MITOCHON PHARMACEUTICALS, Inc.

DISEASE MODIFYING THERAPIES FOR NEURODEGENERATIVE DISEASES

Non - Confidential SUMMARY
2019

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Business Summary

- Mitochondrial targeted compounds **focused on neurodegeneration**
- Small molecule Technology that up-regulates **neurotrophins**, reduces **oxidative stress** by promoting **mitochondrial biogenesis/remodeling**
- **Positive animal data** in Huntington's, MS, Parkinson's, Optic Neuritis, TBI
- **IND Open 4Q 2018 –** P1 to begin in 2019
- **Management team with extensive experience** in developing orphan drugs, efficient use of capital, and exiting
- **Patents recently Issued (2017/2018)** and Orphan Designation Pending
- **$4.5MM Seed Round completed** ($2.0M) **foundations: MJ Fox, NIH**
- Cash needed for next milestone(s): $3.0MM (Through P1) or $30MM (through P2 POC - 2 indications and 2 compounds in clinic)

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Mitochondria are Very Unique Organelles

- Energy Source (ATP producer) for all mammals
- In All Cells Except RBCs
- Distinct/Own DNA
- Evolutionarily conserved
- Main source of oxidative stress
- Key to aging

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Product Platform with Multiple Opportunities

- Lead Orphan compound MP-101
  - Repurposed compound tested in > 100,000 humans
    - New Issued patent – expiry 2040
  - Target Pharmacology - Mitochondrial modulation
    - Increases BDNF, reduces oxidative stress, mitochondria biogenesis
    - Excellent brain penetration
  - Safety index >10x (low dose therapy)
  - Phase II targets: Huntington's Disease, Acute Indications: WBRT and AKI
- Lead compound MP-201, a ProDrug of MP101
  - Striking protective effects in MS and Parkinson models - Lead indications
  - New Molecular Entity (NME) and composition of matter patent filed

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Large Markets with Significant Unmet Needs

- **Adult Orphan Disease (Market Potential > $1billion)**
  - Huntington's Disease: Prevalence 3-7 per 100,000. US estimate 30,000
  - Optic Neuritis: Prevalence 110/100,000, US Estimate 190,000

- **Childhood Orphan Diseases (Market Potential > $500 million)**
  - Duchenne's MD: Prevalence 15 per 100,000 ages 5-24. US estimate= 5,000
  - Wolfram Syndrome: Prevalence 1 per 500,000 ages 5-30. US Est. = 600

- **Adult disease (non-orphan) (Market Potential > $3 billion)**
  - Multiple Sclerosis – Prevalence 2.5 million WW, US estimate = 400,000
  - Parkinson's Disease – Prevalence 6.3 million WW. US estimates = 1 million

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Huntington's Disease

- An adult onset (~40) neurodegenerative disorder
  - Chorea (involuntary movement), loss of muscle coordination, speech.
  - Eventual dementia and premature death.
  - **High levels of Oxidative Stress found Post-Mortem**
- Genetic mutation in huntingtin gene,
  - "tri-nucleotide repeat expansion disorder" of CAG (glutamine).
- Transgenic mouse, N171-82Q
  - Similar to humans
  - "Premanifest" stage showing movement disorders, striatum, intranuclear inclusion / neuritic aggregates and premature death.
- HD mice were treated ~ 17-weeks with MP101 by daily oral gavage at 0.5, 1 and 5mpk - Work done at John Hopkins University

