# ADVANCED-1: Phase 1a Dose-finding, Open-label Study to Evaluate Safety and Toxicity of Intravesical Instillation of TARA-002 in Adults with High-grade Non-muscle Invasive Bladder Cancer

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### **INTRODUCTION**

- Bladder cancer is the most common malignancy involving the urinary system, resulting in approximately 18,000 deaths each year<sup>1</sup>
- Bladder cancer is the 6th most common cancer in the United States, with non-muscle invasive bladder cancer (NMIBC) representing approximately 80% of bladder cancer diagnoses<sup>2,3</sup>
- With the current Bacillus Calmette-Guérin (BCG) shortage and limited effective alternative therapies, there remains a significant unmet need for treatment options for patients with NMIBC
- TARA-002 is a lyophilized biological preparation for instillation containing cells of Streptococcus pyogenes (Group A, type 3) Su strain treated with benzylpenicillin and is being developed for the treatment of high-grade NMIBC
- TARA-002 is manufactured using the same master cell bank as OK-432
- OK-432 is approved in Japan and Taiwan for the treatment of several oncology indications<sup>4</sup>
- The antitumor activity of TARA-002 and OK-432 is thought to occur by direct cytotoxicity and by stimulation of immunocompetent cells (including T cells and natural killer cells) through the induction of helper T-cell type-1 cytokines (including interferon gamma and various interleukins), which then recruit cytotoxic T lymphocytes to tumor cells<sup>3,5</sup>
- Nonclinical toxicology studies with TARA-002 support the starting dose of the Phase 1a dose-finding study (ADVANCED-1)

### **STUDY OBJECTIVES**/ **ENDPOINTS**

- The purpose of this ADVANCED-1 study is to evaluate the safety and toxicity of TARA-002 and to establish the maximum tolerated dose (MTD) and recommended Phase 2 dose (RP2D) in the treatment of HGTa or CIS NMIBC (including CIS with concomitant Ta)
- Primary Endpoints: ADVANCED-1 Dose Escalation
- Incidence of dose limiting toxicity (DLT) adverse events (AEs) in subjects with HGTa or CIS NMIBC (including CIS with concomitant Ta)
- MTD and RP2D of TARA-002 in subjects with HGTa or CIS NMIBC (including CIS with concomitant Ta)

## **METHODS**

### FIGURE 1. PHASE 1A DOSE-FINDING **OPEN-LABEL STUDY OF TARA-002**

**ADVANCED-1 Dose Escalation**<sup>a</sup>



Abbreviations: BCG, Bacillus Calmette-Guérin; CIS, carcinoma in situ; HGTa, highgrade Ta: KE. Klinische Einheit: NMIBC. non-muscle invasive bladder cancer. <sup>a</sup>Subjects will receive weekly intravesical doses of TARA-002 instillation for 6 weeks.

<sup>b</sup>Subjects with HGTa or CIS ± Ta NMIBC who are unable to obtain intravesical BCG, received  $\geq$  1 dose of intravesical BCG, or received  $\geq$  1 dose of intravesical chemotherapy.

- ADVANCED-1 is a Phase 1a, dose-finding, open-label study of TARA-002 in adults  $\geq$  18 years with high-grade NMIBC (HGTa or CIS [including CIS with concomitant Ta])
- Three subjects were enrolled and treated in 3 cohorts of increasing dose levels: 10 KE, 20 KE and 40 KE (Figure 1)
- Across the 3 cohorts, 9 subjects with high-grade NMIBC who were unable to receive intravesical BCG or have received  $\geq$  1 dose of intravesical BCG or chemotherapy. were included
- The overall study duration for each subject was 12-14 weeks (28 days of screening period; 6-week treatment period; 6-week follow-up period)
- During the study, eligible subjects received weekly intravesical doses of TARA-002 instillation for 6 weeks
- Up to 3 dose levels were tested sequentially with 6 weekly intravesical doses, starting with the lowest dose using a 3+3 design in a dose escalation manner until the RP2D was established
- Urinary symptoms and AEs were collected throughout the study duration
- The dose escalation remains ongoing in exploratory cohorts

