STEAP1:
A Therapeutic Target in mCRPC

AMGEN®

Oncology

Do not copy or distribute. © 2020 Amgen Inc. All rights reserved.

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

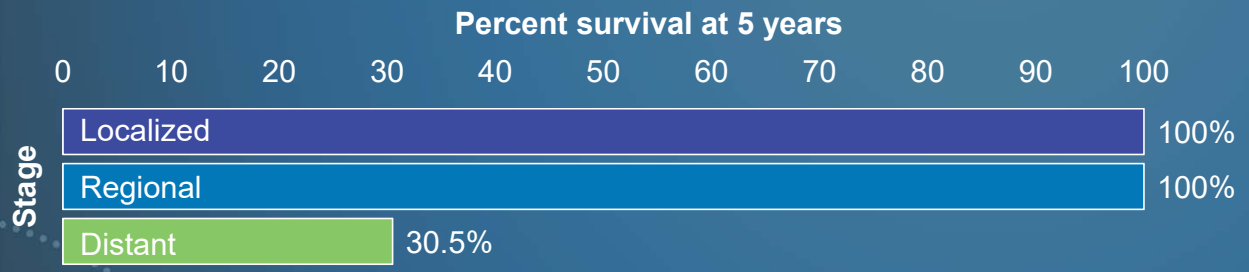
Prostate Cancer Is a Significant Cause of Cancer Death in Men Worldwide[2,3]

~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]

Metastatic Prostate Cancer Is Associated With Reduced Survival[4,*]



- The average stage at which men are diagnosed with prostate cancer varies globally[5]
- 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[5]

*SEER 5-year relative survival rates from 2009–2015 in the US.[4]

SEER=Surveillance, Epidemiology, and End Results.

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.** National Cancer Institute. https://seer.cancer.gov/statfacts/html/prost.html. Accessed March 4, 2020. **5.** Taitt HE. *Am J Mens Health*. 2018;12:1807-1823.

Do not copy or distribute. © 2020 Amgen Inc. All rights reserved.

AMGEN
Oncology

Prostate Cancer Is a Continuum of Progressive Disease[1]

Prostate Cancer Is Characterized by a Defined Disease Continuum, in Which Patients Eventually Experience Disease Progression[1,2]

- Up to 20% of men advance to castration-resistant prostate cancer (CRPC) and are no longer sensitive to hormonal therapy[1,2,*]

Of the men who advance to CRPC,

≥ 84% WILL HAVE METASTASES[2,†]

Progression to Metastatic CRPC (mCRPC) Is Associated With Poor Outcomes[3,4]

~24 MONTHS

predicted survival rate following progression to mCRPC[3,4]

mCRPC IS ASSOCIATED WITH:[2,3]

Decreased quality of life

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

*When CRPC is defined in terms of a rise in PSA levels following castration.[1] †Sites of metastases typically include bone, lymph nodes, liver, and lung.[3]

PSA, prostate-specific antigen.

1. Crawford ED, et al. *Urol Oncol*. 2017;35S:S1-S13. doi:10.1016/j.urolonc.2017.01.020. **2.** Kirby M, et al. *Int J Clin Pract*. 2011;65:1180-1192. **3.** Frieling JS, et al. *Cancer Control*. 2015;22:109-120. **4.** Kantoff PW, et al. *N Engl J Med*. 2010;363:411-422.

Do not copy or distribute. © 2020 Amgen Inc. All rights reserved.

AMGEN® Oncology

Innovative Mechanisms of Action Are Needed to Treat mCRPC[1,2]

Most Men With Advanced Prostate Cancer Become Resistant to ADT, Resulting in Progression to CRPC[3]

- 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[4]

is the average length of ADT treatment prior to progression to CRPC[2,5]

1 IN 3 PATIENTS

with CRPC develop metastases within 2 years of diagnosis[6]

- 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 therapies[1,4]
- As novel hormonal therapies transition into the earlier hormone-sensitive setting, there continues to be a need to identify new targets for patients in the metastatic setting[1,4]

CRPC, castration-resistant prostate cancer; mCRPC, metastatic castration-resistant prostate cancer.

