
MacroGenics®
Developing
Breakthrough Biologics,
Life-changing Medicines®
Post-ESMO Conference Call
September 16, 2024

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Investigational Agents

The safety and efficacy of investigational agents and/or investigational uses of approved products have not been established.

Conference Call Agenda

Introduction
Scott Koenig, M.D., Ph.D. – President and CEO, MacroGenics

Updated TAMARACK Study Results
Stephen Eck, M.D. – SVP, Clinical Development and Chief Medical Officer

Pipeline Update
Scott Koenig, M.D., Ph.D.

Q&A

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Phase 2 TAMARACK Study: Hypothesis & Key Findings

As of July 9, 2024 data cutoff

Hypothesis

Vobra duo safety could be improved while maintaining efficacy observed in Phase 1 study by:

- Reducing starting dose
- Increasing dosing interval

Achieved goal of extending treatment duration and response to therapy while maintaining / improving anti-tumor activity

- Continued encouraging antitumor activity as measured by ORR and PSA response rate
- Extended duration of therapy observed compared to Phase 1 study as measured by median number of doses received
- Improvement in safety and tolerability

Key considerations informing potential vobra duo next steps

- ***Evaluation of mature median rPFS*** *(maturity expected no later than early 2025)*
- ***Assessment of competitive landscape***
- ***Resource allocation across clinical portfolio***
- ***Input from external KOLS***
- ***Potential partnering opportunities***

