Manufacturing Officer
Al Dadson

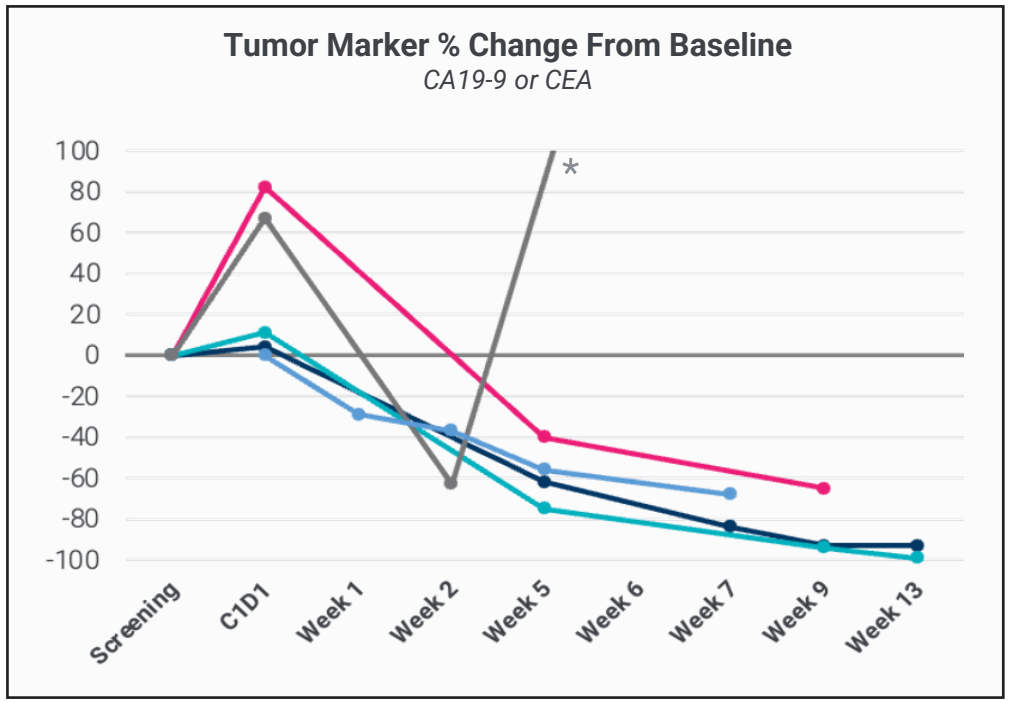
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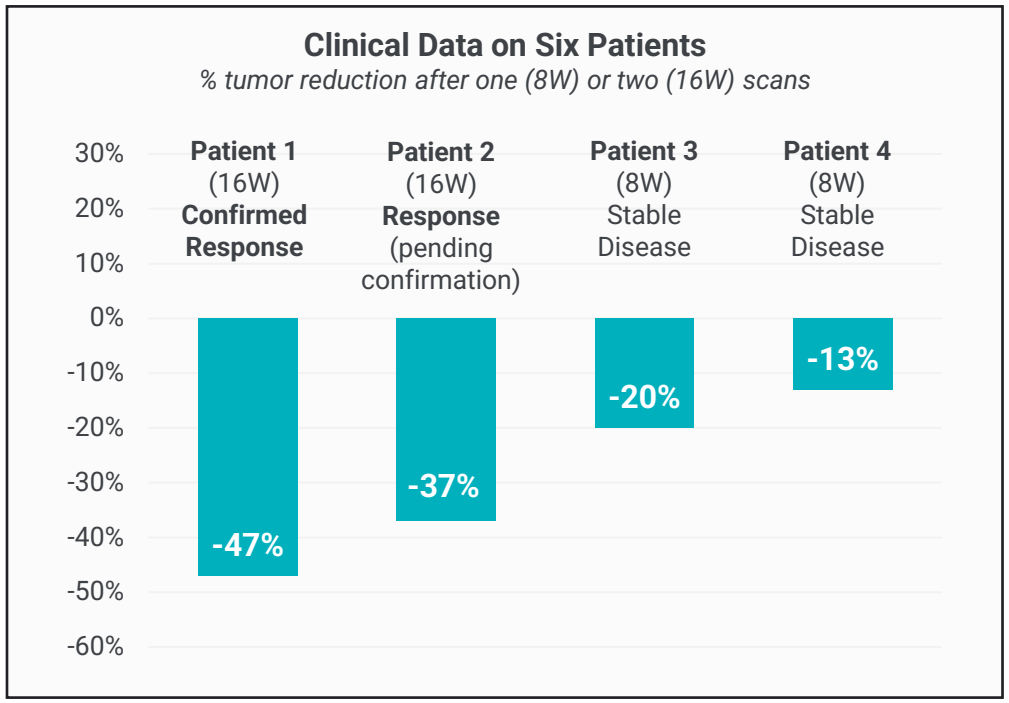
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2L Pancreatic
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Clinical Data in 2L Pancreatic Cancer

Patients (n=6) dosed with 150mg BOT+gem/abraxane after FOLFIRINOX failure for metastatic disease
All patients had liver metastases