Characteristics OF STUDY ADVANCED-1 TARA.002 2016: TARA.002	TABLE 1. OVERVIEW OF DEMOGRAPHICS AND BASELINE TABLE 2. ACTIVITY OUTCOMES OF STUDY ADVANCED-1										
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	CHARACTER	ISTICS OF 9	STUDY AD	ANCED-1			Cohort 1	Cohort 3	Cohort 2	Total	
No. of evaluable subjects         3         3         3         9           Age (years) [a)         No. of let Sa         3         1         2         6           No. of HGTa         3         1         2         6           Modian         72.0         66.0         77.0         72.0           Mix Max         66.80         7.2         7.2.2         42.2         7.2.2         42.2					Total		(10 KE, n=3)	(20 KE, n=3)	(40 KE, n=3)	(N=9)	
Age (part)Mean (SD)72.7 (7.02)62.0 (17.78)76.7 (5.51)70.4 (11.92)Median72.066.077.072.0Min, Max66.565.8042.7577.1249.252Age category (M) (Ja)751.133.311.(33.3)2 (66.7)4.(44.4)5751.633.311.(33.3)2 (66.7)4.(44.4)5752.(65.7)1.(33.3)1.(33.3)5.(55.6)Female2.(65.7)1.(33.3)1.(33.3)4.(44.4)Race category (M)		(N=3)	(N=3)	(N=3)	(N=9)	No. of evaluable subjects	3	3	3	9	
n339Median72.062.017.076.772.0Min, Max66.8077.072.0Min, Max66.8077.072.0Min, Max66.8042, 7.671.82Age category (N) [3]1133.312 (66.7)1 (33.3)2 (65.7)2 (66.7)1 (33.3)2 (66.7)2 (66.7)1 (33.3)32 (66.7)2 (66.7)1 (33.3)4 (44.4)Male1 (33.3)2 (66.7)2 (66.7)5 (55.6)Female2 (66.7)1 (33.3)4 (44.4)Asian0 (0.0)<	Age (years) [a]					No. of HGTa	3	1	2	6	
Mealan         72.0         68.0         70.4         72.0         68.0         70.4         72.0           Min, Max         66.80         42.76         71.82         42.82           Age ctacyon (K) (a)         -         575         2 (65.7)         2 (65.7)         1 (33.3)         2 (65.7)         1 (33.3)         2 (65.7)         1 (33.3)         2 (65.7)         1 (33.3)         2 (65.7)         5 (55.6)           Sean (K3)         -         -         -         Three subjects with GLS reached the three-month (Week 12) activity assessment (Table 2)           Sean (K3)         -	n	3	3	3	9	No. of CIS + Ta	0	2	1	3	
Merian         72.0         66.0         77.0         72.0         Impring model model 12         20.0 (1/3)         0.0 (1/	Mean (SD)	72.7 (7.02)	62.0 (17.78)	76.7 (5.51)	70.4 (11.92)	High grade CP rate in CIS $\pm$ Ta at Week 12	NA	E0% (1/2)	0% (0/1)	220/ (1/2)	
Min, Max         66,80         42,76         71,82         42,82         Methys in Methy	Median	72.0	68.0	77.0	72.0			30% (1/2)	0%(0/1)	55/0 (1/5)	
Age categoryn (%) (a)       > 163.3       163.3       2 (66.7)       4 (44.4)         275       1 (33.3)       2 (66.7)       1 (13.3)       5 (55.6)         Sex (%)       -	Min, Max	66, 80	42, 76	71, 82	42, 82	HGRFS IN HG Ia at Week 12	6/% (2/3)	100% (1/1)	100% (2/2)	83% (5/6)	
>75         1133         12(63         2 (66.7)         4 (44.9)           Sem (%)         - <td< td=""><td colspan="11">Age category n (%) [a]       Abbreviations: CIS = carcinoma in situ; CR = complete response; HGTa = high-grade Ta; HGRFS = high-grade recurrence free survival; KE = Klinische Einheit; NA = not applicable.</td></td<>	Age category n (%) [a]       Abbreviations: CIS = carcinoma in situ; CR = complete response; HGTa = high-grade Ta; HGRFS = high-grade recurrence free survival; KE = Klinische Einheit; NA = not applicable.										
≤75       2 (667)       2 (667)       1 (33.3)       5 (55.6)         Sex (%)	> 75	1 (33.3)	1 (33.3)	2 (66.7)	4 (44.4)	• Three subjects with CIS reach	hed the th	ree-month	(Meek 12)	activity	
Sex n (%)         Sex n (%)           Male         1 (33.3)         2 (66.7)         5 (55.6)           Female         2 (66.7)         1 (33.3)         4 (44.4)           Race n (%)	≤ 75	2 (66.7)	2 (66.7)	1 (33.3)	5 (55.6)	assessment (Table 2)		ince monti		activity	
