PacificEdge

INVESTOR UPDATE

APRIL 2025

INSIDE

LETTER FROM THE CEO

Guideline inclusion validates and accelerates strategy

Dear Shareholders,

The American Urological Association's (AUA) 2025 amendment to the microhematuria guideline was an important moment for the AUA, and highly consequential for urologists, healthcare payers and providers of advanced non-invasive urine-based diagnostics worldwide. It was particularly consequential for Pacific Edge, with Cxbladder Triage receiving a 'Grade A'[1] recommendation in the guideline and specific language on its use.

The amendments stand in sharp contrast to the 2020 guideline, which guided against the use of urine-based biomarkers in lieu of a cystoscopy. In making the change, the AUA has demonstrated its determination to support innovation in urological practice and improvements to the existing standard of care by integrating genomic biomarkers as an alternative for physicians to consider as part of their evaluation of hematuria patients. It is a significant move that aligns the AUA guideline with established practices for prostate, breast, colon and other cancers. It also offers significant benefits to patients, reducing the burden of unnecessary cystoscopies in lower risk patients and improving access to care for a greater number of patients.

Of importance to investors is that the language used in the guideline is among the strongest that could have been envisaged given the available published evidence, the most significant of which is our STRATA randomized controlled study[2]. We will publish more clinical utility evidence for Triage Plus (the focus of the CREDIBLE study) (see page 9) as we look to further expand the indications for our tests in line with our long-term goal to establish Cxbladder as the preferred urine-biomarker for genomic risk stratification of hematuria patients.

Meanwhile, the AUA's recognition of Cxbladder Triage as the only biomarker with 'Grade A' evidence sends a very strong message to the market.

"The guideline clearly marks the 'moat' around our business and that we have no genuine peers."

We have long maintained that the quality of our clinical evidence establishes the greatest possible barrier for our competitors. This recommendation reinforces our first-mover advantage. Meanwhile we are further differentiated from other urine-based biomarkers in hematuria evaluation by the intended use to risk stratify microhematuria populations. Other tests have only established utility as adjunctive tests to resolve atypical cytologies and equivocal cystoscopies. These clear points of difference profoundly mark the 'moat' around our business and that we have no current peers. This achievement, driven by our Clinical Science team, underscores their pivotal role in creating long-term value for our shareholders.

From a business perspective, the guideline is a substantial strategic milestone on which to build our commercial operations. We expect the guideline to catalyze increased testing volume and revenue despite coverage uncertainty. Similarly, we expect this to drive medical policy and commercial contracting conversations with the vast number of healthcare plans in the US such as those with Blue Cross Blue Shield we highlighted in the Q3 25 update in January. It also future proofs Triage against an ever-increasing evidence threshold for reimbursement, and it stands to entrench reliable reimbursement of Cxbladder, so that we can focus on scaling our commercial activities profitably without the distraction of reimbursement risk.

The biggest short-term opportunity is to leverage the guideline language in our ongoing policy dialogue and legal action with Novitas and our engagement with the Centers for Medicare and Medicaid Services (CMS) over the adverse 'Genetic Testing in Oncology: Specific Tests' (L39365) local coverage determination (LCD) (see page 3). This LCD, released in January, and the uncertainty created by its predecessor 'Genetic Testing for Oncology' (DL39365), have continued to limit the growth of our US business to a rate well below its potential (see page 3).

[1] The AUA defines 'Grade A' evidence as evidence with a high certainty rating and notes evidence of this grade makes it "very confident that the true effect lies close to that of the estimate of the effect".
[2] Lotan Y, Daneshmand S, Shore N, Black P, Scarpato KP, Patel A, Lough T, Shoskes DA, Raman JD. A Multicenter Prospective Randomized Controlled Trial Comparing Cxbladder Triage to Cystoscopy in Patients With Microhematuria. The Safe Testing of Risk for Asymptomatic Microhematuria Trial. J Urol 2024

With Cxbladder Triage now in the AUA guideline, our Clinical Science team is focused on coverage and guidelines inclusion for Triage Plus and Monitor Plus, while our R&D Team is focused on simplifying our portfolio of Cxbladder tests as In Vitro Diagnostic (IVD)-ready versions. Implicit in this vision for innovation is that we will need to place greater emphasis on the 'D' in R&D, thus creating the opportunity for decentralized deployment for our tests in the rest of the world.

