PRELIMINARY RESULTS FROM VISTA PHASE 3 PIVOTAL STUDY OF THE NOVEL AGENT VICINIUM IN BCG-UNRESPONSIVE NON-MUSCLE INVASIVE BLADDER CANCER

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Phase 3 Study of Vicinium in BCG-unresponsive Non-muscle Invasive Bladder Cancer: Initial Results
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DISCLOSURES

No industry or financial disclosures or conflict of interests to report

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LACK OF TREATMENT INNOVATION FOR NMIBC

- Bacillus Calmette-Guérin (BCG): primary treatment for all high-grade NMIBC since 1980s
  - Potential for shortages in BCG supply based on single-source provider
- Radical cystectomy remains standard-of-care for BCG-unresponsive NMIBC
  - Significant morbidity and mortality rates
- Last U.S. approved treatment in 1998 limited to BCG-refractory carcinoma *in situ* (CIS) in subjects for whom immediate cystectomy would be associated with unacceptable morbidity or mortality[1]
  - Associated with challenging toxicities and limited use
- Significant need for new treatment for BCG-unresponsive NMIBC

[1] Valstar® (valrubicin) Sterile Solution for Intravesical Instillation package insert

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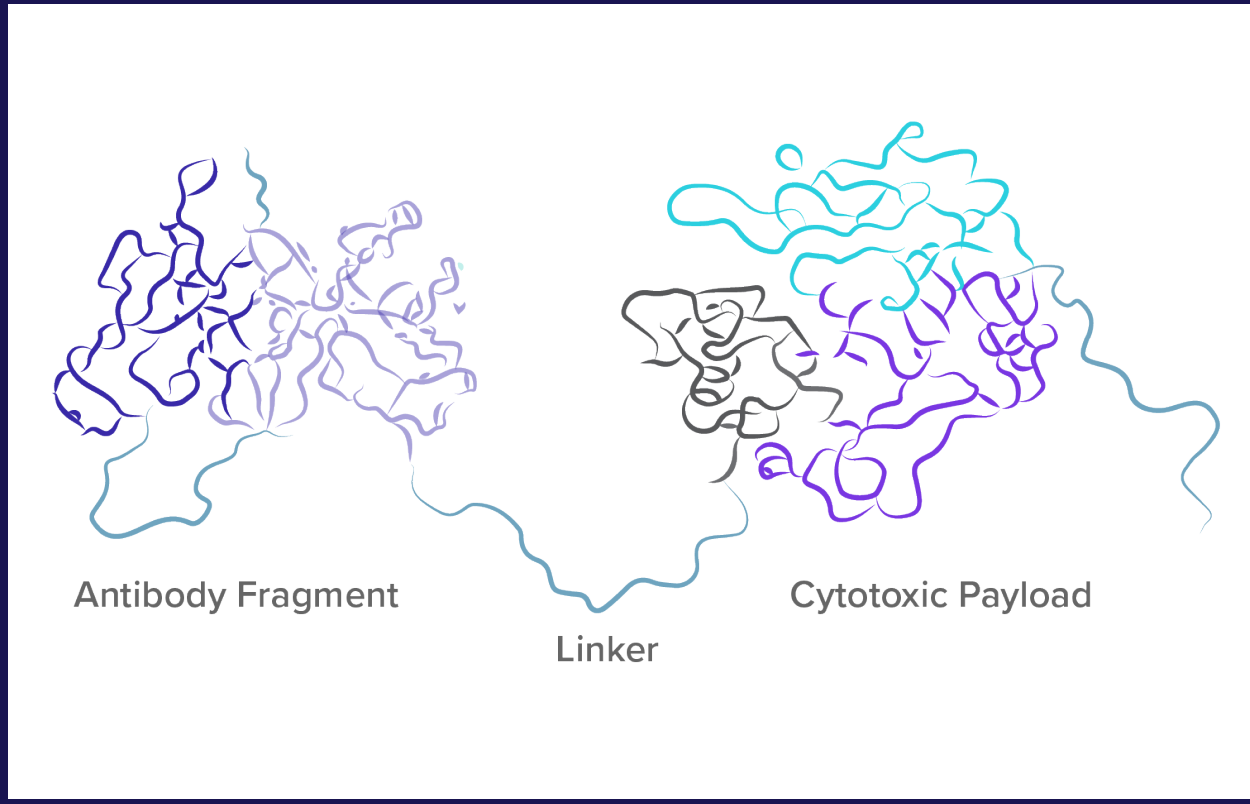
VICINIUM: NOVEL FUSION PROTEIN DESIGNED TO INCREASE TUMOR TARGETING AND DRUG SAFETY

