Descriptive Memorandum

May 2019

Executive Summary

- ERAD Therapeutics Inc. ("ERAD" or the "Company") is a clinical stage biopharmaceutical company that will advance the Company's proprietary modified Cholera toxin ("mCT") to clinical trials to treat disorders associated with misfolded proteins.

- ERAD has demonstrated that its lead molecule prevents the destruction of critical misfolded proteins and rescues them to restore cellular function.

- **mCT readily crosses the Blood Brain Barrier and penetrates into neuronal tissue.**

- The Company's initial therapeutic target is Tay-Sachs Disease, an ultra-rare, fatal pediatric neurological disease caused by a deficiency in the critical enzyme Hexosaminidase A.

- ***There are currently no therapeutics available for treatment of Tay-Sachs Disease.***

Executive Summary

- **ERAD has conclusive *in-vitro* proof of concept data demonstrating the technology's ability to salvage Hexosaminidase A enzyme in Tay-Sachs Disease.**
- **Given the absence of an appropriate animal model for testing, this data should be sufficient for moving to an IND filing.**
- The Company is 18 months from commencing clinical trials and anticipates an expedited clinical study with an NDA filing in early 2021.
- In addition to the benefits of Orphan Drug Designation, ERAD believes successful development of a therapeutic for this indication makes it eligible for a highly valuable Priority Review Voucher.

Modified Cholera Toxin (mCT) Technology

The key therapeutic advance of the ERAD technology is the demonstrated ability of a genetically modified Cholera toxin to prevent destruction of mutated/misfolded proteins in the endoplasmic reticulum and rescue them to restore cellular function.

Misfolded Proteins: Endoplasmic Reticulum-associated Degradation

- Endoplasmic reticulum-associated degradation (ERAD) is a cellular quality control mechanism by which the proper folding of proteins is monitored.

- Proteins with a suboptimal three-dimensional structure are targeted for degradation. This homeostatic pathway ensures that only perfectly folded proteins are allowed to traffic to their functional sites within the cell.

- More than 50 genetic diseases originate from mutations resulting in a **minor misfolding** of a critical protein. In such cases, the ERAD mechanism destroys the mis-folded protein, creating a disease state. **However, many of these mis-folded proteins retain significant activity.**

- Using mCT we have developed methods to rescue mis-folded proteins from ERAD. We possess both cell line and animal data in multiple diseases confirming this ability.

