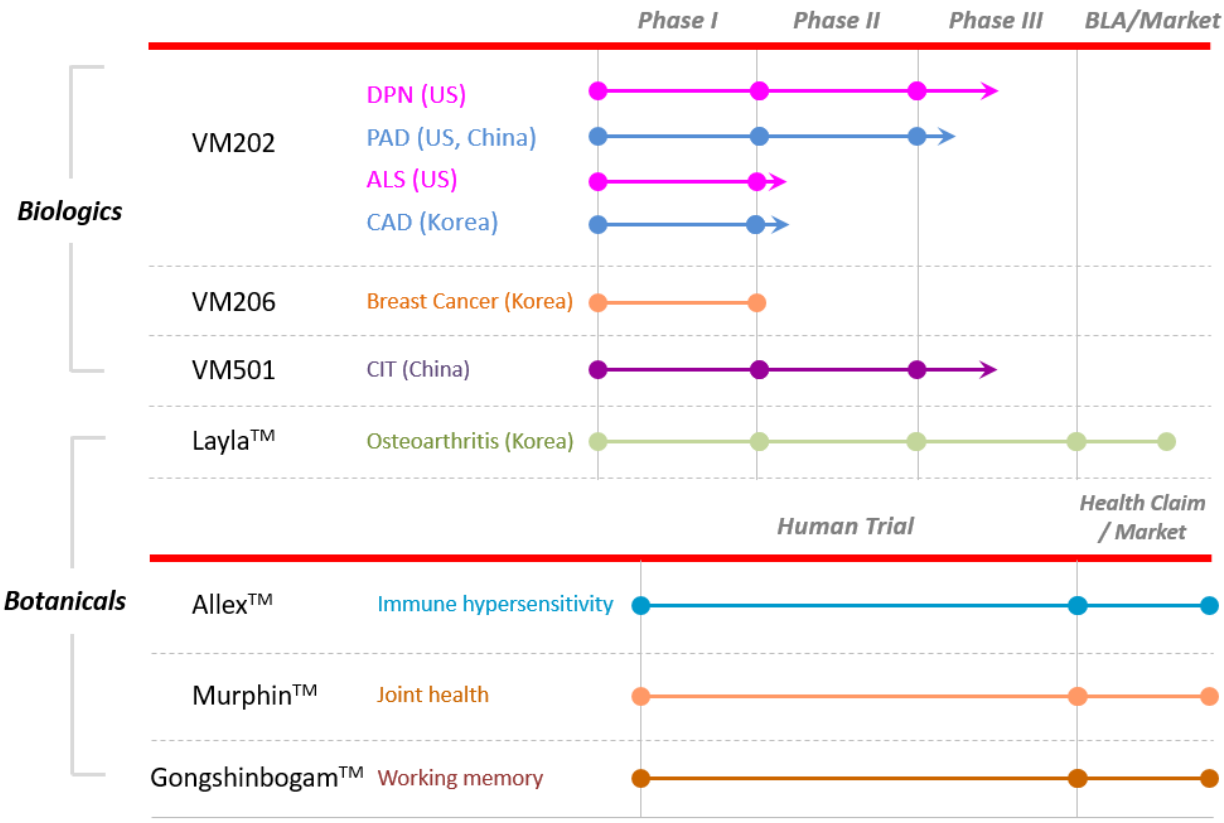
LEADER IN THE DEVELOPMENT OF INNOVATIVE BIOPHARMACEUTICALS

Established in 1996, ViroMed Co., Ltd. (ViroMed), a leading biopharmaceutical company focusing on the development of innovative biological drugs, is headquartered in Seoul, Korea with a US presence in Atlanta, GA. ViroMed has been listed on KOSDAQ (084990) since 2005 with the market capitalization at approximately USD 3.7 billion as of May 29, 2018.

ViroMed has assembled a diverse, yet technologically and conceptually linked pipeline of new and innovative therapeutics in areas such as cardiovascular and neurological diseases, cancers, and immune disorders; seven clinical trials using innovative DNA and protein based drugs are underway in the US, Korea, and China.
Meanwhile, ViroMed is also running a botanical therapeutics program, leveraging synergies and balancing its programs over the long term.



VM202 (*donaperminogene seltoplasmid*)

New and Innovative Drug for Cardiovascular and Neurological Diseases

Two Phase III clinical trials of VM202 are underway for diabetic peripheral neuropathy and chronic, non-healing foot ulcer associated with diabetes.

ViroMed's flagship biologics product VM202 is targeting to enter the market with high unmet medical needs such as cardiovascular and neurological diseases. VM202 is a DNA-based medicine designed to express two isoforms of the protein called hepatocyte growth factor (HGF). HGF is well known to induce the formation of new blood vessels and the growth and regeneration of nerve cells. Currently, VM202 is being tested for 4 major cardiovascular or neurological diseases. In all cases, VM202 is delivered by a series of simple intramuscular injections around the affected site.