- Next-generation antibody drug conjugate (ADC) genetically engineered as a single protein comprising an antibody fragment, peptide linker and cytotoxic payload
- Designed to deliver a potent toxin payload directly to tumor cells while avoiding normal tissue
- Powerful protein synthesis inhibitor payload designed to kill both rapidly proliferating and slower growing cancer cells
- Potential to induce immunogenic cell death



ETA: Pseudomonas exotoxin A
Potent: subpicomolar IC_{50}

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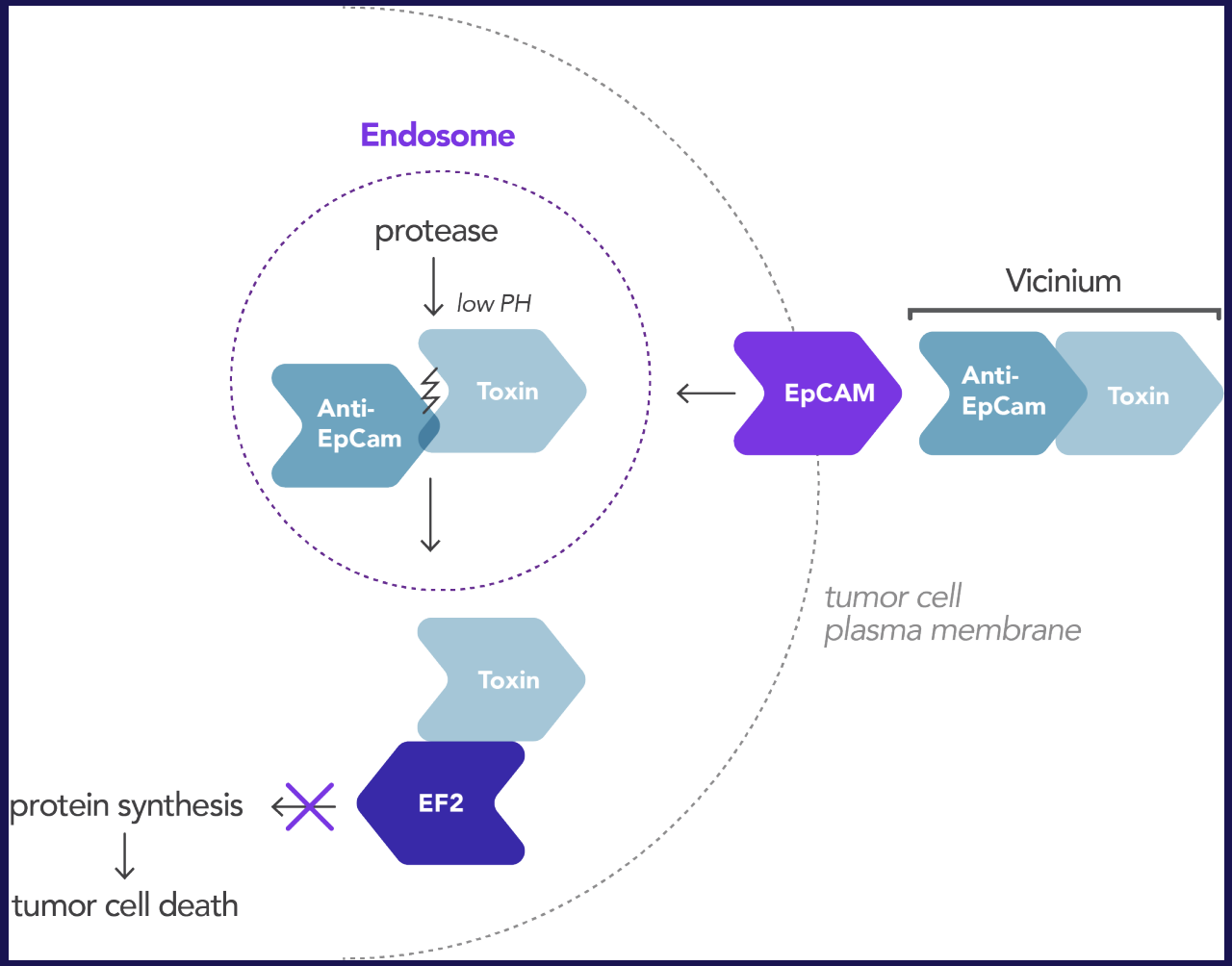
VICINIUM: A UNIQUE MECHANISM OF ACTION FOR TREATING HIGH-GRADE NMIBC



- EpCAM (the target) is overexpressed in >98% of high grade NMIBCs*, minimal expression on healthy bladder tissue
- Stable, genetically engineered peptide linker allows fusion protein to remain intact until internalized by cancer cell
- Anti-EpCAM Ab fragment delivers toxin that kills tumor cells by blocking protein synthesis