Biology of mCT

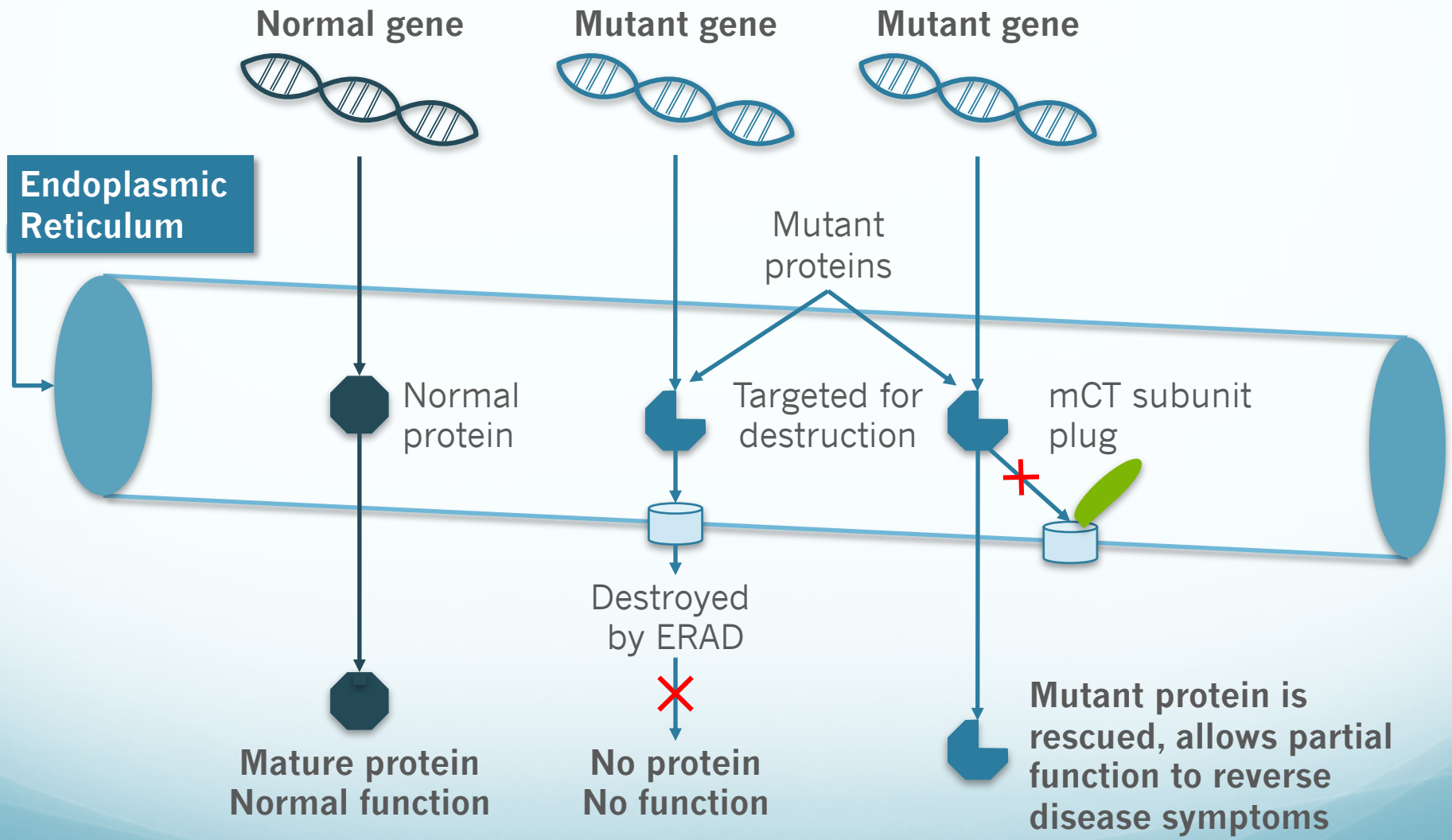
Description of mCT

- Cholera toxin is comprised of an A and a B subunit. The A subunit has enzymatic activity.
- Two point mutations are introduced into the DNA of the A subunit to eliminate its cytotoxic effects while maintaining its other physiological properties.

Mechanism of mCT activity

- The transport activity(translocon) of the endoplasmic reticulum is selectively hijacked by the A subunit of the cholera toxin required for cytosolic access.
- The A subunit and ERAD substrates utilize the same/similar translocon machinery for ER-cytosolic egress - only one protein can occupy the translocon at a time.
- mCT provides a new, general, competitive means to reduce the transit of ERAD substrates into the cytosol for degradation. This allows critical proteins to be rescued, processed and transited to their site of functional activity.
- ERAD inhibition associated with mCT is temporary.

Illustrated Example of mCT Rescue



Lead Therapeutic Candidate: Tay-Sachs Disease

Tay-Sachs Disease

- Tay-Sachs disease is a rare and usually fatal neurodegenerative disorder caused by a deficiency of Hexosaminidase A, a critical lysosomal enzyme.
- This genetically determined disease is inherited in an autosomal recessive manner.
- Deficiency of this enzyme leads to the toxic accumulation of lipid by-products in the brain, resulting in progressive dysfunction of the Central Nervous System.
- Populations most at risk of transmitting this disease include: Ashkenazi Jews, certain French-Canadian communities, the Old Order Amish community, and the Cajun population of Louisiana.
- More than 80 different mutations of the HEXA gene have been identified, but these mutations result in 3 distinct clinical manifestations or subdivisions of Tay-Sachs disease.
- ***There is no recognized treatment for any of the Tay-Sachs disease phenotypes.***

Tay-Sachs Disease

Subdivisions of Tay-Sachs Disease

1. Infantile Tay-Sachs Disease

Initial symptoms develop between 3 and 6 months after birth. These include mild muscle weakness, twitching or jerking of muscles, and an exaggerated startle disorder. Between 6 and 10 months of age, these infants fail to gain new motor skills and no longer make eye contact. These children become progressively more neurologically impaired and usually die from complications of the disease by 3 to 5 years of age.

