Restoring Life’s Potential

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A regenerative medicine company dedicated to creating innovative solutions for the treatment of nerve damage

- NervGen is advancing drug candidates into clinical development for spinal cord injury and peripheral nerve injury
- There are no approved therapeutics that enhance nerve regeneration
- Core technology focuses on protein tyrosine phosphatase sigma (PTPσ), a key neural receptor that inhibits nerve regeneration
- PTPσ inhibition promotes nerve regeneration and improvement of nerve function
- Research is being conducted on other applications of PTPσ including: MS, stroke, cardiac arrhythmia, Alzheimer’s Disease, ...
THE CENTRAL AND PERIPHERAL NERVOUS SYSTEMS

The Body’s Command Center

A complex network of nerves and cells that carries messages to and from the brain and spinal cord to various parts of the body.

They control:

• Movements
• Thoughts
• Senses
• Heartbeat
• Breath
• Everything vital to living

They are impaired by:

• Trauma (CNS & PNS)
• Multiple Sclerosis
• Cardiac arrhythmia
• Stroke
• Epilepsy
• Alzheimer’s
• TBI/concussion
• .......

There are no approved therapeutics that enhance nerve regeneration.
NervGen has created NVG-291

Poised To Be First True Nerve Regeneration Therapeutic

This PTPσ antagonist has the potential to revolutionize the treatment of nerve injury and neurodegenerative diseases

Remarkable and robust effects across every model tested
Professor of Neurosciences at Case Western Reserve University’s School of Medicine and adjunct Professor in the Department of Neurosurgery at the Cleveland Clinic Foundation

Dedicated to spinal cord injury and regeneration research for >30 years

Recipient of multiple prestigious honors and awards including the Reeve-Irvine Research Medal for Critical Contributions to Promoting Repair of the Damaged Spinal Cord and Recovery of Function

Lead or senior author on >180 publications

Inventor of 5+ patents and patent applications

Dr. Silver is an active advisor whose lab will continue to conduct studies for NervGen

The glial scar forms at the site of a nerve injury to begin the healing process and protect the nervous system.

Unfortunately, the glial scar, like all scars, contains “gooey” Chondroitin Sulfate Proteoglycan (CSPG), which acts as flypaper and traps the nerves forever.

The **GLIAL SCAR is highly inhibitory to neuronal growth** and the primary impediment to regeneration in the central and peripheral nervous systems.

Freeing the long immobilized axons could help even chronic spinal cord injuries.
Working together with scientists at Harvard, Dr. Silver identified the locking mechanism underlying the failure of neural regeneration (2000 – 2010).

The PTPσ receptor on neurons binds and locks to the CSPG protein matrix of the glial scar.

Injured Spinal Cord

Shen Y. et al Science 2009 Oct 23;326(5952):592-6
Translational neuroscientist with over 12 years of experience in the regenerative medicine industry

Previously, he served as a scientist on the regenerative medicine team at Athersys, participating in the clinical advancement of its MultiStem system

Dr. Lang received his BS in Biology from the University of Wisconsin-Madison and PhD in Neurosciences from Case Western Reserve University as a grad student under Dr. Silver

>45 publications, presentations and abstracts, 9 major honors and awards, inventor on 3 patent applications

As an Executive-in-Residence at BioEnterprise, Dr. Lang provides consulting to early stage pharmaceutical and biologic companies

Dr. Lang is an active scientific advisor with NervGen
ISP - The “Key” To The Glial Scar Lock

Drs. Silver and Lang co-invented ISP, the predecessor of NVG-291

The first therapeutic to:
• successfully target PTPσ
• relieve inhibition to nerve growth
• promote nervous system recovery
• promote functional improvement

NATIONAL INSTITUTE OF Neurological Disorders And Stroke Video

If the video to the left does not open, click the following link to watch on YouTube
NERVE REGENERATION ACROSS THE GLIAL SCAR

Growth of neurons is restored when treated with ISP


Successfully tested on mice, rats and human cells
DRAMATIC IMPROVEMENT IN SPINAL CORD INJURY