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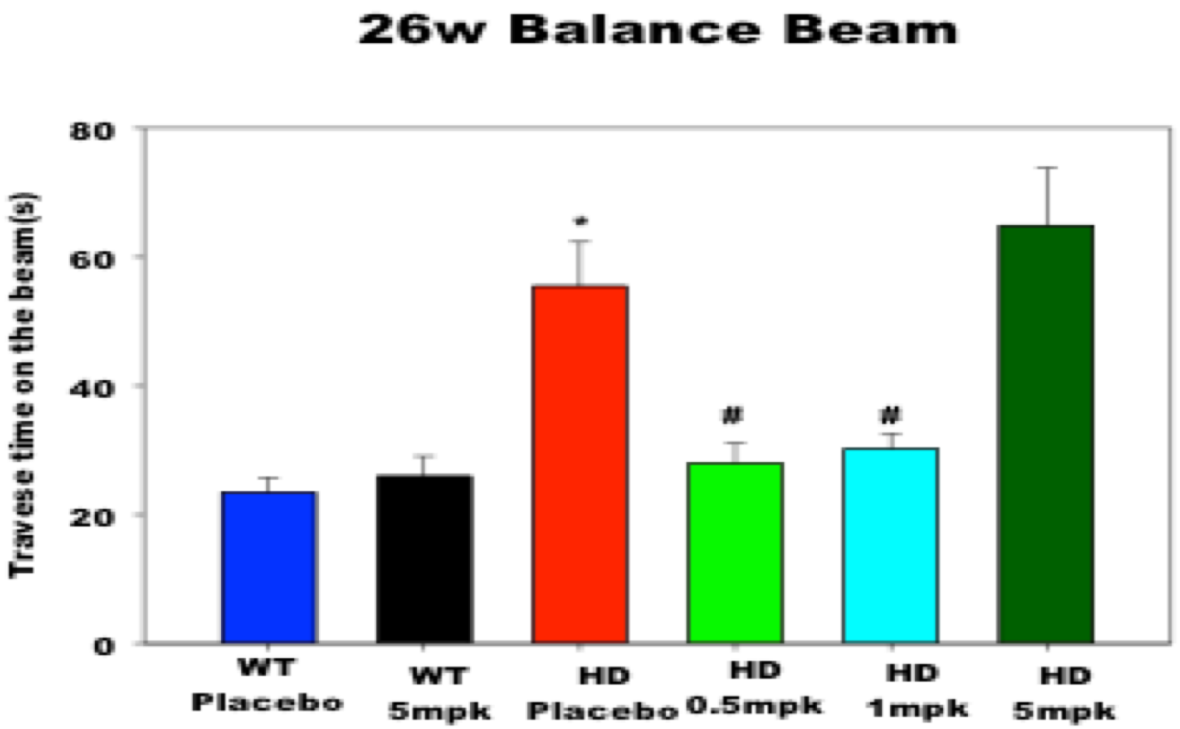
MP101 Improves Motor Function in a N171-82Q HD Mouse Model of Huntington's Disease at Age 26W with 17W Treatment



*p<0.005 versus the WT Placebo group; #p<0.005 versus the HD Placebo group

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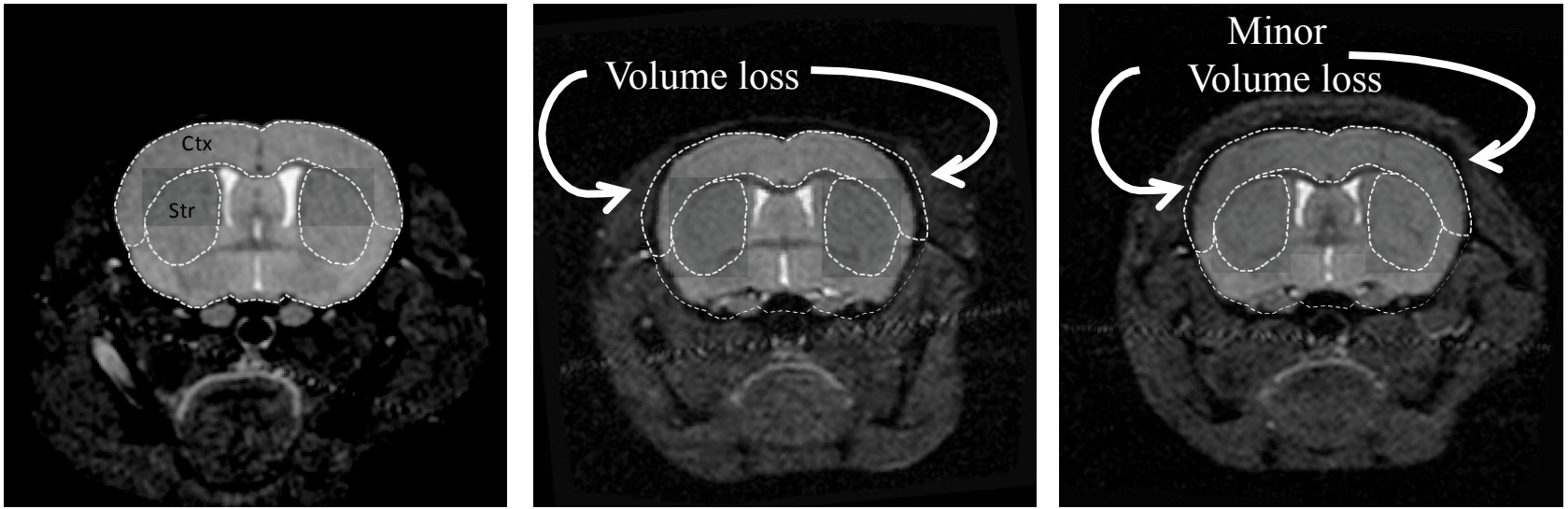
MP101 attenuates brain atrophy (at 26 weeks of age) in N171-82 HD mice

WT | HD | HD-MP101



Wild type (WT) with normal cortex (Ctx) and Striatum (Str). HD placebo (HD) shows loss in both Ctx and Str. MP-101 shows minor loss in Ctx and Str

