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

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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]

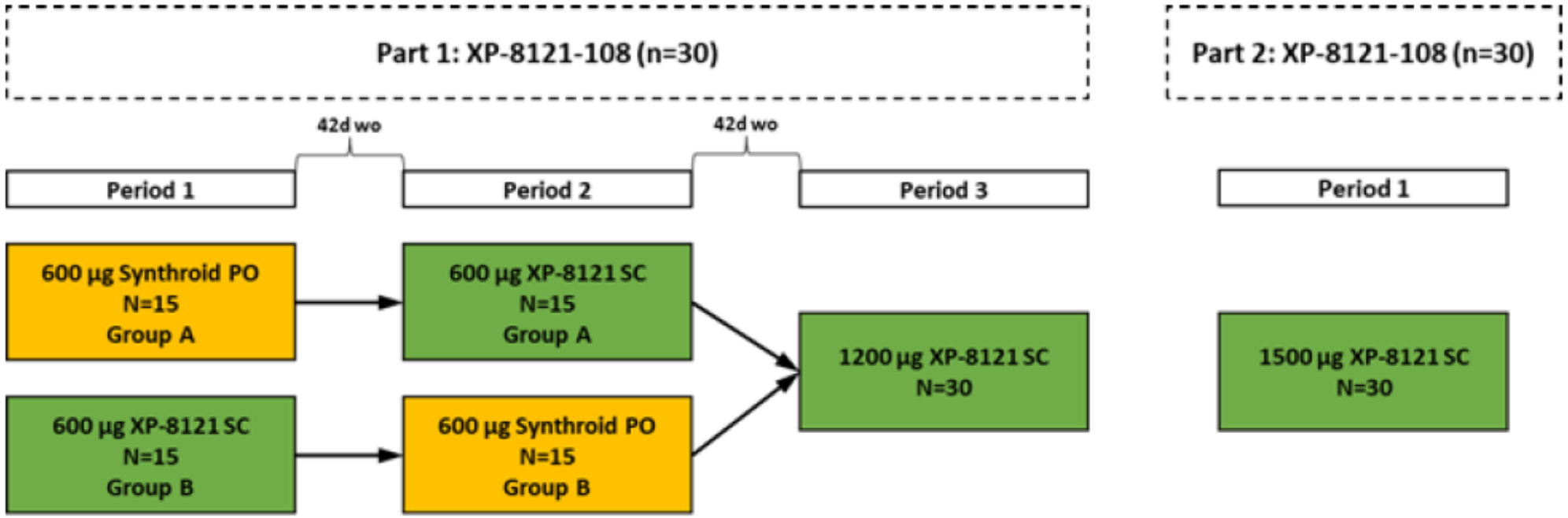
$2-3B Opportunity

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

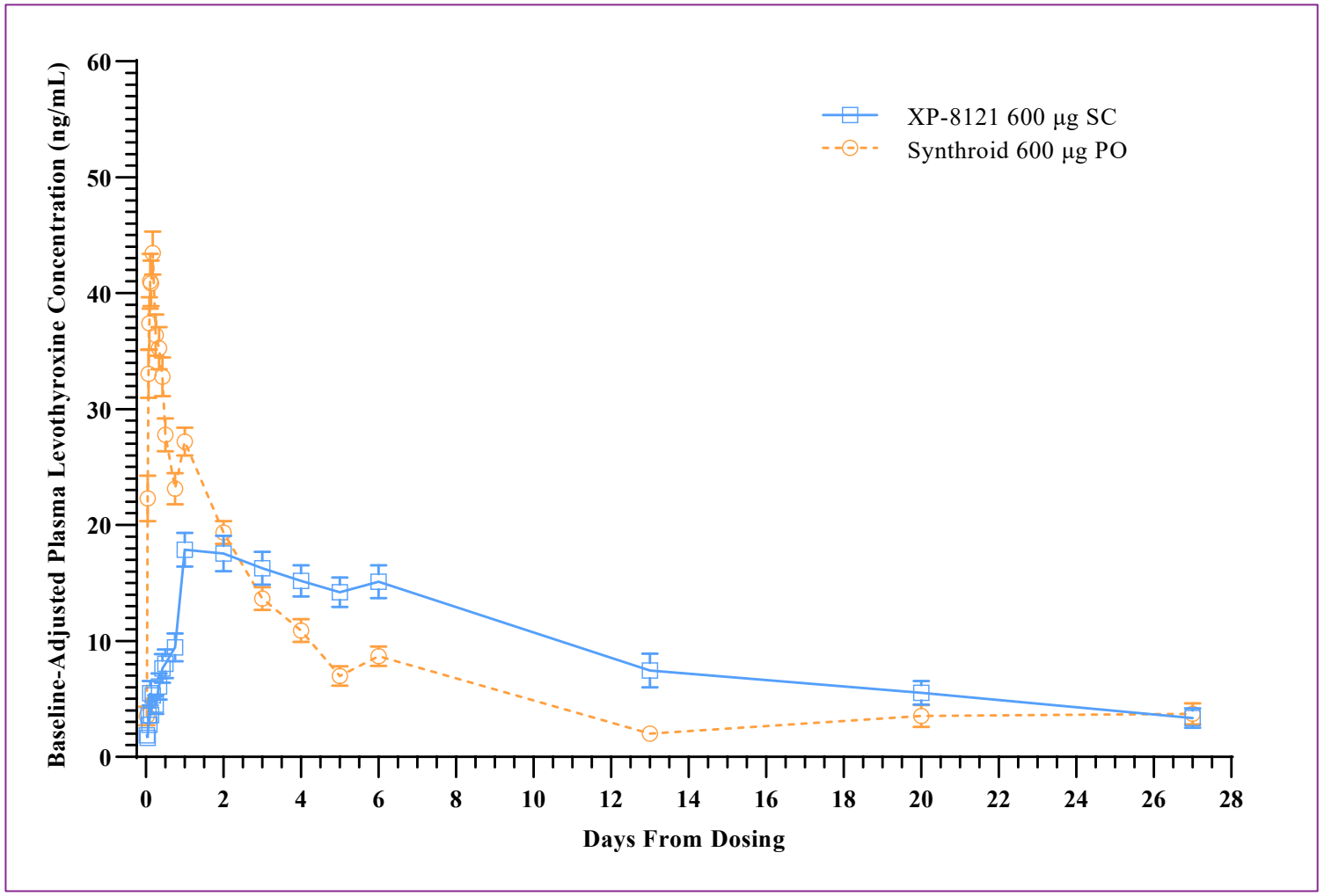
Phase 1 Pharmacokinetic Study Design (XP-8121-108)



