UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): October 20, 2022

XERIS BIOPHARMA HOLDINGS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**001-40880**	**87-1082097**
(State or other jurisdiction of incorporation)	(Commission File Number)	(I.R.S. Employer Identification No.)

180 N. LaSalle Street, Suite 1600
Chicago, Illinois 60601
(Address of principal executive offices, including zip code)

(844) 445-5704
(Registrant's telephone number, including area code)

Not Applicable
(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.0001 per share	XERS	The Nasdaq Global Select Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure

On October 20, 2022, Xeris Biopharma Holdings, Inc. (the "Company") issued a press release announcing topline results from its Phase 1 study of subcutaneous (SC) levothyroxine (XP-8121) in healthy adult volunteers. The Company intends to host a conference call and live webcast to discuss the results on October 20, 2022 at 8:30 a.m. E.T. The Company has made available a slide presentation to accompany the call, a copy of which is being furnished as Exhibit 99.2 to this Current Report on Form 8-K.

The information in this Item 7.01, including Exhibits 99.1 and 99.2 attached hereto, shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or otherwise subject to the liabilities of that section, nor shall they be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, except as expressly set forth by specific reference in such a filing. The Company undertakes no obligation to update, supplement or amend the materials attached hereto.

Item 9.01 Financial Statements and Exhibits

(d) Exhibits

Number	**Description**
99.1	Press release of Xeris Biopharma Holdings, Inc. dated October 20, 2022
99.2	Slide presentation of Xeris Biopharma Holdings, Inc. dated October 20, 2022
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: October 20, 2022

Xeris Biopharma Holdings, Inc.

By: /s/ Steven M. Pieper
Name: Steven M. Pieper
Title: *Chief Financial Officer*

Exhibit 99.1

XERIS BIOPHARMA ANNOUNCES POSITIVE TOPLINE PHASE 1 CLINICAL DATA OF ITS INVESTIGATIONAL SUBCUTANEOUS (SC) LEVOTHYROXINE (XP-8121); HOSTS CONFERENCE CALL AND WEBCAST

Data demonstrate proof-of-concept showing a once weekly subcutaneous injection of XP-8121 provides similar exposure at steady-state as daily oral Synthroid®

Simulation model implies dose conversion factor of 4X

XP-8121 in healthy volunteers was generally well tolerated at all doses

Data supports further development in patients with congenital or acquired hypothyroidism who require thyroid hormone replacement

FDA End-of-Phase 1 interaction expected by year-end

Company to host conference call and webcast today at 8:30 a.m. ET

CHICAGO, IL; October 20, 2022 – Xeris Biopharma Holdings, Inc. (Nasdaq: XERS), a growth-oriented biopharmaceutical company committed to improving patient lives by developing and commercializing innovative products across a range of therapies, today announced topline results from its Phase 1 study of subcutaneous (SC) levothyroxine (XP-8121) in healthy adult volunteers. Using its XeriSol™ technology, the Company is developing a novel formulation of levothyroxine sodium (SC injection) to potentially mitigate many of the challenges associated with oral formulations of levothyroxine.

The Phase 1 study was a randomized, open-label, crossover study conducted in 60 healthy adults. The study was designed to evaluate the pharmacokinetics, dose proportionality and safety and tolerability of 600 µg, 1200 µg, and 1500 µg of XP-8121 following SC administration and to evaluate the relative bioavailability of 600 µg SC XP-8121 versus 600 µg oral (PO) levothyroxine (Synthroid ®). Single dose data from this study were used to develop a population pharmacokinetic model to simulate steady-state exposure (AUC) following weekly SC dosing of XP-8121 or daily PO dosing of Synthroid and to determine the target dose conversion at steady-state from Synthroid PO to XP-8121 SC.

“Oral levothyroxine has been the standard of care treatment for hypothyroidism for many years, and it is one of the most prescribed medicines in the United States, generating more than 100 million prescriptions per year. The Phase 1 study results offer initial proof of concept that our novel subcutaneous formulation of levothyroxine has the potential to provide patients with a once-weekly dosing, thereby potentially improving treatment adherence, as well as bypassing the gastrointestinal (GI) tract, thereby mitigating limitations of oral therapy,” said Paul R. Edick, Xeris’ Chairman and CEO. “We have requested a meeting with the FDA and expect feedback by the end of the year.”

