



PTC Therapeutics Announces FDA Approval of Sephience™ (sepiapterin) for the Treatment of Children and Adults Living with Phenylketonuria (PKU)

July 28, 2025

- Broad labeling inclusive of all disease subtypes for individuals 1 month of age and older -

- PTC will host a conference call on Monday, July 28th at 5:00 pm ET -

WARREN, N.J., July 28, 2025 /PRNewswire/ -- PTC Therapeutics, Inc. (NASDAQ: PTCT) announced today that the U.S. Food and Drug Administration (FDA) has approved SEPHIENCE™ (sepiapterin) for the treatment of children and adults living with phenylketonuria (PKU). The approval includes broad labeling for the treatment of hyperphenylalaninemia (HPA) in adult and pediatric patients 1 month of age and older with sepiapterin-responsive PKU.

"We are excited to have reached this important milestone for those affected by PKU," said Matthew B. Klein, M.D., Chief Executive Officer of PTC Therapeutics. "The broad labeling reflects the potential of Sephience to meet the significant unmet need of PKU patients. The Sephience clinical data along with our expertise in launching rare disease therapies position Sephience to become the future standard of care. Our experienced customer facing teams are ready to bring this therapy to children and adults with PKU in the United States as quickly as possible."

The FDA approval is based on the evidence of significant efficacy and safety from the Phase 3 APHENITY trial as well as durability of treatment effect in the APHENITY long-term extension study.

"The approval marks an exciting milestone for the PKU community," said Catherine Warren, Executive Director of the National PKU Alliance. "This progress brings renewed hope, and we are eager to see the positive impact this new treatment option will have on advancing care and potentially improving quality of life for individuals of all ages and PKU subtypes that respond to this therapy."

SEPHIENCE was recently granted marketing authorization by the European Commission. Review of approval applications is ongoing in several other countries including Japan and Brazil.

Conference Call and Webcast

PTC will hold a conference call Monday, July 28, 2025 at 5:00 pm ET 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 SEPHIENCE™ (sepiapterin)

SEPHIENCE is indicated for the treatment of hyperphenylalaninemia (HPA) in adult and pediatric patients with phenylketonuria (PKU). Sephience is a natural precursor of the enzymatic co-factor BH4, a critical co-factor for phenylalanine hydroxylase (PAH). Through its mechanism of action, Sephience is able to effectively reduce blood phenylalanine (Phe) levels and has the potential to treat a broad range of PKU patients. Sephience is approved in the European Economic Area and the United States.

Indication and Important Safety Information

Indication

SEPHIENCE is indicated for the treatment of hyperphenylalaninemia (HPA) in adult and pediatric patients 1 month of age and older with sepiapterin-responsive phenylketonuria (PKU). SEPHIENCE is to be used in conjunction with a phenylalanine (Phe)-restricted diet.

Contraindications

None

Important Safety Information

Treatment with SEPHIENCE should be directed by physicians knowledgeable in the management of PKU. Biochemical response to SEPHIENCE can only be determined by a therapeutic trial with careful monitoring of ongoing dietary and nutritional balance to ensure adequate Phe control.

Warnings and Precautions

- **Increased Bleeding:** SEPHIENCE may increase the risk of bleeding. Bleeding events, including superficial hematomas, prolonged bleeding, and heavy menstrual bleeding have occurred in patients treated with SEPHIENCE. Inform patients about the risk of bleeding associated with SEPHIENCE and have patients follow up with their healthcare provider should such a bleeding event occur. Consider treatment interruption with SEPHIENCE in patients with active bleeding.
- **Hypophenylalaninemia:** Some pediatric patients receiving SEPHIENCE experienced hypophenylalaninemia. Monitor blood Phe levels during treatment and modify the dosage of SEPHIENCE and/or dietary protein and Phe intake as needed to ensure adequate blood Phe level control. Frequent blood monitoring is recommended in the pediatric population.
- **Interaction with Levodopa:** In a 10-year post-marketing safety surveillance program for a non-PKU indication using

another drug that is a phenylalanine hydroxylase (PAH) activator, 3 patients with underlying neurological disorders experienced seizures, exacerbation of seizures, over-stimulation, and irritability during co-administration with levodopa. Monitor patients who are receiving levodopa for changes in neurological status during treatment with SEPHIENCE.

Adverse Reactions

Most common adverse reactions with SEPHIENCE ($\geq 2\%$ and $>$ placebo) were diarrhea, headache, abdominal pain, hypophenylalaninemia, feces discoloration, and oropharyngeal pain.

Drug Interactions

Avoid concomitant use of drugs known to inhibit folate synthesis dihydrofolate reductase (DHFR) (e.g., trimethoprim, methotrexate, trimetrexate, pemetrexed, pralatrexate, raltitrexed, and piritrexim) while taking SEPHIENCE. Concomitant administration of such drugs may reduce sepiapterin metabolism to BH₄. If concomitant use is not avoidable, monitor blood Phe levels.

SEPHIENCE and PDE-5 inhibitors (e.g., sildenafil, vardenafil, or tadalafil) induce vasorelaxation and may reduce blood pressure. Monitor for signs and symptoms of hypotension.

For medical information, product complaints, or to report an adverse event, please call 1-866-562-4620 or email at usmedinfo@ptcbio.com.

You may also report adverse events directly to FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see [Full Prescribing Information](#).

About Phenylketonuria

Phenylketonuria (PKU) is a rare, inherited metabolic disease, which affects the brain. It is caused by a defect in the gene that helps create the enzyme needed to break down phenylalanine (Phe). If left untreated or poorly managed, Phe—an essential amino acid found in all proteins and most foods—can build up to harmful levels in the body. This causes severe and irreversible disabilities, such as permanent intellectual disability, seizures, delayed development, memory loss, and behavioral and emotional problems. Newborns with PKU initially do not have any symptoms, but symptoms are usually progressive, and damage caused by toxic levels of Phe in the first few years of life is irreversible. Diagnosis of PKU usually takes place during newborn screening programs. There are an estimated 58,000 people living with PKU globally.

About PTC Therapeutics, Inc.

PTC is a global biopharmaceutical company dedicated to the discovery, development and commercialization of clinically differentiated medicines for children and adults living with rare disorders. PTC is advancing a robust and diversified pipeline of transformative medicines as part of its mission to provide access to best-in-class treatments for patients with unmet medical needs. The company's strategy is to leverage its scientific expertise and global commercial infrastructure to optimize value for patients and other stakeholders. To learn more about PTC, please visit www.ptcbio.com and follow on Facebook, X, and LinkedIn.

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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, commercialization and other matters with respect to its products and product candidates; expectations with respect to Sephience, including timing of commercialization and of potential regulatory decisions; 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 Sephience, including any regulatory submissions and potential approvals, commercialization and the potential achievement of 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 Sephience.

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.

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