



# ViroMed

## A Leader in the Development of New and Innovative Biopharmaceuticals

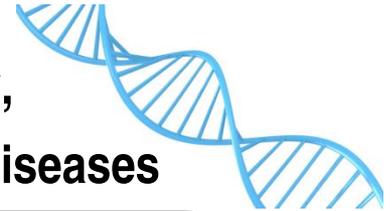
This document has been prepared by ViroMed for the sole purpose of providing information through investigator relations presentation targeting institutional and general investors. The presented material contains future projection and forecasts of the business. The future projection and forecasts provided have been faithfully composed based on rationale and assumption. Such projection and forecasts, however, contain uncertainty and risks and may result different outcomes. The innate uncertainty and risks include changes in overall management, financial markets, related laws and regulations.



# ViroMed Overview

✓ **Develops innovative biologics**

- **Pioneer and global leader in plasmid DNA-based gene therapy, developing therapeutics for cardiovascular and neurological diseases**



- **Established:** Nov. 21, 1996
- **IPO:** Dec. 29, 2005 (KOSDAQ: 084990); latest market cap, \$ >3 Billion
- **No. of employees:** + 90 (R&D >50)
- **Locations:** Seoul, Korea and San Diego, California, US
- **Webpage:** [www.viomed21.com](http://www.viomed21.com)



**Present**



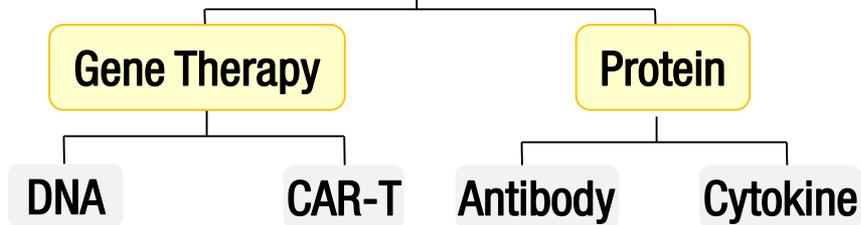
**ViroMed (Magok, Seoul)**  
To be completed in 4Q. 2019



**ViroMed (San Diego, California)**  
Genopis Inc.

# Product Portfolio

## Biologics



Phase III (US)

- Diabetic Peripheral Neuropathy
- Diabetic Non-Healing Foot Ulcer

- Hematological tumors
- Solid tumors

• 1E4

- Thrombocytopenia

Phase III (China)

- Lou Gehrig's Disease ← Phase II (US)
- Ischemic Heart Disease ← Phase II (Korea)
- Neurovascular Diseases
- Neuromuscular Diseases

## Phytotherapeutics

Prescription Drugs

Nutraceuticals with Health Claim

Launched

- Osteoarthritis
- ADHD

- Allergic disease
- Memory improvement
- Joint Health
- Prostate health
- Respiratory health
- Insomnia

# Leadership Highlights

## Proprietary gene therapy platform technologies

Can lead to development of multiple products for various human diseases with high unmet medical needs

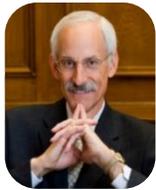


**Seungshin Yu, Ph.D.**

Managing Director,  
Research &  
Business Development

**William Schmidt, Ph.D.**

Vice President,  
Global Clinical Development



## High level skills and expertise in clinical development

### Capabilities of:

- Designing clinical protocols for first-in-class drugs
- Establishing clinical networks
- Conducting clinical studies in time- and cost-honored manners