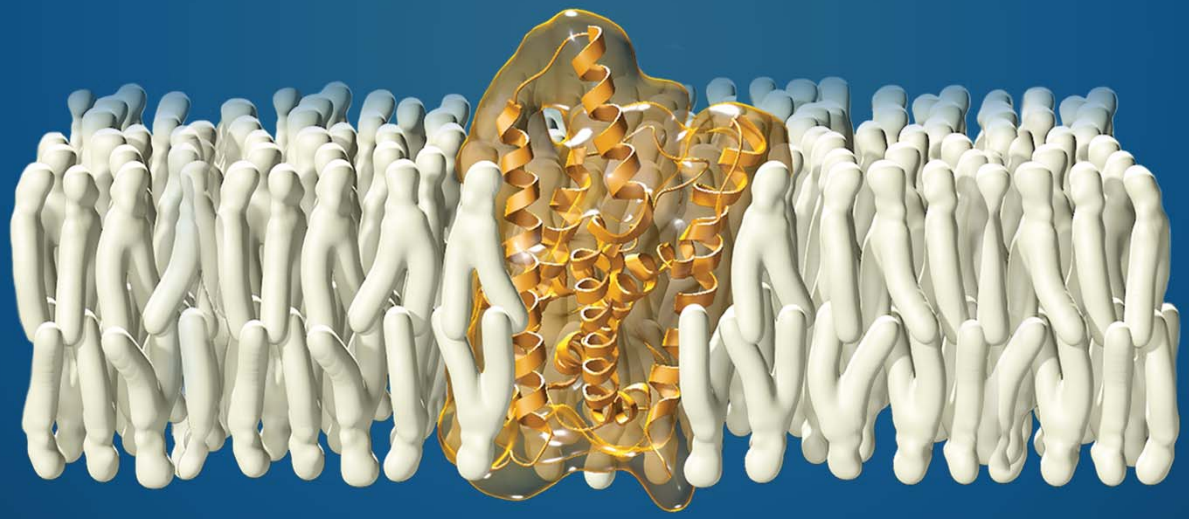
1. Frieling JS, et al. *Cancer Control*. 2015;22:109-120. **2.** Sumanasuriya S, et al. *Cold Spring Harb Perspect Med*. 2018;8:a030635. doi:10.1101/cshperspect.a030635. **3.** Nouri M, et al. *Front Oncol*. 2014;4:370. doi:10.3389/fonc.2014.00370. **4.** Crawford ED, et al. *Urol Oncol*. 2017;35S:S1-S13. doi:10.1016/j.urolonc.2017.01.020. **5.** Petrylak DP, et al. *N Engl J Med*. 2004;351:1513-1520. **6.** Kirby M, et al. *Int J Clin Pract*. 2011;65:1180-1192.

Do not copy or distribute. © 2020 Amgen Inc. All rights reserved.

AMGEN
Oncology

STEAP1 Is a Membrane Protein Primarily Expressed in Prostate Tissue[1]

- Six-transmembrane epithelial antigen of prostate 1 (STEAP1) is localized in the plasma membrane of epithelial cells located at cell to cell junctions and is primarily expressed in prostate tissue[1]
- STEAP1 expression is low or absent in normal prostate tissue with weak cytoplasmic/submembrane staining in liver, testis, thyroid, and lung macrophages[1-3]
  - However, its expression is increased in several types of human cancers, including prostate cancer[1,2]



1. Gomes IM, et al. *Mol Cancer Res*. 2012;10:573-587. **2.** Barroca-Ferreira J, et al. *Curr Cancer Drug Targets*. 2018;18:222-230. **3.** Nolan-Stevaux O. Presented at: American Association for Cancer Research Virtual Annual Meeting I; April 27-28, 2020. Abstract DDT02-04.

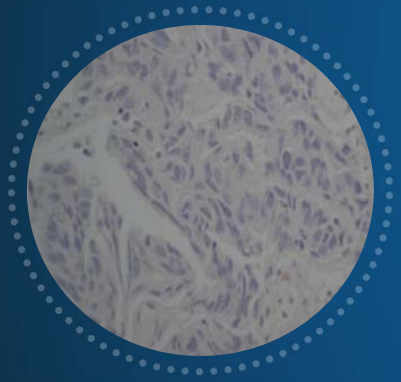
Do not copy or distribute. © 2020 Amgen Inc. All rights reserved.

