



# Eganelisib Addressing Significant Patient Need With Next-Generation Immunotherapies

H.C. Wainwright Global Investment Conference  
May 23-25, 2022



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# Infinity Pharmaceuticals



**Headquarters:** 1100 Massachusetts Avenue,  
Harvard Square, Cambridge, Massachusetts

**Nasdaq:** INFI

**Focus:** First-in-class/best-in-class oncology therapeutics



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# Eganelisib: Potential Best-In-Class Next-Generation Immunotherapy

## **First-in-class, oral, potent and selective macrophage reprogramming therapeutic**

- Strong preclinical/translational medicine data demonstrating reprogramming of tumor associated macrophages
- Uniquely differentiated, next-generation immunotherapy

## **Clinical activity, safety & translational data in P2 settings where CPIs have shown little or no patient benefit**

- 1L advanced/metastatic Triple Negative Breast Cancer (TNBC) in combination with CPI + chemo
- 2L metastatic Urothelial Cancer in combination with CPI
- Clinical/Translational Data releases in 4 tumor types in 2022

**Registration enabling study in frontline advanced/metastatic TNBC - to be initiated by end of 2022**

**Platform clinical program to rapidly and efficiently evaluate eganelisib in indications where tumor associated macrophages limit effectiveness of current therapies - to be initiated in 3Q2022**

# Advancing and Expanding MARIO Clinical Development Program

## Macrophage Reprogramming in Immuno-Oncology



	PHASE 1	PHASE 1B	PHASE 2	PHASE 3	
<b>Frontline mTNBC</b>					
<b>MARIO-4:</b> Registration study eganelisib + CPI + chemo vs. standard of care	[Progress bar: Phase 1, 1B, 2]				Initiate study by YE 2022
<b>MARIO-3:</b> Open label eganelisib triplet on top of Impassion130 doublet of Tecentriq® and Abraxane®	[Progress bar: Phase 1, 1B]				Data in 2H 2022
<b>UC, RCC, HNSCC</b>					
<b>MARIO-275:</b> Randomized controlled study eganelisib + Opdivo® vs. Opdivo in 2L UC	[Progress bar: Phase 1, 1B]				Data in 2H 2022
<b>MARIO-3:</b> Open label study eganelisib + Tecentriq + Avastin® in 1L RCC	[Progress bar: Phase 1, 1B]				Data in 2H 2022
<b>HNSCC:</b> IST WoO monotherapy study	[Progress bar: Phase 1]				Data in 2H 2022
<b>MARIO-P Platform Clinical Program</b>					
<b>Ovarian Cancer</b>	[Progress bar: Phase 1, 1B]				Initiate on a rolling basis in 3Q 2022 (20-40 patients per cohort)
<b>NSCLC</b>	[Progress bar: Phase 1, 1B]				
<b>Soft Tissue Sarcoma</b>	[Progress bar: Phase 1, 1B]				
<b>Prostate Cancer</b>	[Progress bar: Phase 1, 1B]				

Triple Negative Breast Cancer (TNBC)

Urothelial Cancer (UC)

Renal Cell Carcinoma (RCC)

Head and Neck Squamous Cell Cancer (HNSCC)

Non Small Cell Lung Cancer (NSCLC)

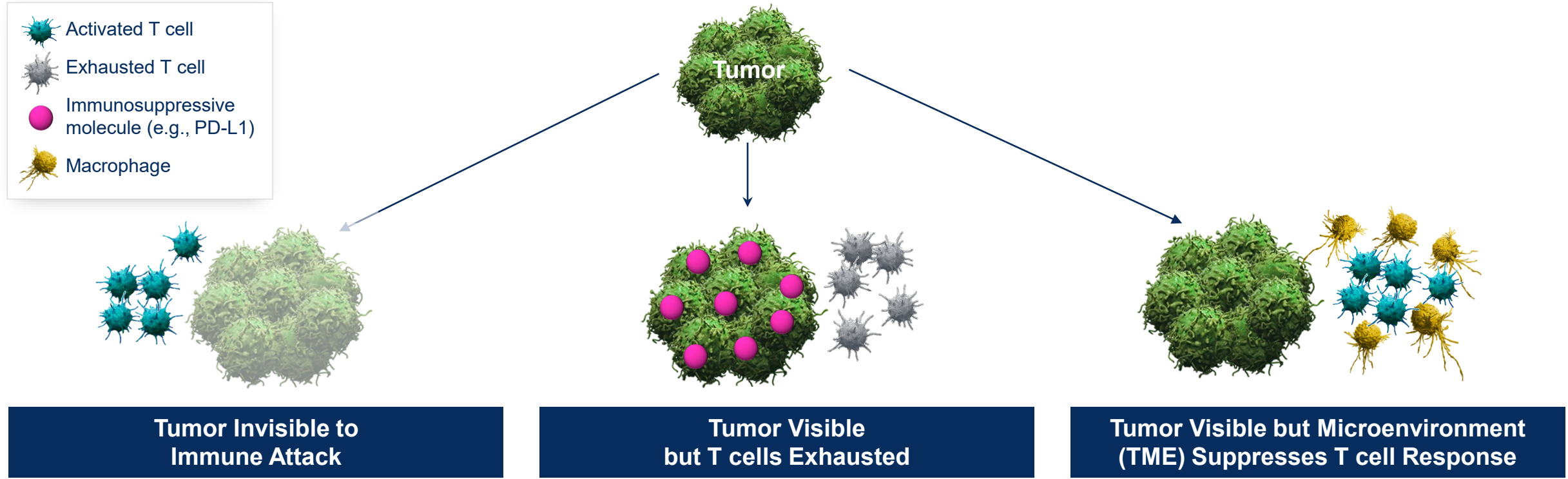
Tecentriq® is a registered trademark of Genentech, Inc.

Abraxane® is a registered trademark of Abraxis BioScience, LLC.

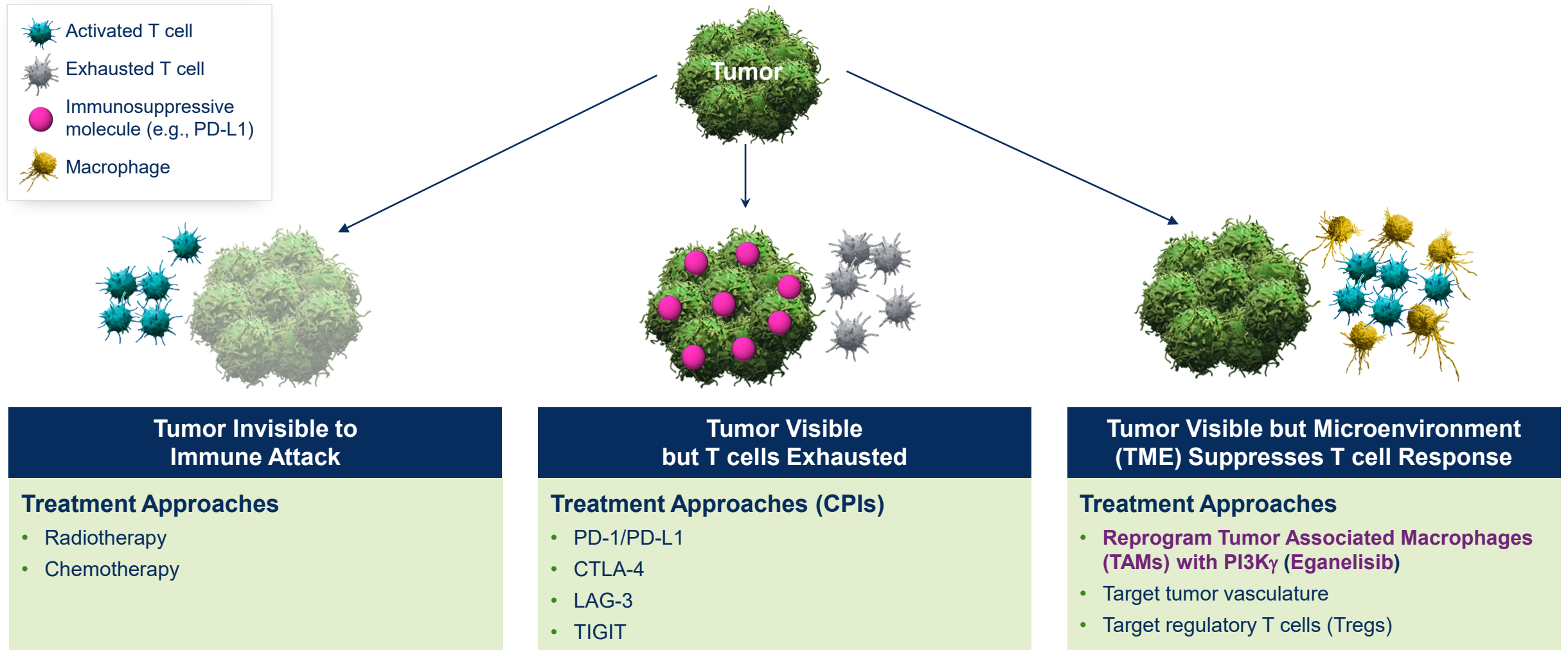
Opdivo® is a registered trademark of Bristol Myers Squibb.