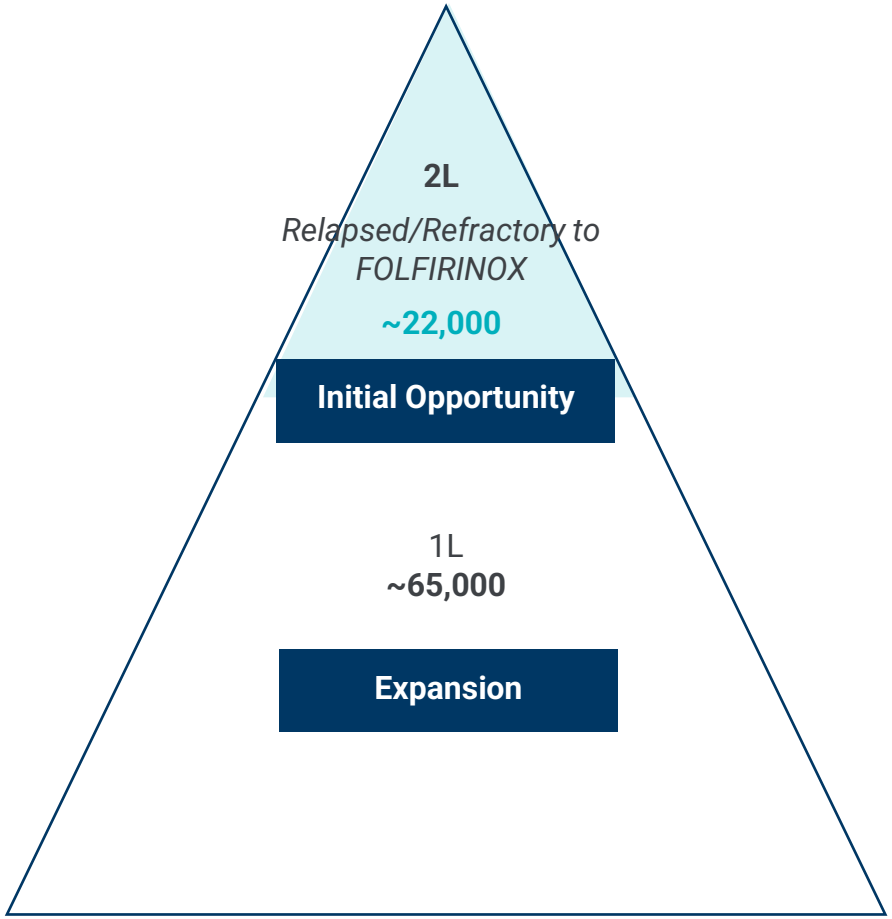
*5th patient had clinical progression and is now off study
6th patient is awaiting their first scan

Source: Data cutoff as of 19OCT2023, tumor marker data is included on 5 patients with an elevated tumor marker at baseline; investigator reported, subject to change

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BOT Potential in Advanced Pancreatic

US/EU5 - Pancreatic Patients Treated Annually



2L Pancreatic Cancer

- Randomized Phase 2 (N=60) ongoing with BOT + gem/Abraxane; expected to be fully enrolled by EOY 2023
- High unmet need: SOC has <15% ORR, 7-8 month mOS
- Potential BLA filing 1H 2025

1L Pancreatic Cancer

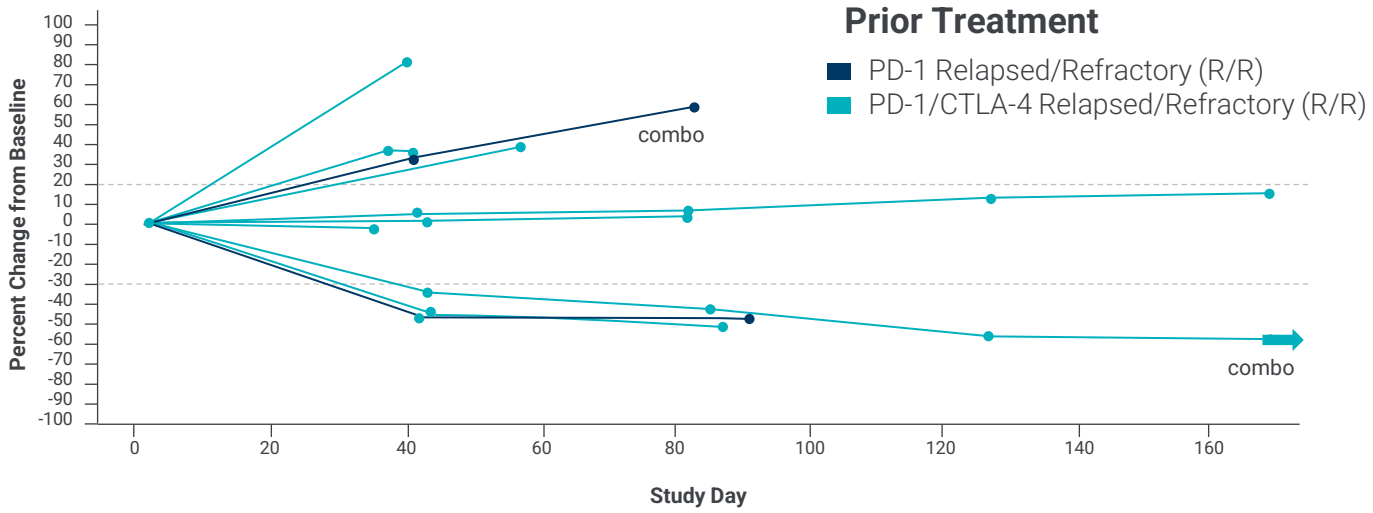
- Registrational study consideration: BOT + SOC (FOLFIRINOX) vs. FOLFIRINOX