Presented at ESMO 2024; Data Cut-off: July 9, 2024

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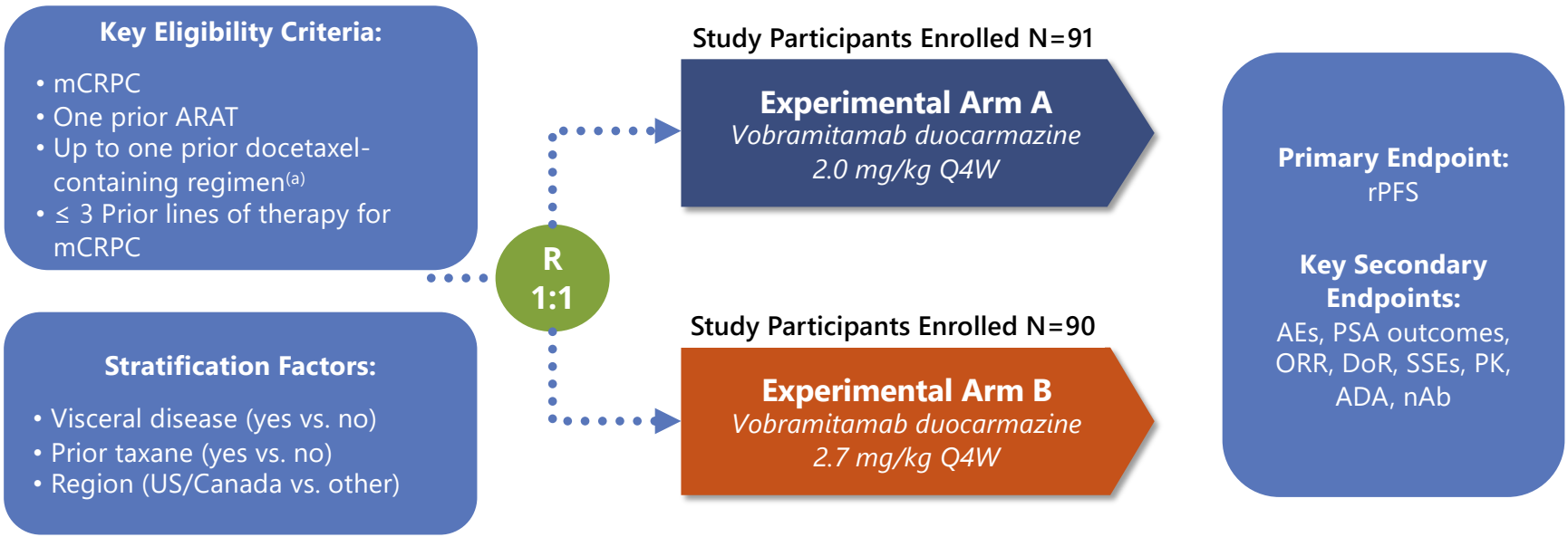
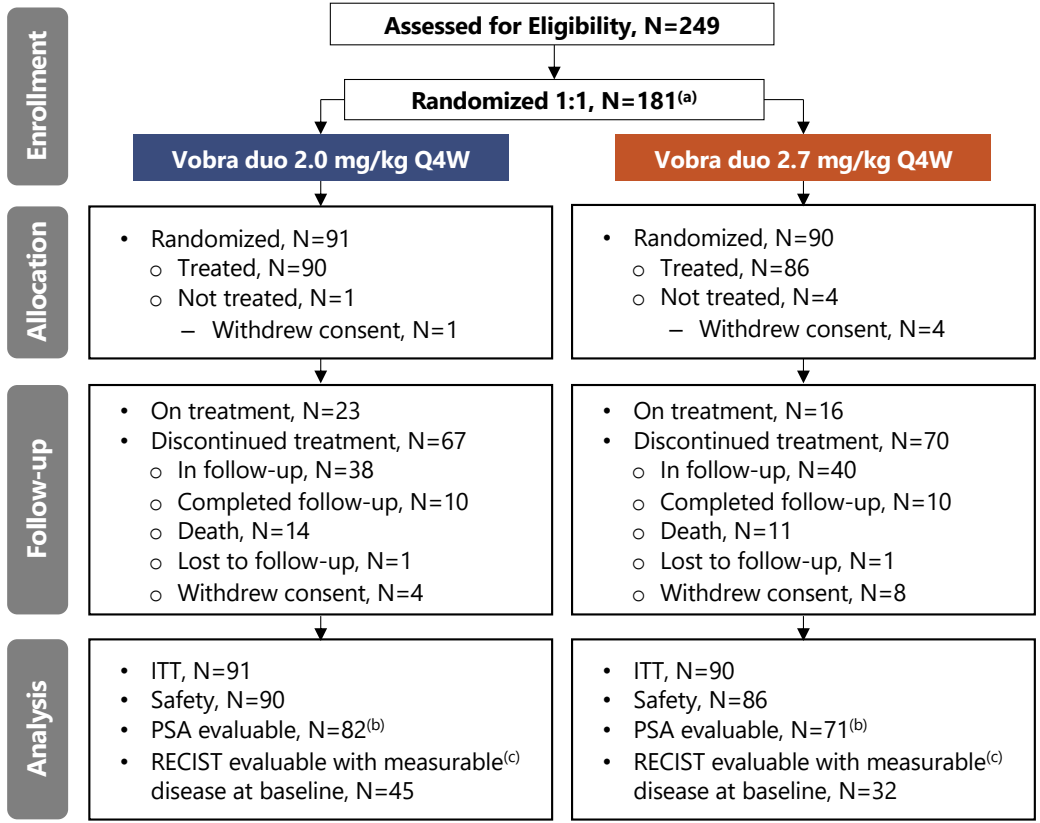
Vobra Duo: mCRPC Phase 2 Study Design Summary



(a) Participants who received an additional taxane or second ARAT (androgen receptor axis-targeted agent [abiraterone, enzalutamide or apalutamide]) for <60 days as bridging therapy while awaiting lutetium-177 vipivotide tetraxetan are also eligible. Other prior chemotherapy for prostate cancer is not allowed.

mCRPC=metastatic castration-resistant prostate cancer; ORR=objective response rate; PSA=prostate-specific antigen; Q4W=every 4 weeks; R=randomize; rPFS=radiographic progression-free survival.

Study Participants Flow



(a) Excludes 3 study participants not dosed with vobra duo who were originally assigned to control arm on earlier version of protocol. These study participants are excluded from all analyses in this presentation.
(b) PSA-evaluable population includes study participants who received at least 1 dose of study treatment, had baseline PSA ≥2 ng/mL, and ≥1 postbaseline PSA measurement.
(c) All study participants who received ≥1 dose of vobra duo, with baseline and postbaseline target lesion measurements (by RECIST v1.1).
ITT=intent-to-treat.