The challenge for Pacific Edge is to make the most of the immediate commercial opportunities we have created. In the US this means being recognized for not only delivering the best clinical outcomes in the market – a title we can now confidently claim for Cxbladder Triage with the AUA's endorsement – but also for offering the simplest user experience.

We will achieve this second goal by investing in digital connections that streamline test ordering and results delivery for an excellent customer experience. These investments include new integrations with electronic medical record and pathology laboratory systems - building on the successful implementations with organizations like Kaiser Permanente and Lumea – and enhancements to our customer portal for clients unable to connect directly to our systems. Additionally, we need to further develop and appropriately incentivize our sales, customer service, and medical affairs teams, empowering them to effectively communicate and deliver Cxbladder's clinical and economic value wherever demand is identified.

We remain steadfast on our vision, while adaptable regarding how we deliver, and I am looking forward to reporting on progress in the new financial year.

With my warm regards,

Dr Peter Meintjes
Chief Executive

TEST VOLUMES

Cxbladder volumes rise with increased US clinical usage

Cxbladder tests processed at Pacific Edge's laboratories in laboratories in Q4 25 improved 6.8% on the prior quarter (Q3 25), lifted by increased adoption in the US.

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Total laboratory throughput (TLT) in Q4 25 rose to 7,577 tests from 7,092 tests in Q3 25.

Q4 25 US TLT was 6,490 tests up 11.7% from the 5,808 tests in Q3 25, lifted by an increase in the number of unique US ordering clinicians to 914 from 866[1] in Q3 25 and an increase in the number of tests each US clinician orders to 7.1 from 6.7[1] in Q3 25. The US volume lift follows continuing incremental improvements in sales force efficiency, up to 406 tests per sales FTE from 379 tests in Q3 25, and a seasonal post-holiday rebound.

The American Urological Association's (AUA) February 2025 inclusion of Cxbladder Triage with a 'Grade A'[2] evidence rating in its new microhematuria guideline has changed our sales pitch to clinicians, medical policy makers and healthcare payers, and generated renewed interest in Cxbladder among the broader urology customer base.

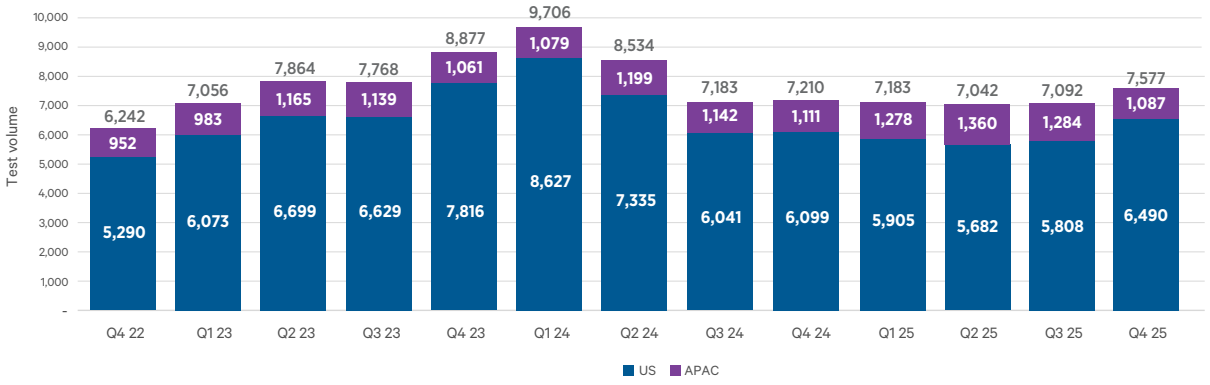
The longer-term impact of this change may take some time to affect the daily lab throughput figures, and as we await various coverage-related events, our commercial team will focus on profitability per sales resource in the wake of the guideline update before seeking to expand the size of the team.

Q4 25 Asia Pacific TLT was 1,087 tests down 15% on the 1,284 tests in Q3 25, with the decrease partly reflecting a reduction in evaluation and clinical study volumes as we continue to focus on commercial testing volumes and see the impact of budgetary constraints within some Health New Zealand – Te Whatu Ora regions.