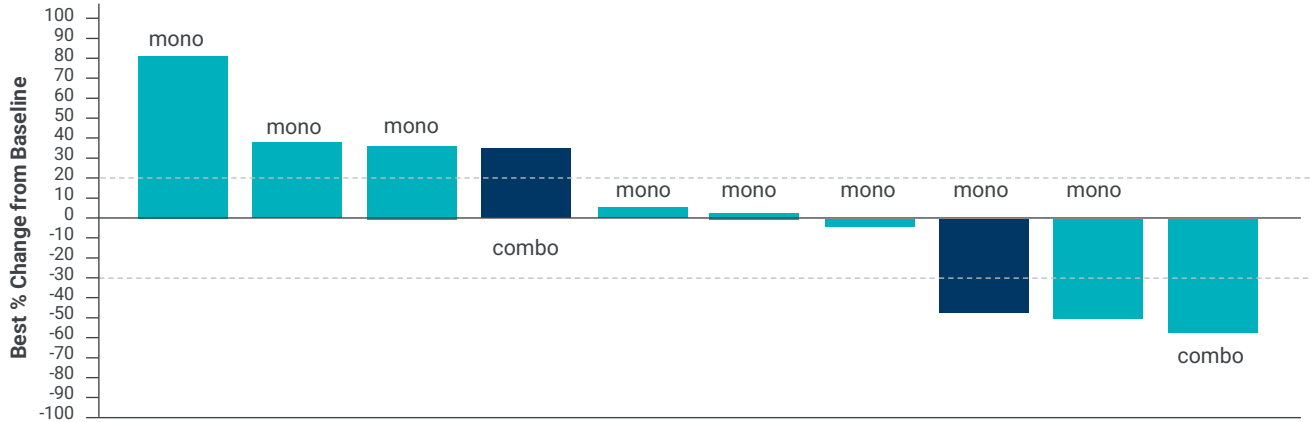
Source: H.F. de Jesus et al. Therapeutic Advances in Medical Oncology 2020; Cerner/Envisa 2022 U.S. Drug Treated Patients and CancerMpact Treatment Architecture


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2L+ Melanoma
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BOT and BOT/BAL Responses in CTLA-4/PD-1 R/R (2L+) Melanoma

Cutaneous melanoma patients receiving BOT monotherapy or BOT/BAL combination





Cutaneous 2L+ Melanoma *Efficacy Evaluable (First study n=10)*	
ORR, %	**30%**
BOR, n (%)	
CR	0 (0)
PR	3 (30)
SD	3 (30)
PD	4 (40)
DCR (CR + PR + SD), %	**60%**
Responses ongoing	33%

PD-1 R/R	1/2 = 50% ORR	(<10% for ipi[1])
CTLA-4/PD-1 R/R	2/8 = 25% ORR	(n/a for ipi[1])

Source: Agenus Data (all evaluable patients on C800-01 as of 05APR2023 who received at least one scan);
Includes investigator-reported data and subject to change;
[1] VanderWalde, Nature Medicine 2023

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BOT Monotherapy Responses in CTLA-4/PD-1 R/R (2L+) Melanoma

Demonstration of BOT differentiated profile

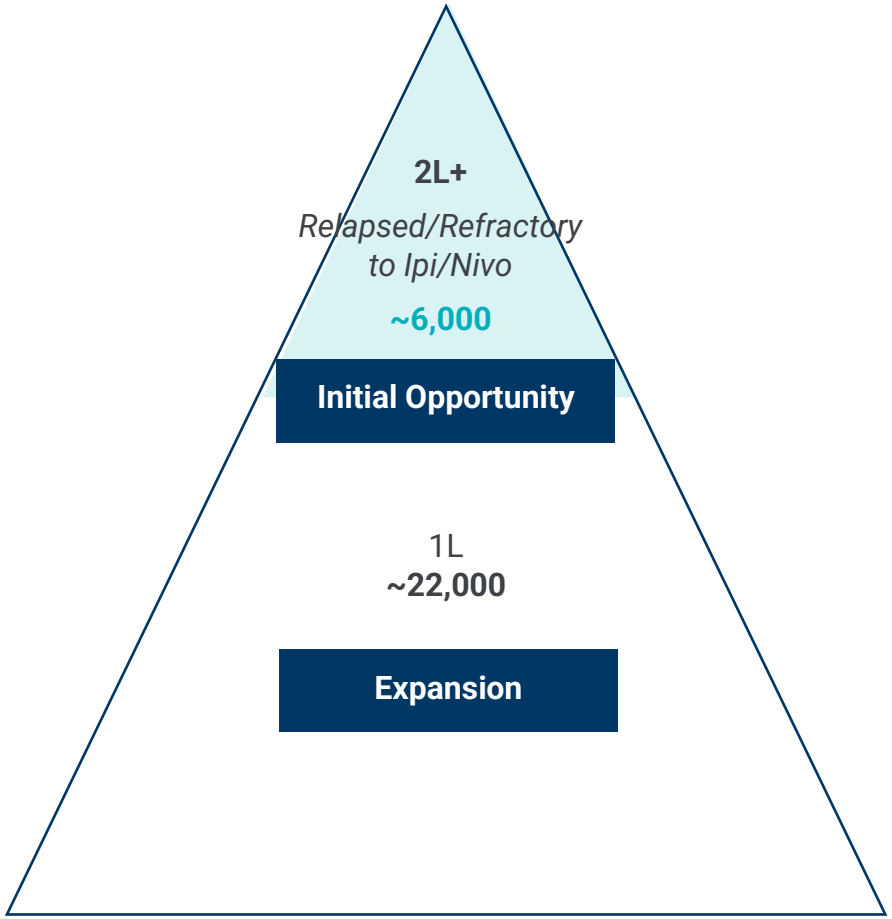
	Dose	BRAF	Prior Tx	BORR	BORR%	Sites
Phase 1 C800-01	2mg/kg	Mutant	**1. BRAF + MEK inhibtor** 2. anti-PD-1 3. anti-CTLA-4 + anti-PD-1	PR	**-50%**	Adrenal, Inguinal, Oral/ Cervical
Phase 2 C800-23	150mg	Mutant	1. anti-PD-1 2. anti-CTLA-4 + anti-PD-1 **3. BRAF + MEK inhibtor**	PR*	**-65%**	**Liver**, Lungs, Soft Tissue
	150mg	WT	1. anti-PD-1 2. anti-CTLA-4 + anti-PD-1	PR	**-48%**	**Liver**, Soft Tissue
	150mg	WT	1. anti-PD-1 2. anti-CTLA-4 **3. anti-PD-1 + anti-LAG3**	PR*	**-60%**	Skin only
	50mg	WT	1. anti-PD-1 2. anti-CTLA-4	PR*	**-39%**	Lungs, Thoracic Nodes

