7 June 2023

MEDICARE COVERAGE OF CXBLADDER EXPECTED TO CEASE

DUNEDIN, New Zealand – Cancer diagnostics company Pacific Edge (NZX, ASX: PEB) today announces Medicare coverage of Cxbladder tests in the US market is expected to cease from 17 July 2023.

This development follows the finalization of a Local Coverage Determination (LCD) (L39365) by Novitas, the Medicare Administrative Contractor (MAC) with jurisdiction for Pacific Edge's laboratory in Hershey Pennsylvania.

The finalized LCD, which includes Cxbladder and tests provided by other companies, specifically notes the Cxbladder tests Triage, Detect, Monitor, Resolve and Detect^{+} as 'not considered medically reasonable and necessary', the threshold required for coverage under the US Social Security Act. A number of other companies are also affected by the LCD.

Over the coming days Pacific Edge will seek to explore all available legal options (including a potential appeal) with our US-based lawyers, the key opinion leaders among our customers, our partners at The Coalition for 21st Century Medicine, and other impacted companies.

As a direct result of the LCD, Pacific Edge's revenue is expected to reduce substantially from current levels until Cxbladder tests regain coverage. In the year ended March 2023 (FY 23), tests for Medicare and Medicare Advantage were ~60% of US commercial tests, or ~13,800 tests, and generated ~$15.3 million, or 77.3%, of FY23 total operating revenue. Post 17 July 2023 all of these tests are expected to be impacted by this determination from Novitas.

Pacific Edge Chief Executive Dr Peter Meintjes says the company is surprised and disappointed with the finalized LCD. He says the local coverage determination appears to materially misunderstand the important role that biomarkers can play in "first line" diagnostics for risk stratifying patients with hematuria into those that would benefit from further potentially more invasive medical attention and those that would not.

Pacific Edge has consistently sought to enhance and to strengthen its research and evidence base with a particular focus on its clinical evidence generation program over the last 18 months under the company's new CEO, Peter Meintjes, further accelerated since Dr. Tamer Aboushwareb joined as the VP of Medical Affairs, now leading the medical organization as CMO. The current program focuses on analytical validity (AV), clinical validity (CV) and clinical utility (CU) in defined patient populations, with conventional end points and at sufficient sample size for future inclusion in guidelines.

"While Novitas appears to have reviewed all available evidence for Cxbladder, we believe that Novitas' analysis has sought to predominantly emphasize negative comments in Cxbladder publications. We believe that focusing predominantly on only negative comments likely mischaracterizes issues or confounding factors with our evidence that were addressed in subsequent publications and routine commercial testing, while also dismissing the support Cxbladder receives from key opinion leading urologists, and the US patient advocacy group BCAN (Bladder Cancer Advocacy Network). Importantly, urologists have identified the value for themselves and their patients as demonstrated by the record number of urologists using the test, 1,151 in FY23Q4, and the record growth in Cxbladder testing volume at 43% CAGR for the last two years.

“Molecular diagnostics is a developing field, and this LCD has made an unprecedented move to change the threshold regarding what’s acceptable evidence and what’s not, by relying on third-party databases[1] that do not adequately cover the current standard of care in bladder cancer diagnosis. Consequently, Novitas does not appear to acknowledge that Pacific Edge’s products improve the standard of care in bladder cancer diagnosis and does not appear to consider the benefits of non-invasive testing alternatives and may result in worse outcomes for patients” Dr Meintjes says.

Private healthcare payers in the USA make independent medical policy decisions and consequently Pacific Edge expects to continue to bill and receive reimbursement from contracted US payers without interruption and from non-contracted private payers in line with historic reimbursement rates. Notably, our largest US customer Kaiser Permanente is expected to continue payment for our Triage and Monitor products, irrespective of the Novitas determination. We also expect continued reimbursement for the small proportion of patients insured by the US Veterans Administration and other direct bill payers.

Pacific Edge is currently unable to fully determine the impact of the new LCD on test volumes in the US market for the 2024 financial year. For the immediate future, the company will continue to promote Cxbladder and process all tests ordered by US clinicians whilst it further considers its strategy and future options.

The company believes that in the short term it is prudent to continue to support Cxbladder as it determines the best path forward, but the approach will be accompanied by cost containment initiatives including, but not limited to an immediate hiring freeze and a halt on discretionary spending and new capital expenditure.