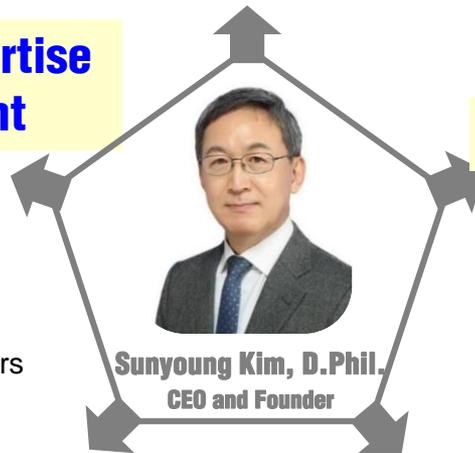
**Jun Tae Park, Ph.D.**

Executive Vice President,  
Licensing & Regulatory Affairs



**Cathy Carroll, Ph.D.**

Director,  
Market Access



**Sunyoung Kim, D.Phil.**  
CEO and Founder

## Manufacturing capability

Manufacturing capability for go-to-market: facility in San Diego



**Keith Hall**

COO  
GENOPIS  
in San Diego

## Commercial potential

- VM202 with blockbuster potential with an aim to enter the market in 2021
- Targeting major human diseases with high unmet medical need

## Innovative botanical pipeline

- Proven records in effective R & D and profitability
- Targeting diseases for which current small molecules and biologics are proved ineffective
- Aiming to enter global market



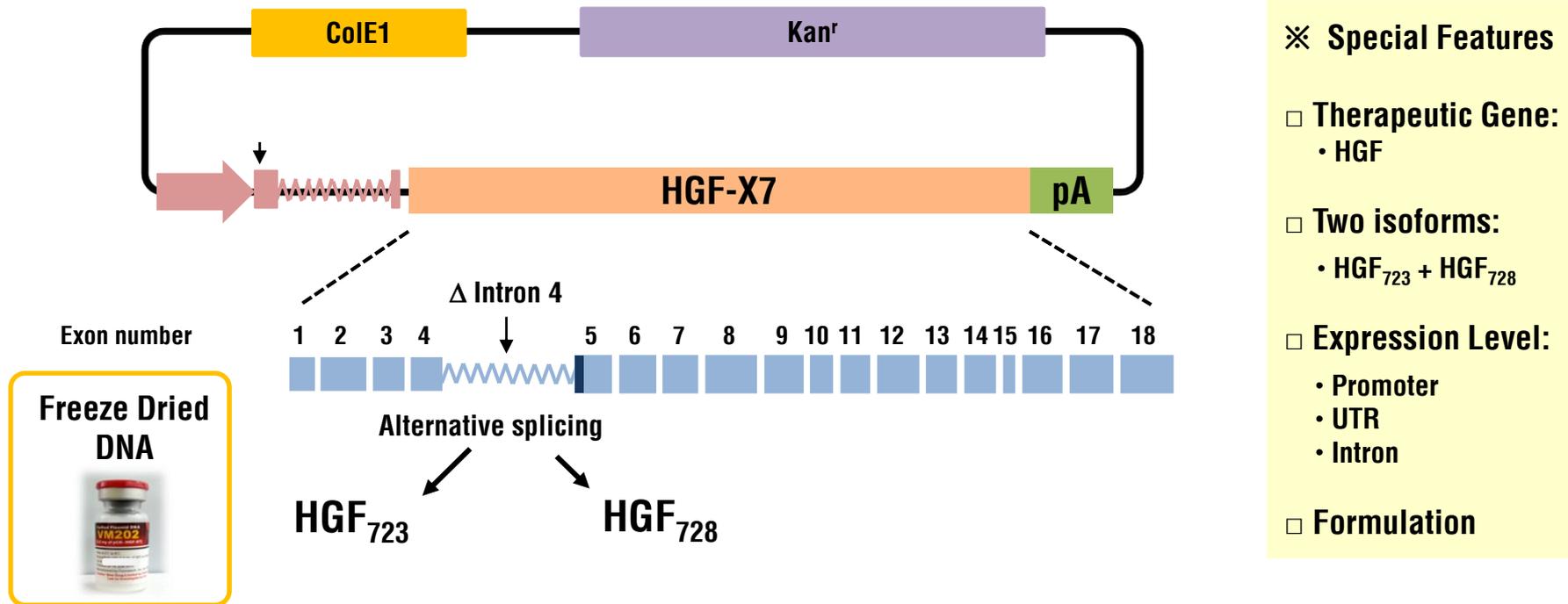
**Miwon Son, Ph.D.**

Senior Managing Director,  
Phytotherapeutics

# Flagship Product – VM202

Innovative DNA medicine that induces **formation of new blood vessels** and **repair of damaged neurons** through a simple series of IM injections