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# How Tumors Evade the Immune System

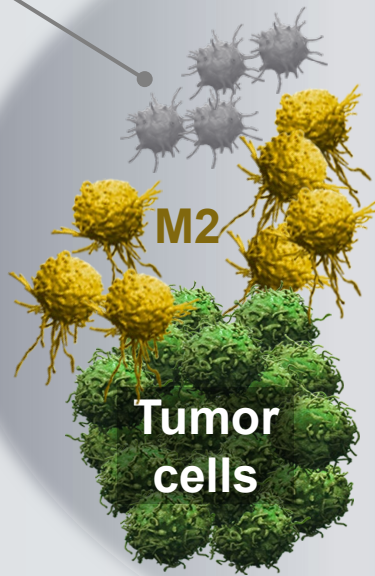


# Eganelisib: Next-Generation Immunotherapy Targeting Tumor Associated Macrophages to Overcome Cancer Immune Evasion



# Eganelisib Reprograms Macrophages to Turn Tumor Microenvironment from Immune Suppressed to Immune Activated

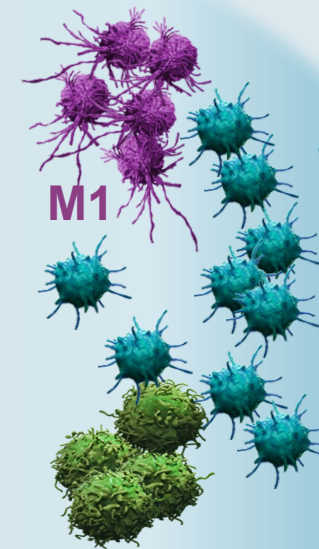
Suppressed  
T cells



PI3K- $\gamma$  inhibitor,  
eganelisib

Eganelisib inhibition of  
PI3K- $\gamma$  reprograms  
protumor (**M2**) to antitumor (**M1**)  
macrophages, expanding and  
activating T cells

Activated  
T cells





# MARIO Clinical Program Demonstrates Eganelisib Clinical Activity and Safety Across Multiple Combinations and Tumor Types

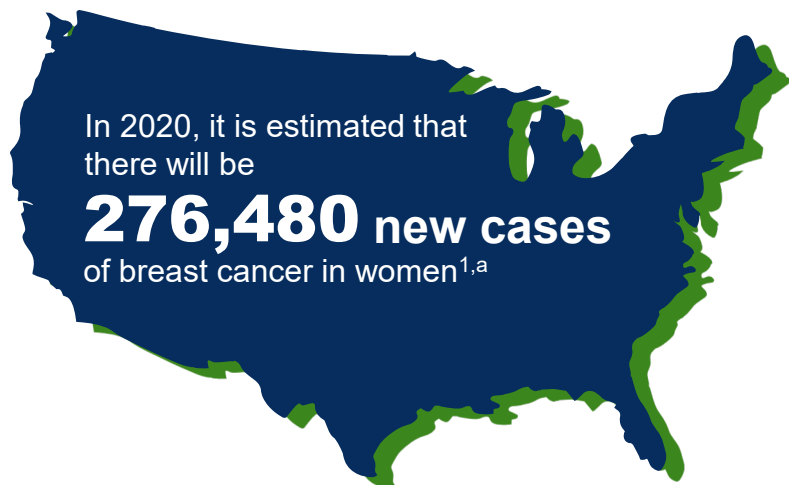


	PHASE 1	PHASE 1B	PHASE 2	KEY STUDY DATA
<b>MARIO-275</b> 2 <sup>nd</sup> Line Urothelial Cancer in combination with Opdivo				ITT mOS of 15.4 mos vs 7.9 mos on Control Arm with HR of 0.62 <sup>1</sup>
<b>MARIO-3</b> Frontline Metastatic TNBC in combination with Tecentriq and Abraxane				PD-L1(+) Pts 47% Extension of mPFS <sup>2</sup> PD-L1(-) Pts 30% Extension of mPFS <sup>2</sup>
<b>ARC-2</b> TNBC and Ovarian Cancer in combination with etrumadenant and Doxil <sup>®</sup>				TNBC ORR: 25% vs. 9% <sup>3</sup> Ovarian ORR: 75% vs. 14% <sup>3</sup>
<b>MARIO-1</b> Checkpoint inhibitor refractory HNSCC and Melanoma in combination with Opdivo				SCCHN ORR (≤ 2 lines): 20% <sup>4</sup> Melanoma ORR (≤ 2 lines): 21% <sup>5</sup>

1. Tomczak et al. ASCO GU 2021; 2. Soliman et al, SABCS 2021 Compared to IMpassion 130 data presented by Emens, LA, 2018 SABCS, abstract GS1-04; 3. Gardner O et al. SABCS 2020 Triplet Arm (Eganelisib + Etrumadenant + Doxil) versus Doublet Arm (Etrumadenant + Doxil); Doxil<sup>®</sup> is a registered trademark of Baxter Healthcare Corporation. 4. Cohen et al. SITC 2020; 5. Postow et al. SITC 2020

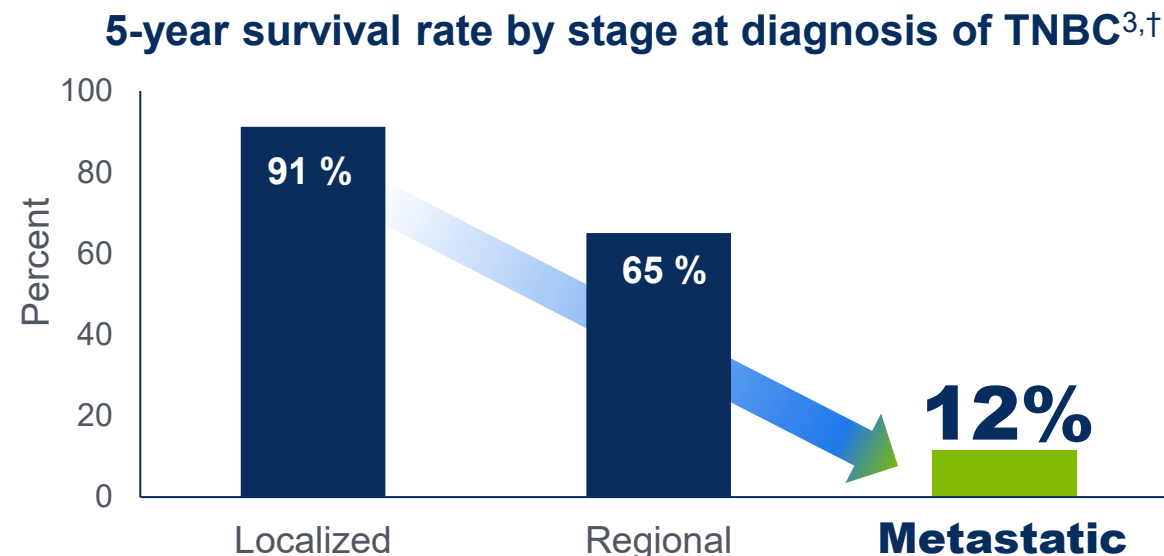
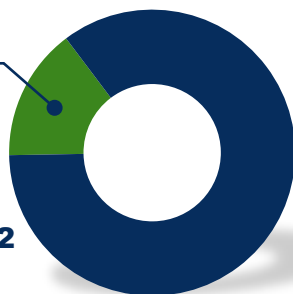
# Metastatic TNBC is Associated with Poor Prognosis

## Advanced TNBC and PD-L1(-) TNBC Are Both Associated With Poor Prognosis



**15%** of breast cancer is **triple negative**<sup>2</sup>

(ie, negative for ER, PR, and HER2)



**PD-L1(-) cancers are associated with poor prognosis<sup>4</sup>**  
≈ 60% of TNBCs are PD-L1(-)<sup>5,‡</sup>

**Forecast of 16K addressable 1L mTNBC patients globally in 2034 suggests market potential of over \$2B<sup>6</sup>**

<sup>a</sup>Estimated cases based on 2013-2017 cases.

<sup>†</sup>5-Year relative survival percent, TNBC by SEER Summary Stage 2000.

<sup>‡</sup>PD-L1—stained tumor-infiltrating immune cells; positive PD-L1 threshold of 0.01 (≥1% of tumor area).