2. Juvenile (Subacute) Tay-Sachs Disease

The onset is between 2 and 10 years of age. The first signs are clumsiness and problems with coordination. Behavioural problems include progressive loss of speech, life skills, and intellectual abilities. Life threatening complications usually occur around 15 years of age.

3. Late-Onset Tay-Sachs Disease

The presentation is variable. The disease progresses relatively slowly, but again presents with progressive clumsiness, mood alterations, and progressive muscle weakness and wasting. Many of these patients require wheel chairs and 40% of patients develop symptoms of psychosis and depression. This is the rarest form of the disease.

mCT Proof of Concept in Tay-Sachs Disease: In-vitro study design

- Lymphocytes from individuals harbouring the Tay-Sachs mutation were tested in vitro to determine if treatment with mCT would result in the rescue of the Hex A enzyme from destruction and hence an increase in enzyme activity.

Below are the experimental conditions for testing:

Treatment conditions

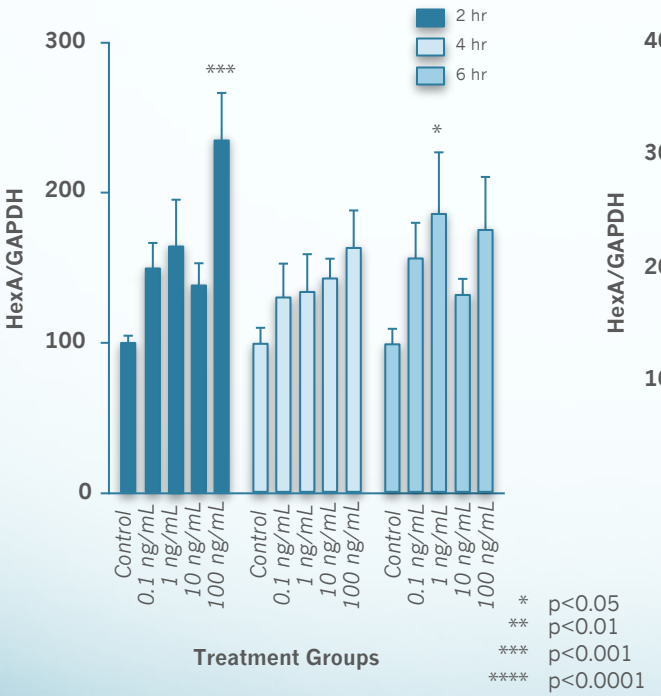
- mCT (lyophilized mCT from NRC received Apr. 2, 2019; 300 µg/mL)
- Cells were plated at 10,000 cells/well in 96 well plates and cultured overnight
- Cells were treated with mCT (0.1 to 100 ng/mL) for 2 – 6 hours
- All experimental groups were run in triplicate to assure consistency
- The cells were then washed with PBS and frozen for later analysis
- Hex A activity was determined according to the standard assay protocol
- GAPDH activity was determined using KDalertTM assay (Invitrogen) according to the manufacturer's protocol

Determination of effect of mCT treatment on HexA activity in Tay-Sachs B-lymphocytes

Effect of mCT treatment on GAPDH normalized HexA activity.

