



# CORPORATE PRESENTATION

January 2025

# FORWARD LOOKING STATEMENTS

Statements contained in this presentation regarding matters that are not historical facts are "forward looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. Protara may, in some cases, use terms such as "predicts," "believes," "potential," "proposed," "continue," "designed," "estimates," "anticipates," "expects," "plans," "intends," "may," "could," "might," "will," "should" or other words or expressions referencing future events, conditions or circumstances that convey uncertainty of future events or outcomes to identify these forward-looking statements. Such forward-looking statements include but are not limited to, statements regarding Protara's intentions, beliefs, projections, outlook, analyses or current expectations concerning, among other things: Protara's business strategy, including its development plans for its product candidates and plans regarding the timing or outcome of existing or future clinical trials (including reporting initial data from 12-month evaluable patients in mid-2025); statements related to expectations regarding interactions with the FDA, Protara's financial footing; statements regarding the anticipated safety or efficacy of Protara's product candidates; and Protara's outlook for the remainder of the year and future periods. Because such statements are subject to risks and uncertainties, actual results may differ materially from those expressed or implied by such forward-looking statements. Factors that contribute to the uncertain nature of the forward-looking statements include: risks that Protara's financial guidance may not be as expected, as well as risks and uncertainties associated with: Protara's development programs, including the initiation and completion of non-clinical studies and clinical trials and the timing of required filings with the FDA and other regulatory agencies; general market conditions; changes in the competitive landscape; changes in Protara's strategic and commercial plans; Protara's ability to obtain sufficient financing to fund its strategic plans and development and commercialization efforts; having to use cash in ways or on timing other than expected; the impact of market volatility on cash reserves; the loss of key members of management; the impact of general U.S. and foreign, economic, industry, market, regulatory, political or public health conditions; and the risks and uncertainties associated with Protara's business and financial condition in general, including the risks and uncertainties described more fully under the caption "Risk Factors" and elsewhere in Protara's filings and reports with the United States Securities and Exchange Commission. All forward-looking statements contained in this presentation speak only as of the date on which they were made and are based on management's assumptions and estimates as of such date. Protara undertakes no obligation to update any forward-looking statements, whether as a result of the receipt of new information, the occurrence of future events or otherwise, except as required by law.

# Promising NMIBC therapy & de-risked rare disease programs

## Oncology



### TARA-002 in NMIBC

- Positive interim results from ADVANCED-2 trial in NMIBC
- Unique product characteristics anticipated to drive significant adoption
- Expanding clinical program into BCG-naïve, combinations and systemic priming dosing

## Rare Disease



### IV Choline for Parenteral Support

- Enrolling pivotal study with PK endpoint
- 30K patient population in the US<sup>1</sup>
- FDA Orphan Drug and Fast Track Designations



### TARA-002 in LMIs

- Dosing underway in Phase 2 STARBORN-1 trial
- TARA-002 predecessor is standard of care in Japan
- U.S. FDA granted Rare Pediatric Disease Designation – PRV eligible

# Multiple upcoming opportunities across our pipeline

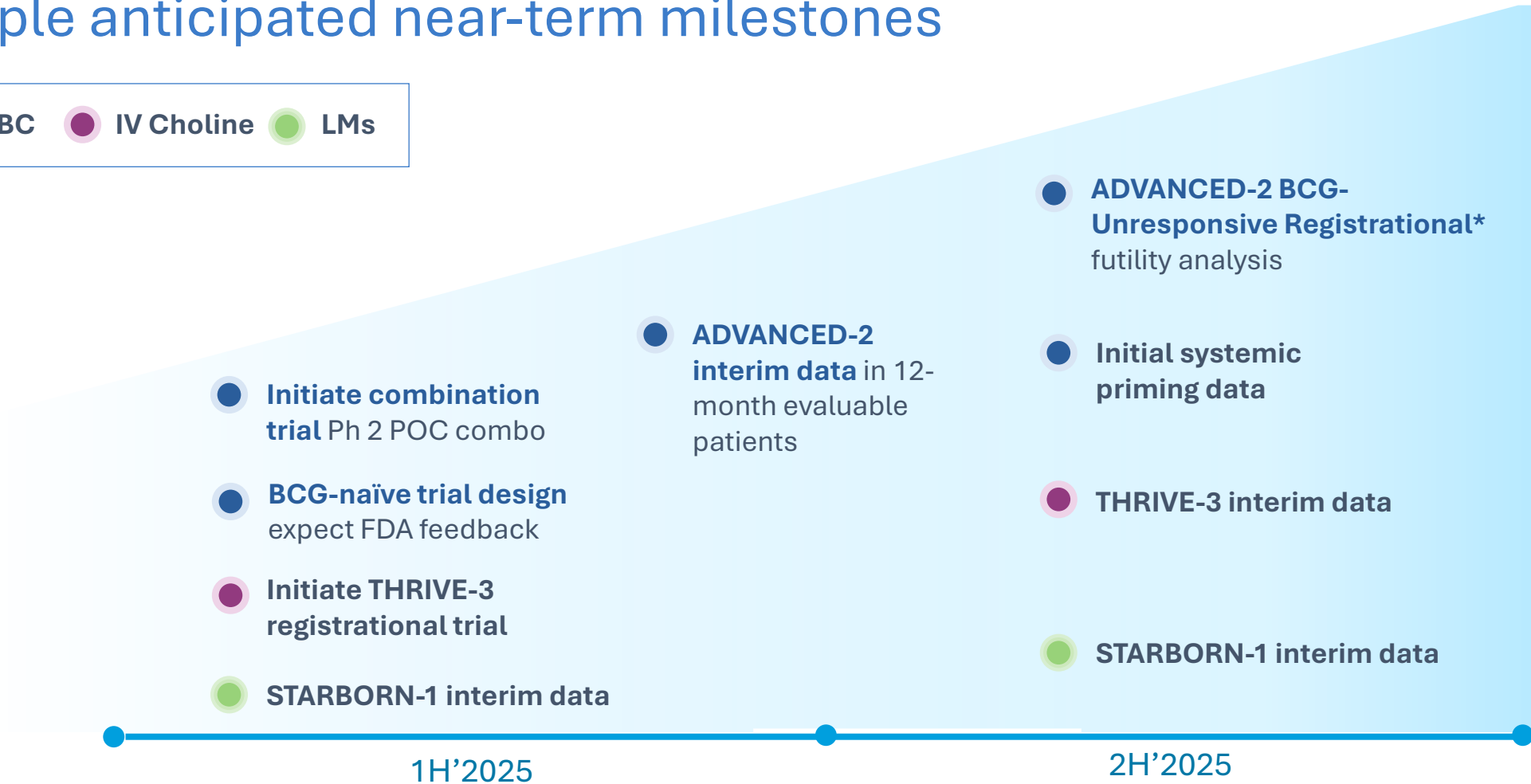
	Indication	Pre-Clinical	Phase 1	Phase 2	Phase 3	Current Status
<b>ONCOLOGY</b>						
TARA-002	NMIBC: BCG-Unresponsive CIS +/- Ta/T1	ADVANCED-2 (Cohort B)				<i>Designed to be registrational</i>
	NMIBC: BCG-Naïve CIS +/- Ta/T1	ADVANCED-2 (Cohort A)				<i>Proof of concept</i>
TARA-002 Systemic Priming	NMIBC: BCG-Naïve & BCG-Exposed CIS +/- Ta/T1	ADVANCED-2 (Cohort C)				<i>Proof of concept</i>
TARA-002 Combination	NMIBC: BCG-Unresponsive CIS +/- Ta/T1	ADVANCED-2 (Cohort D)				<i>Assessing combination potential</i>
<b>RARE DISEASES</b>						
IV CHOLINE	Choline for parenteral support (PS) patients*	THRIVE-3				<i>PK-based registrational study to initiate in 1H'25</i>
TARA-002	Lymphatic Malformations (LMs)**	STARBORN-1				<i>Enrolling safety cohorts</i>

\*Granted Orphan Drug Designations by the U.S. FDA

\*\*TARA-002 granted Rare Pediatric Disease designation by the U.S. FDA and orphan drug designation by the European Medicines Agency for the treatment of LMs.

PK=Pharmacokinetic

# Multiple anticipated near-term milestones

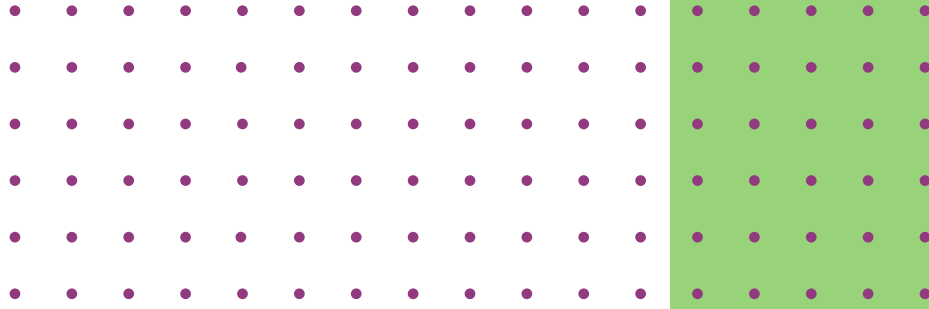


**BALANCE SHEET:** \$81.5M of cash, cash equivalents and investments as of September 30, 2024. Cash runway into 2027 including \$102.7M of gross proceeds from recent public offering

**COMMON SHARE EQUIVALENTS (30.3M)\*\*:** 20.6M Common + 8.0M Preferred + 1.7M Pre-funded warrants on as converted basis as of September 30, 2024 not including 14.1M Common and 2.3M Pre-Funded Warrants issued in recent public offering (46.7M common share equivalents)

\*Designed to be registrational aligned with U.S. FDA guidance on NMIBC clinical trials.

