Galactica Pharmaceuticals, Inc.

Table of Contents

What Is Galactica?

- Galactica is an “IND-ready” biopharmaceutical company focused exclusively on the development of its novel, proprietary RAGE (Receptor for Advanced Glycation End Products)-Ig fusion protein for the treatment of
  - Diabetes and diabetic complications
  - The dry and wet forms of age-related macular degeneration
  - Autoimmune/ inflammatory disorders
  - Possibly Alzheimer’s disease (only with NIH and/or foundation funding)
  - Lung inflammation and cytokine storms symptomatic of COVID-19
- Galactica’s RAGE protein appears to be the first molecule of any type with clinical potential to have demonstrated in vivo efficacy against at least three major diabetic complications – retinopathy/macular edema, neuropathy and nephropathy
  - Enormous clinical significance as many diabetics initially present with one major complication but subsequently develop multiple complications
- Galactica’s first-in-class molecule, to be administered via subcutaneous injection, should be the drug of choice for the treatment of any patient presenting with any of the three major diabetic complications or either form of macular degeneration, and generate a very attractive reimbursement profile
- The Company has successfully worked through all manufacturing issues and has a clear path to its first IND filing in 15 -18 months (much sooner for COVID)
  - The time to IND filing is dictated by the results of a second round of clonal selection

What is RAGE?

- RAGE is a multi-ligand receptor that exists as a membrane and soluble protein
- Its most important ligands appear to be:
  - Advanced Glycation End Products (AGE)
    - Implicated in diabetes and diabetic complications
  - High Mobility Group Box Protein Family
    - HMGB1 implicated in autoimmune/inflammatory disorders and age-related macular degeneration
  - Calgranulin (S100) Protein Family
    - Possibly implicated in autoimmune/inflammatory disorders
  - Amyloid β
    - Study published in The Journal of Neuroscience Research (March 3, 2011) concluded that amyloid β originates in the liver, not the brain, which would enable its inhibition by a RAGE fusion protein systemically delivered (study led by J. Gregor Sutcliffe, Ph.D. of Scripps Research Institute)
- RAGE also has an important NF-κB-mediated signaling function, a process that precedes virtually all inflammatory cytokine cascades and is believed to play a role in other disease areas as well

MARKET OPPORTUNITIES

Market Opportunities - Diabetes

- **Diabetes in the U.S.**
  - There were estimated to be approximately 34.2 million diabetics, or 10.5% of the population, in 2018
    - Many remain undiagnosed until presenting with one of the complications of the disease
  - The incidence of diabetes still is increasing ~ 7% per year
  - In 2017, per CDC, U.S. spent $327 billion caring for diabetic population
    - IMS estimates that drugs treating the underlying disease, including insulin, accounted for less than $30 billion of that amount, thus >$300 billion attributable to major diabetic complications
  - American Diabetes Association also estimates that the aggregate economic cost of diabetes in 2017 was $327 billion, a 26% increase since 2012
  - Type 2 diabetes accounts for >90% of all diabetes in the U.S.
  - Diabetes occurs in >20% of all people over the age of 60 years
  - Diabetes is the leading cause of blindness in people between 20 and 74 years of age
  - There are estimated to be ~1 million cases of progressive diabetic retinopathy. Each year, an additional 12,000 to 24,000 new cases are reported
  - Type I's not well controlled also suffer from complications

- **Diabetes in ROW**
  - The incidence of diabetes in most of ROW is at least equal to U.S. rate, although much higher in China and the Arab Gulf States

Market Opportunities - Diabetes

- **Unmet Clinical Needs**
  - Diabetic retinopathy/macular edema remain growing and debilitating conditions with significant unmet medical need, for which no efficacious, **non-invasive**, therapy currently exists
  - Truly efficacious therapies for diabetic neuropathy and nephropathy do not exist

- **Commercial Potential**
  - Diabetic complications in the U.S. alone likely represent at least a $25-35 billion market, and probably much larger if RAGE-Fc is adopted prophylactically for diabetic patients before they present with complications and/or inhibits the development of cardiovascular disease in diabetic patients
  - The global diabetic complications market likely exceeds $200 billion

Market Opportunities - AMD

- **Dry and Wet Forms of Age-Related Macular Degeneration**
  - In the U.S. alone, the National Eye Institute estimates that the aggregate prevalence of the wet form in 2010 was approximately 2 million, and by 2050, that number is expected to grow to approximately 5.4 million
  - In 2016 there were approximately 11 million people in the U.S. affected with any AMD, with a global prevalence of approximately 170 million

- **Unmet Clinical Needs**
  - For the wet form, Genentech's Lucentis (and off-label Avastin), Regeneron/Bayer's Eylea and Novartis' Beovu are efficacious, but are all administered via intraocular injection, which is extremely onerous for patients and can result in certain toxicities
  - No therapeutic treatment is currently available for the dry form, which represents 90% of all cases

- **Commercial Potential**
  - For the wet form, Lucentis, Eylea and off-label Avastin generated ~ $4.5 billion in 2014 sales, prior to approval of Eylea and Lucentis for diabetic retinopathy/macular edema
  - By extrapolation, the market for a therapeutic for the dry form of AMD could approximate $45 billion
  - With rapidly ageing global population, this market is likely to continue growing rapidly

COMPETITION

Competition – Diabetic Complications

- For the treatment of diabetic retinopathy/macular edema, the current standard of care is the VEGF inhibitors, Genentech's Lucentis, Regeneron/Bayer's Eylea and Novartis' Beovu
- All of these drugs have two major drawbacks relative to Galactica's RAGE molecule:
  - Many diabetic patients presenting with retinopathy or macular edema may concurrently suffer from, or be at high risk of, other diabetic complications
    - There is no evidence to date that any of these drugs may be effective against those other complications
  - All three drugs must be administered via intraocular injection, which is extremely onerous for patients and can result in certain toxicities
    - Ophthalmologists also dislike intraocular injections as they routinely cause eye irritation
- For the treatment of diabetic neuropathy, the most commonly used drug is Lyrica, initially developed for epilepsy, but with marginal efficacy treating neuropathic pain
- For diabetic nephropathy, beta blockers are the best available treatment, but their efficacy for this indication is marginal

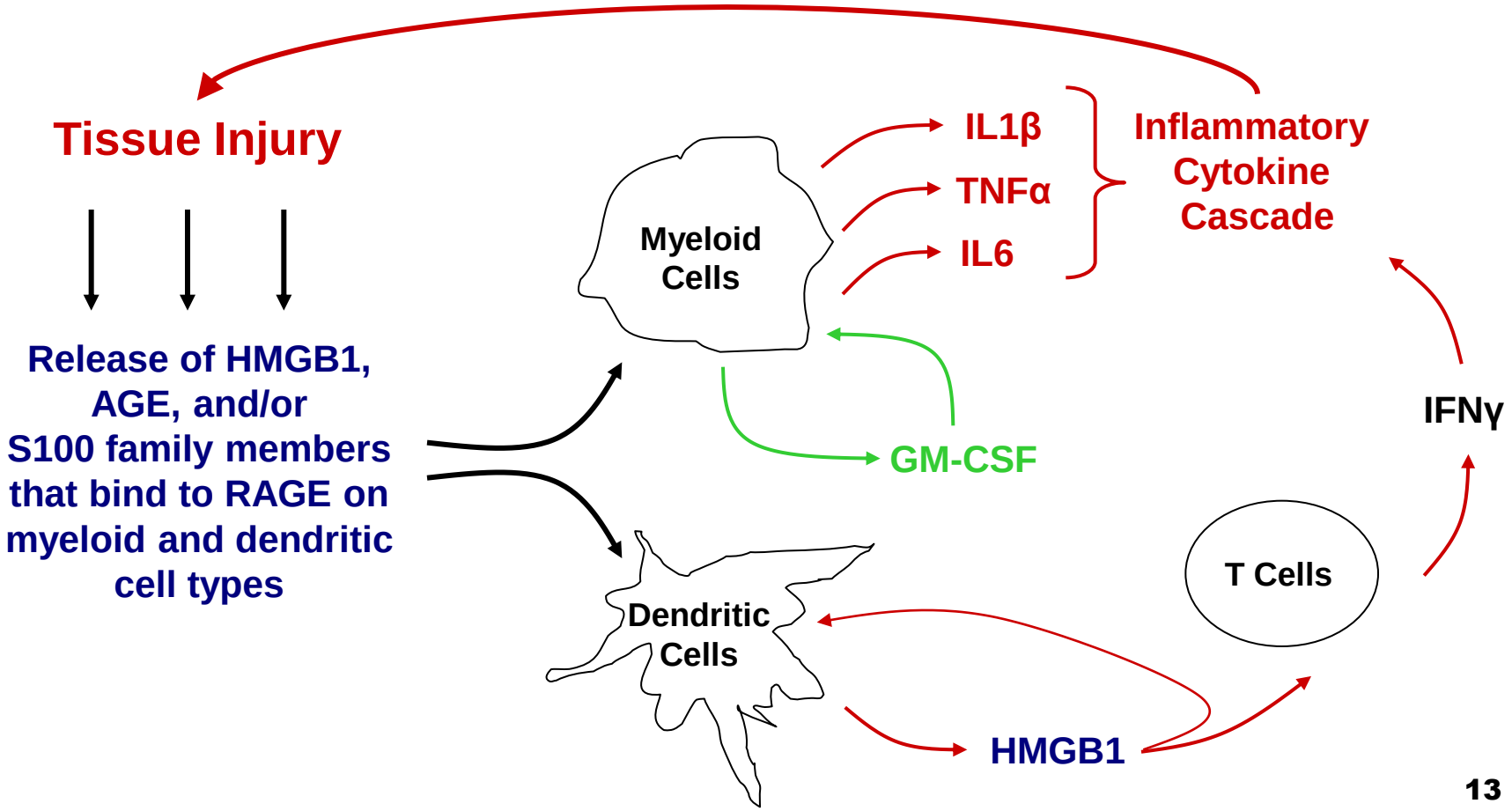
Competition – Diabetic Complications

- Galactica's first-in-class RAGE protein should be the drug of choice for the treatment of any of the three major diabetic complications – retinopathy/macular edema, neuropathy and nephropathy
- Ours appears to be the only drug, either currently marketed or under development, with the ability, demonstrated across short- and long-term studies in two species, not only to treat, but also prevent the development of, every one of these major diabetic complications
- Administration of Galactica's molecule by subcutaneous injection is far superior to the intraocular injection of Lucentis, Eylea or Beovu
- With such broad and compelling data for the treatment of the three major diabetic complications, it would not be surprising if Galactica's protein also prevents the development of cardiovascular disease among diabetic patients
- Based on a few studies suggesting a strong correlation between capillary density and insulin resistance, Galactica's molecule may also play a role in regulating insulin resistance, in which case it would be prescribed for earlier intervention in diabetes
- As a first-in-class molecule addressing enormous unmet clinical needs and potentially saving governments and other healthcare providers billions of dollars annually, Galactica's drug should generate a very favorable reimbursement profile