- Plasmid DNA designed to simultaneously express two isoforms of HGF -



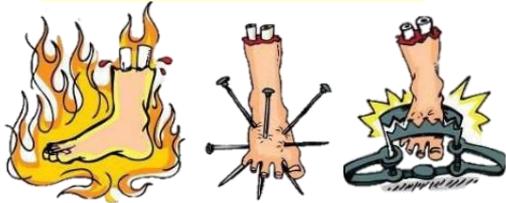
## ✘ Special Features

- Therapeutic Gene:
  - HGF
- Two isoforms:
  - HGF<sub>723</sub> + HGF<sub>728</sub>
- Expression Level:
  - Promoter
  - UTR
  - Intron
- Formulation

**ViroMed has a strong patent position with VM202.**

# Simple intramuscular injections of VM202 can create new blood vessels and repair damaged neurons.

## • Neuropathic Pain



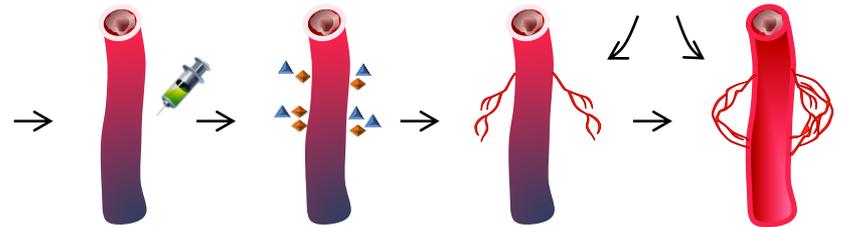
## • Peripheral Artery



## • Coronary Artery



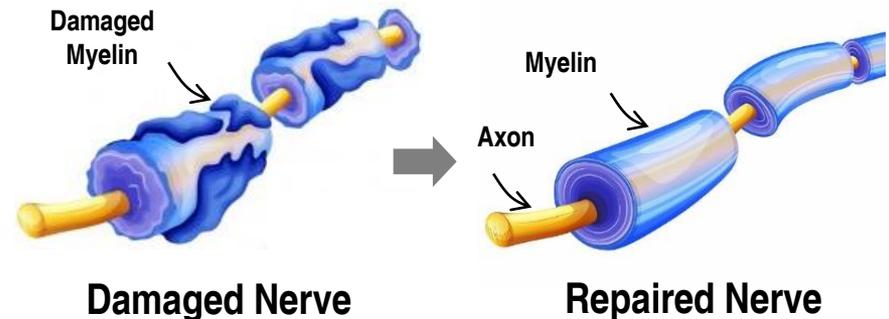
## ① Angiogenesis



## ② Reduction in the level of pain factors

(CSF-1, IL-6,  $\alpha 2\delta 1$ , 5-HTT, etc.)

## ③ Regeneration of damaged nerves

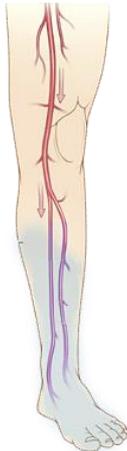
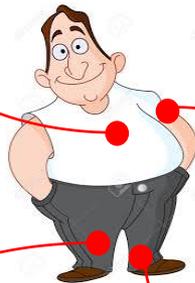
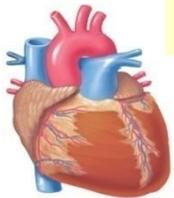


