Preliminary Efficacy and Safety Results From ADVANCED-2: A Phase-2 Open-label Study of Intravesical TARA-002 In Adults With High-grade Non-muscle Invasive Bladder Cancer

Gautam Jayram[1], Eugene Kramolowsky[2], Myroslava Doronina[3], William Tabayoyong[4], Brian Mazzarella[5], Jacqueline Zummo[6], Wei Sun[6], Khushboo Belani[6], Eppie Brown[6], Andrea DiFiglia[6], Claire Middleton[6], Brian Desch[6], Chen Quin Lam[7], Neal Shore[8], Zoreslava Lysak[3], Evgeny Levenko[3]

[1]Urology Associates P.C., Nashville, TN, United States; [2]Virginia Urology, Richmond, Virginia, United States; [3]Arensia Exploratory Medicine LLC, Kyiv, Ukraine; [4]Department of Urology, University of Rochester, Rochester, NY, United States; [5]Urology Austin, Austin, Texas, United States; [6]Protara Therapeutics, Inc., New York, NY, United States; [7]Pharmapace Inc., San Diego, CA, United States; [8]Carolina Urologic Research Center, Myrtle Beach, SC, United States

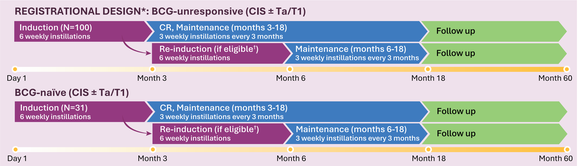
INTRODUCTION

- Effective management of non-muscle invasive bladder cancer (NMIBC) remains a critical unmet medical need, further complicated by an ongoing shortage and limited availability of Bacillus Calmette-Guérin (BCG).
- TARA-002 is a unique formulation containing inactivated cells of *Streptococcus pyogenes* (Group A, type 3) Su strain administered intravesically.
- TARA-002 is a broad spectrum immune potentiator that elicits a TH1 pro-inflammatory cytokine response.
- This study reports updated efficacy and safety data of TARA-002 in participants with NMIBC with CIS ± Ta/T1, including 9-month and 12-month evaluable participants.

METHODS

- ADVANCED-2 (NCT05951179) is an ongoing, actively enrolling, Phase 2, open-label study to evaluate the safety and efficacy of intravesical instillation of TARA-002 (40 KE) in adults ≥18 years with BCG-unresponsive and BCG-naïve (defined as patients who have never been exposed and those who have not received intravesical BCG for at least 24 months) NMIBC with CIS ± Ta/T1 who have active disease (**Figure 1**).
- The primary endpoint is high-grade complete response (CR) at any time up to Month 6.
- Key secondary endpoint is durability of response at Month 12.
- Participants are followed for safety throughout the study.
- The data cutoff date is April 16, 2025.

FIGURE 1. ADVANCED-2 STUDY SCHEMA



ABBREVIATIONS: BCG = Bacillus Calmette-Guérin; CR = complete response; CIS = carcinoma in situ ; FDA = Food and Drug Administration; HG = high-grade

*Aligned with the U.S. FDA's 2024 BCG-unresponsive NMIBC: Developing Drugs and Biologics for Treatment Guidance for Industry.
†Residual CIS and/or recurrence of HGTa

- Enrollment of BCG-unresponsive participants is ongoing.
- Enrollment of BCG-naïve participants is complete.

Baseline Characteristics

TABLE 1. BASELINE DEMOGRAPHICS AND CLINICAL CHARACTERISTICS

	BCG-unresponsive N=19*	BCG-naïve N=31†
Age, years		
Median	80.0	71.0
Min, max	47, 92	45, 89
Sex, n (%)		
Male	15/19 (78.9)	25/31 (80.6)
Race, n (%)		
White	16/19 (84.2)	29/31 (93.5)
Black	0/19 (0.0)	1/31 (3.2)
Asian	2/19 (10.5)	0/31 (0.0)
Not reported	1/19 (5.3)	1/31 (3.2)
Ethnicity, n (%)		
Non-Hispanic	19/19 (100.0)	28/31 (90.3)
ECOG Score, n (%)		
0	13/15 (86.7)	25/30 (83.3)
Baseline Diagnosis, n (%)		
CIS Only	16/17 (94.1)	18/31 (58.1)
CIS+Ta	1/17 (5.9)	9/31 (29.0)
CIS+T1	0/17 (0.0)	4/31 (12.9)

