UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of The Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): **March 6, 2024**

XENCOR, INC.
(Exact name of registrant as specified in its charter)

Delaware	**001-36182**	**20-1622502**
(State or other jurisdiction of incorporation)	(Commission File Number)	(IRS Employer Identification Number)
465 North Halstead Street, Suite 200 Pasadena, California		**91107**
(Address of principal executive offices)		(Zip Code)

(626) 305-5900
(Registrant's telephone number, including area code)
(Former name or former address, if changed since last report.)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.01 per share	XNCR	Nasdaq Global Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD

On March 6, 2024, the Company posted a presentation on the "Investors" section of the Company's website (www.xencor.com), which includes additional clinical data from the Phase 2 study of vudalimab (PD1 x CTLA-4) monotherapy in patients with metastatic castration resistant prostate cancer. The information contained in, or that can be accessed through, the Company's website is not a part of this filing. A copy of the presentation is attached as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated herein by reference.

The information in "Item 7.01" and in Exhibit 99.1 attached hereto is being furnished and shall not be deemed to be "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall such information be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, Except as expressly set forth by specific reference in such a filing.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	Description
99.1	Presentation dated March 6, 2024.
104	Cover Page Interactive Data File (formatted as inline XBRL).

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: March 6, 2024

XENCOR, INC.

By: /s/ Celia Eckert
Celia Eckert
General Counsel & Corporate Secretary

Proteins by Design®

XmAb® Antibody Therapeutics

Corporate Overview

March 2024

Forward-Looking Statements

Certain statements contained in this presentation, other than statements of historical fact, may constitute forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Such statements include, but are not limited to, statements regarding Xencor's development plans and timelines; potential regulatory actions; expected use of cash resources; the timing and results of clinical trials; the plans and objectives of management for future operations; and the potential markets for Xencor's product and development candidates. Forward-looking statements are based on the current expectations of management and upon what management believes to be reasonable assumptions based on information currently available to it, and involve numerous risks and uncertainties, many of which are beyond Xencor's control. These risks and uncertainties could cause future results, performance or achievements to differ significantly from the results, performance or achievements expressed or implied by such forward-looking statements. Such risks include, but are not limited to, potential delays in development timelines or negative preclinical or clinical trial results, reliance on third parties for development efforts and changes in the competitive landscape including changes in the standard of care, as well as other risks described in Xencor's filings with the Securities and Exchange Commission (SEC). Xencor expressly disclaims any duty, obligation or undertaking to update or revise any forward-looking statements contained herein to reflect any change in Xencor's expectations with regard thereto of any subsequent change in events, conditions or circumstances on which any such statements are based, except in accordance with applicable securities laws. For all forward-looking statements, we claim the protection of the safe harbor for forward looking statements contained in the Private Securities Litigation Reform Act of 1995.

Xencor: Engineering Antibody Immune Functions to Make Better Drugs

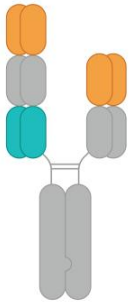
XmAb® Protein Engineering: small changes, big functional impacts
- XmAb Fc Domains augment native immune functions and/or control structure
- Preserves half-life, stability and production
- Over 1,500 issued patents and pending patents worldwide

Advancing XmAb bispecific antibody drug candidate portfolio
- 8 XmAb bispecific antibodies in Phase 1 or 2 clinical studies internally and with partners
- Multiple preclinical programs

3 XmAb antibodies commercialized by partners
- Ultomiris® (Alexion) multiple indications approved worldwide
- Sotrovimab (Vir) was granted global authorizations for mild-to-moderate COVID-19
- Monjuvi® (Incyte) global approvals for relapsed or refractory DLBCL

Partnership portfolio leverages modular XmAb technology
- Multiple partnerships for technology licenses: little/no effort and greatly broadens scope

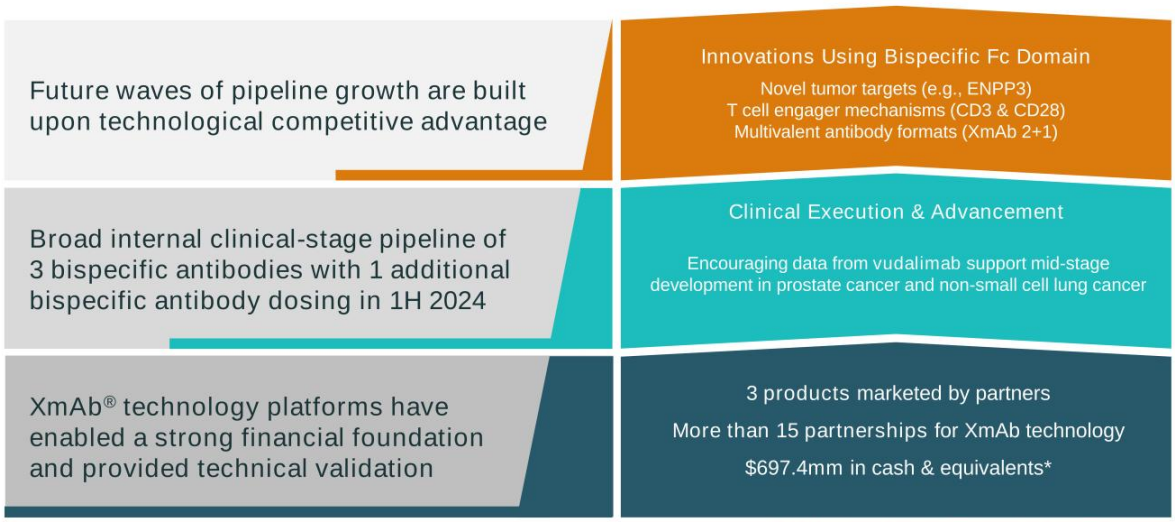
XmAb 2+1 Bispecific Antibody Format



XmAb Fc Domains

Johnson&Johnson Innovative Medicine
ALEXION AstraZeneca Rare Disease
Incyte
Genentech A Member of the Roche Group
AMGEN
GILEAD
astellas
aimmune THERAPEUTICS
VIR
xencor

Layers of Value Creation Built on XmAb® Technology



* As of 12/31/2023. Includes marketable debt. Updated 02/27/2024.