VM202-DPN (Lead Indication, Painful Diabetic Peripheral Neuropathy, PDPN)

Diabetic Peripheral Neuropathy (DPN) is a common complication that affects 30 to 50% of patients with type 2 diabetes whose blood vessels are prone to damage due to high blood sugar levels, affecting the neighboring nerve cells and causing abnormally high levels of pain. Diminished sensory perception or abnormally heightened pain reception are the main symptoms, which may be accompanied by insomnia and depression. Other than analgesics, there is no effective treatment available that addresses the indication at a fundamental level. The annual market for DPN pain relievers is estimated to be USD 3 to 4 billion. However, not all patients are able to control their symptoms through painkillers, and adverse side effects from the use of painkillers are also reported.

High level of pain relieving effect and superior safety: The pain relieving effects of VM202 are greater than those of other pain killers on the market, with no serious drug-related adverse effects.

Convenient to use: Two rounds of VM202 injection – considered to be one treatment – can provide 9 (or more) months of pain relieving effect**.**

From the model used in clinical development and based on the results of the Phase II trial, VM202 would be categorized as an injectable gene therapy for the long term relief of pain associated with diabetic peripheral neuropathy. In our Phase II trial of VM202-DPN, two days of VM202 treatment demonstrated significant pain reduction effect in patients and improvement in quality of life for the 9 month follow-up period. Patients not on pregabalin or gabapentin had the largest reductions in their pain, suggesting that VM202 potentially can provide medical benefits for patients for whom no pain relievers have, to date, been available.

The therapeutic advantages that VM202 has as compared to other currently available PDPN treatments are its prolonged analgesic effect and lack of adverse side effects, which renders the cost benefit model completely different from other analgesics: while in-office VM202 administration may have a relatively high initial cost, some patients may only require 1 or 2 treatments per year; the response rate would be superior to other analgesics; and currently there are no adverse events or safety issues.

Potential as a disease modifying drug: VM202 not only reduces pain symptoms but has the potential to modify PDPN progression by repairing the damaged neurons.

As the potential of VM202 to improve sensation in patients with diabetic neuropathy was confirmed in Phase II through monofilament test, should Phase III data also demonstrate VM202 to be disease-modifying, the labeling and target population of VM202 may be significantly expanded. It could be potentially introduced to patients with DPN in its earlier stages, who would then benefit from the therapeutic effect of VM202 in restoring nerve function rather than simply relieving symptoms. Recognizing VM202's potential, the US FDA granted RMAT (Regenerative Medicine Advanced Therapy) designation to VM202-DPN in May, 2018.

In summary, the efficacy and safety records of VM202 are outstanding as compared to other currently used drugs. VM202 is positioned to not only take a significant fraction of the current PDPN market but also create a new market by providing pain relief to patients for whom virtually nothing is available at present, and by stopping or reversing disease progression.

VM202-PAD (Non-healing ischemic foot ulcers in patients with diabetes, NHU)

For the treatment of non-healing foot ulcers in diabetic patients with peripheral arterial disease (PAD), VM202 offers a therapeutic modality completely different from therapies currently in use.

Therapeutic modality completely different from therapies currently in use:
VM202 aims to improve blood flow into the foot through collateral vessel formation.

In our Phase II trial of VM202-CLI (critical limb ischemia), VM202 treatment resulted in significant reductions in ulcer area and meaningful improvement of tissue oxygenation in patients. Moreover, complete ulcer healing was seen in a higher percentage in VM202 treated patients. Rather than manipulating the wound environment with local application of growth factors and specialized dressings, VM202 aims to improve blood flow into the foot while compensating for the underlying PAD with collateral vessel formation. The expectation is that, by addressing the underlying vascular pathology, healed ulcers would reopen less frequently and new ulcers would not form, hence infection and amputation rates would potentially decrease.

Treatment would consist of 4 days of in-clinic VM202 injections, each day spaced 2 weeks apart, in the target leg combined with standard wound care dressings and offloading. As these patients are already subject to weekly or biweekly clinic visits for dressing changes, incorporating VM202 in their care would be straightforward. While VM202 may seem expensive, extended periods of wound care, dressings, and other auxiliary wound therapies (e.g. hyperbaric oxygen) could be even costlier over time and may not improve the long term infection and amputation rates since they do not address the underlying PAD.

VM202-CAD (Ischemic heart disease, IHD)

VM202-CAD is currently under development to target ischemic heart disease (IHD), a cardiovascular disease also known as coronary artery disease (CAD). CAD occurs when the coronary artery is narrowed or occluded. Myocardial infarction and angina pectoris are the two types of CAD, for which treatment options include bypass surgery, stent insertion, and the use of drugs such as cholesterol lowering agents and thrombolytic agents. The estimated annual medical costs associated with CAD are almost USD 20 billion, and it remains a leading cause of death in developed countries. As such, there is a high demand for medical treatments that are effective and safe.

For the indication of IHD, VM202 would be administered as multiple myocardial injections via intravascular catheter following acute myocardial infarction. Preclinical and Phase I data suggest VM202 improves myocardial perfusion and function while reducing post-infarction scarring. Phase II data are eagerly awaited for the role of VM202 in the treatment of ischemic heart disease.

