Xeris Biopharma Announces Positive Topline Phase 2 Clinical Data of Its Investigational XeriSol™-Formulated Once-Weekly Subcutaneous (SC) Levothyroxine (XP-8121)

May 30, 2024

XeriSol™ formulation enabled predictable bioavailability and sustained levels of levothyroxine in a once-weekly subcutaneous presentation

Once-weekly SC levothyroxine (XP-8121) participants normalized TSH/T4 levels using 45% less drug than would be needed for their daily oral dose on a weekly basis

Data established an average once-weekly SC dose of XP-8121 and confirmed previous Phase 1 study of a 4X target dose conversion factor when switching from once-daily oral administration of levothyroxine

Participants who completed the study rated higher treatment satisfaction with XP-8121 compared to oral and a majority (72%) indicated a strong preference for the SC route of administration

Study exposed the challenges of achieving and maintaining normal TSH with daily oral levothyroxine therapy

FDA End-of-Phase 2 interaction to facilitate a Phase 3 pivotal study program is expected by year-end

CHICAGO--(BUSINESS WIRE)--May 30, 2024-- Xeris Biopharma Holdings, Inc. (Nasdaq: XERS), a growth-oriented biopharmaceutical company committed to improving patients' lives by developing and commercializing innovative products across a range of therapies, today announced topline results from its recently completed Phase 2 multi-center, open label, study of XP-8121 for the treatment of adults with hypothyroidism. XP-8121 employs the Company's XeriSol™ formulation technology to enable a novel once-weekly SC injection of levothyroxine. This novel formulation significantly increases the bioavailability of levothyroxine reducing overall drug exposure and enabling a dosing regimen with the potential to mitigate the many challenges associated with achieving and maintaining a normal level of thyroid stimulating hormone (TSH) with daily oral formulations of levothyroxine.

The Phase 2 study (NCT05823012) was a non-randomized, open-label, single arm, self-controlled study of XP-8121 (levothyroxine sodium) to determine a target dose conversion factor from stably dosed oral levothyroxine to XP-8121 (levothyroxine sodium) in 46 patients with hypothyroidism and to assess the safety and tolerability of XP-8121 (levothyroxine sodium) after once-weekly SC injections. The Phase 2 study leveraged the bioavailability observations of a previous Phase 1 study in which PK analysis showed that participants could achieve comparable systemic exposure with XP-8121 at only 57% of a weekly oral dose. The Phase 2 study included the following periods: Screening, Titration Period (2 to 8 weeks), and Maintenance Period (4 weeks). Participants entered the study on a stable oral dose (≥ 3 months) with normal TSH and free T4 laboratory values.

Participants were receiving a daily oral levothyroxine dose of 83.7 ± 31.14 mcg (mean ± SD) at study entry. To ensure the safety of study participants, once-weekly SC injection of XP-8121 was initiated at 2X their daily dose and titrated every 2 weeks to a target of 4X their daily dose. Participants completing the Maintenance Period were receiving a weekly XP-8121 dose of 324.4 ± 125.59 mcg. The geometric mean ratio of the once-weekly dose of XP-8121 to the daily dose levothyroxine (aka dose conversion factor) was 4.02 [90% CI 3.79, 4.27]. A total of 30 participants (65.2%) experienced at least 1 TEAE (Treatment Emergent Adverse Event) with most rated mild (87%) and moderate (13%) in severity. The most frequent (> 2 participants) TEAE included fatigue (21.7%), injection site pain (10.9%), headache (8.7%) and urinary tract infection (6.5%). No deaths or other serious adverse events (SAEs) were reported. Injection site tolerability was assessed with every SC administration of XP-8121 (> 450 injections). There were very few reports of discomfort (18%; mostly mild intensity), erythema (7%; Draize scale) or edema (1%; Draize scale). No participant discontinued from the study due to an injection site reaction. The Treatment Satisfaction Questionnaire for Medication (TSQM-9) was administered to assess patient satisfaction. XP-8121 scored consistently higher in all three domains (effectiveness, convenience, and global satisfaction) compared to oral levothyroxine. At the conclusion of the study, participants were asked to rate preference for once-weekly XP-8121. A majority (72%) indicated a strong preference for the SC route of administration based on categorical attributes of convenience (60.6%), ease of administration (45.5%), frequency of administration (54.5%), level of compliance (27.3%) and confidence in therapy (36.4%).

"A 2022 study published in the Journal of the Endocrine Society estimated the prevalence of hypothyroidism in the U.S. grew to 11.7% or approximately 30 million adults in 2019*. Innumerable reports have been published documenting the various compliance and absorption challenges that can interfere with the bioavailability of oral levothyroxine. Interestingly, in our own Phase 2 study, 40% of patients considered stable at the time of screening were found to have their TSH or T4 outside of normal range. We believe our once-weekly SC injection can enable control in patients who struggle with oral preparations for a variety of reasons," said Paul R. Edick, Xeris' Chairman and CEO.

"We are excited by the initial top line results of our Phase 2 dose-finding study of XP-8121. These results are further evidence of our target dose conversion and consistent with the estimates generated from the prior Phase 1 study in healthy volunteers," said Kenneth E. Johnson, PharmD, Xeris' Senior Vice President, Global Development and Medical Affairs. "Given the known challenges of oral bioavailability of levothyroxine and further by the high rate of screen failures observed in our phase 2 study, we believe that XP-8121 could fill a substantial unmet medical need. We look forward to meeting with the FDA later this year and expect to present complete study results at upcoming medical meetings as well as submission to peer-reviewed medical journals."

