

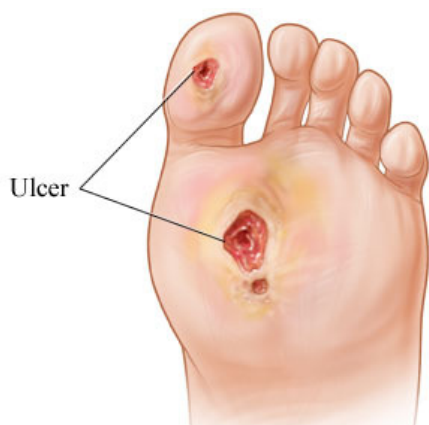
Amputation Prevention Molecule

Product Description

To prevent amputations resulting from diabetic foot ulcers, OmegaGenesis is developing a topical formulation of novel pro-angiogenic inorganic nanoparticles. A topical formulation of nanorods is periodically applied to diseased tissues to promote and improve local microvascular circulation and thereby, speed healing of tissues directly affected. A liquid suspension of nanorods will be formulated in a cream or gel using GRAS ingredients to enhance healing and ease application.

The ideal product will be dispensed using a metered dose pump or collapsible aluminum tube designed for frequent multi-dose applications to treat a chronic condition.

The product will be regularly applied to the ulcerous tissue and adjacent areas to stimulate the body's own defense and regenerative systems.



Foot Ulcer Area

A topical application of nanorods to the affected tissues stimulates blood flow and accelerates the healing process by growing new blood vessels.

Application and Patient Benefit

Foot amputation is an unfortunate outcome for as much as 12% of the affected population¹. Delaying or healing diabetic foot ulcers allows patients to experience normal walking and load bearing and potentially reduces the risk of or delays amputation.

Applications of OmegaGenesis formulated nanorods results in neogenesis (regeneration of biological tissues) through new microvasculature growth resulting improved local blood circulation. With blood flow restored, the patient avoids or delays surgical intervention and possible partial or whole foot amputation. Advanced cases may be treated with pro-angiogenic nanorod formulations resulting in improved function and rehabilitation.

1) Diabetes: foot ulcers and amputation, Dereck Hunt, Bmj Clinical evidence handbook, p.129, 2008.

Market Opportunity

Diabetic foot ulceration impacts over 3 million patients in the U.S. and over \$18.9 billion in treatment spent annually². According to the Centers for Disease Control and Prevention (CDC), the estimated incidence of diabetes in the US exceeds 1.5 million new cases annually, with an overall prevalence of 20.8 million

Amputation Prevention Molecule



people, or 7% of the US population. By 2030, the International Diabetes Federation predicts that the Global prevalence of diabetes will almost double from 193 million people to 366 million.

The most common cause of non-traumatic lower extremity amputations in the U.S. and Europe is diabetic foot ulcer, with an average of 166,000 amputations per year in the US costing an estimated \$11.7 billion annually². An estimated 25% of patients with diabetes will develop a lower extremity ulcer during the course of their disease³.

2) Journal of the American Podiatric Medical Association, March/April 2008, Vol 98, No 2, page 166

3) SINGH N, ARMSTRONG DG, LIPSKY BA: Preventing foot ulcers in patients with diabetes. JAMA 293: 217, 2005.

Scientific Insights

The underline risk factors for foot ulceration are peripheral neuropathy and ischemia. These changes can lead to pure neuropathic ulcers, pure ischemic ulcers or neuro-ischemic ulcers. The loss of pain sensation in the foot can lead to injure either suddenly or gradually. Low microvascular circulation reduces sweating and oxygenation of the tissue thus leading to local infection. The resultant ischemia hinders wound healing, turning the wound into a chronic ulcer.

Ischemia resulting from peripheral vascular disease is a risk factor for developing diabetic foot ulcer and infection. This disorder is considered a small vessel disease. Peripheral vascular disease manifests as insufficient blood tissue perfusion.

Pro-angiogenic products such as the OG nanorods have been shown to induce microvascular sprouting similar to VEGF. Formulating OG nanorods in a vehicle designed to enhance tissue contact and cell permeation results in endothelial cell proliferation and localized microvascular sprouting. With blood flow restored to affected tissues, it is anticipated that a normal healing process may be promoted.

Scientific evidence also demonstrates that OmegaGenesis nanorods have ROS (antioxidant) activity^{4,5}. Migration, adhesion, proliferation, neovascularization, remodeling, and apoptosis are main processes in wound healing regulated, or at least modulated by ROS mechanisms.

