Oxysterols for Treatment of Perinatal Brain Injury

A First-In-Class Therapy to Prevent Cerebral Palsy in Premature Infants

A TRANSLATIONAL SCIENCE BENEFITS MODEL CASE STUDY
**Significance of the Project**

Diffuse white matter injury is the most common brain injury leading to poor neurologic outcomes in survivors of premature birth. The clinical outcomes are diverse depending on severity and its precise location but may include motor disabilities such as cerebral palsy (CP), which is the most common motor disability in childhood.

Population based studies have estimated that ~3 per 1,000 children in the United States are affected and this number is higher in developing countries. The greatest risk factor for the development of CP is premature birth, with an inverse relationship between CP risk and gestational age and birth weight.

Per the CDC, CP has been reported in up to 10% of survivors of premature birth. The economic impact of this injury is high with lifetime costs of care for one child with CP estimated at 1.5 million U.S. dollars. Other outcomes of neonatal WMI include permanent cognitive and/or neurosensory impairment.

There are no treatment options for infants with this injury, only supportive care. Therefore, the development of an effective therapy would constitute a major medical breakthrough in this underserved patient population.

**Summary of the Project**

The goal of this work is to develop an intravenous formulation of an oxysterol (TT-20), which was found in human breast milk, for the treatment of white matter injury (WMI) in preterm infants to preclude CP.

TT-20 is a small molecule that reverses WMI and motor abnormalities in preclinical animal models. Unlike current palliative care options, TT-20 is a first-in-class remyelination treatment that can preclude CP and reduce lifetime costs.

WMI results from the loss of preoligodendrocytes subsequent to inflammation or hypoxic injury experienced by premature infants in the NICU. The loss of these myelinating precursors results in significant and permanent hypomyelination and associated clinical deficits.

Dr. Benner and his team have identified multiple oxysterols in human maternal breast milk that promote the production of new oligodendrocytes from postnatal neural stem cells. In a mouse model of neonatal inflammatory WMI, administration of TT-20 promoted the production of new periventricular oligodendrocytes, improved myelination in the white matter regions most commonly injured in premature babies, and rescued associated motor deficits.

This figure examines the efficacy of treatment in a neonatal mouse model of WMI. Shown are uninjured control, injured without treatment, and injured with treatment.
Impact of the Project

Clinical

Dr. Benner and his team are developing an intravenous formulation of a drug to treat WMI in preterm infants, to preclude CP.

Currently, there is no treatment for WMI in preterm infants, and no treatment or prevention for CP. As of April 2020, pilot data have been collected in rodent models, and early IND-enabling studies are on-track with the aim of submitting a pre-IND meeting request to the FDA in Q3 2021.

The team plans to file an IND and initiate a phase 1b clinical trial as early as Q4 2022 to obtain initial safety data and determine optimal drug dosing for this population. The end result will be an intravenous formulation for preterm infants that is a first-in-class remyelination treatment able to prevent CP and reduce lifetime costs.

Economic

Shorter-term economic benefits include license agreements and patents to protect the intellectual property of the use of TT-20. A startup company, Tellus Therapeutics Inc., was established in October 2018 and is leading the efforts to translate the technology for clinical use in the pediatric population.

Longer-term economic benefits include cost savings and effectiveness, including the potential to avoid the approximately $1.5 million U.S. lifetime costs for caring for one child with CP, decreasing caregiver burden, and improving quality of life of patients.

This technology doesn’t just have the capacity to lower healthcare costs, however: this technology is designed to save lives and improve the quality of life of patients.

Community

One of the benefits of this technology is the potential for preventing CP, which will greatly improve the quality of life for patients and those around them, while significantly reducing lifetime care costs and the associated caregivers’ burden.

Prevention of CP or the reduction of severity will be a lifelong benefit for affected infants and their communities.