Total volumes for the year to the end of March 2025 (FY 25) were down 11.5% to 28,894 tests from 32,633 in FY 24, with the fall reflecting the reduction in the sales force compared to the prior financial year in response to the uncertainty over Medicare coverage of Cxbladder.

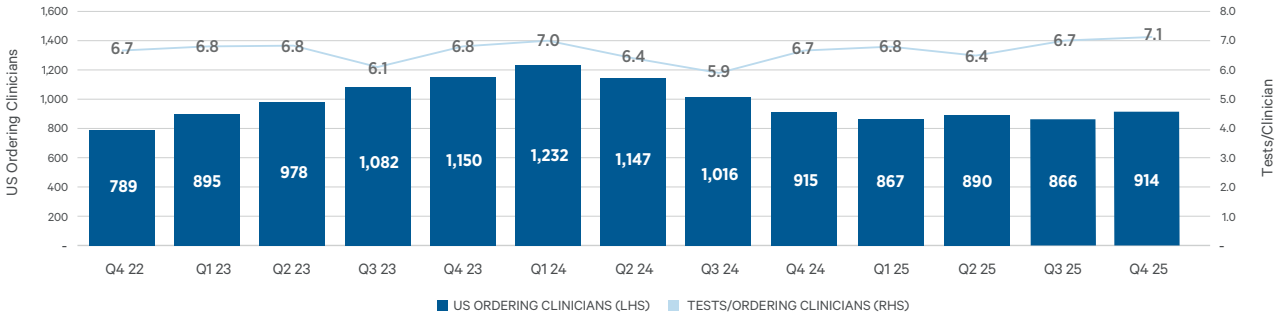
[1] The number of ordering clinicians in Q3 25 and the tests per ordering clinician has been restated to reflect post period adjustments.
[2] The AUA defines 'Grade A' evidence as evidence with a high certainty rating and notes evidence of this grade makes it "very confident that the true effect lies close to that of the estimate of the effect".

FIGURE 1: TOTAL TEST VOLUMES[1]



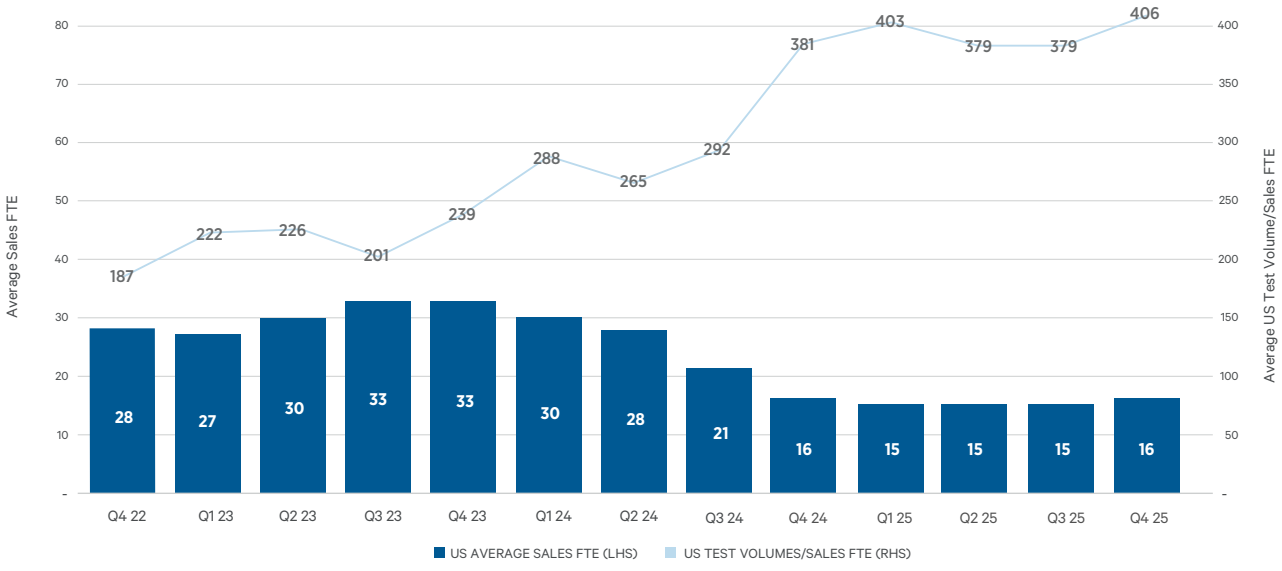
[1] Volumes in some prior quarters of FY24 are marginally different from those reported in earlier investor updates reflecting post period adjustments.