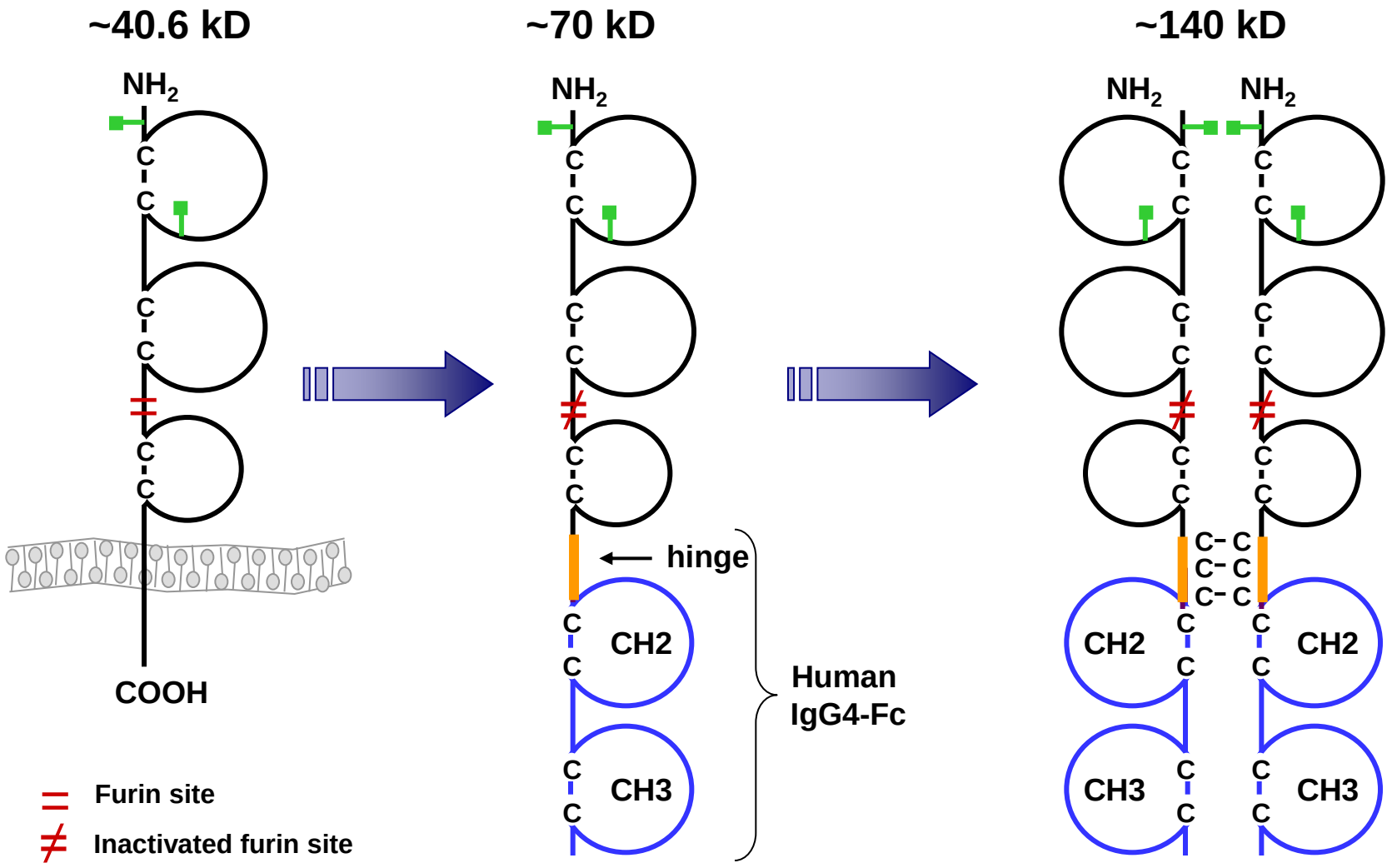
Competition - AMD

- As for diabetic retinopathy/macular edema, intraocular injections of Lucentis (Avastin off-label), Eylea and Beovu represent the standard of care for the wet form of macular degeneration
- Administration of Galactica's drug by subcutaneous injection is far superior to intraocular injection
- Based on data from Galactica's diabetes studies in rats showing that administration of RAGE-Fc reduces VEGF levels, we would expect our drug to be more efficacious than a VEGF inhibitor in the treatment of wet AMD
- There does not appear to be any drug under development for the treatment of wet AMD with a profile superior to Galactica's molecule
- For the dry form of AMD, there currently are no approved therapies, thus Galactica's drug, if approved for this indication, would satisfy an enormous unmet clinical need
  - Roche's lampalizumab was considered one of the most promising candidates under development for dry AMD but it failed in a Phase III clinical study

Mechanism of Action In Autoimmune Diseases



Composition of Galactica's Molecule



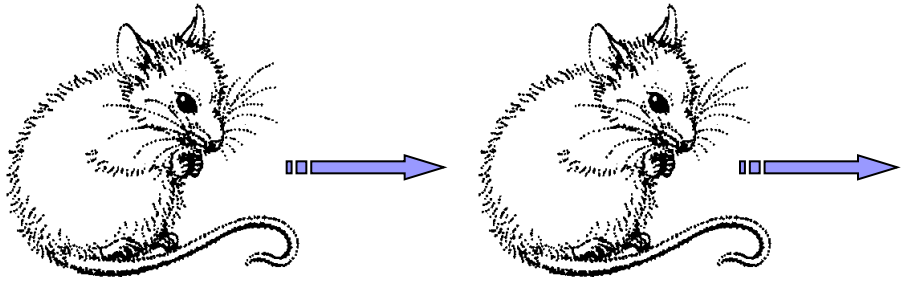
Strong Science/Preclinical Data

- In a 10-week murine study of collagen-induced arthritis (CIA), demonstrated the ability of mRAGE-Fc to significantly inhibit the development of arthritis
  - **The CIA model has been extremely predictive of efficacy of molecules in man**
- In an 8-week murine study of diabetic retinopathy, demonstrated the ability of mRAGE-Fc to significantly inhibit diabetes-induced increase in retinal permeability
- In a 44-week murine study of diabetic retinopathy, demonstrated the ability of mRAGE-Fc to significantly inhibit diabetes-induced degeneration of the retinal vasculature
- In the same 44-week study, also demonstrated the ability of mRAGE-Fc to significantly inhibit the development of diabetic neuropathy
- In a 42-week rat study, demonstrated the ability of mRAGE-Fc to significantly inhibit diabetes-induced degeneration of the retinal vasculature and the development of diabetic nephropathy
- **There were no observed toxicities in any of five total studies**

IN-VIVO ANIMAL DATA

Assessing mRAGE-Fc in 10 Week Murine CIA Model

DBA-1 male mice (10 mice per treatment group)



Administration (ip) of mRAGE-Fc (0, 10, 100, or 300 µg/mouse/day) beginning on Day 0

