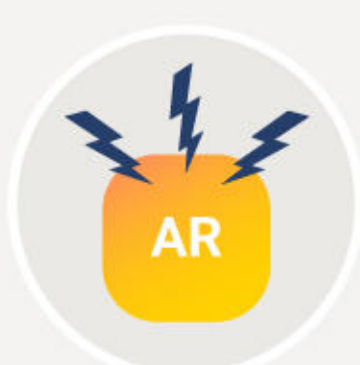


Augmenting AR inhibition in prostate cancer: Rationale for targeting the cell cycle

The androgen signaling pathway is a key driver of PCa pathogenesis and progression¹.

Patients with mCRPC progress due to **continued activation of the androgen receptor**



despite castrate levels of circulating testosterone²

Average life expectancy **2-3 YEARS**³



Patients with mCRPC experience disease progression and cancer-specific mortality despite recent improvements^{4,5}

Novel approaches are needed to²:

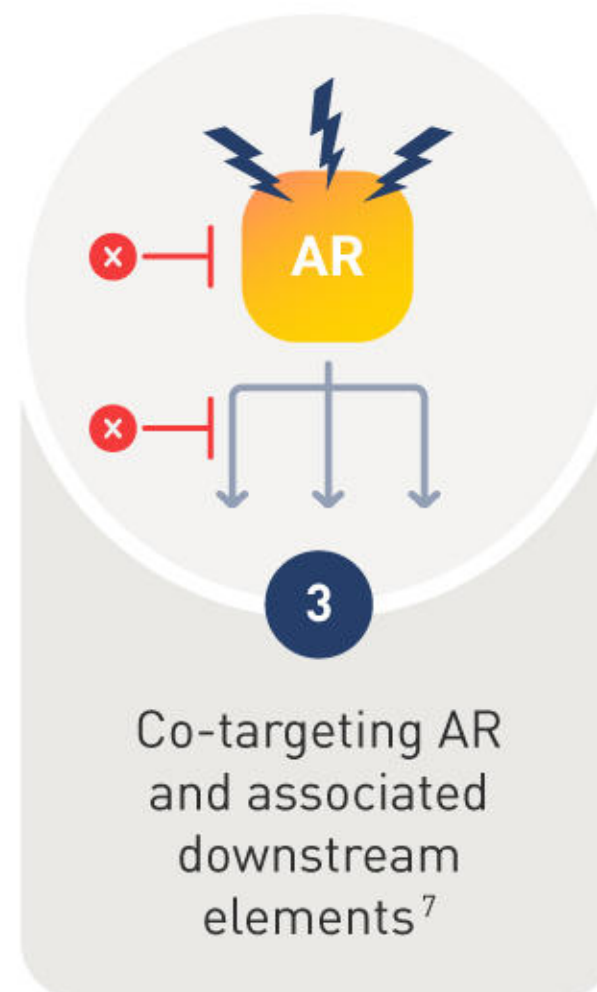
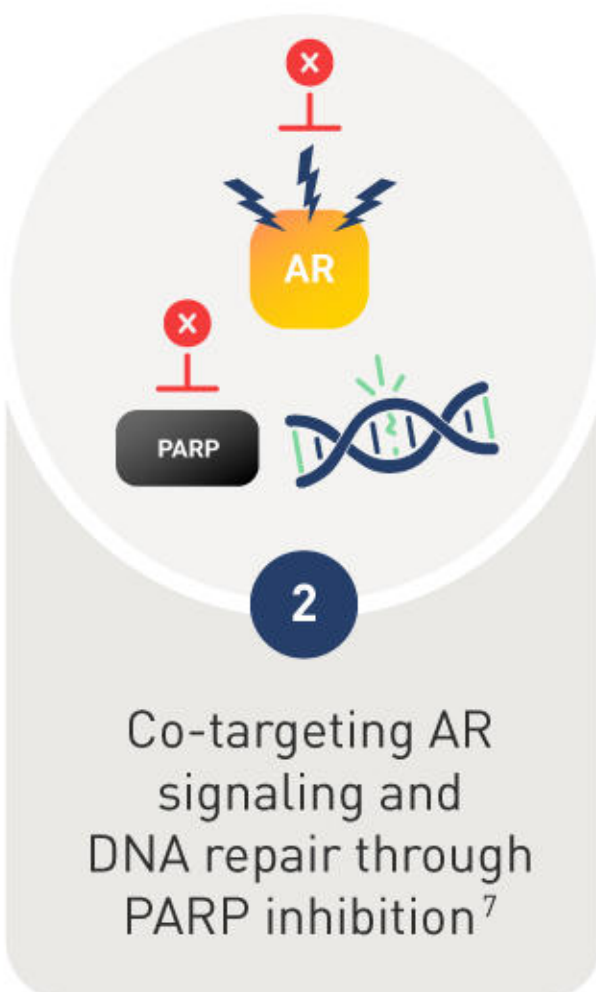