# Clinical Development of VM202

## Cardiovascular

Coronary Artery Disease  
Acute Myocardial Infarction

Phase II (Korea) planned



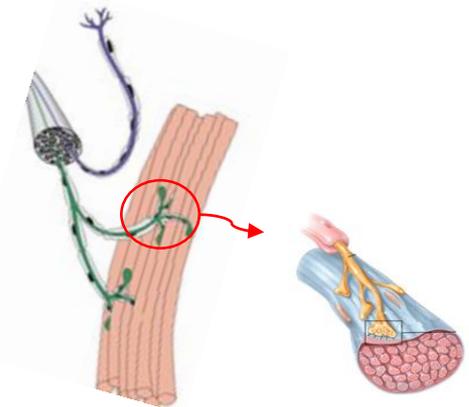
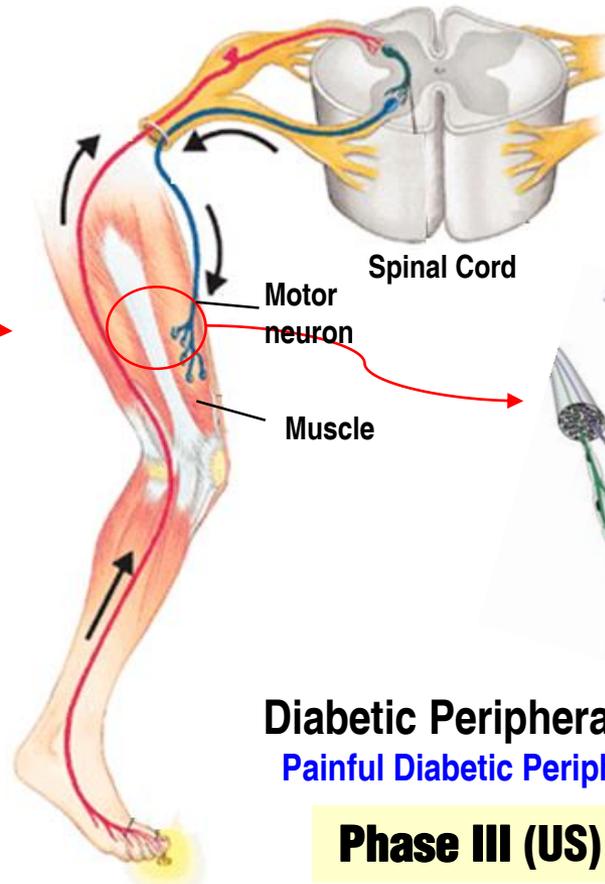
Peripheral Artery Disease  
Diabetic Foot Ulcer

Phase III (US) ongoing

## Neurological

Amyotrophic Lateral Sclerosis  
Lou Gehrig's Disease

Phase II (US) planned



Diabetic Peripheral Neuropathy  
Painful Diabetic Peripheral Neuropathy

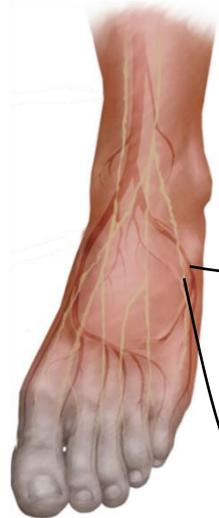
Phase III (US) ongoing

# 1<sup>st</sup> Target Disease of VM202

## Painful Diabetic Peripheral Neuropathy (PDPN)

- One of the most frequently observed neuropathies associated with 30% of all diabetes patients
- Patients suffer from **sensory loss, dysesthesia, and night time pain.**

### Hyperglycemia



### Blood vessel damage



Nerves shrivel  
when blood vessels disappear

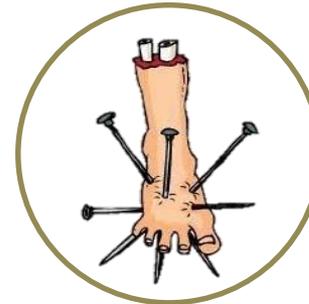
Normal

Blood vessel

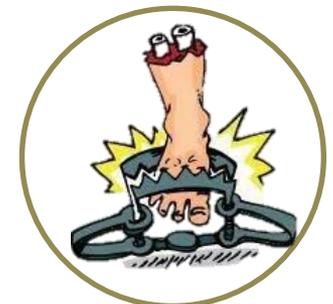
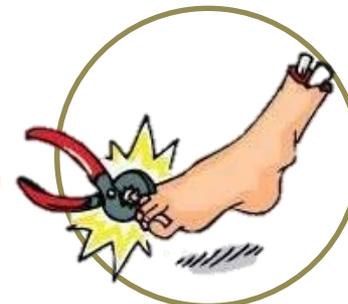
Nerve