* Data generated in prior EBIO studies using internal antibody

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VISTA TRIAL: PHASE 3 STUDY OF VICINIUM FOR NMIBC

- Single-arm, open label, multi-center phase 3 study of subjects with BCG-unresponsive NMIBC
  - BCG-unresponsive defined as having completed 2+ courses (≥ 5 and ≥ 2 treatments resp.) of full dose BCG starting within 13 months of each other

- 3 cohorts by histology and time to recurrence after adequate BCG
  - Cohort 1: CIS with or without papillary tumors that recurred within 6 months of BCG
  - Cohort 2: CIS with or without papillary tumors that recurred >6 months but ≤11 months of BCG
  - Cohort 3: Papillary tumors (without CIS) that recurred within 6 months of BCG

- Dosing: intravesical instillation of 30mg Vicinium in 50 ml buffered saline held for 2 hours
  - Induction: biweekly for 6 weeks → weekly for 6 weeks
  - Subjects with CR proceed to maintenance of every other week for 2 years total

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VISTA TRIAL: ASSESSMENT OF RESPONSE

- Primary Endpoint: Complete response rate and duration of response in subjects enrolled in Cohort 1

- Complete response defined as negative central urine cytology or pathology, or local cystoscopy

- Key Secondary Endpoints
  - Event-free survival (EFS) in all subjects, time to disease recurrence, time to cystectomy, progression-free survival, overall survival, safety and tolerability

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VISTA TRIAL PATIENT DEMOGRAPHICS

CHARACTERISTICS	COHORT 1	COHORT 2	COHORT 3
	CIS that recurred within 6 months of BCG	CIS that recurred >6 months but ≤11 months of BCG	Papillary (without CIS) that recurred within 6 months of BCG
Total subjects enrolled	87	6	40
Evaluable subjects at 3-months	72	5	34
Median age (current)	75	71	77
Males/Females	54/18	4/1	29/5
Median prior treatment for NMIBC BCG cycles Intravesical chemotherapy TURBT	4 (range 2-14) 1 (range 0-23) 4 (range 0-11)		

Data as of 20 April 2018 cut off

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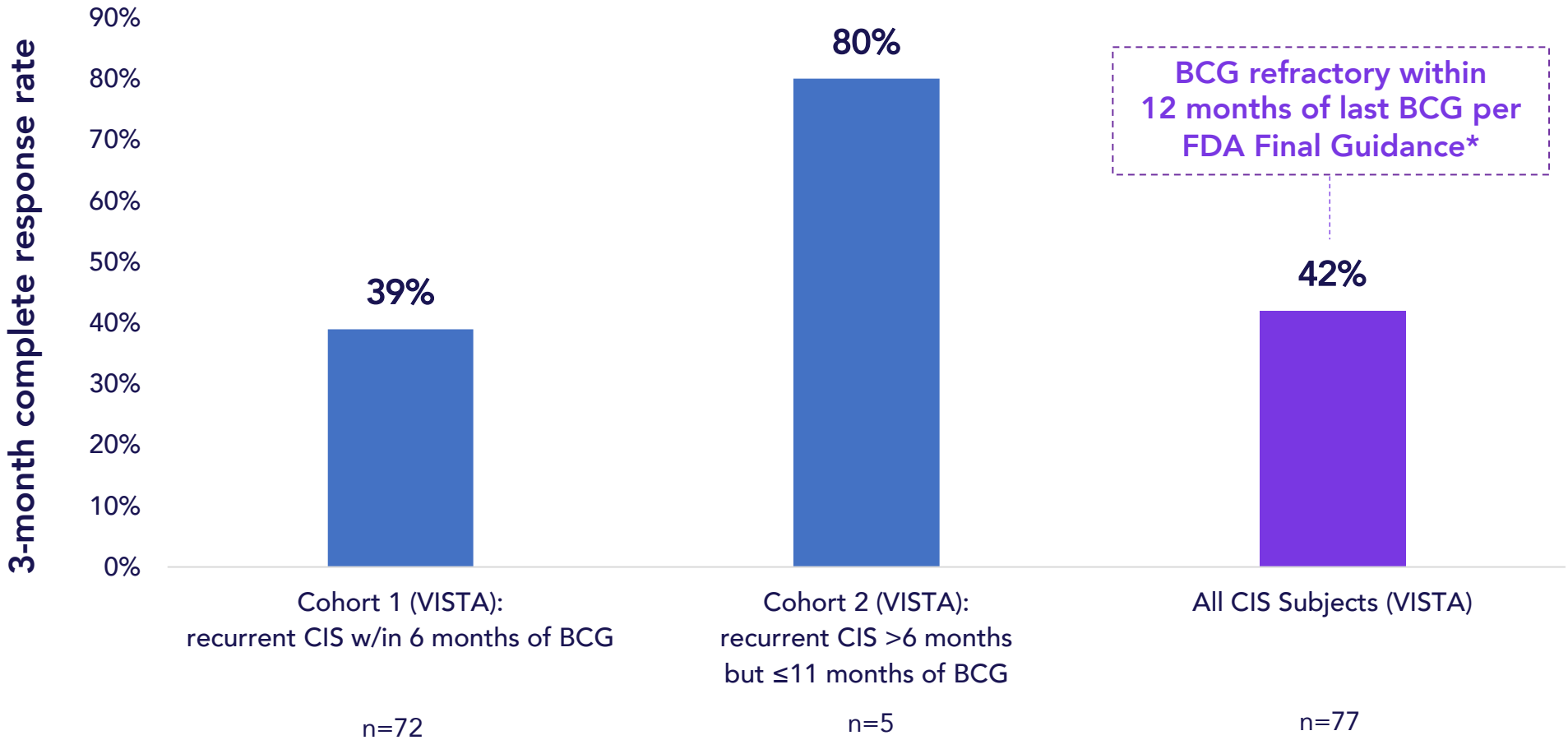
VICINIUM DEMONSTRATES 42% COMPLETE RESPONSE RATE AT 3-MONTHS IN CIS PATIENTS



