PTC Therapeutics Provides Key Regulatory Updates

March 19, 2024

- BLA submitted to FDA for Upstaza™ for the treatment of AADC deficiency -

- NDA to be submitted mid-year for Translarna™ based on FDA feedback -

SOUTH PLAINFIELD, N.J., March 19, 2024 /PRNewswire/ -- PTC Therapeutics, Inc. (NASDAQ: PTCT) today announced the submission of a BLA to the U.S. FDA for Upstaza™ (eladocagene exuparvovec), a gene therapy for the treatment of aromatic L-amino acid decarboxylase (AADC) deficiency. In addition, based on recent feedback from the FDA, PTC plans to re-submit an NDA for Translarna™ (ataluren) for the treatment of nonsense mutation Duchenne muscular dystrophy (nmDMD). PTC expects to make the NDA resubmission by mid-year.

"We are excited to bring Upstaza one step closer to children in the United States with the highly mortal and fatal disease of AADC deficiency. The data collected to date continue to demonstrate the transformative clinical benefits the gene therapy provides to patients," said Matthew B. Klein, M.D., Chief Executive Officer of PTC Therapeutics. "In addition, we look forward to the Translarna NDA resubmission this summer. We know U.S. patients and families have been waiting for an approved therapy that specially targets nmDMD."

In addition, the sepiapterin MAA for PKU remains on schedule for submission to the EMA by the end of this month.

About Upstaza ™ (eladocagene exuparvovec)
Upstaza is a one-time gene replacement therapy indicated for the treatment of patients aged 18 months and older with a clinical, molecular, and genetically confirmed diagnosis of aromatic L–amino acid decarboxylase (AADC) deficiency with a severe phenotype. It is a recombinant adeno-associated virus serotype 2 (AAV2)-based gene therapy, containing the human DDC gene.[1] It is designed to correct the underlying genetic defect, by delivering a functioning DDC gene directly into the putamen, increasing the AADC enzyme and restoring dopamine production.[2,3]

The efficacy and safety profile of Upstaza has been demonstrated across clinical trials and compassionate use programs.[1] The first patient was dosed in 2010. In clinical trials, Upstaza demonstrated transformational neurological improvements. The most common side effects were initial insomnia, irritability and dyskinesia.

Administration of Upstaza occurs through a stereotactic surgical procedure, a minimally invasive neurosurgical procedure used for the treatment of a number of pediatric and adult neurological disorders. The Upstaza administration procedure is performed by a qualified neurosurgeon in centers specialized in stereotactic neurosurgery.

Upstaza has received marketing authorization in Europe, Great Britain and Israel.

About aromatic L-amino acid decarboxylase (AADC) deficiency
AADC deficiency is a fatal, rare genetic disorder that typically causes severe disability and suffering from the first months of life, affecting every aspect of life – physical, mental and behavioral. The suffering of children with AADC deficiency may be exacerbated by: episodes of distressing seizure-like oculogyric crises causing the eyes to roll up in the head, frequent vomiting, behavioral problems, and difficulty sleeping.

The lives of affected children are severely impacted and shortened. Ongoing physical, occupational and speech therapy, and interventions, including surgery, also are often required to manage potentially life-threatening complications such as infections, severe feeding and breathing problems.

About Translarna™ (ataluren)
Translarna (ataluren), discovered and developed by PTC Therapeutics, is a protein restoration therapy designed to enable the formation of a functioning protein in patients with genetic disorders caused by a nonsense mutation. A nonsense mutation is an alteration in the genetic code that prematurely halts the synthesis of an essential protein. The resulting disorder is determined by which protein cannot be expressed in its entirety and is no longer functional, such as dystrophin in Duchenne. Translarna, the tradename of ataluren, is licensed in multiple countries for the treatment of nonsense mutation Duchenne muscular dystrophy (nmDMD) in ambulatory patients aged 2 years and older. Ataluren is an investigational new drug in the United States.

About Duchenne Muscular Dystrophy (Duchenne)
Primarily affecting males, Duchenne is a rare and fatal genetic disorder that results in progressive muscle weakness from early childhood and leads to premature death in the mid-20's due to heart and respiratory failure. It is a progressive muscle disorder caused by the lack of functional dystrophin protein. Dystrophin is critical to the structural stability of all muscles, including skeletal, diaphragm, and heart muscles. Patients with Duchenne can lose the ability to walk (loss of ambulation) as early as 10 years old, followed by loss of the use of their arms. Duchenne patients subsequently experience life-threatening lung complications, requiring the need for ventilation support, and heart complications in their late teens and 20s.

