Protara Therapeutics Announces Alignment with FDA on Registrational Path Forward for IV Choline Chloride in Patients Dependent on Parenteral Nutrition

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- *New development pathway significantly expands addressable patient population for IV Choline Chloride*
- *IV Choline Chloride has the potential to become the first FDA-approved IV formulation of choline for the 40,000 PN patients in the U.S.*
- *Approximately 80% of PN patients are choline deficient, which can lead to liver damage and hepatic failure; ASPEN recommends choline replacement for PN patients*
- *Company expects to start registrational trial to support FDA approval of IV Choline Chloride for PN patients in the first half of 2025*

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 that it has reached alignment with the U.S. Food and Drug Administration (FDA) on a registrational path forward for intravenous (IV) Choline Chloride, an investigational phospholipid substrate replacement. The Company had previously been pursuing an indication in intestinal failure-associated liver disease (IFALD) and following feedback from FDA, will now pursue a broader indication in patients on parenteral nutrition (PN) who are or may become unable to synthesize choline from oral or enteral nutrition sources. The Company plans to advance the development of IV Choline Chloride as a source of choline for adult and adolescent patients on long-term PN. The FDA has granted IV Choline Chloride Orphan Drug Designation for the prevention of choline deficiency in PN patients.

“There are currently no IV formulations of choline available or in development for PN patients. The FDA recognizes this as a serious unmet need and has been instrumental in helping us define an efficient regulatory path to provide a much-needed source of IV choline for these patients,” said Jesse Shefferman, Chief Executive Officer of Protara Therapeutics. “We look forward to advancing the clinical development of IV Choline Chloride, which we believe has the potential to become the first FDA approved IV choline therapy for patients dependent on PN. In parallel, we remain keenly focused on advancing our lead product candidate, TARA-002, for patients with non-muscle invasive bladder cancer and lymphatic malformations.”

“Approximately 80 percent of PN-dependent patients are choline-deficient and have some degree of liver damage, which may be reversible with effective supplementation,” said Palle Bekker Jeppesen M.D., Ph.D., Clinical Professor and Head of the Department of Intestinal Failure and Liver Diseases, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark. “Top professional medical societies in both the U.S. and Europe recognize the impact of long-term choline deficiency on liver health, particularly, the development of liver disease with progressive steatosis, fibrosis, and eventually end-stage liver cirrhosis, and recommend treatment with choline. Access to an IV formulation of choline has the potential to make a meaningful impact for intestinal failure patients for whom oral or enteral choline supplementation is not an option.”

Choline is recommended for patients on PN by the American Society for Parenteral and Enteral Nutrition (ASPEN) Recommendations for Changes in Commercially Available Parenteral Multivitamin and Multi–Trace Element Products, as well as by the European Society for Clinical Nutrition and Metabolism (ESPEN) in their Guideline on Home Parenteral Nutrition.

The FDA indicated that a single study with an endpoint of restoring choline levels in PN patients could serve as the basis for a regulatory filing for IV Choline Chloride. Based on this feedback, the Company intends to assess the safety and efficacy of IV Choline Chloride in its planned seamless Phase 2b/3 double-blinded, randomized, placebo-controlled THRIVE-3 study in adolescents and adults on long-term PN when oral or enteral nutrition is not possible, insufficient, or contraindicated. The Phase 2b portion of the study, which will seek to establish the pharmacokinetics (PK) profile of IV Choline Chloride, will enroll approximately 24 patients who will receive one of three daily doses of IV Choline Chloride for 24 weeks. During the randomized, double-blind Phase 3 portion of the study, approximately 100 patients will receive either high dose IV Choline Chloride, low dose Choline Chloride, or placebo for 24 weeks. The primary endpoint of this portion of the study will seek to demonstrate IV Choline Chloride as a durable source of choline. Secondary endpoints will assess the impact of choline replacement on liver function. All patients will be eligible to enter an open-label extension. The Company intends to initiate this study in the first half of 2025.

In previous studies, treatment with IV Choline Chloride successfully increased plasma choline concentrations in patients on PN and was also shown to improve steatosis, a key marker of liver injury.

About IV Choline Chloride

IV Choline Chloride is an investigational, intravenous (IV) phospholipid substrate replacement therapy initially in development for patients receiving parenteral nutrition (PN). Choline is a known important substrate for phospholipids that are critical for healthy liver function and also plays an important role in modulating gene expression, cell membrane signaling, brain development and neurotransmission, muscle function, and bone health. PN patients are unable to synthesize choline from enteral nutrition sources, and there are currently no available PN formulations containing choline. Approximately 80 percent of PN-dependent patients are choline-deficient and have some degree of liver damage, which can lead to hepatic failure. There are currently no available PN formulations containing choline. In the U.S. alone, there are approximately 40,000 patients on long-term parenteral nutrition who would benefit from an IV formulation of choline. IV Choline Chloride has the potential to become the first FDA approved IV choline formulation for PN patients. IV Choline Chloride has been granted Orphan Drug Designation by the FDA for the prevention of choline deficiency in PN patients. The Company was issued a U.S. patent claiming a choline composition with a term expiring in 2041.

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.

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, 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; statements related to expectations regarding interactions with the FDA; Protara's financial position; statements regarding the anticipated safety or efficacy of Protara's product candidates; and Protara's outlook for the remainder of the year. 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 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 press release 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.

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