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Efficient XmAb® Platform Builds Differentiated Pipeline & Early Clinical Testing Rigorously Vets Lead Programs

Select a program for late-phase commit, if compelling data and competitive landscape

Broad platform enables strategy with renewable pipeline and cash flows

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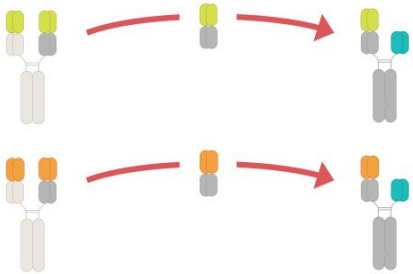
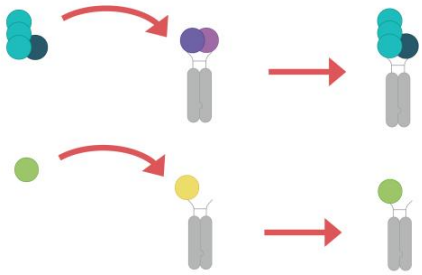
Plug-and-play Fc Domain Enables Rapid Prototyping of Target Combinations and Pipeline Generation

XmAb® Bispecific Antibodies



XmAb® Cytokines



XmAb® Bispecific Fc Domains Retain Beneficial Antibody Properties

- Highly stable, modular scaffold
- Antibody-like half-life in vivo
- Compatible with standard manufacturing and development processes

→ Enable Multiple Classes of New Biologics

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Pipeline Focus on T-Cell Engagers and Vudalimab

XmAb technology enables selective target engagement and increases addressable target space

Program (Targets/Design)	Fc Domain	Indications	Preclinical	Phase 1	Phase 2	Phase 3	Commercial Rights
T Cell Selective, Dual Checkpoint Inhibitor							
Vudalimab PD-1 x CTLA-4	Bispecific Xtend	1L NSCLC mCRPC	+ chemotherapy +/- chemotherapy combination				xencor
T Cell Engagers (CD3 & CD28)							
XmAb819 ENPP3 x CD3 (2+1)	Bispecific	Renal cell carcinoma					xencor
XmAb808 B7-H3 x CD28 (2+1)	Bispecific Xtend	Prostate cancer, Oncology	+ pembrolizumab				xencor
XmAb541 CLDN6 x CD3 (2+1)	Bispecific Xtend	Ovarian cancer, Oncology					xencor
Engineered Cytokines							
XmAb662 IL12-Fc	Bispecific Xtend	Oncology					xencor
XmAb564 IL2-Fc	Bispecific Xtend	Autoimmune					xencor

Key: Solid tumors | Opportunistic

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XmAb® Technologies Create Numerous Differentiated Antibodies for Technology Partners

Technology licensing expands pipeline with very little opportunity cost

Selected Programs	Fc Domain	Indications	Preclinical	Phase 1	Phase 2	Phase 3	Marketed	Commercial Rights
Ultomiris®	Xtend™	PNH, aHUS, gMG, NMOSD						Alexion, AstraZeneca Rare Disease
Monjuvi®	Cytotoxic	DLBCL						Incyte
Xevudy®	Xtend	COVID-19				NOT CURRENTLY AUTHORIZED IN U.S.		VIR
Obexelimab	Immune Inhibitor	IgG4-RD, wAIHA						Zenas BioPharma
Tobevibart (VIR-3434)	Cytotoxic Xtend	Hepatitis B Hepatitis D						VIR
Xaluritamig (AMG 509) STEAP1 x CD3	2+1 Bispecific	Prostate cancer						Amgen
Efbalropendekin alfa (XmAb306) IL15/IL15Rα-Fc	Bispecific Xtend	r/r multiple myeloma + daratumumab r/r multiple myeloma + cevostamab Oncology + atezolizumab						Genentech, A Member of the Roche Group [1]
Plamotamab CD20 x CD3	Bispecific	B-cell malignancies						Johnson&Johnson Innovative Medicine [2]
ASP2138 CLDN18.2 x CD3	2+1 Bispecific	Oncology						Astellas
JNJ-9401 PSMA x CD28	Bispecific	Prostate cancer						Johnson&Johnson Innovative Medicine
JNJ-1493 CD20 x CD28	Bispecific	Heme-Onc						Johnson&Johnson Innovative Medicine

Key: XmAb Bispecific; XmAb Tech (Non-BsAb)

[1] Co-development with Genentech, through May 2024
[2] Co-development with J&J Innovative Medicine

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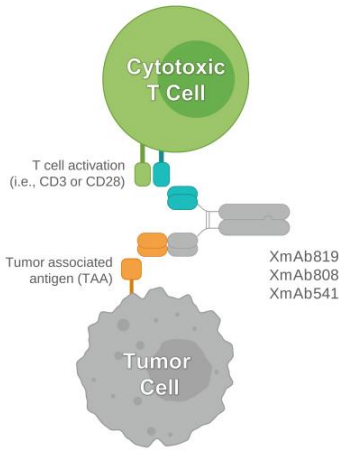
XmAb® Bispecific Fc Domain

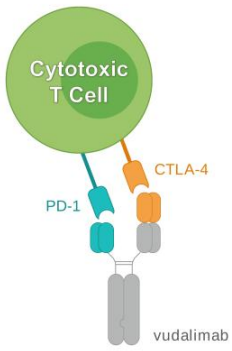
Enabling New Classes of Biologics and Therapeutic Mechanisms of Action

Distinct and Novel Mechanisms-of-Action Enabled By Xencor's XmAb® Bispecific Fc Domain

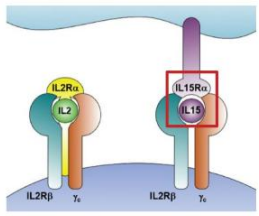
CD3 and CD28 T Cell Engagers

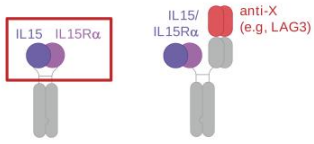


T Cell Selective Dual Checkpoint Inhibition



Engineered Cytokine-Fc Fusions





Efbalropendekin alfa (XmAb306)