Data was extracted on from a live database (C800-01 on 05Apr 2023 & C800-23 on 03Sept2023) that is being actively queried.
Prior therapies, dates and responses are subject to confirmation; *unconfirmed.
BORR (best overall RECIST v1.1 response)

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BOT Potential in Advanced Melanoma

US/EU5 - Melanoma Patients Treated Annually



2L+ Melanoma

- Phase 2 cohorts with BOT monotherapy enrollment complete; expansion with BOT/BAL cohorts ongoing
- High unmet need: no established Standard of Care in IO relapsed/refractory setting
- Potential BLA filing 1H 2025

1L Melanoma

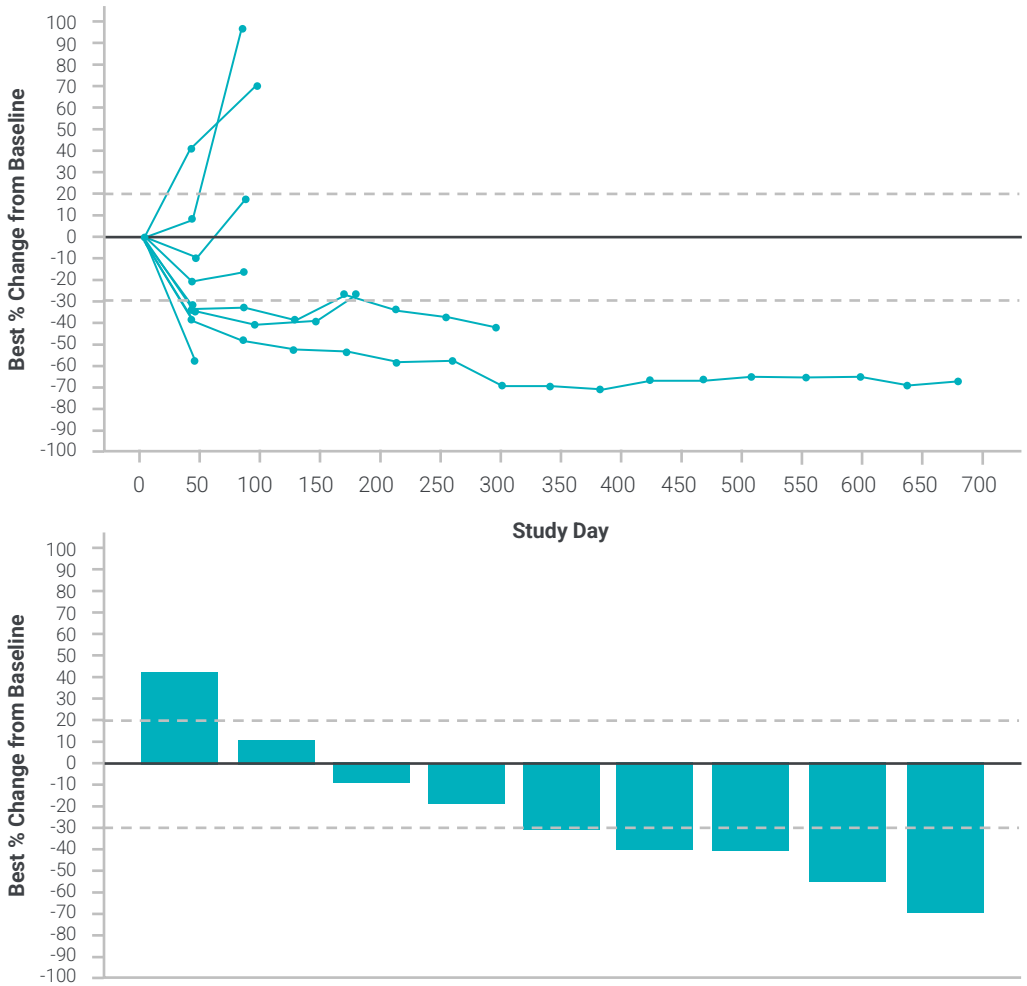
- Registrational study consideration: BOT/BAL vs. 1L SOC

Source: Cerner/Envisa 2022 Drug Treated Patients and CancerMpact Treatment Architecture

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2L+ NSCLC
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Responses from Phase 1 in 2L+ NSCLC



Efficacy Evaluable (n=9)	
ORR, %	**56%**
BOR, n (%)	
CR	0 (0)
PR	5 (56)
SD	3 (33)
PD	1 (11)
DCR (CR + PR + SD), %	**89%**

Current Status & Go-forward Plan

- Phase 1b expansion ongoing (46 patients enrolled as of October 10, 2023)
- Anticipated enrollment of 100 patients by 1Q 2024
- Initial readout expected midyear 2024
- Potential registration path if data supports