“We see this LCD as a delay to our future commercialization plans. Now that Novitas has codified their views in a finalized LCD, we are able to consider and assess the potential necessary adjustments required to regain Medicare coverage. The generation of clinical evidence that supports the further integration of Cxbladder into clinical practice is expected to be at the foundation of these efforts.

Chief Medical Officer, Dr Tamer Aboushwareb notes: “The language and framework adopted in this LCD has reinforced our recent decision to develop and commercialize Cxbladder Detect^{+} as a single test for hematuria evaluation. The clinical evidence for Detect^{+} has, and will be, developed in a more structured framework for AV, CV and CU, using a defined patient population, conventional end points and a sample size sufficient for future inclusion in guidelines.

“By building a solid and focused clinical development plan based on the foundations of AV, CV and CU (which are requirements for guidelines inclusion and coverage), the Detect^{+} test will likely be the strongest candidate for future potential inclusion in both the NCCN[2] and AUA[2] guidelines for the stratification of microscopic hematuria patients. We have an ongoing study (DRIVE) expected to be ready for publication by early 2024 and another two validation studies (microDRIVE, and AUSSIE) set to start soon with a target completion date at the end 2024,” Dr Tamer Aboushwareb says.

In light of this new LCD, management and the Board at Pacific Edge are reviewing the scenario planning commenced last year to determine a strategic path forward that potentially includes: a) legal challenges

[1] The finalized LCD relies on three knowledge bases to determine coverage. They are Clinical Genome Resource (ClinGen); National Comprehensive Cancer Network (NCCN); Oncology Knowledge Base (OncoKB) knowledge bases.
[2] NCCN: National Comprehensive Cancer Network; AUA American Urological Association.

or appeals, b) seeking to regain coverage through Novitas, c) seeking to be awarded coverage through an alternative MAC, d) alternative billing practices that would increase patient responsibility and e) remaining open to other strategic alternatives.

Which of these we adopt, will be determined by considering a number of factors including the potential impact on revenue, expenditure and cash reserves, the time and resources required to regain coverage, shareholder value implications, and the expected likelihood of success.

Chairman Chris Gallaher notes: “Pacific Edge is well funded with cash and cash equivalents and short-term deposits of $77.8 million at the end of March 2023. Despite this current setback, the company believes that it can still deliver on the significant opportunities we see for Cxbladder in the US and around the world. We will update the market as we gain greater clarity and have determined our strategic path forward.”

A copy of the LCD can be downloaded from the following link: HERE

Pacific Edge is holding a conference call at 11.00am (NZT) today (Wednesday 7 June 2023)

Webcast link: www.virtualmeeting.co.nz/pebjun23

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Released for and on behalf of Pacific Edge by Grant Gibson Chief Financial Officer.

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OVERVIEW

Pacific Edge: www.pacificedgedx.com

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.

Cxbladder: www.cxbladder.com

Cxbladder is a urine-based genomic biomarker test optimized for the detection and surveillance of bladder cancer. The Cxbladder evidence portfolio developed over the past 14 years includes more than 20 peer reviewed publications for primary detection, surveillance, adjudication of atypical urine cytology

and equivocal cystoscopy. Cxbladder is the focal point of numerous ongoing and planned clinical studies to generate an ever-increasing body of clinical utility evidence supporting adoption and use in the clinic to improve patient health outcomes. Cxbladder is reimbursed by CMS and has been trusted by over 4,400 US urologists in the diagnosis and management of more than 100,000 patients, including the option for in-home sample collection. In New Zealand, Cxbladder is accessible to 75% of the population via public healthcare and all residents have the option of buying the test online.

Pacific Edge
NOVITAS LCD DECISION
Investor presentation

Chris Gallaher
Chairman

Dr Peter Meintjes
Chief Executive

7 June 2023

PACIFIC EDGE
CANCER DIAGNOSTICS COMPANY

Pacific Edge's ordinary shares trade on the NZX and the ASX under the ticker code: PEB

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NOVITAS DETERMINATION TIMELINE