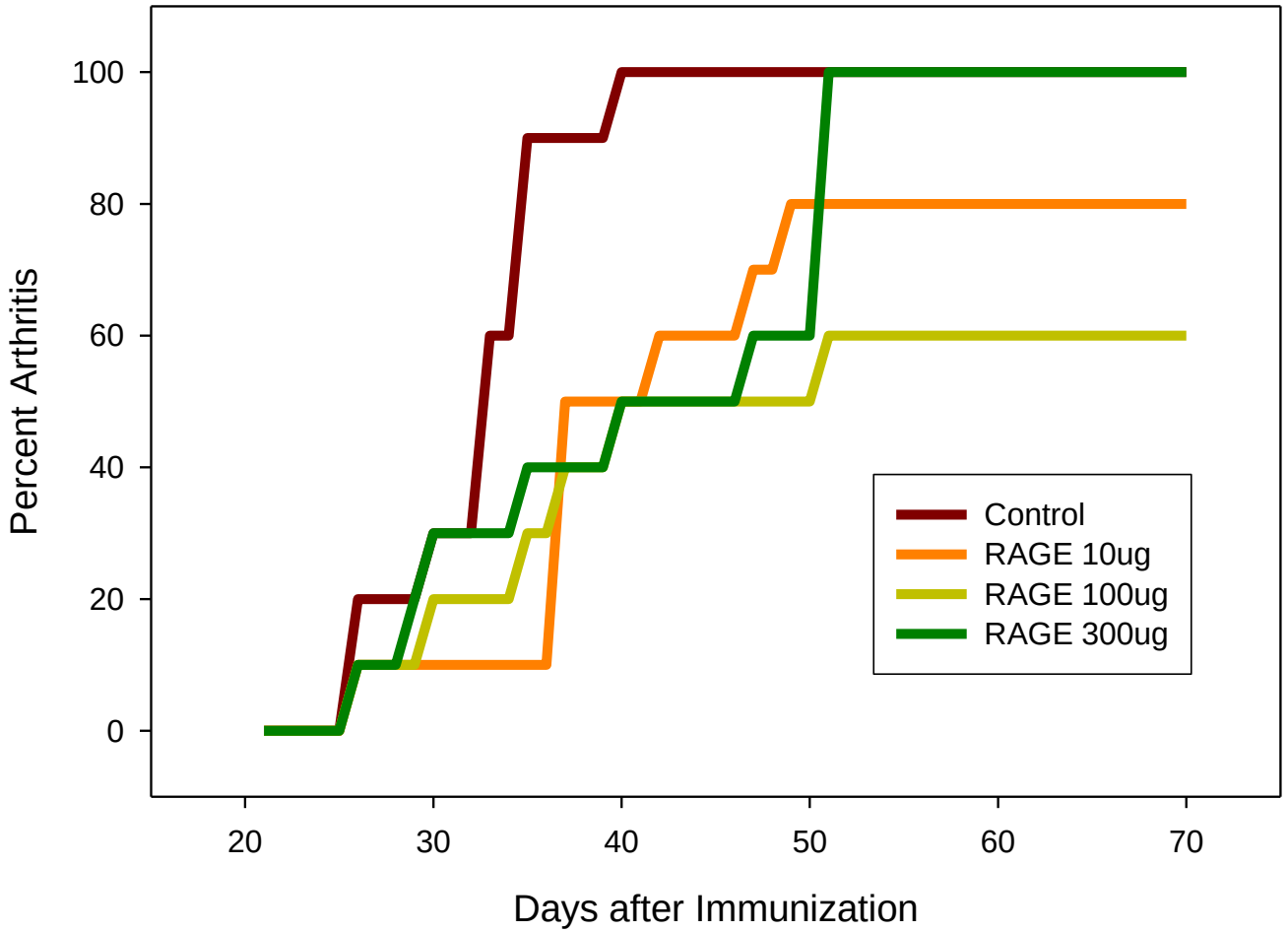
Bovine type II collagen in CFA administered intradermally on Day 3

Assessments

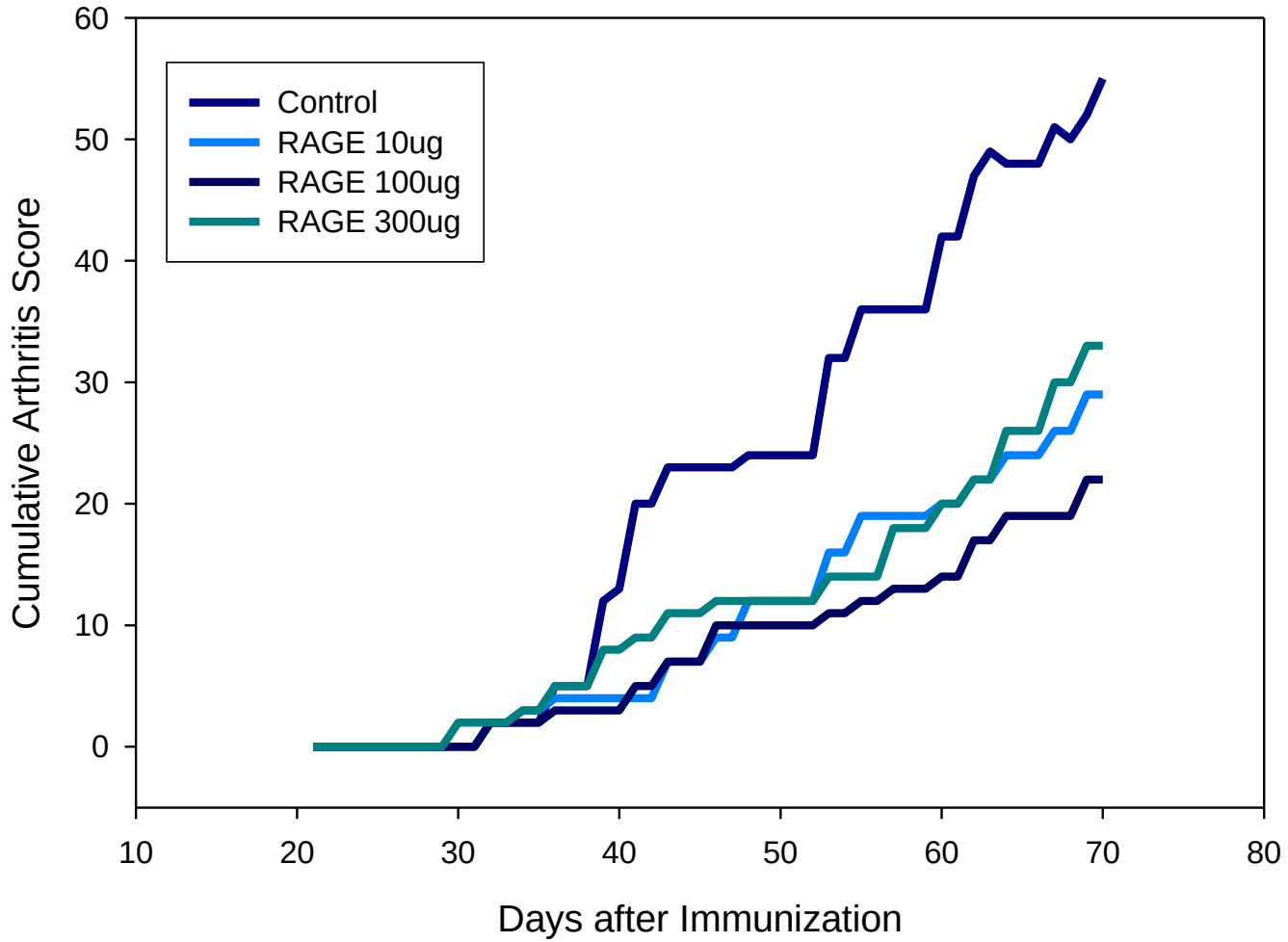
- Daily examination for disease onset
- Body weights determined weekly
- Overall health status noted daily
- Clinical assessment of arthritis 5X/week
- Paw edema assessed 3X/week
- Symptom-free mice at ten weeks post-immunization considered disease negative

Galactica-sponsored experiment performed in the laboratory of Paul Wooley using mRAGE-Fc produced at Gala Biotech

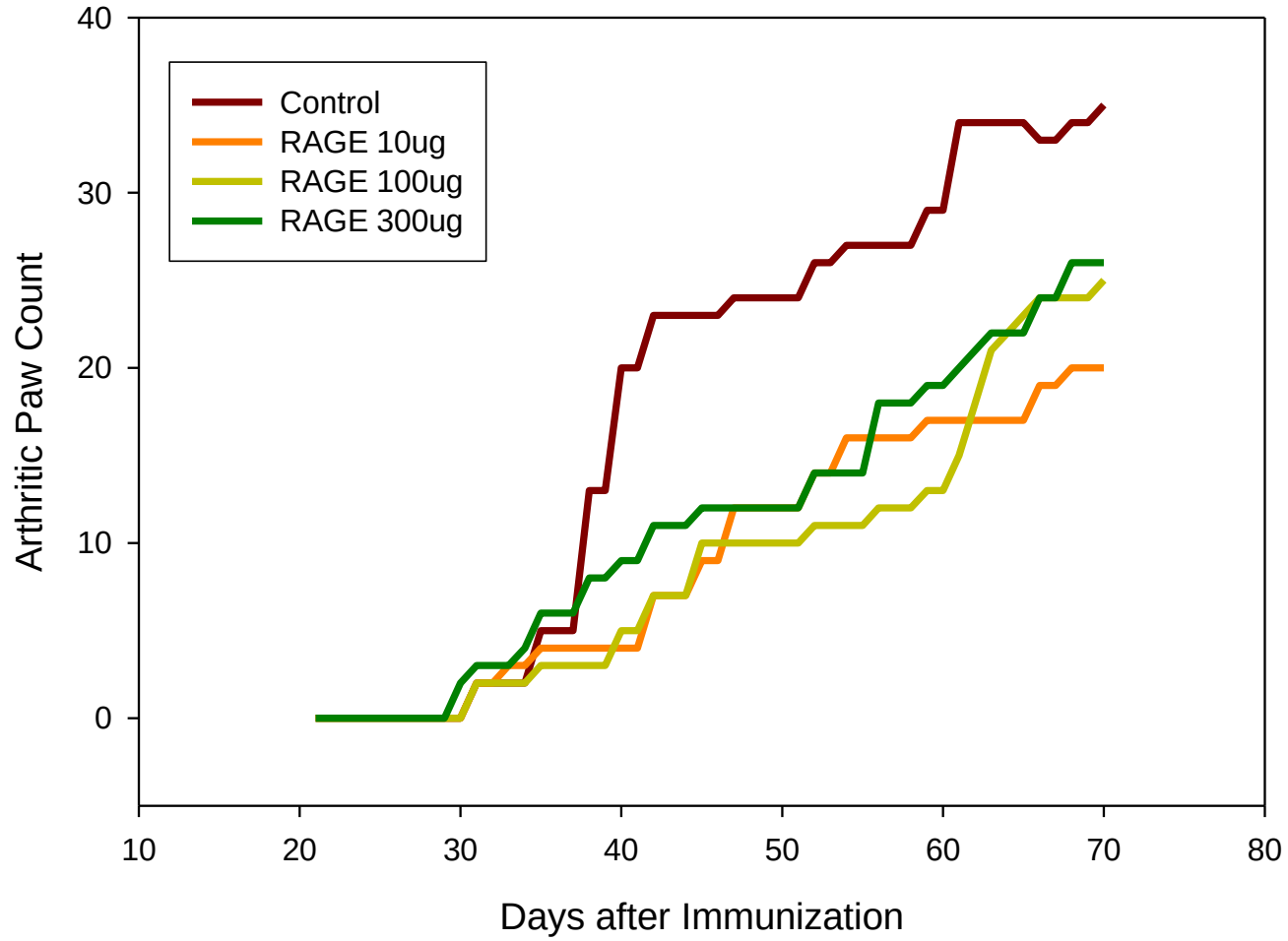
mRAGE-Fc Decreases Incidence of Arthritis