Male         1 (33.3)         2 (66.7)         2 (66.7)         5 (55.6)           Female         2 (66.7)         1 (33.3)         4 (44.4)           Race n (%)	Sex n (%)					• In Cohort 2 (20 KE cohort) 1	heavily n	ro-troated	RCG_unresn	oncive	
Female         2 (66.7)         1 (33.3)         1 (33.3)         4 (44.4)           Race n (\$)         Image: Constrained const	Male	1 (33.3)	2 (66.7)	2 (66.7)	5 (55.6)	narticipant with CIS + Ta achieved complete response					
Race n (%)         Control	Female	2 (66.7)	1 (33.3)	1 (33.3)	4 (44.4)	- In the other 2 CIS + Ta subjects visible tymor regression was					
American Indian or Alaska Native         0 (0.0)         0 (0.0)         0 (0.0)         0 (0.0)         0 (0.0)           Asian         0 (0.0)         0 (0.0)         0 (0.0)         0 (0.0)         0 (0.0)           Native Hawaiian or Pacific Islander         0 (0.0)         0 (0.0)         0 (0.0)         0 (0.0)           White         3 (100.0)         3 (100.0)         3 (100.0)         9 (100.0)           Other         0 (0.0)         0 (0.0)         0 (0.0)         0 (0.0)           No         3 (100.0)         3 (100.0)         3 (100.0)         9 (100.0)           No         3 (100.0)         3 (100.0)         9 (100.0)         Any DLTS         Cohort 1         Cohort 3         Cohort 3         Nola           No         3 (100.0)         3 (100.0)         3 (100.0)         9 (100.0)         Any DLTS         0 (0.0)         0 (0.0)         0 (0.0)         0 (0.0)         0 (0.0)         0 (0.0)         0 (0.0)         0 (0.0)         0 (0.0)         0 (0.0)         0 (0.0)         1 (13.3)         0 (0.0)         1 (11.1)           Any TEALS selating to TARA-002         3 (100.0)         3 (100.0)         3 (100.0)         0 (0.0)         0 (0.0)         0 (0.0)         0 (0.0)         0 (0.0)         0 (0.0)         0	Race n (%) observed										
Asian       0 (0.0)       0 (0.0)       0 (0.0)       0 (0.0)       0 (0.0)         Bick or African American       0 (0.0)       0 (0.0)       0 (0.0)       0 (0.0)       0 (0.0)         White       3 (100.0)       3 (100.0)       3 (100.0)       9 (100.0)       0 (0.0)       0	American Indian or Alaska Native	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	<ul> <li>Five of 6 subjects with HGTa achieved high-grade recurrence free survival at Week 12</li> </ul>					
Black or African American         0 (0,0)         0 (0,	Asian	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)						
Native Hawaiian or Pacific Islander         0 (0.0)	Black or African American	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)						
White         3 (100.0)         3 (100.0)         9 (100.0)           Other         0 (0.0)         0	Native Hawaiian or Pacific Islande	r 0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	TABLE 3. OVERVIEW OF IN	<b>CIDENCE</b>	OF TREAT	MENT EM	ERGENT	
Other         0 (0.0)	White	3 (100.0)	3 (100.0)	3 (100.0)	9 (100.0)	ADVERSE EVENTS THROUGHOUT THE STUDY DURATION					
Ethnicity n (%)       Child L2       Colloi L2 <thcolloi <="" l2<="" td=""><td>Other</td><td>0 (0.0)</td><td>0 (0.0)</td><td>0 (0.0)</td><td>0 (0.0)</td><td></td><td>Cohor</td><td>t 1 Cohor</td><td>2 Cohort 2</td><td>Total</td></thcolloi>	Other	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)		Cohor	t 1 Cohor	2 Cohort 2	Total	
Hispanic         0 (0.0)         <	Ethnicity n (%)						(10 KE, I	n=3) (20 KE, i	n=3) (40 KE, n=:	3) (N=9)	
Non-Hispanic         3 (100.0)         3 (100.0)         3 (100.0)         9 (100.0)           BMI (kg/m²)         Any TEAEs         3 (100.0)         2 (66.7)         3 (100.0)         2 (66.7)         3 (100.0)         2 (66.7)         3 (100.0)         3 (1	Hispanic	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	Any DITs	0 (0 (	)) 0(0(	) 0 (0 0)	0 (0 0)	