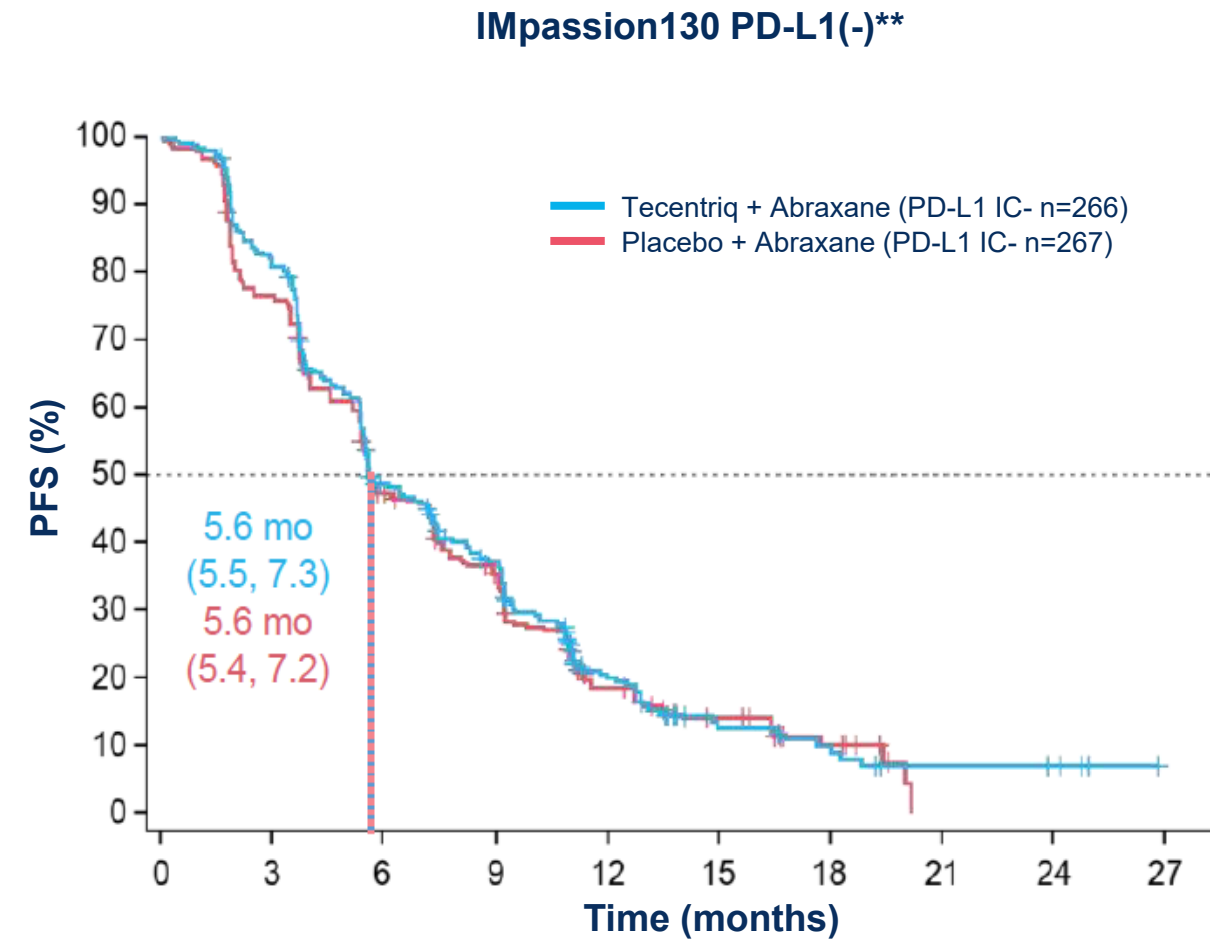
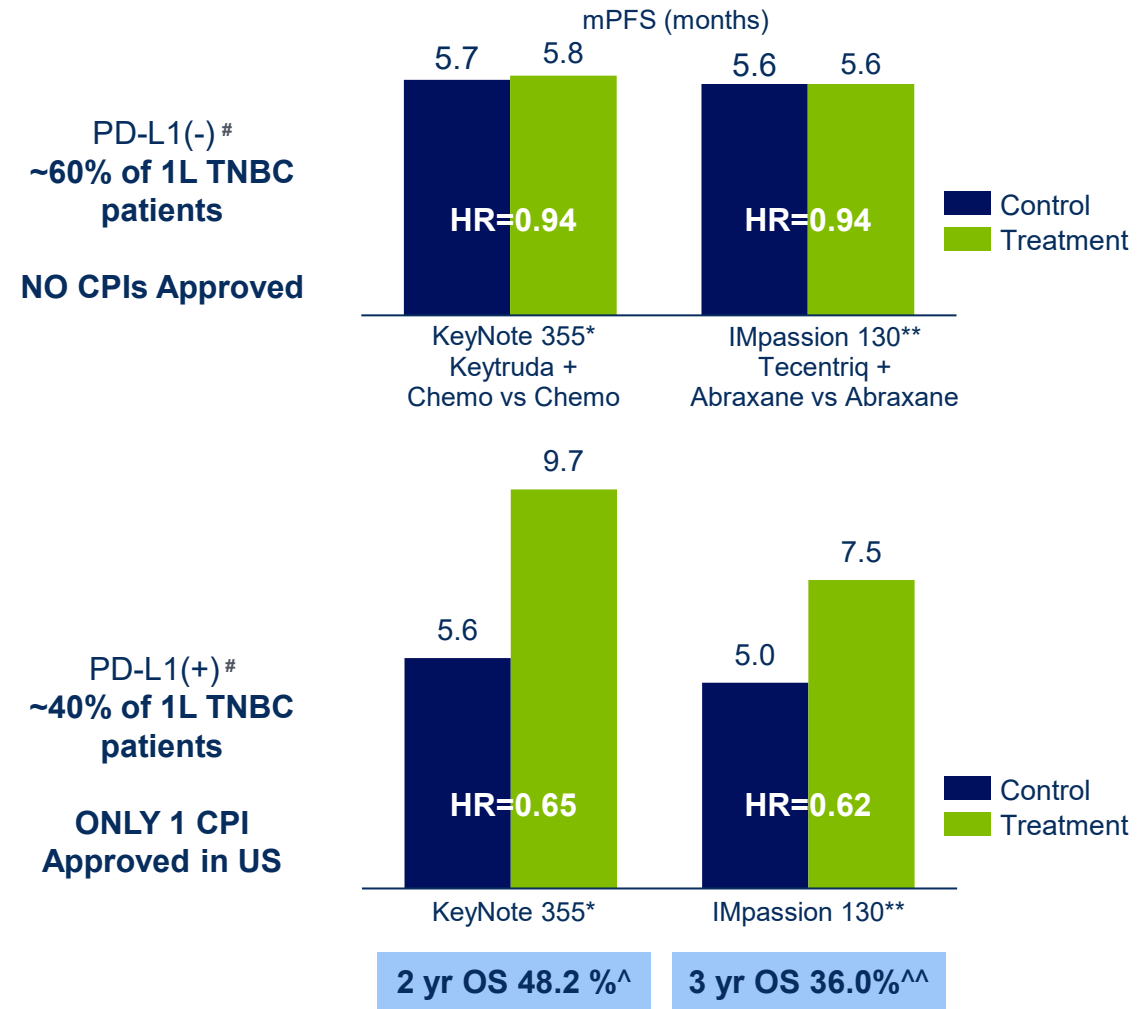
1. National Cancer Institute. Accessed November 24, 2020. <https://seer.cancer.gov/statfacts/html/breast-subtypes.html> 2. American Cancer Society. Accessed November 24, 2020.

<https://www.cancer.org/cancer/breast-cancer/understanding-a-breast-cancer-diagnosis/types-of-breast-cancer/triple-negative.html> 3. National Cancer Institute. Accessed November 23, 2020.

<https://seer.cancer.gov/statfacts/html/breast-subtypes.html> 4. Davis AA, Patel VG. *J Immunother Cancer*. 2019;7(1):278. 5. Matikas A et al. *Clin Cancer Res*. 2019;25(18):5717-5726. 6. LEK

forecast based on LEK interviews, research and analysis, Decision Research Group data Dec 2020

# PD-L1(-) Patients: No CPI Has Demonstrated Benefit Over SOC Chemo



\*Cortes, Lancet December 5, 2020; 396:1817-28, \*\*Emens, LA, IMpassion130, 2018 SABCS Abstract GS1-04, ^Rugo, ESMO 2021, Abstract LBA16, ^^Emens, LA July 1, 2021, Annals of Oncology, # Keynote 355 PD-L1 expression assessed by The 22C3 Dako PharmDx IHC assay, which factors in expression in both tumor cells and tumor-infiltrating immune cells. A CPS score is calculated and a score of ≥10% is positive and CPS <10% is negative. IMpassion130 PD-L1 expression assessed by IC ≥1% of tumor area is positive and IC <1% is negative as determined by the VENTANA PD-L1 (SP142) Assay.