- **July 2020**
  - Novitas informs Pacific Edge that Cxbladder is covered under LCD 35396 with a comment in Local Coverage Article (A58529) “the CxBladder test is now covered utilizing the reasonable and necessary guidelines”
- **June 2022**
  - Novitas proposed a new approach to Cxbladder coverage in Draft LCD (DL39365/DL3967) and a Draft Local Coverage Article (DA59125)
  - Seeks to link coverage relying to third party knowledge bases[1]
  - Cxbladder not mentioned in the LCD or LCA
- **July 2022**
  - Revision of the draft explicitly excluded Cxbladder from coverage, Pacific Edge shares put in trading halt and the market notified of the new draft determination
  - Pacific Edge advised that cessation of Medicare coverage had a low chance of succeeding, was unprecedented and unlawful (21st Century Cures Act).
- **July 2022 – September 2022**
  - With customers, the patient advocacy group BCAN (Bladder Cancer Advocacy Network) and our industry partner the Coalition for 21st Century Medicine (C21) and several other affected diagnostic test companies submitted written comments for consideration supported by in person representations.
- **September 2022 – May 2023**
  - Contingency planning underway for multiple outcomes amid expectations that coverage would be maintained.
- **November 2022**
  - A58529 is retired and Pacific Edge is guided by Novitas to use A58917 as the basis for coverage with Medicare Advantage Plans
- **January 2023**
  - Triage gains coding and then coverage under the older LCD (L35396) based on it being included in the LCA 58917
- **2 June 2023 (June 3 NZT):**
  - Novitas finalized draft LCD (L39365), noting multiple tests, including Cxbladder Triage, Detect, Monitor, Resolve and Detect+ as ‘not considered medically reasonable and necessary’.
- **17 July 2023:**
  - Medicare coverage of Cxbladder to cease

[1] The knowledge bases are Clinical Genome Resource (ClinGen); National Comprehensive Cancer Network (NCCN); Oncology Knowledge Base (OncoKB)

NOVITAS DETERMINATION HAS A SIGNIFICANT IMPACT ON PACIFIC EDGE

NOVITAS SUMMARY CONCLUSIONS

Finalized LCD (L39365) notes Cxbladder tests 'not considered medically reasonable and necessary', the threshold required for coverage under the US Social Security Act, based on:

- Insufficient validation in confounding clinical circumstances
- Population and gender biases
- High numbers of false positives
- Questions credibility of Pacific Edge funded research

- L39365 is focused on diagnostic, prognostic and predictive tests following or as an adjunct to a confirmed pathological diagnosis of cancer
- Novitas continues to reimburse Pacific Edge at US$760/test, but this is expected to cease on 17 July 2023

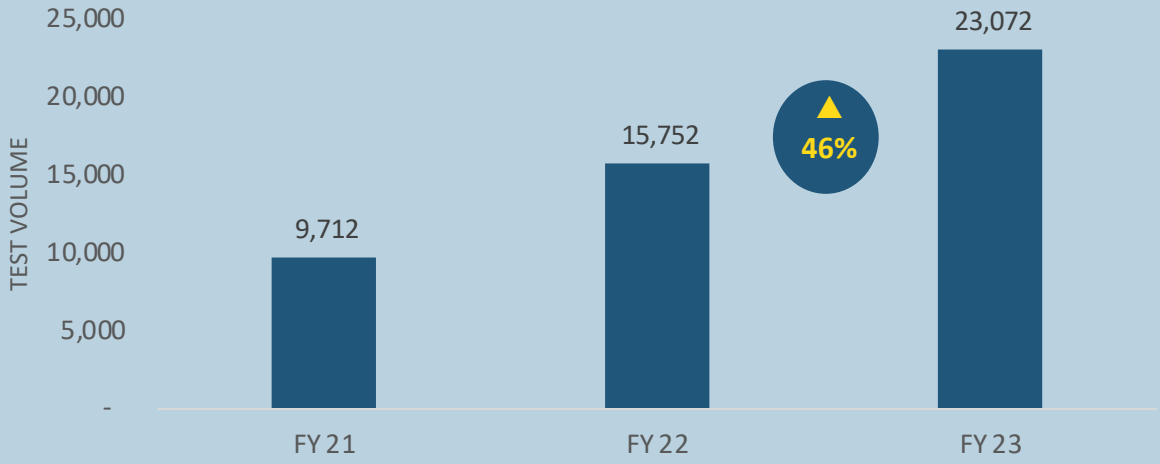
Novitas is the Medicare Administrative Contactor (MAC) with jurisdiction for Pacific Edge's US laboratory.