\*\*Does not include 10.8M common warrants issued with the April 2024 private placement exercisable at a \$5.25 per share at the earlier or April 10, 2027 or 90 days after public announcement of a minimum 42% six-month CR rate from at least 25 BCG-Unresponsive patients in the ADVANCED-2 clinical trial.

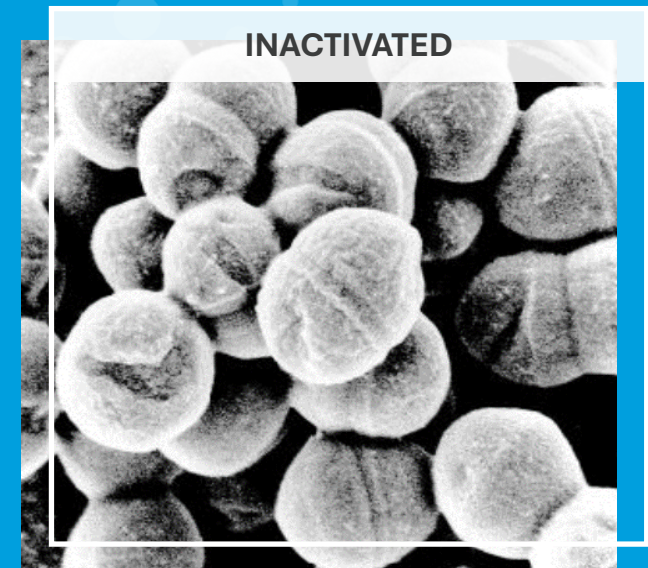
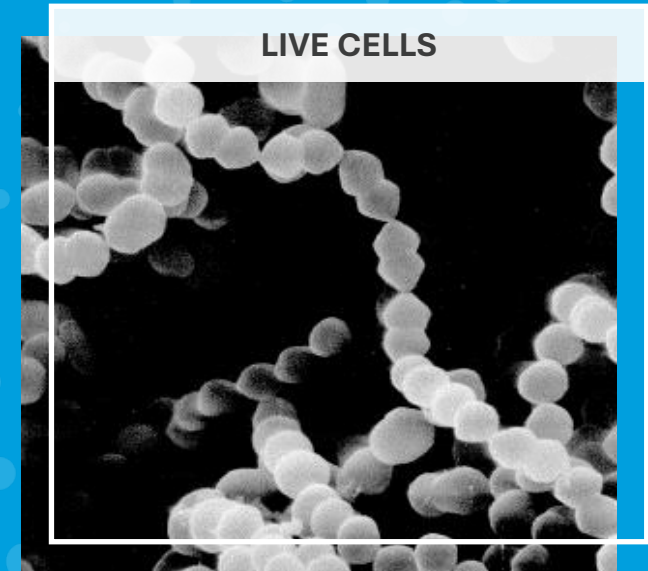


# TARA-002

Lyophilized, Inactivated Group A *Streptococcus pyogenes*

# TARA-002: Broad Immunopotentiator with significant potential

- TARA-002 is an investigational, genetically distinct strain of *Streptococcus pyogenes* that is inactivated while retaining its immune-stimulating properties
- TARA-002 is manufactured under cGMP conditions from the same Master Cell Bank as originator therapy OK-432,<sup>(1)</sup> approved for LMs and a number of oncology indications in Japan
- There are close to 2,000 publications for OK-432 in Pubmed
- Protara has worldwide rights, excluding Japan & Taiwan, for TARA-002 / OK-432



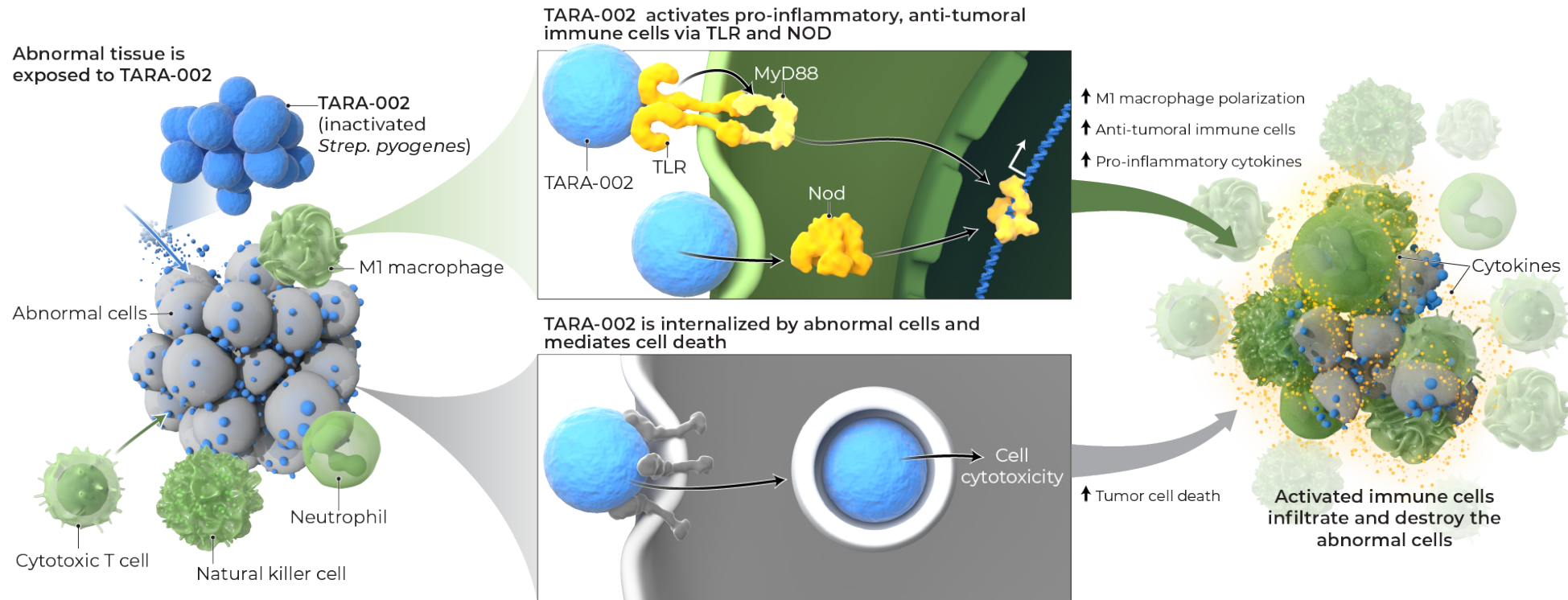
1. Marketed in Japan as Picibanil<sup>®</sup>.

# Broad immunopotential = potential for durable response

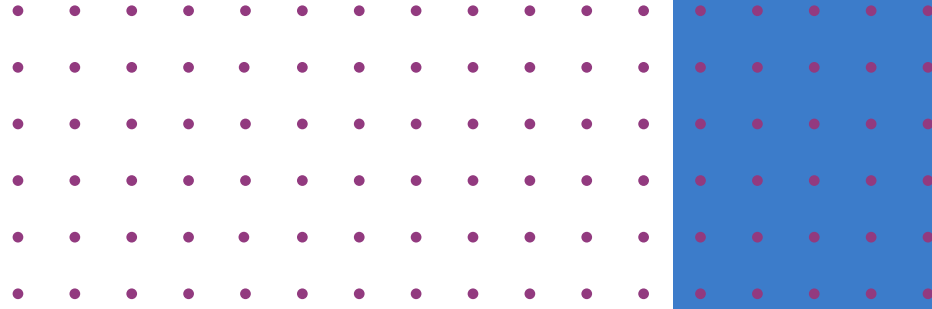
*Mechanism similar to BCG, unique to other agents in development*

Activates Th1 Immune Cascade <sup>(1)(2)(3)</sup>

IL-1b   IL-6   IL-12   TNF- $\alpha$    IFN- $\gamma$    GM-CSF   NK-Cells







# TARA-002

Non-Muscle Invasive Bladder Cancer

# Unique product characteristics anticipated to drive significant adoption



## Encouraging interim ADAVNCED-2 data

- Compelling response rates in BCG-UN and BCG-naïve
- 100% durability observed from 3-to 6-months and 80% reinduction salvage rate seen across all patients



## Favorable safety & tolerability

- To date, no Grade 2 or greater treatment-related adverse events
- To date, majority of adverse events are grade 1 and transient



## Anticipated low burden on physicians & patients

- No additional administration procedures or safety protocols required
- Fast administration typically performed by nurse
- Dedicated to ensuring access with minimal burden

