Protara Therapeutics Announces Positive Three-Month Data from TARA-002 Clinical Program in NMIBC

April 5, 2024

- *TARA-002 demonstrated a complete response rate of 43% at three months in BCG-Unresponsive/Experienced patients in ongoing NMIBC program*
- *TARA-002 demonstrated a complete response rate of 63% at three months in CIS-only patients in ongoing NMIBC program*
- *TARA-002 demonstrated a favorable safety and tolerability profile with no Grade 3 or greater treatment-related adverse events*
- *Preliminary data from six-month evaluable patients in ADVANCED-2 trial of TARA-002 in NMIBC expected in 2H 2024*

NEW YORK, April 05, 2024 (GLOBE NEWSWIRE) -- Protara Therapeutics, Inc. (Nasdaq: TARA), a clinical-stage company developing transformative therapies for the treatment of cancer and rare diseases, today announced positive data from three-month evaluable carcinoma in situ (CIS) patients treated across its ongoing clinical program of TARA-002, the Company's investigational cell-based therapy, in high-risk Non-Muscle Invasive Bladder Cancer (NMIBC), including Bacillus Calmette-Guérin (BCG)-Unresponsive, BCG-Experienced and BCG-Naïve patient populations.

"These promising three-month results support the continued development of TARA-002 for patients with NMIBC for whom there are currently limited treatment options," said Timothy Lyon, M.D., Associate Professor of Urology and the Urology Residency Program Director at Mayo Clinic in Florida, and TARA-002 study investigator. "Given our understanding that up to half of patients treated with intravesical immune therapies that do not initially respond can be salvaged with repeat induction, there is reason to believe that the promising three-month response rates shared today could be further improved through reinduction with TARA-002. This encouraging anti-tumor activity coupled with a favorable safety profile and mode of administration that is both convenient and familiar to urologists indicates that, if confirmed in future studies, TARA-002 could potentially play a meaningful role in NMIBC treatment in the future."

Enrollment continues in the Company's ADVANCED-2 Phase 2 clinical trial of TARA-002 in patients with high-grade NMIBC with BCG-Unresponsive CIS and BCG-Naïve CIS. The ADVANCED-2 trial design incorporates both reinduction and maintenance dosing. The Company expects to share preliminary results from a pre-planned risk-benefit analysis of the ADVANCED-2 trial in ten patients, who are six-month evaluable in the second half of 2024.

"We are highly encouraged by these early results observed in these three-month evaluable patients across our ADVANCED-1 and ADVANCED-2 clinical trials, which clearly demonstrate TARA-002's activity in both BCG-Unresponsive and BCG-Naïve patients. We look forward to sharing data from post-reinduction, six-month evaluable patients in our ADVANCED-2 trial in the second half of 2024," said Jesse Shefferman, Chief Executive Officer of Protara Therapeutics.

Overview of Three-Month Evaluable Data

Data reported today highlight the potential of TARA-002 in patients with NMIBC. Data were derived from three-month evaluable NMIBC patients with CIS pooled across the Company's ADVANCED-1 Phase 1a, Phase 1b-expansion and ADVANCED-2 Phase 2 trials of TARA-002 in patients with high-risk NMIBC, including BCG-Unresponsive, BCG-Experienced and BCG-Naïve patients. The overall three-month complete response (CR) rate prior to reinduction for 16 evaluable patients treated across the three trials with varying BCG status was 38% (6/16), with a CR rate of 63% (5/8) in CIS-only patients and 13% (1/8) in patients with CIS +Ta/T1. The Company believes that reinduction and planned enhancements to dosing and administration will lead to an increased CR rate at six months in patients who did not achieve a CR at three months, as reinduction with other immune agents in NMIBC patients with CIS has demonstrated a 30%-50% salvage rate. The Company plans to explore additional dosing cohorts, which may prove effective in patients who might benefit.

	Three Month Evaluable Patients		
	# Patients	**# of CRs**	**CR %**
BCG-Unresponsive/ Experienced			
CIS-only	6	3	50%
CIS +Ta/T1	1	-	-%
	7	3	43%
BCG-Naïve			
CIS-only	2	2	100%
CIS +Ta/T1	7	1	14%
	9	3	33%
	16	6	38%
By Stage of Disease at Baseline			
CIS-only	8	5	63%

CIS +Ta/T1	8	1	13%
	16	6	38%
By Study			
Phase 1a	3	1	33%
Phase 1b-EXP	8	3	38%
Phase 2 Naïve	5	2	40%
	16	6	38%

The majority of reported adverse events were Grades 1 and 2 across all dose levels, and treatment emergent adverse events (TEAEs), as assessed by study investigators, were in line with typical responses to bacterial immunopotentiation, and included fatigue, headache, fever, and chills. The most common urinary symptoms were urinary urgency, urinary frequency, urinary tract pain/burning, incomplete emptying, and bladder spasm. Most bladder irritations resolved soon after administration or in a few hours to a few days.