“We are very encouraged with the results of the Phase 1 study of XP-8121, our subcutaneous injection of levothyroxine. The data show that subjects receiving XP-8121 SC have slower absorption, lower peak plasma, and higher extended exposure compared to Synthroid PO at the comparable dose of 600 µg. In addition, exposure was proportional over the range of ascending XP-8121 doses studied. Simulations based on the population pharmacokinetic model indicate that exposure from weekly XP-8121 1200 µg SC doses overlaps daily Synthroid PO 300 µg suggesting a dose conversion factor of 4x,” said Ken Johnson, PharmD, Xeris’ Senior Vice President, Global

Development and Medical Affairs. “Importantly, single SC doses of XP-8121 at all doses were safe and well tolerated and no XP-8121 studied dose was different from Synthroid 600 µg PO with respect to the safety findings.”

Conference Call and Webcast Details

Xeris will host a conference call and webcast today, Thursday, October 20, 2022, at 8:30 a.m. Eastern Time. To pre-register for the conference call please use this link: https://www.netroadshow.com/events/login?show=f4a7da25&confId=43411

After registering, a confirmation email will be sent, including dial-in details and a unique code for entry. The Company recommends registering a minimum of ten minutes prior to the start of the call. Following the conference call, a replay will be available until Thursday, November 8, 2022, at US:1 929 458 6194, US Toll Free: 1 866 813 9403, UK: 0204 525 0658, Canada: 1 226 828 7578, or all other locations: +44 204 525 0658 Access Code: 573410. In addition, a live audio of the conference call will be available as a webcast. To join the webcast, please visit “Events” on investor relations page of the Company’s website at www.xerispharma.com or use this link https://events.q4inc.com/attendee/711397177

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 solvents 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®, the first and only FDA-approved therapy for primary periodic paralysis, and Recorlev® for the treatment of endogenous Cushing’s syndrome. Xeris also has a 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 Twitter, LinkedIn, or Instagram.

Forward-looking Statement

Any statements in this press release about future expectations, plans and prospects for Xeris Biopharma Holdings, Inc., including the development of a sub-cutaneous formulation of levothyroxine, the market and therapeutic potential of Xeris' products and product candidates, expectations regarding clinical data or results from planned clinical trials, the timing of clinical trials, the timing or likelihood of regulatory approval and commercialization of its product candidates, the timing or likelihood of expansion of current marketed products into new indications and uses or into additional markets, the potential utility of its proprietary formulation technology platforms, and other statements containing the words "expected," "will," "would," "continue," 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, 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. Various factors 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, including the impact of COVID-19 on our business operations and clinical activities, our ability to fund our product development programs or commercialization efforts, whether our clinical trials demonstrate efficacy and safety to the satisfaction of the FDA or other regulatory authorities, and whether our products will achieve and maintain market acceptance. No assurance can be given that our expectations will be realized and persons reading this communication are, therefore, cautioned not to place undue reliance on these forward-looking statements. Additional information about economic, competitive, governmental, technological, and other factors that may affect Xeris is set forth in the "Risk Factors" section of the most recently filed Quarterly Report on Form 10-Q filed with the U.S. Securities and Exchange Commission, the contents of which are not incorporated by reference into, nor do they form a part of, this communication. Forward-looking statements in this communication are based upon information available to Xeris, as of the date of this communication and, while believed to be reasonable, actual results may differ materially. Subject to any obligations under applicable law, Xeris does 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.