ABBREVIATIONS: ECOG= Eastern Cooperative Oncology Group; n = number of participants
FOOTNOTE: *Figure 2 excludes 2 participants who withdrew prior to the response assessment; Table 4 excludes 6 participants who had not yet been exposed to TARA-002. †Figure 3 excludes 1 participant who withdrew prior to the response assessment; Table 4 excludes 1 participant who had not yet been exposed to TARA-002.

RESULTS

Response Assessment

FIGURE 2. TARA-002 MONOTHERAPY DEMONSTRATES 100% HIGH-GRADE COMPLETE RESPONSE AT ANY TIME IN BCG-UNRESPONSIVE PARTICIPANTS

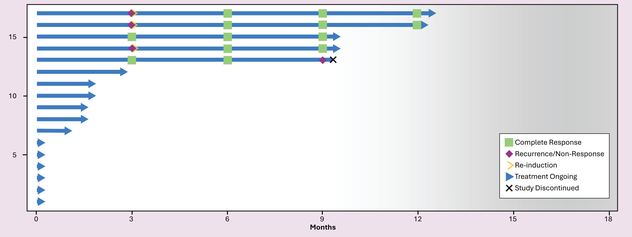


TABLE 2. TARA-002 MONOTHERAPY DEMONSTRATES PROMISING EFFICACY AND ENCOURAGING DURABILITY IN BCG-UNRESPONSIVE PARTICIPANTS

	BCG-unresponsive n/N (%)
High-grade CR at any time	**5/5 (100.0)**
CIS only	5/5 (100.0)
CIS + Ta/T1	N/A
High-grade CR at Month 6	**5/5 (100.0)**
CIS only	5/5 (100.0)
CIS + Ta/T1	N/A
High-grade CR at Month 9	**4/5 (80.0)**
CIS only	4/5 (80.0)
CIS + Ta/T1	N/A
High-grade CR at Month 12	**2/3 (66.7)**
CIS only	2/3 (66.7)
CIS + Ta/T1	N/A

FOOTNOTE (FIGURE 2 AND TABLE 2): At the time of data cutoff, 5 participants were evaluated for high-grade CR at Month 3 and later. Five participants were evaluated for high-grade CR at Month 6, 5 participants at Month 9, and 3 participants at Month 12. Evaluable participants include those who had at least one dose of study drug before the response assessment time point and were discontinued due to disease progression or treatment failure. Participants who have not yet completed the visit time point were not included.

- For BCG-unresponsive participants, the rate of high-grade CR at any time was 100% (5 of 5), 100% (5 of 5) at Month 6, 80% (4 of 5) at Month 9, and 67% (2 of 3) at Month 12.
- Among the three BCG-unresponsive participants who did not achieve an initial CR and received re-induction, all converted to a CR by Month 6, which was maintained at Month 9 (100%, 3 of 3).

FIGURE 3. TARA-002 MONOTHERAPY DEMONSTRATES 76% HIGH-GRADE COMPLETE RESPONSE AT ANY TIME IN BCG-NAÏVE PARTICIPANTS

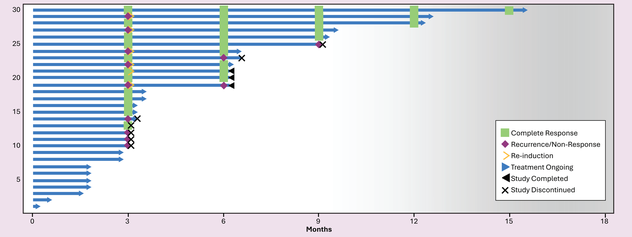


TABLE 3. TARA-002 MONOTHERAPY DEMONSTRATES PROMISING EFFICACY AND ENCOURAGING DURABILITY IN BCG-NAÏVE PARTICIPANTS

	BCG-naïve n/N (%)
High-grade CR at any time	**16/21 (76.2)**
CIS only	10/11 (90.9)
CIS + Ta/T1	6/10 (60.0)
High-grade CR at Month 6	**10/16 (62.5)**
CIS only	5/6 (83.3)
CIS + Ta/T1	5/10 (50.0)
High-grade CR at Month 9	**5/8 (62.5)**
CIS only	4/5 (80.0)
CIS + Ta/T1	1/3 (33.3)
High-grade CR at Month 12	**3/7 (42.9)**
CIS only	3/5 (60.0)
CIS + Ta/T1	0/2 (0.0)