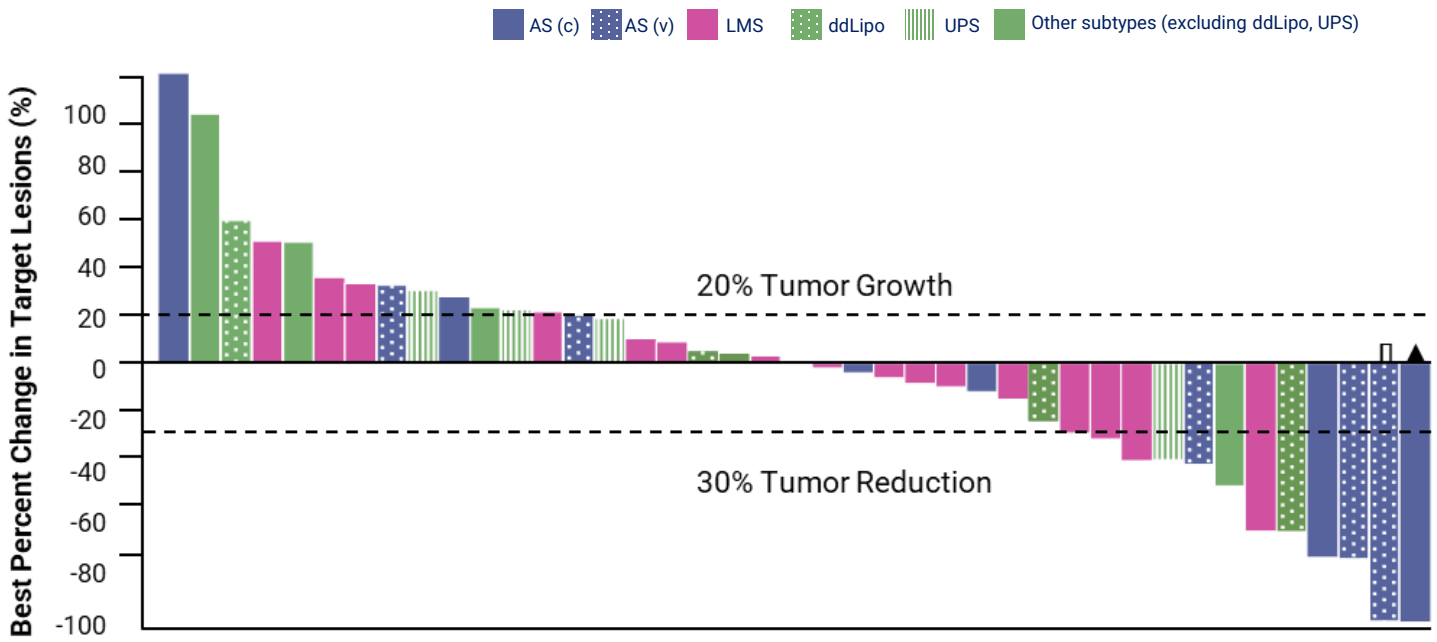
Data cutoff as of 07JUN2023

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2L+ Sarcomas
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BOT/BAL Combination Response in Refractory Sarcomas

Responses in heterogenous sarcoma population



Two additional patients showed significant clinical response (NOT INCLUDED in RECIST v1.1 response rate):

▯ 1 deep PR in AS (v) by iRECIST; patient had minor early progression at 6 weeks followed by a deep response in target lesion (-98%) that is durable at 102+ weeks.

▲ 1 unconfirmed CR in AS (c); patient had a visible skin lesion that disappeared on exam, images on file.

Efficacy Evaluable (N=41)*	iRECIST	RECIST v1.1
ORR†, % (95% CI)	**20%** (9—35)	**17%** (7—32)
1mg/kg (n=27)	15%	11%
2mg/kg (n=14)	29%	29%
BOR, n (%)		
CR	0	0
PR	8 (20)	7 (17)
SD	18 (44)	18 (44)
PD	15 (37)	16 (39)
Median DOR, months (95% CI)	**19.4** (1.9—NR)	**11.8** (1.9—NR)
DCR (CR + PR + SD), % (95% CI)	**63%** (47-78)	**61%** (45—76)
CBR (CR + PR + SD at 6 months), % (95% CI)	**27%** (14-43)	**24%** (12-40)
6-month PFS, % (95% CI)	**40%** (23—57)	**37%** (20—54)