"TARA-002 is a broad spectrum immunopotentiator with a similar mechanism of action as the standard of care, BCG. Because TARA-002 is an inactivated bacteria, there are no special dosing and administration protocol requirements, which makes it ideal for administration in the community urology practice setting," said Gautam Jayram, MD., Director, Advanced Therapeutics Center, Urology Associates PC in Nashville and TARA-002 study investigator. "I am encouraged by the early three-month data in a challenging disease state and look forward to continued participation in the TARA-002 clinical program."

NMIBC Clinical Program

The ADVANCED-1 expansion trial is evaluating intravesical TARA-002 at the 40KE[1] dose in up to 12 NMIBC patients with CIS and CIS +Ta/T1, including BCG-Unresponsive, BCG-Naïve, and BCG-Experienced patient populations. The primary endpoint is safety and complete response (CR) rate at the preliminary three-month assessment timepoint.

The Phase 2 open-label ADVANCED-2 trial is assessing intravesical TARA-002 in at least 102 NMIBC patients with CIS (± Ta/T1) who are BCG-Unresponsive (n=75-100) and BCG-Naïve (n=27). The BCG-Unresponsive cohort has been designed to be registrational aligned with the FDA's 2018 BCG-Unresponsive Non-muscle Invasive Bladder Cancer: Developing Drugs and Biologics for Treatment Guidance for Industry. Trial subjects receive an induction course of six weekly intravesical instillations, followed by either reinduction (if eligible) or maintenance for up to 24 months.

Two additional exploratory cohorts will be added to the ADVANCED-2 trial assessing higher dosing at an 80KE dose (Cohort C) and systemic priming prior to initiation of intravesical administration (Cohort D). In addition, the Company intends to initiate a proof-of-concept study of TARA-002 in combination with pembrolizumab in NMIBC patients with CIS to assess the potential synergistic effects of the combination regimen.

About TARA-002

TARA-002 is an investigational cell therapy in development for the treatment of NMIBC and of lymphatic malformations (LMs), for which it has been granted Rare Pediatric Disease Designation by the U.S. Food and Drug Administration. TARA-002 was developed from the same master cell bank of genetically distinct group A Streptococcus pyogenes as OK-432, a broad immunopotentiator marketed as Picibanil® in Japan and approved in Taiwan by Chugai Pharmaceutical Co., Ltd. Protara has successfully shown manufacturing comparability between TARA-002 and OK-432.

When TARA-002 is administered, it is hypothesized that innate and adaptive immune cells within the cyst or tumor are activated and produce a pro-inflammatory response with release of cytokines such as tumor necrosis factor (TNF)-alpha, interferon (IFN)-gamma, IL-1b, IL-6, IL-12, granulocyte-macrophage colony-stimulating factor (GM-CSF) and natural killer cells. TARA-002 also directly kills tumor cells and triggers a host immune response by inducing immunogenic cell death, which further enhances the antitumor immune response.

About Non-Muscle Invasive Bladder Cancer (NMIBC)

Bladder cancer is the 6th most common cancer in the United States, with NMIBC representing approximately 80% of bladder cancer diagnoses. Approximately 65,000 patients are diagnosed with NMIBC in the United States each year. NMIBC is cancer found in the tissue that lines the inner surface of the bladder that has not spread into the bladder muscle.

About Protara Therapeutics, Inc.

Protara is a clinical-stage biotechnology company committed to advancing transformative therapies for people with cancer and rare diseases. Protara's portfolio includes its lead candidate, TARA-002, an investigational cell-based therapy in development for the treatment of non-muscle invasive bladder cancer (NMIBC) and lymphatic malformations (LMs). The Company is evaluating TARA-002 in an ongoing Phase 2 trial in NMIBC patients with carcinoma in situ (CIS) who are unresponsive or naïve to treatment with Bacillus Calmette-Guérin (BCG), as well as a Phase 2 trial in pediatric patients with LMs. Additionally, Protara is developing IV Choline Chloride, an investigational phospholipid substrate replacement for patients on parenteral nutrition who are otherwise unable to meet their choline needs via oral or enteral routes. For more information, visit www.protaratx.com.

References

1. Klinische Einheit, or KE, is a German term indicating a specified weight of dried cells in a vial.

Forward-Looking Statements

Statements contained in this press release 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,

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Company Contact:

Justine O'Malley
Protara Therapeutics
Justine.OMalley@protaratx.com
646-817-2836

Source: Protara Therapeutics