# Bladder cancer: significant unmet need

## All Bladder Cancers



**~80,000**

People **diagnosed with bladder cancer** annually in the U.S.<sup>1</sup>

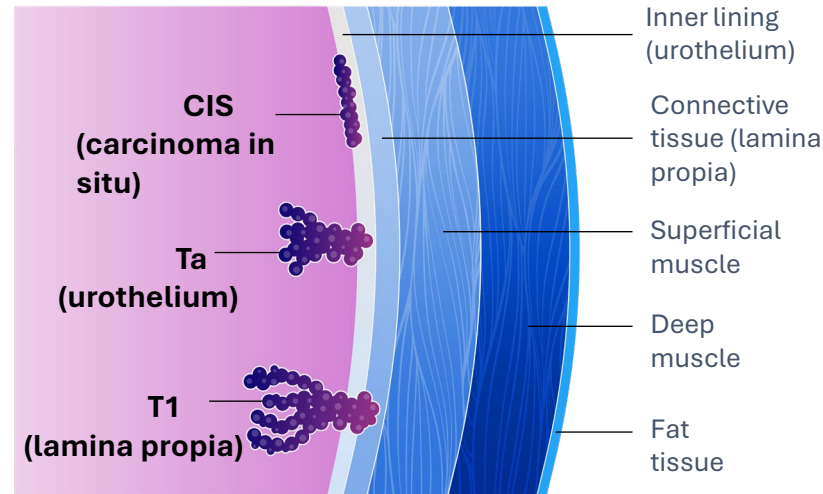
**~725,000**

People estimated **living with bladder cancer** annually in the US<sup>1</sup>

**Average age 73**

1. National Cancer Institute. SEER Bladder Cancer – Stat Facts. Accessed April 25, 2023. | 2. Anastasiadis et al. Therapeutic Advances in Urology, 2012. | 3. Campbell Walsh 11th edition, 2014, Elsevier. | 4. J Gual Frau et al. Arch Esp Urol. 2016.

## NMIBC



**~75%**

Of all bladder cancer diagnoses are **NMIBC**<sup>2</sup>



**80%**

Estimated to **recur in 3 years**<sup>3</sup>

## BCG-UN; Significant unmet need



**~40% to 50%**

**BCG failure rate**

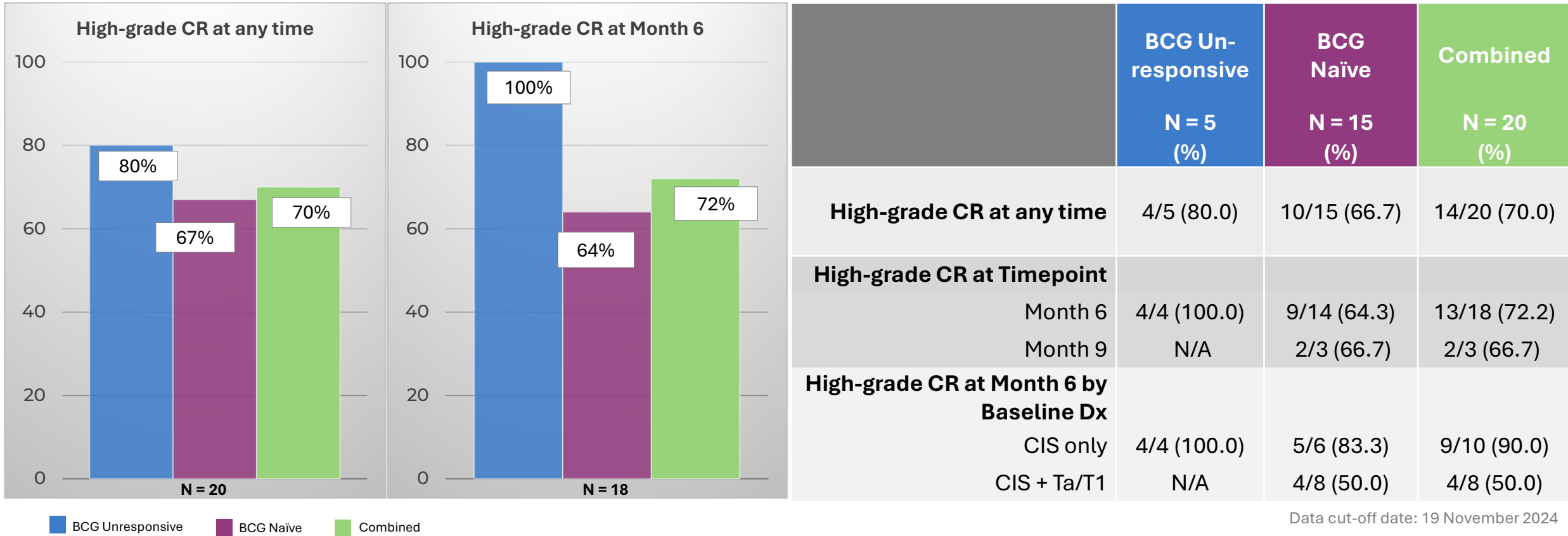
radical cystectomy is the SOC after BCG failure<sup>4</sup>



**FDA**

Currently approved therapies for **BCG-unresponsive NMIBC** were approved on the basis of **single arm trials**

# TARA-002 demonstrated 72% six-month CRR and 70% CRR at any time across BCG exposures

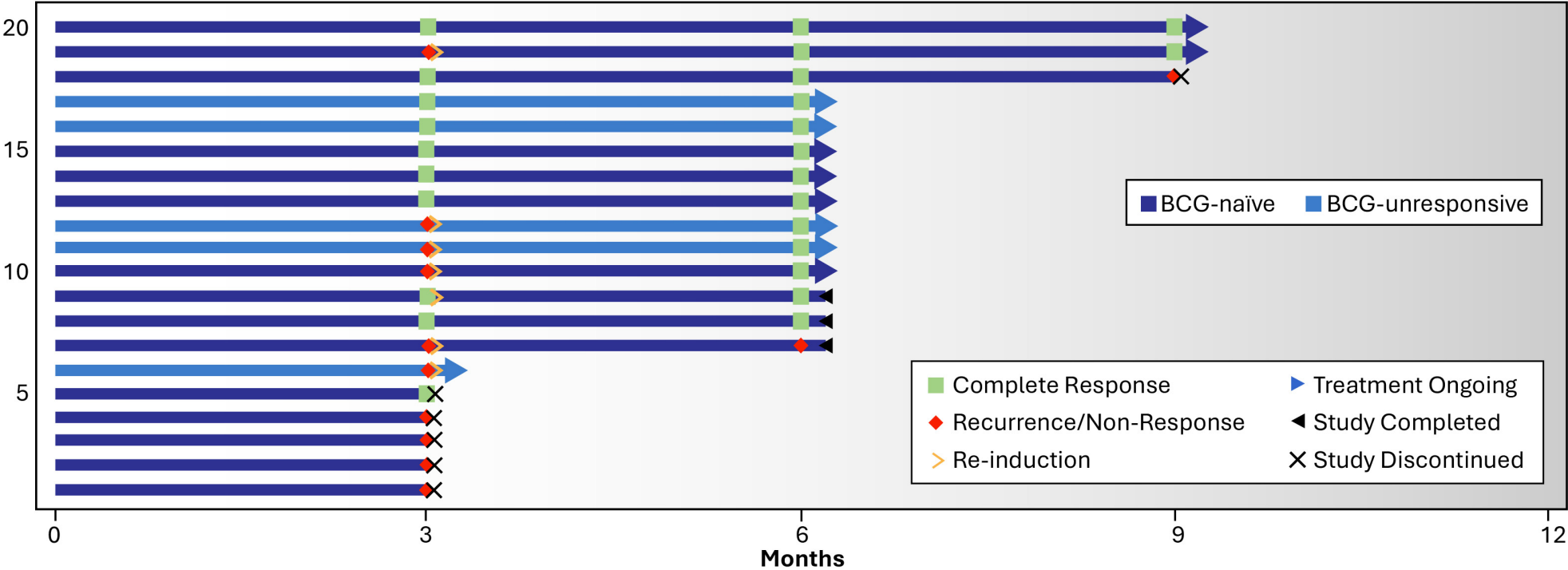


Data cut-off date: 19 November 2024

Abbreviations: BCG = Bacillus Calmette-Guérin; CR = complete response; CIS = carcinoma in situ; Dx = diagnosis; NMIBC = non-muscle invasive bladder cancer

Notes: At the time of data cutoff, 20 subjects were evaluated for high-grade CR at Month 3 and later. Eighteen subjects were evaluated for high-grade CR at Month 6 and 3 subjects at Month 9; Evaluable subjects include those who had at least one dose of study drug before the response assessment of time point and were discontinued due to dx progression or treatment failure. Subjects who have not yet completed week 12 visit as of study cut off date are not included; Central urine cytology is pending for 3 subjects at Month 6 and 1 subject at Month 9.

# TARA-002 demonstrated 100% durability from 3 months to 6 months with a reinduction salvage rate of 80%<sup>1</sup>



Data cut-off date: 19 November 2024

Abbreviations: BCG = Bacillus Calmette-Guérin; CR = complete response; CIS = carcinoma in situ

NOTES: At the time of data cutoff, of the 24 subjects enrolled, 20 subjects were evaluated for high-grade CR at Month 3 and later. Eighteen subjects were evaluated for high-grade CR at Month 6 and 3 subjects at Month 9. Evaluable subjects include those who had at least one dose of study drug before the response assessment of time point and were discontinued due to diagnosis of progression or treatment failure. Subjects who have not yet completed the week 12 visit as of study cut of date were not included. Central urine cytology is pending for 3 subjects at Month 6 and 1 subject at Month 9.