# MARIO-4: First Registration Study of Eganelisib

- Based on strength of efficacy, safety and translational medicine data from MARIO-3
- Randomized, double-blind, placebo-controlled study with PFS and OS endpoints
- PD-L1(-) patients: eganelisib + chemotherapy + checkpoint inhibitor vs chemotherapy
- PD-L1(+) patients: eganelisib + chemotherapy + checkpoint inhibitor vs chemotherapy + checkpoint inhibitor
- Study design to be finalized pending feedback from global regulatory authorities
- MARIO-4 Study to be initiated by end of 2022

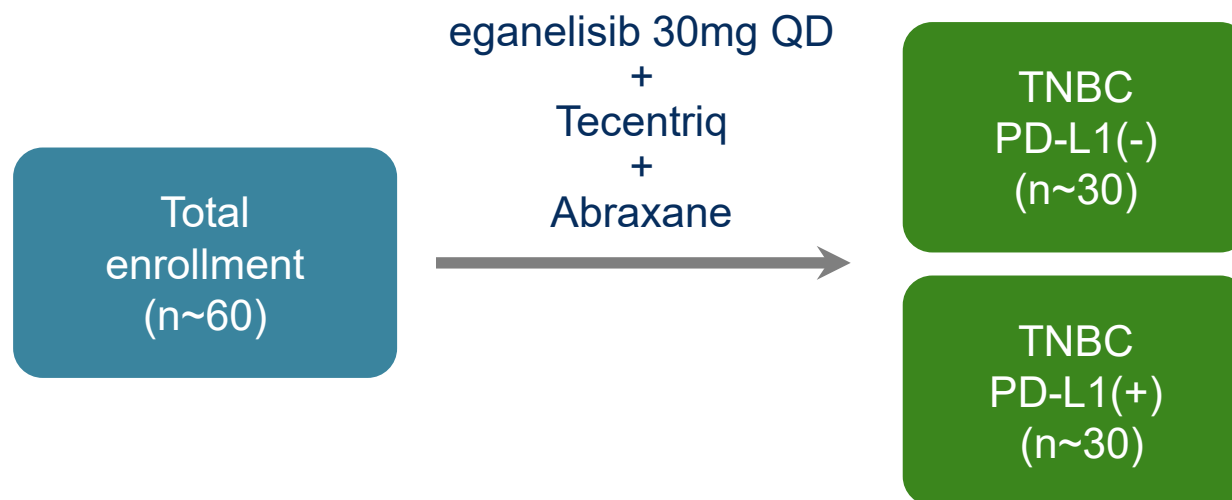
# Designed to Demonstrate Eganelisib's Ability to Improve and Extend the Clinical Benefit of Tecentriq + Abraxane in 1L mTNBC

## Eganelisib FDA Fast Track Designation for TNBC

### MARIO-3 TNBC evaluating the potential of eganelisib to improve on IMpassion130 results\*

#### Addition of eganelisib to Tecentriq and Abraxane in front-line TNBC

- Inclusion/exclusion criteria per IMpassion130 study
- Two prespecified cohorts: PD-L1(-) and PD-L1(+)
- Primary objective: CR rate  
CR benchmark ~7% ITT; 10% PD-L1(+)
- Secondary objectives: PK, PD, ORR, DCR, and PFS; ORR for PD-L1(-) cohort
- PD-L1 status determined via central lab (histogeneX) with Ventana SP142 antibody to align with IMpassion130



CR, complete response; DCR, disease control rate; ITT, intent-to-treat; ORR, overall response rate; PD, pharmacodynamics; PD-L1, programmed death-ligand 1; PFS, progression-free survival; PK, pharmacokinetics; QD, once daily; SOC, standard of care; mTNBC, metastatic triple-negative breast cancer; TNBC, triple-negative breast cancer.

Immune Cell Score ≥ 1% cutoff for PD-L1(+)

\*Schmid P et al, N Engl J Med. 2018;379(22):2108-2121.

# No New Safety Signals: Profile Consistent with Expectations for the 3 Component Drugs

## Most Common Treatment-Related TEAEs in ≥ 10% of All Treated Patients\*\* (N=50)

Preferred or Grouped Term#	Treatment-related TEAE (All)	Treatment-related TEAE (≥ Gr. 3)
Nausea	25 (50.0)	0 (0.0)
Fatigue	24 (48.0)	3 (6.0)
Skin AEs	18 (36.0)	6 (12.0)
Diarrhea	15 (30.0)	3 (6.0)
Hepatic AEs*	14 (28.0)	9 (18.0)
Alopecia	13 (26.0)	0 (0.0)
Vomiting	11 (22.0)	1 (2.0)
Neutropenia AEs	11 (22.0)	8 (16.0)
Pyrexia	9 (18.0)	0 (0.0)

Preferred or Grouped Term	Treatment-related TEAE (All)	Treatment-related TEAE (≥ Gr. 3)
Peripheral sensory neuropathy	9 (18.0)	3 (6.0)
Decreased appetite	8 (16.0)	0 (0.0)
Headache	8 (16.0)	0 (0.0)
Stomatitis	7 (14.0)	0 (0.0)
Dysgeusia	7 (14.0)	0 (0.0)
Constipation	6 (12.0)	0 (0.0)
Weight decreased	5 (10.0)	1 (2.0)
Hypokalaemia	5 (10.0)	0 (0.0)

Presented in descending order of All Treatment-Related TEAE

\*One Grade 4 event and No Hy's Law

\*\*No treatment-related Grade 5 AEs

# Grouped terms:

Skin AEs: rash maculo-papular, rash, pruritus, dermatitis, dry skin, photosensitivity reaction, rash erythematous

Hepatic AEs: ALT increased, AST increased, ALP increased, blood bilirubin increased, autoimmune hepatitis

Neutropenia AEs: neutropenia and neutrophil count decreased

Soliman H, et al. SABCS 2021

# Triplet Manageability Compares Favorably to Historical Doublet

	<b>MARIO-3*</b> Eganelisib+Tecentriq+Abraxane (N=50) n (%)		<b>IMpassion130**</b> Tecentriq+Abraxane (N=460) n (%)	
<b>All-causality AEs</b>				
Any grade	47	(94.0)	457	(99.3)
Grade 3 or 4	32	(64.0)	233	(50.7)
Grade 5	2	(4.0)	6	(1.3)
Serious AEs	15	(30.0)	110	(23.9)
AE leading to any treatment withdrawal	9	(18.0)	88	(19.1)
AE leading to Atezo withdrawal	8	(16.0)	37	(8.0)
AE leading to Nab-Pac withdrawal	8	(16.0)	85	(18.5)
<b>Treatment-related AEs***</b>				
Any grade	47	(94.0)	444	(96.5)
Grade 3 or 4	30	(60.0)	191	(41.5)
Grade 5	0	(0.0)	2	(0.4)
Serious AEs	9	(18.0)	58	(12.6)

\* MARIO-3: Data listed are treatment emergent adverse event (TEAE).

\*\* Emens et al., Annal of Oncology 2021

\*\*\* In MARIO-3, the data listed are for TEAEs that were related to any study drug

Soliman H, et al. SABCS 2021

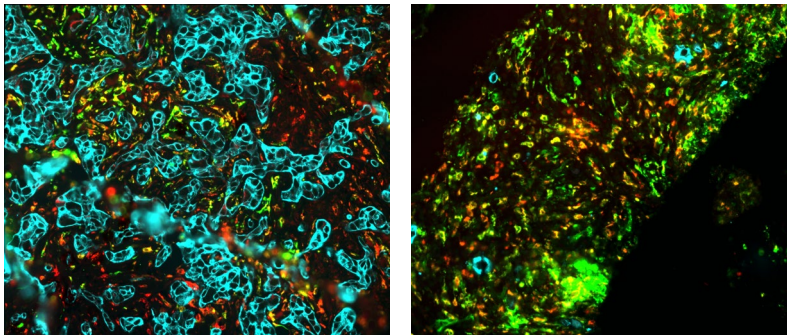
# Immune Activation Shrinks Tumors Regardless of PD-L1 Status