AMGEN®
Oncology

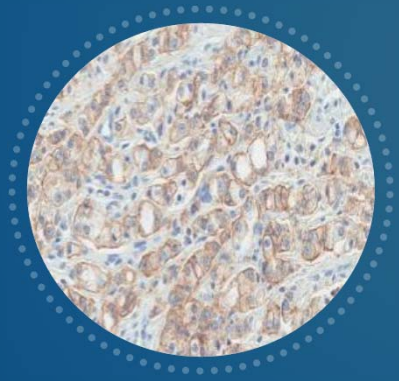
STEAP1 Is a Differentially Expressed Tumor-Associated Antigen in Prostate Cancer[1]

In mCRPC tumor samples, STEAP1 is expressed in primary tumors and metastatic tumors[1]

Prostate Cancer (Negative Control)[2]



Prostate Cancer (STEAP1)[1]



STEAP1 Membrane Detection in mCRPC Tumor Samples by Immunohistochemistry[1]

Samples	STEAP1 % Positive
Primary prostate tumor (n=88)	80
mCRPC bone metastases (n=25)*	84
mCRPC liver metastases (n=27)*	81
Other mCRPC metastases (n=62)*	94

*University of Washington – warm autopsy program samples.[1]

mCRPC, metastatic castration-resistant prostate cancer; STEAP1, six-transmembrane epithelial antigen of prostate 1.

1. Nolan-Stevaux O. Presented at: American Association for Cancer Research Virtual Annual Meeting I; April 27-28, 2020. Abstract DDT02-04. 2. Gomes LM, et al. *Urol Oncol.* 2014;32:53.e23-53.e29.

Do not copy or distribute. © 2020 Amgen Inc. All rights reserved.

AMGEN
Oncology

Overexpression of STEAP1 Correlates With Disease Progression in Prostate Cancer[1]

STEAP1 is induced by the androgen receptor and is overexpressed in **> 80% of prostate cancers**, including bone and lymph node metastases[1-4]

Overexpression of STEAP1 Is Associated With:[1-3]

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).[5,6]

STEAP1, six-transmembrane epithelial antigen of prostate 1.

1. Barroca-Ferreira J, et al. *Curr Cancer Drug Targets*. 2018;18:222-230. **2.** Gomes IM, et al. *Mol Cancer Res*. 2012;10:573-587. **3.** Ihlaseh-Catalano SM, et al. *Histopathology*. 2013;63:678-685. **4.** Nolan-Stevaux O. Presented at: American Association for Cancer Research Virtual Annual Meeting I; April 27-28, 2020. Abstract DDT02-04. **5.** Epstein JI, et al. *Am J Surg Pathol*. 2016;40:244-252. **6.** Bravaccini S, et al. *Sci Rep*. 2018;8:4254. doi:10.1038/s41598-018-22594-1.

Do not copy or distribute. © 2020 Amgen Inc. All rights reserved.

AMGEN®
Oncology

Targeting STEAP1 Is A Potential Strategy for Treating mCRPC[1,2]