Presented at ESMO 2024; Data Cut-off: July 9, 2024

Demographics and Baseline Characteristics

TAMARACK

ITT population, N=181[(a)]

Parameter	Vobra duo 2.0 mg/kg Q4W N=91	Vobra duo 2.7 mg/kg Q4W N=90
Median (range) age, years	71 (46-89)	69 (35-86)
ECOG PS, n (%)		
0	42 (46.2)	51 (56.7)
1	48 (52.7)	37 (41.1)
2	1 (1.1)	2 (2.2)
Disease status at first diagnosis, n (%)		
Local resectable	28 (30.8)	37 (41.1)
Locally advanced unresectable	12 (13.2)	9 (10.0)
Metastatic	51 (56.0)	44 (48.9)
Type of disease progression at study entry, n (%)		
Radiographic progression of measurable disease	43 (47.3)	31 (34.4)
Radiographic progression of bone disease (in >2 new bone lesions)	33 (36.3)	41 (45.6)
PSA progression only	24 (26.4)	25 (27.8)
PSA progression with any other type of progression	39 (42.9)	32 (35.6)
Study participants with visceral disease, n (%)	15 (16.5)	15 (16.7)
Study participants with prior taxane, n (%)	48 (52.7)	49 (54.4)
Study participants with prior PARP, n (%)	6 (6.6)	8 (8.9)
Number of prior ARAT, n (%)		
1	82 (90.1)	84 (93.3)
>1	9 (9.9)	6 (6.7)
Baseline PSA		
n	89	85
Mean (standard deviation), ng/mL	180.5 (542.60)	182.6 (433.06)
Median (range), ng/mL	26.4 (0.8-3447.0)	24.7 (0.2-2778.0)
PSA ≥2 ng/mL, n (%)	83 (91.2)	74 (82.2)

(a) All randomized study participants, including the study participants not treated.
PARP=poly (ADP-ribose) polymerase.

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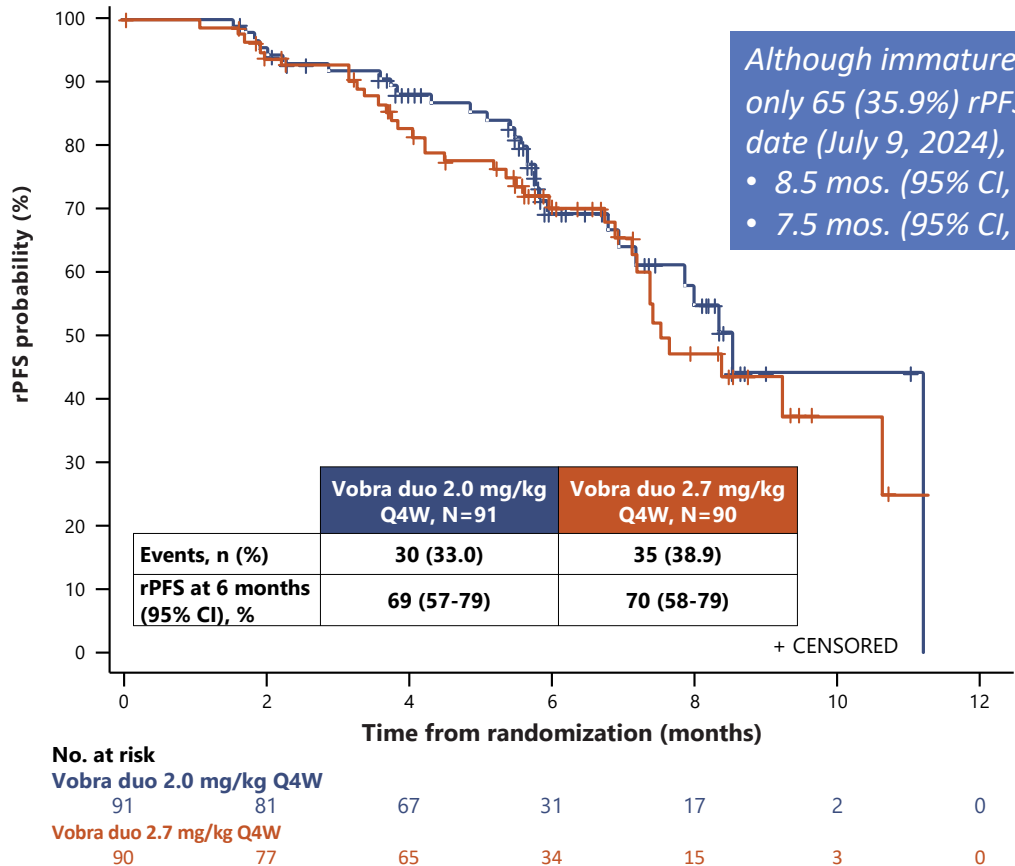
rPFS per Investigator by PCWG3