### Painful diabetic peripheral neuropathy



**Throbbing, Burning, Stabbing, Tingling**



# Currently Used Medicines for Painful DPN

- **There are 3 major drugs, generating \$ 3 - 4 billion market.**

- **Anticonvulsants:** **Pregabalin (Lyrica<sup>®</sup>, Pfizer)**  
\$ ~5.1 B (2014), Neuropathic pain market: 30-50%
- **Gabapentin (Neurontin<sup>®</sup>, Pfizer)**  
\$ ~ 210 M (2014)
- **Antidepressants:** **Duloxetine (Cymbalta<sup>®</sup>, Eli Lilly)**  
\$ 5 B (2013), Neuropathic pain market > \$1 B
- NSAIDs
- **Opioids:** **Tapentadol (Nucynta<sup>®</sup> ER, Depomed)**  
\$ 281 Million (US, 2016)

## Improvement Needed in

- Safety and tolerability profile
- Efficacy profile
- Curative or disease-modifying capability

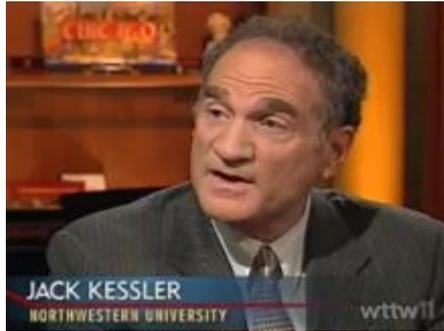
## Limitations

- Pain relief only → No disease-modifying capability
- Modest treatment benefit
- Tolerability issue and side effects minimize compliance
- 40% PDPN patients with no option to control or manage their pain

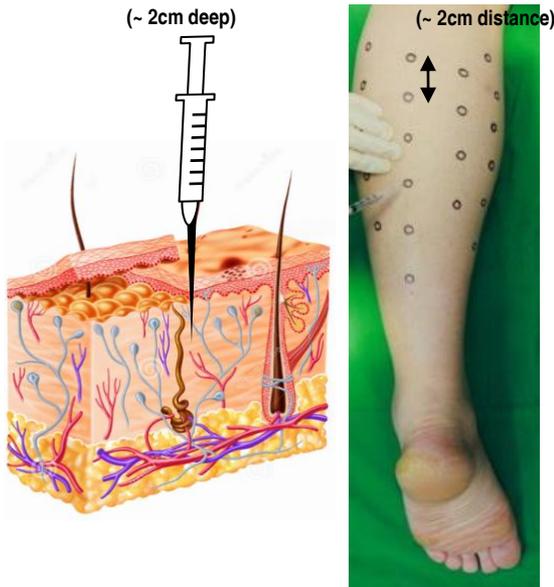
# Study Outline of VM202-DPN Phase II

A Double-Blind, Randomized, Placebo-Controlled, Multicenter Study (US, Korea)

Principal Investigator  
JOHN (JACK) A. KESSLER, M.D.  
(Northwestern Medical School)