## PD-L1(-) Patient with PR

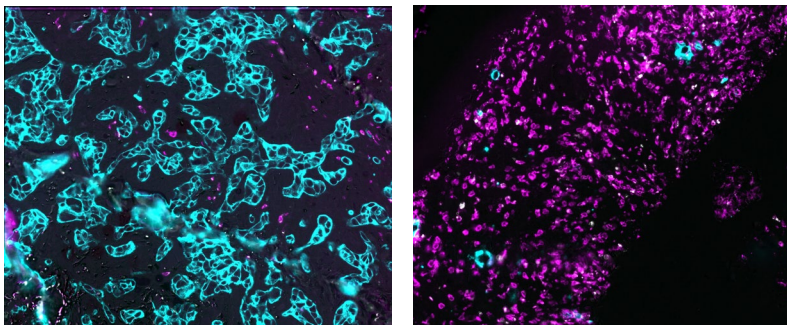
Day 0

2 mo

Tumor M2 HLADR+ M1



Tumor CD8 T Cells Activated T Cell



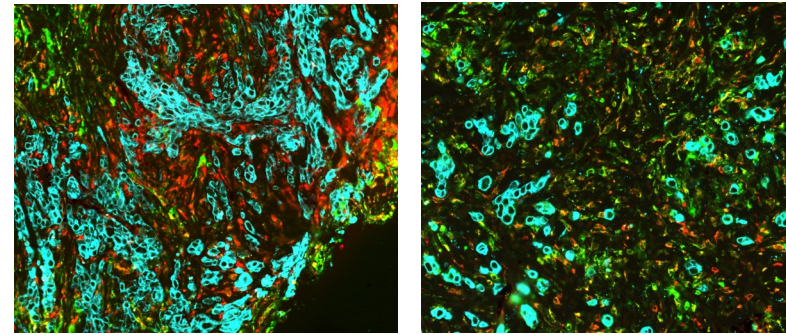
Patient Ongoing Over 13 Months

## PD-L1(+) Patient with PR

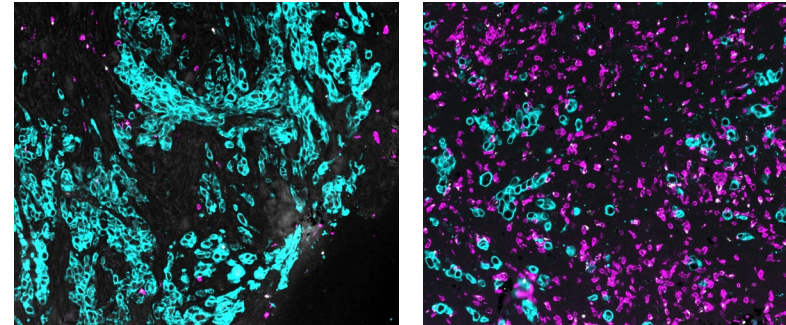
Day 0

2 mo

Tumor M2 HLADR+ M1



Tumor CD8 T Cells Activated T Cell

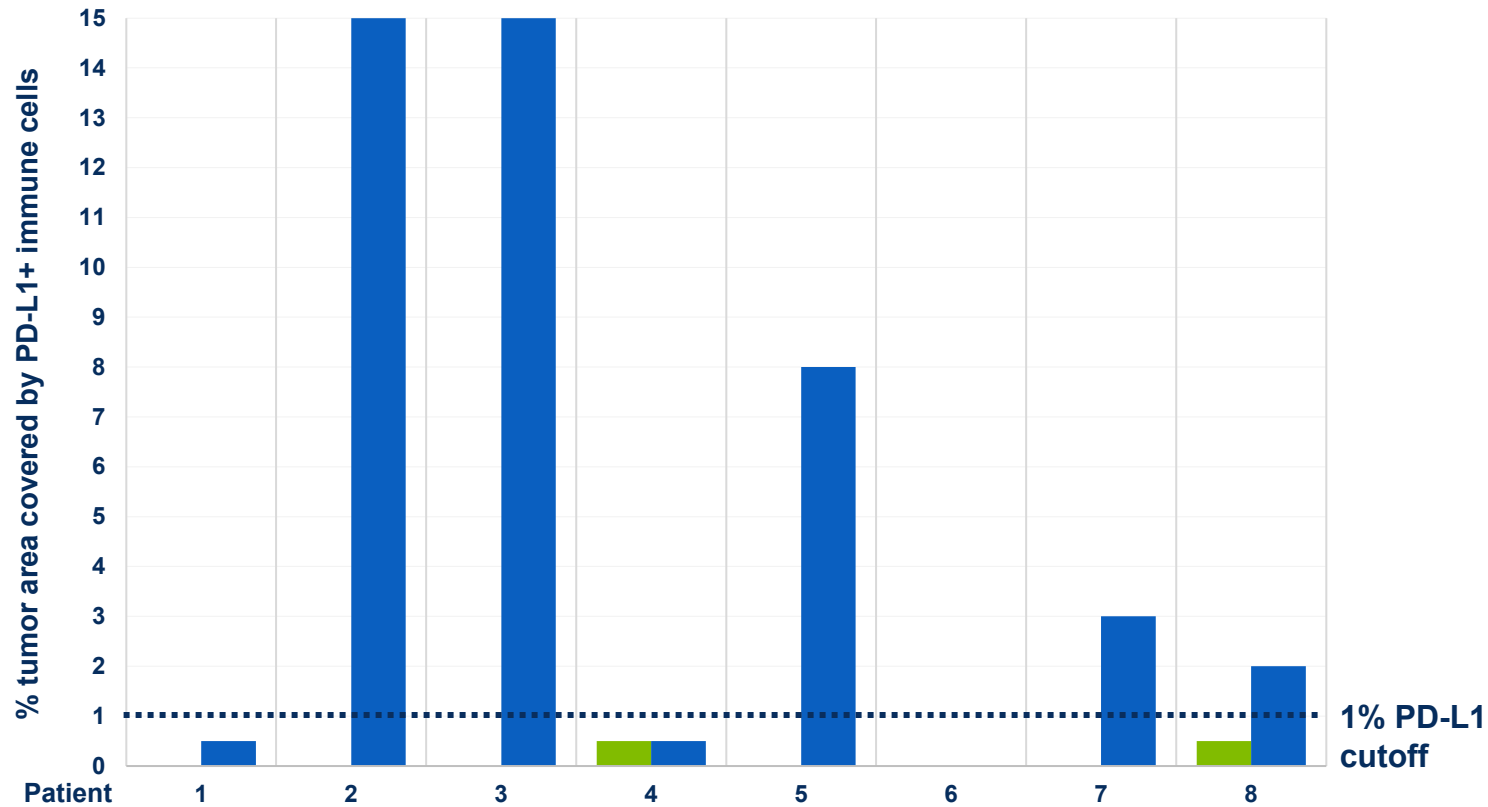


Patient Ongoing Over 13 Months

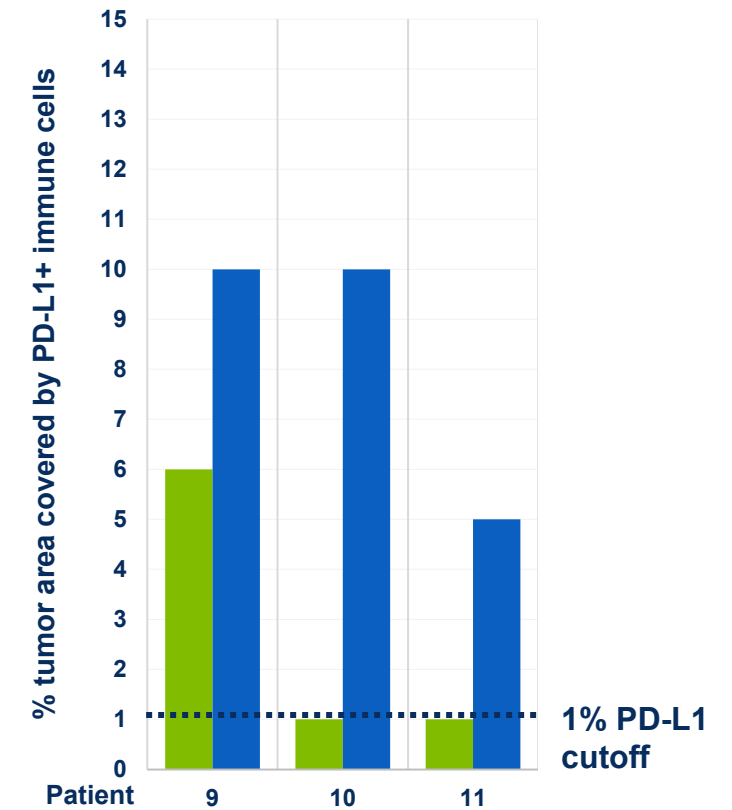


# PD-L1 Expression Increased Following Eganelisib Treatment

PD-L1(-) at Baseline



PD-L1(+) at Baseline

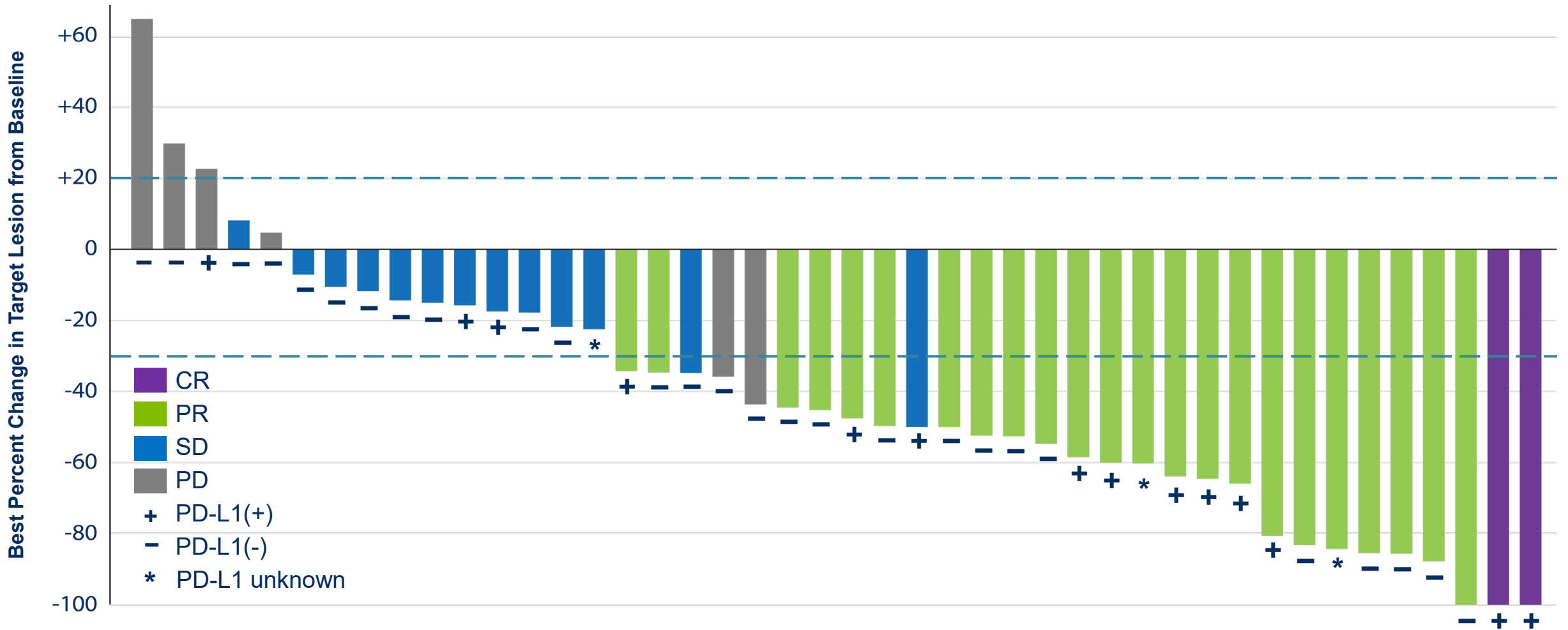


11 Paired Tumor Biopsies

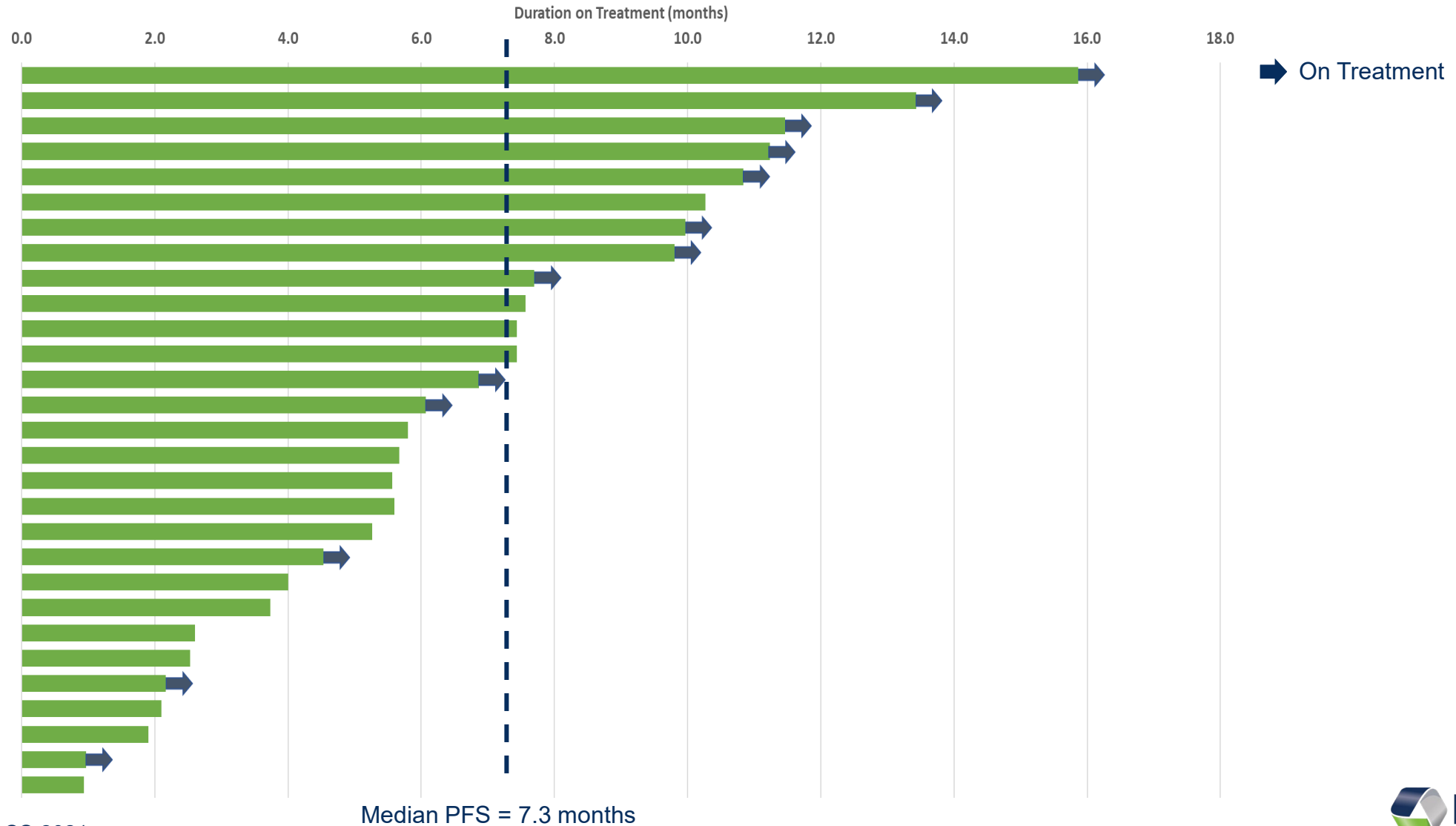
■ Baseline ■ 2 months