ITT population, N=181



	Vobra duo 2.0 mg/kg Q4W, N=91	Vobra duo 2.7 mg/kg Q4W, N=90
Events, n (%)	30 (33.0)	35 (38.9)
rPFS at 6 months (95% CI), %	69 (57-79)	70 (58-79)

*Although immature[(a)] and subject to change, with only 65 (35.9%) rPFS events as of data cut-off date (July 9, 2024), **median rPFS** was:*

- *8.5 mos. (95% CI, 7.2-11.2) on 2.0 mg/kg arm*
- *7.5 mos. (95% CI, 7.2-10.6) on 2.7 mg/kg arm*

(a) Company anticipates having final median rPFS no later than early 2025 based on collection of events no later than January 2025 (as per study design).
PCWG3=Prostate Cancer Working Group 3

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Tumor and PSA Responses

	Vobra duo 2.0 mg/kg Q4W	Vobra duo 2.7 mg/kg Q4W
RECIST response-evaluable population w/baseline measurable disease[(a)]	**N=45**	**N=32**
Best overall response (confirmed), n (%)		
CR	0	1 (3.1)
PR	9 (20.0)	12 (37.5)
SD	30 (66.7)	15 (46.9)
PD	5 (11.1)	2 (6.3)
NE	1 (2.2)	2 (6.3)
Confirmed ORR (CR + PR), n (%)	9 (20.0)	13 (40.6)
Confirmed + unconfirmed ORR, n (%)	12 (26.7)	15 (46.9)
Median (range) DOR of confirmed RECIST responders, months [n]	4.9 (1.94-6.47) [9]	NE (1.54-9.46) [13]
PSA response-evaluable population[(b)]	**N=82**	**N=71**
PSA50 response (confirmed), n (%)	37 (45.1)	28 (39.4)
PSA50 response (confirmed + unconfirmed), n (%)	41 (50.0)	37 (52.1)
Median (range) DOR of confirmed PSA50 responders, months [n]	NE (0.95-9.23) [37]	NE (0.95-9.49) [28]

(a) All study participants who received ≥1 dose of vobra duo, with baseline and postbaseline target lesion measurements (by RECIST v1.1).

(b) All study participants who received ≥1 dose of vobra duo, with a baseline PSA ≥2 ng/mL and ≥1 postbaseline PSA measurement.

NE=not evaluable; SD=stable disease.

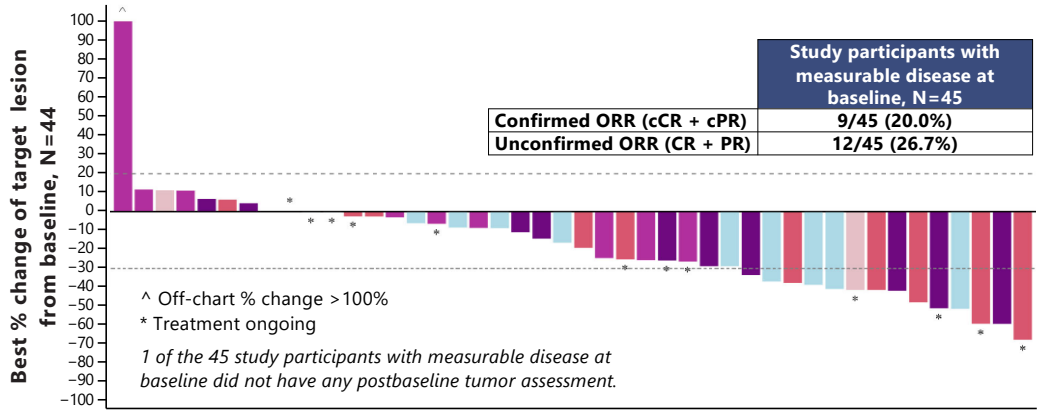
Presented at ESMO 2024; Data Cut-off: July 9, 2024

