PTC Therapeutics Receives Positive CHMP Opinion for Upstaza™ for the Treatment of AADC Deficiency

May 20, 2022

– First ever gene therapy directly administered into the brain –

– Recommended for regulatory approval by EMA –

– Results demonstrated sustained improvements in motor and cognitive function –

– Conference call scheduled for Monday, May 23, at 8 a.m. ET –

SOUTH PLAINFIELD, N.J., May 20, 2022 /PRNewswire/ -- PTC Therapeutics, Inc. (NASDAQ: PTCT) today announced that Upstaza™ (eladocagene exuparvovec; PTC-AADC) received a positive opinion from the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA). Once ratified by the European Commission, Upstaza will be the first approved disease-modifying treatment for aromatic L-amino acid decarboxylase (AADC) deficiency for patients 18 months and older and the first marketed gene therapy directly infused into the brain.

"We are thrilled with the positive opinion from the CHMP, and are eager to bring Upstaza to patients living with AADC deficiency," said Stuart W. Peltz, Ph.D., Chief Executive Officer, PTC Therapeutics. "Upstaza will be the first marketed gene therapy that is directly administered into the brain, the first gene therapy approved in a major market in several years, the third gene therapy that is on the market now, and only the fourth in vivo gene therapy ever approved. It's important for the biotech community to have gene therapy products achieving approvals at regulatory bodies, as well as it being an important milestone for PTC that will help us build the gene therapy franchise and grow our revenue base."

The CHMP opinion is based on the findings of clinical studies conducted in Taiwan. In addition, data from the compassionate use treatment of patients in Europe were included in the application. In the clinical studies, patients went from no display of any motor milestone development to developing clinically meaningful motor skills and neuromuscular function from as early as three months following treatment, with transformational improvements shown to continue up to nine years after treatment.[1] Cognitive and communication skills improved in all treated patients.[1,2]

"The difference Upstaza, a one-time gene therapy, can make is life-changing," said Paul Wuh-Liang Hwu, M.D., Ph.D., Lead Investigator, National Taiwan University Hospital. "AADC deficiency is a devastating neurological disorder with no effective treatment. Before therapy, affected children couldn't even lift their head, but now many can sit, stand with help, feed themselves and some can walk and talk."

PTC expects the European Commission to ratify the marketing authorization for Upstaza under exceptional circumstances in approximately two months. The decision will be applicable to all 27 European Union member states, as well as Iceland, Norway and Liechtenstein.

About Upstaza™ (eladocagene exuparvovec)
Upstaza, formerly PTC-AADC, is a one-time gene replacement therapy for the treatment of AADC deficiency. 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 more than 10 years ago. In the clinical trials, Upstaza demonstrated transformational neurological improvements, which have continued for up to nine years following treatment. The most common side effects were initial insomnia, irritability and dyskinesia. The full indication proposed by the CHMP for ratification is: Upstaza is 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.

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 will be performed by a qualified neurosurgeon in a center specialised in stereotactic neurosurgery.

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, which can happen daily and last for hours, causing the eyes to roll up in the head, frequent vomiting, behavioral problems, difficulty sleeping, and life-threatening complications such as respiratory infections and gastrointestinal problems.

There is no disease-modifying treatment approved for AADC deficiency and the lives of affected children are severely impacted, and shortened, with the use of many different medications to help manage symptoms. Ongoing physical, occupational and speech therapy, and interventions, including surgery, are also often required to manage potentially life-threatening complications such as infections, severe feeding and breathing problems and scoliosis.

About PTC Therapeutics, Inc.
PTC is a science-driven, 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.

Conference Call on Monday, May 23
PTC will host a conference call to discuss the positive opinion from the CHMP on its AADC deficiency gene therapy, Upstaza, on Monday, May 23 at 8 a.m. ET.

Access the call by dialing (877) 303-9216 (in the United States) or +1 (973) 935-8152 (outside of the United States) five minutes prior to the start of the call and providing the passcode 3275436.

An audiocast replay will be available approximately two hours after completion of the call. The audiocast will be archived on the company's website for 30 days.

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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 clinical trials and studies, availability of data, regulatory submissions and responses and other matters; expectations with respect to Upstaza, including any regulatory decision made by the European Commission; PTC's expectations with respect to the licensing, regulatory submissions and commercialization of its other products and product candidates; PTC's strategy, future operations, future financial position, future revenues, projected costs; 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; expectations with respect to Upstaza and other programs within PTC's gene therapy platform, including any regulatory submissions and potential approvals, manufacturing capabilities and the potential financial impact and benefits of its leased biologics manufacturing facility and 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 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.

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.

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