4) Adv. Mater. 2008, 20, 753–756

5) Digest Journal of Nanomaterials and Biostructures Vol. 3, No.4, December 2008, p. 159 – 162

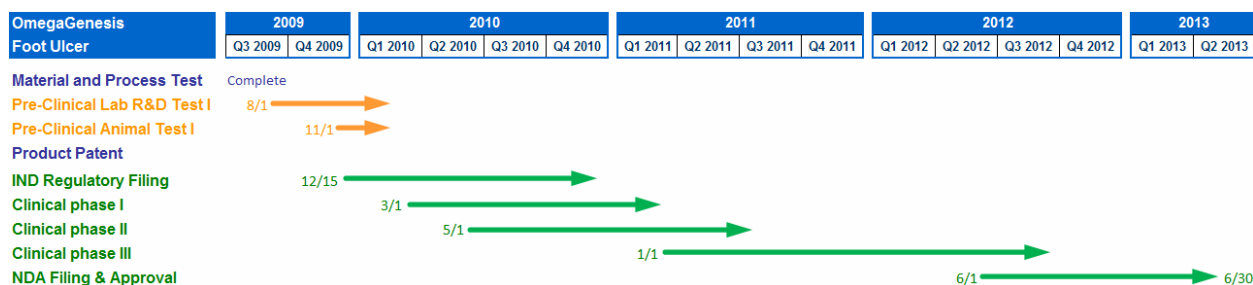
Test Phases and Timeline

While much work has been done to demonstrate the use of inorganic nanoparticles as therapeutic targets, laboratory studies have been started to formulate nanorods into a product which will be readily accepted in the market for over the counter or prescription use.

The planned stages are:

- Laboratory Research and Development to produce and formulate nanorods - June 2009
- In vitro pro-angiogenic formulation screening - July 2009
- In vivo animal model for example diabetic mice - October 2009
- FDA - IND filing - January 2010
- Phase 1 Clinical Trial - March 2010
- Subsequent Clinical trials - 2011

Amputation Prevention Molecule



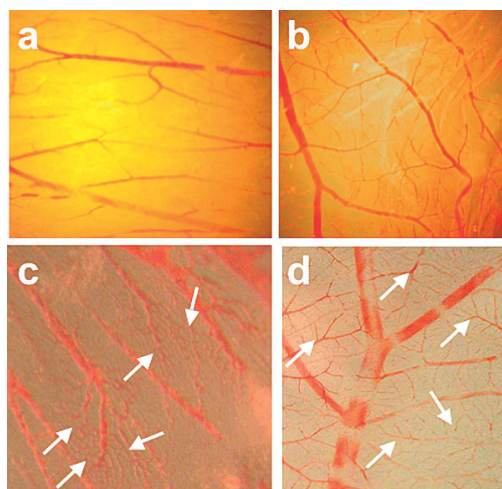
Test Results

In vitro and in vivo studies have been conducted to demonstrate the safety and efficacy of formulated nanorods in laboratory models. Findings from this work and additional studies will lead to initial clinical trials in diabetic foot ulcer patients.

Thus far we have shown:

- MAPK activation: mitogen activated protein kinase (MAPK) activation, a key signaling pathways for angiogenesis
- Cell cycle analysis using PI staining in HUVECs revealed a significant increase in the percentage of cells in the S-phase when treated with Eu III(OH)₃ nanorods as compared with that of untreated control cells.
- Internalization of Nanorods in the cytoplasm of HUVECs
- No induction of apoptosis in HUVECs.
- Chick CAM assays - induced CAMs angiogenesis and vascular sprouting
- Formation of Reactive Oxygen Species (ROS) - mechanism for angiogenesis
- Mice ear model for angiogenesis
- In vivo toxicity experiments on C57BL6 mice did not show any biochemical or hematological toxicity when the mice were treated with europium hydroxide nanorods (125mg/Kg/day).

Chick CAM Assay Demonstrates Blood Vessel Sprouting in Viable Tissue



Chick CAM assay demonstrating sprouting. (a) Treated with vehicle, (b) VEGF, (c and d) 1 and 10 µg nanorods

Partnership

In April, 2009 OmegaGenesis announced a partnership with The Department of Surgery at The University of Arizona College of Medicine to collaborate on potential remedies to address diabetic foot ulcers.