MEDICARE COVERS >61.5M US CITIZENS OVER 65

Medicare

- Cxbladder has a majority Medicare and Medicare Advantage population; average age of 73 for presentation with hematuria
- In FY23, Medicare and Medicare Advantage delivered 13,800 tests (~60%) of US commercial Cxbladder tests generating ~$15.3m in total operating revenue (~77.3%)

PACIFIC EDGE US COMMERCIAL TEST VOLUMES



NOVITAS MISUNDERSTANDS THE VALUE OF CXBLADDER TO UROLOGISTS

WHERE WE AGREE WITH NOVITAS:

- Molecular diagnostics is a developing field, and it is important to assess genetic testing in the context of oncology with a rigorous, evidence-based approach to facilitate the appropriate testing for all eligible Medicare beneficiaries
- The review of Pacific Edge's evidence emphasized negative comments and confounding factors where further research and evidence can and are being undertaken – all research was peer reviewed and published in well-respected journals

WHERE WE DISAGREE WITH NOVITAS:

- Does not acknowledge the support Cxbladder is attracting from urologists the US with 1151 clinicians ordering in Q4FY23 and rapidly growing testing volume of 43% CAGR over the last 2 years
- Misunderstands the value of non-invasive primary 'first line' testing
- Misunderstands the value of our tests in the context of the current AUA standards of urological care:
    - Does not consider hematuria as substantiated suspicion of bladder cancer. Current guidelines recognize this and require a cystoscopy, many of which Cxbladder can safely avoid
    - Misunderstands the central value proposition of tests like Cxbladder with high NPV in that they allow urologists to reduce unnecessary tests and procedures
    - Misunderstands how to interpret a positive result, i.e. that physicians should continue the evaluation of the patient for any other cause of disease, including upper tract assessment
- The LCD is an unprecedented change to the threshold and mechanism regarding what's acceptable evidence and what's not

Cxbladder™

TRIAGE

Used in primary care to:

- Assist clinicians to **safely de-intensify** hematuria evaluation from low incidence populations
- **Sensitivity 95% / NPV 99%**

DETECT

Used in primary and secondary care:

- Assist clinicians to adjudicate diagnostic dilemmas (e.g., equivocal cystoscopy & atypical cytology) in any patient population
- Sensitivity 82% / Specificity 85% / NPV 97%

MONITOR

Used in bladder cancer surveillance to

- Assist clinicians in **monitoring for UC recurrence**. Intended to reduce the frequency of surveillance cystoscopy and improve patient compliance
- **Sensitivity 93% / NPV 97%**

Sensitivity: the likelihood of the test to be positive in a patient with the disease
Specificity: the likelihood of the test to be negative when the patient does not have the disease;
NPV: the likelihood of a negative test being a true negative.

STRATEGIC OPTIONS: SHORT-TERM

CONTAINING COSTS AS WE REVIEW STRATEGY

TAKING A PRUDENT APPROACH

- Continue to promote Cxbladder and process all tests ordered by US clinicians with the current team
- Cost containment including, but not limited to immediate hiring freeze, and a halt on discretionary spending and new CAPEX
- Contracted payers (Kaiser, VA and other minor health plans) will continue to be billed and we expect to receive reimbursement from them in line with historic rates.

The Veterans Administration serves >9m veterans each year

- DRIVE[1] clinical study, has enrolled 80% of target patients
- DRIVE is a key engagement with VA urologists to determine clinical validity in a cohort of VA patients

The Kaiser Health Plan covers >12.5m members

- 2 Kaiser sites in PEB's Top 20 Accounts. 14 Kaiser sites across Southern California ordering in FY23
- EMR software development and integration testing complete; KP and PE working towards "go live"

[1] Detail of Pacific Edge's clinical studies are included in the appendix to this presentation.

STRATEGIC OPTIONS: LONGER TERM

ENSURING WE ARE RIGHT-SIZED IN LIGHT OF THE LCD

CLINICAL EVIDENCE SETS THE PATH TO REGAINING MEDICARE COVERAGE

- Reconfiguring the evidence generation program over the last 12-18 months has refocused and accelerated our path to guideline inclusion and regaining Medicare coverage
- Detect+ will be the strongest candidate for inclusion in the NCCN and AUA guidelines as single product for hematuria evaluation
- Clinical studies accelerated[1]:
  - DRIVE ready for publication in CY24
  - microDRIVE, and AUSSIE target completion in end of CY24

REVIEWING OUR BUSINESS IN LIGHT OF THE LCD

- Management and Board are reviewing the scenario planning commenced last year to determine a path forward that includes
  - Legal challenges or appeals
  - Regaining coverage through Novitas
  - Regaining coverage through an alternative MAC
  - Alternative billing practices, such increasing patient responsibility
  - Other strategic alternatives
- Impact on revenue, expenditure, cash reserves, required time and resources to regain coverage and shareholder value are determinative.
- Management and Board are committed to right-size the business to fit any revision to strategy