About the Research Team

Eric J. Benner, MD, PhD - Principal Investigator
- Assistant Professor of Pediatrics, Duke University School of Medicine
- George W. Brumley, Jr. M.D. Distinguished Assistant Professor of Developmental Biology
- Co-founder and Chief Science Officer, Tellus Therapeutics

Jason Kralic, PhD
- Co-founder and Chief Executive Officer, Tellus Therapeutics

Austin Schwarz, PhD, MBA
- Vice President of Operations, Tellus Therapeutics

Jaron Ballentine, MBA
- VP of Commercial Strategy, Tellus Therapeutics

Simon Gregory, PhD
- Duke University School of Medicine, Department of Neurology
- Co-founder and Scientific Advisory Board Member

Maria Iglesias de Ussel, PharmD, PhD
- Research Project Leader II, Duke Clinical & Translational Science Institute

Kelly Pegram, MSc, RACC
- Research Analyst and Lab Manager
**Project Milestones to Date**

**Project Start**
- Preclinical studies show efficacy in a rodent model

**2014 - 2018: EARLY PHASE DISCOVERY**
- Duke CTSI Translational Accelerator Award

**Licensing**
- Exclusive worldwide license granted

**JAN 2019**
- Duke CTSI Transformative Award

**CTSA Funding**
- Tellus Therapeutics is formed

**Funding**
- $75K from MedBlue

**OCT 2018**
- Tellus Therapeutics is formed

**New Company**
- $75K from MedBlue

**Award**
- MassChallenge Diamond Award ($100K)

**CTSA Funding**
- Duke CTSI Accelerator and BioLabs NC “Golden Ticket”

**Funding**
- $250K loan from NC Biotech Center

**Award**
- R01 is funded by NIH

**Grant Funding**
- DEC 2019

**RPD Designation**
- Rare Pediatric Disease application to the FDA is accepted

**ODD Designation**
- Orphan Drug application to the FDA for TT-20 is accepted

**SEPTMBER 2020**
- ODD designation awarded

**Anticipated Future Milestones**

**Pre-IND Work**
- May 2021: Xontogeny seed funding will enable IND work

**Phase 1b Clinical Trial**
- Clinical trial to determine dosing and initial safety data

**Projected Date of Completion**
- 2026: Drug in clinic
Translational Science Benefits Summary

**Therapeutic Procedures:**
Use of oxysterols to prevent Cerebral Palsy (CP) *(Demonstrated in animal models)*

**Drugs:**
Novel TT-20 based formulation *(Demonstrated)*

**Guidelines:**
Change practice in ICUs caring for infants with White Matter Injury *(Potential)*

**License Agreement:**
Worldwide license for use of oxysterols for repair of myelin *(Demonstrated)*

**Commercial Entity:**
Launch of a startup (Tellus Therapeutics) to develop TT-20 *(Demonstrated)*

**Patents:**
Two patents filed for use of oxysterols for myelin repair and treatment of inflammation-related diseases *(Demonstrated)*

**Cost Savings:**
Reduced lifetime costs associated with CP, resulting in lower societal and financial cost of illness *(Potential)*

**Life Expectancy & Quality of Life:**
Prevention of CP will increase life expectancy for infants with WMI, improve quality of life of patients, and reduce caregiver burden *(Potential)*

**Disease Prevention & Reduction:**
Prevention of CP *(Potential)*
CTSA Resources Used

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<th>Core</th>
<th>Type of Service</th>
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<tbody>
<tr>
<td>CTSI Accelerator</td>
<td>Grant Support; Project Management Support; Strategic Inputs</td>
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<tr>
<td>Office of Regulatory Affairs and Quality</td>
<td>Regulatory Support</td>
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Other Institutional Resources Used

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<tr>
<td>Duke Clinical Research Institute Pharmacokinetics</td>
<td>Pharmacokinetic Analysis</td>
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<td>Duke Office of Licensing and Ventures</td>
<td>Licensing Agreements</td>
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<td>Duke Proteomics and Metabolomics Shared Resource</td>
<td>Oxysterol Detection in Plasma and Brain</td>
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For More Information

About Dr. Eric Benner: [https://scholars.duke.edu/person/eric.benner](https://scholars.duke.edu/person/eric.benner)

About Duke Clinical & Translational Science Institute: Visit [ctsi.duke.edu](http://ctsi.duke.edu) or email us at DukeCTSI@dm.duke.edu


Translational Science Benefits Model citation:


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