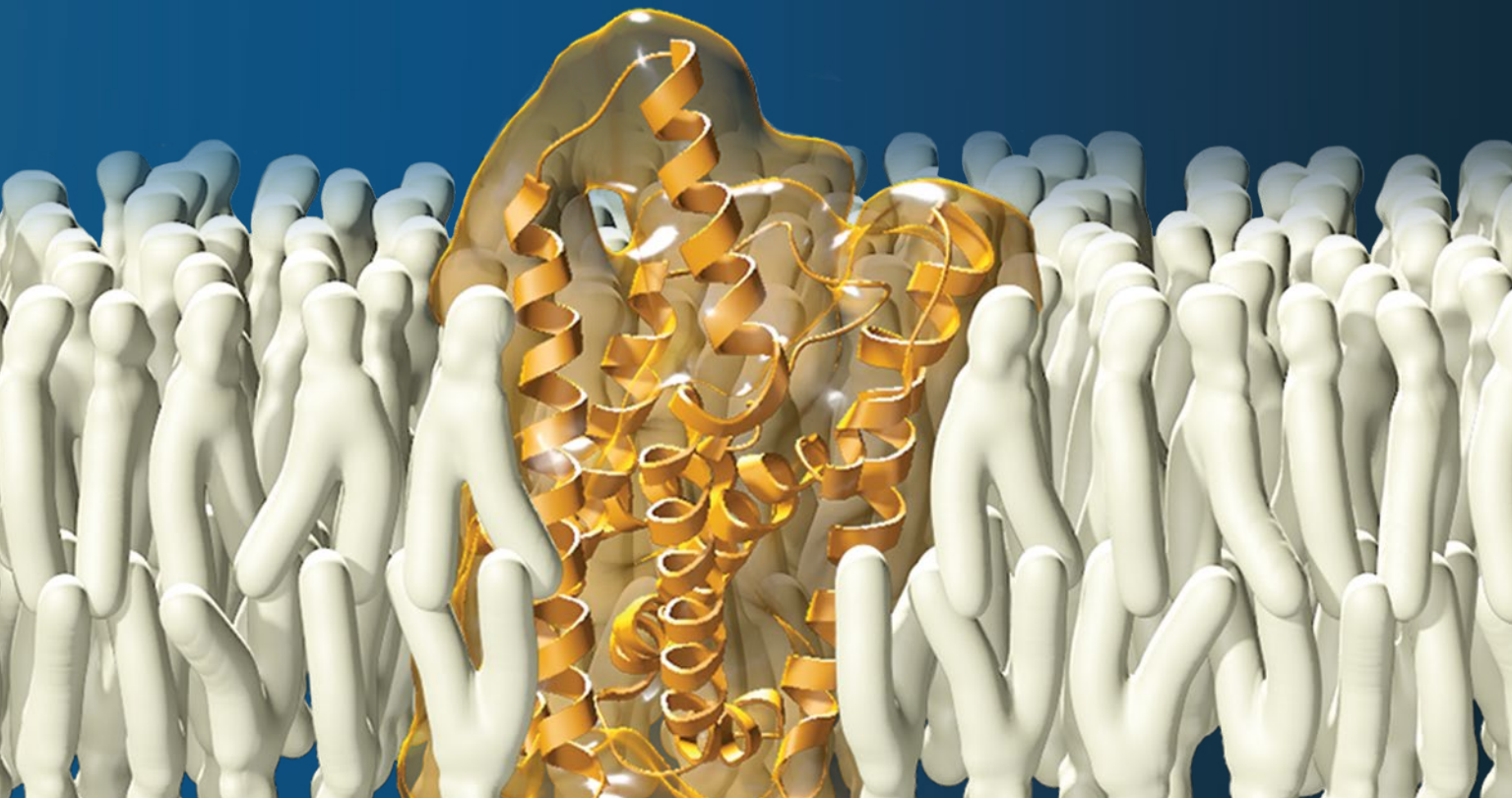
STEAP1:
A Therapeutic Target in mCRPC



Progression of Prostate Cancer Is Associated With Low Survival Rates[1]