American Urological Association **www.auanet.org**

- Most influential and largest urological association in the world with 23,000 members worldwide.
- Standards of care relevant to Cxbladder are hematuria and micro-hematuria management and non-muscle invasive bladder cancer (NMIBC) (allows for biomarkers in surveillance)
- Guidelines reviewed as new evidence emerges

NCCN National Comprehensive Cancer Network® **www.nccn.org**

- US-based not-for-profit alliance of 32 leading US cancer centres
- Bladder cancer standard suggests biomarkers may be considered during surveillance of high-risk non-muscle-invasive bladder cancer
- Guidelines reviewed annually. PEB will resubmit in every year where there is new peer-reviewed evidence for Cxbladder

[1] Detail of Pacific Edge's clinical studies are included in the appendix to this presentation.

SUMMARY AND OUTLOOK:

- Disappointed by the new LCD
  - Highlights some areas of improvement in Pacific Edge's evidence portfolio that either have been or are being addressed
  - Does not acknowledge the value Cxbladder offers in the patient diagnosis and management, or the record demand from urologists
- The single most important determinant of coverage is high-quality clinical evidence
  - The clinical evidence program has already been accelerated
  - On the back of DRIVE, microDRIVE and AUSSIE, Detect^{+} is the strongest candidate for guidelines inclusion
- We will continue to bill and collect revenue from contracted payers in the US and in APAC
- We have world-leading technology, a strong balance sheet with $77.8 million cash on hand at the end of March
- Despite this setback we still expect to deliver on the significant opportunities we see for Cxbladder in the US and around the world.

QUESTIONS

APPENDIX

CLINICAL EVIDENCE GENERATION TOWARDS GUIDELINE INCLUSION (1/2)

STUDY	AIM	LOCATIONS	ENROLLED SITES*	STATUS**
STRATA	**S**afe **T**esting of **R**isk for **A**symptoma**TI**c Microhematuri**A** Demonstrate the clinical utility (CU) of Cxbladder using a prospective, two-arm randomized design to risk-stratify patients and rule out from cystoscopy • Establish CU for Cxbladder Triage in MH populations to identify patients at low risk of bladder cancer that can safely avoid cystoscopy • Retrospective analysis with Cxbladder Detect+ to show equivalent or greater CU in MH populations with the improved performance characteristics • CU evidence supports AUA/NCCN guidelines inclusion using Cxbladder Triage and/or Cxbladder Detect+ to risk stratify MH populations	USA Canada	11 / 13	- Enrolment total is 492, including 113 'low risk' subjects that are the focus of the study - Target enrolment: ~600 patients, including 120 low risk subjects randomized to test arm - Last patient in: Q3 2023 - Follow up: until Q3 2024
DRIVE	**D**etection and **RI**sk Stratification in **VE**terans Presenting with Hematuria Prospective recruitment of patients to a single-arm observational study to demonstrate the CV of Cxbladder tests in risk stratifying Veterans presenting with hematuria • CV evidence for Triage in MH & GH patients supplementing NZ Studies • Demonstrate CV of Cxbladder Detect+ within a Veterans cohort • Retrospective analysis with Cxbladder Detect+ to demonstrate CV evidence supporting AUA/NCCN Guidelines inclusion in MH & GH patients • Contribute data to pooled-analysis to establish CV for Detect+ in MH patients	VA Sites (USA)	10 / 11	- Enrolment total is 562 - Target enrolment: ~600 patients - Last patient in: Q3 2023 - Follow up: until Q2 2025
AUSSIE	**A**ustralian **U**rologic risk **S**tratification of patient**S** w**I**th h**E**maturia Prospective recruitment of patients to a single-arm observational study to demonstrate CV in an Australian healthcare setting for patients presenting with hematuria • Demonstrate CV of Cxbladder Detect+ with an Australian cohort • Demonstrate accurate risk stratification of hematuria patients to intensify or de-intensify evaluation • Contribute data to pooled-analysis to establish CV for Detect+ in MH patients	Australia	1 / 1	- Enrolment due to start May 2023

*Estimated number of enrolled sites
**All dates are best-case estimates and subject to change

CLINICAL EVIDENCE GENERATION TOWARDS GUIDELINE INCLUSION (2/2)