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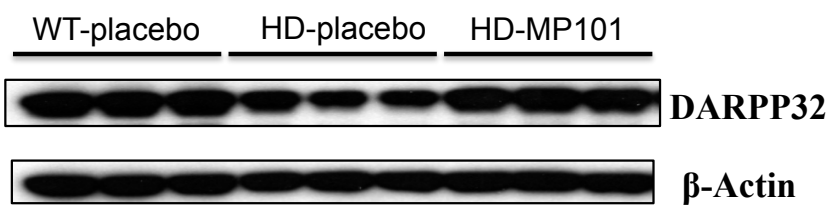
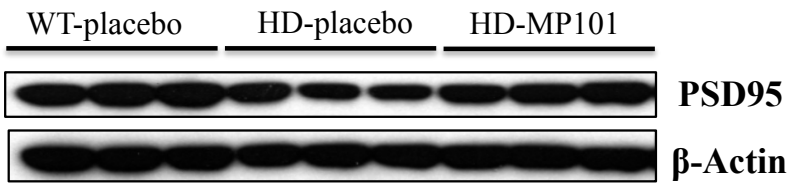
MP101 preserves medium spiny neurons (DARPP32) and General Neurons (PSD95) to near normal

A

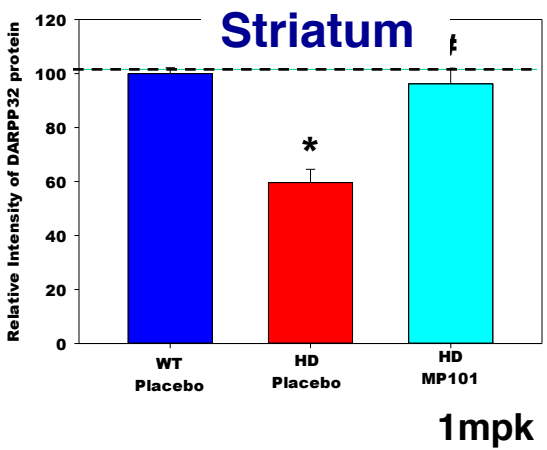


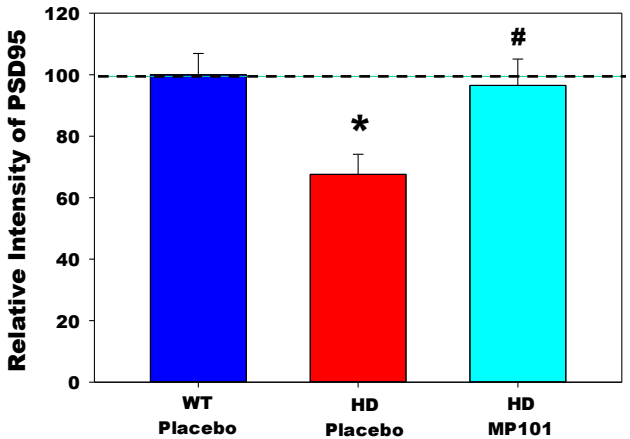
26w DARPP32 protein



26w PSD95 protein

B





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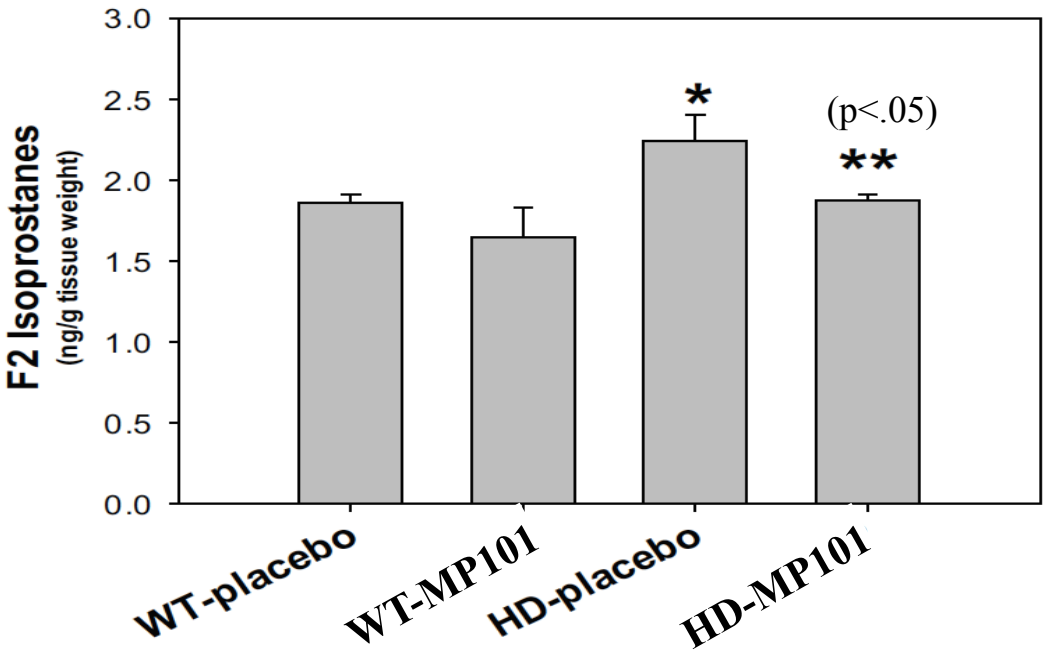
MP101 Significantly Lowers Oxidative Stress in HD Brain

F2 Isoprostanes Biomarker in HD Mice Cortex



Wu, B., et al., *2,4 DNP Improves Motor Function, Preserves Medium Spiny Neuronal Identity, and Reduces Oxidative Stress in a Mouse Model of Huntington's disease.* Experimental Neurology, 2017. **293**: p. 83-90.

