

AROUND THE CORNER:

Top Developments in Genitourinary Cancer Therapeutics

The third quarter of 2026 was defined less by new readouts than by regulatory follow-through. Data from ASCO GU and the ASCO Annual Meeting turned into FDA approvals in muscle-invasive bladder cancer and metastatic hormone-sensitive prostate cancer, and biomarker-selected strategies moved firmly into routine practice. The following seven developments, ranked by near-term clinical impact, are the most consequential non-renal GU advances of the quarter.

1. Enfortumab Vedotin Plus Pembrolizumab Approved for All Cystectomy-Eligible MIBC Representative trial: KEYNOTE-B15/EV-304. FDA approval July 10, 2026

Last quarter we described KEYNOTE-B15 as the most practice-changing readout of ASCO GU. The FDA has now acted on it. It expanded perioperative enfortumab vedotin plus pembrolizumab (EVP) to adults with MIBC who are candidates for cystectomy, regardless of cisplatin eligibility.

In the phase 3 trial of 808 cisplatin-eligible patients, EVP outperformed neoadjuvant gemcitabine-cisplatin across every major endpoint: event-free survival HR 0.53 (2-year EFS 79.4% vs 66.2%) overall survival HR 0.65 pathologic complete response 55.8% vs 32.5%.

It is the first non-platinum regimen in roughly 25 years to displace cisplatin-based chemotherapy in this setting. For the first time, the perioperative decision in MIBC no longer begins with cisplatin eligibility.

2. Lutetium-177 PSMA-617 Moves Into Hormone-Sensitive Disease Representative trial: PSMAddition (NCT04720157). FDA approval July 31, 2026

The FDA approved [¹⁷⁷Lu]Lu-PSMA-617 in combination with an androgen receptor pathway inhibitor for PSMA-positive metastatic prostate cancer that is androgen pathway modulation-naïve or -sensi-

tive. In PSMAddition (n=1,144), adding radioligand therapy to an ARPI improved radiographic progression-free survival (HR 0.72; 95% CI 0.58–0.90; P=.002). Median rPFS was not reached in either arm, and overall survival data remain immature.

This approval moves PSMA-targeted radioligand therapy from late-line castration-resistant disease into the hormone-sensitive setting. That will increase demand for PSMA PET imaging and nuclear medicine capacity well before the survival question is settled.

3. Capivasertib Brings PTEN Testing Into mHSPC Representative trial: CAPitello-281. FDA approval June 2026

After a favorable 7–1 ODAC vote in April, the FDA approved capivasertib plus abiraterone and prednisone for PTEN-deficient metastatic hormone-sensitive prostate cancer. Median rPFS was 33.2 months, compared with 25.7 months for abiraterone alone (HR 0.81; P=.034).

About one in four men with newly diagnosed mHSPC have PTEN-deficient tumors. The approval makes PTEN immunohistochemistry at diagnosis a practical necessity. It is also the first AKT-targeted therapy in prostate cancer.

4. TALAPRO-3 Extends PARP Inhibition Into Castration-Sensitive Disease Representative trial: TALAPRO-3. Phase 3 results at ASCO 2026; FDA Priority Review July 22, 2026

In patients with metastatic castration-sensitive prostate cancer and homologous recombination repair (HRR) gene alterations, talazoparib plus enzalutamide cut the risk of radiographic progression or death by about half compared with enzalutamide alone (HR 0.481; P<.0001). Median rPFS was not reached, versus 45.8 months in the control arm.

With Priority Review granted, a PARP inhibitor–ARPI combination in the castration-sensitive setting appears likely. HRR testing will then be needed at the point of metastatic di-



agnosis, not only after castration resistance.

5. Perioperative Apalutamide Reaches the ASCO Plenary Representative trial: PROTEUS (NCT03767244). Phase 3 results presented as LBA1, ASCO 2026

PROTEUS randomized 2,109 men with high-risk localized or locally advanced prostate cancer undergoing radical prostatectomy to perioperative apalutamide plus ADT or placebo plus ADT. Metastasis-free survival improved significantly (HR 0.80; 5-year MFS 78.2% vs 73.5%), and pathologic complete response rose from 1% to 8.9%.

The absolute MFS difference is modest, but this is the first phase 3 evidence that intensifying hormonal therapy around surgery improves a meaningful long-term endpoint. It may support apalutamide plus ADT with prostatectomy as a new standard for high-risk patients choosing surgery.

6. ctDNA-Guided Adjuvant Therapy Arrives in Bladder Cancer Representative trial: IMvigor011. FDA approval May 15, 2026

The FDA approved adjuvant atezolizumab for patients with MIBC who have ctDNA-defined molecular residual disease after radical cystec-

tomy. A companion diagnostic, Signatera CDx, was approved at the same time. In the randomized, placebo-controlled trial (n=250), atezolizumab improved disease-free survival (median 9.9 vs 4.8 months; HR 0.64) and overall survival (median 32.8 vs 21.1 months; HR 0.59).

It is the first approval in solid tumors that uses a molecular residual disease assay to select patients for adjuvant immunotherapy. It is likely a template for other GU malignancies.

7. EV-302 Five-Year Data Suggest a Survival Plateau Representative trial: EV-302 / EV-103. Long-term follow-up at ASCO 2026

Extended follow-up of first-line EVP in metastatic urothelial carcinoma showed about 40% of patients alive at five years. Among complete responders, 83.6% maintained their response through four years, and the survival curve began to flatten at around 3.5 years.

For a disease in which metastatic five-year survival was once measured in single digits, these data raise a question that was hard to imagine only a few years ago: whether some patients with metastatic urothelial cancer may be functionally cured.