ERAD

THERAPEUTICS

AN ORPHAN DRUG COMPANY FOCUSING ON GAUCHER DISEASE AND CYSTIC FIBROSIS

JULY 2017

For Discussion Purposes-All content in this presentation is the property of ERAD Therapeutics Inc.

ERAD Therapeutics Inc. (ETI) Overview

Private Orphan Drug company with Two Exciting Preclinical Assets

Developing two novel, but related biological technologies to treat Orphan Diseases[1,2] with a primary focus on **the unmet medical need and frequently fatal neurological consequences of Gaucher Disease** (a Lysosomal Storage Disease-LSD) and a secondary focus on Cystic Fibrosis (a respiratory and gastrointestinal disease).

ETI is developing a Patent Portfolio for a proprietary drug delivery mechanism which is based on the unique targeting capabilities of the CTB subunit[3] which binds to and enters cells through its specific cell-surface receptor **AND** is capable of crossing the Blood-Brain-Barrier

Successful achievement of Orphan Drug Designation (February, 2017) for mCT Technology

ERAD 2017

1 https://www.fda.gov/regulatoryinformation/lawsenforcedbyfda/significantamendmentstothefdcact/orphandrugact/default.htm
2 See Slide 4
3 See Slide 7

Investment Highlights

Proprietary CTB Technology	• Two platform technologies addressing significant unmet medical needs in Orphan Diseases • Primary focus on Gaucher Disease Type 1 & Type 3 • Fully Completed Seed Round enabling achievement of transitional milestones by 12-2017
Large Market Opportunity	• Gaucher Disease Type 1 $1.6 B+ • -game changing enzyme delivery mechanism opening entire GD market • Gaucher Disease Type 3 $350M+ **no current therapies address this high-need market**
Exclusivity & Fast Track	• Orphan Drug Designation (ODD) successfully achieved for mCT • Fast-track opportunity for CTB-GCC in Gaucher Type 3 • Potential for multiple ODD opportunities • Clear Orphan Drug Strategy
Additional Opportunities	• Our unique drug delivery mechanism enables delivery of drugs to tissues not currently accessible by traditional therapeutic strategies
Right leadership To execute the plan	• Seasoned management team with broad expertise in drug development

Gaucher Disease-Improving Clinical Outcomes by Revolutionizing Enzyme Replacement Therapy

Gaucher Disease

There are **~8,000 total U.S. cases** with a predominance in **Ashkenazi Jews.** Gaucher is classified into 3 types according to neurological deterioration, age and progression rate

Type 1

Most common; not previously known to impact the Central Nervous System, and usually presents in adulthood with an enlarged liver, enlarged spleen, anemia, and bone disease

- 6,000 – 7,000 U.S. patients
- 5 therapies on the market with $1.6 billion in sales per year
- Many Type 1 patients eventually experience neurological manifestations called "Parkinsonism" that cannot be controlled by conventional ERT

Type 2

Exceedingly rare; involves the CNS, affects infants and is uniformly fatal by 2 years of age

- ~250 U.S. patients
- **There are no therapies for Type 2**

Type 3

Begins at any time in childhood, involves the CNS, and is characterized by slowly progressive neurological deterioration and premature death

- 750-1,000 U.S. patients
- **There are no therapies for Type 3**

Note: Information from: National Gaucher Foundation website http://www.gaucherdisease.org

FDA Approved Treatments for Gaucher Disease & Their Shortcomings

FDA approved treatments for Gaucher Disease revolve around two approaches

Enzyme Replacement Therapy (ERT) (intravenous)

Biologics aimed to replace the critical enzyme deficiency; administered through IV infusion every 2 to 4 weeks

- 3 drugs: Marketed by **Sanofi (Genzyme), Pfizer**, and **Shire**
- Avg. Price of $405,000 / year/ patient
- **~$1.6 billion in total annual sales***
- Current ERT cannot cross the BBB to address the neurological manifestations of Gaucher Disease

Substrate Reduction Therapy (SRT) (oral)

Small molecule drugs aimed to decrease the accumulation of harmful storage material; administered through daily pills

- 2 drugs: Marketed by **Sanofi (Genzyme)** and **Acetelion Pharma**
- Avg. Price of $302,000 /year/patient
- Significant side effects restricting adoption
- **~$150 million** in total annual sales

Neither of these approaches address the neurological deterioration that accompanies Gaucher Disease Types 1, 2 & 3 as they do not cross the Blood Brain Barrier (BBB). Patients with Types 2 & 3 disease currently have no therapeutic options to treat the fatal neurological complications of their disease.