Best % Change in Target Lesions From Baseline per Investigator

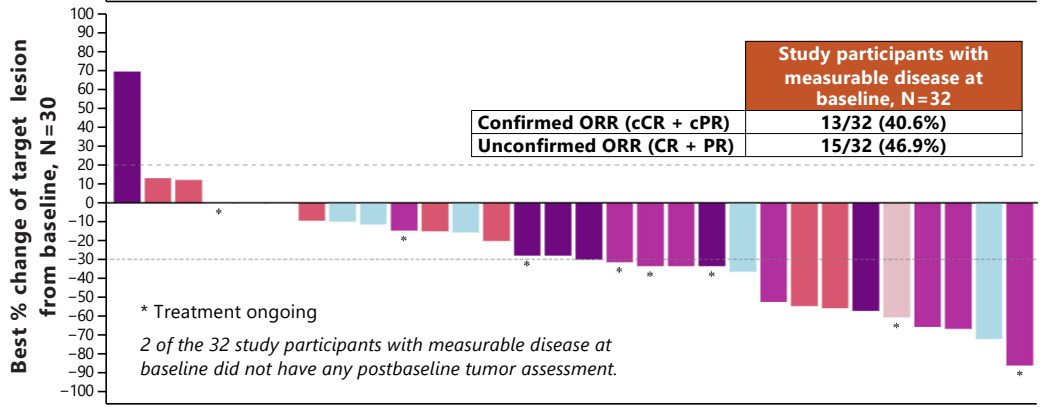
TARMARACK

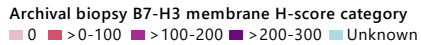
RECIST response-evaluable population with measurable disease, N=77[(a)]

Vobra Duo 2.0 mg/kg Q4W



Vobra Duo 2.7 mg/kg Q4W





ORRs across both dosing cohorts indicate robust anti-tumor activity

(a) All study participants who received ≥1 dose of vobra duo, with baseline and postbaseline target lesion measurements (by RECIST v1.1).
cCR=confirmed complete response; CR=complete response; cPR, confirmed partial response; PR, partial response.

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Treatment Exposure and Reason for Treatment Discontinuation

TAMARACK

	TAMARACK vobra duo 2.0 mg/kg Q4W	TAMARACK vobra duo 2.7 mg/kg Q4W	CP-MGC018-01 vobra duo 3.0 mg/kg Q3W[(b)]
Treated with any study treatment, n	90	86	41
Treatment discontinued, n (%)	67 (74.4)	70 (81.4)	41 (100)
Adverse event	22 (24.4)	31 (36.0)	15 (36.6)
Death	2 (2.2)	2 (2.3)	0
Physician decision	5 (5.6)	2 (2.3)	0
Progressive disease	28 (31.1)	28 (32.6)	24 (58.5)
Subject decision/withdrew consent	10 (11.1)	7 (8.1)	2 (4.9)
Treatment ongoing, n (%)	23 (25.6)	16 (18.6)	0
Mean (standard deviation) number of doses	6.1 (2.35)	5.5 (2.39)	5.0 (2.98)
Median (range) number of doses	6 (1-11)	6 (1-12)	4.0 (1.0-15.0)
Median (range), duration study treatment, months	6.4 (1.0-11.1)	6.7 (1.0-12.9)	4.2 (2.1-15.0)
Median (range) dose intensity,[(a)] %	92.6 (64.2-106.1)	81.7 (40.5-104.3)	66.4 (26.7-102.9)

Results indicate improvement in duration of therapy for vobra duo in TAMARACK compared to that of Phase 1 mCRPC expansion cohort (i.e., median of 6 vs. 4 doses, respectively)

*(a) Total dose intensity is calculated as total dose administered / total planned dose × 100. Total planned dose = assigned dose at randomization * baseline weight * [(last dose date – first dose date) / 28 + 1] rounded to nearest whole number.*

(b) Expansion cohort data from Phase 1 study (NCT03729596) of vobra duo in men with mCRPC who had progressed after 1 prior line of chemotherapy for metastatic disease and no more than 2 prior lines of antihormonal therapy; participants were required to have PSA ≥2 ng/mL and documented progressive disease per PCWG2 criteria; data as of final cut-off date of August 3, 2023.

