PTC518 PIVOT-HD Study Achieves Primary Endpoint

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- Study met primary endpoint with dose-dependent blood HTT protein lowering at Week 12 -

- Favorable dose-dependent trends across clinical scales in Stage 2 patients at Month 12 -

- Signals of dose-dependent clinical benefit relative to matched natural history cohort as well as dose-dependent lowering of NfL in Stage 2 patients at Month 24 -

- Continued favorable safety and tolerability profile with no treatment-related NfL spikes -

- PTC will host a conference call on May 5, 2025, at 8:00 am ET-

WARREN, N.J., May 5, 2025 /PRNewswire/ -- PTC Therapeutics, Inc. (NASDAQ: PTCT) today announced results from the Phase 2 PIVOT-HD study of PTC518 (votoplam) in Stage 2 and Stage 3 Huntington's disease (HD) patients. The study met its primary endpoint of reduction in blood Huntingtin (HTT) protein levels ($p<0.0001$) at Week 12 and favorable safety and tolerability. In addition, the 12-month data from the Stage 2 patients are consistent with the previously reported dose-dependent lowering of HTT protein and dose-dependent trends across clinical scales.

"These PIVOT-HD results confirm that PTC518 lowers Huntingtin protein and shows early signals of clinical benefit with a favorable safety profile," said Matthew B. Klein, M.D., Chief Executive Officer, PTC Therapeutics. "In addition, at 24 months, we observed favorable dose-dependent trends on the cUHDRS and the TFC and SDMT subscales relative to natural history as well as dose-dependent lowering of neurofilament light chain protein. We look forward to discussions on the next development and regulatory steps including the potential for accelerated approval as we work to potentially bring the first disease-modifying therapy to those affected by Huntington's disease."

Results from the full 12-month cohort demonstrate dose-dependent lowering in blood HTT levels, with 23% at the 5mg dose level for both Stage 2 and 3 patients and 39% and 36% at the 10mg dose level for Stage 2 and 3 patients, respectively. For Stage 2 patients, there were dose-dependent trends of benefit on clinical scales including the Composite Unified Huntington's Disease Rating Scale (cUHDRS) and Total Motor Score (TMS) subscale. For Stage 3 patients, there were trends favoring the 5mg dose group relative to placebo, but not the 10mg dose group, suggesting that treatment effect may differ in Stage 3 patients relative to Stage 2 patients.

For all dose levels and disease stages, PTC518 showed a favorable safety and tolerability profile with no treatment-related serious adverse events or neurofilament light chain protein (NfL) spikes.

In addition, 24-month treatment data from the patients on whom data were shared last year (N=21) demonstrate signals of dose-dependent trends on the cUHDRS, Total Function Capacity (TFC) and Symbol Digit Modalities Test (SDMT) subscales when compared to a propensity matched natural history cohort from the ENROLL-HD Registry. At Month 24, there was also dose-dependent lowering of plasma NfL from baseline of -8.9% (nominal $p=0.12$) for the 5mg dose level and -14% (nominal $p=0.03$) for 10mg dose level.

Conference Call and Webcast Details:
PTC will hold a conference call at 8:00 am ET today to discuss this news. To access the call by phone, please click here to register and you will be provided with dial-in details. To avoid delays, we recommend participants dial in to the conference call 15 minutes prior to the start of the call. The webcast conference call can be accessed on the Investor section of the PTC website at https://ir.ptcbio.com/events-presentations. A replay of the call will be available approximately two hours after completion of the call and will be archived on the company's website for 30 days following the call.

About PIVOT-HD
PIVOT-HD was designed as a 12-month placebo-controlled trial to assess pharmacodynamic effect and safety of PTC518 at two dose levels--5mg and 10mg, relative to placebo. Initially, the study included only Stage 2 patients. A Stage 3 cohort of similar size was subsequently added to help identify the best study population for future studies. The primary endpoints of PIVOT-HD were total blood Huntingtin (HTT) lowering at 12 weeks and safety events. Secondary endpoints included 12-month blood HTT levels, and other blood-and central nervous system (CNS) biomarkers as well as changes in Composite Unified Huntington's Disease Rating Scale (cUHDRS).

Following 12 months, patients were eligible to enroll in a long-term extension study in which all subjects would receive PTC518. Those originally randomized to 5mg and 10mg would continue at that dose level; those initially randomized to placebo would be randomized 1:1 to 5mg or 10mg. All subjects and investigators remain blinded to initial treatment assignment.

Presentation of study results is expected at a scientific meeting later in the year.

About PTC518
PTC518 is a small molecule splicing modifier that acts via a unique mechanism to promote the inclusion of a novel pseudoexon containing a premature termination codon, thus triggering Huntingtin (HTT) mRNA degradation and subsequent reduction in HTT protein levels. PTC518 was discovered from PTC's validated splicing platform, following the successful discovery and development of Evrysdi® (risdiplam) for spinal muscular atrophy (SMA).

About Huntington's Disease
Huntington's disease (HD) is a fatal, hereditary, genetic disorder of the central nervous system.[1] It is caused by a defective gene. This gene produces

a protein, called Huntingtin (HTT), which is involved in the functioning of the nerve cells in the brain (neurons). When the gene is defective, it produces an abnormal (or mutated) HTT protein that is toxic and causes neuron damage and neuron death.[2] HD usually presents in people who are in their 30s or 40s. Symptoms can present earlier in life, and this is called Juvenile HD.[2,3] There are also cases of infantile HD, when symptoms develop in children who are younger than 10 years old.[2] While symptoms vary from person to person, the disease primarily affects the brain and results in abnormal movements, difficulties with speech, swallowing and walking, as well as a number of other symptoms including behavioral, cognitive and motor symptoms.[4,5] While there are therapies approved for specific disease symptoms, currently, there is no cure for HD and there are no approved drugs that delay the onset or slow disease progression.

About PTC Therapeutics, Inc.
PTC is a global biopharmaceutical company that discovers, develops and commercializes clinically differentiated medicines that provide benefits to children and adults living with rare disorders. PTC's ability to innovate new therapies and to globally commercialize products is the foundation that drives investment in a robust and diversified pipeline of transformative medicines. To learn more about PTC, please visit www.ptcbio.com and follow on Facebook, X, and LinkedIn.

For More Information:

Investors:
Ellen Cavaleri
+1 (615) 618-6228
ecavaleri@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 press release, other than statements of historic fact, are forward-looking statements, including statements with respect to the future expectations, plans and prospects for PTC, PTC's strategy, including with respect to the expected timing of clinical trials and studies, availability of data, regulatory submissions and responses and other matters, 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 PTC's license and collaboration agreement with Novartis Pharmaceuticals Corporation including its right to receive development, regulatory and sales milestones, profit sharing and royalty payments from Novartis; 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; the sufficiency of PTC's cash resources and its ability to obtain adequate financing in the future for its foreseeable and unforeseeable operating expenses and capital expenditures; 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.

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:

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