1. 100% durability from 3 to 6 months in 9/9 patients; reinduction salvage rate of 80% in 4/5 patients

# TARA-002 demonstrated favorable safety and tolerability in interim analysis of ADVANCED-2 trial

**AEs reflect urinary tract instrumentation effects and known safety profile of an immune-potentiating drug**

N=24	Any Grade	Grade 1	Grade 2	Grade 3	Grade 4/5
<b>Number of Subjects with TEAEs, n^ (%)</b>	16 (67)	11 (46)	7 (29)	3 (13)	0
<b>Number of Subjects with Related TEAEs^, n (%)</b>	6 (25)	6 (25)	0	0	0
Dysuria	3 (13)	3 (13)	0	0	0
Bladder Discomfort	1 (4)	1 (4)	0	0	0
Bladder Spasm	1 (4)	1 (4)	0	0	0
Chills	1 (4)	1 (4)	0	0	0
Fatigue	1 (4)	1 (4)	0	0	0
Hematuria	1 (4)	1 (4)	0	0	0
Micturition Urgency	1 (4)	1 (4)	0	0	0
Urinary Incontinence	1 (4)	1 (4)	0	0	0
<b>Number of Subjects with Serious TEAEs+, n (%)</b>	3 (13)	0	1 (4)	2 (8)	0
<b>Number of Subjects with TEAEs leading to Study Drug Withdrawal, n (%)</b>	0	0	0	0	0

Abbreviations: AE = adverse event; NMIBC = non-muscle invasive bladder cancer; TEAE = treatment emergent AE

Data cut-off date: 19 November 2024

^ Subjects may be counted in multiple categories

+ Non-drug related Serious TEAEs included urinary tract infection (UTI; N = 2) and urosepsis (N = 1)

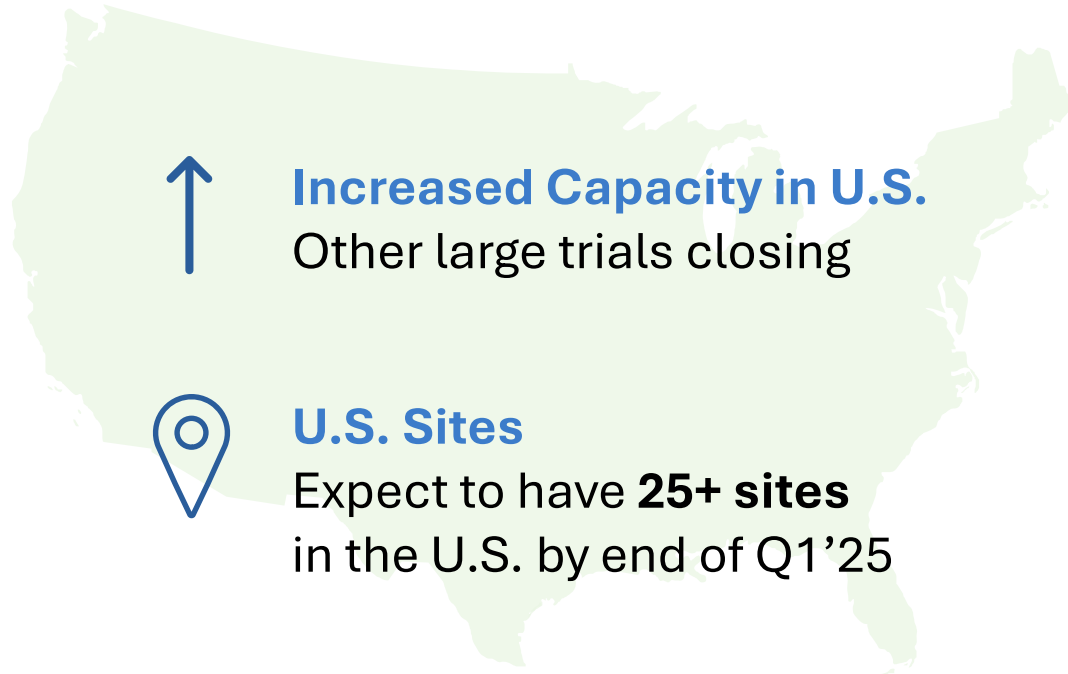
Note: the safety population includes any patients who have had at least 1 dose of TARA-002. The 24 patients in safety analysis include 3 patients who have not reached their week 12 assessment, and 1 patient withdrew consent prior to their week 12 assessment

# BCG-Unresponsive: Accelerating trial enrollment

## Registrational Trial Enrollment



**International expansion**  
Expansion ongoing across  
**South America and Asia**



**Increased Capacity in U.S.**  
Other large trials closing



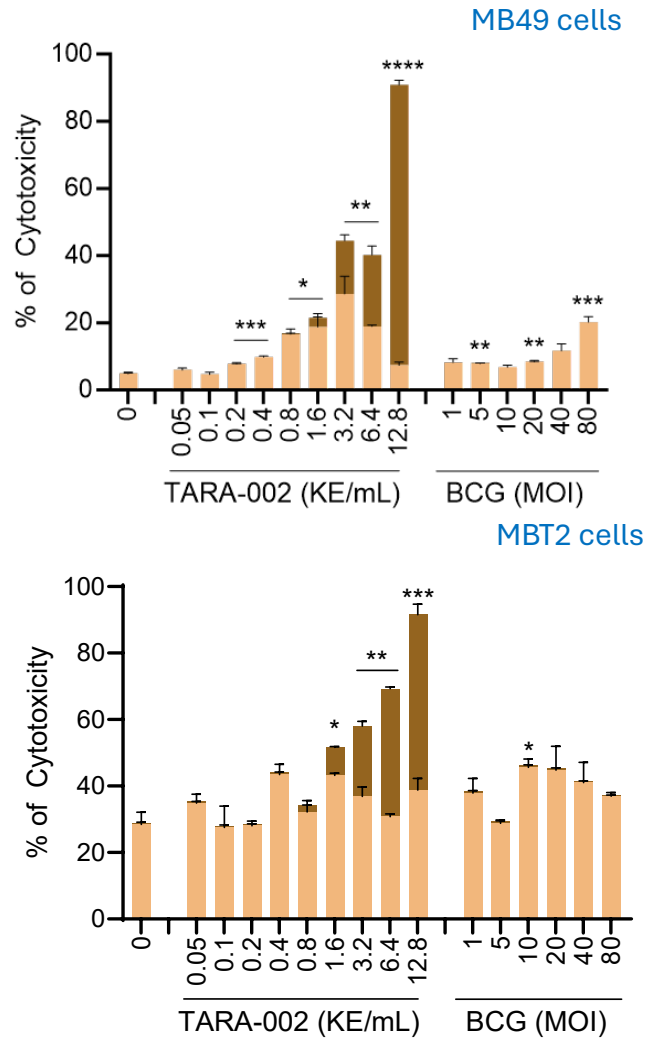
**U.S. Sites**  
Expect to have **25+ sites**  
in the U.S. by end of Q1'25



**Positive TARA-002 data**  
Positive data expected  
to drive participation

# TARA-002 demonstrates differentiated profile to BCG<sup>(1)</sup>

## 1 TARA-002 induces higher cytotoxicity than BCG in bladder cancer cells



## 2 TARA-002 treatment promotes higher release of pro-inflammatory TH1-type cytokines than BCG in co-culture

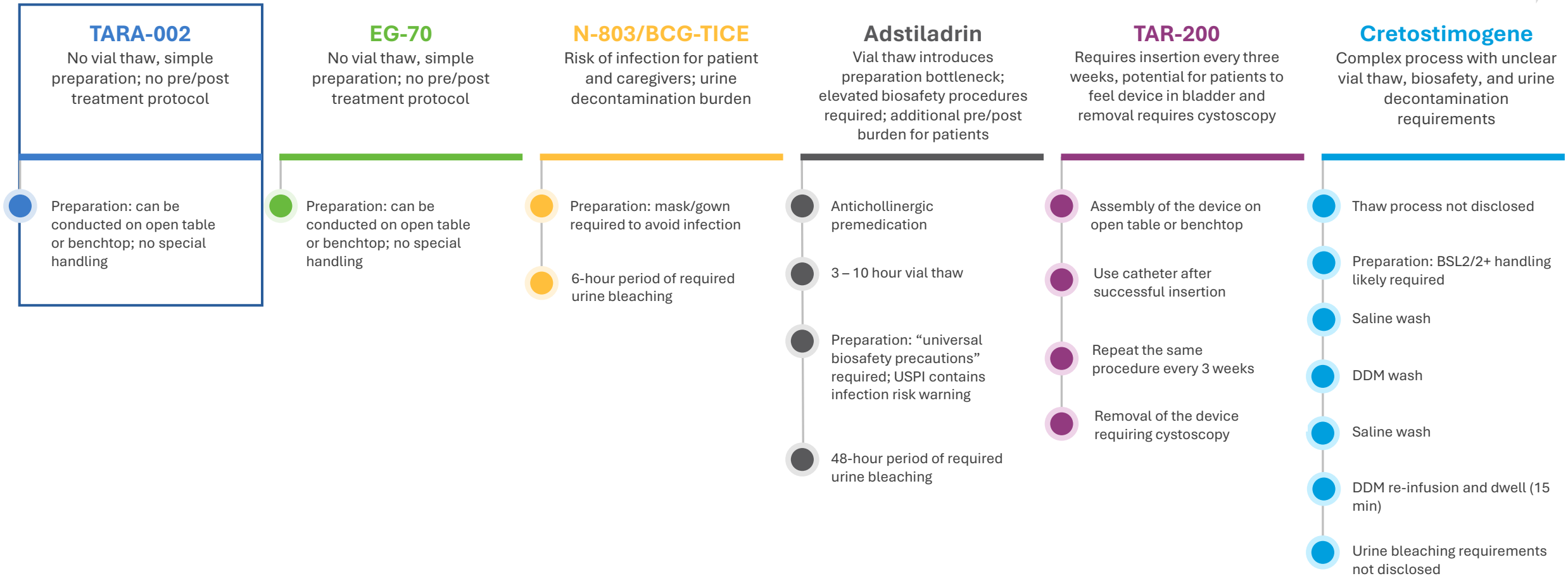
Cytokines	BCG	TARA-002
IFN- $\gamma$	---	+
TNF- $\alpha$	+	+++
IL-12p70	=	+
IL-6	+	+
IL-1 $\beta$	+++	+++
IL-10	=	+
IL-4	+	+
IL-13	=	=
IL-8	=	-
IL-2	--	--