* **Life Capital Equity Research** Analysis of Orphan Drug Market February 4, 2016

OUR CTB-GCC & Gaucher Disease: ETI's Approach to fatal complications

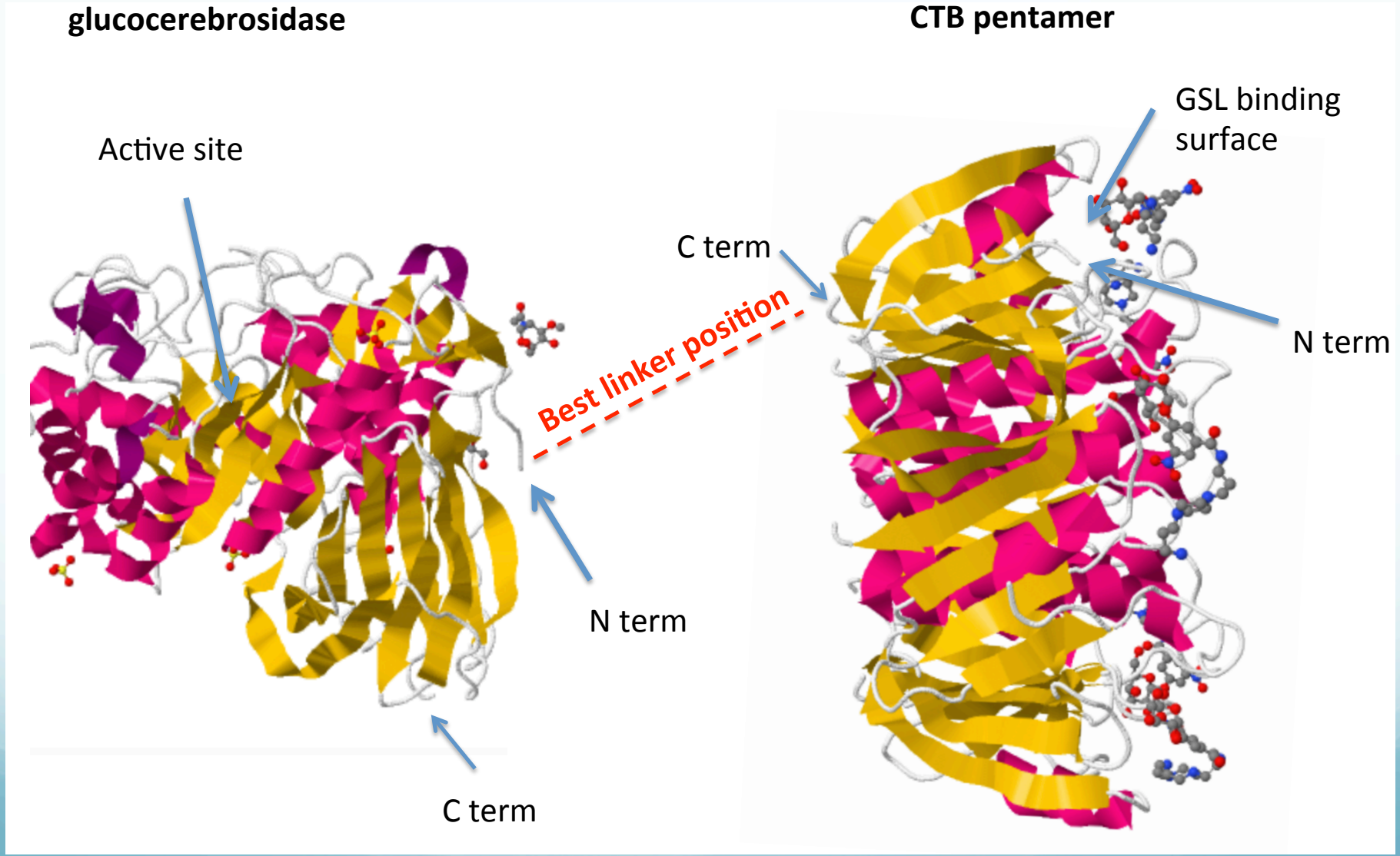
CTB-GCC Trans-Blood Brain Barrier Delivery Technology

A **revolutionary** approach to delivering **E**nzyme **R**eplacement **T**herapy **(ERT)** across the Blood-Brain Barrier (BBB) to the CNS tissues in Gaucher Disease patients