About Hypothyroidism

Hypothyroidism, or underactive thyroid, happens when your thyroid gland doesn't make enough thyroid hormones to meet your body's needs. Your thyroid is a small, butterfly-shaped gland in the front of your neck. It makes hormones that control the way the body uses energy. These hormones affect nearly every organ in your body and control many of your body's most important functions. For example, they affect your breathing, heart rate,

weight, digestion, and moods. Without enough thyroid hormones, many of your body's functions slow down.

About Levothyroxine

Therapeutically, levothyroxine is administered when the body is deficient in the endogenous hormone. Administration of levothyroxine is thus indicated for acquired thyroid disease (primary hypothyroidism), in cases of decreased secretion of TSH from the anterior pituitary gland (secondary hypothyroidism), and in cases of decreased secretion of TRH from the hypothalamus (tertiary hypothyroidism) and for congenital hypothyroidism. In most patients, hypothyroidism is a permanent condition requiring lifelong treatment. The goal of therapy is restoration of the euthyroid state, which can reverse the clinical manifestations of hypothyroidism and significantly improve quality of life.

About XeriSol™

The proprietary XeriSol™ non-aqueous formulation technology platform is designed to address the limitations of aqueous formulations for peptide and small molecule drugs. The solutions are formulated using biocompatible, non-aqueous solutions that impart high stability and solubility to drugs allowing for development of room temperature stable, ready-to-use formulations. XeriSol™ formulations have been used extensively in global commercial products (Gvoke®/Ogluo®) and clinical trials. The technology is protected by an extensive patent estate, trade secrets and know-how, and it is available for licensing.

About Xeris

Xeris (Nasdaq: XERS) is a growth-oriented biopharmaceutical company committed to improving patient lives by developing and commercializing innovative products across a range of therapies. Xeris has three commercially available products; Gvoke®, a ready-to-use liquid glucagon for the treatment of severe hypoglycemia, Keveyis®, a proven therapy for primary periodic paralysis, and Recorlev® for the treatment of endogenous Cushing's syndrome. Xeris also has a robust pipeline of development programs to extend the current marketed products into important new indications and uses and bring new products forward using its proprietary formulation technology platforms, XeriSol™ and XeriJect®, supporting long-term product development and commercial success.

Xeris Biopharma Holdings is headquartered in Chicago, IL. For more information, visit www.xerispharma.com, or follow us on X, LinkedIn, or Instagram.

Forward-looking Statement

Any statements in this press release other than statements of historical fact are forward-looking statements. Forward-looking statements include, but are not limited to, statements about future expectations, plans and prospects for Xeris Biopharma Holdings, Inc. including statements regarding expectations for the release of clinical data or results from clinical trials, the timing of meetings with regulatory authorities, the market and therapeutic potential of its products and product candidates, including the therapeutic potential of XP-8121, the potential utility of its formulation platforms, including XeriSol™-formulated subcutaneous levothyroxine's potential benefits compared to daily oral formulations, the intellectual property rights associated with XeriSol™ and its availability for licensing and other statements containing the words "will," "would," "continue," "expect," "should," "anticipate" and similar expressions, constitute forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. These forward-looking statements are based on numerous assumptions and assessments made in light of Xeris' experience and perception of historical trends, current conditions, business strategies, operating environment, future developments, geopolitical factors and other factors it believes appropriate. By their nature, forward-looking statements involve known and unknown risks and uncertainties because they relate to events and depend on circumstances that will occur in the future. The various factors that could cause Xeris' actual results, performance or achievements, industry results and developments to differ materially from those expressed in or implied by such forward-looking statements, include, but are not limited to, its financial position and need for financing, including to fund its product development programs or commercialization efforts, whether its products will achieve and maintain market acceptance in a competitive business environment, its reliance on third-party suppliers, including single-source suppliers, its reliance on third parties to conduct clinical trials, the ability of its product candidates to compete successfully with existing and new drugs, and its and collaborators' ability to protect its intellectual property and proprietary technology. No assurance can be given that such expectations will be realized and persons reading this communication are, therefore, cautioned not to place undue reliance on these forward-looking statements. Additional risks and information about potential impacts of financial, operational, economic, competitive, regulatory, governmental, technological, and other factors that may affect Xeris can be found in Xeris' filings, including its most recently filed Annual Report on Form 10-K filed with the Securities and Exchange Commission, the contents of which are not incorporated by reference into, nor do they form part of, this communication. Forward-looking statements in this communication are based on information available to us, as of the date of this communication and, while we believe our assumptions are reasonable, actual results may differ materially. Subject to any obligations under applicable law, we do not undertake any obligation to update any forward-looking statement whether as a result of new information, future developments or otherwise, or to conform any forward-looking statement to actual results, future events, or to changes in expectations.

- Wyne, Kathleen L., et al. "Hypothyroidism Prevalence in the United States: A Retrospective Study Combining National Health and Nutrition Examination Survey and Claims Data, 2009–2019." *Journal of the Endocrine Society*, vol. 7, no. 1, 2023, pp. bvac172–bvac172, https://doi.org/10.1210/jendso/bvac172

View source version on businesswire.com: https://www.businesswire.com/news/home/20240530612890/en/

Investor Contact
Allison Wey
Senior Vice President, Investor Relations and Corporate Communications
awey@xerispharma.com

Source: Xeris Biopharma Holdings, Inc.