# 88.6% of Evaluable Patients Achieved Tumor Reduction

## Tumor Reduction in 92.8% of PD-L1(+) and 85.2% of PD-L1(-) Patients



# Durable, Ongoing Benefit in PD-L1(-) Patients



# mPFS Longer than IMpassion130 PD-L1(-) and PD-L1(+) Benchmarks



Median Duration of Follow Up of 9.9 Months

Median PFS in Patients With Both PD-L1(-) and PD-L1(+) Tumors		
	PD-L1(-)	PD-L1(+)
MARIO-3 (eganelisib + Tecentriq + Abraxane)	7.3 months (N=27)	11.0 months (N=14)
Benchmark IMpassion130 <sup>1</sup> (Tecentriq + Abraxane)	5.6 months (N=266)	7.5 months (N=185)

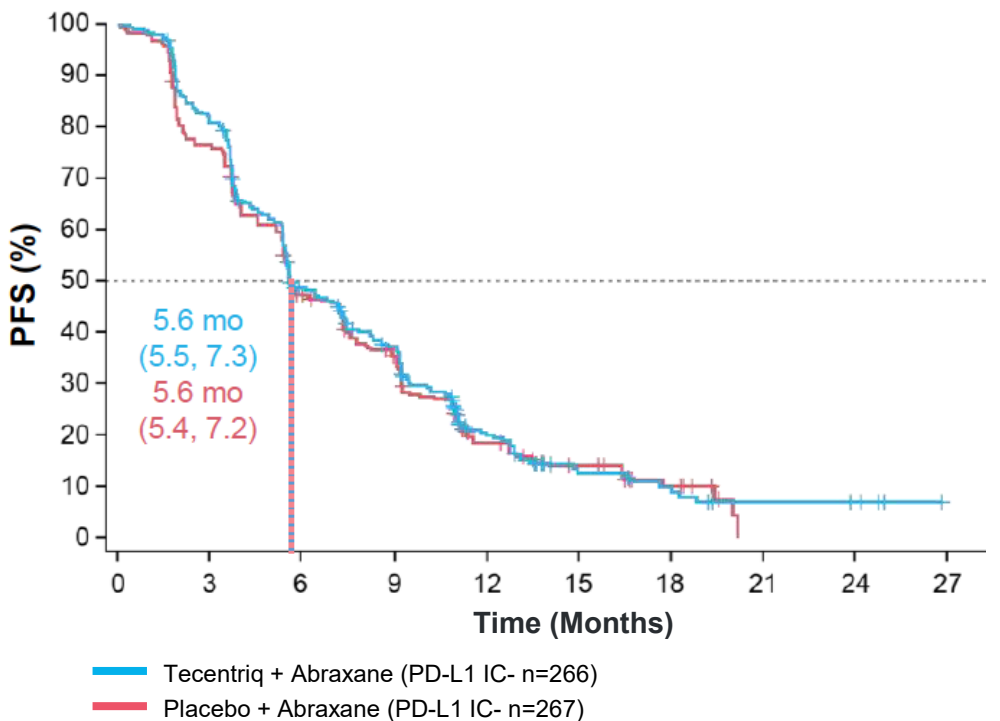
1. Schmid P et al. *Lancet*. 2020; Soliman H, et al. SABCs 2021

# Positive Signal of PFS Durability in PD-L1(-) Patients vs SOC Chemo

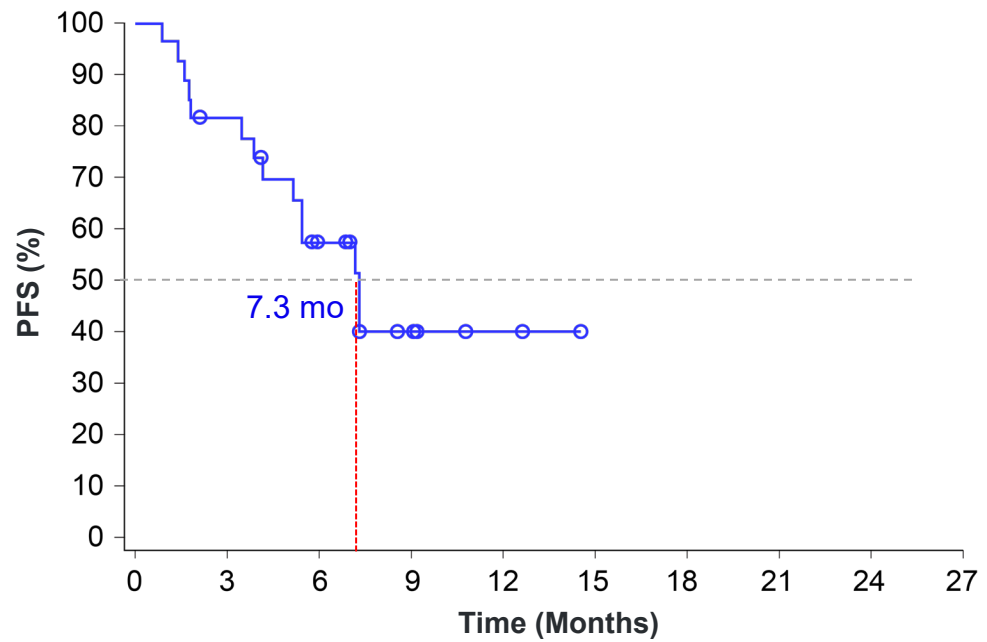


## Potential to Address Need for Improvement Over SOC Chemo

Historical IMpassion130 PD-L1(-)\*



MARIO-3 PD-L1(-)