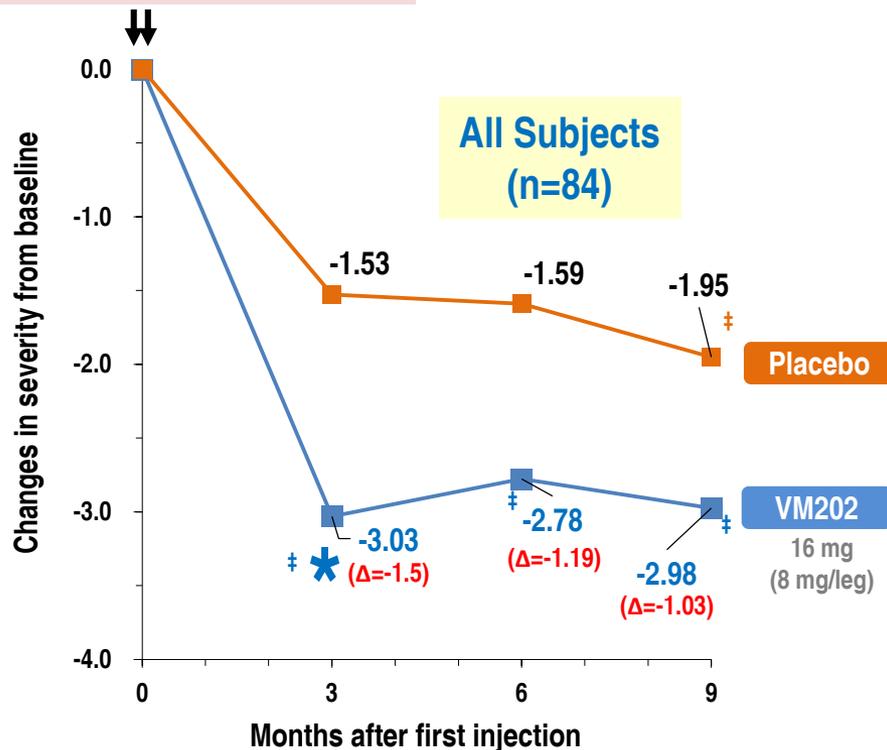


- 1. Indication:** Painful Diabetic Peripheral Neuropathy
- 2. Total administered subjects:** 103
- 3. Injection scheme**  
Bilateral 2 injection cycles along the calf line (day 0 & 14)
- 4. Follow-up period:** 9 months
- 5. Efficacy**
  - Pain score (Daily Pain and Sleep Interference Diary)\*
  - VAS\*, BPI-DPN\*, MNSI, PGIC\*, etc.
- 6. Safety**



# Effect on Pain Severity (Daily Pain Diary)

2 Rounds of IM injection of VM202

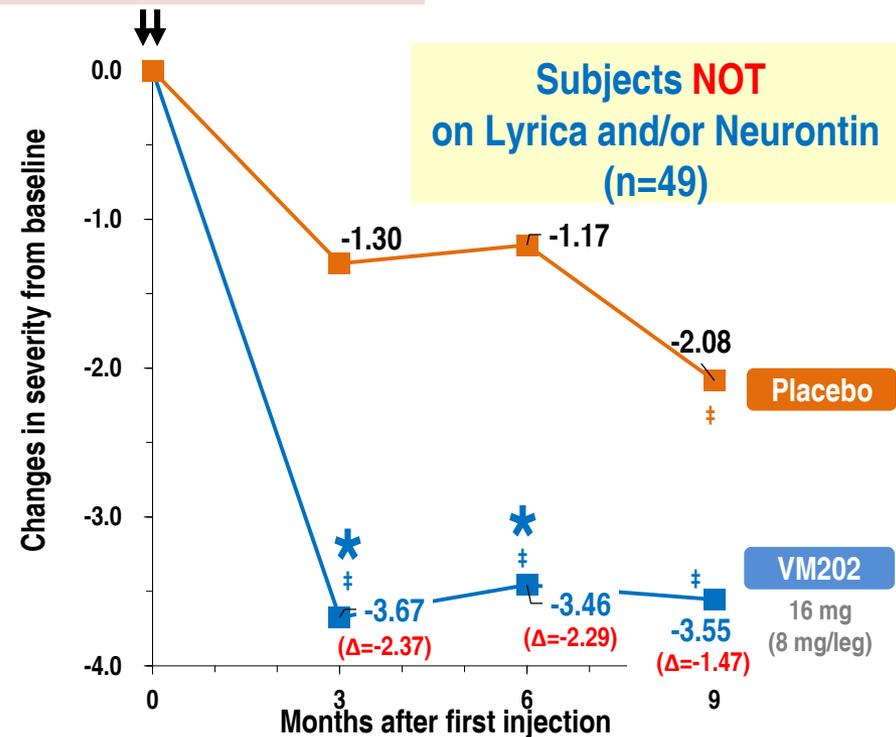


[\* $p<0.05$ , vs. placebo, † $p<0.05$ , vs. baseline,  $\Delta$  VM202 16mg – Placebo]