Prostate cancer is a significant cause of cancer death in men worldwide [2,3]

~1.3 MILLION NEW PATIENTS

diagnosed and 360,000 estimated deaths due to prostate cancer **worldwide** in 2018[2]

~234,000 NEW PATIENTS

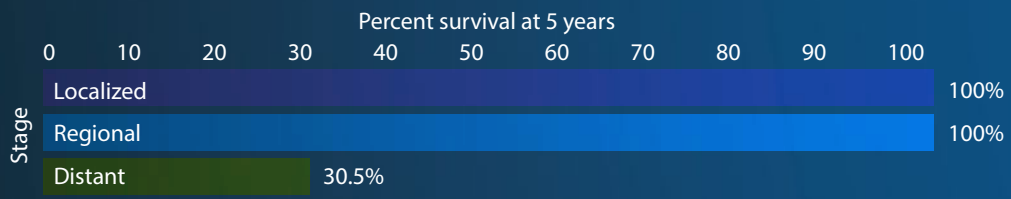
diagnosed and 33,000 estimated deaths due to prostate cancer in **North America** in 2018[2]

~450,000 NEW PATIENTS

diagnosed and 110,000 estimated deaths due to prostate cancer in the **EU** in 2018[2]

The average stage at which men are diagnosed with prostate cancer varies globally. Because of the limited screening for early disease detection in developing countries, men in these countries are more likely to be diagnosed at an advanced stage compared with men in developed countries.[4]

Metastatic prostate cancer is associated with reduced survival[5,*]



Prostate cancer is a continuum of progressive disease[3]

Prostate cancer is characterized by a defined disease continuum, in which patients eventually experience disease progression; up to 20% of men advance to castration-resistant prostate cancer (CRPC) and are no longer sensitive to hormonal therapy.[3,6,‡]

Of the men who advance to CRPC,

≥ 84% WILL HAVE METASTASES[6,†]

*SEER 5-year relative survival rates from 2009–2015 in the US.[5]
†Sites of metastases typically include bone, lymph nodes, liver, and lung.[1]
‡When CRPC is defined in terms of a rise in PSA levels following castration.[3]
SEER=Surveillance, Epidemiology, and End Results.

Innovative Mechanisms of Action Are Needed to Treat Metastatic Castration-Resistant Prostate Cancer (mCRPC), as Novel Hormonal Therapies Transition into the Hormone-Sensitive Prostate Cancer Setting[1,7]

For over 40 years, the mainstay of treatment in regional or advanced prostate cancer has been hormonal therapy, also known as androgen-deprivation therapy (ADT), either alone or in combination with chemotherapy.[3] However, most men with advanced prostate cancer become resistant to ADT, resulting in progression to CRPC.[8]

is the average length of ADT treatment prior to progression to CRPC[7,9]

1 IN 3 PATIENTS
with CRPC develop metastases within 2 years of diagnosis[6]

Progression to mCRPC is associated with poor outcomes[1,10]

~24 MONTHS predicted survival rate following progression to mCRPC[1,10]

mCRPC is associated with:[1,6]