Investor Contact

Allison Wey

Senior Vice President, Investor Relations and Corporate Communications

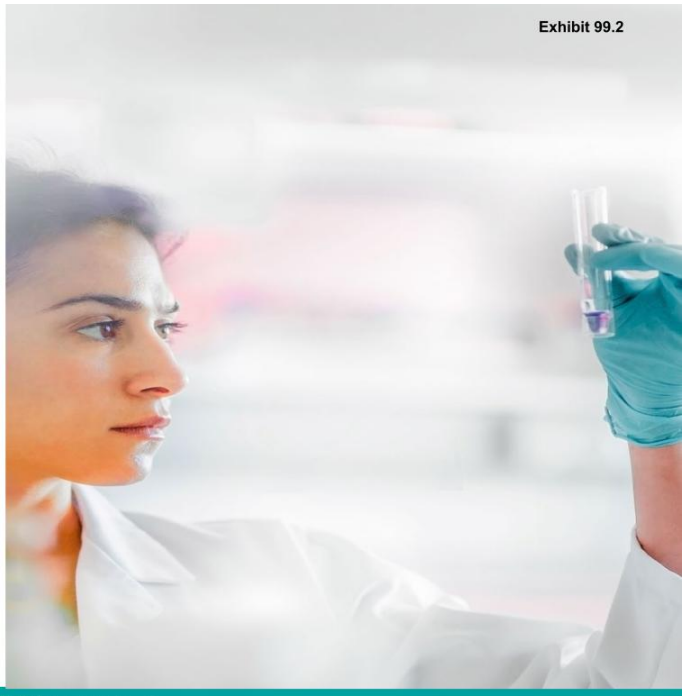
awey@xerispharma.com

312-736-1237

Exhibit 99.2

Xeris Biopharma (Nasdaq: XERS)

A growth-oriented biopharmaceutical company committed to improving patient lives by developing and commercializing innovative products across a range of therapies



Topline Results of Phase 1 Study of Levothyroxine: PO vs SC (XP-8121-108)

Agenda

Opening Remarks: Paul Edick, Chairman and CEO

Study Results: Ken Johnson, PharmD
SVP, Global Development and Medical Affairs

Q&A

xeris® PHARMACEUTICALS

Forward-looking statements

Any statements in this presentation about future expectations, plans and prospects for Xeris Biopharma Holdings, Inc., including the development of a sub-cutaneous formulation of levothyroxine, the market and therapeutic potential of Xeris' products and product candidates, expectations regarding clinical data or results from planned clinical trials, the timing of clinical trials, the timing or likelihood of regulatory approval and commercialization of its product candidates, the timing or likelihood of expansion of current marketed products into new indications and uses or into additional markets, the potential utility of its proprietary formulation technology platforms, and other statements containing the words "expected," "will," "would," "continue," 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, 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. Various factors 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, including the impact of COVID-19 on our business operations and clinical activities, our ability to fund our product development programs or commercialization efforts, whether our clinical trials demonstrate efficacy and safety to the satisfaction of the FDA or other regulatory authorities, and whether our products will achieve and maintain market acceptance. No assurance can be given that our expectations will be realized and persons reading this communication are, therefore, cautioned not to place undue reliance on these forward-looking statements. Additional information about economic, competitive, governmental, technological, and other factors that may affect Xeris is set forth in the "Risk Factors" section of the most recently filed Quarterly Report on Form 10-Q filed with the U.S. Securities and Exchange Commission, the contents of which are not incorporated by reference into, nor do they form a part of, this communication. Forward-looking statements in this communication are based upon information available to Xeris, as of the date of this communication and, while believed to be reasonable, actual results may differ materially. Subject to any obligations under applicable law, Xeris does 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.

XeriSol™ Levothyroxine may enable 1x/weekly subcutaneous (SC) therapy

With over 100M Rx/yr, oral levothyroxine is one of the most prescribed therapies in US

XP-8121 — Levothyroxine

For maintenance therapy in patients with congenital or acquired hypothyroidism who require thyroid hormone replacement

Value Proposition

- 1st injectable levothyroxine indicated for hypothyroidism
- Bypasses GI tract, avoid the spectrum of oral absorption challenges
- Improved regimen compliance with 1x/week administration
- Demonstrate safety at comparable exposure
- Small volume, ready-to-use, room temperature stable SC injection enabled by XeriSol™ formulation technology

US Market Opportunity Overview

105M Rx/yr dispensed for oral levothyroxine[1]

47% associated with a comorbid GI condition impacting oral absorption[2]

21% concomitant medication known to interfere with absorption of levothyroxine[3]

17% admit to compliance issues with daily oral regimen[3]

15% w/hard to control symptoms[2]

62M weekly doses per year[1]

$30-$50 per weekly dose comparable to branded orals[4]