FIGURE 2: CXBLADDER CLINICAL ADOPTION



The number of ordering clinicians in Q3 25 and Q1 25 and the tests per ordering clinician in Q3 25 have been restated to reflect post period adjustments.

FIGURE 3: US SALES FORCE EFFICIENCY



APPROVED BY THE AUA BOARD OF DIRECTORS FEBRUARY 2025

Authors' disclosure of potential conflicts of interest and author/staff contributions appear at the end of the article.

MICROHEMATURIA: AUA/SUFU GUIDELINE (2020, AMENDED 2025)

Guideline Panel

Daniel A. Barocas, MD, MPH; Stephen Boorjian, MD;* Ronald Alvarez, MD, MBA; Tracy M. Downs, MD; Cary P. Gross, MD; Blake Hamilton, MD; Kathleen Kobashi, MD; Robert Lipman; Yair Lotan, MD; Casey Ng, MD; Matthew Nielsen, MD, MS; Andrew Peterson, MD; Jay Raman, MD; Rebecca Smith-Bindman, MD*

** Equal author contribution*

Guideline supportive of commercial operations

The American Urological Association's inclusion of Cxbladder Triage as a recommended alternative to the standard of care in the evaluation of microhematuria (MH) patients, represents a substantial strategic milestone on which to build our commercial operations.

The guideline, released in late February, will help to reduce the burden of unnecessary cystoscopies for lower risk patients, resulting in less patient discomfort, lower morbidity, and improved access to care by reducing wait times.

It states urologists may use urine-based biomarkers for intermediate-risk patients presenting with MH to assist their decision on whether to defer a cystoscopy: "In appropriately counseled intermediate-risk patients who want to avoid cystoscopy and accept the risk of forgoing direct visual inspection of the bladder urothelium, clinicians may offer urine cytology or validated urine-based tumor markers… to facilitate the decision regarding the utility of cystoscopy. Renal and bladder ultrasound should still be performed in these cases."

Intermediate risk' patients represent a large serviceable market for Triage, amounting to anywhere from 40-70% of all MH patients, or up to 3.5 million patients per year in the US alone[1]. This figure represents the base-line population indicated by the guideline, but we expect through the development of further evidence and clinician education to extend our addressable market to almost all patients presenting with hematuria.

In a significant achievement, the guideline mentions Cxbladder Triage as the only urine-based biomarker test that has 'Grade A' evidence from a randomized controlled trial (the STRATA study[2]) in support of this recommendation. The study was the first randomized controlled trial of any urine biomarker and demonstrated that Cxbladder Triage could safely and effectively reduce cystoscopies by as much as 59% without missing tumors.

The specific mention of Cxbladder Triage in the guideline reinforces our first mover advantage and establishes a high evidentiary standard that any other test must meet to be competitive.

The largest immediate opportunity is to leverage the guideline language in our ongoing policy dialogue with Medicare Administrative Contractor Novitas and the Centers for Medicare and Medicaid Services over the adverse 'Genetic Testing in Oncology: Specific Tests' (L39365) local coverage determination (LCD) released in January.

Should these discussions not yield the certainty we seek, and the LCD comes into effect on 24 April 2025, we will use the new guideline, and the evidence ignored by Novitas as it finalized the LCD (including the STRATA study and updated Analytical Validation studies of Triage and Detect[3]). In the meantime, we have submitted a reconsideration request for Cxbladder Triage under the 'Biomarkers for Oncology' LCD (L35396) using all current evidence and Novitas has deemed our submission valid.

Separately, the new guideline provides additional support to our contracting negotiations with healthcare plans across the US and in new markets and will help to catalyze change in the practice of independent urologists worldwide.