Decreased quality of life

Increased risk of skeletal-related events, such as bone pain and fractures

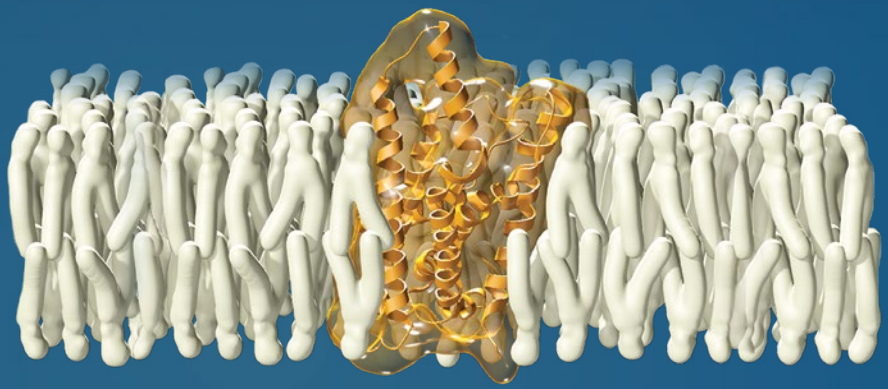
Novel hormonal therapies have improved outcomes in some patients with mCRPC; however, mCRPC remains an incurable and difficult to treat disease because patients may develop resistance to these newer therapies. As novel hormonal therapies transition into the HSPC setting, there continues to be a need to identify new targets for patients in the metastatic setting.[1,3]

HSPC, hormone-sensitive prostate cancer.

Overexpression of STEAP1 Drives Disease Progression in Prostate Cancer[11]

Six-transmembrane epithelial antigen of prostate 1 (STEAP1) is a membrane protein primarily expressed in the prostate tissue, where it is localized in the plasma membrane of epithelial cells located at cell to cell junctions.[12]