**High long-term pain-relieving effects**

Simplified from Kessler et al. *Annals of Clinical and Translational Neurology*, 2: 465-478 (2015)

2 Rounds of IM injection of VM202

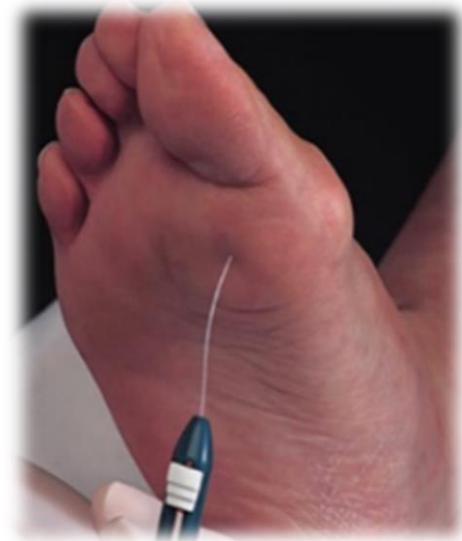


[\* $p<0.05$ , vs. placebo, † $p<0.05$ , vs. baseline,  $\Delta$  VM202 16mg – Placebo]

**Higher pain-relieving effects in subjects NOT on gabapentin and/or pregabalin**

# Key Discoveries of DPN Phase II Trial

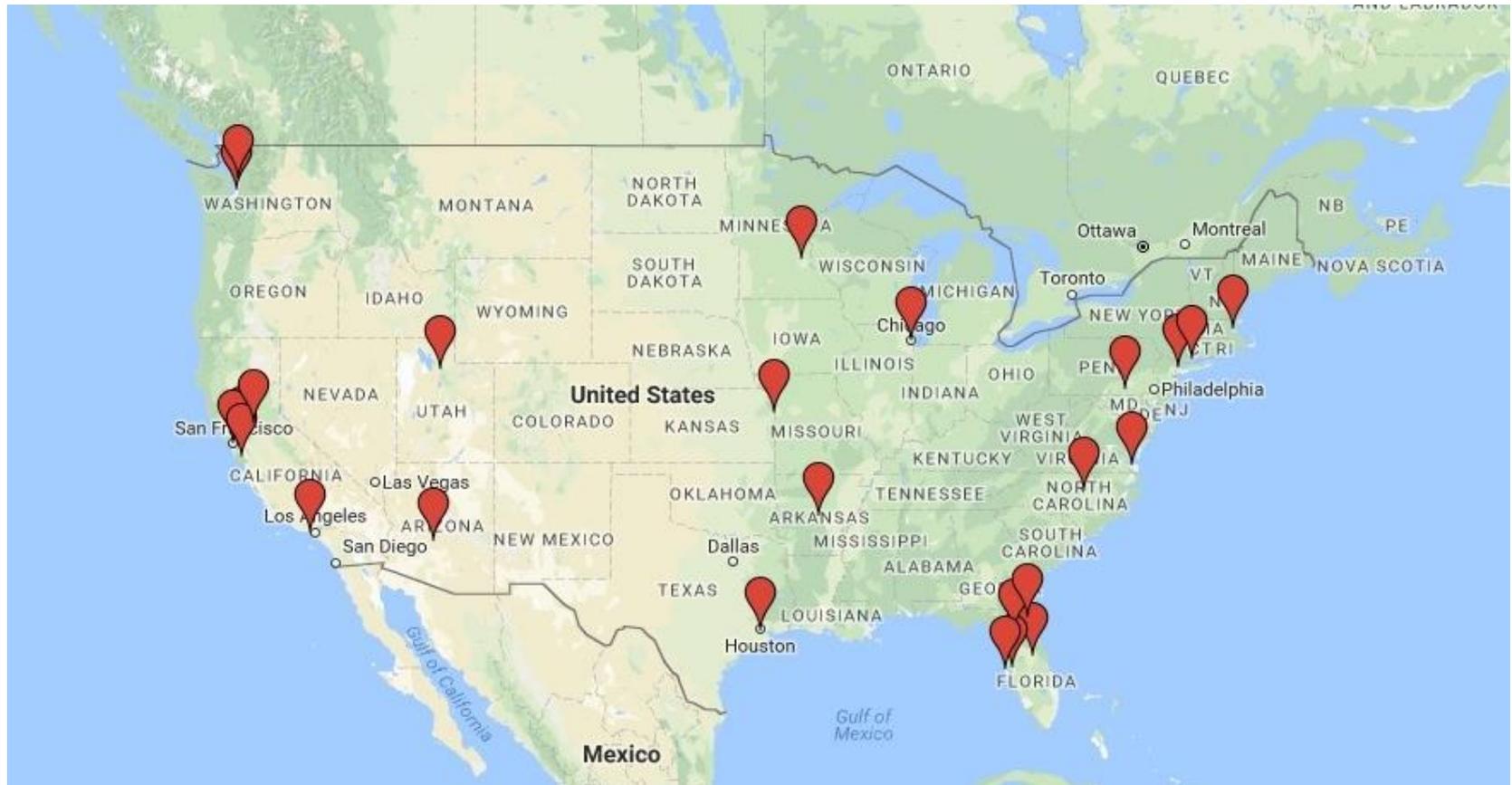
1. An **excellent safety profile** compared to current prescription drugs.  
(No antibody to HGF, No change in HGF serum level).
2. **Significant improvements in all pain measurements** for a long period of time. (Daily pain diary, BPI-DPN, VAS, PGIC)
3. Pain relieving effects **were more pronounced in patients not taking Lyrica and/or Neurontin.**
4. Data from monofilament tests suggested that VM202 might aid recovery of sensory functions and have the potential to be a **disease-modifying drug.**