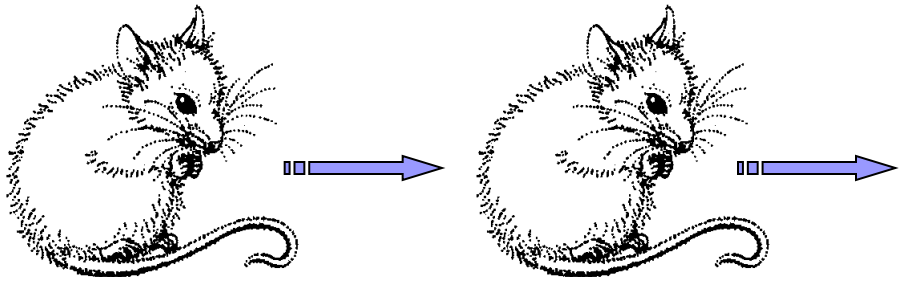
mRAGE-Fc Decreases Severity of Arthritis



mRAGE-Fc Decreases Paw Numbers Affected with Arthritis



8 Week Murine Model of Streptozotocin-Induced Diabetes



Administration (ip) of 45 mg/Kg streptozotocin (STZ) for 5 days

mRAGE (0, 10, 100, 300 µg/mouse/injection) administered ip. 3X/week for 8 weeks

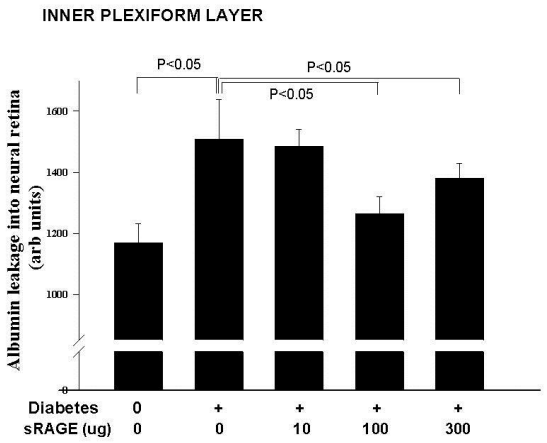
Assessments

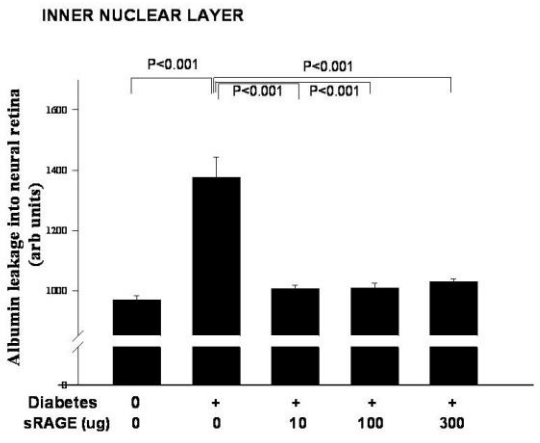
- Blood glucose levels assessed on d0, d28, and d56
- Body weights determined weekly
- Glycohemaglobin (GHb) assessed on d56
- Tactile sensitivity assessed on d56
- Post-mortem assessment of:
  - Vascular permeability
  - Leukocyte adherence to retinal capillaries
  - NFkB-regulated expression of COX-2, ICAM, iNOS

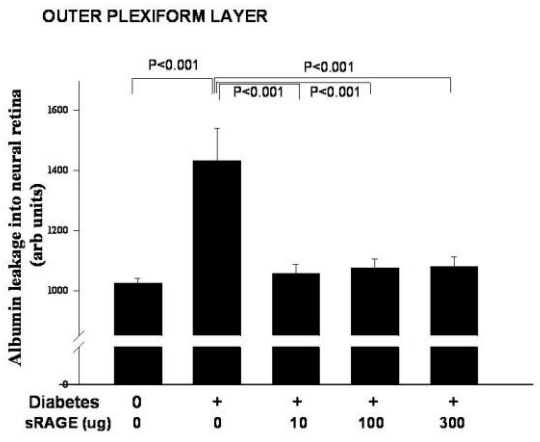
25 mice per treatment group

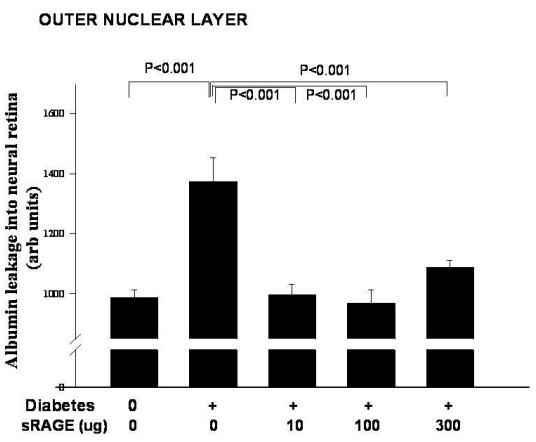
Galactica-sponsored experiment performed in the laboratory of Timothy Kern using mRAGE-Fc produced at Gala Biotech

mRAGE-Fc Inhibits Vascular Permeability in Retina of Diabetic Mice









ONL
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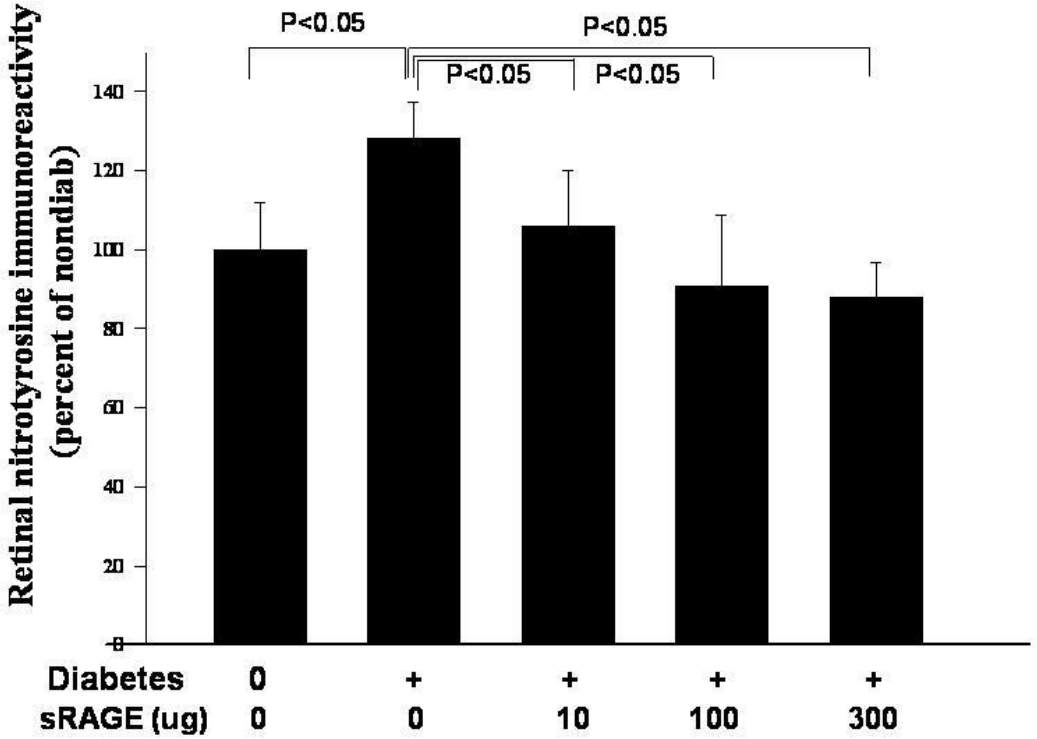
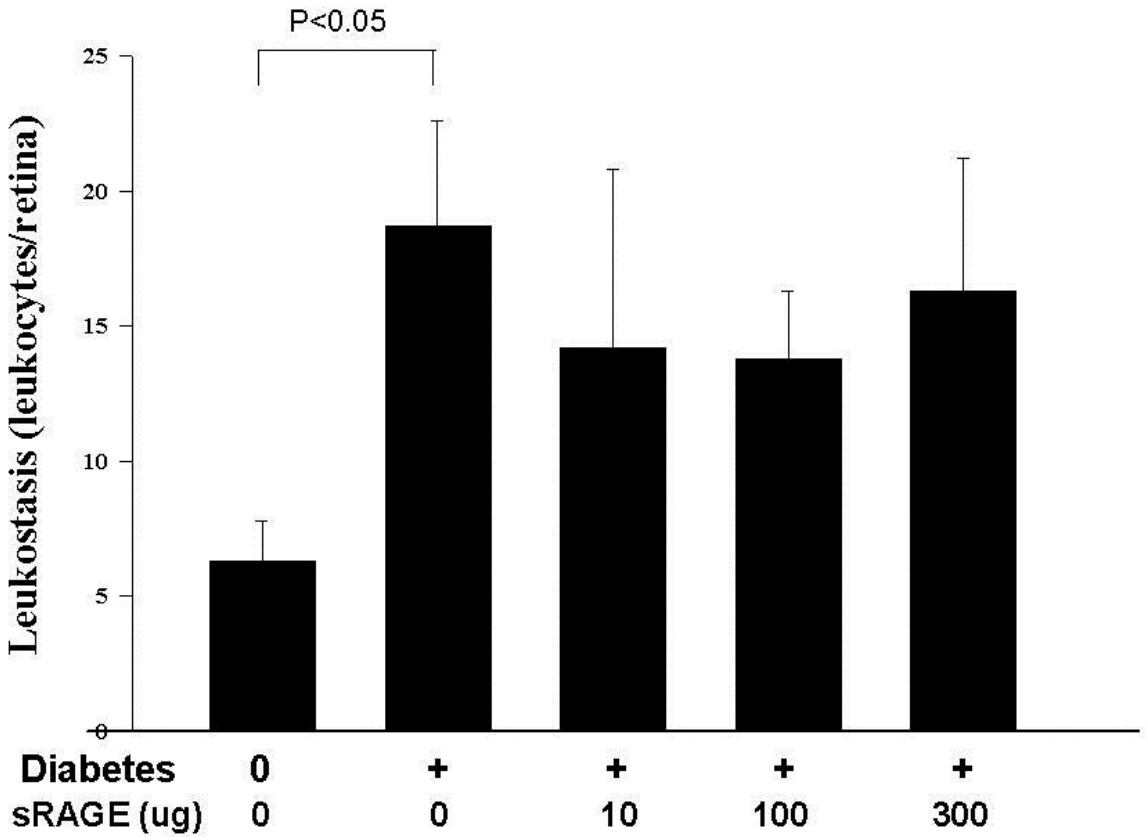
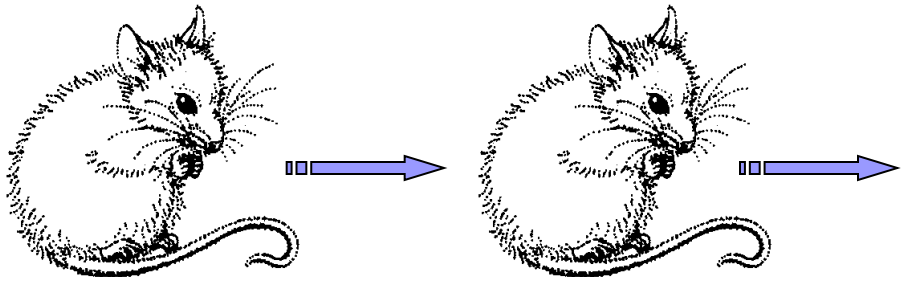
mRAGE-Fc Inhibits Nitration of Proteins in Retina of Diabetic Mice