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Multiple Sclerosis

- No known etiology
- Autoimmune disorder of the CNS
- Antibodies attack the myelin sheaths surrounding and protecting the axons
- **High levels of Oxidative Stress found Post-Mortem**
- Intermitting episodes, called Relapsing Remitting, the body repairs itself to some degree
- Voluntary movement is disrupted/involuntary control of bladder and bowels
- Work done at Asahikawa Medical University

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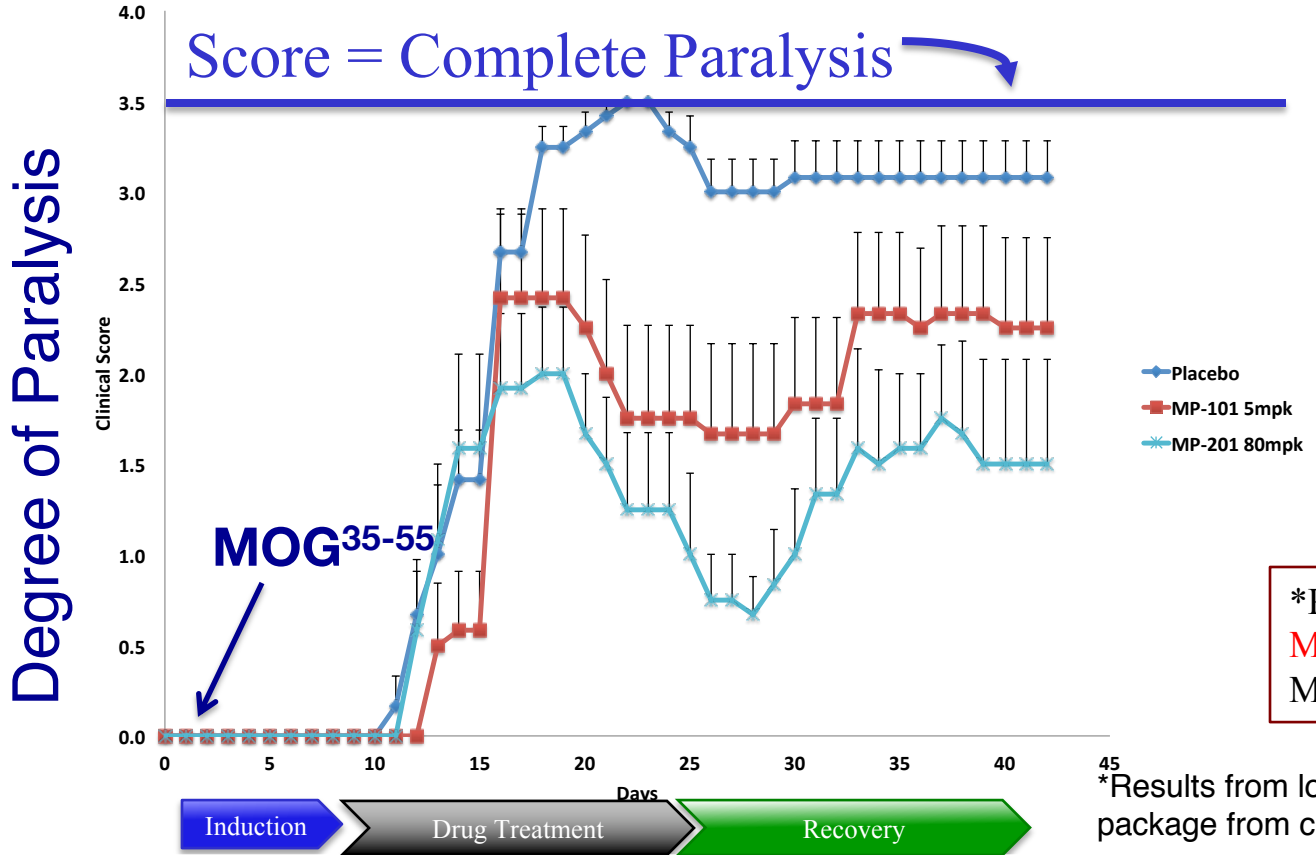
MP101 & MP201 attenuates Multiple Sclerosis using the EAE Model



