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ADVANCED-2: Phase 2 Open-label Study to Evaluate Safety and Anti-tumor Activity of Intravesical Instillation of TARA-002 in Adults with High-grade Non-muscle Invasive Bladder Cancer

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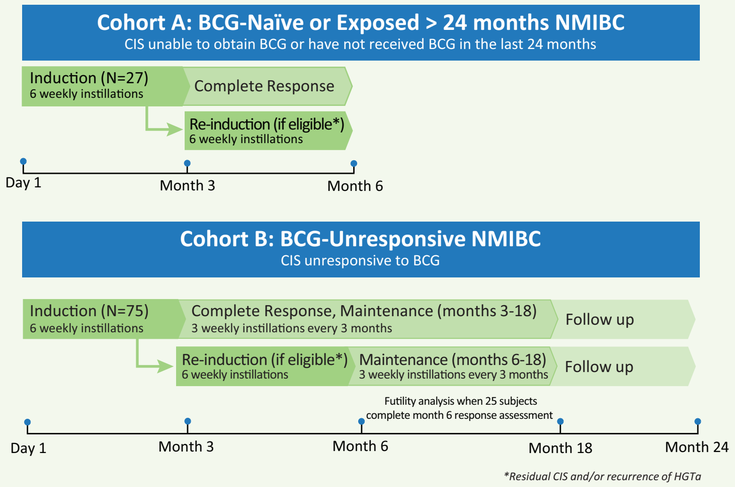
INTRODUCTION

- Bladder cancer is the most common malignancy involving the urinary system, resulting in ~18,000 US deaths/year[1]
- 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[2,3]
- With the current Bacillus Calmette-Guérin (BCG) shortage and limited effective alternative therapies, there continues to be 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 (HG) NMIBC
- TARA-002 is manufactured using the same master cell bank as OK-432 (Picibanil®)
- OK-432 is approved in Japan and Taiwan for the treatment of several oncology indications[4]
  - Prolongation of survival time in patients with gastric cancer (postoperative cases) or primary lung cancer in combination with chemotherapy
  - Reduction of cancerous pleural effusion or ascites in patients with gastrointestinal cancer or lung cancer
  - Head and neck cancer (maxillary cancer, laryngeal cancer, pharyngeal cancer, and tongue cancer) and thyroid cancer that are nonresponsive to other drugs
  - Lymphangioma
- 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[3,5]
- The dose for the Phase 2 study is 40 KE, which is based on the recommended Phase 2 dose (RP2D) established in the Phase 1a study.

METHODS

FIGURE 1. STUDY DESIGN



ADVANCED-2

- ADVANCED-2 is a Phase 2 open-label study of intravesical TARA-002 in adults ≥ 18 years with CIS NMIBC (±Ta/T1)
- This study includes ~102 subjects enrolled in 2 cohorts based on prior BCG experience (**Figure 1**):
  - Cohort A includes 27 subjects with:
    - CIS (± Ta/T1) who are BCG naïve and are unable to obtain intravesical BCG, or
    - CIS (± Ta/T1) who are BCG exposed and have not received intravesical BCG for 24 months prior to CIS diagnosis
  - Cohort B includes 75 subjects with:
    - CIS (± Ta/T1) who are BCG unresponsive after completion of adequate BCG therapy (minimum of 5/6 doses induction and 2/3 doses maintenance or 2/6 doses reinduction)
  - The study duration per subject is:
    - 6 months for Cohort A (includes induction, reinduction [if eligible])
    - 24 months for Cohort B (includes induction; reinduction [if eligible]; maintenance until 18 months)

STUDY OBJECTIVES/ENDPOINTS

ADVANCED-2

- The purpose of the ADVANCED-2 Phase 2 study is to assess the safety and anti-tumor activity of TARA-002, at the established RP2D, for the treatment of subjects with CIS NMIBC (±Ta/T1) with active disease
- Primary Endpoint:
  - Incidence of high-grade complete response at any time
- Safety Endpoints:
  - Incidence and severity of AEs
  - Incidence and severity of treatment emergent AEs (TEAEs)
  - Incidence and severity of serious AEs (SAEs)
  - Incidence and severity of treatment emergent SAEs (TESAEs)

ADVANCED-2 ELIGIBILITY

TABLE 1. KEY INCLUSION AND EXCLUSION CRITERIA

Key Inclusion Criteria

- CIS ± Ta/T1 (active disease present at last tumor evaluation prior to signing consent)
- Cohort A – BCG naïve or BCG exposure > 24 months prior to CIS diagnosis
- Cohort B – CIS BCG unresponsive
- For CIS with concomitant Ta/T1, all visible papillary tumors must be removed prior to treatment

Key Exclusion Criteria

- Penicillin allergy
- Concomitant prostatic or upper tract urothelial involvement per Investigator's assessment
- Has significant urinary incontinence or otherwise unable to hold intravesical immunotherapy in the bladder for 2 hours
- Participation in any other anti-cancer therapy (including investigational agents) within 6 weeks prior to signing informed consent

- The key inclusion and exclusion criteria are summarized in **Table 1**

CURRENT ENROLLMENT STATUS

- Phase 2 (ADVANCED-2) is currently open for enrollment
- ClinicalTrials.gov Identifier: NCT05951179

NOTE: Please contact Protara for additional information at clinicaltrials@protaratx.com

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