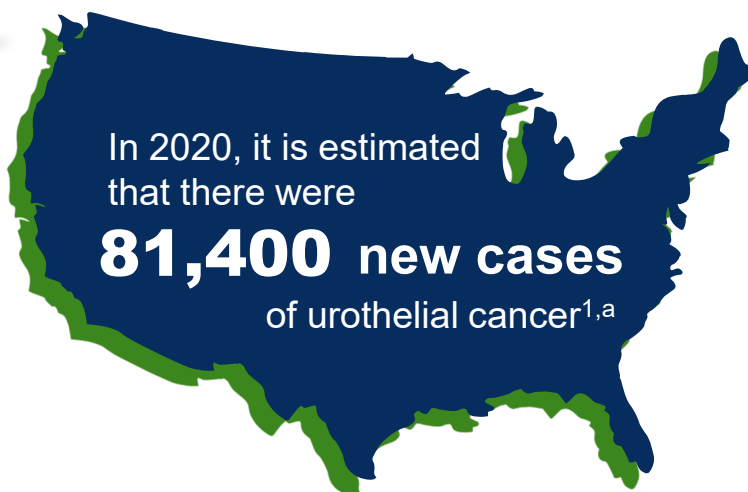


\*Emens LA, et al. IMpassion130. SABCS 2018 (program #GS1-04)

# Significant Unmet Need in Metastatic Urothelial Cancer

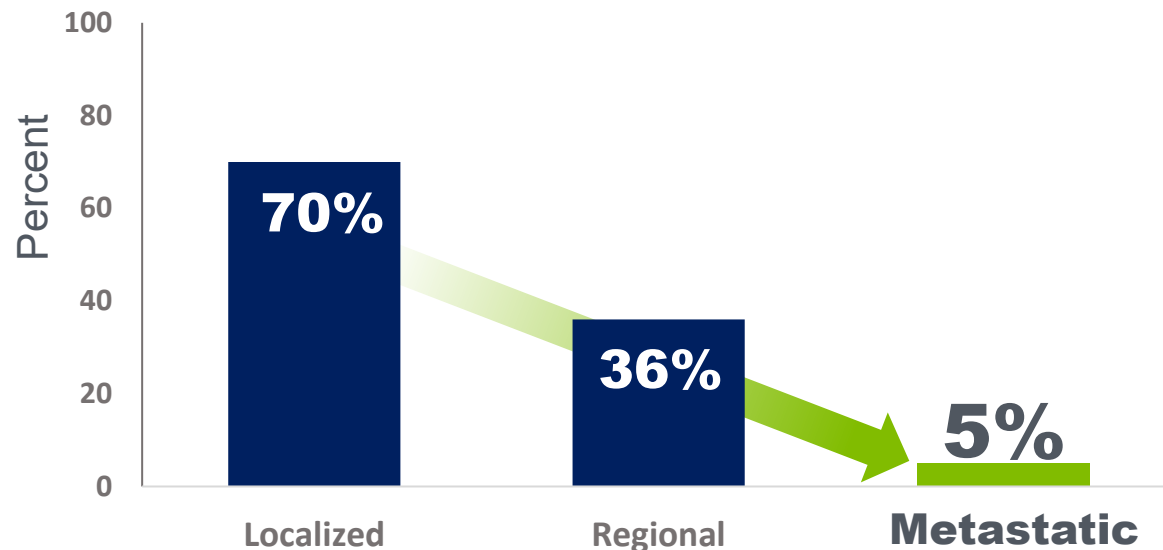
## UC Is the Most Common Type of Bladder Cancer<sup>1</sup>

**95%**  
of bladder cancers are **urothelial cancer**



**Majority of mUCs are PD-L1 negative<sup>3</sup>**

## 5-Year Survival Rate by Stage at Diagnosis of UC<sup>2,\*</sup>



## Median Overall Survival for 2L mUC Patients with SOC Opdivo

	PD-L1(-)	ITT
Checkmate 275	6.0 months (n=146, 54%)	8.6 months (n=270)

<sup>a</sup>Estimated cases based on 2013-2017 cases. <sup>\*</sup>5-Year relative survival percent, UC by SEER Summary Stage 2000.

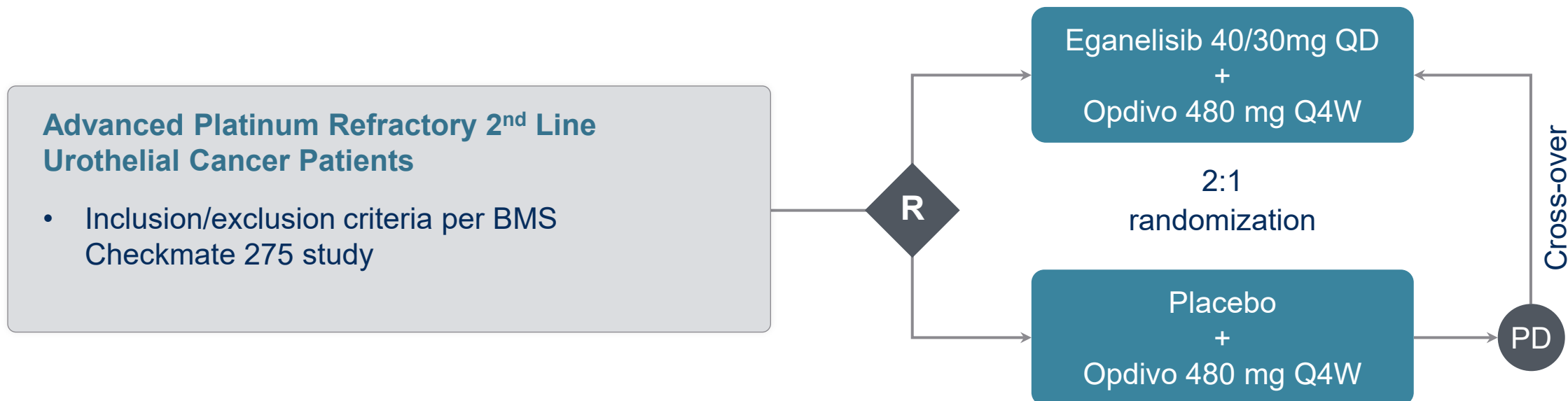
mUC, metastatic urothelial cancer; PD-L1, programmed death-ligand 1; SEER, Surveillance, Epidemiology, and End Results; UC, urothelial cancer.

1. National Cancer Institute. Accessed December 16, 2020. <https://seer.cancer.gov/statfacts/html/urinb.html> 2. National Cancer Institute. Accessed December 16, 2020.

<https://www.cancer.gov/types/bladder/patient/bladder-treatment-pdq#Keypoint2> 3. Bellmunt J et al. *Ann Oncol*. 2015;26(4):812-817. 4. National Cancer Institute. Accessed July 20, 2021. <https://seer.cancer.gov/statfacts/html/urinb.html>

# MARIO-275: Addition of Eganelisib to Standard of Care Opdivo in I/O Naïve Urothelial Cancer Patients, Including PD-L1(-) Patients