BMI (kg/m²)       Any TEAEs with CTCAE Severity Grade 23       0 (0.0)       1 (33.3)       0 (0.0)       1 (13.1)         n       3       3       9       Any TEAEs with CTCAE Severity Grade 23       0 (0.0)       1 (33.3)       0 (0.0)       1 (13.1)         Mean (SD)       30.87 (6.385)       26.80 (4.531)       27.93 (2.916)       28.53 (4.555)       Any TEAEs with CTCAE Severity Grade 23       0 (0.0)       1 (33.3)       0 (0.0) <td>Non-Hispanic</td> <td>3 (100.0)</td> <td>3 (100.0)</td> <td>3 (100.0)</td> <td>9 (100.0)</td> <td></td> <td>3 (100</td> <td>0) 2 (66</td> <td>7) 3 (100 0)</td> <td><u> </u></td>	Non-Hispanic	3 (100.0)	3 (100.0)	3 (100.0)	9 (100.0)		3 (100	0) 2 (66	7) 3 (100 0)	<u> </u>	
n         3         3         9           Mean (SD)         30.87 (6.385)         26.80 (4.531)         27.93 (2.916)         28.53 (4.555)           Median         30.10         24.70         26.30         26.30           Min, Max         24.9, 37.6         23.7, 32.0         26.2, 31.3         23.7, 37.6           ECOG PS at Baseline n (%) [a]	BMI (kg/m²)					Any TEAEs with CTCAE Severity Grade >3	0.010	.0) 2 (00. )) 1 (33	(100.0)	1 (11 1)	
Mean (SD)       30.87 (6.385)       26.80 (4.531)       27.93 (2.916)       28.53 (4.555)         Median       30.10       24.70       26.30       26.30         Min, Max       24.9, 37.6       23.7, 32.0       26.2, 31.3       23.7, 37.6         ECOG PS at Baseline n (%) [a]        3 (100.0)       3 (100.0)       2 (6.7)       3 (100.0)       0 (0.0) <t< td=""><td>n</td><td>3</td><td>3</td><td>3</td><td>9</td><td>Any TEAEs Polated to TABA 002</td><td>2 (100</td><td>1(33)</td><td>7) 2(66.7)</td><td>T (11.1)</td></t<>	n	3	3	3	9	Any TEAEs Polated to TABA 002	2 (100	1(33)	7) 2(66.7)	T (11.1)	
Median         30.10         24.70         26.30         26.30           Min, Max         24.9, 37.6         23.7, 32.0         26.2, 31.3         23.7, 37.6           ECOG PS at Baseline n (%) [a]               0         2 (66.7)         3 (100.0)         3 (100.0)         8 (88.9)           1         1 (33.3)         0 (0.0)         1 (11.1)         1 (11.1)         No         1 (13.3)	Mean (SD)	30.87 (6.385)	26.80 (4.531)	27.93 (2.916)	28.53 (4.555)	Any TEAEs Related to TARA-002	0 (100 S (100	$\frac{10}{200}$	(00.7)	/ (//.0)	
Min, Max         24.9, 37.6         23.7, 32.0         26.2, 31.3         23.7, 37.6           ECOG PS at Baseline n (%) [a]         Any TEAEs Leading to Study Discontinuation         0 (0.0) </td <td>Median</td> <td>30.10</td> <td>24.70</td> <td>26.30</td> <td>26.30</td> <td>Any TEAEs Leading to Treatment Discontinua</td> <td></td> <td>0 (0.0</td> <td>(0.0)</td> <td>0 (0.0)</td>	Median	30.10	24.70	26.30	26.30	Any TEAEs Leading to Treatment Discontinua		0 (0.0	(0.0)	0 (0.0)	
ECOG PS at Baseline n (%) [a]       Any Serious TEAEs       0 (0.0)       0 (0.0)       0 (0.0)       0 (0.0)       0 (0.0)       0 (0.0)         0       2 (66.7)       3 (100.0)       3 (100.0)       8 (88.9)       1       1 (33.3)       0 (0.0)	Min, Max	24.9, 37.6	23.7, 32.0	26.2, 31.3	23.7, 37.6	Any TEAEs Leading to Study Discontinuation	0 (0.0	0) 0 (0.0	0) 0 (0.0)	0 (0.0)	
0         2 (66.7)         3 (100.0)         8 (88.9)           1         1 (33.3)         0 (0.0)         0 (0.0)         1 (11.1)           Prior Doses of Non-BCG Bladder Cancer Therapies         Any TEAEs with Outcome of Death         0 (0.0)         0 (0.0)         0 (0.0)         0 (0.0)         0 (0.0)           Yes         2 (66.7)         2 (66.7)         1 (33.3)         2 (66.7)         4 (44.4)           Prior Doses of BCG Therapy         Yes         1 (33.3)         2 (66.7)         2 (66.7)         2 (66.7)         4 (44.4)           Yes         1 (33.3)         2 (66.7)         2 (66.7)         5 (55.6)         A cross all 3 cohorts, 8 of 9 (88.9%) subjects experienced at least one treatment emergent adverse event.         - Across all 3 cohorts, 8 of 9 (88.9%) subjects experienced at least one treatment emergent AE           Yes         1 (33.3)         1 (33.3)         1 (33.3)         4 (44.4)           No         2 (66.7)         1 (33.3)         4 (44.4)	ECOG PS at Baseline n (%) [a]					Any Serious TEAEs	0 (0.0	0) 0 (0.0	0) 0 (0.0)	0 (0.0)	