=, no change; +: 2- 5 fold upregulation  
 +++:  $\geq$  15-fold upregulation; -: 2- 5 fold upregulation;  
 --: 5-14-fold upregulation; ---:  $\geq$  15-fold upregulation



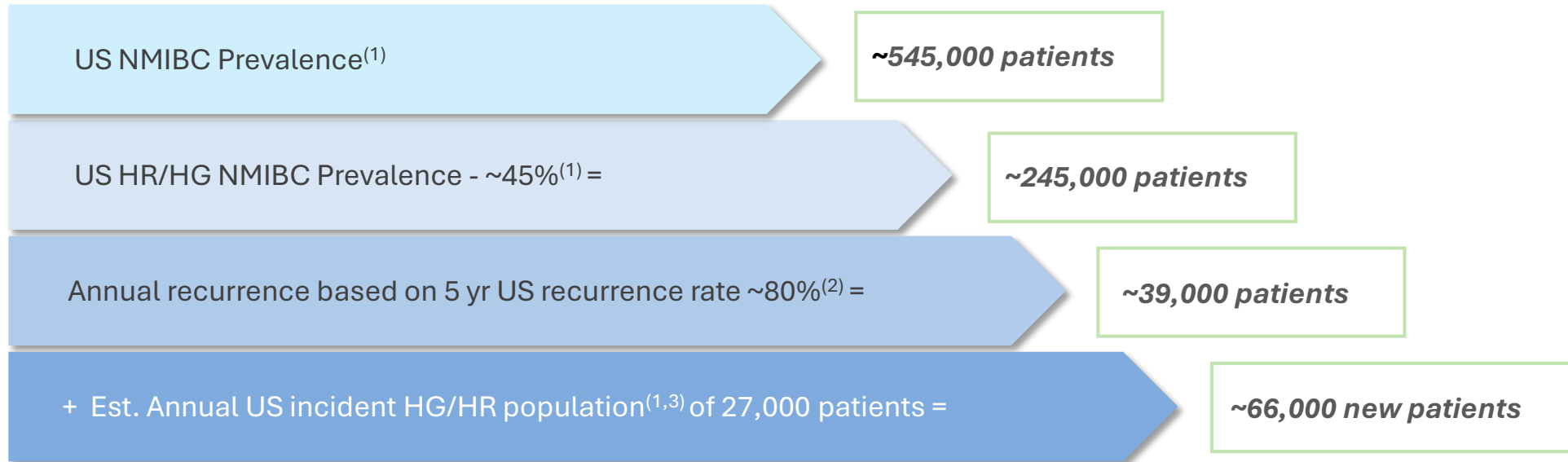
# TARA-002 administration among the easiest of approved and experimental NMIBC treatments

TARA-002 has reduced burden for physicians and patients



# High-risk, high grade NMIBC: A significant addressable market in the US

*Even in highly competitive scenarios, the market is large enough to sustain multiple entrants*



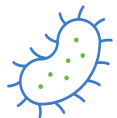
Over 65K HR/HG NMIBC annual patients, at branded therapeutics pricing = ~\$5bn-\$6bn addressable US market broad enough for a variety of modalities and mechanisms of action (MOAs) to succeed

# TARA-002 HAS A DIFFERENTIATED PROFILE IN NMIBC WITH ENCOURAGING INTERIM DATA



## PROMISING CLINICAL DATA

- Positive interim results across BCG exposures



## UNIQUE MOA

- Only broad immunopotentiator in the industry pipeline
- Non-clinical data points to encouraging durability
- No overlapping toxicities with other novel therapeutic in NMIBC



## POTENTIAL EASE ON PROVIDERS & PATIENTS

- To date, no Grade 2 or greater treatment-related adverse events
- Simple, fast administration via catheter



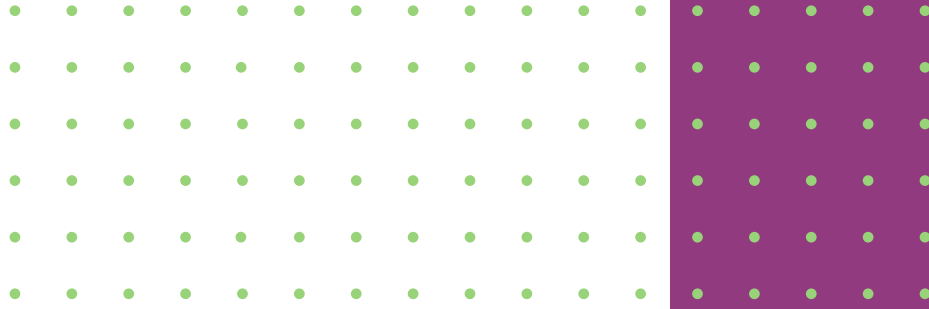
## OPPORTUNITIES TO EXPAND

- First to publish efficacy in BCG-naïve patients; assessing potential next steps
- Only novel agent with the ability to dose systemically – potentially replacing intravesical administration



## RELIABLE MANUFACTURING

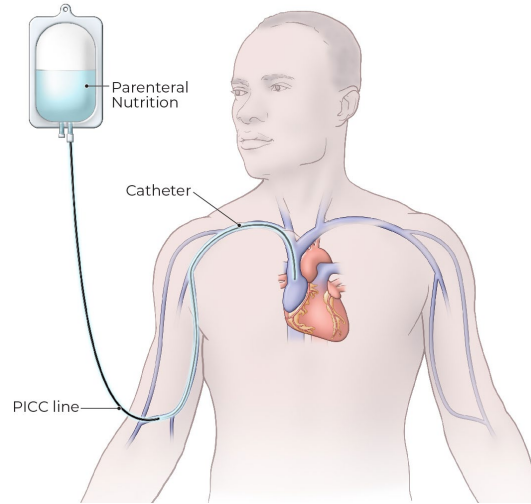
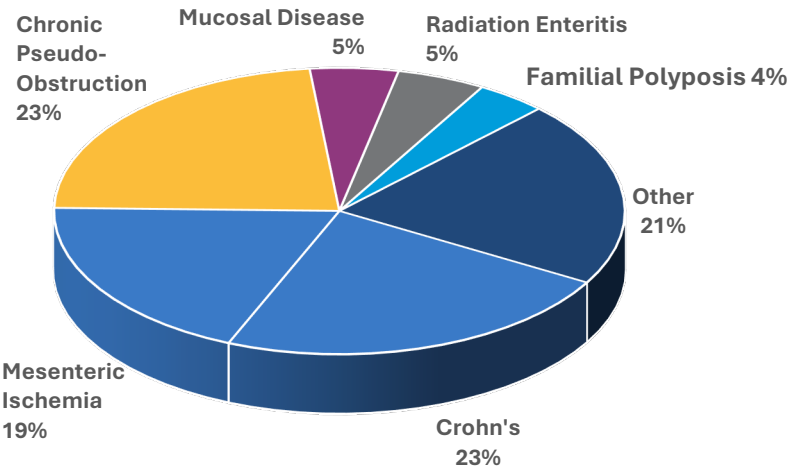
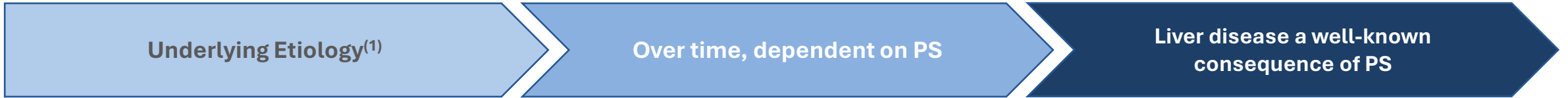
- Advanced, FDA-inspected, cGMP manufacturing with 20mm vial annual capacity
- Doubling time (2 hrs) vs. BCG (16 hrs) adds to TARA-002's benefit over BCG in the non-refractory setting
- Dedicated to ensuring access with minimal burden