Rodents with severe spinal cord contusion to model severe human injury

Representative 3D model of injury

Histological sections

Rodents had remarkable motor recovery: consistent coordination, toe clearance, tail held consistently high
UNPRECEDENTED RECOVERY WITH ISP

Measurement of Locomotion
(7 weeks of daily treatment)
33% response rate

Measurement of Balance
12 weeks post SCI

Improvement continues after cessation of therapy

First drug to achieve a remarkable 6 point improvement on the BBB scale
UNPRECEDENTED RECOVERY OF BLADDER FUNCTION

Dose dependent bladder function improvement in 100% of injured animals

- Recovery of urinary function is a critical quality of life issue to the paralyzed population
- Eliminating catheterization would reduce:
  - urinary tract infections
  - hospitalizations
  - morbidity
  - healthcare cost


Bladder, bowel and sex function related to same nerve region
UNPRECEDEDNTED RECOVERY

- Significant recovery of locomotion, with a significant percentage of animals fully recovered
- 100% of the animals recovered voluntary bladder function
- Reproduced in multiple studies, labs and models including 6 separate SCI studies
- Published in Nature - the highest standard (image linked to paper)

Modulation of the proteoglycan receptor PTPσ promotes recovery after spinal cord injury

Bradley T. Lang¹, Jared M. Cregg¹, Marc A. DePaul¹, Amanda P. Tran¹, Kui Xu², Scott M. Dyck³, Kathryn M. Madalena¹, Benjamin P. Brown⁴, Yi-Lan Weng⁵, Shuxin Li⁶, Soheila Karimi-Abdolrezaee³, Sarah A. Busch¹, Yingjie Shen² & Jerry Silver¹

Of the hundreds of drugs for regenerating nerve function that Dr. Silver’s lab has tested, ISP is by far the most effective
Protective mechanisms in the body inhibit regeneration of the nervous system affecting millions of people and costing hundreds of billions of healthcare dollars.
SPINAL CORD INJURY

- Every year 12,000 - 17,000 people suffer a debilitating spinal cord injury in the US
- 250,000-300,000 are currently living with permanent paralysis
- Direct medical costs can exceed $1 million in the first year alone
- Estimated public health costs of $40 billion annually
- No approved regenerative or restorative therapeutics

Paralysis takes away life’s potential and NervGen intends to restore it
PERIPHERAL NERVE INJURY

• Every year ~1.4 million people suffer a debilitating peripheral nerve injury in the US caused by trauma and medical disorders.

• Scarring in peripheral nerves also curtails regeneration.

• ~20 million people in the US are living with after-effects including permanent numbness and loss of sensation, chronic and debilitating pain, partial or full loss of movement, and decreased quality of life.

• Current treatments are nerve grafts, nerve blockers and numbing agents.

Nerve injuries cost the US health care system ~$150 billion annually.
Enhanced regeneration and functional recovery after spinal root avulsion by manipulation of the proteoglycan receptor PTPσ

Heng Li, Connie Wong, Wen Li, Carolin Ruven, Liumin He, Xiaoli Wu, Bradley T. Lang, Jerry Silver & Wutian Wu

Resulted in significant increased axonal density, numbers and accelerated motor recovery

OTHER INDICATIONS
Inflammation causes scarring and oligodendrocyte progenitors cannot grow through the scar to remyelinate

**ISP TREATMENT IN MS MOUSE MODEL**

**ISP:**
- stimulates the production of OPC’s (oligodendrocyte precursor cells)
- allows remyelination and regeneration of damaged nerves
- increases specific proteases that digest and break down the scar (CSPG’s)

**MS Symptoms**

- Numbness, tingling
- Headache
- Cognitive dysfunction
- Depression
- Speech/swallowing problems
- Breathing problems
- Fatigue
- Sexual dysfunction
- Muscle spasms
- Itching
- Walking difficulty

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**MS MOUSE MODEL VIDEO**

*ISP administered at 5 day intervals by collaborator Dr. Yan Yang at Case Western*