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Overall Summary of TEAEs on TAMARACK and CP-MGC018-01

AEs, n (%)	Vobra duo 2.0 mg/kg Q4W N=90	Vobra duo 2.7 mg/kg Q4W N=86	CP-MGC018-01 3.0 mg/kg Q3W[(b)] N=41
Any TEAE	89 (98.9)	86 (100)	41 (100)
Treatment-related AEs[(a)]	87 (96.7)	84 (97.7)	41 (100)
Any grade ≥3 TEAE	59 (65.6)	54 (62.8)	33 (80.5)
Grade ≥3 treatment-related AE[(a)]	42 (46.7)	45 (52.3)	32 (78.0)
Any SAE	34 (37.8)	38 (44.2)	23 (56.1)
Treatment-related SAEs[a]	23 (25.6)	24 (27.9)	19 (46.3)
Fatal treatment-related AEs	5 (5.6)	3 (3.5)	2 (4.9)
TEAEs resulting in vobra duo discontinuation	23 (25.6)	33 (38.4)	15 (36.6)
TEAEs resulting in vobra duo dose reductions	45 (50.0)	47 (54.7)	28 (68.3)
TEAEs resulting in vobra duo interruption	46 (51.1)	51 (59.3)	28 (68.3)

Overall improvement in safety and tolerability in TAMARACK compared to that of Phase 1 mCRPC expansion cohort

(a) Includes events with causality assessments of "possible," "probable," or "definite," per investigator.

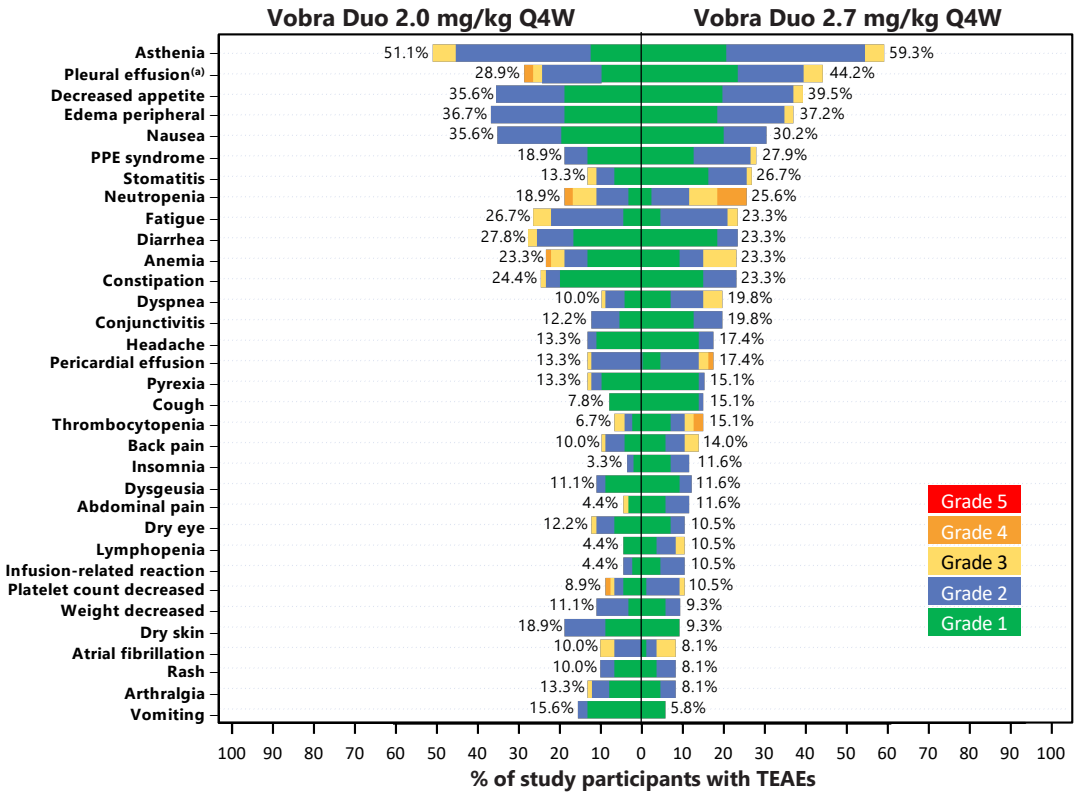
(b) Expansion cohort data from Phase 1 study (NCT03729596) of vobra duo in men with mCRPC who had progressed after 1 prior line of chemotherapy for metastatic disease and no more than 2 prior lines of antihormonal therapy; participants were required to have PSA ≥2 ng/mL and documented progressive disease per PCWG2 criteria; data as of final cut-off date of August 3, 2023.

