DISRUPTIVE THERAPIES

BARDA INDUSTRY DAY
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CEO and Founder, United Therapeutics Corporation
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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.

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FOCUSED ON OUR PATIENTS

Commercial Products

PULMONARY ARTERIAL HYPERTENSION (PAH)

TABLET

INFUSION

INHALATION

TABLET

ONCOLOGY

INJECTION
ADVANCE AUTONOMOUS DRUG DELIVERY FOR MASS CASUALTY CARE

» Example: Implantable Remodulin is FDA-approved

» Transforms any limited use short $T^{1/2}$ drug or biologic into a clinically viable therapy

» Patch pump safely applied by rescuer; appropriate for steady state antibiotics, naloxone (weaponized opiate) or atropine (chemical weapons)
ADVANCE NOVEL SYNERGISTIC THERAPIES

» Treprostinil in next generation inhaler

» Multiple therapies in SNS can have route, spectrum and PK expanded for mass casualty care

SNS=Strategic National Stockpile
Focus | Advance | Create | Transform
Example: (1) Inhaled treprostinil (PAH) adapted to ILD; (2) use NSAIDs to boost NAI plasma levels in severe flu

- UT aero-medicinals deliver to precise regions of lung (80nm-100um)
- Novel biologics (mAB) cellular and adenoviral therapy given as aerosols
UT FACTS

Focus  Advance  Create  Transform
WORLDWIDE EVLP PATIENTS TO DATE

1636 LIVES SAVED*

*Global figure including all EVLP technologies. To date, our EVLP clinical trial has successfully transplanted EVLP lungs into more than 50 patients.
UNITED THERAPEUTICS LUNG RECIPIENTS

HEATHER LEVERINGTON

20 months post double lung transplant, Heather won two gold medals at the 2018 US Transplant Games in Utah.

CHUCK BOETSCH

I did my first 5k in early May, and this was my second. I have also traveled to Colorado, up to 10,500 feet with no issues.
UT LUNG SERVICE MODEL

LUNG BIOENGINEERING
EVLP CENTER (LB-1)
Silver Spring, MD

Construction in progress
EX-VIVO ORGAN PERFUSION EXPANSION MODEL
LONGER TERM VISION
DE NOVO LUNGS + CELLULARIZATION
DOUBLE / TRIPLE SUPPLY
CELL THERAPY

How cell therapy works?

EXAMPLE
Restoring nitric oxide enzyme in PAH patients using their cells

Endothelial progenitor cells (EPCs)
eNOS gene
Cell expansion
Transfection

1. Adapted from Callahan et. Al. Severe Immune Complication Committee (SICC), MGH and the U.U. FDA
CELL THERAPY

How cell therapy works?

EXAMPLE

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CELL THERAPY

How cell therapy works?

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CELL THERAPY

How cell therapy works?

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- eNOS gene
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- Transfection

LEUKAPHERESIS

1. ISOLATE EPCs FROM PATIENT (DAY 0)

2. XPAND EPCS 2000X (DAY 1-26)

3. TRANSFECT WITH ENOS GENE

4. FREEZE CELLS FOR FUTURE USE

MANUFACTURING PROCESS

1. Adapted from Callahan et. Al. Severe Immune Complication Committee (SICC), MGH and the U.U. FDA
UT CELL THERAPY

How cell therapy works?

EXAMPLE

Sapphire: restore nitric oxide enzyme in PAH patients

1. Adapted from Callahan et. Al. Severe Immune Complication Committee (SICC), MGH and the EMA/SFDA
SAPPHIRE STUDY*

Study of Angiogenic Cell Therapy for Progressive Pulmonary Hypertension: Intervention With Repeat Dosing of eNOS-enhanced EPCs

*The SAPPHIRE study is being conducted entirely in Canada, and is sponsored by Northern Therapeutics, Inc., a Canadian entity in which UT has a 49.7 percent voting stake and a 71.8 percent financial stake. UT has the exclusive right to pursue this technology in the United States, and plans to seek FDA approval of Aurora-GT if SAPPHIRE is successful.
Cellular therapies, given intravenously provide an opportunity to transfer beneficial responses observed in sepsis survivors. The code book for sepsis survival can be encoded in a multipurpose, long lived, cryopreserved product.
SEPSIS IN THE US

OVER 1.7M CASES\(^{(1)}\) AND 265,000 DEATHS IN US PER YEAR\(^{(2)}\)

SEPSIS IN THE U.S. IS INCREASING

» Aging population and increased immune-suppressed population
» Imported and domestic pan-resistant bacteria
» 1 patient dies every 2 minutes from sepsis

1. Hershey TB; NEJM, 2017  2. Rhee, C; JAMA, 2017
A UNIVERSAL CELL THERAPY FOR SEPSIS

Aurora GT

Proprietary cryopreserved COTS MSCs

Expanded 2000X

Engineered anti-sepsis MSCs

1. INSERT SEPSIS SURVIVAL GENES

2. 4-H THAW TO TREAT

Vial

Bioreactor

Sepsis survival genes

MSC | Mesenchymal Stem Cell
POC: MSC THERAPY FOR SEPSIS

MESENCHYMAL STEM CELLS REDUCE INFLAMMATION
WHILE ENHANCING BACTERIAL CLEARANCE AND
IMPROVING SURVIVAL IN SEPSIS

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Mei & Haitsma, American Journal of Respiratory and Critical Care Medicine, 2010
CO-TREATMENT OF MSC AND ANTIBIOTICS → IMPROVED SURVIVAL OF SEPTIC ANIMALS BY 36%

1. Mei & Haitsma, AJRCCM, 2010

Survival %

0 25 50 75 100

0 24 48 72 96 120 144 166

TIME (hours)

Sepsis animals

Sepsis animals treated with MSCs

p < 0.005
LYING MICE VS. TRUTHFUL PATIENTS

SEOK et al. GENOMIC RESPONSES IN MOUSE MODELS POORLY MIMIC HUMAN INFLAMMATORY DISEASES (PLOS 2013)

Rare mRNA found in both survivor mice and humans

HUMAN SEPSIS

R .01

MOUSE SEPSIS

1/160 septic patients have elevated survival protein with 65% lower mortality

Sepsis survival gene inserted into allogeneic MSCs

Aurora GT sepsis cells stored for treatment
UTHR — FOCUSED ON TODAY WHILE BUILDING THE BRIDGES TO FIND CURES