ISP promotes remyelination and enhances functional recovery
Sudden Arrhythmic Death (SAD): 180,000 to 250,000 cases per year – 50% of all sudden cardiac deaths

Lack of nerve regeneration (or sympathetic denervation) following heart attack is a leading risk factor for SAD

ISP:

- the first drug to regenerate nerves through a scar after a heart attack, thereby reducing susceptibility to arrhythmia
- sympathetic nerve regeneration cures rodents of heart-attack induced arrhythmias

OTHER OPPORTUNITIES

ALS (Lou Gehrig’s Disease) & Parkinson’s Disease
Neuron retraction precedes neuron cell death in ALS and Parkinson’s Disease. This retraction could be due to scarring and inflammation. Therefore, promoting motor axon regeneration may prevent progression of both of these diseases.

Epilepsy
One of the major triggers for epileptic seizures is scarring, causing an imbalance in excitatory/inhibitory waves in the brain. ISP should be able to help neurons regenerate and return the excitatory/inhibitory balance.

Concussion/Traumatic Brain Injury
Same mechanism of trauma - inflammation - scarring suggests that TBI’s should respond to ISP as well

Others
Stroke, Alzheimer’s Disease, Vascular Dementia, Macular Degeneration, Huntington’s Disease, Bell’s Palsy, Carpal Tunnel, Brachial Plexus injury, Restless Leg Syndrome, Cancer Resection, Guillain-Barre Syndrome…
MOVING FORWARD
MANAGEMENT TEAM

Ernest Wong, PhD MBA, President & CEO
- 20+ years of industry experience, 15+ in corporate and business development roles at both private and publicly listed companies
- Global project leader for 2 Phase III drugs
- Led campaign that resulted in sale of YM BioSciences to Gilead for US$510 M

Bill Radvak, BASc, Co-Founder & Executive Chairman of the Board
- 30+ years as Founder, CEO and Director of startup companies
- Founder & CEO of Response Biomedical, a publicly listed medical device company. Grew Response Biomedical from inception to a 100+ employee sales and manufacturing company

Rob Pilz, CPA, BComm (Finance), Chief Financial Officer
- 20+ years in strategic and operational planning, corporate finance, M&As, partnering, accounting, audit, HR and project management
- CFO positions in 3 Deloitte Technology Fast 50™ companies

Over 70+ years of corporate and managerial experience
Mike Abrams  
*Board of Directors*
Successfully transformed scientific discoveries into commercially successful products. Dr. Abrams co-invented Cardiolite which achieved +$500M peak annual sales of 500M. Founder, President & CEO of AnorMED for 10 years prior to its 2006 acquisition by Genzyme for $580M.

Brian McAlister  
*Advisor*
Prolific startup specialist for the past 30 years
Assisted +25 early stage biotechnology, enterprise software and natural resources companies including Novadigm, ManageIQ and Cohbar

Brian Bayley, MBA  
*Board of Directors*
30+ years of public issuer experience both as a director / officer, and has transaction experience over $2b
Currently, the Executive Chairman of Earlston Investments, a private merchant bank

Dr. Harold Punnett, DMD  
*Co-Founder, Board of Directors*
Founder and angel investor with a passion for developing solutions for helping those with spinal cord injuries and nerve related injuries
Plays active role in fostering early finance and partnering relationships for early stage companies

• FTO analysis revealed no issues

• Extensive IP estate with patent applications covering method of use for treating multiple diseases (cardiovascular, neurotrauma and CNS diseases)

• New IP generating studies underway
SCALABLE MANUFACTURING PROCESS

• Manufacturing using well established scalable peptide chemical synthetic techniques
• No bioprocessing production required
• Multiple small batches of NVG-291 successfully made at contract manufacturing facility
• Multiple GMP contract manufacturers available to perform synthesis
HIGHLIGHTS

PTPσ inhibitors - Breakthrough for nerve regeneration

- Unmet need for spinal cord and peripheral nerve injury
- Scientific leaders in the field
- Unmatched results in multiple independent studies
- Grants and peer reviewed papers
- Multiple disease indication
- Orphan Drug potential
- Product pipeline
For more information, please contact:

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