Improve disease control

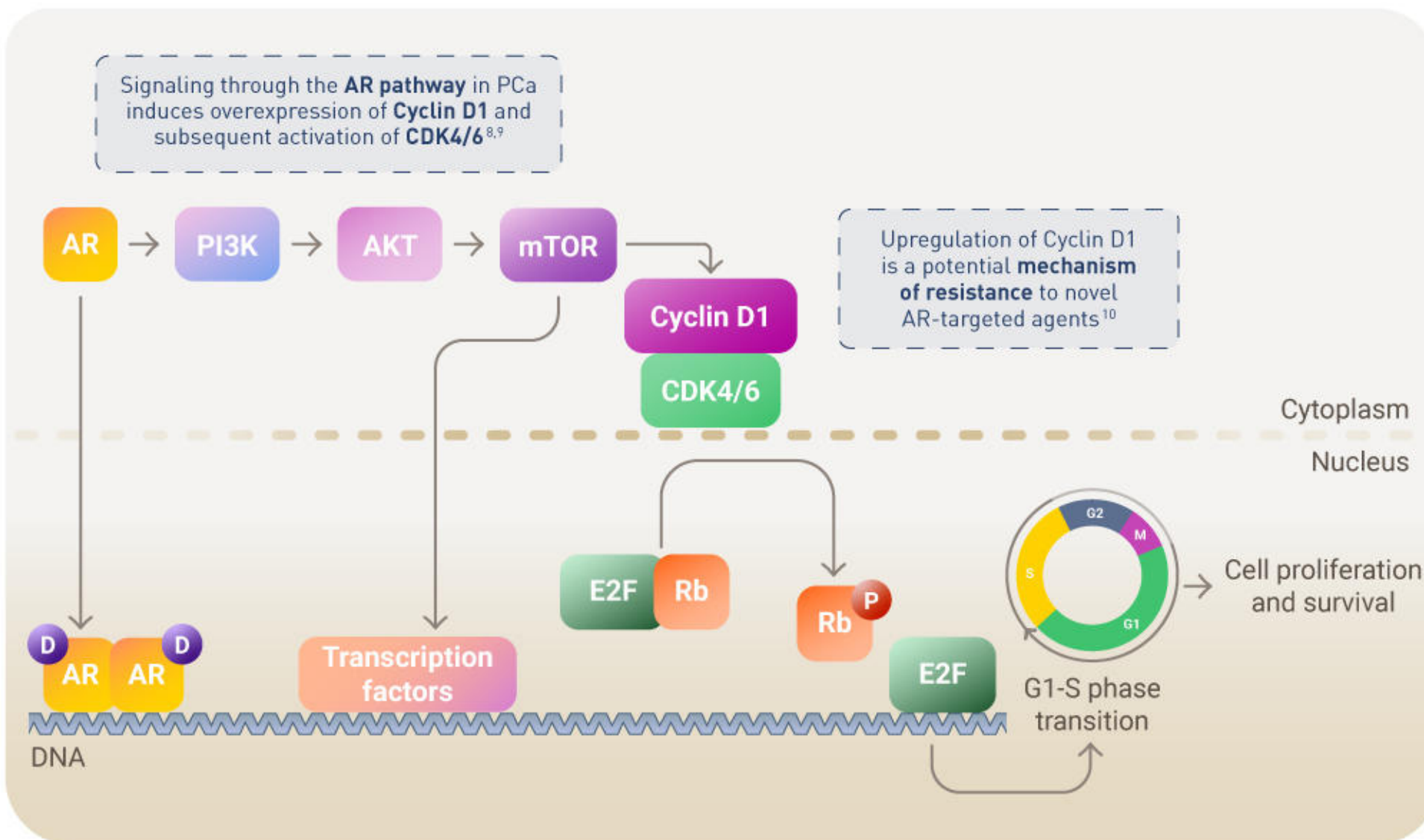


Delay the need for chemotherapy

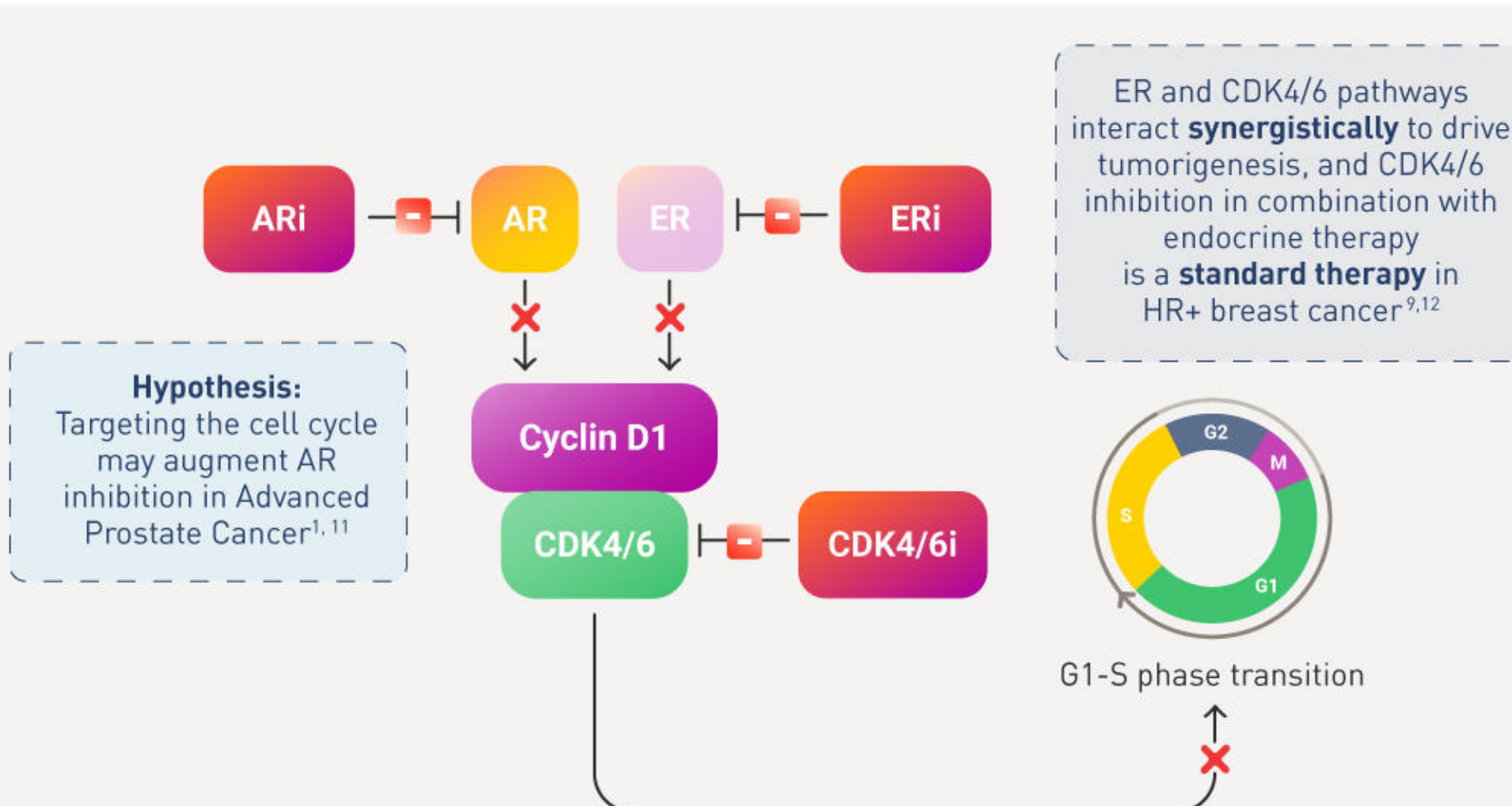
Examples of current and emerging approaches in advanced PCa management:



The interaction between AR and other molecular pathways results in PCa cell cycle progression and cancer proliferation



Biological parallels between PCa and HR+ BCa: continued ER and AR signaling drive uncontrolled cellular proliferation by activating CDK4 & 6^{8,9}



Dual inhibition of AR and CDK4/6 is being actively investigated in clinical trials

AR=androgen receptor; Ari=androgen receptor inhibitor; BCa=breast cancer; CDK4/6=cyclin dependent kinase 4 & 6 inhibitor; E2F=E2F family of transcription factors; ER=estrogen receptor; Eri=estrogen receptor inhibitor; HR+=hormone receptor positive; mCRPC= metastatic castrate resistant prostate cancer; PARP=poly (ADP-ribose) polymerase; PCa=prostate cancer; PI3K=phosphoinositide 3-kinase; PSMA=prostate-specific membrane antigen; Rb=retinoblastoma protein

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