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[1] Pacific Edge estimates

[2] Lotan Y, Daneshmand S, Shore N, Black P, Scarpato KP, Patel A, Lough T, Shoskes DA, Raman JD. A Multicenter Prospective Randomized Controlled Trial Comparing Cxbladder Triage to Cystoscopy in Patients With Microhematuria. The Safe Testing of Risk for Asymptomatic Microhematuria Trial. J Urol 2024.

[3] Harvey JC, Cambridge LM, Ellen CW, Colonval M, Hazlett JA, Newell J, Zhou X, Guilford PJ. Analytical Validation of Cxbladder® Detect, Triage, and Monitor: Assays for Detection and Management of Urothelial Carcinoma. Diagnostics. 2024; 14(18):2061.

GUIDELINES

Guideline success featured at key meeting

A Pacific Edge symposium – Cxbladder Triage: Risk Stratification for Patients with Microhematuria – attracted significant interest at the Annual Meeting of the Southeastern Section of the American Urological Association (SESAUA) in mid-March.

SESAUA was the first opportunity for Pacific Edge to promote Cxbladder Triage since its inclusion in the guideline. The symposium was a standing room only event and was led by Dr Zachary Klaassen, Urologic Oncologist and Associate Professor of Urology; Wellstar MCG Health and the Georgia Cancer Center. It covered the details of the guideline, and the benefits Cxbladder Triage offered in reducing the burden of unnecessary cystoscopies for those with a lower risk of cancer, resulting in less patient discomfort and morbidity.

Watch the symposium online here

EVIDENCE INTEGRITY

Novitas' flawed understanding of Cxbladder evidence

Pacific Edge on 20 February released a point-by-point rebuttal of the evidentiary review used to support the finalization of the adverse 'Genetic Testing in Oncology: Specific Tests' (L39365) LCD that threatens to end Medicare coverage of our tests.

Our goal in releasing this rebuttal was to ensure all our stakeholders – patients, clinicians, medical policy makers, healthcare payers, our investors and our own people – understand our confidence in the clinical value of Cxbladder.

Pacific Edge's clinical evidence program is focused on developing high-quality clinical evidence for Cxbladder tests in a structured framework of Analytical Validity, Clinical Validity, and Clinical Utility, with the endpoints and sample sizes required for coverage decisions and guideline inclusion. Cxbladder Triage's February inclusion in the AUA microhematuria guideline with a 'Grade A' classification of the evidence supporting the use of it is an unequivocal validation of this approach and contrasts starkly with Novitas' review of our evidence portfolio.

Our analysis of the LCD evidentiary review found:

- Novitas conflates feasibility testing of biomarkers in urine with test development of a specific clinical diagnostic lab test.
- Novitas misinterprets evidence for Cxbladder Triage and Detect by framing them as screening tests for an asymptomatic population, rather than tests to support clinical decision making.
- Novitas misinterprets evidence for Cxbladder Detect and Triage because it misunderstands the patient population targeted by the tests (patients presenting with hematuria, not asymptomatic patients).
- Novitas misinterprets evidence for Cxbladder because it does not understand how the information generated by the tests is used to guide clinical decision making.
- Novitas has based its evidentiary review on a preliminary version of the Cxbladder test, referred to as uRNA-D, which is not the test offered to Medicare patients.

Our full rebuttal can be downloaded here

New evidence supports the clinical and economic value of Cxbladder Monitor

Two new studies examining the deployment of Cxbladder Monitor in Australia and New Zealand have demonstrated the clinical utility of the test for the surveillance for the recurrence of bladder cancer and the cost savings it delivers to healthcare payers. This real-world evidence is further supported by a new health economics study that demonstrates the savings the test offers to healthcare payers against the American Urological Association standard of care.

Monitor garners support in Australia

A new real world evidence study conducted by Northern Health in Melbourne, Australia, has demonstrated the effectiveness and safety of Cxbladder Monitor as an alternative approach in the surveillance for bladder cancer recurrence[1].

The retrospective study was designed to determine whether clinically significant bladder cancer recurrences, specifically progression to invasive or metastatic disease, were missed using Northern Health's protocol, which alternated annually between a Cxbladder Monitor test and flexible cystoscopy, compared to the standard yearly cystoscopy recommended by the European Association of Urology (EAU).