Targeted Cytokines

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XmAb® Bispecific T Cell Engagers

*XmAb **2+1** Bispecific Antibody Format*

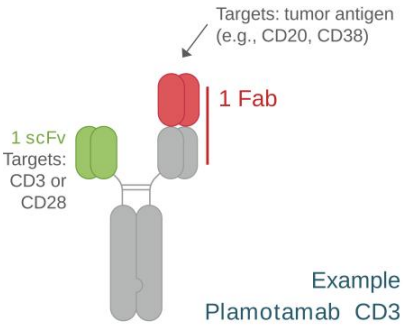
XmAb819 (ENPP3 x CD3)

XmAb541 (CLDN6 x CD3)

XmAb808 (B7-H3 x CD28)

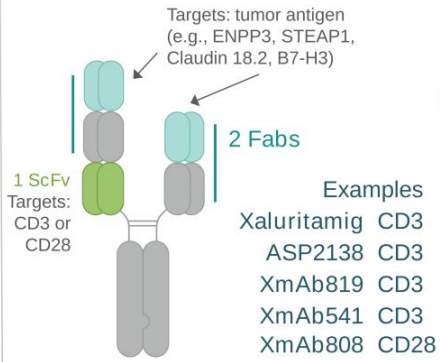
XmAb® T Cell Engagers Use Multiple Formats and Affinity Designs to Customize for Each Tumor Target

XmAb® 1+1

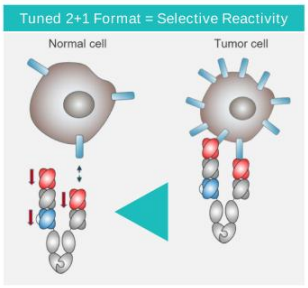


Example
Plamotamab CD3

XmAb® 2+1



Examples
Xaluritamig CD3
ASP2138 CD3
XmAb819 CD3
XmAb541 CD3
XmAb808 CD28



CD3 affinity tuned for reduction of cytokine release syndrome and off-tumor cell killing
Tumor antigen binding affinity tuned for tumor expression density and to match format

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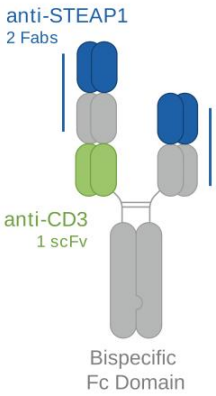
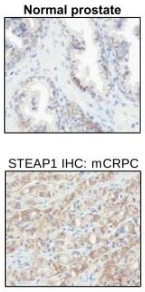
XmAb® 2+1 T-cell Engager Clinical Experience: Xaluritamig (AMG 509; STEAP1 x CD3)

XmAb 2+1 Design



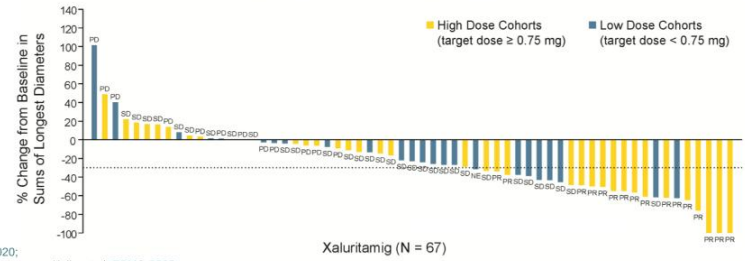
Amgen's Phase 1 Study of Xaluritamig in mCRPC; Interim Results at ESMO 2023

- First TCE to target STEAP1, a challenging membrane target with limited extracellular exposure
- Phase 1 expansion & optimization ongoing; Amgen plans to initiate additional studies in earlier treatment lines
- Safety profile clinically manageable with generally low-grade CRS, primarily in Cycle 1 of treatment



Nolan-Stevaux O, Cancer Res 2020; 80(16 Suppl):Abstract nr DDT02-03

- 41% ORR in high dose cohorts; 24% total (RECIST 1.1)
- Preliminary durability encouraging but early: mDOR 9.2 months (n=16, 10/16 still in response)



Kelly, et al. ESMO 2023.

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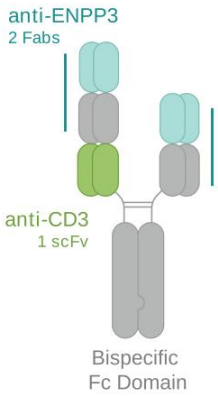
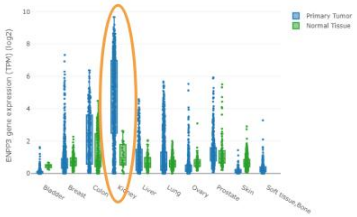
XmAb®819: CD3 T-cell Engager for Renal Cell Carcinoma in Phase 1

XmAb 2+1 Design

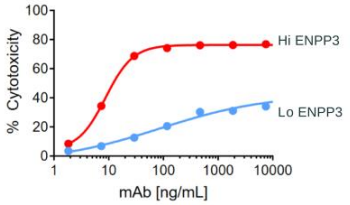


XmAb819 (ENPP3 x CD3)

ENPP3: high RCC; low healthy tissues



Selective T cell directed cytotoxicity



Phase 1 Dose Escalation Study

- Relapsed/refractory clear cell RCC (ccRCC)
  - Nearly uniformly high ENPP3 expression
- Dose escalation ongoing
- Administration: IV and subcutaneous cohorts dosing weekly, with priming and step-up doses
- Following determination of RP2D, expansion cohorts planned in ccRCC and other histologies with high ENPP3 expression
- Companion diagnostic under development for potential patient selection in other histologies