SAE=serious adverse event.

Presented at ESMO 2024; Data Cut-off: July 9, 2024

TEAEs Reported in ≥10% of Study Participants in Either Arm

(Safety population, N=176)

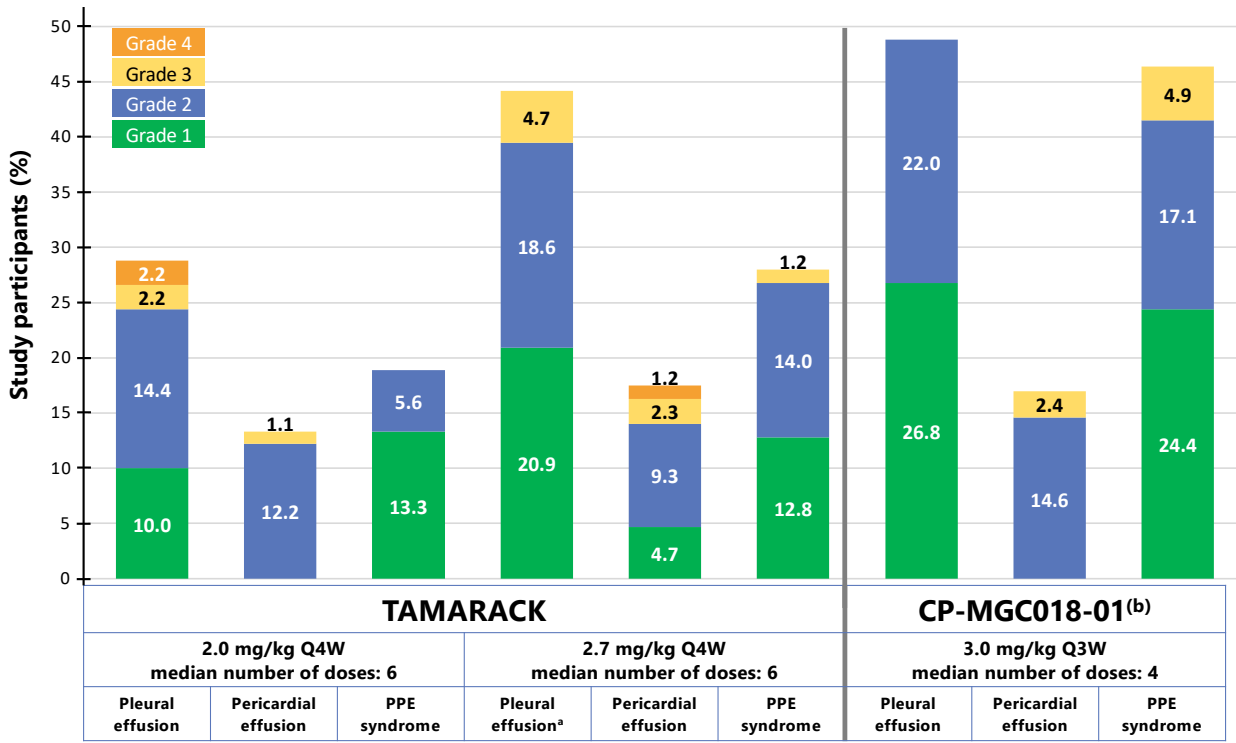


(a) Includes one treatment-related pleural effusion event reported to be grade 3 but with a fatal outcome; site query to correct the discrepancy is pending.