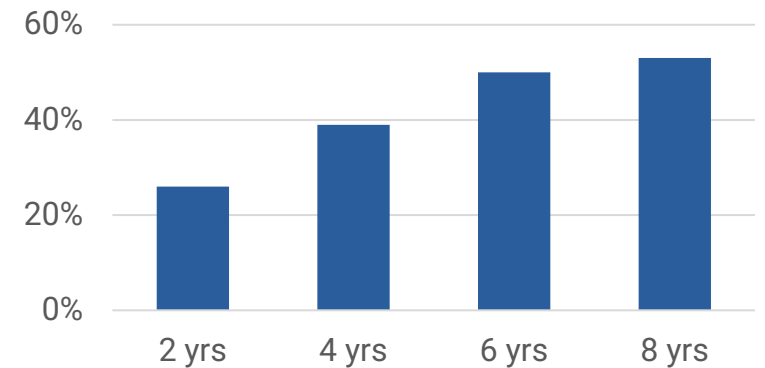
# IV CHOLINE CHLORIDE

Phospholipid substrate replacement therapy for patients dependent on parenteral support (PS)

# Overview of Parenteral Support



Complicated Liver Disease in PS<sup>(2)</sup>



Patients are dependent on PS to meet their nutritional needs; cannot sufficiently create or absorb many important nutrients, **most notably Choline**

Majority of nutrition is delivered via **central line as a sterile injectable drug** – only approved via NDA

No currently available PS formulations contain choline

# Choline deficiency in PS is among the largest rare disease indications



## ~30,000<sup>1</sup> PS patients in the U.S. and the majority are choline deficient

- 78% of PS-dependent patients are choline-deficient and of those 63% have some degree of liver damage<sup>2</sup>
- Data confirm choline deficiency results in liver, bone, muscle and cognitive impairment<sup>3,4</sup>

## Phase 2 study confirmed choline replacement restored normal levels






- Independently conducted Phase 2 data demonstrated significant improvement in serum choline concentrations and a pronounced impact on steatosis<sup>4</sup>
- Choline replacement is included in guidelines and recommendations by key PS professional associations

## FDA has cleared the way for “source of choline” label with single study

- FDA granted a targeted indication of “source of choline for PS patients who are, or may become, choline-deficient”
- Single study demonstrating an increase in choline levels required (already demonstrated in Ph 2 trial)
- Both a compound patent and a method of treatment patent in U.S. to 2041

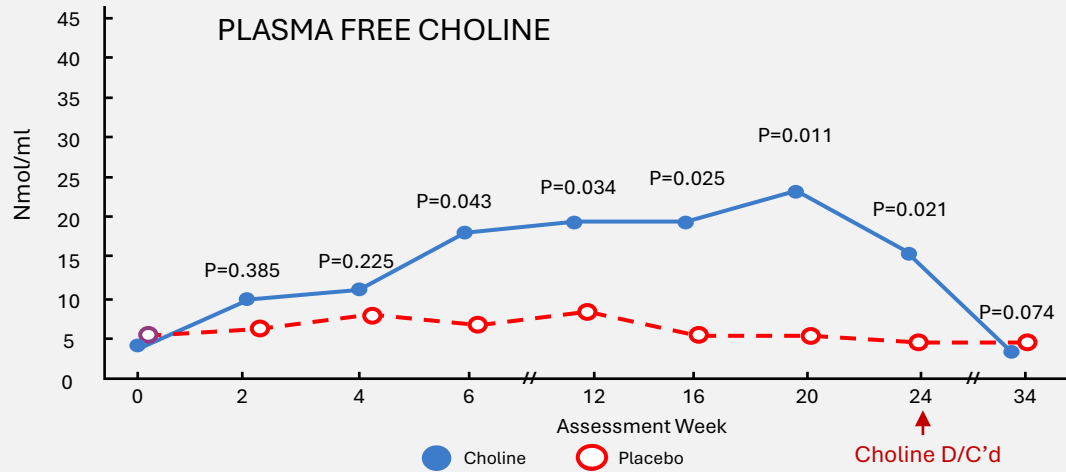
# Choline replacement recommended in key PS Guidelines

## Parenteral Support Professional Societies' Position on Choline

 <p><b>Guidelines / Position Paper</b></p>	<p><b>ASPEN 2012 Position Paper (Vanek et al.)<sup>3</sup>:</b></p> <ul style="list-style-type: none"><li>• Includes recommendations for Multivitamins &amp; Multi-Trace Elements</li><li>• Recognises the impact of long-term choline deficiency on the development of steatosis and hepatocellular carcinoma</li><li>• Recommends that a commercially available parenteral choline product, either as an individual product or incorporated into a multivitamin product, should be developed and routinely added to adult parenteral formulas at a dose of 550 mg per day</li></ul>  	<p><b>ESPEN Micronutrient Guideline 2022 (Berger et al.)<sup>4</sup>:</b></p> <ul style="list-style-type: none"><li>• (Can/may) monitor choline in patients with abnormal liver function</li><li>• (Can/may) consider treatment of HPN patients with abnormal liver function or proven deficiency with 550mg-2g/day choline</li><li>• (Can/may) prescribe a dose of 400-550 mg choline via EN or PN per day has been suggested to support lipid metabolism</li></ul>  
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# Independent studies demonstrate that treatment with IV Choline rapidly restores choline levels and improves steatosis