*P values by Ordinal Regression
MP101 5mpk = 0.0192
MP201 80mpk = 0.00014

*Results from logistic regression model using ordinal package from cran project (www.cran.r-project.org)

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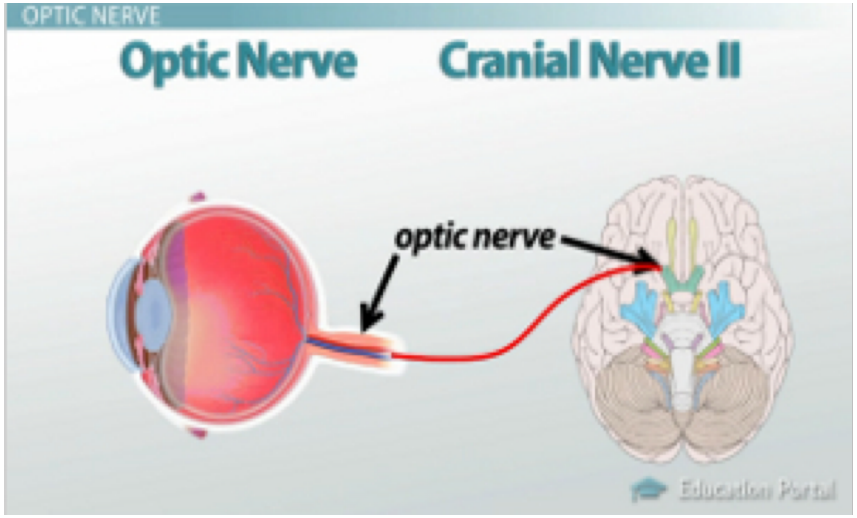
Optic Neuritis
(pre-Multiple Sclerosis)



- Inflammatory demyelinating disease of the optic nerve
- Either idiopathic or associated with multiple sclerosis
- Presentation: Acute unilateral vision loss
- Work done at Univ. Pennsylvania

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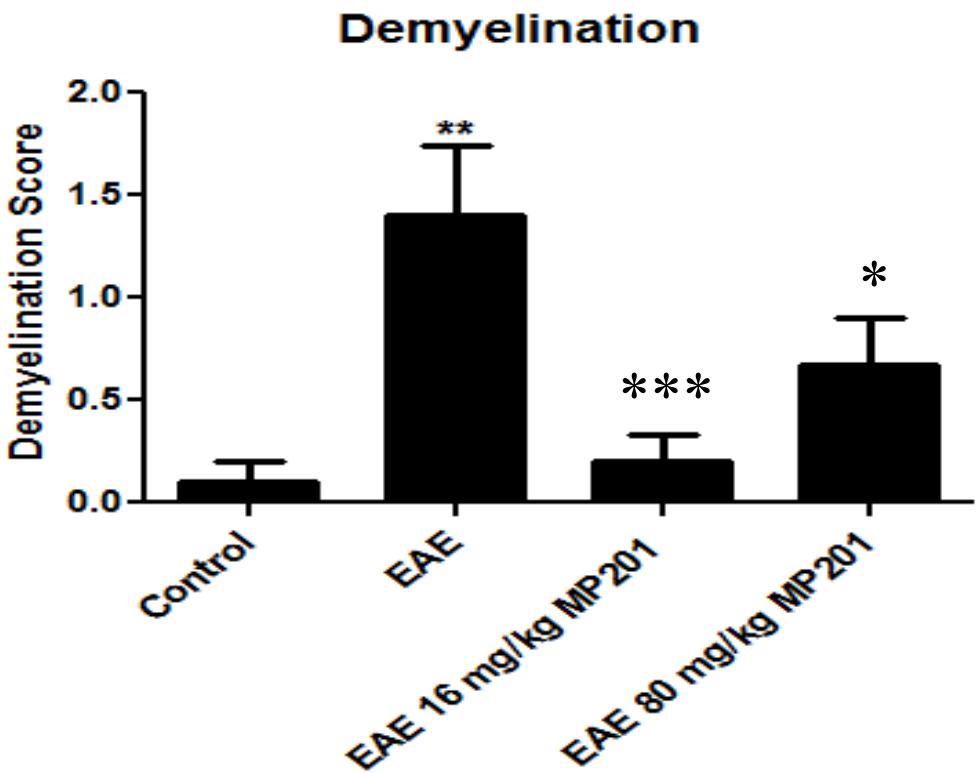
MP201 Protects Optic Nerve from Demyelination



Immunization Day 0. MP201 treatment started day 15, repeated daily until sacrifice

Statistics: one way ANOVA, **p<0.01 EAE vs control, ***p<0.001 EAE vs EAE + 16 mpk MP201, *p<0.05 EAE vs EAE + 80 mpk MP201