- Each experiment is normalized to control = 100%
- Results from the three experiments were combined

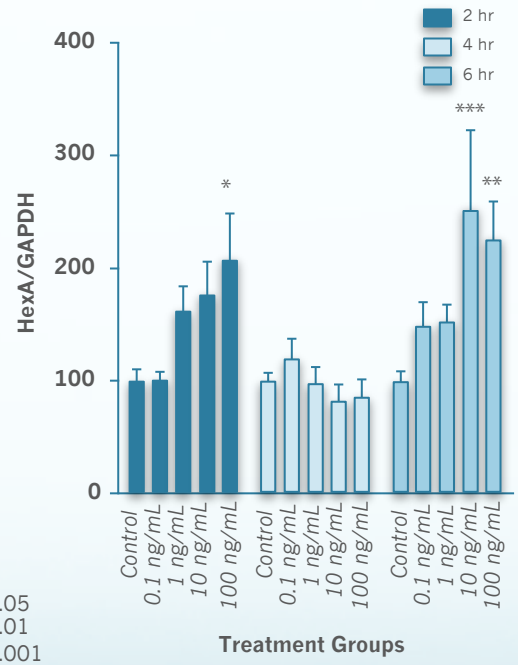
Effect of mCT on normalized HexA activity in GM03441 cells



Factors:

Duration = ns
mCT = ****

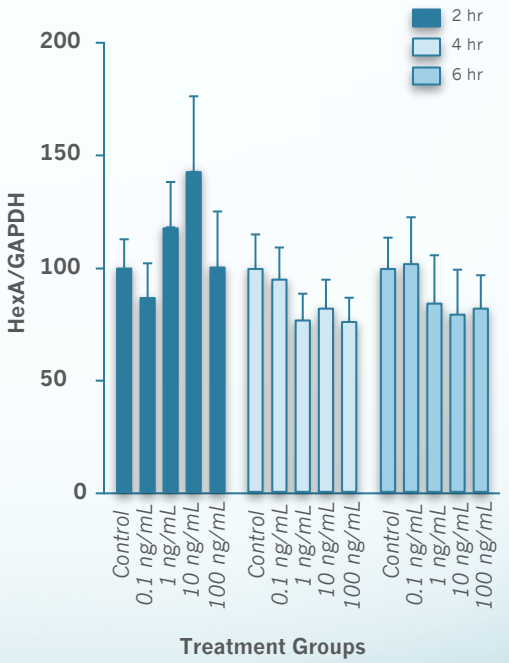
Effect of mCT on normalized HexA activity in GM03461 cells



Factors:

Duration = **
mCT = ****

Effect of mCT on normalized HexA activity in GM03575 cells



Factors:

Duration = ns
mCT = ns

mCT Proof of Concept in Tay-Sachs Disease: In-vitro study design

Conclusions from mCT testing on Tay-Sachs Cells

- Analysis of combined experiments shows demonstrably increased GAPDH normalized HexA activity
- Statistically significant increases observed in 2 of 3 cell lines
- 2-way ANOVA indicated that mCT is a highly significant factor in salvaging functional enzyme activity in GM03441 and GM03461 cells

Applicable Drug Development Incentive Programs for ERAD Therapeutics Lead Molecule (mCT)

Orphan Drug Designation

- FDA program to promote the development of therapeutics for indications with a patient population in the US of less than 200,000.
- Tax credits and deductions provided for qualified development expenses.
- Waiver of PDUFA fees for marketing approval in certain circumstances.
- Provides seven years of market exclusivity to developer of orphan drug.

Priority Review Voucher

- FDA program to promote the development of therapeutics for neglected tropical diseases, later expanded to include rare pediatric conditions and medical countermeasures to terrorism.
- Awarded to company upon FDA approval.
- **Transferable voucher** reduces PDUFA review time to six months – an average of 12 months less then standard review.
- **14 vouchers awarded since program introduction – 10 for rare pediatric disorders.**
- **Highly valued – Regeneron/Sanofi paid Biomarin $67.5 million for voucher in 2014. United Therapeutics sold voucher in 2015 for $350 million.**

Other Identified Disease Targets for mCT

- S1P Lyase Insufficiency Syndrome (SPLIS)
- Gaucher Disease

Characteristics of SPLIS

Disorder	• S1P Lyase Insufficiency Syndrome ("SPLIS")
Physiological manifestations	• Range of intracellular imbalances including signaling molecule sphingosine-1-phosphate upstream to SPL cleavage and downstream degradation products phosphoethanolamine (PE) and hexadecenal leading to array of phenotypic expressions
Clinical presentation	• Highly variable, but includes renal failure, adrenal insufficiency, rapid neurological deterioration, and immunodeficiencies
Life expectancy	• Depending on severity < 6 months to adolescence if left untreated • Renal failure necessitates dialysis or transplant for extended survival
Disease incidence	• Estimated to be <1,000 cases worldwide • 45 cases currently identified - largely undiagnosed given recent discovery of condition
Current disease treatments	• **No known treatment for disorder**