mRAGE-Fc Does Not Inhibit Leukostasis in Retina of Diabetic Mice



44 Week Murine Model of Streptozotocin-Induced Diabetes



Administration (ip) of 45 mg/Kg streptozotocin (STZ) for 5 days

mRAGE (0, 10, 100, 300 µg/mouse/injection) administered ip. 3X/week for 44 weeks

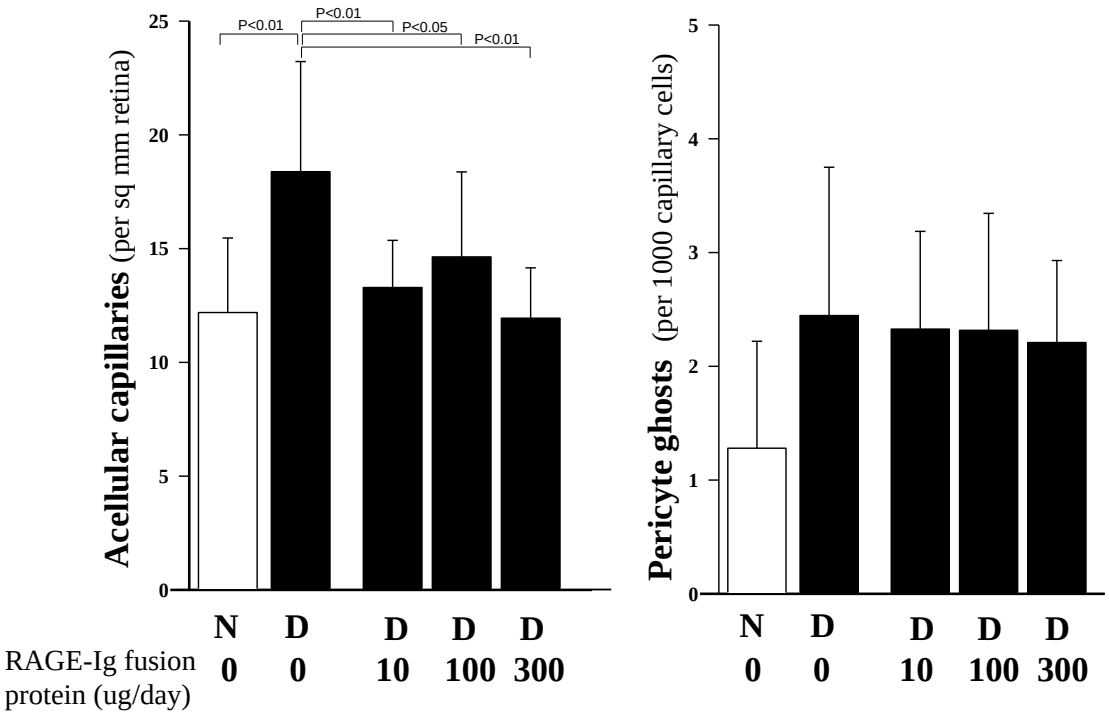
25 mice per treatment group

Assessments

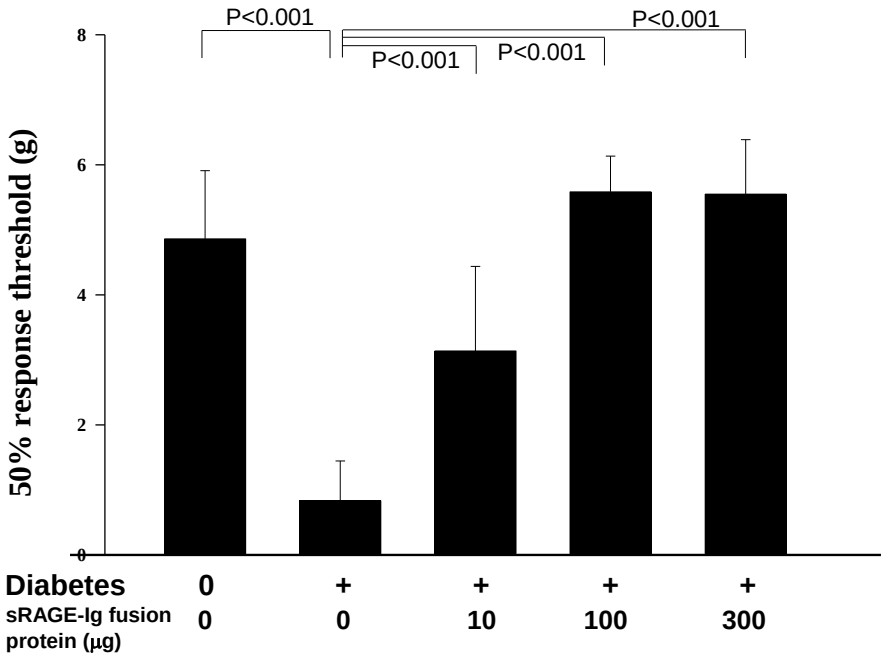
- Body weight, every 4 weeks
- Blood glucose levels assessed prior to mRAGE-Fc administration and at 16 week intervals
- Glycohemaglobin (GHb) assessed at weeks 12, 24, and 32.
- Albuminuria, week 16 and 32
- Tactile sensitivity, week 16 and 32
- Post-mortem assessment of:
  - Vascular lesions and non-vascular lesions
  - Capillary cell apoptosis, IRMA, and micro-aneurysms
  - ganglion/axon representation

Galactica-sponsored experiment performed in the laboratory of Timothy Kern using mRAGE-Fc produced at Gala Biotech