STEAP1 expression is low or absent in normal tissues, and its expression is increased in several types of human cancers.[11,12]



STEAP1 is overexpressed in **> 80% of prostate cancers**, including bone and lymph node metastases.[11-13]

Overexpression of STEAP1 is associated with:[11-13]

Worse prognosis in patients with prostate cancer

Higher risk/grade of disease[§]

Cellular proliferation and disease progression

[§]Gleason score (GS) is used to grade prostate cancers from GS ≤ 6 (overall low risk/grade 1) to GS 8–10 (high risk/grade 4–5).[14,15]

Targeting STEAP1 Is a Promising Strategy for Treating mCRPC[11,12]

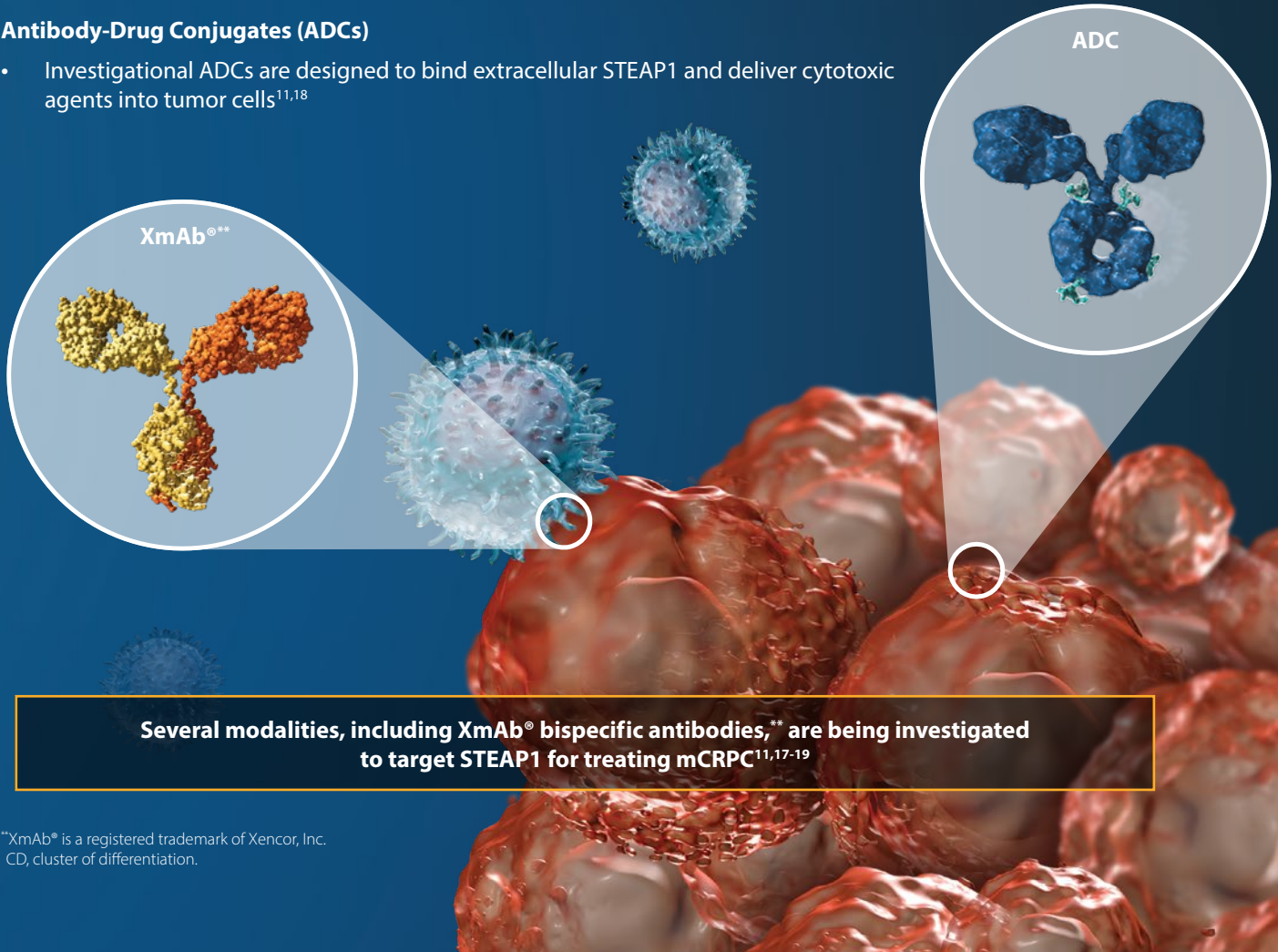
Due to its cell surface expression and role in disease progression, therapies that target STEAP1 are being investigated in clinical trials.[11,12]