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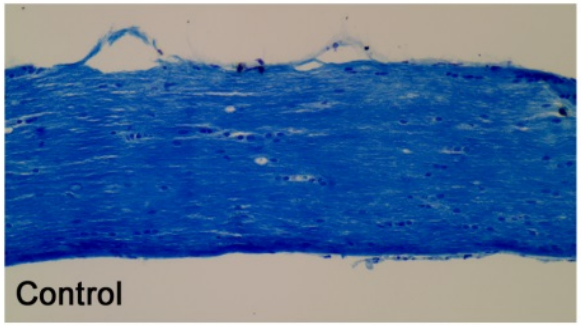
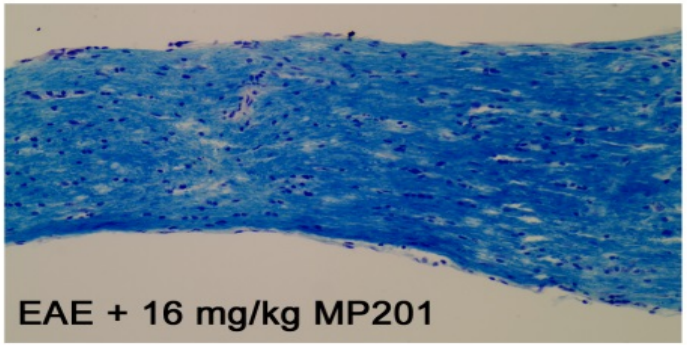
MP201 Significantly Prevents Demyelination in Optic Nerve

Blue Stain shows Myelin around 1000's of Nerves

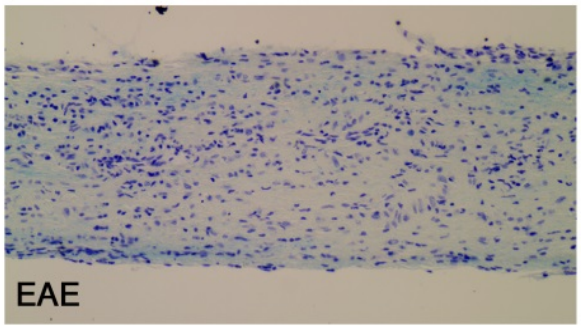
Normal Myelin in healthy mouse

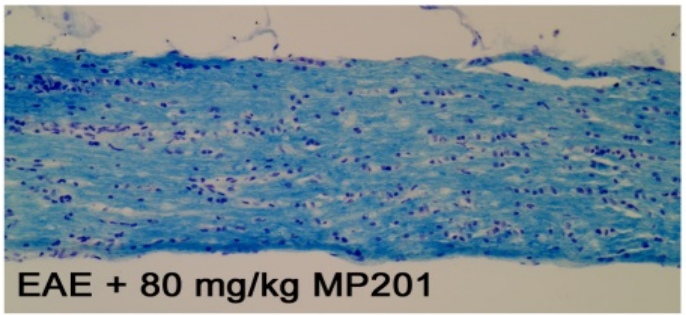




Almost complete Protection of Myelin

Almost complete loss of Myelin





Significant protection

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Parkinson's Disease

- No known genetic cause
  - Movement issues, depression and later stages dementia.
- Mouse Model: Sirt3 KO mice, which
  - exhibit increased vulnerability of striatal and hippocampal neurons
  - 6-OHDA injected into the right striatum
  - Following day provided MP101 at 1 and 5mpk for two weeks.
- The dopaminergic neurons are slowly destroyed over the course of two weeks and mice are then tested on a constant speed rotarod for duration (3-min max).
- Work done at Nat'l Inst. Ageing