Presented at ESMO 2024; Data Cut-off: July 9, 2024

Select TEAEs by Grade and Dose in TAMARACK and CP-MGC018-01

TAMARACK safety population, N=176; CP-MGC018-01 safety population, N=41



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Summary

As of July 9, 2024 data cutoff

- Data demonstrated vobra duo's antitumor activity by ORR and PSA response rate
- Anticipate having final TAMARACK median rPFS no later than early 2025
- Company believes it has better understanding of vobra duo's overall safety and tolerability and is considering ways to further improve molecule's safety as it awaits final median rPFS
- Through dose reduction and increase in dosing interval, events of neutropenia, anemia, thrombocytopenia, pleural effusion and PPE syndrome improved compared to Phase 1 dose expansion in mCRPC; also, on average, TAMARACK study participants stayed on treatment longer than did those in Phase 1
- Company is considering exploring whether adverse events associated with prolonged exposure to vobra duo could be mitigated by strategies such as further increasing dosing intervals or utilizing loading doses

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Deep and Differentiated Proprietary Pipeline with Retained Commercial Rights

Program (Target)	Potential Indication(s)	Modality/ Platform	Preclinical	Phase 1	Phase 2	Phase 3	Partner / Sponsor
Vobramitamab Duocarmazine (B7-H3)	mCRPC TARACK Study	ADC					
	Multiple Solid Tumors *(+lorigerlimab)*	ADC + DART®					
Lorigerlimab (PD-1 × CTLA-4)	mCRPC *(+docetaxel)* ORIKEET Study	DART					
Enoblituzumab (B7-H3)	Neo-adj. Prostate Cancer HEAT Study[a]	Fc-optimized mAb					JOHNS HOPKINS MEDICINE
Tebotelimab[b] (PD-1 × LAG-3)	Solid Tumors & Heme Malignancies	DART					
MGC026 (B7-H3)	Multiple Solid Tumors	ADC					
MGC028 (ADAM9)	Multiple Solid Tumors	ADC					

The safety and efficacy of investigational agents and/or investigational uses of approved products have not been established. Pipeline reflects current status of each program or most recently completed phase of development.
(a) The "Help Elucidate & Attack Longitudinally" (HEAT) study is an investigator-sponsored trial.
(b) MacroGenics currently has no active/ongoing tebotelimab studies.

Partnered Programs: Potential Future Cash Flow & Platform Validation

Program (Target)	Potential Indication(s)	Modality/ Platform	Preclinical	Phase 1	Phase 2	Phase 3	Marketed	Partner
MARGENZA® (HER2)	HER2+ Metastatic Breast Cancer	Fc-optimized mAb						EVERSANA™ [(a)]
ZYNYZ® (PD-1)	Merkel Cell Carcinoma	mAb						Incyte
	Squamous Cell Anal Carcinoma	mAb						
	Non-Small Cell Lung Cancer	mAb						
TZIELD® (CD3)	Stage 2 "At Risk" T1D	mAb						sanofi
	Stage 3 "Early Onset" T1D	mAb						
MGD024 (CD123 × CD3)	CD123+ Heme Malignancies	DART						Exclusive Option GILEAD
Bispecific (Undisclosed)	Multiple Solid Tumors	DART/TRIDENT®						GILEAD

$435M Non-dilutive funding achieved since mid-2022

The safety and efficacy of investigational agents and/or investigational uses of approved products have not been established. Pipeline reflects current status of each program or most recently completed phase of development.

(a) MacroGenics entered risk-sharing collaboration with Eversana in November 2020, under which MacroGenics books U.S. sales and Eversana leads execution of U.S. commercialization of MARGENZA. For all other currently partnered programs for which a license option has been exercised, the partner would book any future worldwide sales, if approved, and MacroGenics would be entitled to receive milestones and royalties.

Unique Capabilities to Develop Next Generation Antibodies for Treating Cancer

Multiple Phase 2 Programs in Prostate Cancer

Multiple data catalysts

Studies:

TIMARACK

TORIKEET

HEAT[b]

Broad Capabilities for Drug Conjugates

Experience in combining novel targets with differentiated drug-linker technology

Proprietary Platforms for Multispecifics

Flexible platforms with clinical and/or partner validation

Proven R&D Track Record

Three approved products generated from our pipeline[a] fuel potential revenue

Margenza®

Tzield®

ZYNYZ®

Well Funded to Deliver on Plan

$140M Cash as of 6/30/24, plus $100M in milestones subsequently received from Incyte, and other anticipated and potential future payments, should provide cash runway into 2026

(a) *TZIELD® was sold to Provention Bio (Sanofi) and is marketed by Sanofi; ZYNYZ™ was licensed to, and is marketed by, Incyte.*
(b) *The "Help Elucidate & Attack Longitudinally" (HEAT) neo-adjuvant prostate cancer study is an investigator-sponsored trial.*

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Thank You!

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