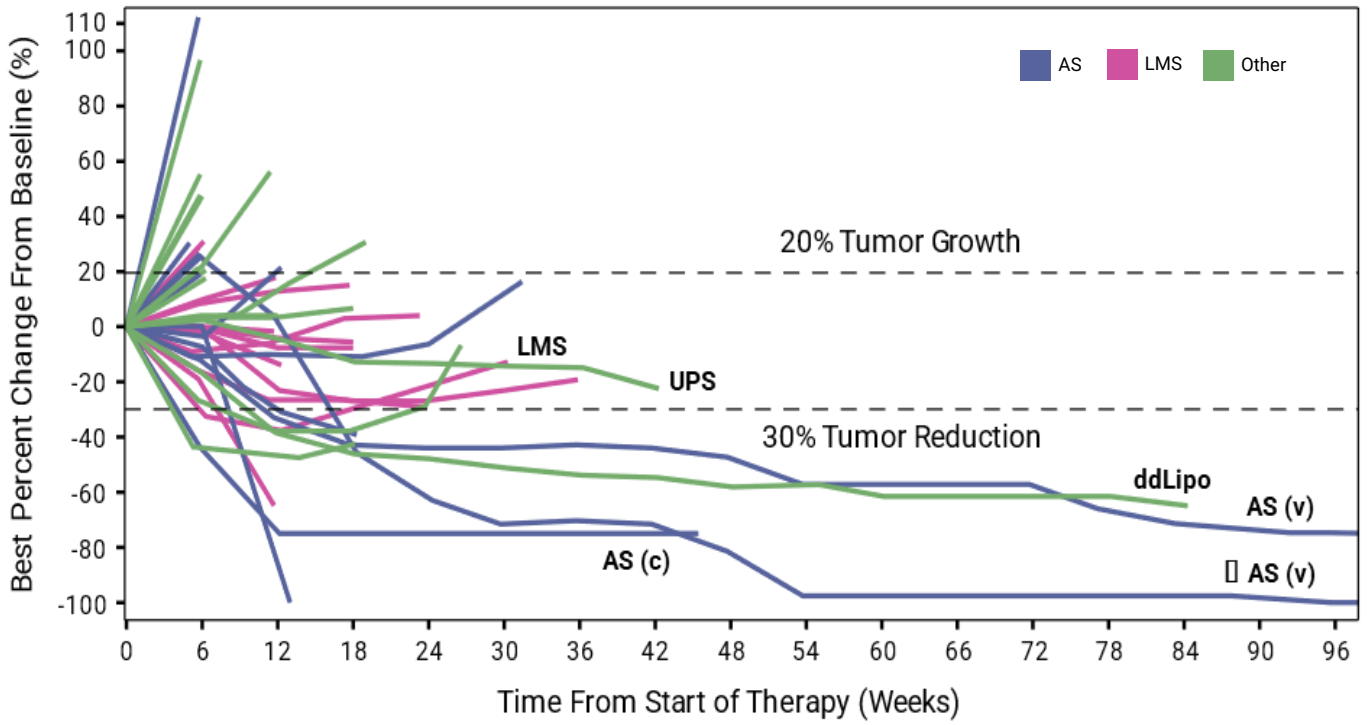
Data cutoff as of 17AUG2023; Source: Wilky et al. ESMO 2023

* Median f/u: 5.7 months (range, 1.4—28.4); † One response confirmed after data cutoff

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BOT/BAL Combination Response in Refractory Sarcomas

Broad activity in heterogenous sarcoma population



One additional patient showed significant durability (NOT INCLUDED in RECIST v1.1 response rate):

1 deep PR in AS (v) by iRECIST; patient had minor early progression at 6 weeks followed by a deep response (-98%) that is durable at 102+ weeks.