The findings highlighted notable clinical and operational benefits including the significant potential of Monitor to optimize bladder cancer surveillance programs, reduce healthcare costs, and substantially improve patient satisfaction and overall healthcare system efficiency.

Notably, the new protocol achieved a 59% reduction in the hospital's surveillance cystoscopy waitlist, greatly improving patient access and resource allocation.

"...the new protocol achieved a 59% reduction in the hospital's surveillance cystoscopy"

Financial analysis revealed substantial cost savings, with each Monitor test being approximately A$850 cheaper compared to conventional cystoscopy, leading to savings for Northern Health.

The budget impact benefits of Monitor were also affirmed in a Pacific Edge study accepted for publication in the JU Open Plus journal (see page 8).

The researchers concluded, "An alternating Cxbladder Monitor and Flexible Cystoscopy surveillance protocol can be safely used for NMIBC[2] patients eligible for annual surveillance, without clinically significant recurrences being missed. This can also alleviate a health center's surveillance cystoscopy waitlist and allow improved patient access to cystoscopy. Cxbladder Monitor was found to be cheaper, and the patients enthusiastically accepted it as an alternative to cystoscopy."

[1] Guduguntla A, Whish-Wilson T, Chandler L, Gyomber D. A novel bladder cancer surveillance schedule using bladder Cx for patients on annual surveillance. BJUI Compass. 2025;6(1).
[2] Non-muscle invasive bladder cancer

Cxbadder Monitor delivers savings in New Zealand

A retrospective study at Te Whatu Ora Health in Auckland found Cxbladder Monitor, for the surveillance for the recurrence of low-risk non-muscle invasive bladder cancer, is more patient-friendly, safe and saved the health provider $39,000[1] over a three-year period.

A study led by Dr Alexandra Gower and colleagues evaluated 206 urine-based Cxbladder Monitor tests conducted between 2020 and 2023. Researchers found Cxbladder Monitor detected 19 positive results, with follow-up cystoscopies confirming recurrence in four cases. Among negative results, 7% later showed recurrence in follow up examinations including a single high-grade case (0.5%). Patients reported preferring Cxbladder Monitor, highlighting the benefits of less anxiety, reduced discomfort, and fewer logistical issues associated with the test when compared to a cystoscopy.

Meanwhile the analysis found substantial cost savings, with Cxbladder Monitor costing $395 per test versus $643 for a traditional cystoscopy. Over three years, using Cxbladder Monitor, alternated annually with cystoscopy reduced total expenses at the health provider by nearly $39,000, averaging about $13,000 saved per year.

The researchers concluded: “Our findings indicate Cxbladder Monitor provides a safe, efficient, and patient-preferred alternative to routine cystoscopy surveillance. These results could prompt broader adoption, significantly impacting how bladder cancer surveillance is managed, balancing cost control and patient well-being.”

[1] All references to dollar amounts in this item are NZ dollars.

... and against the AUA standard of care

A new health economics study has shown that the inclusion of Cxbladder Monitor into bladder cancer recurrence surveillance protocols can save healthcare payers as much as $686[2] per patient over a five year surveillance period.

The study[3], accepted for publication in the JU Open Plus journal, compared the American Urological Association (AUA) bladder cancer surveillance protocols, with a new protocol that included Monitor in the surveillance program nine months after diagnosis. Under the Cxbladder protocol, cystoscopies were deferred if the Monitor test returned negative results, postponing invasive examinations until the next routine check-up.

Compared to the AUA standard of care, Cxbladder Monitor reduced mean total costs by $68,621 for 100 patients over 5 years or $137 per patient per year. Additionally, this approach reduced the number of cystoscopies by 129 examinations per 100 patients (0.31 per patient per year), with no difference in delayed cancer diagnosis, highlighting both the economic and clinical efficiencies of the Cxbladder Monitor test.

[2] All references to dollar amounts in this item are US dollars.
[3] Mark Tyson MD, MPH, John P. Sfakianos MD, Daniel A Shoskes MD, Tobias Muench, Kim Seemann, Rhodri Saunders, Siamak Daneshmand. Economic Impact Model of Incorporating Cxbladder Monitor in the Surveillance of Non-Muscle Invasive Bladder Cancer; article accepted for publication.