Our CTB-subunit (see slide 9) transports the deficient enzyme in Gaucher Disease, "Glucocerebrosidase" (GCC), across the BBB into neurological tissues

Capability to treat the **fatal neurological complications** of all three Types of Gaucher Disease

Structure of CTB-GCC



Advantages of ETI's Therapeutic Approach for Gaucher Disease

Our CTB-GCC approach to ERT is novel and should address unmet medical needs in Gaucher Disease Type 1 and Type 3

- Our engineered construct has 2 distinct protein regions, (CTB and GCC) that are manufactured by the cell as a single protein (hybrid molecule)
- Our **CTB subunit** is a unique drug delivery mechanism that attaches to the cell surface of virtually every cell in the body and is well-demonstrated to cross the Blood Brain Barrier
- Current ERT addresses only the systemic manifestations of Gaucher Disease Type 1 but cannot address the neurologic manifestations seen in Gaucher Disease Type 1 and Type 3
- We anticipate that the GCC enzyme will be transported across the BBB by our proprietary CTB-GCC molecule, and delivered to neuronal cells to correct the GCC deficiency and **treat the neurological deterioration** that accompanies all forms of Gaucher Disease
- By crossing the BBB, CTB-GCC potentially addresses the recently noted neurological manifestations of Gaucher Disease Type 1 (Parkinsonism), expanding market potential for CTB-GCC

Gaucher Market

- The total Gaucher Type 1 market exceeds $1.6 billion dollars and is estimated to reach $2.35 B
- All 5 approved Type 1 drugs continue to show year over year growth
- Premium pricing is preserved with average annual drug cost per patient exceeding $360,000**
- Type 1 market can expand to address “Parkinsonism”, a neurological manifestation recently linked to Gaucher Type 1
- **Our CTB-GCC technology provides a Unique Opportunity to address unmet clinical needs in Gaucher Type 3 patients**

LifeSci Capital Equity Research Analysis of Orphan Drug Market February 4, 2016

** Blended average of Enzyme Replacement Therapy and Substrate Reduction Therapy

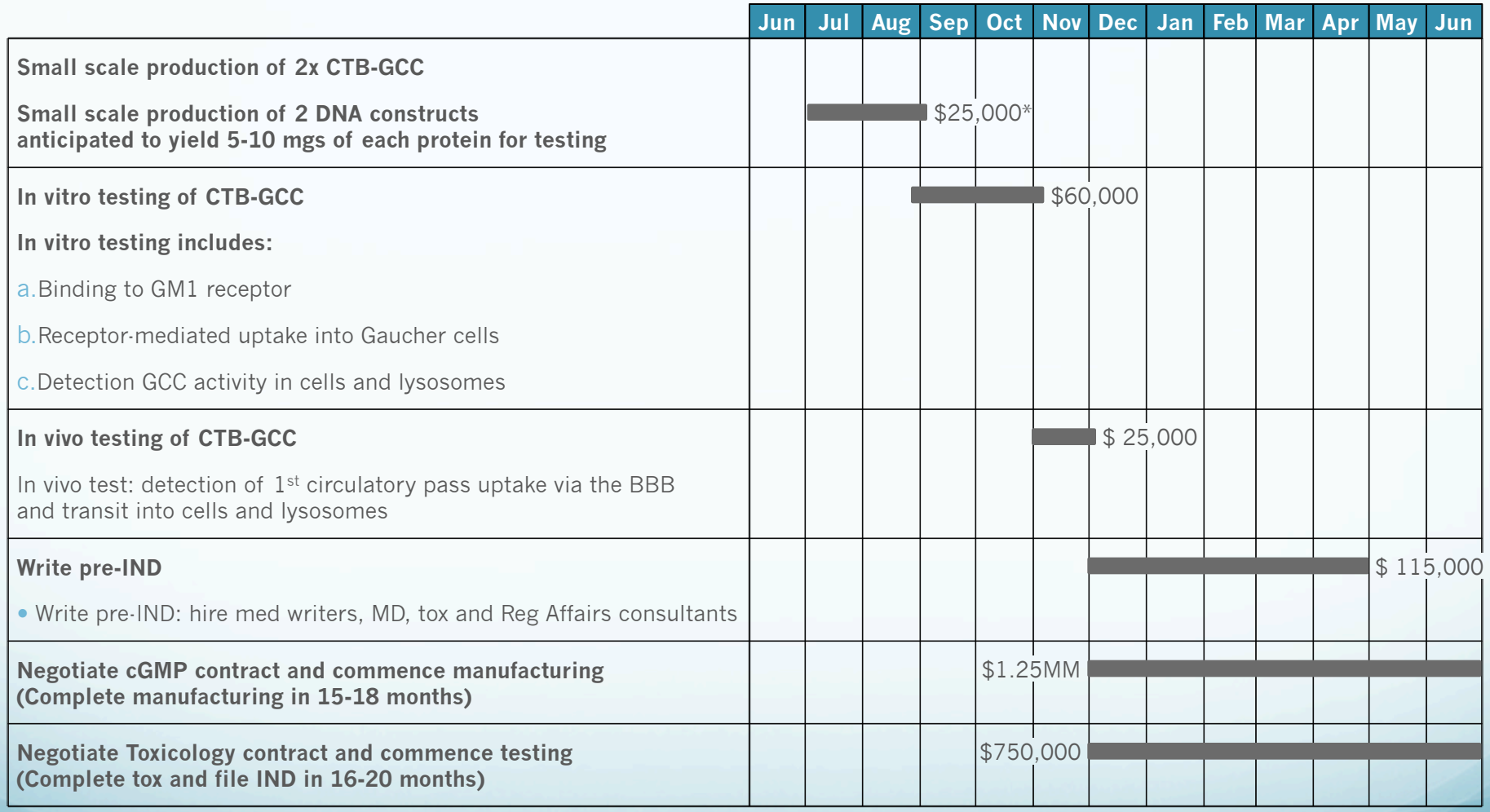
Gaucher type 3 market opportunity-
$325 million without competition