STUDY	AIM	LOCATIONS	ENROLLED SITES*	STATUS**
Microhematuria Pooled-analysis	Pooled-analysis of Cxbladder Detect+ performance from multiple studies involving prospectively recruited patients from single-arm observational studies including eligible microhematuria patients • CV of Cxbladder Detect+ with microhematuria (MH) patients • Combines data from DRIVE, AUSSIE and a future MH-focused clinical trial • CV evidence supports AUA/NCCN guidelines inclusion using Cxbladder Detect+ to risk stratify MH populations	USA, Aus	N/A	- DRIVE underway, AUSSIE and microDRIVE projected to start in 2023
microDRIVE	**D**etection and **RI**sk Stratification in **VE**terans Presenting with **Micro**hematuria • Demonstrate the clinical validity of Cxbladder Detect^{+} in detecting urothelial cancer in patients presenting with microhematuria. • MicroDRIVE will compare the performance of Detect^{+} against the current gold-standard for the detection of urothelial cancer, diagnostic cystoscopy and pathology.	USA	0/1	- Projected to start recruitment Sep/Oct 2023 - Target is 1000 patients and 50 tumour confirmed - Last patient in: March/April 2024
LOBSTER	**LO**ngitudinal **B**ladder Cancer **S**tudy for **T**umor R**E**cur**R**ence Prospective recruitment of patients to a single-arm observational study to evaluate the clinical validity of CxbM • To safely risk stratify patients under surveillance for recurrence of UC • To demonstrate that it is safe to alternate CxbM with cystoscopy for intermediate and high-risk patients under surveillance for recurrence of UC • Targeting AUA/NCCN guidelines inclusion for biomarkers as an alternative to cystoscopy in a surveillance setting	USA (including some VA sites) Australia	3 / 10	- Three sites are open - Two due to open in April - Another 6 are at pre-activation. - Enrolment is now 63 patients with 98 samples collected to date - Each site will enroll 100 patients within 12 months and follow up for another 12 months

*Estimated number of enrolled sites
**All dates are best-case estimates and subject to change

SUMMARY OF CLINICAL EVIDENCE

		Study	Pop. Type	Sensitivity (Sn)	NPV	Specificity (Sp)	Comment
Detect+	**AV**	Lotan et al., 2022	MH + GH*	97%	99.7%	90%	Pooled data from US and Singapore cohorts (*n*=804)
	CV	DRIVE (unpublished) (**1**)	MH + GH*				*Study in progress*
		AUSSIE (unpublished) (**4**)	MH + GH*				*Study to start this year*
		microDRIVE (unpublished) (**5**)	MH*				*Study to start this year*
Triage	**AV**	Kavalieris et al., 2015	MH + GH*	95.10%	98.50%	45%	**Sn, Sp, NPV** values when test-negative rate is 40%
	CV	Davidson et al., 2019	MH + GH*	95.5% (**1**)	98.6% (**1**)	34.3%	GH only: **Sn** (95.1%), **NPV** (98%), **Sp** (32.8%); MH only: **Sn** (100%), **NPV** (100%), **Sp** (42.6%)
		Konety et al., 2019	(**2**)	100%			Cxbladder (**3**) correctly adjudicated all UC confirmed patients (*n*=26) with atypical urine cytology results (*n*=153, **4**)
		Lotan et al., 2022	MH + GH*	89%	99%	63%	Pooled data from US and Singapore cohorts (*n*=804)
	CU	Davidson et al., 2020	MH + GH*	89.4% (**5**)	98.9% (**5**)	59% (**5**)	39% of patients testing negative for Cxb Triage & imaging did not get cystoscopy & were managed at primary care (**6**)
		STRATA (unpublished) (**7**)	MH + GH*				*Study in progress*
Detect	**AV**	O'Sullivan et al., 2012	GH*	81.8%	97%	85.1%	Cxb Detect detected 97% of HG tumors & 100% of Stage 1 or greater tumors.
	CV	Lotan et al., 2022	MH + GH*	74%	97%	82%	Pooled data from US and Singapore cohorts (*n*=804)
		DRIVE (unpublished) (1)	MH + GH*				*Study in progress*
Monitor	**AV**	Kavalieris et al., 2017	(**1**)	88% (**2**)	97% (**2**)	N/A	(**3**)
	CV	Konety et al., 2019	(**4**)	100%			Cxbladder (**5**) correctly adjudicated all UC confirmed patients (*n*=26) with atypical urine cytology results (*n*=153, **6**)
	CU	Koya et al., 2020	(**7**)				Integration of Cxb Monitor into the surveillance schedule reduced annual cystoscopies (39%) (8,9)