XmAb® Bispecific Antibodies**

- Investigational XmAb® bispecific antibodies** are designed to bind simultaneously to STEAP1 on tumor cells and CD3 on cytotoxic T cells[16,17]

Antibody-Drug Conjugates (ADCs)

- Investigational ADCs are designed to bind extracellular STEAP1 and deliver cytotoxic agents into tumor cells[11,18]

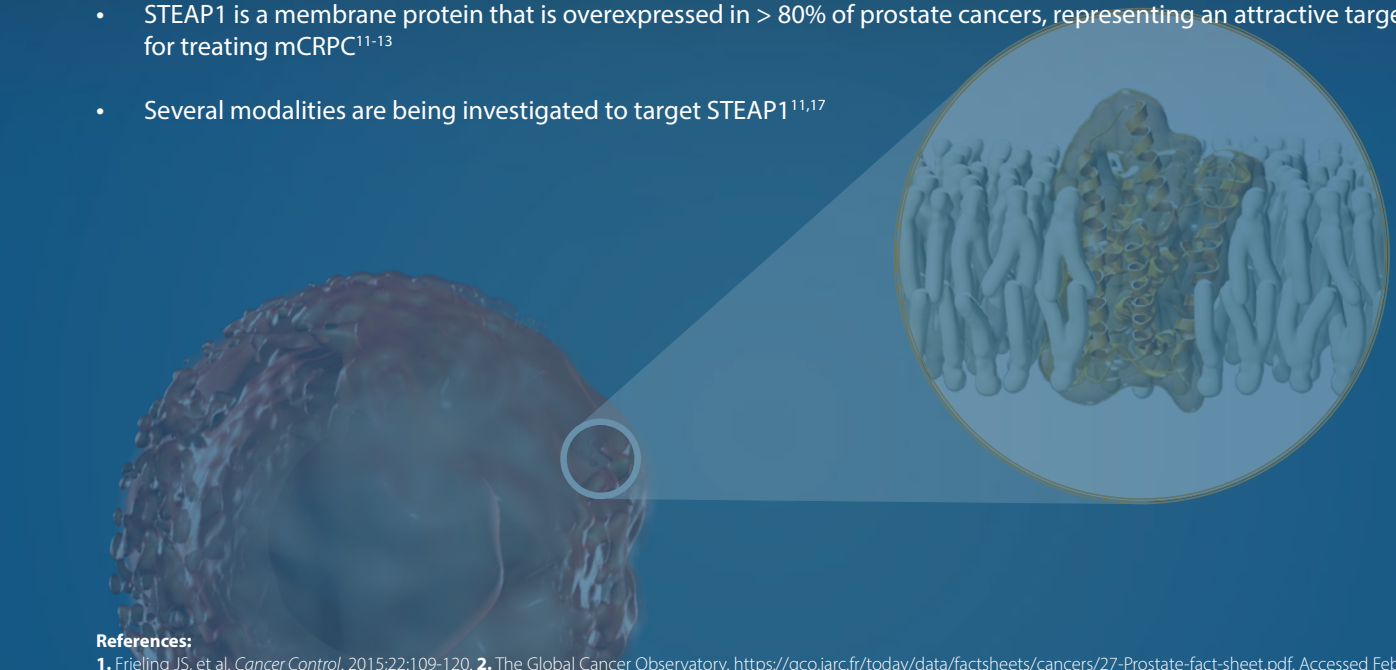


Several modalities, including XmAb® bispecific antibodies, are being investigated to target STEAP1 for treating mCRPC[11,17-19]**

**XmAb® is a registered trademark of Xencor, Inc.
CD, cluster of differentiation.

Key Takeaways

- mCRPC remains an incurable and difficult to treat form of prostate cancer[1]
- STEAP1 is a membrane protein that is overexpressed in > 80% of prostate cancers, representing an attractive target for treating mCRPC[11-13]
- Several modalities are being investigated to target STEAP1[11,17]



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1. Frieling JS, et al. *Cancer Control*. 2015;22:109-120. **2.** The Global Cancer Observatory. https://gco.iarc.fr/today/data/factsheets/cancers/27-Prostate-fact-sheet.pdf. Accessed February 21, 2020. **3.** Crawford ED, et al. *Urol Oncol*. 2017;35S:S1-S13. doi:10.1016/j.urolonc.2017.01.020. **4.** Taitt HE. *Am J Mens Health*. 2018;12:1807-1823. **5.** National Cancer Institute. https://seer.cancer.gov/statfacts/html/prost.html. Accessed March 4, 2020. **6.** Kirby M, et al. *Int J Clin Pract*. 2011;65:1180-1192. **7.** Sumanasuriya S, et al. *Cold Spring Harb Perspect Med*. 2018;8:a030635. doi:10.1101/cshperspect.a030635. **8.** Nouri M, et al. *Front Oncol*. 2014;4:370. doi:10.3389/fonc.2014.00370. **9.** Petrylak DP, et al. *N Engl J Med*. 2004;351:1513-1520. **10.** Kantoff PW, et al. *N Engl J Med*. 2010;363:411-422. **11.** Barroca-Ferreira J, et al. *Curr Cancer Drug Targets*. 2018;18:222-230. **12.** Gomes IM, et al. *Mol Cancer Res*. 2012;10:573-587. **13.** Ihlaseh-Catalano SM, et al. *Histopathology*. 2013;63:678-685. **14.** Epstein JI, et al. *Am J Surg Pathol*. 2016;40:244-252. **15.** Bravaccini S, et al. *Sci Rep*. 2018;8:4254. doi:10.1038/s41598-018-22594-1. **16.** Xencor. https://www.xencor.com/technology/bispecific-fc-domains/. Accessed March 3, 2020. **17.** Xencor. https://investors.xencor.com/news-releases/news-release-details/xencor-reports-third-quarter-2019-financial-results. Accessed March 3, 2020. **18.** Danila DC, et al. *J Clin Oncol*. 2019;37:3518-3527. **19.** ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT04221542. Accessed March 4, 2020.

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