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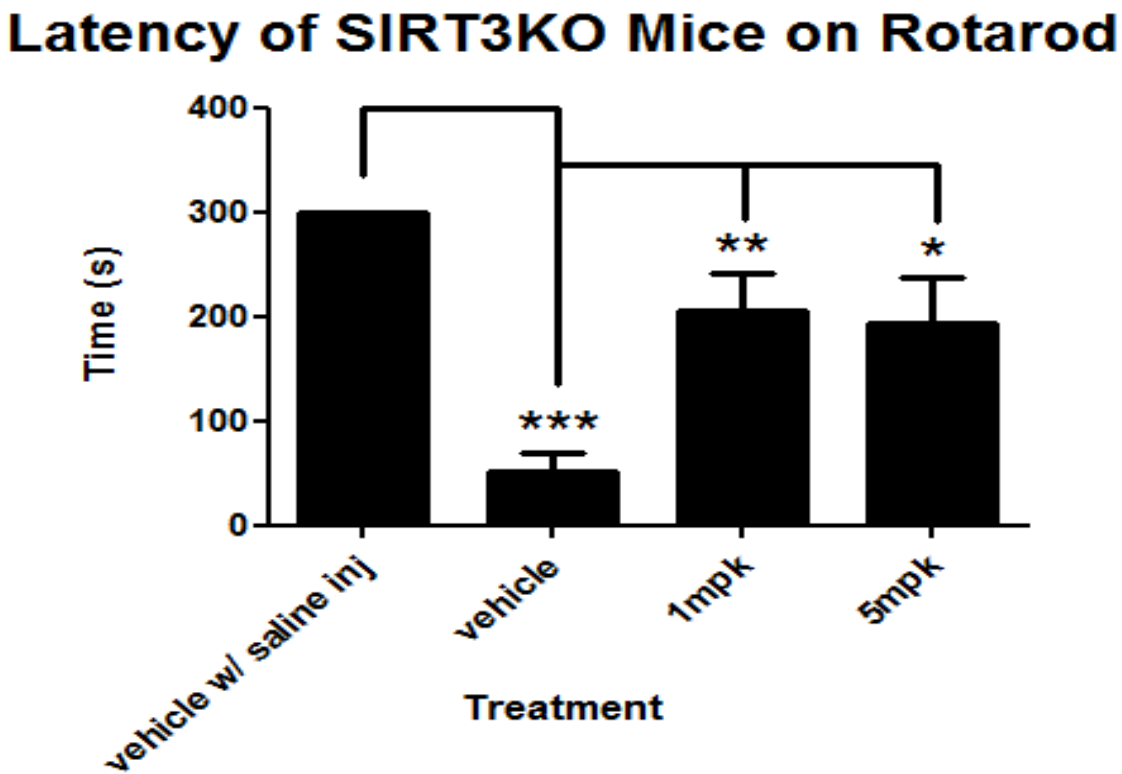
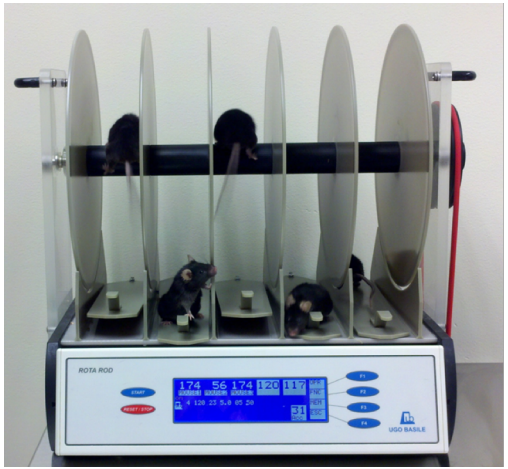
MP101 Significantly Improves Motor Scores with 6'OHDA model of PD





Measures coordination and fall time

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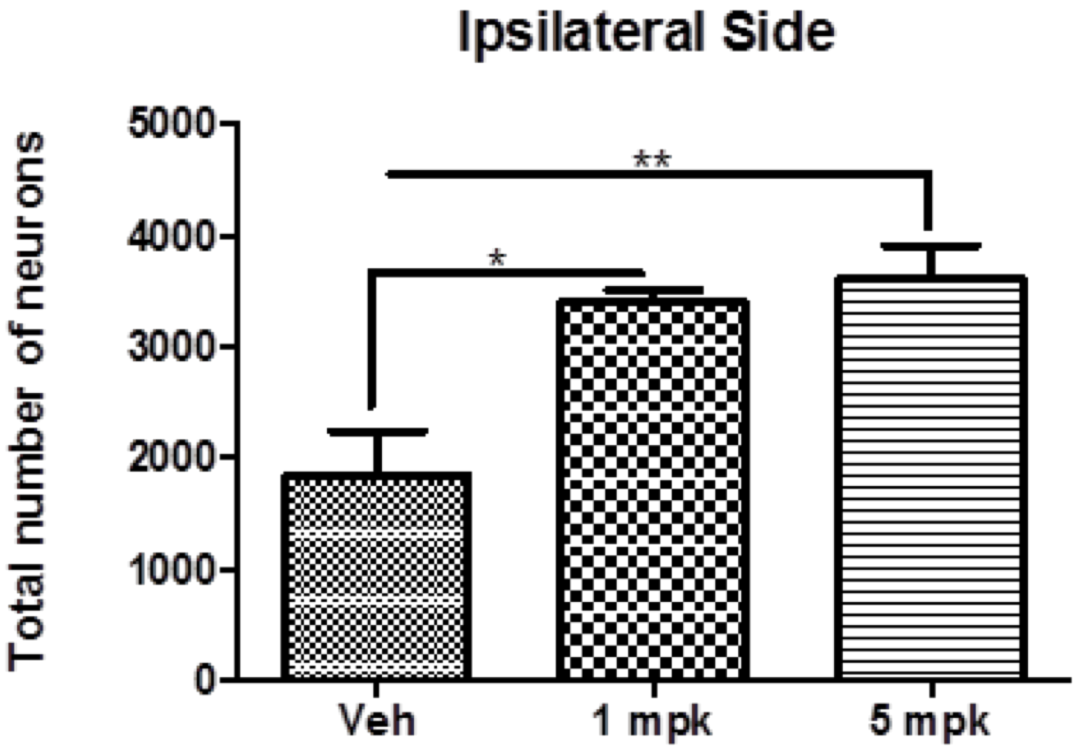
MP101 Significantly Protects Dopaminergic Neurons with 6'OHDA model of PD