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

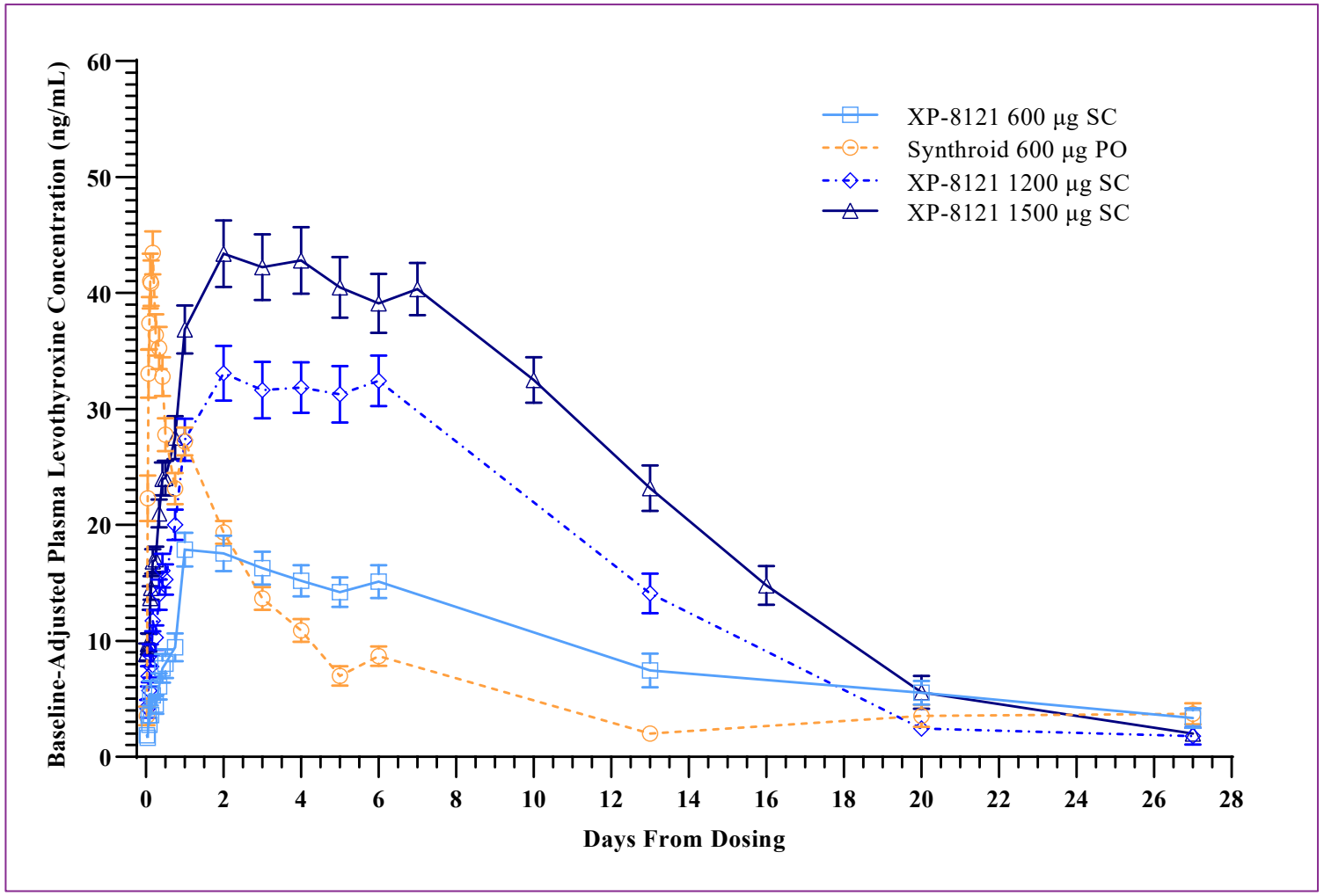
- Mean Concentration Profile Over Time
- Key PK Parameters - Cmax, Tmax, AUCs