1       1 (33.3)       0 (0.0)       0 (0.0)       1 (11.1)         Prior Doses of Non-BCG Bladder Cancer Therapies       Any TEAEs with Outcome of Death       0 (0.0)       0 (0.0)       0 (0.0)       0 (0.0)       1 (33.3)         Yes       2 (66.7)       2 (66.7)       1 (33.3)       5 (55.6)       Any TEAEs Leading TARA-002 Dose Interruption       0 (0.0)       1 (33.3)       0 (0.0)       1 (11.1)         Mo       1 (33.3)       2 (66.7)       1 (33.3)       2 (66.7)       4 (44.4)       Any TEAEs with Outcome of Death       0 (0.0)       0 (0.0)       0 (0.0)       0 (0.0)       1 (11.1)         Mo       1 (33.3)       2 (66.7)       2 (66.7)       4 (44.4)       Any TEAEs Leading TARA-002 Dose Interruption       0 (0.0)       1 (33.3)       0 (0.0)       1 (11.1)         Mo       1 (33.3)       2 (66.7)       2 (66.7)       5 (55.6)       A (44.4)       Any TEAEs Leading TARA-002 Dose Interruption       0 (0.0)       1 (33.3)       0 (0.0)       1 (11.1)         Mo       2 (66.7)       2 (66.7)       2 (66.7)       5 (55.6)       -0 one subject experienced a TEAE with a maximum severity of Grade 3 (hypoxia after TURBT), which was not related to TARA-002       -0 one subject experienced a TEAE with a maximum severity of Grade 3 (hypoxia after TURBT), which was not related to TARA-002	0	2 (66.7)	3 (100.0)	3 (100.0)	8 (88.9)	Any Serious TEAEs Related to TARA-002	0 (0.0	0) 0 (0.0	0) 0 (0.0)	0 (0.0)	
Prior Doses of Non-BCG Bladder Cancer TherapiesAny TEAEs Leading TARA-002 Dose Interruption0 (0.0)1 (33.3)0 (0.0)1 (11.1)Yes2 (66.7)2 (66.7)1 (33.3)5 (55.6)4 (44.4)Prior Doses of BCG Therapy	1	1 (33.3)	0 (0.0)	0 (0.0)	1 (11.1)	Any TEAEs with Outcome of Death	0 (0.0	0) 0 (0.0	0 (0.0)	0 (0.0)	
Yes2 (66.7)2 (66.7)1 (33.3)5 (55.6)No1 (33.3)1 (33.3)2 (66.7)4 (44.4)Prior Doses of BCG TherapyYes1 (33.3)2 (66.7)2 (66.7)5 (55.6)No2 (66.7)1 (33.3)1 (33.3)4 (44.4)No2 (66.7)1 (33.3)1 (33.3)4 (44.4)	Prior Doses of Non-BCG Bladder Cancer Therapies					Any TEAEs Leading TARA-002 Dose Interrupt	tion 0 (0.0	)) 1 (33.	3) 0 (0.0)	1 (11.1)	
No         1 (33.3)         1 (33.3)         2 (66.7)         4 (44.4)           Prior Doses of BCG Therapy         -	Yes	2 (66.7)	2 (66.7)	1 (33.3)	5 (55.6)	Abbreviations: CTCAE = Common Terminology Criteria for Adverse Event; DLT = Dose Limiting Toxicity; KE = Klinische Einheit;					
Prior Doses of BCG Therapy- Across all 3 cohorts, 8 of 9 (88.9%) subjects experienced at least one treatment emergent AEYes1 (33.3)2 (66.7)2 (66.7)5 (55.6)No2 (66.7)1 (33.3)1 (33.3)4 (44.4)No2 (66.7)1 (33.3)4 (44.4)	No	1 (33.3)	1 (33.3)	2 (66.7)	4 (44.4)	I LAE = treatment emergent adverse event.					
Yes         1 (33.3)         2 (66.7)         2 (66.7)         5 (55.6)           No         2 (66.7)         1 (33.3)         4 (44.4)   — One subject experienced a TEAE with a maximum severity of Grade 3 (hypoxia after TURBT), which was not related to TARA-002	Prior Doses of BCG Therapy	Prior Doses of BCG Therapy • Across all 3 conorts, 8 of 9 (88.9%) subjects experienced at least one treatment emergent AE (TEAE. Table 3)									
No         2 (66.7)         1 (33.3)         4 (44.4)         which was not related to TARA-002	Yes	1 (33.3)	2 (66.7)	2 (66.7)	5 (55.6)	<ul> <li>One subject experienced a TEAE with</li> </ul>	th a maximun	n severity of G	ade 3 (hypoxia a	fter TURBT),	
	No	2 (66.7)	1 (33.3)	1 (33.3)	4 (44.4)	which was not related to TARA-002					