* Referred

MH: Microhematuria, GH: Gross Hematuria. For definitions of Sensitivity, NPV and Specificity please see the glossary on page 33 of this presentation

FOOTNOTES FOR CLINICAL EVIDENCE SUMMARY

	Footnotes	
Detect+	1	Observational study to validate performance characteristics and clinical utility of Cxbladder tests (Cxb Triage, Cxb Detect, Cxb Detect^{+}).
	2	Observational study to validate performance characteristics of Cxb Detect^{+} in patients with UC of the upper tract.
	3	Patients with suspected upper tract UC (UTUC) or surveillance patients with a history of UTUC.
	4	Observational study to validate performance characteristics and clinical utility of Cxbladder tests (Cxb Triage, Cxb Detect, Cxb Detect^{+}).
	5	Observational study to validate performance characteristics of Cxb Detect^{+} in microhematuria (MH) patients.

Triage	**1**	Cxb Triage performance; Cxb Triage & imaging combined performance had a **Sn** of 97.7% & **NPV** of 99.8%.
	2	Patients included hematuria evaluation (*n*=436) or surveillance previously diagnosed with UC (*n*=416) with both Cxbladder & urine cytology results.
	3	Cxbladder includes Cxbladder Triage & Cxbladder Monitor.
	4	This included *n*=70 for patients with hematuria & *n*=83 for patients with previously diagnosed UC and overall test negative rate of 30.7%.
	5	Cxb Triage performance; Cxb Triage & imaging combined performance had a **Sn** of 98.1%, **NPV** of 99.9% & **Sp** of 98.4%.
	6	Cxb Triage negative rate was 53%; Follow-up period of 21-months showed no missed cancers, demonstrating safety.
	7	The intent of STRATA is to show that it is safe to risk stratify low risk microhematuria patients and not undertake cystoscopy.

Detect	**1**	Observational study to validate performance characteristics and clinical utility of Cxbladder tests (Cxb Triage, Cxb Detect, Cxb Detect^{+}).

Monitor	**1**	Surveillance patients previously diagnosed with primary or recurrent UC.
	2	Cxb Monitor performance characteristics on surveillance patients diagnosed with primary UC; Cxb Monitor had a **Sn** of 93% and **NPV** of 94% on patients with recurrent UC.
	3	Using Kavalieris et al., (2017) data set, Lotan et al., (2017) compared relative performance of Cxb Monitor against NMP22 ELISA, NMP22 BladderChek and urine cytology.
	4	Patients included hematuria evaluation (*n*=436) or previously diagnosed UC (*n*=416) with both Cxbladder & urine cytology results.
	5	Cxbladder includes Cxbladder Triage & Cxbladder Monitor.
	6	This included *n*=70 for patients with hematuria & *n*=83 for patients with previously diagnosed UC; test negative rate of 30.7%.
	7	All patients were being evaluated for recurrence of UC (*n*=309 providing 443 samples).
	8	Cxb Monitor identified all seven confirmed recurrence events idnetified on the first cystoscopy.
	9	Patients returning negative Cxb Monitor results (n=235) had no pathology-confirmed recurrence at 1st cystoscopy

REFERENCES SUMMARY OF CLINICAL EVIDENCE

	References
Detect+	Lotan et al., (2022). Urinary Analysis of FGFR3 and TERT Gene Mutations Enhances Performance of Cxbladder Tests and Improves Patient Risk Stratification. The Journal of Urology, 10-1097.

Triage	Davidson et al., (2019). Inclusion of a molecular marker of bladder cancer in a clinical pathway for investigation of haematuria may reduce the need for cystoscopy. NZ Med J, 132(1497), 55-64.
	Davidson et al., (2020). Assessment of a clinical pathway for investigation of haematuria that reduces the need for cystoscopy. The New Zealand Medical Journal (Online), 133(1527), 71-82.
	Kavalieris et al., (2015). A segregation index combining phenotypic (clinical characteristics) and genotypic (gene expression) biomarkers from a urine sample to triage out patients presenting with hematuria who have a low probability of urothelial carcinoma. BMC urology, 15(1), 1-12.
	Konety et al., (2019). Evaluation of cxbladder and adjudication of atypical cytology and equivocal cystoscopy. European urology, 76(2), 238-243.
	Lotan et al., (2022). Urinary Analysis of FGFR3 and TERT Gene Mutations Enhances Performance of Cxbladder Tests and Improves Patient Risk Stratification. The Journal of Urology, 10-1097.