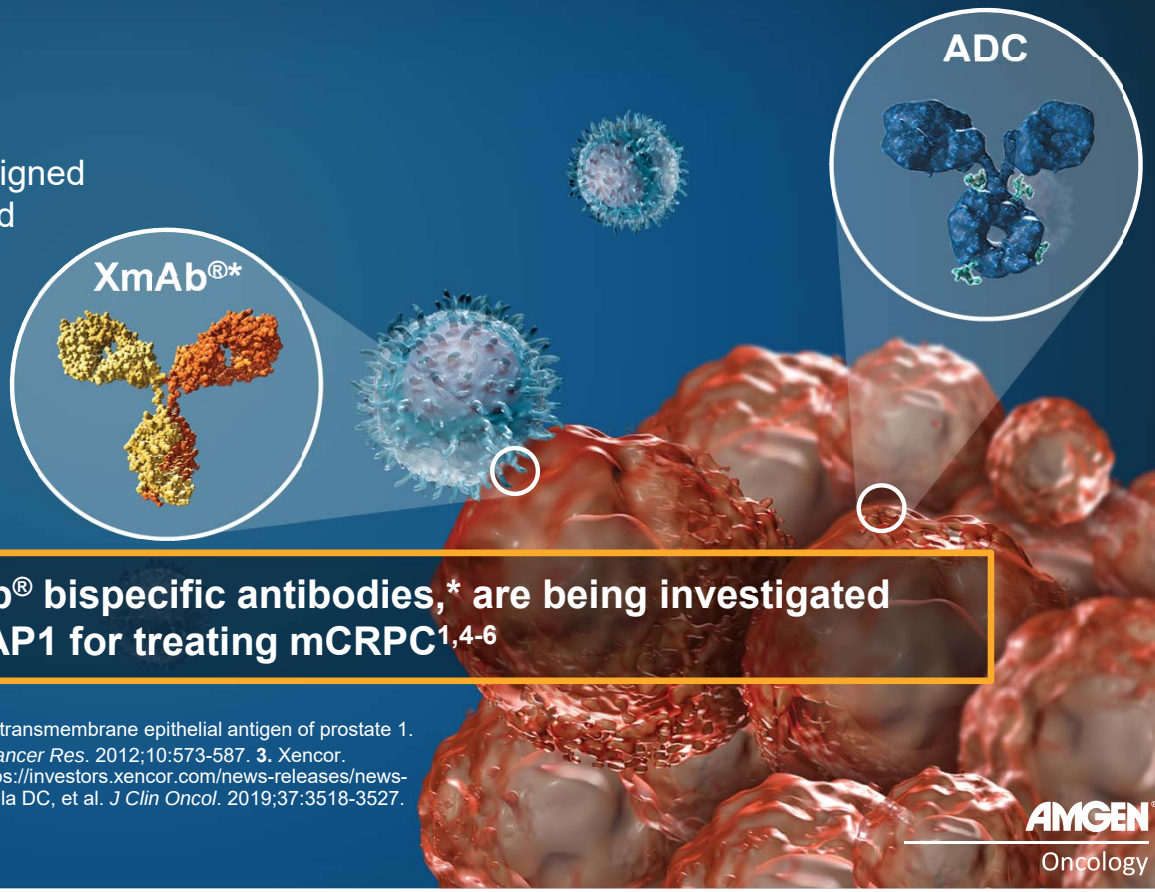
Due to its cell surface expression and role in disease progression, therapies that target STEAP1 are being investigated in clinical trials[1,2]

XmAb® Bispecific Antibodies*

- Investigational XmAb® bispecific antibodies* are designed to bind simultaneously to STEAP1 on tumor cells and CD3 on cytotoxic T cells[3,4]

Antibody-Drug Conjugates (ADCs)

- Investigational ADCs are designed to bind extracellular STEAP1 and deliver cytotoxic agents into tumor cells[1,5]



Several modalities, including XmAb® bispecific antibodies,* are being investigated to target STEAP1 for treating mCRPC[1,4-6]

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

CD, cluster of differentiation; mCRPC, metastatic castration-resistant prostate cancer; STEAP1, six-transmembrane epithelial antigen of prostate 1.