NCT05433142

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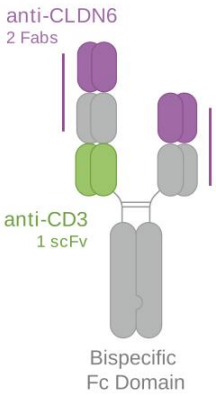
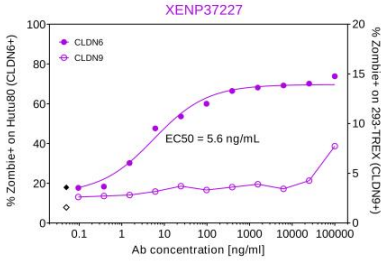
XmAb®541: CD3 T-cell Engager for Ovarian Cancer & Solid Tumors

XmAb 2+1 Design



XmAb541 (CLDN6 x CD3)

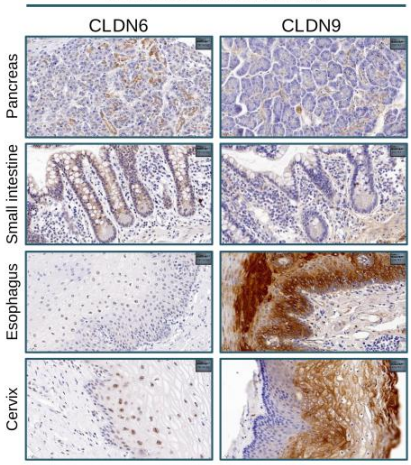
CLDN6 selective over CLDN9



- Differential expression in cancerous tissue presents CLDN6 as an intriguing target
- CLDN family members, which are small membrane proteins, have high sequence identity, complicating antibody design
- XmAb541 engineered for CLDN6 selectivity over similar CLDN9, CLDN3 and CLDN4
- Clinical status: IND open; planned dosing 1H24

CLDN6 Avoids Normal Tissue

FDA999w normal tissue staining



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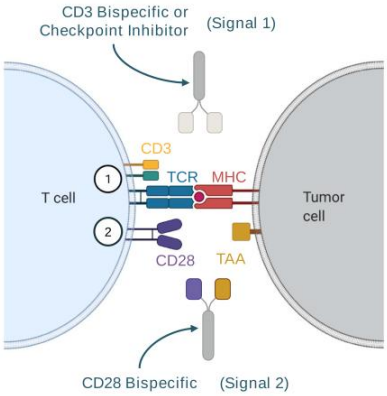
CD28 Bispecific Antibodies Provide a Boost to T Cell Activation

CD28 provides "Signal 2" activation



XmAb® CD28 T cell engagers feature low affinity, monovalent binding

- Avoid historic CD28 safety concerns (superagonism)
- Well behaved: stable, silent FcγR interactions, with Xtend™ Fc technology
- Potential to combine with anti-PD1 and/or CD3 T cell engagers

Multiple wholly owned early-stage and actively advancing programs

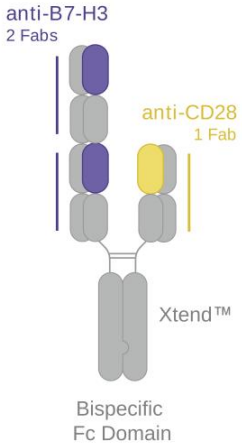
- Ongoing Phase 1 study of XmAb808 (B7-H3 x CD28) in combination with pembrolizumab in solid tumors
- Presented preclinical data from multiple research-stage programs targeting CEACAM5, STEAP1, ENPP3, Trop2 and MSLN

Two narrow, target-limited collaborations with J&J for CD28 bispecifics

- JNJ-9401 (PSMA x CD28; Phase 1) for combination with J&J CD3 bispecifics; collaboration includes access to J&J prostate-cancer franchise for clinical combinations across Xencor's portfolio
- JNJ-1493 (CD20 x CD28; Phase 1) for J&J's use in combination with plamotamab and other agents, such as CD3 bispecifics

XmAb808: Tumor-specific CD28 T-cell Engager Targeted to Broadly Expressed Tumor Antigen B7-H3 in Phase 1

XmAb 2+1 Design



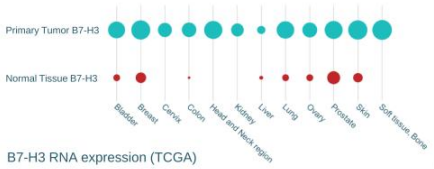
XmAb CD28 T Cell Engagers

Designed to enhance selective T cell activation through CD28 (Signal 2) when in the presence of tumor cells

- Feature low affinity, monovalent binding to CD28
- Avoid CD28 safety concerns (superagonism)
- Well behaved: stable, silent FcγR interactions, with Xtend™ Fc technology
- Potential to combine with anti-PD1 and/or CD3 T cell engagers (Signal 1)

B7-H3 is Broadly Expressed in Solid Tumors

High expression in prostate cancer and others (kidney, breast, lung, etc.)



B7-H3 RNA expression (TCGA)

Clinical Programs

XmAb808: Phase 1 dose-escalation in solid tumors

- Combination with anti-PD1 (Signal 1); pembrolizumab added on third dose, included in all dose escalation cohorts
- Enrolling patients with prostate cancer, ovarian cancer, HNSCC, urothelial cancer and others

NCT05585034

Two narrow, target-limited collaborations with J&J for XmAb CD28 bispecifics; 2 programs in Phase 1

- JNJ-9401: PSMA x CD28
- JNJ-1493: CD20 x CD28

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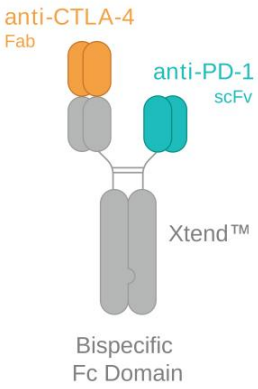
T Cell Selective, Dual Checkpoint Inhibitor