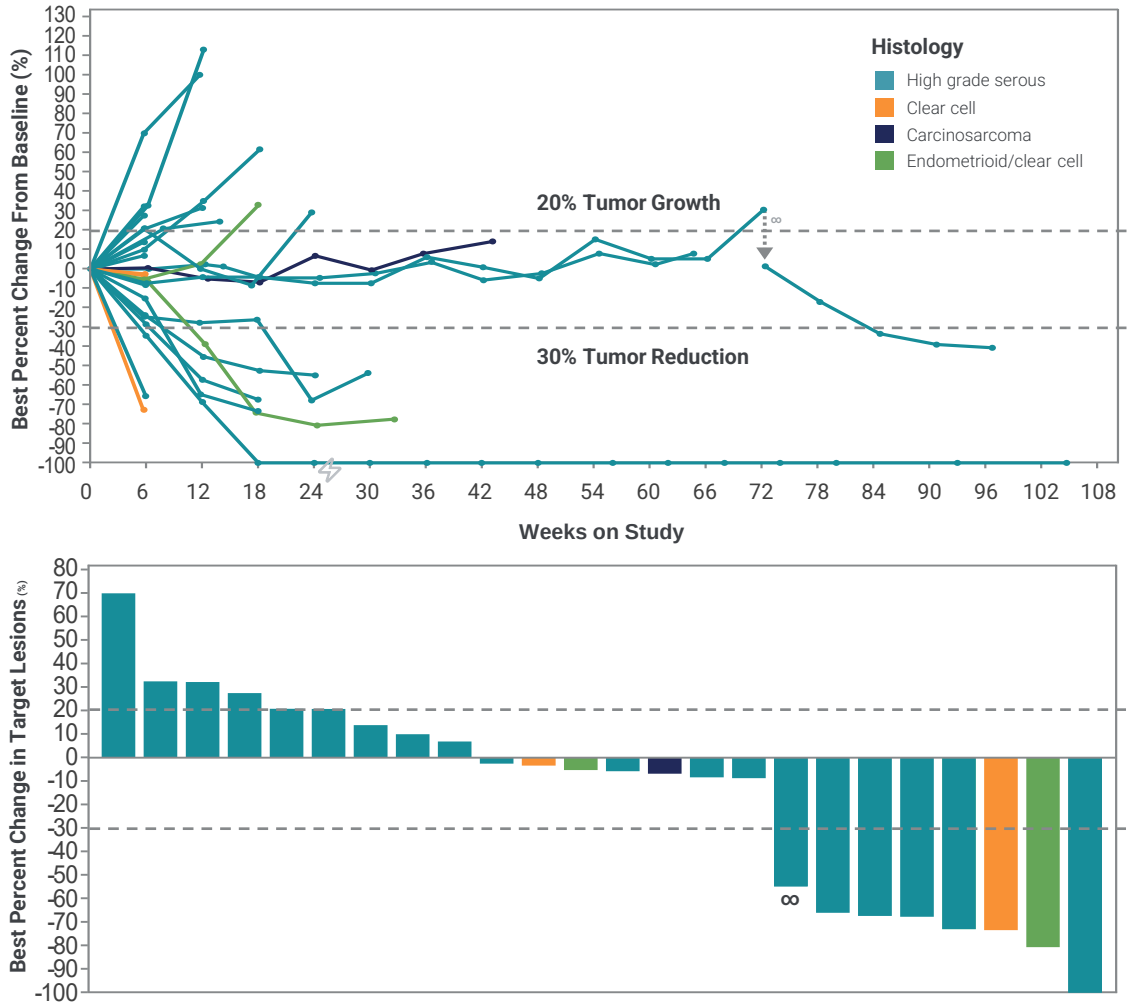
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Data cutoff as of 17AUG2023; Source: Wilky et al. ESMO 2023
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2L+ Ovarian
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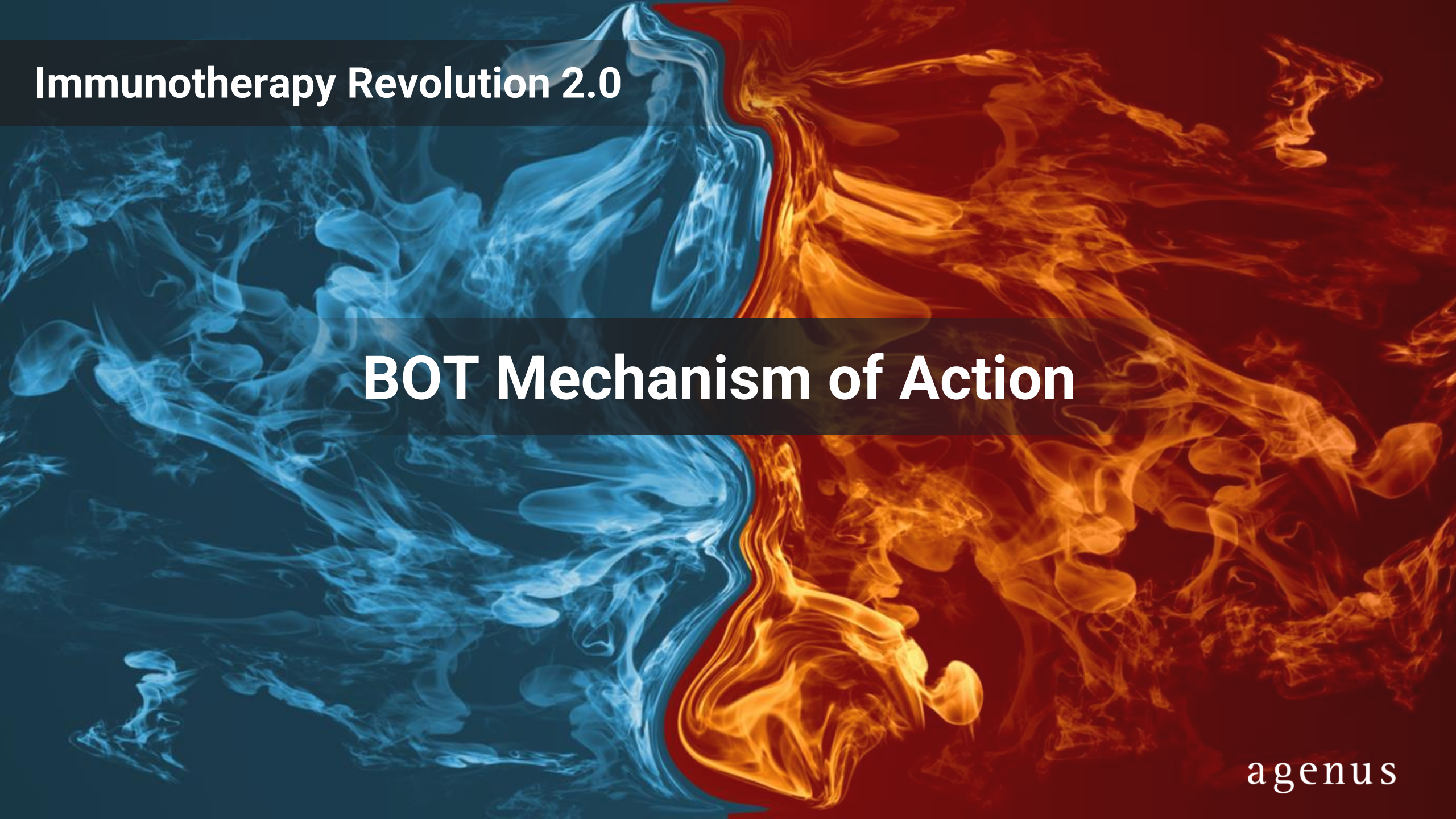
Platinum R/R Ovarian BOT/BAL Efficacy



Efficacy Evaluable (n=24)	
ORR, %*	**33%** (95% CI, 15.6-55.3%)
BOR, n (%)	
CR	1* (4)
PR	7* (29)
SD	8 (33)
PD	8 (33)
DCR (CR + PR + SD), %	**67%** (95% CI, 44.7-84.4%)
Median DOR, months	NR (4.2-NR)
12-month OS, months	78% (95% CI, 43-93%)
Median F/U, months	6.9 (Range, 1.7-29.2)