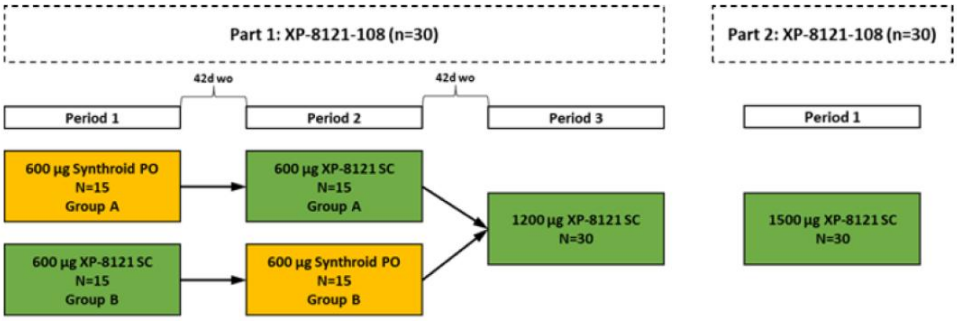
$2-3B Opportunity

Sources: 1. IQVIA NPA Y2021; 2. McMillan M et al. *Drugs R D.* 2016 16(1):53-68; 3. Robertson HM et al *Thyroid : Official Journal of the American Thyroid Association.* 2014 24(12):1765-1771. 4. Tirosint WAC and 5x premium to Synthroid

XP-8121-108: Study Overview

- **Background**
  - Reliance on the FDA's previous findings of safety and effectiveness for the listed drug, Synthroid® (Levothyroxine sodium tablets; NDA 21402 [Abbvie]); selected as reference standard for oral (PO) levothyroxine
  - Single 600 ug dose comparison based on FDA guidance *Levothyroxine Sodium Tablets – In Vivo Pharmacokinetic and Bioavailability Studies and In Vitro Dissolution Testing* (2000)
  - Three (3) ascending doses of XP-8121 SC to determine dose proportionality
- **Study Objectives**
  - Characterize the pharmacokinetics of XP-8121 SC (600 ug, 1200 ug, and 1500 ug) compared to Synthroid PO (600 ug)
  - Evaluate XP-8121 dose proportionality (600 ug, 1200 ug, and 1500 ug)
  - Assess the safety and tolerability of XP-8121
- **Chronic Dosing Simulations: Population Pharmacokinetic Model**
  - Compare steady state exposure (e.g. AUC) with weekly dosing of XP-8121 SC versus daily dosing of Synthroid PO
  - Determine dose conversion from Synthroid PO to XP-8121 SC

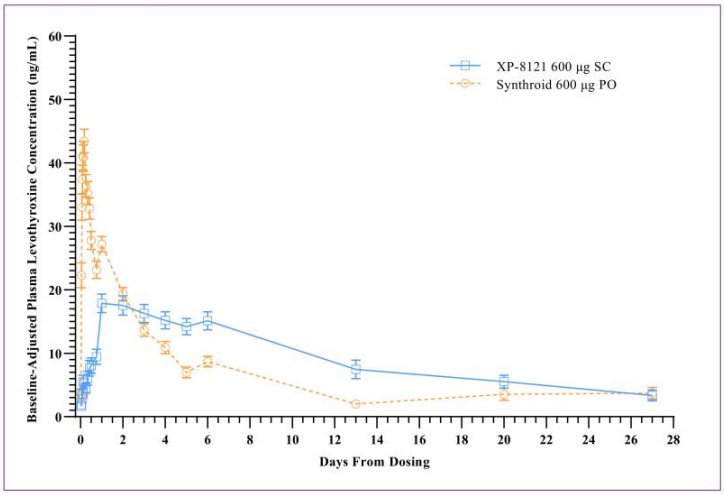
Phase 1 Pharmacokinetic Study Design (XP-8121-108)



PK results based on Baseline-Adjusted T4 Concentrations to determine:

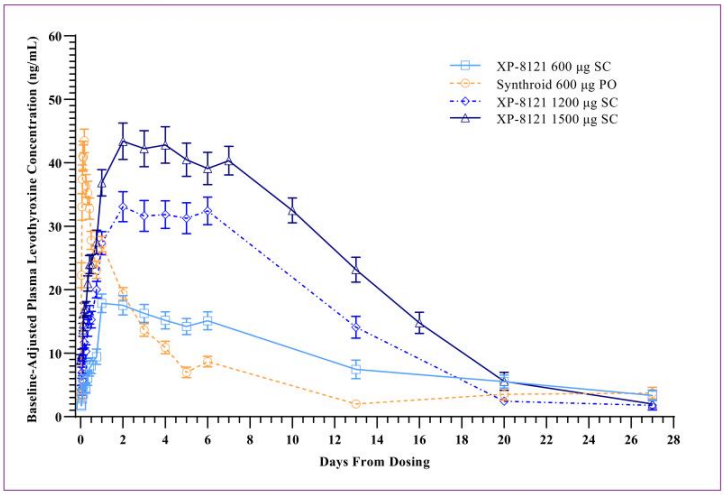
- Mean Concentration Profile Over Time
- Key PK Parameters - Cmax, Tmax, AUCs

Baseline Adjusted T4 Concentration by Time Profile Day 1 to Day 28 Following Single Dose Administration (XP-8121-108)



- **Synthroid PO 600 ug exhibits a rapid rise in levothyroxine levels followed by a rapid decline**
- **XP-8121 SC exhibits a lower maximum concentration (Cmax), longer time to maximum concentration (Tmax) with sustained exposure profile relative to Synthroid PO administration**

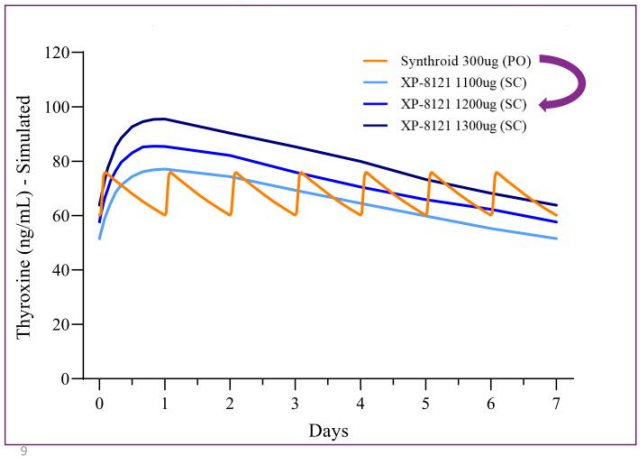
Baseline Adjusted T4 Concentration by Time Profile Day 1 to Day 28 Following Single Dose Administration (XP-8121-108)



- Synthroid PO 600 ug exhibits a rapid rise in levothyroxine levels followed by a rapid decline
- XP-8121 SC exhibits a lower maximum concentration (Cmax), longer time to maximum concentration (Tmax) with sustained exposure profile relative to Synthroid PO administration
- **Confirmation of dose proportional exposure with ascending doses of XP-8121**
- **No major safety concerns were identified**

PopPK Model: Simulation of Chronic Dosing

XP-8121 SC 1200 µg/week has similar exposure to Synthroid PO 300 µg/day at steady state



- All data from XP-8121-108 combined to generate PopPK model
- Simulated pharmacokinetic profile (Baseline Adjusted T4 Concentration) to estimate the exposure of XP-8121 and Synthroid PO with chronic dosing (e.g. steady state)
- Implies that 1200 ug once-weekly dose of XP-8121 SC could provide similar exposure (e.g. Cmax and AUC) to Synthroid PO 300 µg/day at steady state; 4x conversion factor

XP-8121 Highlights and Next Steps

- Large market opportunity: Oral levothyroxine is one of the most prescribed therapies in US with over 100 million prescriptions annually
- Demonstrated proof-of-concept: A once weekly subcutaneous injection of XP-8121 can provide comparable exposure to daily oral Synthroid® supporting further development in patients with congenital or acquired hypothyroidism who require thyroid hormone replacement
- Dose conversion ratio established: Chronic dosing simulation implies dose conversion ratio of 4X
- Safe and well tolerated: XP-8121 in healthy volunteers was generally well tolerated at all doses
- Next Steps: FDA End-of-Phase 1 meeting requested; interaction expected by year-end

Q&A