Detect	Lotan et al., (2022). Urinary Analysis of FGFR3 and TERT Gene Mutations Enhances Performance of Cxbladder Tests and Improves Patient Risk Stratification. The Journal of Urology, 10-1097.
	O'Sullivan et al., (2012). A multigene urine test for the detection and stratification of bladder cancer in patients presenting with hematuria. The Journal of urology, 188(3), 741-747.

Monitor	Kavalieris et al., (2017). Performance characteristics of a multigene urine biomarker test for monitoring for recurrent urothelial carcinoma in a multicenter study. *The Journal of Urology*, *197*(6), 1419-1426.
	Konety et al., (2019). Evaluation of cxbladder and adjudication of atypical cytology and equivocal cystoscopy. European urology, 76(2), 238-243.
	Koya et al., (2020). An evaluation of the real world use and clinical utility of the Cxbladder Monitor assay in the follow-up of patients previously treated for bladder cancer. *BMC urology*, *20*(1), 1-9.
	Lotan et al., (2017). Clinical comparison of noninvasive urine tests for ruling out recurrent urothelial carcinoma. *Urologic Oncology: Seminars and Original Investigations*, 35 (8), 531-539.

GLOSSARY

- ***Sensitivity*** - the frequency with which a test correctly identifies patients with a disease.
- ***Specificity*** - the frequency with which a test correctly identifies patients without a disease.
- ***Negative Predictive Value (NPV)*** - the percentage of negative tests being true negatives (by standard of care).
- ***Positive Predictive Value (PPV)*** - the percentage of positive tests being true positives (by standard of care).
- ***Rule-out Rate (ROR)*** - the percentage of tests that return a negative result.
- ***Evidence definitions:***
  - ***Analytical validity***: Develop a test that is repeatable in the lab for a given indication and population.
  - ***Clinical validity:*** Make sure the test works in the same way on an independent eligible population for the given indication.
  - ***Clinical utility:*** Put the test in the hands of a physician to establish that it can usefully change patient management within the context of care for the defined population and indication.

PACIFIC EDGE: RESEARCH, INNOVATION, COMMERCIALIZATION

2001
Pacific Edge established

2003
Listed on the NZX

2007
Commercial pivot to focus on urothelial cancer diagnostics

2008
Holyoake et al: Urine-based RNA detection of urothelial cancer. Clin Cancer Res

2010
Pacific Edge Diagnostics New Zealand (PEDNZ) established

2012
O'Sullivan et al: Cxbladder Detect performance validation. Journal of Urology

Dec 2012
Launch of Pacific Edge Diagnostics USA and Cxb Detect

Mar 2013
PEDUSA receives CLIA accreditation

May 2013
First commercial sale (Cxb Detect) for PEDNZ

Mar 2013
First commercial sale (Cxb Detect) for PEDUSA

Dec 2014
Launch of Cxbladder Triage

Mar 2015
Kavalieris et al: Cxb Triage performance validation. BMC Urology

Dec 2015
Launch of Cxbladder Monitor

Nov 2016
Clinical trials commence in Singapore

Feb 2018
Cxb Triage adopted into Canterbury Community Health Pathways with primary care referral

Aug 2019
Konety et al: Clinical Utility of Cxb Detect in adjudicating atypical cytology and equivocal cystoscopy. European Urology

Apr 2020
Patient in-home sampling initiated in the US

Jun 2020
Kaiser Permanente, approves commercial use of Cxbladder

Jul 2020
CMS confirms reimbursement of Cxbladder at $760/test

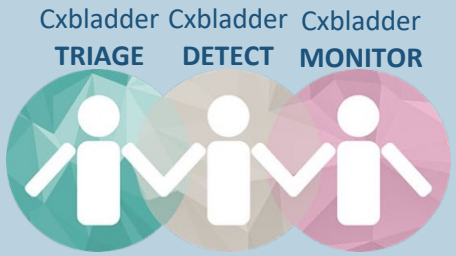
Aug 2021
Cxbladder reaches 70% public healthcare coverage in NZ

Oct 2021
PEB raises $103.5m (~US$72.5m)

Dec 2021
First commercial sale of Cxbladder in Australia

Dec 2022
Lotan et al: Enhanced Cxbladder Tests Deliver Improved Performance. Journal of Urology

2001 2007 2008 2011 2012 2013 2014 2015 2016 2018 2019 2020 2021 2022



Cxbladder®

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