VM202-ALS (Amyotrophic Lateral Sclerosis, ALS)

VM202-ALS is currently under development to target ALS (Lou Gehrig's disease), a neurodegenerative disease. The condition is characterized by the destruction of motor neurons necessary for the mobility muscle groups such as the tongue, neck, and limbs, with the disease development mechanism yet undefined. It is estimated that there are about 30,000 ALS patients in the US alone. ALS mostly occurs in adults with 2 to 5 years of expected survival period. As the disease progresses, everyday activities are gradually compromised, and patients eventually become dependent on a ventilator for respiration. According to the ALS Therapy Development Institute (US), a market of USD 2 to 4 billion would be created when an innovative drug becomes available for ALS. In our Phase I study, some patients demonstrated slower disease progression while some patients' ALSFRS-R showed their body functions improved, suggesting VM202 may provide medical benefits in the care of ALS patients.

List of Publications on VM202

Expression vector pCK and therapeutic gene HGF

1. Lee *et al.,* Improved expression of vascular endothelial growth factor by naked DNA in mouse skeletal muscles: implication for gene therapy of ischemic diseases., *Biochemical and Biophysical Research Communications,* 2000;272:230-235.
2. Pyun *et al.*, Naked DNA expressing two isoforms of hepatocyte growth factor induces collateral artery augmentation in a rabbit model of limb ischemia., *Gene Therapy*, 2010;17:1442-1452.

Preclinical

3. Carlsson *et al.,* Quantitative MR measurements of regional and global left ventricular function and strain after intramyocardial transfer of VM202 into infarcted swine myocardium., *American Journal of Physiology - Heart and Circulatory Physiology*, 2008;295:H522-532.
4. Cho *et al.,* Therapeutic angiogenesis using naked DNA expressing two isoforms of the hepatocyte growth factor in a porcine acute myocardial infarction model., *European Journal of Cardio-thoracic Surgery*, 2008;34:857-863.
5. Saeed *et al.,* MR assessment of myocardial perfusion, viability, and function after intramyocardial transfer of VM202, a new plasmid human hepatocyte growth factor in ischemic swine myocardium., *Radiology*, 2008;249:107-118.
6. Saeed *et al.*, Cardiovascular magnetic resonance imaging in delivering and evaluating the efficacy of hepatocyte growth factor gene in chronic infarct scar., *Cardiovascular Revascularization Medicine*, 2011;12:111-122.
7. Perin *et al.*, Human hepatocyte growth factor (VM202) gene therapy via transendocardial injection in a pig model of chronic myocardial ischemia., *Journal of Cardiac Failure*, 2011;17:601-611.
8. Hahn *et al.*, Enhanced cardio-protective effects by coexpression of two isoforms of hepatocyte growth factor from naked plasmid DNA in a rat ischemic heart disease model., *The Journal of Gene Medicine*, 2011;13:549-555.
9. Nho *et al.,* Effective control of neuropathic pain by transient expression of hepatocyte growth factor in a mouse chronic constriction injury model., *The FASEB Journal,* 2018 Apr 16, doi: 10.1096/fj.201800476R [Epub ahead of print]
10. Ko *et al.,* Hepatocyte growth factor (HGF) promotes peripheral nerve regeneration by activating repair Schwann cells., *Scientific Reports,* 2018 May 29, doi: 10.1038/s41598-018-26704-x [Epub ahead of print]

Clinical

1. ***VM202-PAD (Critical Limb Ischemia)***
   Henry *et al.,* Safety of a non-viral plasmid-encoding dual isoforms of hepatocyte growth factor in critical limb ischemia patients: a phase I study., *Gene Therapy*, 2011;18:788-794.
2. ***VM202-PAD (Critical Limb Ischemia)***
   Gu *et al.,* A phase I clinical study of naked DNA expressing two isoforms of hepatocyte growth factor to treat patients with critical limb ischemia., *The Journal of Gene Medicine*, 2011;13:602-610.
3. ***VM202-CAD (Ischemic Heart Disease)***
   Kim *et al.,* Intramyocardial transfer of hepatocyte growth factor as an adjunct to CABG: phase I clinical study., *Gene Therapy*, 2013;20:717-722.
4. ***VM202-DPN (Diabetic Peripheral Neuropathy)***
   Ajroud-Driss *et al.,* Phase 1/2 open-label dose-escalation study of plasmid DNA expressing hepatocyte growth factor in patients with painful diabetic neuropathy, *Molecular Therapy*, 2013;21:1279-1286.
5. ***VM202-DPN (Diabetic Peripheral Neuropathy)***
   Kessler *et al.,* Double-blind, placebo-controlled study of HGF gene therapy in diabetic neuropathy, *Annals of Clinical and Translational Neurology*, 2015;2:465-478.
6. ***VM202-PAD (Critical Limb Ischemia)***
   Kibbe *et al.,* Safety and efficacy of plasmid DNA expressing two isoforms of hepatocyte growth factor in patients with critical limb ischemia., *Gene Therapy*, 2016;3:306-312.
7. ***VM202-ALS (Amyotrophic Lateral Sclerosis)***
   Robert L. Sufit *et al.,* Open label study to assess the safety of VM202 in subjects with amyotrophic lateral sclerosis., *Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration*, 2017 May;18(3-4):269-27.

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