Neublastin: A Novel Potential Treatment for Neuropathic Pain

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Biogen Idec, with our partner NsGene, is pursuing clinical development of neublastin as an innovative, first-in-class, potentially restorative therapy for the treatment of neuropathic pain.

| Background | Neublastin (NBN, Artemin, Enovin)  
| Receptors (GFRα3) are highly expressed in pain-sensing neurons |
| Promising Efficacy | Neublastin **reverses chronic pain** induced by sensory nerve damage  
| Neublastin induces **long-lasting improvements in sensory and motor function** following nerve injury |
| Addresses High Unmet Need | Most patients have **inadequate response** to approved therapies (Lyrica, Neurontin, Cymbalta)  
| –54 to 86% have less than 50% improvement |
| | Tolerability of approved NP therapies is poor  
| –20% of patients **discontinue therapy** annually |
| | Many patients live with **disabling pain** and desire more effective therapies |
Neublastin

- NBN signals through its receptor GFRα3
- GFRα3 expression is limited to small fiber sensory neurons
- NBN is a potent survival factor for sensory neurons in vitro and in vivo
- Opportunity for targeted alleviation of pain, minimal CNS side effects
Animal Models of Neuropathic Pain

- Nerve Injury Models:
  - Distal Root Crush
  - Chronic Nerve Constriction
  - Chemotherapy Neuropathy

- Clinical Disorders:
  - Disc Compression
  - Diabetic Neuropathy
  - PHN
  - Root Avulsion

Sah, Ossipov and Porreca, 2003
Compelling Efficacy in Models of Neuropathic Pain

*NBN treatment normalizes changes in gene expression and signaling molecules that are associated with heightened sensitivity to pain.*
Systemic NBN Stimulates Repair and Reinnervation Following Dorsal Root Injury

*NBN treatment promotes long distance and long lasting repair of sensory axons following nerve crush*
Systemic Treatment with NBN Produces Long-term Recovery of Sensorimotor Behavior

NBN or vehicle given 3x per week for 2 weeks to rats subjected to distal nerve crush
Neublastin
Summary of Opportunity

• NBN treatment **reverses neuropathic pain** resulting from nerve injury

• NBN **restores synaptic connectivity** after root injury

• NBN produces **long-lasting recovery of sensorimotor function** following nerve injury

• NBN may represent an **innovative, first-in-class, potentially restorative** treatment for neuropathic pain and neuropathy associated with nerve damage