mRAGE-Fc Significantly Inhibits Capillary Degeneration



mRAGE-Fc Significantly Inhibits Sensitivity to Light Touch



4 and 8 Week Rat Model of Streptozotocin-Induced Diabetes

Administration (ip) of 45 mg/Kg streptozotocin (STZ) for 5 days

mRAGE (1.5 mg/rat/injection) administered IP or SC 3X/week for 4 or 8 weeks

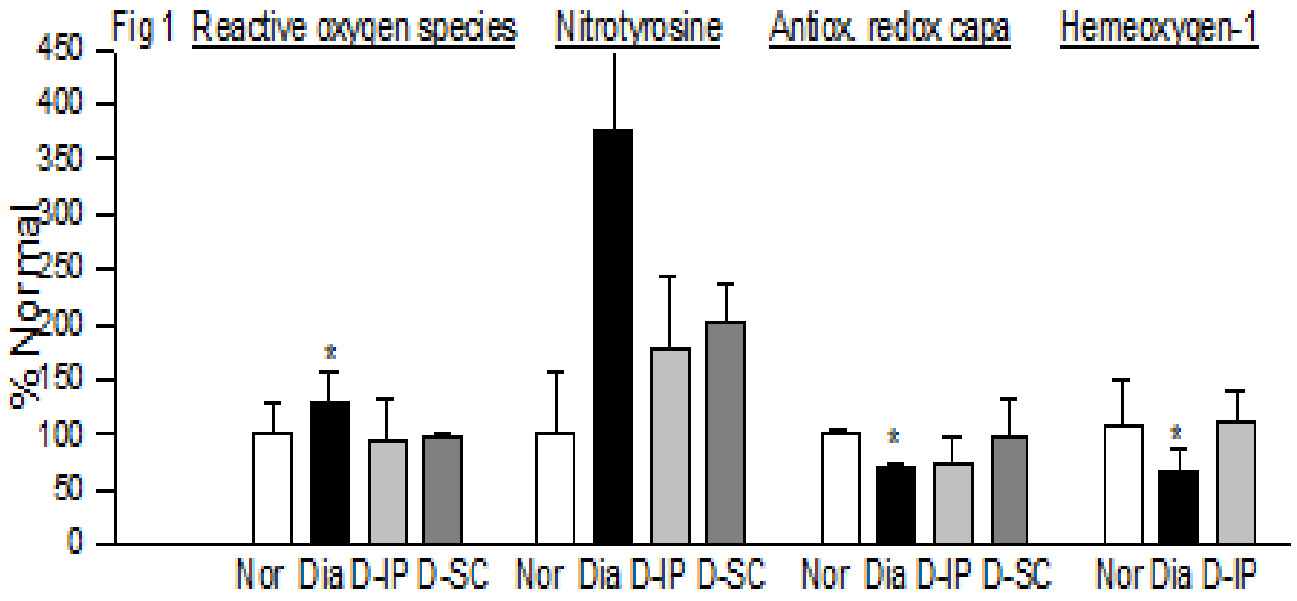
8-10 rats per treatment group

Assessments

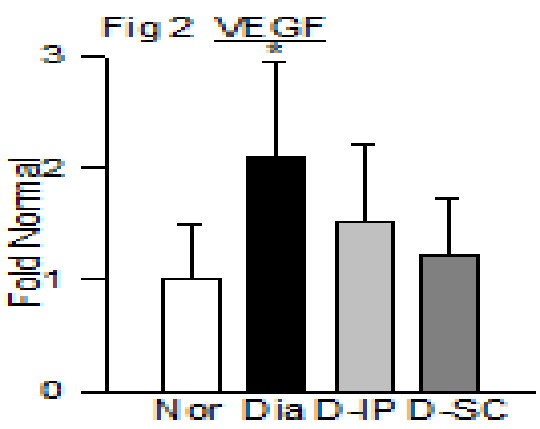
- Compare efficacy of SC vs. IP @ 4 weeks
- Test immunogenicity of drug in rats @ 8 weeks
- Retinal function by electroretinograms
- Kidney function by quantifying total urine albumin
- Assessment of:
  - Retinal oxidative stress
  - Protection against increased retinal VEGF levels
  - Severity of hyperglycemia

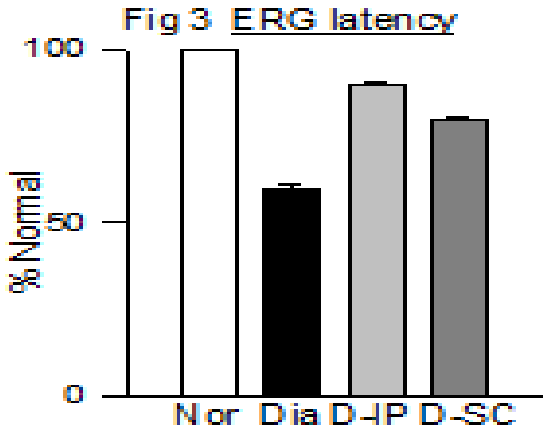
Galactica-sponsored (NIDDK supported) experiment performed in the laboratory of Renu Kowluru using mRAGE-Fc produced at Gala Biotech

mRAGE-Fc (at 4 weeks) Ameliorates Retinal Oxidative Stress

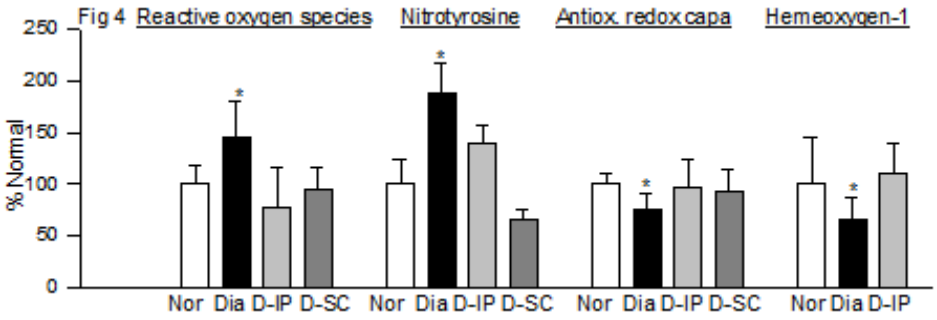


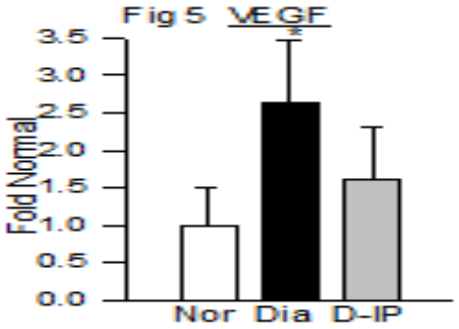
mRAGE-Fc (at 4 weeks) Inhibits Increase in Retinal VEGF Levels and Partly Restores Retinal Function





mRAGE-Fc (at 8 weeks) Ameliorates Retinal Oxidative Stress and Inhibits Increase in Retinal VEGF Levels





42 Week Rat Model of Streptozotocin-Induced Diabetes

Administration (ip) of 45 mg/Kg streptozotocin (STZ) for 5 days

mRAGE (1.5 mg/rat/injection) administered SC 3X/week for 42 weeks

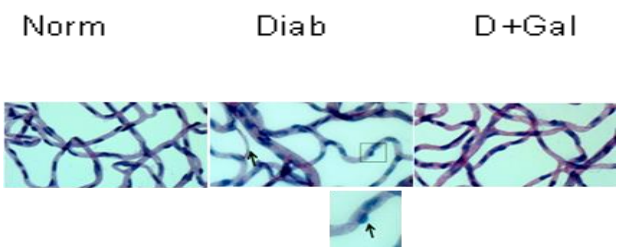
Assessments

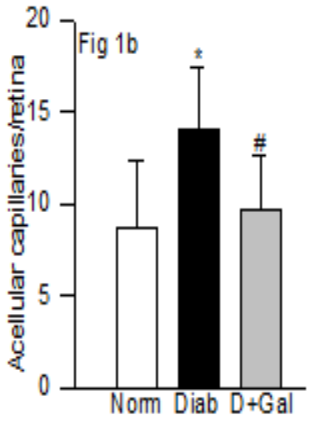
- Body weight, 2X/week
- Blood glucose levels and 24 hour urine output, 1X/week
- Retinal function by electroretinograms ~2 and ~8 months after initiation
- Kidney function by quantifying total urine albumin ~2 weeks before termination
- Post-mortem assessment of:
  - Retinal microvasculature
  - Capillary cell apoptosis
  - Oxidative stress and mitochondrial integrity in retina and kidney
  - Inflammatory mediators in retina and kidney
  - Retinal VEGF levels

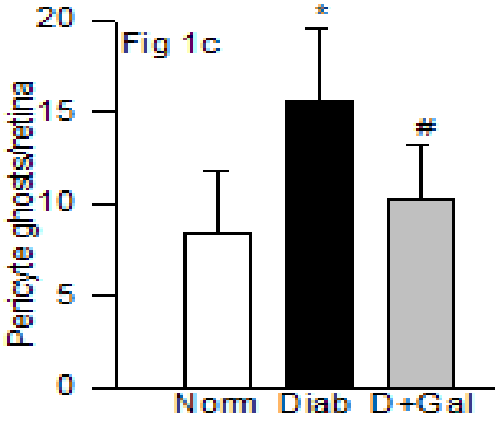
10-12 rats per treatment group

Galactica-sponsored (NIDDK supported) experiment performed in the laboratory of Renu Kowluru using mRAGE-Fc produced at Gala Biotech

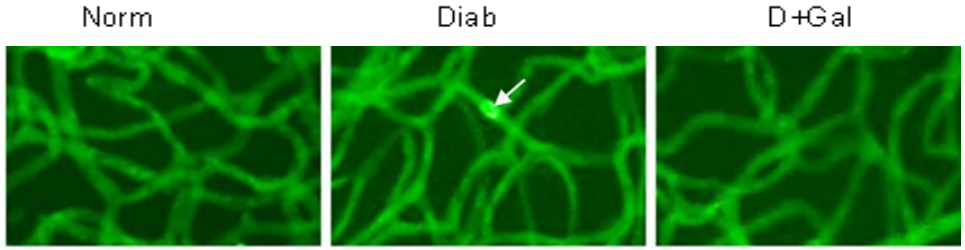
mRAGE-Fc Significantly Protects Retinal Vasculature From Development of Histopathology Characteristic of Diabetic Retinopathy