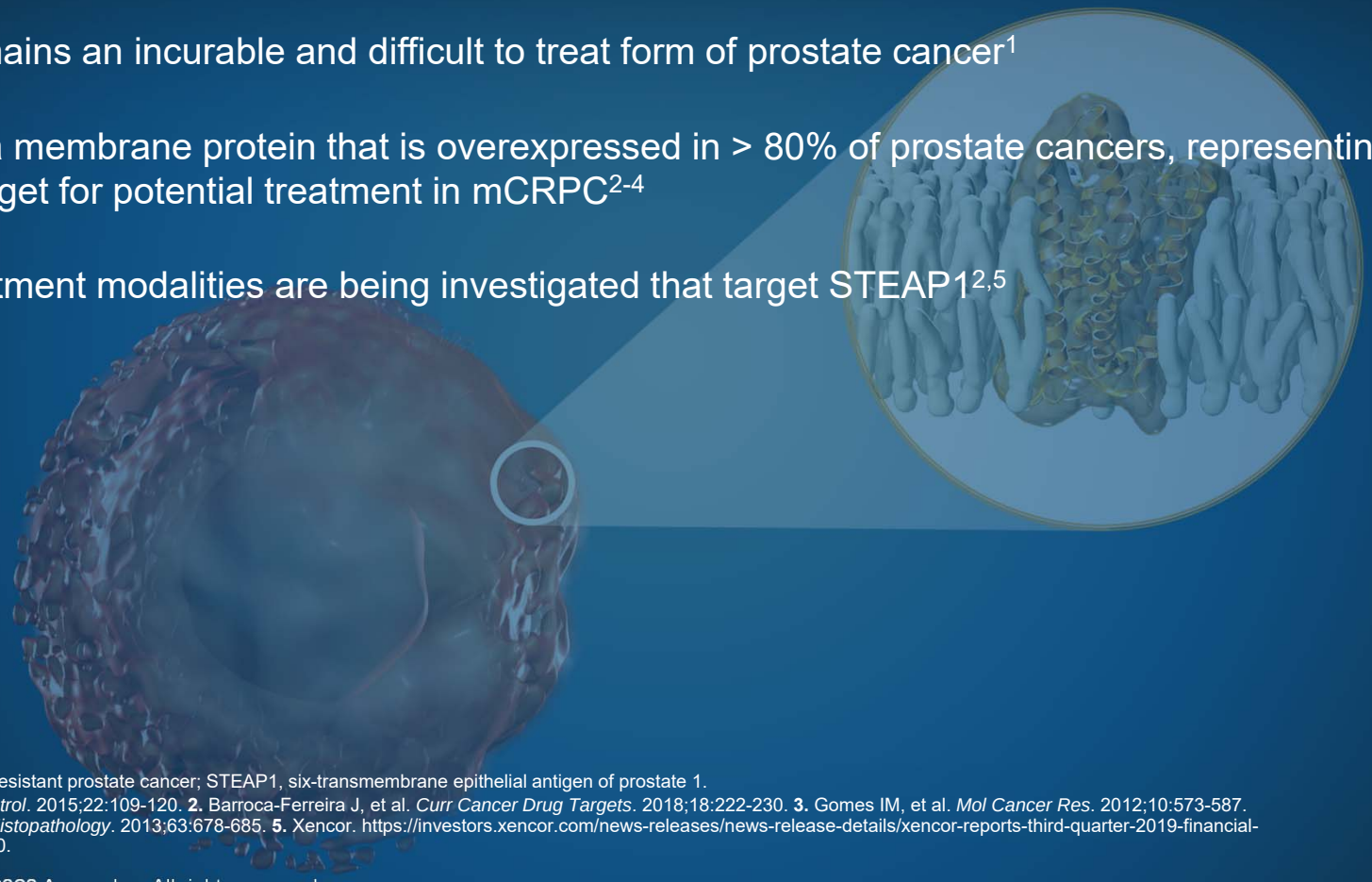
1. Barroca-Ferreira J, et al. *Curr Cancer Drug Targets*. 2018;18:222-230. **2.** Gomes IM, et al. *Mol Cancer Res*. 2012;10:573-587. **3.** Xencor. https://www.xencor.com/technology/bispecific-fc-domains/. Accessed March 3, 2020. **4.** Xencor. https://investors.xencor.com/news-releases/news-release-details/xencor-reports-third-quarter-2019-financial-results. Accessed March 3, 2020. **5.** Danila DC, et al. *J Clin Oncol*. 2019;37:3518-3527. **6.** ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT04221542. Accessed March 4, 2020.

Do not copy or distribute. © 2020 Amgen Inc. All rights reserved.

AMGEN® Oncology

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 potential treatment in mCRPC[2-4]
- Several treatment modalities are being investigated that target STEAP1[2,5]



mCRPC, metastatic castration-resistant prostate cancer; STEAP1, six-transmembrane epithelial antigen of prostate 1.

1. Frieling JS, et al. *Cancer Control*. 2015;22:109-120. **2.** Barroca-Ferreira J, et al. *Curr Cancer Drug Targets*. 2018;18:222-230. **3.** Gomes IM, et al. *Mol Cancer Res*. 2012;10:573-587. **4.** Ihlaseh-Catalano SM, et al. *Histopathology*. 2013;63:678-685. **5.** Xencor. https://investors.xencor.com/news-releases/news-release-details/xencor-reports-third-quarter-2019-financial-results. Accessed March 3, 2020.

Do not copy or distribute. © 2020 Amgen Inc. All rights reserved.

AMGEN
Oncology

Disclosures

This slide deck contains forward-looking statements that are based on Amgen's current expectations and beliefs and are subject to a number of risks, uncertainties, and assumptions that could cause actual results to differ materially from those described. All statements, other than statements of historical fact, are statements that could be deemed forward-looking statements. Forward-looking statements involve significant risks and uncertainties, including those more fully described in the Risk Factors found in the most recent Annual Report on Form 10-K and periodic reports on Form 10-Q and Form 8-K filed by Amgen with the U.S. Securities and Exchange Commission, and actual results may materially vary. Except where otherwise indicated, Amgen is providing this information as of June 29, 2020 and does not undertake any obligation to update any forward-looking statements contained in this booklet as a result of new information, future events, or otherwise.

Do not copy or distribute. © 2020 Amgen Inc. All rights reserved.