## PLASMA FREE CHOLINE LEVELS: ALL PATIENTS<sup>(1)</sup>

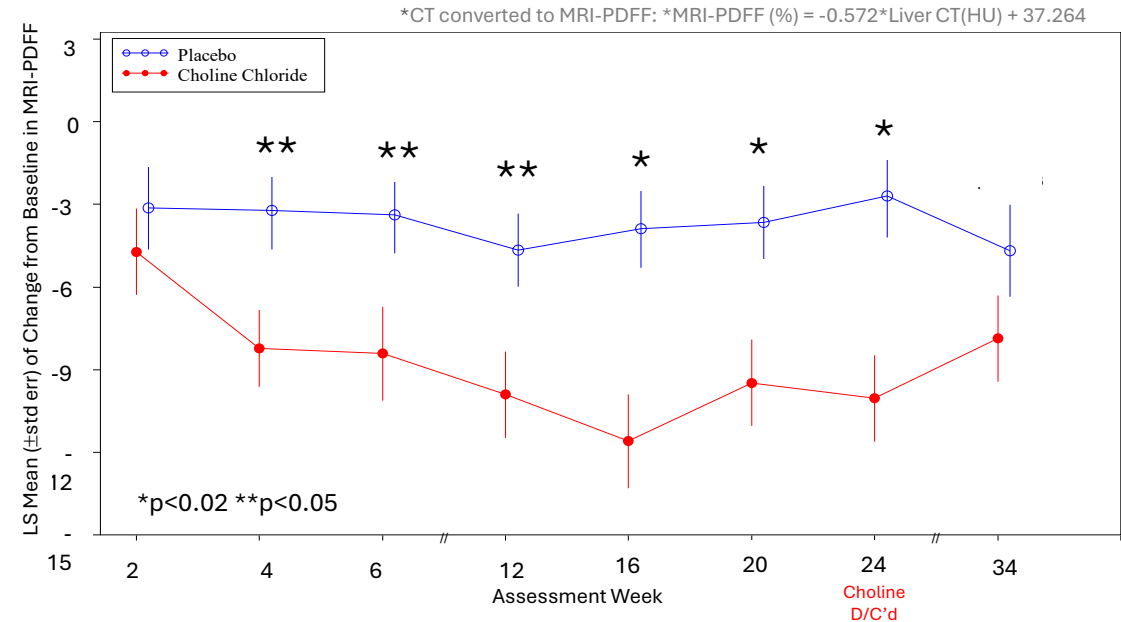


Studies conducted by independent academic institution

1. Buchman et al. JPEN, 2002 - Protara Therapeutics re-analysis of patient CRFs, data on file.

**Primary endpoint to replicate in registrational trial**

## CLINICALLY MEANINGFUL IMPROVEMENT IN STEATOSIS<sup>(1)</sup>



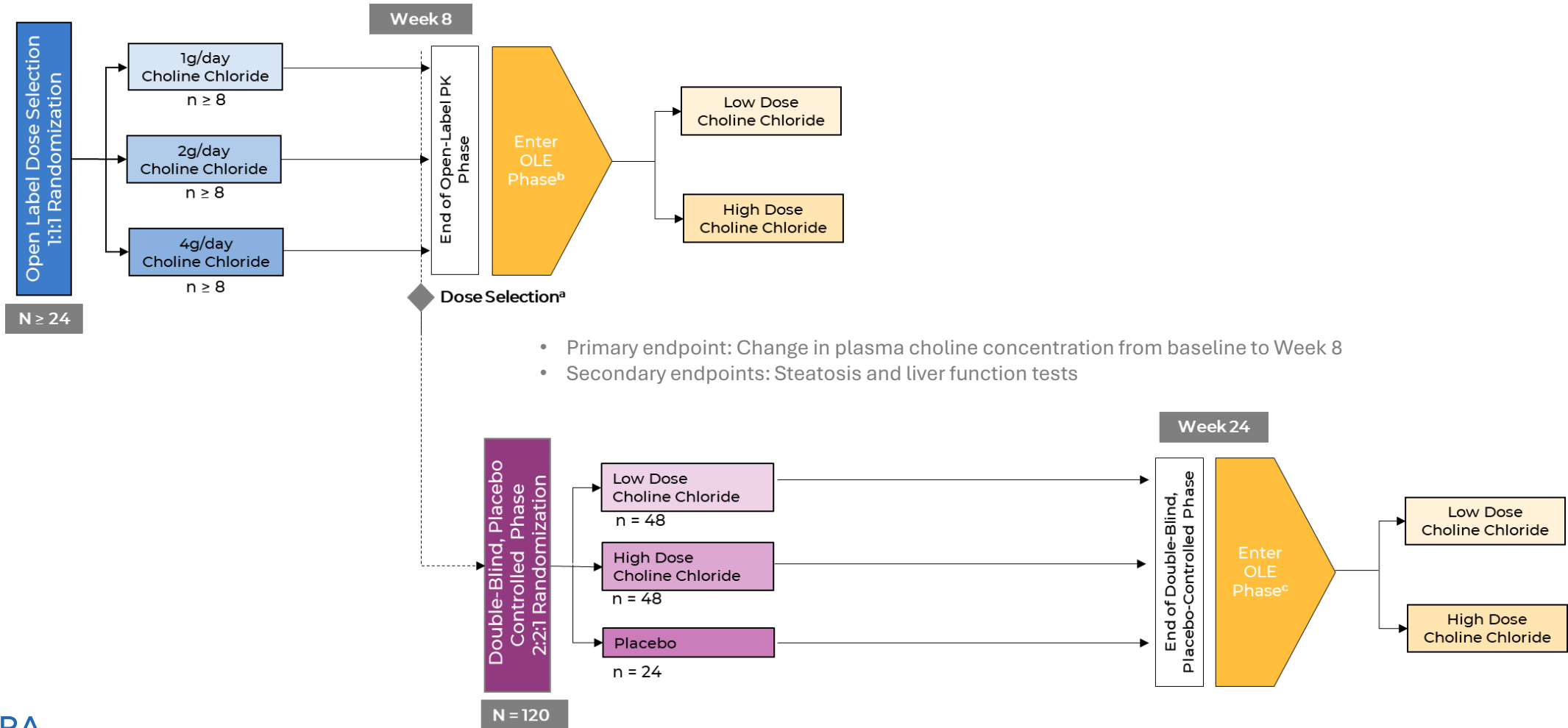
Significant differences in the LS mean change from baseline in MRI-PDFF observed in Choline group vs. placebo at Weeks 4 - 24, demonstrating a clinically meaningful and statistically significant reduction in steatosis (range 31%-54%)

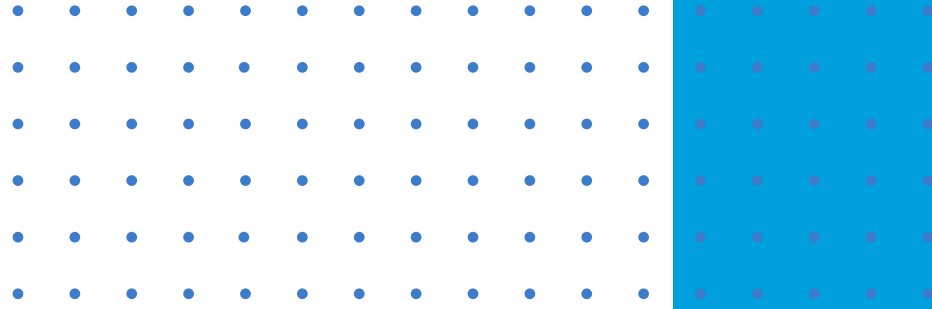
**Secondary endpoint to replicate in registrational trial to support clinical benefit**



# Pivotal trial with PK-based endpoints expected to initiate in 1H'25

THRIVE-3 is a seamless Phase 2b/3 trial with dose confirmation followed by double-blinded, randomized, placebo-controlled trial to assess the safety and efficacy of IV Choline Chloride in adolescents and adults on long-term PS when oral or enteral nutrition is not possible, insufficient, or contraindicated (n=120)





# TARA-002

Lymphatic Malformations (LMs)



# TARA-002 in LMs



## Lymphatic Malformations

Rare, non-malignant lesions consisting of dilated, lymphatic fluid-filled sacs caused by abnormal development of the lymphatic endothelial system<sup>(1)</sup>

Epidemiology: incidence of lymphatic malformations is  $\approx$ 1,400-1,800 LM cases per year<sup>(2)</sup>



## Current treatment options

Current treatment options include surgical excision with high complication (33%) and recurrence (55%) rates<sup>(3)</sup> as well as off-label use of sclerosants



## Potential for Priority Review Voucher upon approval

Granted RPDD in 2021



## Ongoing Ph 2 clinical trial

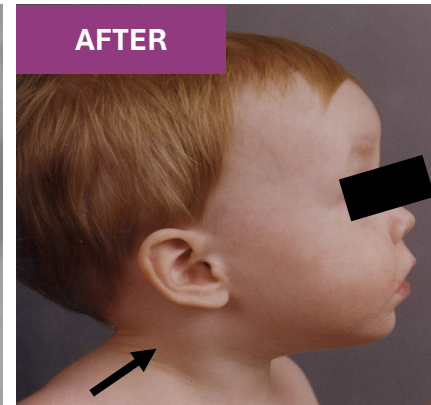
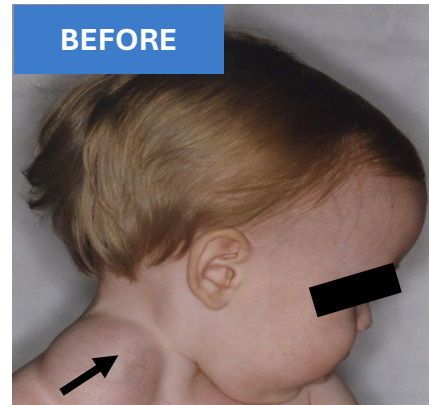
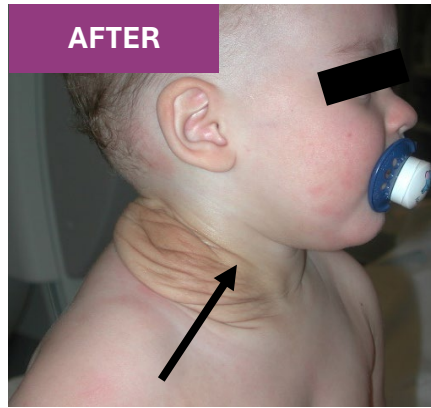
Ph 2 STARBORN-1 trial in pediatric LMs patients is ongoing



## Additional indications

Historical literature and patient experience indicate that TARA-002 could have the potential to treat other maxillofacial cysts

# Clear evidence of biologic activity observed with OK-432\*



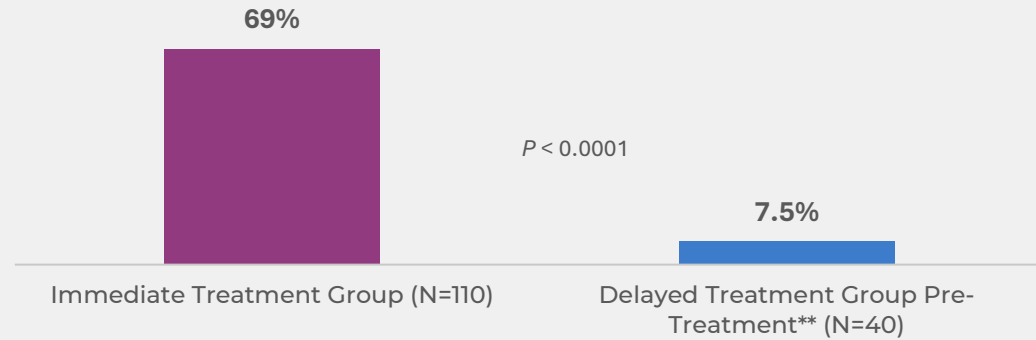
Completed clinical study of OK-432 (TARA-002 predecessor therapy) in U.S. suggests effectiveness with strong support for safety profile

\*TARA-002 is developed from the same master cell bank as OK-432

# Robust clinical results in large, academic study of OK-432

## 69% CLINICAL SUCCESS<sup>†</sup> IN IMMEDIATE TREATMENT GROUP 6 MONTHS AFTER ENROLLMENT

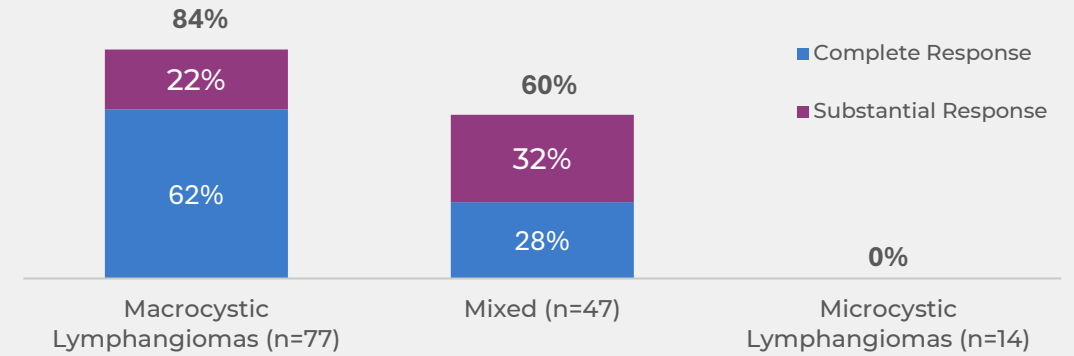
ITT: Observations 6 Months After Enrollment



- During this same period, 7.5% of patients in the delayed treatment group experienced spontaneous regression of LM
- Treatment: 1-4 injections at 8-week intervals max of 0.2mg/session (2KE)

## 84%\* CLINICAL SUCCESS<sup>†</sup> IN PATIENTS WITH MACROCYSTIC LESION TYPES

Complete or Substantial Response by Radiographically Confirmed Lesion Type\*\*



- Patients with radiographically confirmed macrocytic lesions had the greatest chance for clinical success
- In those patients with mixed lesions, clinical success was still achieved

<sup>†</sup> Clinical Success was defined as complete or substantial response.

