SAFE HARBOR STATEMENT

Remarks today concerning
United Therapeutics may include forward-looking statements which represent United Therapeutics’ expectations or beliefs regarding future events. We caution that such statements involve risks and uncertainties that may cause actual results to differ materially from those in the forward-looking statements. Consequently, all such forward-looking statements are qualified by the cautionary language and risk factors set forth in United Therapeutics’ periodic and other reports filed with the SEC.

There can be no assurance
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This presentation
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United Therapeutics and MannKind entered into an exclusive license and collaboration agreement related to the TreT program on September 3, 2018. That agreement has not yet closed, and is subject to a number of conditions, including the expiration or termination of the Hart-Scott-Rodino Antitrust Improvements Act.
TECHNOSPHERE® PLATFORM: INNOVATIVE ORAL INHALATION TECHNOLOGY

POWDER FORMULATIONS

DEVICES

DIGITAL TECHNOLOGY
MANNKIND HAS CREATED A SUITE OF TECHNOLOGIES FOCUSING ON PULMONARY DELIVERY OF THERAPEUTIC AGENTS

**Lungs have a large surface area**
- Rapid drug exposure – similar to I.V.
- Avoids first pass liver metabolism
- Consistent dose to dose delivery

**Business advantages**
- Significant investments in IP platform
- Proven approval track record
- FDA approved excipient

**Compatibility with diverse APIs**
- Small molecules, peptides and biologics
- Local drug delivery for lung disease
- Systemic delivery for vaccines

**Patient-focused design**
- Portable and discreet devices
- Non-invasive therapy – needle free
- Wide user compatibility due to ease of use
TECHNOSPHERE® PARTICLES: WHAT ARE THEY?

FDKP

» Crystalline plate assembly

» Extremely high surface area

CRISTALLINE PARTICLE

AMORPHOUS PARTICLE

DRUG PRODUCT IS RELEASED FROM FDKP WHEN IT REACHES THE LUNG
PROVEN PLATFORM TO ENHANCE THERAPEUTIC PROFILES ON NEW AND EXISTING TREATMENTS

Technosphere® Technology enables systemic delivery of therapies

Rapid drug absorption that mimics intra-arterial delivery due to bypassing the liver

Formulations have been prepared with a diverse assortment of drugs

99mTechnetium-labeled particles demonstrate uniform distribution to the deep lung

Excellent Aerodynamics
MANNKIND INHALATION DELIVERY DEVICES

Re-usable
Dreamboat®
Family

Single Use
Cricket®
Family
FEEDBACK LOOPS AND DIGITAL INTEGRATION
OUR TECHNOLOGY IS PROTECTED BY ~800 PATENTS IN FORCE WORLDWIDE COVERING BOTH UTILITY AND DESIGN OUT TO 2035

1. Formulation technology including optimized particles and characteristics (2034)

2. 35 Patents listed in FDA’s Orange Book, Patent term extends to 2032. Trademarks Registered in major markets

3. Methods of making/manufacturing the formulations and particles (2035)

4. Inhalers, cartridges, inhalation systems, blister package and methods of using them (2032)

5. Inhaler testing and support technologies (2030)

6. Methods of treatment using the formulations and inhalation systems (2031)
FIRST PREVIEW OF PHASE 1 TREPROSTINIL TECHNOSPHERE® (TreT)

A DOSE-RISING CLINICAL TRIAL TO EVALUATE THE PHARMACOKINETICS, SAFETY AND TOLERABILITY OF TREPROSTINIL INHALATION POWDER IN HEALTHY NORMAL VOLUNTEERS

TECHNOSPHERE® (TreT) is a development stage product not approved for sale in any jurisdiction.
TreT: SINGLE ASCENDING DOSE IN HEALTHY NORMAL VOLUNTEERS

- **DOSING COHORTS**: 6
- **SUBJECTS PER COHORT**: 6
- **TOTAL OF 36 SUBJECTS DOSED WITH TreT**

**TreT DOSES**
- 30 mcg – 1 x 30 mcg cartridge
- 60 mcg – 1 x 60 mcg cartridge
- 90 mcg – 1 x 90 mcg cartridge
- 120 mcg – 1 x 90 mcg + 1 x 30 mcg
- 150 mcg – 1 x 90 mcg + 1 x 60 mcg
- 180 mcg – 2 x 90 mcg

TECHNOSPHERE® (TreT) is a development stage product not approved for sale in any jurisdiction.
TREPROSTINIL PK: $C_{\text{max}}^*$

**Graph:**
- **C$_{\text{max}}$ (pg/mL)** vs. **dose (mcg)**
- **Parallel to Tyvaso Curve**

**TECHNOSPHERE® (TreT)** is a development stage product not approved for sale in any jurisdiction.
TREPROSTINIL PK: AUC LAST (EXPOSURE)*

TECHNOSPHERE® (TreT) is a development stage product not approved for sale in any jurisdiction.
**DOSING SUMMARY**

1. **150 mcg**
   
   Doses up through 150 mcg were tolerated

2. **90 mcg**
   
   Doses up to 90 mcg fall within range of doses evaluated with Tyvaso

3. **SINGLE USE**
   
   Treprostinil Technosphere enables simple single use inhalation in <3 seconds

TECHNOSPHERE® (TreT) is a development stage product not approved for sale in any jurisdiction.
THANK YOU
2 | NEXT GENERATION DELIVERY SYSTEMS

» **TREVYENT®** / Parenteral Treprostinil Sodium
  Jonathan M.N. Rigby

» **TECHNOSPHERE®** / Drug Delivery Platform
  Michael Castagna, PharmD