Potential to address an **UNMET CLINICAL NEED** In Type 3 Gaucher patients

Gaucher Type 3 Market Opportunity

- No existing therapies on market or under development
- We address the fatal neurological deterioration of Type 3 disease
- All 800-1,000 Type 3 patients should be eligible for treatment
- ~Premium pricing: We assume $405,000 /patient/year which is the average annual cost of ERT drug therapy

CTB-GCC
Development & Signal Assessment



* Denotes that if initial DNA constructs do not yield appropriately configured CTB-GCC it will be required to re-engineer new DNA constructs and create additional rounds of small scale production. By necessity, this will delay completion of in vitro testing and will increase the cost of the project.

mCTs and Cystic Fibrosis: ETI's Paradigm Shift

Our mCT technology & Cystic Fibrosis: Restoring Cellular Function

ETI's ERAD (mCT) Blockade Technology is based on interrupting the **E**ndoplasmic **R**eticulum **A**ssociated **D**egradation **(ERAD)** pathway

- Our proprietary modified Cholera toxin (mCT) molecules are designed to **address the disease manifestations** caused by the destruction of misfolded but functional proteins (caused by ERAD) and serve to restore cellular function
- Our mCT technology received Orphan Drug Designation in February, 2017
- The delF508CFTR mutation in CF is the **current** key target of our mCT technology
- Peer reviewed publication[4]

Cystic Fibrosis (CF) is a disease resulting from multiple genetic mutations leading to the loss of several functional proteins;

- Many of these proteins are misfolded but maintain at least partial function but are destroyed by the **ERAD** process
- The most common mutation is del F508CFTR which results in the well-known respiratory distress of CF patients
- Many other mutations result in the lesser-known gastro-intestinal manifestations of CF
- CF is the most prevalent Orphan Disease