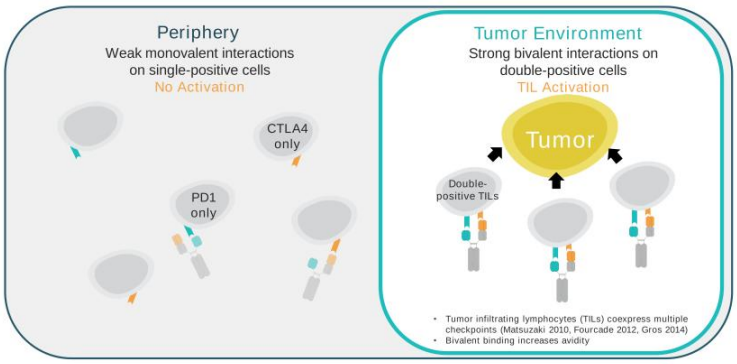
Vudalimab (PD-1 x CTLA-4)

Vudalimab: Selective PD-1 x CTLA-4 Bispecific Antibody

- Monotherapy generally well tolerated, with a potentially differentiated profile from two-antibody combination therapy (PD-1 + CTLA-4)
- Xencor's initial focus on tumors with poor PD-1 inhibitor activity: e.g., prostate cancer



Vudalimab is Designed to Promote Tumor-Selective T Cell Targeting



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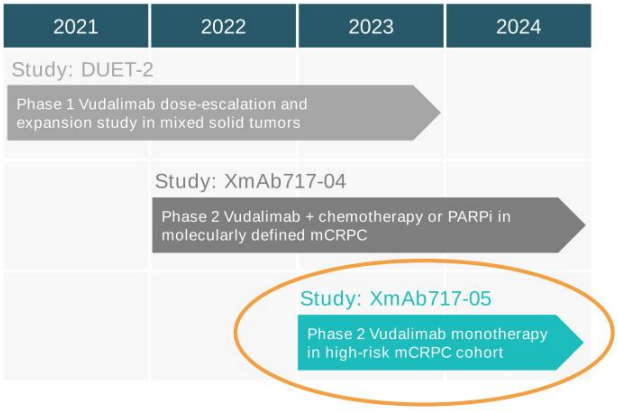
Evolution of Vudalimab Development Program for mCRPC



mCRPC Cohort in Study XmAb717-05

- Visceral, soft tissue, or lymph node metastases ("high-risk" mCRPC)
- Measurable disease by RECIST 1.1
- Progressed after all approved, medically appropriate therapies
- < 2 prior chemotherapy regimens
- No prior treatment with anti-CTLA-4 or PD-1

Study status (February 7, 2024)

- 14/30 mCRPC patients enrolled

Vudalimab Q3W flat dose schedule: 1000 (< 80 kg) or 1200 mg (≥ 80 kg) IV

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Preliminary Data for Vudalimab Monotherapy in mCRPC

Vudalimab monotherapy has been associated with clinical response in 5 out of 12 evaluable mCRPC patients with visceral or lymph node metastases

- Findings consistent with observations of durable responses (41 and 27 weeks) in Phase 1 mCRPC cohort in 2 patients with visceral and lymph node (extrapelvic and/or intrapelvic) metastases

Vudalimab monotherapy safety profile has been consistent with other checkpoint inhibitor therapies

- Low rate of discontinuation of treatment due to adverse events

Additional data will inform future development efforts in monotherapy, and/or contribution of monotherapy to combination treatment

NCT05032040 Data cut February 7, 2024.

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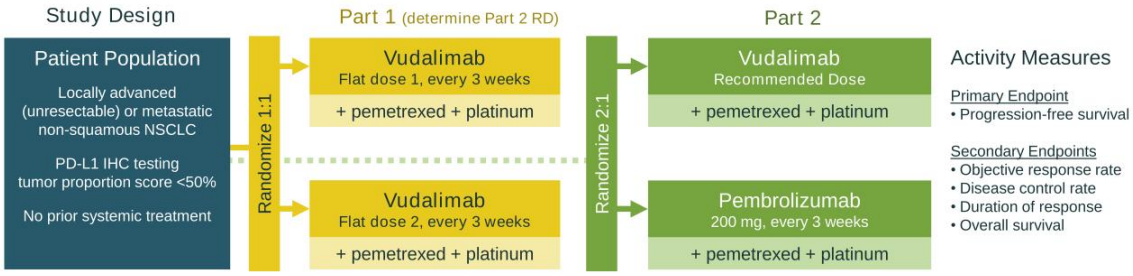
Phase 1b/2 Study in 1L NSCLC in combination with chemotherapy

Part 1 dose comparison, Part 2 randomized vs. pembro; ***First patient dosed in Q4 2023***



Encouraging proof-of-concept data in NSCLC supports evaluation of vudalimab in 1L

- Study of volrustomig (PD-1 x CTLA-4) in checkpoint-naïve NSCLC shows superior PFS over pembrolizumab
  - Volrustomig + chemo vs. pembrolizumab + chemo
- Vudalimab Phase 1 Cohort C (20 patients with NSCLC) activity in 3-4L patients
  - Heavily-pretreated population: 95% checkpoint experienced, 40% ≥ 2 prior checkpoints, median 3 prior therapies
  - 14% objective response rate (2 partial responses of 14 evaluable); 50% disease control rate (7/14)

NCT06173505

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Progress Across XmAb® Portfolio Programs in 2024

XmAb Drug Candidate		2024 Priority
T cell selective, dual checkpoint inhibitor		
XmAb819	ENPP3 x CD3	Advance dose escalation toward target dose levels in 2024
XmAb808	B7-H3 x CD28	Advance dose escalation toward target dose levels in 2024
XmAb541	CLDN6 x CD3	Dose first patient during 1H 2024, enroll Phase 1 study
T Cell Engagers (CD3 & CD28)		
Vudalimab	PD-1 x CTLA-4	Data update and go-forward decision on vudalimab monotherapy (mCRPC) in 1H 2025
		Data update and go-forward decision on vudalimab combination with docetaxel (mCRPC) in 1H 2025
		Enroll Phase 1b portion of vudalimab in front-line metastatic non-small-cell lung cancer
Engineered Cytokines		
XmAb662	IL12-Fc	Complete internal data package from Phase 1 study during 1H 2024
XmAb564	IL2-Fc	Complete internal data package from Phase 1 multiple-ascending dose (MAD) study during 1H 2024