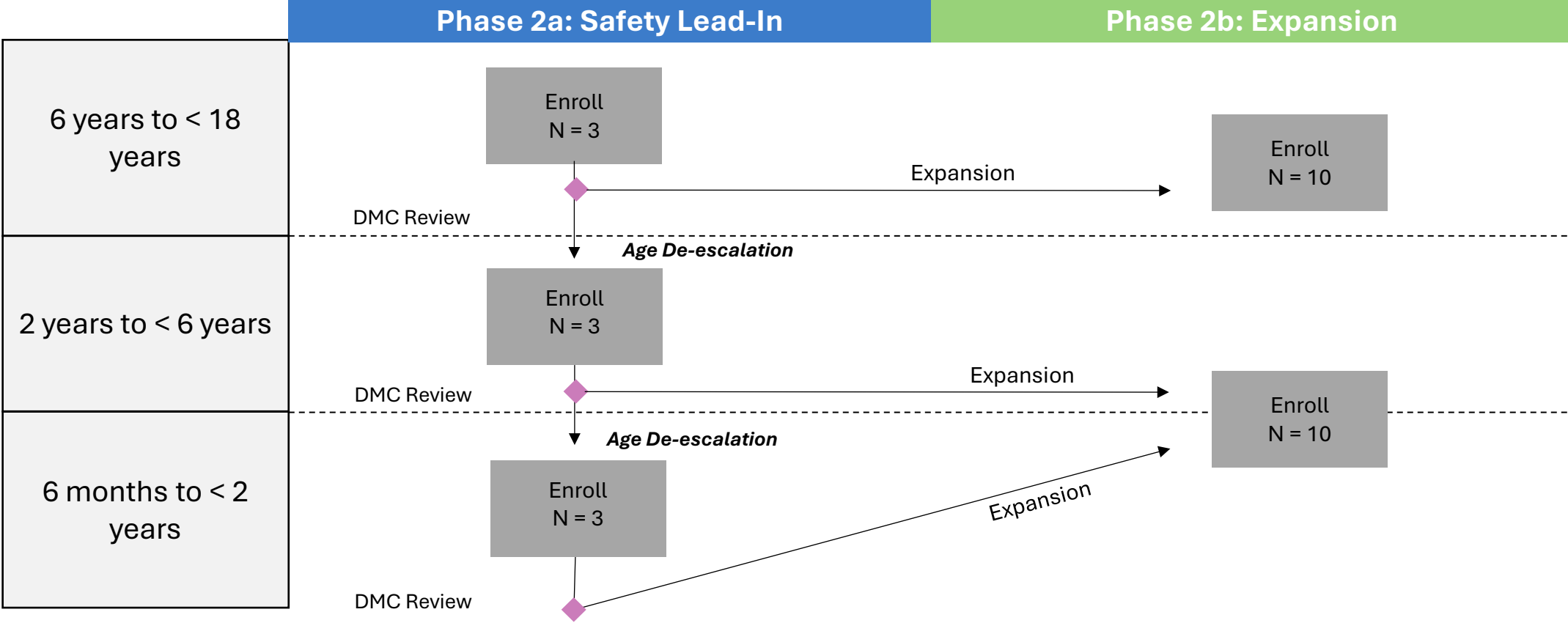
\*Reflects data prior to dosing with OK-432. After dosing, the clinical success rate was 66%, which was not statistically different from the Immediate Treatment Group.

\*\*Results were analyzed by lesion type across all treatment groups

1. Results based on retrospective analysis of source verified data that included the full dataset of subjects enrolled in randomized study between January 1998 and August 2005, including data in the published study (Smith et al. 2009) which included subjects enrolled between January 1998 and November 2004.

# TARA-002 in LMs: Phase 2 STARBORN-1 Trial underway

Single Arm Open-Label Safety and Efficacy Study of TARA-002 in Pediatric Patients with Macrocytic and Mixed-cystic LMs (N=29)



# APPENDIX



# Led by a team of experienced professionals



**Jesse Shefferman**

Co-founder, Director,  
Chief Executive Officer



**Jacqueline Zummo, PhD,  
MPH, MBA**

Co-founder, Senior Vice President, Chief  
Scientific Operations Officer



**Pat Fabbio**

Chief Financial Officer



**Mary Grendell**

General Counsel, Corporate Secretary



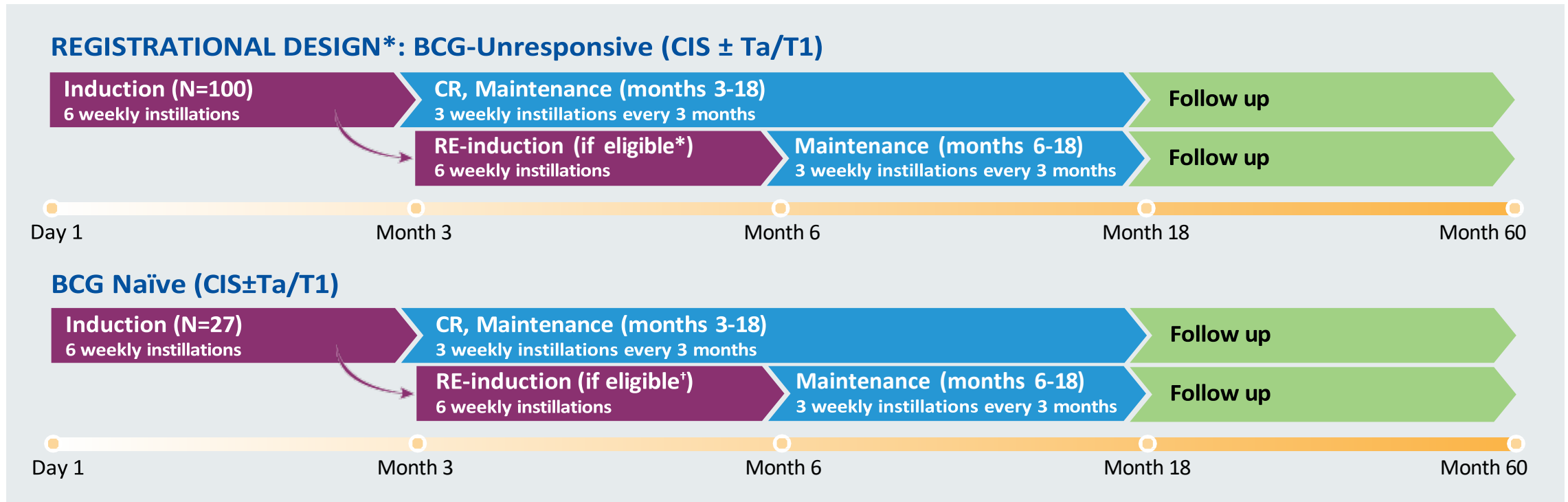
**Justine O'Malley**

Senior Vice President, Investor  
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# TARA-002 in NMIBC: ADVANCED-2 clinical trial design

Primary endpoint of high-grade complete response (CR) at any time at 6 months; Key secondary of 12-month DOR



Abbreviations: CR = complete response; CIS = carcinoma in situ

\*Aligned with the FDA's 2024 BCG Unresponsive NMIBC: Developing Drugs and Biologics for Treatment Guidance for Industry.

†Residual CIS and/or recurrence of HGTA

# ADVANCED-2 demographics and disease characteristics

	N = 24		N = 24
<b>Age (years)</b>		<b>Prior BCG Status, n (%)</b>	
Mean (SD)	71 (10.9)	BCG Naïve	17 (71)
Median	71	BCG Exposed	2 (8)
Min, Max	45, 92	BCG Unresponsive	5 (21)
<b>Sex, n (%)</b>		<b>Prior No. of BCG Doses, n (%)</b>	
Male	19 (79)	≥ 12 BCG doses	5 (21)
Female	5 (21)	< 12 BCG doses	2 (8)
<b>Race, n (%)</b>		<b>Prior non-BCG Treatment, n (%)</b>	
White	24 (100)	Gemcitabine/Docetaxel	2 (8)
<b>Ethnicity, n (%)</b>		Gemcitabine	1 (4)
Hispanic	1 (4)	Mitomycin	3 (12)
Non-Hispanic	23 (96)	Other	2 (8)
<b>ECOG Score, n (%)</b>		<b>Prior TURBT Status, n (%)</b>	
0	18 (75)	> 3 TURBTs	5 (21)
1	5 (21)	≤ 3 TURBTs	19 (79)
2	1 (4)		
<b>Baseline Diagnosis, n (%)</b>			
CIS only	14 (58)		
CIS + Ta	6 (25)		
CIS + T1	4 (17)		

# TARA-002: Manufacturing is a potential competitive advantage



**20M** vial capacity ability to expand capacity **5X**



Efficient 2 hour doubling time with two-week batch completion



**47** successful batches to date



**Completed FDA inspection** without Form 483s