4 PLOS ONE | DOI:10.1371/journal.pone.0166948 December 9, 2016

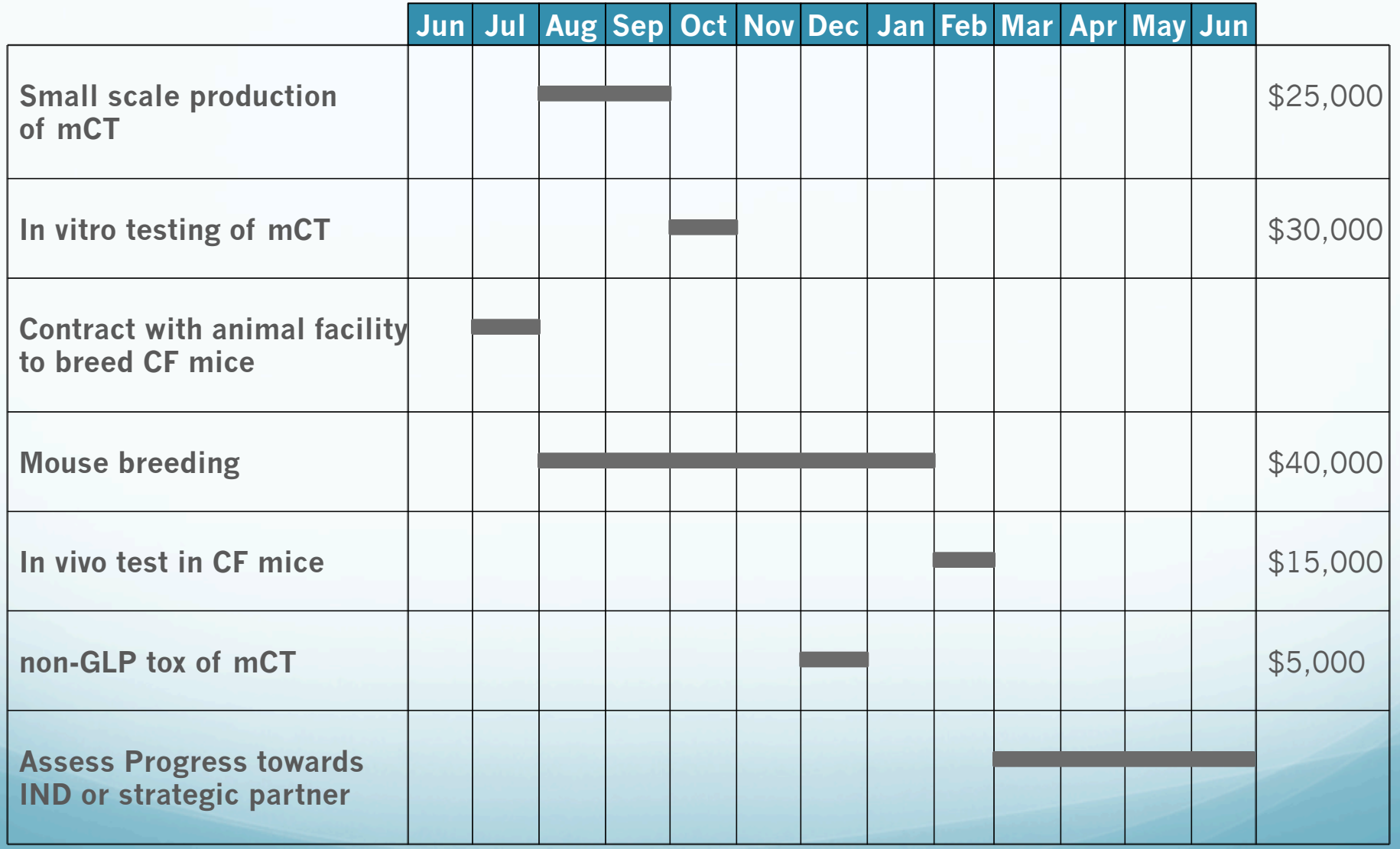
Advantages of ETI's Therapeutic Approaches to Cystic Fibrosis

Our ERAD (mCT) Blockade approach offers a unique approach to treatments for Cystic Fibrosis and other Orphan Diseases

- Our peer-reviewed and published principal discovery gives us the ability to prevent destruction of mutated or misfolded proteins and rescue them to restore cellular function[4]
- Our engineered mCT molecules have 2 distinct proteins, (A and B subunits) joined together
  - The B subunit is the targeting vector that attaches to the cell surface of virtually every cell in the body;
  - The A subunit has been modified to eliminate the cytotoxic enzymatic activity of the CT molecule but maintain its other physiological properties
  - The modified A subunit temporarily blocks normal ERAD preventing the degradation of misfolded enzymes and allowing them to be rescued, processed and transited to their site of action;
- Our mCT technology has been shown to correct the F508delCFTR deficiency responsible **for Cystic Fibrosis.**
- Potential for injectable and oral formulations

4 PLOS ONE | DOI:10.1371/journal.pone.0166948 December 9, 2016

mCT Testing and Development



Orphan Drug Development- Compelling Strategic and Financial Market Appeal

Large Pharma is Active in Orphan Drugs

Large Pharma is extremely active in the orphan drug space:

- 40% of acquired biotechs between 2008-2012 had an orphan drug in development
- Novartis, GSK, Roche and Pfizer are largest orphan drug companies
- Pfizer, Gilead, Roche, Shire, BMY and Celgene are leading orphan drug acquirers
- 50% of top 20 orphan drugs were either acquired or in-licensed by Large Pharma

Key Market Statistics:

- Worldwide orphan drug sales forecast to grow to $178 billion by 2020 with a **CAGR of +11.7%** (2015 to 2020); almost **double** overall prescription market growth
- Orphan drugs set to be 20% of worldwide prescription sales by 2020 (excluding generics)
- 7 of top 10 orphan drug companies in 2020 will be Large Pharma

Source: 1. Nature Biotechnology: Acquiring orphans, 2014; 2. EvaluatePharma: Orphan Drug Report, 2015

Advantages of Orphan Drug Development

Orphan drugs are often brought to market quickly, yield impressive sales in small, targeted patient populations increasing the potential for strategic partnerships and/or sale with large Pharma

Key Advantages

- Shorter timeline to market
- Requires significantly less resources
  - <100 patients for Gaucher Phase III clinical trials
  - <550 patients for all orphan drug Phase II/III studies
  - Tax credits (<50% of R&D costs & clinical trial incentives)
  - Phase III up to 50-75% cheaper than non-orphan drugs
  - Waived FDA fees and protocol assistance
- FDA is often more flexible with approvals
- Marketing exclusivity (7 years from approval in the U.S.)
- Lower marketing costs as patients are easily located
- Faster uptake and market acceptance
- Payors recognize the need for and cover the high costs of Orphan Drugs

Source: 1. FDA; 2. EvaluatePharma: Orphan Drug Report, 2015

Exit Strategy

Acquisition or Partnership

Large Pharma is extremely active in this space both acquiring and/or partnering with smaller drug development companies

- 50% of top 20 orphan drugs were either acquired or in-licensed by large Pharma
- ~40% of acquired biotechs between 2008-2012 had an orphan drug in development

Compelling Valuations

Rare disease companies have premium valuations

- Alexion has a market cap of $29B
- Biomarin has a market cap of $16B

Multiple $100M+ deals for pre and clinical stage orphandrugs

- Sanofi/Genzyme: $20B - Lysosomal storage disease
- Shire/Acceleron: $498M - Duchenne muscular dystrophy
- Shire/Nimbus Discovery: - Lysosomal storage disease
- Roche/ISIS: $362M - Huntington's disease
- Biogen Idec/KNOPP Neurosciences: $265M - ALS

The People & The Opportunity

Management Team

Oscar Bronsther, M.D., F.A.C.S – Chief Executive Officer

- Former CEO and current Director at MetaStat, Inc.
- Clinical Professor at George Washington University
- Former Chairman, Section of General Surgery at Inova Fairfax Hospital

George Spitalny, Ph.D. – Chief Scientific Officer, Director, Co-Founder

- 25+ years in the biotech and pharmaceutical industry
- Former Director of Immunology at Bristol-Myers Squibb

Craig Sibley, MB, HBSc. – Executive Vice President, Director, Co-Founder

- 25+ years in the healthcare and life sciences industry
- Former companies include AMGEN Canada, Schering Canada, and Ares-Serono

Board of Directors

Robert Bender – Chairman of the Board

- Serial entrepreneur with 35+ years in biotech and devices
- Multiple startups with successful exits
- Private and public offering experience on both sides

Michael Beaubaire, MD

- Chair of the Scientific Advisory Board for Lincoln Park Capital.
- Oversees and assists LPC in evaluating and investing in the health science space, with over hundreds of millions of dollars invested to date
- Served as Financial Analyst of Salomon Brothers and Donaldson, Lufkin and Jenrette

Brad Thompson, PhD

- Biotechnology founder with 22 years experience as CEO of a public company
- Chairman, Director, and Audit Committee member of numerous public companies
- Has initiated and overseen Phase 1, 2, and 3 clinical studies approved by MHRA, EMA, FDA and Health Canada

Near-Term Corporate Objectives

- Synthesize GLP material for CTB-GCC and mCT0 for pre-clinical development
- Conduct additional non-GLP toxicology studies
- Submit and obtain additional Orphan Drug Designations
- Arrange Series A Financing
- Hold Pre-IND meeting with FDA

Value-creating milestones for the next 18 months

ERAD
THERAPEUTICS

Thank You

Source: 1. FDA; 2. EvaluatePharma: Orphan Drug Report, 2015