FOOTNOTE (FIGURE 3 AND TABLE 3): At the time of data cutoff, 21 participants were evaluated for high-grade CR at Month 3 and later. Sixteen participants were evaluated for high-grade CR at Month 6, 8 participants at Month 9, and 7 participants at Month 12. Evaluable participants include those who had at least one dose of study drug before the response assessment time point and were discontinued due to disease progression or treatment failure. Participants who have not yet completed the visit time point were not included. Central urine cytology is pending for 1 participant at Month 12. Six participants (10, 11, 12, 19, 20, 21) were enrolled and treated under a protocol version that ended at Month 6; re-consent for further treatment was not obtained prior to study end. These participants are not included in the denominator from Month 9 onwards.

- For BCG-naïve participants, the rate of high-grade CR at any time was 76% (16 of 21), 63% (10 of 16) at Month 6, 63% (5 of 8) at Month 9, and 43% (3 of 7) at Month 12.
- Among BCG-naïve participants who achieved a CR at Month 3 and remained on study, 86% (6 of 7) maintained their response through Month 6. Of those evaluable at later time points, 75% (3 of 4) maintained a response through Month 9, 100% (2 of 2) maintained a response at Month 12
- Of the five BCG-naïve participants who did not achieve an initial CR and received re-induction, the CR rate at Month 6 was 80% (4 of 5).

SAFETY

TABLE 4. FAVORABLE AND WELL-TOLERATED SAFETY PROFILE ACROSS BCG EXPOSURES

N=43	Any Grade	Grade 1	Grade 2	Grade 3	Grade 4/5
Participants with TEAEs, n (%)	32 (74)	26 (60)	13 (30)	8 (19)	0 (0)
Participants with Related TEAEs, n (%)	13 (30)	12 (28)	1 (2)	0 (0)	0 (0)
Participants with Serious TEAEs, n (%)	6 (14)	0 (0)	2 (5)	6 (14)	0 (0)
Participants with Related TEAEs Leading to Study Drug Withdrawal, n (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

ABBREVIATIONS: TEAE = Treatment-Emergent Adverse Event

FOOTNOTE: A total of 43 participants were exposed to at least one dose of TARA-002; 13 were BCG-unresponsive and 30 were BCG-naïve. Adverse events that are recorded after the initiation of treatment are classified as TEAEs. Severity of adverse event is based on NCI-CTCAE Version 5.0. Non-treatment-related serious TEAEs included urosepsis, urinary tract infection, small intestinal obstruction, incarcerated hernia, hydronephrosis, cellulitis, lower urinary tract symptoms, and ataxia.

- Majority of TEAEs were Grade 1 and transient (**Table 4**).
- No participants experienced treatment-related serious AEs (SAEs) or related TEAEs leading to withdrawal or death (**Table 4**).
- Common urinary AEs reflect urinary tract instrumentation effects, such as bladder spasm, burning sensation, and UTI.
- Systemic AEs were consistent with the known safety profile of an immune-potentiating drug, such as flu-like symptoms.

CONCLUSIONS

- TARA-002 was well tolerated and demonstrated encouraging clinical activity in both BCG-naïve and BCG-unresponsive participants with high-risk NMIBC with CIS ± Ta/T1.
- TARA-002 demonstrated encouraging durability of response up to 12 months after initiation of TARA-002 therapy in both BCG-naïve and BCG-unresponsive participants.
- These interim findings support the potential of TARA-002 as an intravesical immunotherapy for high-risk NMIBC.
- Additional data from this study will further the understanding of the efficacy and safety profile of TARA-002 in both BCG-naïve and BCG-unresponsive high-risk NMIBC patients.

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