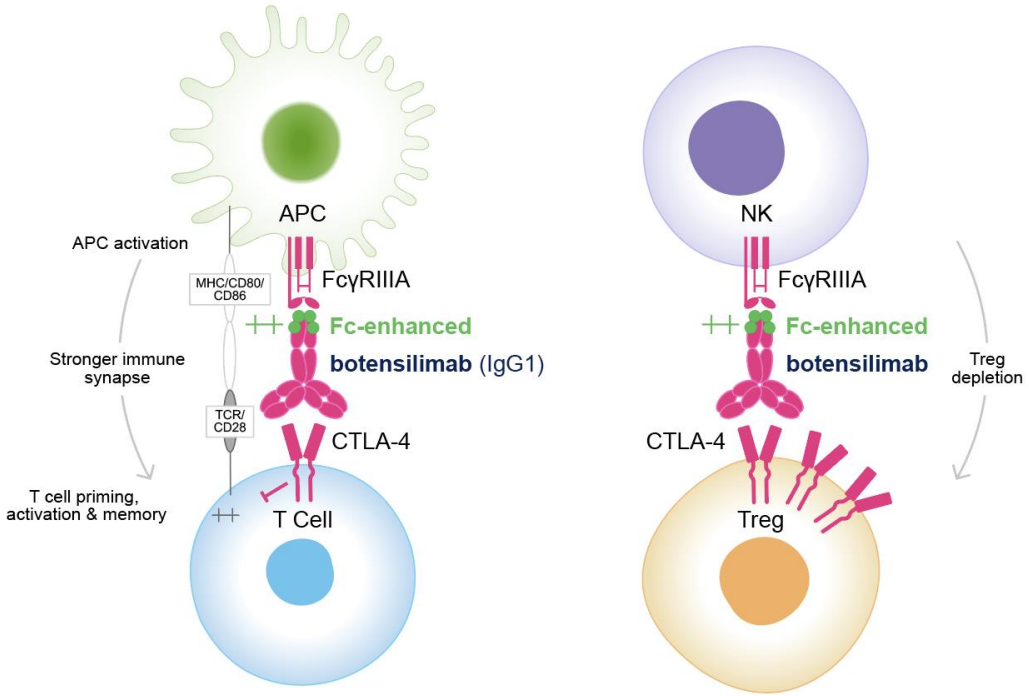
Source: Bockorny et al. SGO 2023; *uCR is a confirmed PR, 1 uPR (will not confirm); ∞ SD for 72 weeks on monotherapy prior to switching to combination, new RECIST baseline; ⚡Received radiation, no evidence of disease.

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Immunotherapy Revolution 2.0
BOT Mechanism of Action
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BOT: Multi-Functional Anti-CTLA-4 Immune Activator

BOT Mechanism of Action



"Turning Cold Tumors Hot"

- **Primes and expands** T cells to eradicate tumor
- **Activates** Natural Killer (NK) cells, and antigen presenting cells (APCs) to identify and attack the cancer
- **Reduces regulatory T cells** that suppress the activity of cytotoxic (tumor killing) T cells
- **Establishes memory** with T cells and dendritic cells

Source: El-Khoueiry AB. SITC 2021. Poster #479; Waight et al. Cancer Cell. 2018;33(6): 1033-1047; Agenus data

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Immunotherapy Revolution 2.0
BOT/BAL Safety
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BOT Has a Manageable Toxicity Profile

TRAEs of ≥10% related to BOT; data from expanded Phase 1b study

All Patients Treated with BOT/BAL Combo at 1mg/kg or 2mg/kg BOT (n = 255)			
n (%)	**All Grade**	**Grade 3**	**Grade 4**
Any TRAE	204 (80)	70 (27)	5 (2)
GASTROINTESTINAL			
Immune-mediated diarrhea/colitis*	84 (33)	36 (14)	1 (0)
Nausea	49 (19)	5 (2)	0 (0)
Vomiting	28 (11)	3 (1)	0 (0)
CONSTITUTIONAL			
Chills	40 (16)	0 (0)	0 (0)
Decreased appetite	45 (18)	0 (0)	0 (0)
Fatigue	73 (29)	6 (2)	0 (0)
Pyrexia	44 (17)	4 (2)	0 (0)
SKIN			
Pruritus	38 (15)	0 (0)	0 (0)
Rash Maculo-Papular	37 (15)	3 (1)	0 (0)
MUSCULOSKELETAL			
Arthralgia	29 (11)	1 (0)	0 (0)

Source: Agenus data extracted 26MAY2023; *Immune-mediated diarrhea/colitis includes investigator-reported cases or patients who received steroids or immunosuppressants/infliximab; Median follow-up of 5.4 months
Note: discontinuation due to a BOT TRAE = 22%

Immunotherapy Revolution 2.0

Achievements & Upcoming Catalysts

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Achievements & Upcoming Catalysts

2023 (Completed)

- ✓ Data from Phase 1b: 2/3L+ MSS CRC (ASCO GI 2023)
- ✓ Data from Phase 1b: ovarian cancer (SGO 2023)
- ✓ Fast Track designation from U.S. FDA for BOT/BAL in CRC (April 2023)
- ✓ Data from Phase 1b: 2/3L+ MSS CRC (ESMO GI 2023)
- ✓ Phase 2 CRC enrollment completed (October 2023)
- ✓ Data from Phase 1b: advanced sarcomas (ESMO 2023)
- ✓ Data from CRC, pancreatic, lung, melanoma studies (Corporate Event, ESMO 2023)

1H 2024

- Phase 2 Data: 2L Pancreatic
- Phase 1b Data: 2/3L+ MSS CRC
- IST Data: 1L MSS CRC
- IST Data (Expanded): Neoadjuvant CRC

Mid 2024

- **Planned BLA filing: 2/3L+ MSS CRC**
- Phase 1b Data: PD-(L)1 +/- chemotherapy relapsed/refractory 2L+ NSCLC

2H 2024

- Phase 2 Data: 2L+ Melanoma
- Phase 2 Data: 2/3L+ MSS CRC

1H 2025

- Potential BLA filing: Pancreatic
- Potential BLA filing: Melanoma