About PTC Therapeutics, Inc.
PTC is a global biopharmaceutical company focused on the discovery, development and commercialization of clinically differentiated medicines that provide benefits to patients with rare disorders. PTC's ability to innovate to identify new therapies and to globally commercialize products is the foundation that drives investment in a robust and diversified pipeline of transformative medicines. PTC's mission is to provide access to best-in-class treatments for patients who have little to no treatment options. PTC's strategy is to leverage its strong scientific and clinical expertise and global commercial infrastructure to bring therapies to patients. PTC believes this allows it to maximize value for all its stakeholders. To learn more about PTC, please visit us at **www.ptcbio.com** and follow us on Facebook, Instagram, LinkedIn and Twitter at @PTCBio.

For More Information:

Investors:
Kylie O'Keefe
+1 (908) 300-0691

kokeefe@ptcbio.com

Media:
Jeanine Clemente
+1 (908) 912-9406
jclemente@ptcbio.com

Forward-Looking Statement

This press release contains forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. All statements contained in this release, other than statements of historic fact, are forward-looking statements, including statements regarding: the future expectations, plans and prospects for PTC, including with respect to the expected timing of regulatory submissions and responses, commercialization and other matters with respect to its products and product candidates; PTC's strategy, future operations, future financial position, future revenues, projected costs; the extent, timing and financial aspects of our strategic pipeline prioritization and reductions in workforce; and the objectives of management. Other forward-looking statements may be identified by the words, "guidance", "plan," "anticipate," "believe," "estimate," "expect," "intend," "may," "target," "potential," "will," "would," "could," "should," "continue," and similar expressions.

PTC's actual results, performance or achievements could differ materially from those expressed or implied by forward-looking statements it makes as a result of a variety of risks and uncertainties, including those related to: the outcome of pricing, coverage and reimbursement negotiations with third party payors for PTC's products or product candidates that PTC commercializes or may commercialize in the future; PTC's ability to use the results of Study 041, a randomized, 18-month, placebo-controlled clinical trial of Translarna for the treatment of nmDMD followed by an 18-month open-label extension, and from its international drug registry study to support a marketing approval for Translarna for the treatment of nmDMD in the United States; whether investigators agree with PTC's interpretation of the results of clinical trials and the totality of clinical data from our trials in Translarna; expectations with respect to Upstaza, including any regulatory submissions and potential approvals, commercialization, manufacturing capabilities, the potential achievement of development, regulatory and sales milestones and contingent payments that PTC may be obligated to make; significant business effects, including the effects of industry, market, economic, political or regulatory conditions; changes in tax and other laws, regulations, rates and policies; the eligible patient base and commercial potential of PTC's products and product candidates; PTC's scientific approach and general development progress; and the factors discussed in the "Risk Factors" section of PTC's most recent Annual Report on Form 10-K, as well as any updates to these risk factors filed from time to time in PTC's other filings with the SEC. You are urged to carefully consider all such factors.

As with any pharmaceutical under development, there are significant risks in the development, regulatory approval and commercialization of new products. There are no guarantees that any product will receive or maintain regulatory approval in any territory, or prove to be commercially successful, including Translarna and Upstaza.

The forward-looking statements contained herein represent PTC's views only as of the date of this press release and PTC does not undertake or plan to update or revise any such forward-looking statements to reflect actual results or changes in plans, prospects, assumptions, estimates or projections, or other circumstances occurring after the date of this press release except as required by law.

Acronyms:
BLA: Biologics License Application

DMD: Duchenne Muscular Dystrophy
EMA: European Medicines Agency

FDA: U.S. Food and Drug Administration

MAA: Marketing Authorization Application

NDA: New Drug Application
PKU: Phenylketonuria

References:

1. Tai CH, *et al.* Long-term efficacy and safety of eladocagene exuparvovec in patients with AADC deficiency. *Mol Ther.* 2022;30(2):509-518.
2. Chien *et al.* AGIL-AADC gene therapy results in sustained improvements in motor and developmental milestones through 5 years in children with AADC deficiency. Poster presented at the 48th Annual Meeting of the Child Neurology Society, Charlotte, NC, USA, Oct 23-26, 2019.
3. Chien YH, *et al.* Efficacy and safety of AAV2 gene therapy in children with aromatic L-amino acid decarboxylase deficiency: an open-label, phase 1/2 trial. *Lancet Child Adolesc Health.* 2017;1(4):265-273.