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**

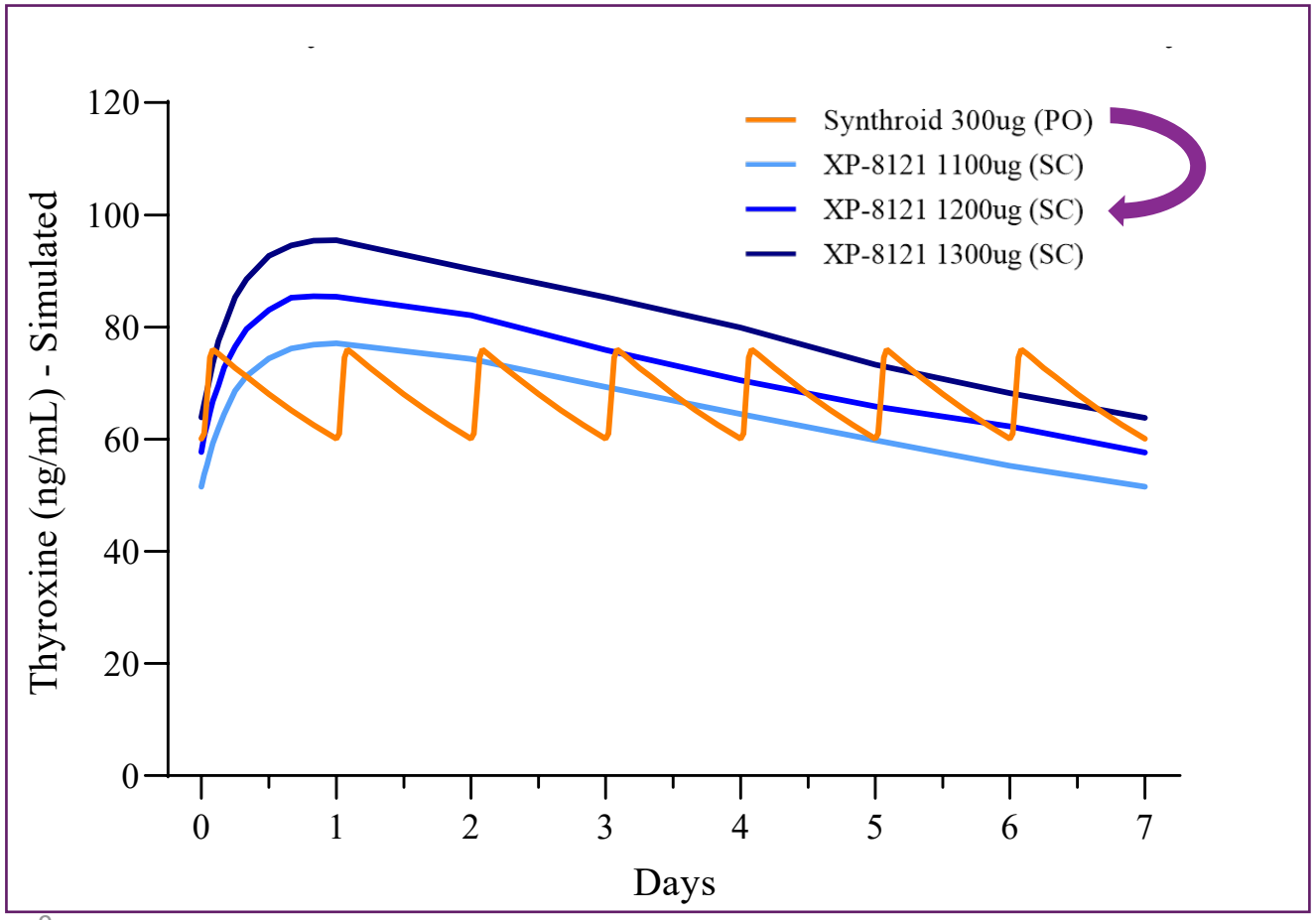
Baseline Adjusted T4 Concentration by Time Profile Day 1 to Day 28 Following Single Dose Administration (XP-8121-108)



- 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