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Operational/Milestones 2017 – 2020 ($30MM)

Task	Completion Date	Use of funds
IND Filing MP-101	3Q 2018	Completed/Open
Phase I SAD/MAD MP-101	3Q 2019	$2.5 million
Phase II Ready Activities MP-101	3Q 2019	$1.5 million
Phase II MP-101	2Q 2021	$7.0 million
MP-201 Activities thru Phase I	1Q 2020	$4.0 million
Phase II MS or Parkinson's – MP-201	2Q 2022	$10 million
G&A costs for 3 years		$5.0 million

Planned Exit through M&A post phase 2 (POC)

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Exit Comps for Neuro Disease Companies PH2 > $500MM

- Recent Activity shows high correlation with high exit values for rare disease companies in neurodegeneration:
  - Prexton/Lundbeck (Parkinson's PI) = $1B ($130M upfront)
  - Raptor/Horizon (Huntington's PII) = $800MM (M&A)
  - Karyopharm/Biogen (ALS/TBI Pre-clin) = $217MM (M&A)
- Pediatric Voucher worth $125MM on last sale
  - Sarepta/Gilead

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Competitive landscape shows mitochondrial targeted companies attracting capital but focus not on Neuro

- **Bioelectron (formerly Edison Pharma)–** Anti-oxidants (EPI-743) with main focus is on mitochondrial disease with Leigh Syndrome and Friedreich's Ataxia most advance, 2014 deal with Dainippon up to $4.3B
- **NeuroVive** – NeuroStat (Cyclosporine) to target Mitochondrial Permeability Transition Pore (mPTP). Main focus on traumatic brain injury. IPO Swedish and NASDAQ
- **CohBar** – Peptide (CB4211) for *de novo* lipids. Main focus NASH. IPO on NASDAQ pre-clinical
- **Mitobridge –** nuclear hormone PPAR delta targeted (MA-0211). Early stage discovery company. Programs across mitochondrial diseases including neuro, 2018 buy-out by Astellas for $225MM
- **Gencia** – Mitochondrial Agonists of the Glucocorticoid Receptor (MAGR). Main focus on Steroid/inflammatory conditions. 2015 deal with Takeda $500MM
- **Stealth Biotherapeutics–** Cardiolipin stabilizers. Main focus on Cardio/renal, Ocular indications and Mito diseases. Raised > $100MM from Morningstar

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Experienced Management Team

- **Robert Alonso, Founder, CEO – MBA, Serial Entrepreneur**
  - + 25 years Pharmaceutical experience, MRK, Roche (15 years entrepreneur)
  - Founding CEO Ceptaris Therapeutics (Exit > $250MM)
- **John G. Geisler, Founder, CSO PhD Mammalian Genetics**
  - +25 years research experience (Pfizer, Isis, JnJ)
  - Expertise in mitochondrial energy expenditure
- **Marcus Keep, Acting CMO, MD Board Certified Neurologist**
  - Neurosurgeon
- **Peter Crooks, SVP Chemistry – PhD Medicinal Chemistry**
  - World expert in medicinal chemistry - over 400 published papers, 100 Patents
- **Eve Damiano, Head Regulatory – MS Biology**
  - Expert in regulatory affairs filing multiple INDs and NDAs

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Scientific Advisory Board

- Mark Mattson, Ph.D. – National Institute on Aging
  Expert in neurodegeneration and aging
- Lawrence Steinman, MD- Stanford University
  Professor of Neurology, Neurological Sciences and Pediatrics
- Steven Hersch, MD – Mass General Hospital
  Expert in Huntington's Disease and study leader Huntington Study Group
- Martin Brand, Ph.D. – Bucks Institute on Aging, CA
  Aging, ROS Production, Mitochondrial Bioenergetics
- Lee Sweeney, PhD – U. Florida
  - Expert on neuromuscular diseases
- Ken Shindler, MD/PhD- Schea Eye/University of Pennsylvania
  Expert in Optic Neuritis

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SUMMARY

- **Two Compounds** in Pipeline focus on Neurodegeneration
  - MP-101 – Target Huntington's, Optic Neuritis
  - Patent issued 2017, expiry ~ 2040
  - MP-201 – Target MS and Parkinson's, TBI (DOD)
    - Novel chemistry, NME patent Pending
- **First in Class Compounds**
  - Huntington's Disease – Improves movement and coordination
  - MS and Optic Neuritis – Prevents Demyelination
  - Parkinson's – Protects dopamine neurons and improves motor skills
- **Experienced team** with FDA/orphan development and exit capabilities
- Early Stage Valuation with potential **>20x return**

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