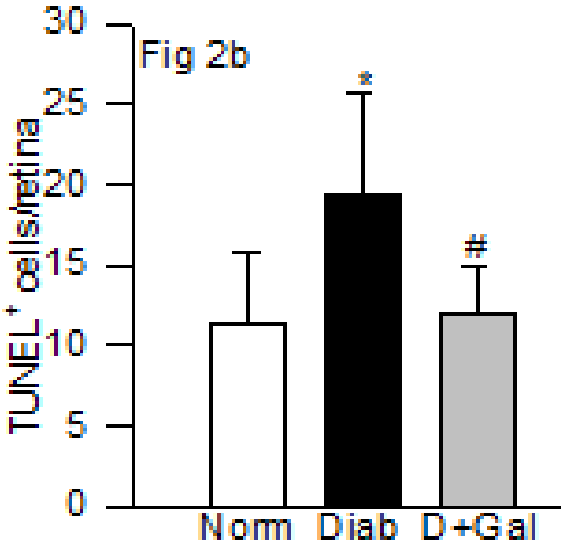




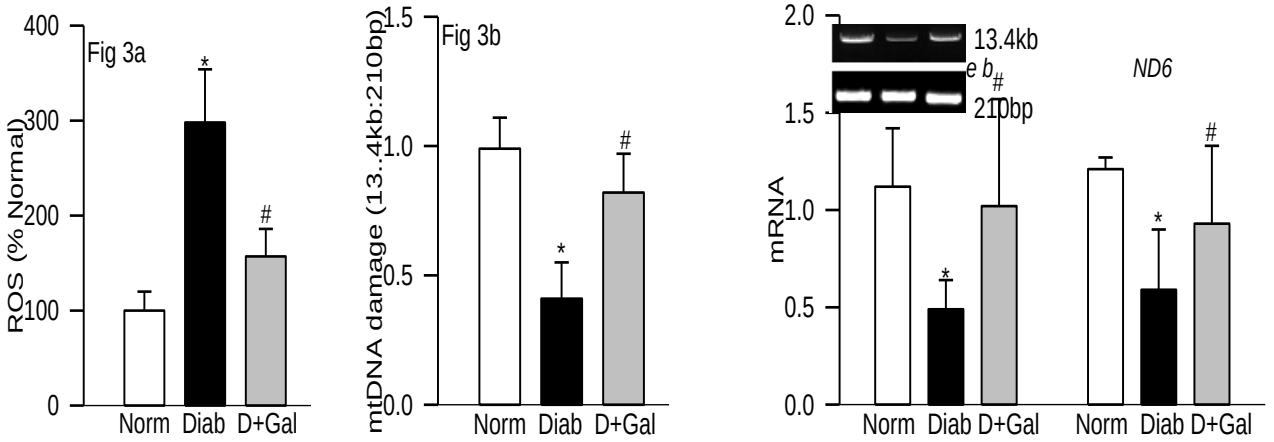


mRAGE-Fc Prevents Increase in Capillary Cell Apoptosis

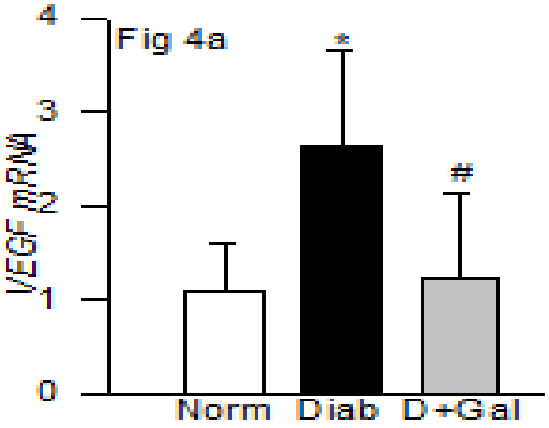


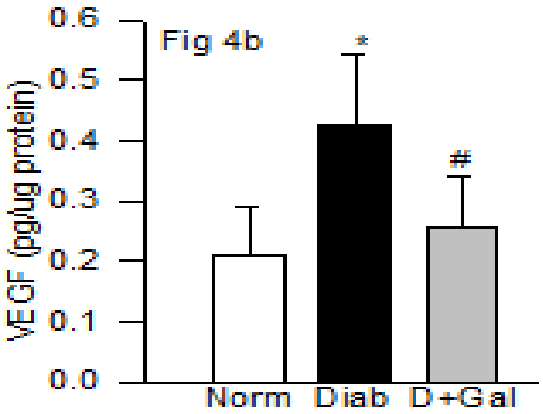


mRAGE-Fc Ameliorates Retinal Oxidative Stress and Restores Mitochondrial Integrity

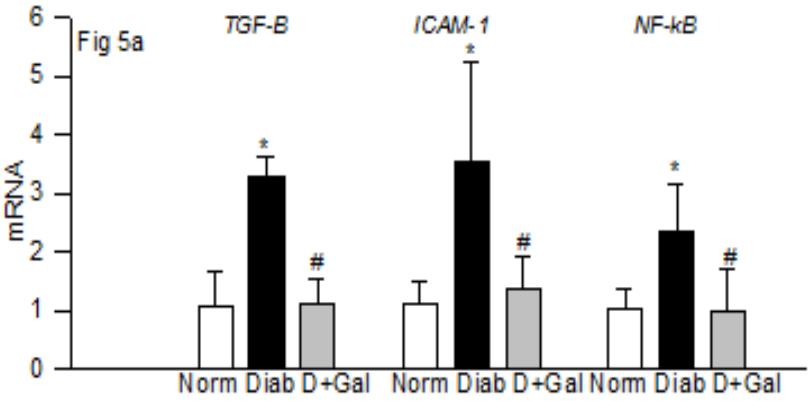


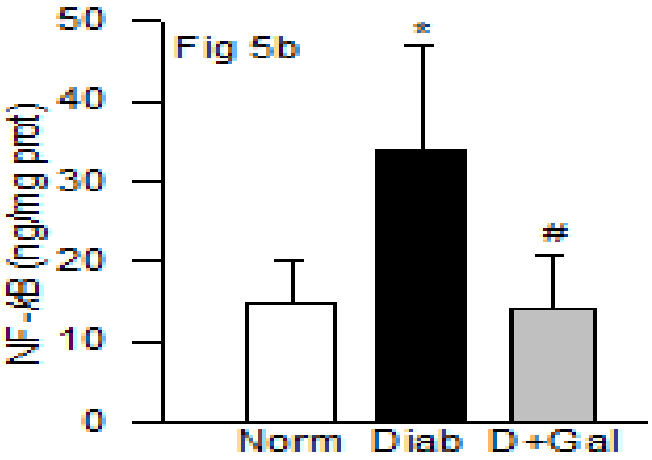
mRAGE-Fc Inhibits Increase in Retinal VEGF Levels





mRAGE-Fc Prevents Increase in Inflammatory Mediators in Retina

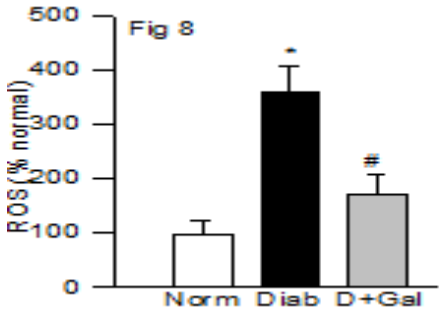


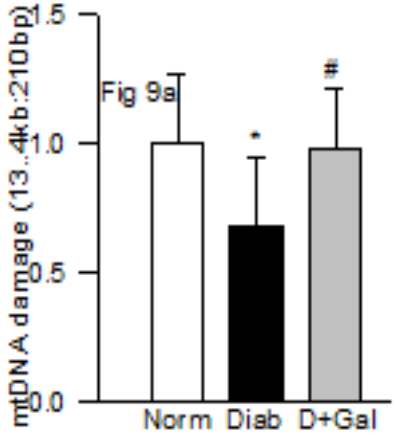


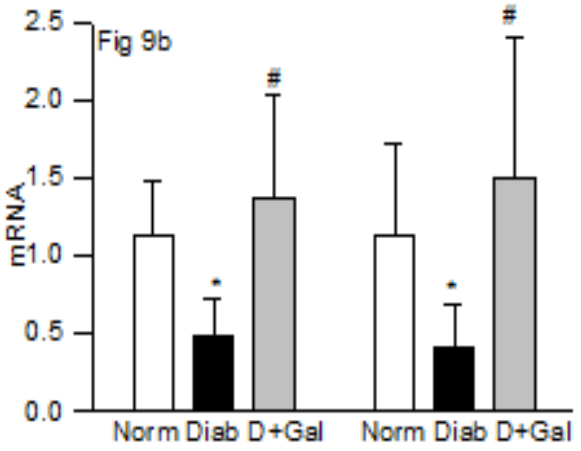
mRAGE-FC Ameliorates Increase in Albumin Output

Group	Duration of Diabetes/RAGE administration	Urine Volume (ml/24 hour)	Urine albumin (mg/24hrs)	Kidney weight (g)	Kidney/BW ($gx10^{-3}$)
Normal	42 weeks	12±6	2.41±0.93	4.96±0.54	8±1
Diabetes	42 weeks	59±32*	10.27±7.2*	6.56±2.50	15±6*
Diabetes- RAGE (SC)	42 weeks	47±24*	4.71±2.78	5.33±1.16	12±3*