Therapeutic Area Key: Solid tumors | Opportunistic

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Proteins by Design®

XmAb® Antibody Therapeutics

Corporate Overview

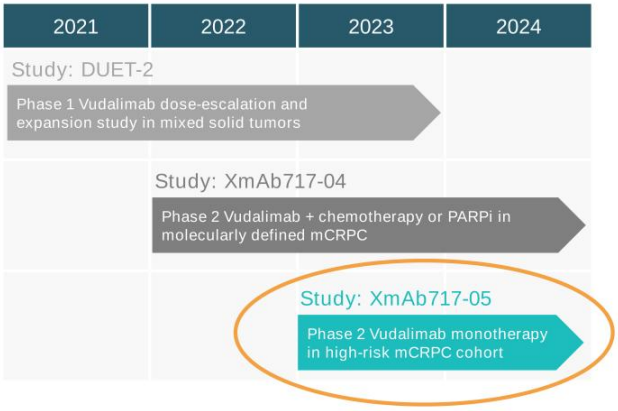
March 2024

Vudalimab Monotherapy in Patients with mCRPC

Study XmAb717-05

Data cut 7 February 2024

Evolution of Vudalimab Development Program for mCRPC



mCRPC Cohort in Study XmAb717-05

- Visceral, soft tissue, or lymph node metastases ("high-risk" mCRPC)
- Measurable disease by RECIST 1.1
- Progressed after all approved, medically appropriate therapies
- < 2 prior chemotherapy regimens
- No prior treatment with anti-CTLA-4 or PD-1

Study status

- 14/30 mCRPC patients enrolled

Vudalimab Q3W flat dose schedule: 1000 (< 80 kg) or 1200 mg (≥ 80 kg) IV

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Summary of Preliminary Data

Vudalimab monotherapy has been associated with clinical response in 5 out of 12 evaluable mCRPC patients with visceral or lymph node metastases

- Findings consistent with observations of durable responses (41 and 27 weeks) in Phase 1 mCRPC cohort in 2 patients with visceral and lymph node (extrapelvic and/or intrapelvic) metastases

Vudalimab monotherapy safety profile has been consistent with other checkpoint inhibitor therapies

- Low rate of discontinuation of treatment due to adverse events

Additional data will inform future development efforts in monotherapy, and/or contribution of monotherapy to combination treatment

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Demographics and Baseline Characteristics and Prior Treatment

Characteristic	mCRPC (n = 14)
Age, median (range)	72 (58-89)
Liver or Lung metastases at baseline, (%)	6 (42.9)
PSA (ng/ml) at baseline, median (range)	152.9 (35-1873)
ECOG 1, n (%)	12 (85.7)
Metastatic disease at diagnosis, n (%)	11 (78.6)

Prior Treatment	mCRPC (n = 14)
Median (range) lines of prior therapy	4 (2-8)
Chemotherapy, n (%)	13 (92.8)
Lines of chemotherapy, median (range)	1 (1-2)
Prior AR Therapy	14 (100.0)
Abiraterone, n (%)	11 (78.6)
Enzalutamide, n (%)	8 (57.1)
Lu-177 PSMA, n (%)	4 (28.6)
Prior radiation, n (%)	9 (64.3)

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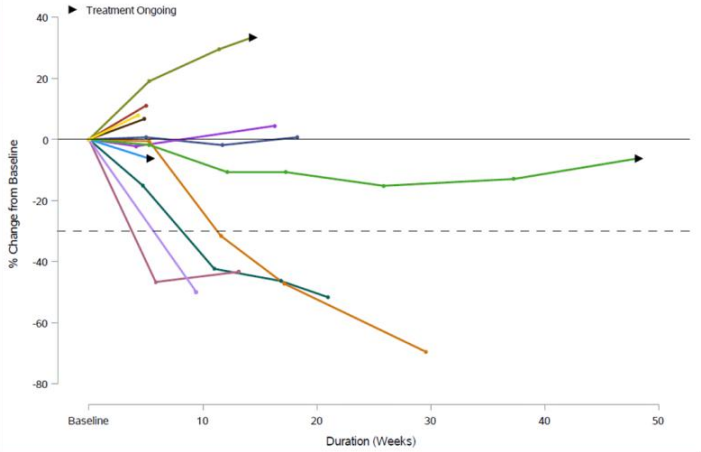
Response to Treatment and Percent Change in Target Lesions

RECIST 1.1 (PCWG3), n (%)	mCRPC (n = 12*)
Objective response rate	4 (33)
Best overall response	
Complete response	0
Partial response	4 (33)
Confirmed	3 (25)
Unconfirmed	1 (8)
Stable disease	2 (17)
Progressive disease	3 (25)
Not evaluable	3 (25)
Disease control rate	6 (50)

*Subjects who have baseline and at least one post-baseline RECIST assessment.



Duration of response for confirmed responders: 18, 10 and 7 weeks

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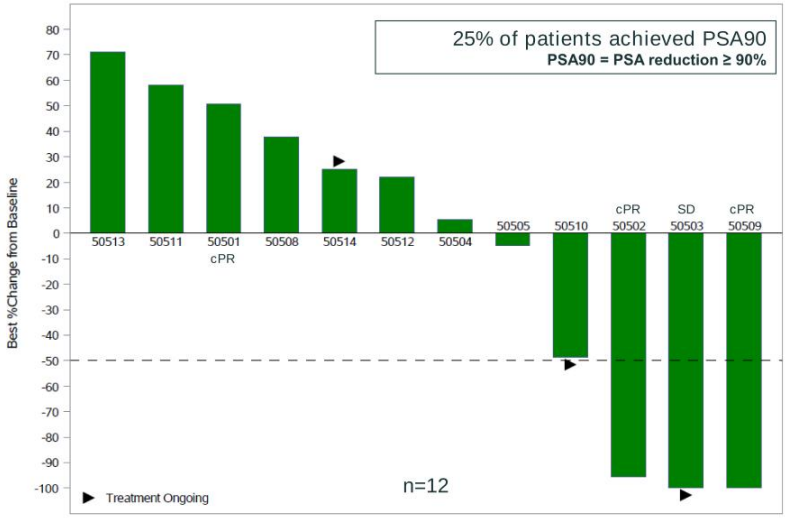
Best Percent Change in PSA From Baseline