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 annual revenues**
- Many Type 1 patients develop 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

Results of Non-GLP Toxicology Studies

- Study performed at the National Center of Experimental Biology in Montreal
- Animals with same genetic background as CFTR mice, injected IV with a single dose of either 10x (4 ug) or 100x (40 ug) of anticipated therapeutic (400 ng/30 gm mouse)
- No evidence of any serious adverse events in mice after 2 weeks of observation; none of the animals died
- Second study conducted in which mice were injected IV daily for 7 days with 40 ug; as previously, no evidence of any adverse events observed
- In second study blood chemistry and organ function tested along with gross observations upon necropsy (animals sacrificed 2 weeks after last injection).
- Conclusions were the no-observed adverse effect level (NOAEL) and the no-observed effect level (NOEL) were established at > 40 ug in the mouse or 4.87 mg/60 Kg human.
- **No toxicological adverse events detected at the highest dose used.**

Issued mCT Patents

Title	"Use of Holotoxin to reduce Endoplasmic Reticulum-associated Degradation of Misfolded Proteins."
USPTO application no.	14/309558
Filing date	August 9, 2012
US notice of allowance	April 18, 2017
US Patent No.	9,901,612
Current status	Patents on the technology have been issued in both the U.S. and the E.U.

mCT Provisional Patent Applications

Title	"Treatment of SPLIS via ERAD Blockade with Modified Bacterial Toxin."
Filing date	2019
Title	"Treatment of Tay-Sachs Disease via Blockade with Modified Bacterial Toxin"
Filing Date	2019

CMO has completed small scale manufacturing of mCT

Contract Manufacturing Organization	• NRC Canada
Development status	• Good functional mCT expressing clone constructed • Preliminary expression conditions identified • Initial fermentation process developed • Initial purification process for recombinant mCT completed
Current manufacturing scale	• 20L bioreactor
Next steps	• Optimize fermentation and purification processes • Initiate pilot-scale to 500L and then to 1000 L cGMP manufacturing

Management

Oscar Bronsther, M.D., F.A.C.S – Chief Executive Officer	• Former CEO and 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	• 30+ years in the biotech and pharmaceutical industry • SVP, Drug Development, Global Clinical Development with Kyowa Hakko Kirin • 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 • Founding management of numerous biotechnology companies • Commercial operations management with Schering-Plough, Amgen and Ares Serono. • Participated in planning, launch and marketing of Intron-A, Neupogen, and Rebif

Board of Directors

Robert Bender (Chairman)	• Life science and healthcare investor and entrepreneur • Executive management and board participant for numerous public and private companies. • Formerly with venture capital firm VenturesWest
Michael Beaubaire, M.D.	• CEO, Immunomodulation • Founding Principal, MSB Advisors • Previous positions with HSA capital Partners, Salomon Brothers
Oscar Bronsther, M.D.	• *see management profile*
Bennedetto Marotta	• Toronto-based developer of residential homes and condominiums • Founding investor and largest current ERAD shareholder
Craig Sibley	• *see management profile*
George Spitalny, Ph.D.	• *see management profile*
Brad Thompson, Ph.D.	• Life science entrepreneur and executive • 20+ years public company CEO • Board participant – numerous public and private companies

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

Comparable Valuations

Multiple $100M+ deals for pre and clinical stage orphan drugs

- Sanofi/Principia: $790M – Multiple Sclerosis
- Sanofi/Genzyme: $20B – Lysosomal storage disease
- Shire/Acceleron: $498M – Duchenne muscular dystrophy
- Roche/ISIS: $362M – Huntington's disease
- Biogen Idec/KNOPP Neurosciences: $265M – ALS