breviations: BCG, Bacillus Calmette-Guérin; BMI = Body Mass Index; ECOG = Eastern Cooperative Oncology Group; KE = Klinische Einheit; n = number; PS = performance status; SD = standard deviation.

• The study screened 15 participants, of which 9 participants enrolled (HGTa: 6; CIS ± Ta: 3) within 3 cohorts of increasing dose levels (10 KE, 20 KE and 40 KE), with 3 subjects per cohort (**Table 1**)

- Median age of the participants was 72 years
- Four participants (44.4%) were female
- All participants were non-Hispanic and White

### **RESULTS**

- The most commonly reported AEs were general disorders and administration site conditions (including fatigue, chills, influenza-like illness, and pyrexia) and renal and urinary disorders (bladder spasm, micturition urgency, pollakiuria, urinary tract pain, dysuria, and urinary retention)
- These events spontaneously resolved without treatment or after the use of antipyretics/ analgesics
- No serious TEAEs, study discontinuations, or deaths occurred
- No DLTs were observed; MTD was not established

### CONCLUSIONS

- In the ADVANCED-1 study. TARA-002 was generally well tolerated at all three evaluated dose levels
- TARA-002 demonstrated a favorable safety profile for the treatment of high-grade NMIBC
- Because no DLTs were observed, an MTD was not established for TARA-002
- Therefore, higher doses are currently being explored - Dose escalation remains ongoing in
- exploratory Phase 1a cohorts
- No serious TEAEs were observed Most TEAEs resolved by the end of the study
- RP2D was determined at 40 KE for the treatment of high-grade NMIBC
- Additionally, anti-tumor activity was observed at 20 KE and 40 KE suggest that 40 KE, suggesting a therapeutically active dose at the RP2D of 40 KE

### **FUTURE DIRECTIONS**

- Enrollment is ongoing in the open-label expansion trial (ADVANCED-1EXP) to evaluate intravesical TARA-002 at the 40 KE dose in 12 CIS ± Ta patients
- A Phase 2 study (ADVANCED-2) is ongoing to assess the anti-tumor activity and safety of TARA-002 at 40 KE in subjects with highgrade CIS NMIBC ± Ta/T1 based on prior BCG experience
- Cohort A: BCG naive CIS  $\pm$  Ta/T1 unable to access BCG or BCG exposed > 24 months prior to CIS diagnosis
- Cohort B: BCG unresponsive CIS ± Ta/T1

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