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Characteristics of Patients with Clinical Response

Patient	Age/ Race	Prior Systemic Therapies	Prior Radiation	Metastases at Baseline	PSA (ng/mL)	BOR/ Duration of Response	EOT reason
50509	66/AA	Docetaxel Enzalutamide Abiraterone	None	Bone Extrapelvic LN Pelvic LN (SoD = 45.1 mm)	Baseline: 165 Nadir: <0.02 Last: <0.02	cPR 10 weeks	AE: Immune mediated hepatitis
50506	69/W	Carboplatin Bicalutamide Leuprolide + abiraterone	Unspecified RT: Non-castrate clinically localized disease	Retroperitoneal LN (SoD = 34.5 mm)	Baseline: 111 Nadir: Not available Last: Not available	uPR	Lost to follow up
50503	79/AA	Bicalutamide Leuprolide	None	1 liver lesion Bone (SoD = 44.8 mm)	Baseline: 1873 Nadir: 4 Last: 12	SD (PSA90)	Still on study >48 weeks
50502	89/AA	Bicalutamide Leuprolide + abiraterone Enzalutamide Docetaxel Cabazitaxel Olaparib	External beam IMRT (thoracic spine)	3 liver lesions Bone (SoD = 118.5 mm)	Baseline: 180 Nadir: 8 Last: 47	cPR 18 weeks	PD
50501	60/W	Leuprolide + enzalutamide Docetaxel	None	Bone Retroperitoneal LN (SoD = 30 mm)	Baseline: 140 Nadir:211 Last: 549	cPR 7 weeks	PD

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AE: adverse event; BOR: best overall response; cPR: confirmed partial response; SD: stable disease; PD: progressive disease; uPR: unconfirmed partial response

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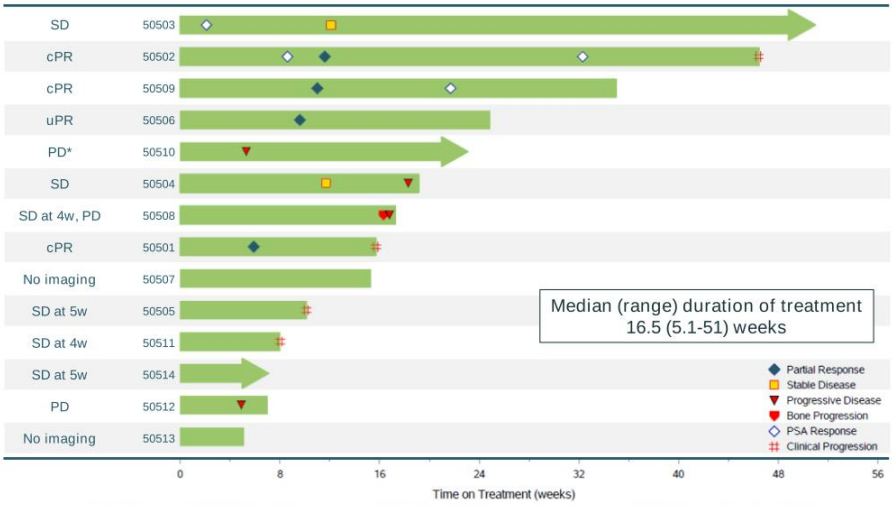
Time on Treatment (n=14)



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RECIST 1.1: end of Cycle 2 then Q6W through Cycle 8, Q9W thereafter. Bone scans: end of cycle 2, Q9W through cycle 12, Q12W, thereafter. PSA: end of Cycle 1, Q6W thereafter. * Patient is seeing clinical benefit and is being treated beyond progression.

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Summary of Treatment-Emergent Adverse Events

Event, n (%)	mCRPC (n = 14)
Any	13 (92.9)
Grade ≥ 3	9 (64.3)
Treatment related	9 (64.3)
Serious adverse event	7 (50.0)
Related serious adverse event	4 (28.6)
Leading to dose modification*	8 (57.1)
Leading to treatment discontinuation	2 (14.3)
Leading to death	1 (7.1)

* Dose modification includes dose reduced and/or held.

One Grade 5 adverse event of autoimmune hepatitis was deemed treatment related; there have been no known additional cases of Grade 5 autoimmune hepatitis among three clinical studies of vudalimab with more than 240 patients treated.

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irAEs of Any Grade in ≥ 2 Patients and Grade ≥ 3 in Any Patients

Any Grade, n (%)	mCRPC (n = 14)
Number of subjects with ≥ 1 event	8 (57.1)
Rash maculo-papular	4 (28.6)
ALT increased	3 (21.4)
Amylase increased	2 (14.3)
AST increased	2 (14.3)
Blood bilirubin increased	2 (14.3)
Hyperthyroidism	2 (14.3)

Grade ≥ 3, n (%)	mCRPC (n = 14)
Number of subjects with ≥ 1 event	3 (21.4)
ALT increased	1 (7.1)
AST increased	1 (7.1)
Blood AP increased	1 (7.1)
Blood bilirubin increased	1 (7.1)
Diabetic ketoacidosis	1 (7.1)
Hyperkalaemia	1 (7.1)
Immune-mediated hepatitis	1 (7.1)
Lipase increased	1 (7.1)

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Benchmark Rates of Immune-Mediated Hepatitis

Drug (Target)	Vudalimab (PD-1 x CTLA-4)	Ipilimumab (CTLA-4)	Ipilimumab (CTLA-4)	Ipilimumab (CTLA-4) + Nivolumab (PD-1)	Ipilimumab (CTLA-4) + Nivolumab (PD-1)
Dosage	N=218*, includes 10 mg/kg Q2W & 1000 mg/1200mg Q3W	3 mg/kg	10 mg/kg	1 mg/kg ipilimumab + 3 mg/kg nivolumab for RCC or mCRC	3 mg/kg ipilimumab + 1 mg/kg nivolumab for melanoma or HCC
Immune-Mediated Hepatitis†, All Grade	7.3%	4.1%	15.0%	7.0%	15.0%
Immune-Mediated Hepatitis†, Grade 3 - 5	5.0%	1.6%	10.8%	6.1%	13.4%

† Immune-Mediated Hepatitis defined as:

For vudalimab: Treatment-related adverse event (TRAE) immune-mediated hepatitis, hepatitis, autoimmune hepatitis, hepatic cirrhosis, hepatic failure, hepatitis acute, hyperbilirubinemia, immune-mediate cholangitis, or liver injury.