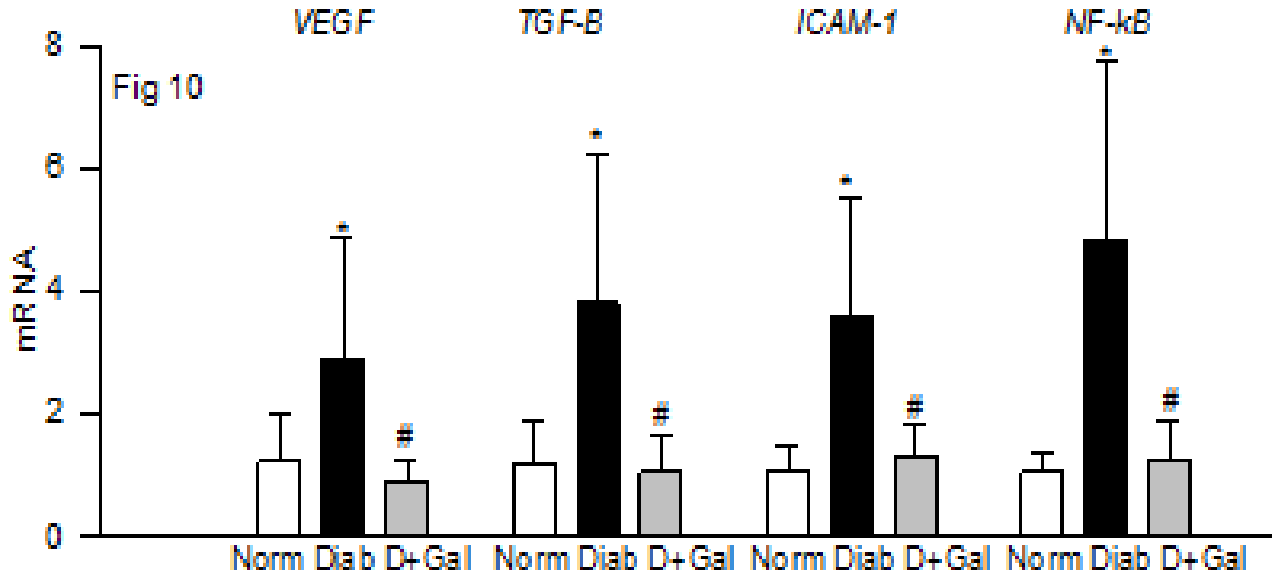
mRAGE-Fc Ameliorates Oxidative Stress in the Kidney and Restores Mitochondrial Integrity







mRAGE-Fc Prevents Increase in Inflammatory Mediators in Kidney



Other Achievements To Date

- Manufacturing
  - Produced, purified and characterized mRAGE-Fc for preclinical experimentation
  - Produced, purified and characterized pilot batches (<100 mg) of 4 hRAGE-Fc variants
  - Generated and tested cGMP Master Cell Bank for optimal hRAGE-Fc variant for preclinical and clinical use
  - Completed extensive upstream and downstream process development work and short-term stability study

- Assay Development
  - Successfully developed quantitative concentration and functional assays for RAGE-Fc proteins
  - Optimized development of hRAGE-Fc through selection of biologically active variants
    - Galactica substituted two amino acids from monkey RAGE to minimize the formation of multimeric aggregates during fermentation
    - This substitution is the key claim in Galactica's composition-of-matter patents issued globally

Management

- **Galactica is operating as a virtual company**
- **Lawrence B. Brown, J.D., M.B.A.**
  - CEO, President, and Chairman
  - Senior pharmaceutical/biotechnology executive with 33 years experience
  - Independent pharmaceutical consultant
  - Positions previously held:
    - Vice President, Business Development, Savient Pharmaceuticals, Inc., East Brunswick, NJ. Management Committee member
    - Director (Head), Business Development, Centocor, Inc., Malvern, PA. Pharmaceutical Management Committee member
  - Expertise in corporate governance, business development, finance, mergers and acquisitions, venture capital, strategic planning and drug development

Active Consultants

- **Gene Burton, Ph.D., DNA Bridges, Inc.**
  - Head, Protein Manufacturing Strategies, DNA Bridges, Inc., 2008 – Present
  - Vice President, Process Sciences and Product Development, Receptor BioLogix, Inc., 2005-2008
  - Director, Purification and Isolation Development, Bayer Corporation, 1999-2004
  - Senior Scientist and Group Leader, Recovery Process Research and Development, Genentech, Inc., 1982- 1999
- **Ronald P. Danis, M.D.**
  - Professor Emeritus of Ophthalmology, Former Director of the Fundus Photograph Reading Center, University of Wisconsin Medical School, Madison, WI
  - Principal investigator for numerous national clinical trials
  - Subject matter expert for many leading pharmaceutical and ophthalmic companies
  - Standing member of the Diabetic Retinopathy Clinical Research Network (affiliated with the National Eye Institute)
  - Dr. Danis has published over 60 articles in the areas of diabetes, ophthalmology, retinopathy, infectious disease, and macular degeneration

Regulatory Considerations

- Since Galactica's RAGE fusion protein is a fully human biologic, it will **NOT** be subject to the very high regulatory hurdles to which small molecule diabetes drugs have been subjected following the market withdrawal of the glitazones (Avandia)

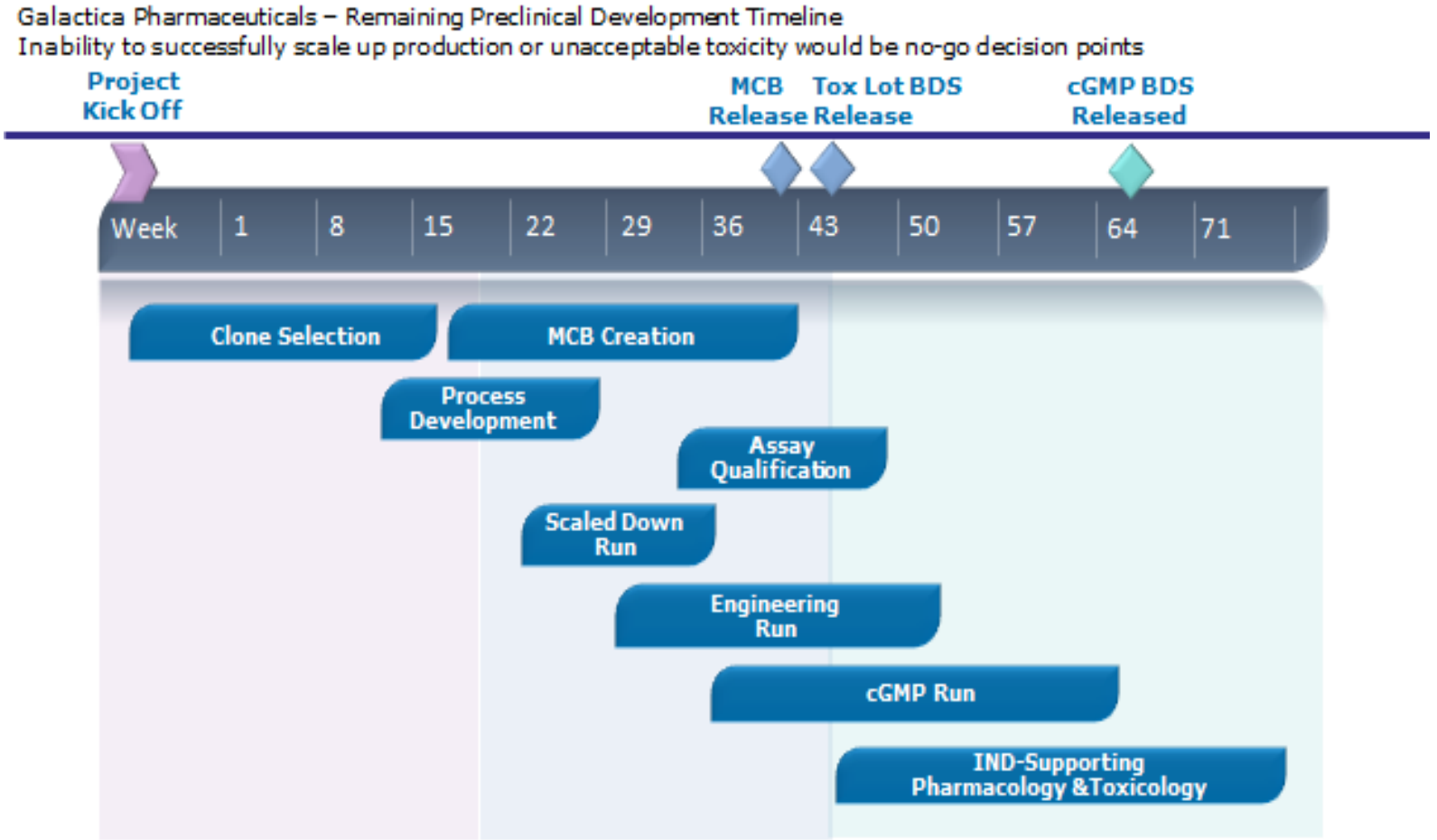
Galactica Intellectual Property

- Galactica Patent Application (U.S. Patent Application No. 12/664,111, International Application No. PCT/US08/066956) RAGE Fusion Proteins
  - Priority date: June 14 2007
  - International filing date: June 13 2008
  - International publication date: December 24 2008 (Publication No. 2008/157378)
  - Global composition claims, and certain method of use claims, have issued
  - In U.S. and Europe (and likely Japan), patent expirations will be extendable through standard pediatric and regulatory extensions

First Clinical Study

- Initial clinical study has been designed as a 40-patient Phase I/II proof-of-concept trial of hRAGE-Fc in the treatment of diabetic macular edema
  - Dr. Carl Regillo, Director, Retina Service, Wills Eye Hospital, and Professor of Ophthalmology, Thomas Jefferson University, will serve as Principal Investigator
  - Participants' HbA1C levels will be monitored to assess whether Galactica's protein helps to regulate insulin resistance

RAGE-Fc Development Timeline



Galactica Pharmaceuticals Summary

- Galactica's RAGE protein appears to be the first molecule of any type with clinical potential to have demonstrated in vivo efficacy against the three major diabetic complications – retinopathy/macular edema, neuropathy and nephropathy
- Galactica's first-in-class molecule, to be administered via subcutaneous injection, should be the drug of choice for the treatment of any patient presenting with any of the three major diabetic complications or either form of macular degeneration, and generate a very attractive reimbursement profile
- The enormous unmet clinical needs which Galactica's RAGE protein will address conservatively represent a **$250+ billion** global market opportunity
- Since Galactica's RAGE fusion protein is a fully human biologic, it will **NOT** be subject to the very high regulatory hurdles to which small molecule diabetes drugs have been subjected following the market withdrawal of the glitazones (Avandia)
- The Company has successfully worked through all manufacturing issues and has a clear path to its first IND filing in 15 months (much sooner for COVID)
  - The time to IND filing is dictated by the results of a second round of clonal selection
- Global composition-of-matter patent claims, and certain method of use claims, have issued
- Strong scientific and management team