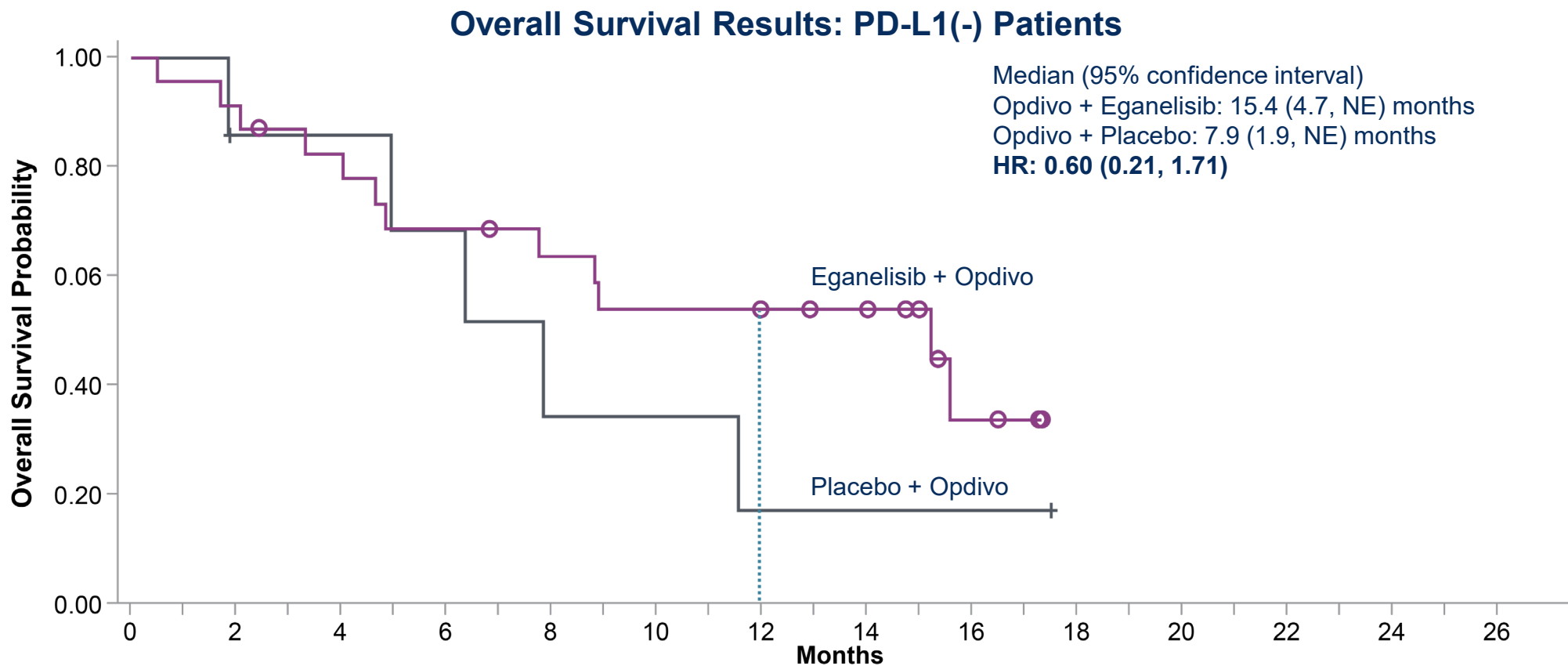
## FDA Fast-Track Designation



DOR, duration of response; MDSC, myeloid-derived suppressor cells; ORR, overall response rate; OS, overall survival; PD-L1, programmed death-ligand 1; PFS, progression-free survival; Q4W, once every four weeks; QD, once a day.

\* PD-L1 expression measured in baseline/archival tumor biopsies with Dako PD-L1 immunohistochemical 28-8 pharmDx kit approved for nivolumab in UC, except 2 biopsies tested with 22C3 PD-L1 antibody prior to study (Tumor Proportion Score < 1% cutoff for PD-L1 (-)); Findings presented include data up to June 26, 2021

# mOS of PD-L1(-) Pts on Combo Arm: 15.4 mos vs 7.9 mos on Control HR of 0.60 Indicating 40% Reduction of Risk of Death



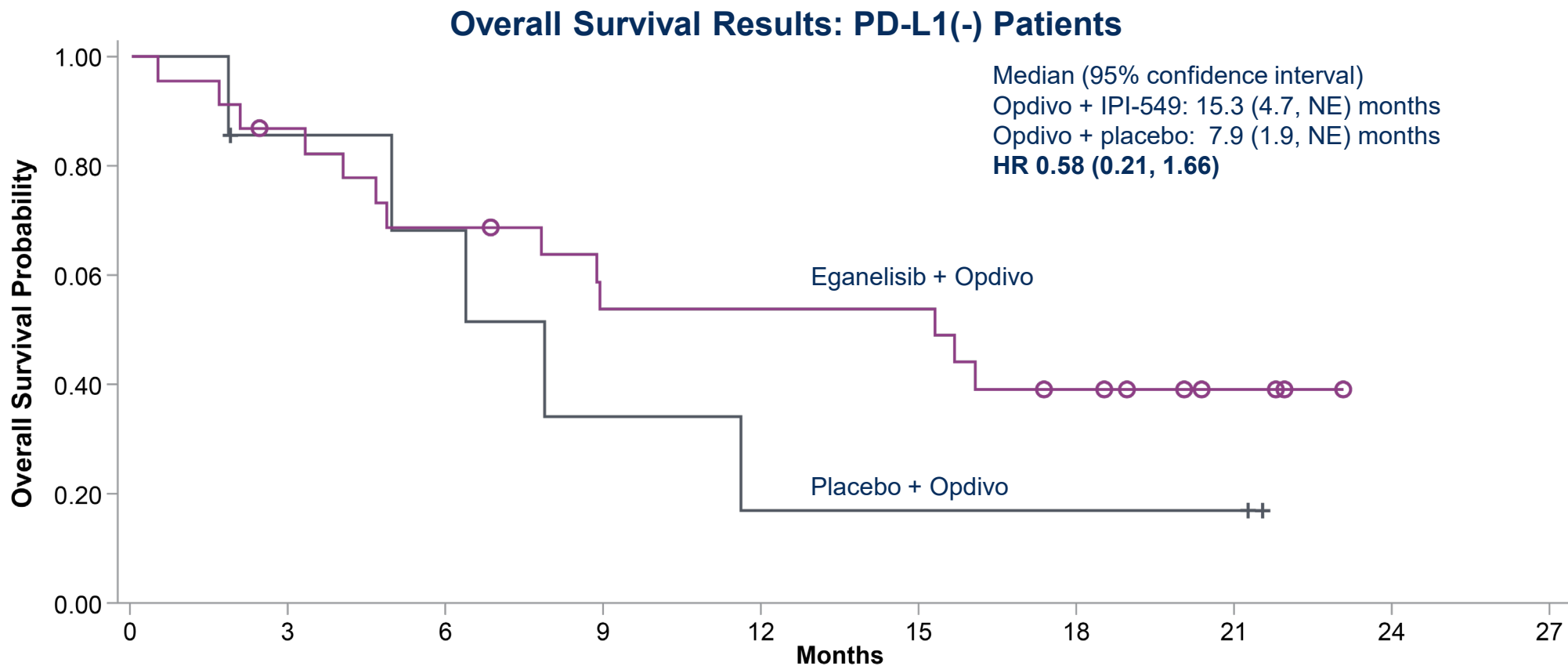
Eganelisib+Opdivo (N=23)	23	21	18	15	13	11	10	9	3	0		
Placebo+Opdivo (N=7)	7	5	5	4	2	2	1	1	1	0		

One Year OS Landmark:  
54% on Combo versus  
17% on Opdivo

Censoring based on last available clinical visit; Tumor Proportion Score < 1% cutoff for PD-L1 (-)  
Data Snapshot: 26 June 2021



# mOS of PD-L1(-) Pts on Combo Arm: 15.3 mos vs 7.9 mos on Control HR of 0.58 Indicating 42% Reduction of Risk of Death



Eganelisib+Opdivo (N=23)	23	19	15	11	11	11	7	3	0	0
Placebo + Opdivo (N=7)	7	5	4	2	1	1	1	1	0	0

OS (mITT): censoring based on last available clinical visit (Figures 14.1.1.3.5, Table 14.2.5.4)

# 2022 Milestones: Two Study Starts and Four Data Readouts

## Initiation of New Studies

1. MARIO-4 registration enabling study in frontline mTNBC by end of 2022
2. MARIO-P Platform Clinical Program in 3Q 2022

2022 new study starts and data to inform additional registration studies in 2023 and beyond

## Data in 2H 2022

- MARIO-3 TNBC
- MARIO-275 UC
- MARIO-3 RCC
- HNSCC Window of Opportunity IST

# Advancing and Expanding MARIO Clinical Development Program

## MACrophage Reprogramming in Immuno-ONcology



	PHASE 1	PHASE 1B	PHASE 2	PHASE 3	
<b>Frontline mTNBC</b>					
<b>MARIO-4:</b> Registration study eganelisib + CPI + chemo vs. standard of care					Initiate study by YE 2022
<b>MARIO-3:</b> Open label eganelisib triplet on top of Impassion130 doublet of Tecentriq® and Abraxane®					Data in 2H 2022
<b>UC, RCC, HNSCC</b>					
<b>MARIO-275:</b> Randomized controlled study eganelisib + Opdivo® vs. Opdivo in 2L UC					Data in 2H 2022
<b>MARIO-3:</b> Open label study eganelisib + Tecentriq + Avastin® in 1L RCC					Data in 2H 2022
<b>HNSCC:</b> IST WoO monotherapy study					Data in 2H 2022
<b>MARIO-P Platform Clinical Program</b>					
<b>Ovarian Cancer</b>					Initiate on a rolling basis in 3Q 2022 (20-40 patients per cohort)
<b>NSCLC</b>					
<b>Soft Tissue Sarcoma</b>					
<b>Prostate Cancer</b>					

Triple Negative Breast Cancer (TNBC)  
 Urothelial Cancer (UC)  
 Renal Cell Carcinoma (RCC)  
 Head and Neck Squamous Cell Cancer (HNSCC)  
 Non Small Cell Lung Cancer (NSCLC)

# 2022 Financial Guidance

- **Cash at March 31, 2022 (unaudited): \$67.1 million**
- **2022 Net Loss: \$45 million to \$55 million**
- **2022 Year-End Cash: \$25 million to \$35 million**

**Infinity's financial guidance does not include potential additional funding or business development activities.**



# Eganelisib Addressing Significant Patient Need With Next-Generation Immunotherapies

H.C. Wainwright Global Investment Conference  
May 23-25, 2022