Data as of 20 April 2018 cut off
Efficacy assessment based on cystoscopy as well as centrally read cytology and, where suspicious lesions found on cysto, central pathology
* BCG-Unresponsive Nonmuscle Invasive Bladder Cancer: Developing Drugs and Biologics for Treatment Guidance for Industry, February 2018

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CIS PATIENT JOURNEY TO COMPLETE RESPONSE

- 76 year old female
- CIS diagnosed in March 2016
- Post TURBT treated BCG per AUA guidelines (induction course of 6 doses over 6 weeks followed by maintenance course of 3 doses over 3 weeks)
- CIS remained confirmed by local and central pathology at September 2016
- Enrolled into VISTA Trial cohort 1 in October 2016; treated with Vicinium
- Confirmed complete response observed January 2017

Subject remains on treatment with complete response at last observation out to

19 MONTHS

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RECURRENCE-FREE RATE AT 3-MONTHS IN COHORT 3 SUBJECTS WITH PAPILLARY TUMORS ONLY

68%

recurrence-free rate at 3-months in papillary only subjects

(n=34)

- Subjects deemed to have no visible evidence of disease when starting Vicinium treatment
- Disease recurrence remains appropriate response criteria
- Time to disease recurrence remains standard clinical endpoint

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VICINIUM WELL-TOLERATED IN TREATED PATIENTS[1]

Treatment-Emergent Adverse Event[2]	Subjects (n=129) with: All TEAEs		Treatment-Related TEAEs	
	All Grades	Grade ≥3	All Grades	Grade ≥3[3]
Any TEAE	104 (81%)	36 (28%)	52 (41%)	5 (4%)
Urinary tract infection	37 (29%)	5 (4%)	13 (10%)	2 (%)
Dysuria	25 (19%)	0 (0%)	14 (11%)	0 (0%)
Hematuria	21 (16%)	2 (2%)	11 (9%)	0 (0%)
Pollakiuria (frequency of urination)	16 (12%)	0 (0%)	12 (9%)	0 (0%)
Diarrhea	13 (10%)	0 (0%)	2 (2%)	0 (0%)
Fatigue	13 (10%)	0 (0%)	8 (6%)	0 (0%)
Micturition urgency	11 (9%)	0 (0%)	8 (6%)	0 (0%)
Nausea	10 (8%)	1 (1%)	3 (2%)	0 (0%)
Lipase increased (all asymptomatic)	10 (8%)	4 (3%)	2 (2%)	1 (0%)

Subjects (n=129)	Treatment-Emergent SAEs[4]	Treatment-Related SAEs
Any Serious AE	17 (13%)	4 (3%)
Acute kidney injury or renal failure	4	3
Hematuria	3	0
Cholestatic hepatitis	0	1

1. <1% (n=4) treatment discontinuations due to AEs or progression of bladder cancer
2. Includes named TEAE and Lab Investigations occurring in more than 10 (8%) subjects regardless of treatment relationship
3. No grade 5 treatment-related adverse events observed
4. All SAEs that occurred in more than 1 subject

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SUMMARY

- 3-month data demonstrate Vicinium efficacy in subjects with NMIBC
  - 42% complete response rate at 3-months in cohort 1 and 2 subjects with recurrent CIS within 12 months of last BCG treatment, according to FDA Final Guidelines
  - 68% recurrence-free rate in subjects with papillary tumor
- Vicinium safety profile was tolerable and manageable
- Phase 3 findings consistent with Vicinium experience in Phase 1 and 2 clinical trials
- Convenient BCG-like instillation
- VISTA Trial enrollment complete; 12-month complete response data anticipated by mid-2019
- Unmet need in BCG-unresponsive NMIBC supports continued development of Vicinium

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