Evidence to drive clinical practice change

Our clinical study program is at the foundation of Pacific Edge's value. We are focused on generating the compelling clinical evidence required to drive behavior change in physicians. Specifically, we seek to produce evidence that is founded on the frameworks of Analytical Validity (AV), Clinical Validity (CV) and Clinical Utility (CU), with the endpoints and sample sizes required for coverage decisions and guideline inclusion.

STUDY	GOAL	POPULATION AND USE	STATUS
STRATA **S**afe **T**esting of **R**isk for **A**symptoma**T**ic Microhematuri**A**	• CU for Triage • CV/CU for Triage Plus (retrospective)	• Microhematuria (MH) • Risk stratification	- Recruitment closed with 555 patients including 223 low risk patients (test and control) with interim analysis results published in Journal of Urology and led to Guidelines inclusion for 2025 update. - Monitoring for final analysis completed mid-Aug, some re-work needed. Database lock expected Q2 2025 and final Clinical Study Report (CSR) expected Q3-4 2025.
DRIVE **D**etection and **R**isk stratification **I**n **VE**terans presenting with hematuria	• CV for Triage Plus for a Veterans' cohort • Data for MH pooled analysis	• MH and gross hematuria (GH) • Risk stratification	- Enrolment closed with 710 patients enrolled including 46 tumour confirmed patients (target was 45) from across 10 US Veteran Affairs (VA) sites. - Database lock completed and publication submission expected by March 2025.
microDRIVE **D**etection and **R**isk stratification **I**n **VE**terans presenting with microhematuria	• CV of Triage Plus • Data for MH pooled analysis	• MH • Detection	- Currently a decentralised study across all VAMC[1] coordinated using a single US VA. - Protocol amendment approved - 3 more sites to join in Q2 2025 to increase enrolment. - 467 patients have consented for the study with 305 samples received to date. - The target is 1000 patients with 35 tumour confirmed patients. - Last patient in is now projected to be Q3 2025.
AUSSIE **A**ustralian **U**rologic risk **S**tratification of patient**S** w**I**th h**E**maturia	• CV of Triage Plus (Australian cohort) • Data for MH pooled analysis	• MH and GH • Risk stratification	- The target is 35 Urothelial Cancer (UC) confirmed patients including a minimum of 10 MH patients. - Currently 543 subjects enrolled with 35 UC confirmed including 5 MH patients. - Last patient in projected to be Q3 2025.
POOLED ANALYSIS	• CV of Triage Plus	• MH and GH • Risk stratification	- MH (and separately GH patient data where available) from DRIVE, AUSSIE and microDRIVE will be pooled and performance determined. - Paper submission is one quarter after publication of DRIVE, microDRIVE and AUSSIE.
LOBSTER **LO**ngitudinal **B**ladder cancer **S**tudy for **T**umor **R**ecurrence	• CV of Monitor and Monitor+	• Surveillance • Risk stratification	- Enrolment will be complete when 75 UC recurrences are observed across 10–15 sites. - Enrolment is 388 subjects providing 894 samples with 52 UC recurrences observed to date. - We project last patient in (to observe 75 recurrences) between Q4 2025 to Q2 2026.
CREDIBLE **C**ystoscopic **RED**uction **I**n **BL**adder **E**valuations for microhematuria	• CU of Triage Plus	• MH • Risk stratification	- Study level Institutional Review Board (IRB) approvals received, site level IRB approvals for 7 sites, contracts finalized for 10 of expected 15 sites. - Currently amending the protocol to address KOL feedback and adjust to AUA guideline changes. - Enrolment due to commence 1 April 2025.

Quarterly dates are calendar year not financial years

[1] Veterans Affairs Medical Centers

ABOUT US

Pacific Edge Limited (NZX/ASX: PEB) is a global cancer diagnostics company leading the way in the development and commercialization of bladder cancer diagnostic and prognostic tests for patients presenting with hematuria or surveillance of recurrent disease. Headquartered in Dunedin, New Zealand, the company provides its suite of Cxbladder tests globally through its wholly owned, and CLIA certified, laboratories in New Zealand and the USA.

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