For ipilimumab: U.S. FDA label, Yervoy® (ipilimumab) injection, for intravenous use, as revised 2/2023. Yervoy is a registered trademark of Bristol-Myers Squibb Company.

* Excludes 27 patients treated at vudalimab doses less than 10 mg/kg.

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Novel Therapeutic Development Landscape for mCRPC

Drug	Vudalimab[1]	Xaluritamig[2]	Pluvicto + SoC[3]	Lorigerlimab[4]	MK-5684 (ODM-208)[5]	ARX517[6]	Vobramitamab Duocarmazine[7]
Study	Phase 2	FIH / Dose Escalation	Phase 3 (VISION)	Phase 1 Expansion Cohort	Phase 2	Phase 1b Dose Expansion	Phase 1 Expansion Cohort
MoA	PD1xCTLA4	STEAP1xCD3	177Lu-PSMA-617	PD1xCTLA4	CYP11A1 Inhibitor	PSMA ADC	B7xH3 ADC
Selected Population	No	No	PSMA+	No	AR-LBD mut	No	No
Xencor Interest	Wholly Owned	Mid- to High-Single Digit Royalty	-	-	-	-	-
Dosing	1000 or 1200 mg IV Q3W	1.5 mg IV QW (3-step, D1/8/15/22: 0.1/0.3/1.0/1.5 mg)	7.4 GBq IV Q6W for 4-6 cycles + SoC	6 mg/kg IV Q3W	5 mg BID with dexamethasone 1 mg/fludrocortisone 0.1 mg	Tested up to 2.88 mg/kg Q3W, putative therapeutic doses ≥2.0 mg/kg	3 mg/kg IV Q3W
Enrolled (N)	14	97	385	42	66	32 (≥2.0 mg/kg)	40
ECOG PS 0 / 1	85.7% ECOG 1	46% / 54%	91.4% (ECOG 0 or 1)	28.6% / 71.4%	24.2% / 74.2%	37% / 59%	42.5% / 57.5%
Measurable Disease	100%	69%	48%	83%	59%	15.5% (C4 - C8)	40%
Prior Lines Median (Range)	4 (2 - 8)	4 (1, 9)	~4*	2 (1, 9)	~3 - 4*	4 (1, 13)	3 (2 - 7)
Prior Taxane	93%	85%	98%	98%	98.5%*	66%	100%
PSA50	25%	40% Low Dose (N=43)/ 59% High Dose (N=44)	46%	28.6% (N=42)	56%	52% (2.0 - 2.88 mg/kg) (N=23)	54% (N=39)
PSA90	25% (N=12)	19% Low Dose (N=43)/ 36% High Dose (N=44)	33% PSA80	21.4% (N=42)	24%*	26% (2.0 - 2.88 mg/kg) (N=23)	~10% (est.) (N=39)
PR (RECIST v1.1)	25% cPR, 33% uPR (N=12)	3% cPR Low Dose (N=30)/ 41% cPR High Dose (N=37)	51%	25.7% cPR (N=35)	21%	22% cPR (Dose Levels 1.4 - 2.88 mg/kg) (N=9)	12.5% cPR, 25% uPR (N=16)
Grade 3+ TEAE	64%	76%	53%	62%	48%	12.5% (TRAE)	56%
TRAE Disc.	14%	19%	11.9% (Lu-PSMA-617)	25%	3% hospitalization rate for adrenal insufficiency	3%	7%

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Novel Therapeutic Development Landscape for mCRPC - Sources

* Xencor Estimate

[1] Xencor.

[2] Interim Results From a Phase 1 Study of Xaluritamig (AMG 509), a STEAP1 x CD3 XmAb® 2+1 Immune Therapy, in Patients With Metastatic Castration Resistant Prostate Cancer (mCRPC), Kelly and Appleman et al.; Amgen, ESMO 2023.

[3] Lutetium-177–PSMA-617 for Metastatic Castration-Resistant Prostate Cancer, de Bono and Krause et al.; NEJM, Sept 2021.

[4] Lorigerlimab, a Bispecific PD-1 ×CTLA-4 DART® Molecule in Patients With Metastatic Castration-Resistant Prostate Cancer: A Phase 1 Expansion Cohort, Luke and Cybulska-Stopa et al.; MacroGenics, ASCO GU 2023.

[5] MK-5684 (ODM-208), a CYP11A1 inhibitor, in metastatic castration-resistant prostate cancer (mCRPC) patients with and without AR-LBD mutations: CYPIDES Phase 2 results; Fizazi and Antonarakis et al.; Merck, ASCO GU 2024.

[6] ARX517, an Anti-Prostate-Specific Membrane Antigen (PSMA) Antibody-Drug Conjugate (ADC), Demonstrates Promising Safety and Efficacy in Heavily Pre-Treated Patients With Metastatic Castration-Resistant Prostate Cancer (mCRPC); Shen and Tagawa et al.; Ambrx Biopharma, ESMO 2023.

[7] MGC018, an Anti-B7-H3 Antibody-Drug Conjugate (ADC), in Patients With Advanced Solid Tumors: Preliminary Results of Phase 1 Cohort Expansion; Shenderov and Lugowska et al.; MacroGenics ESMO 2021.

Vudalimab Monotherapy in Patients with mCRPC

Study XmAb717-05

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