# Current Phase III Clinical Trial

- **Enrollment Goal:**
  - **477 subjects randomized in a 2:1 ratio of VM202 to placebo**
- **Enrollment as of 31 Jul, 2018:**
  - **494** randomized (103%)
  - **230** completed study to full 9 months
- **Dropouts: 37 discontinued study (7.5% = much lower than other trials)**
- **Concomitant DPN medications as of Jul 31, 2018 (N = 487):**
  - **Receiving Lyrica (35) or Neurontin (203) or Both (4) = 242 total**
  - **Not receiving Lyrica and Neurontin = 245**

# Phase III Clinical Trial Sites



- 25 geographically-distributed sites in the USA

# RMAT Designation

## (Regenerative Medicine Advanced Therapy)

**VM202 for PDPN was granted RMAT by FDA on 21 May 2018, the first and only RMAT for a gene therapy targeting a prevalent disease.**

### Eligibility

- A regenerative medicine therapy in cell and gene therapy
- Drugs intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition
- Preliminary clinical evidence indicates potential to address unmet medical needs.

### Benefits

- Include all of the benefits of *Fast track* and *Breakthrough* designation programs
- Allows **shorter timeline for BLA approval** including early interactions with FDA

### RMAT Status

- 20 designations granted (as of Jun, 2018)
- Among them, 15 also have orphan designation (cancer: 2, inherited disease: 6)  
5 are in gene therapy (cancer: 1, inherited disease: 3)
  - ✓ Autologous hematopoietic stem cell transplantation in beta-thalassemia (LentiGlobin)
  - ✓ CD19 activity of modified T cells (CAR-T) in large B cell NHL (JCAR017)
  - ✓ Autologous gene-corrected cell therapeutics in recessive RDEB (EB-101)
  - ✓ AAV delivery of SGSH gene in MPS IIIA (ABO-102)
  - ✓ **Plasmid delivery of HGF gene in painful diabetic peripheral neuropathy (VM202)**

# New PDPN Drug Candidates in Late Stage Clinical Studies

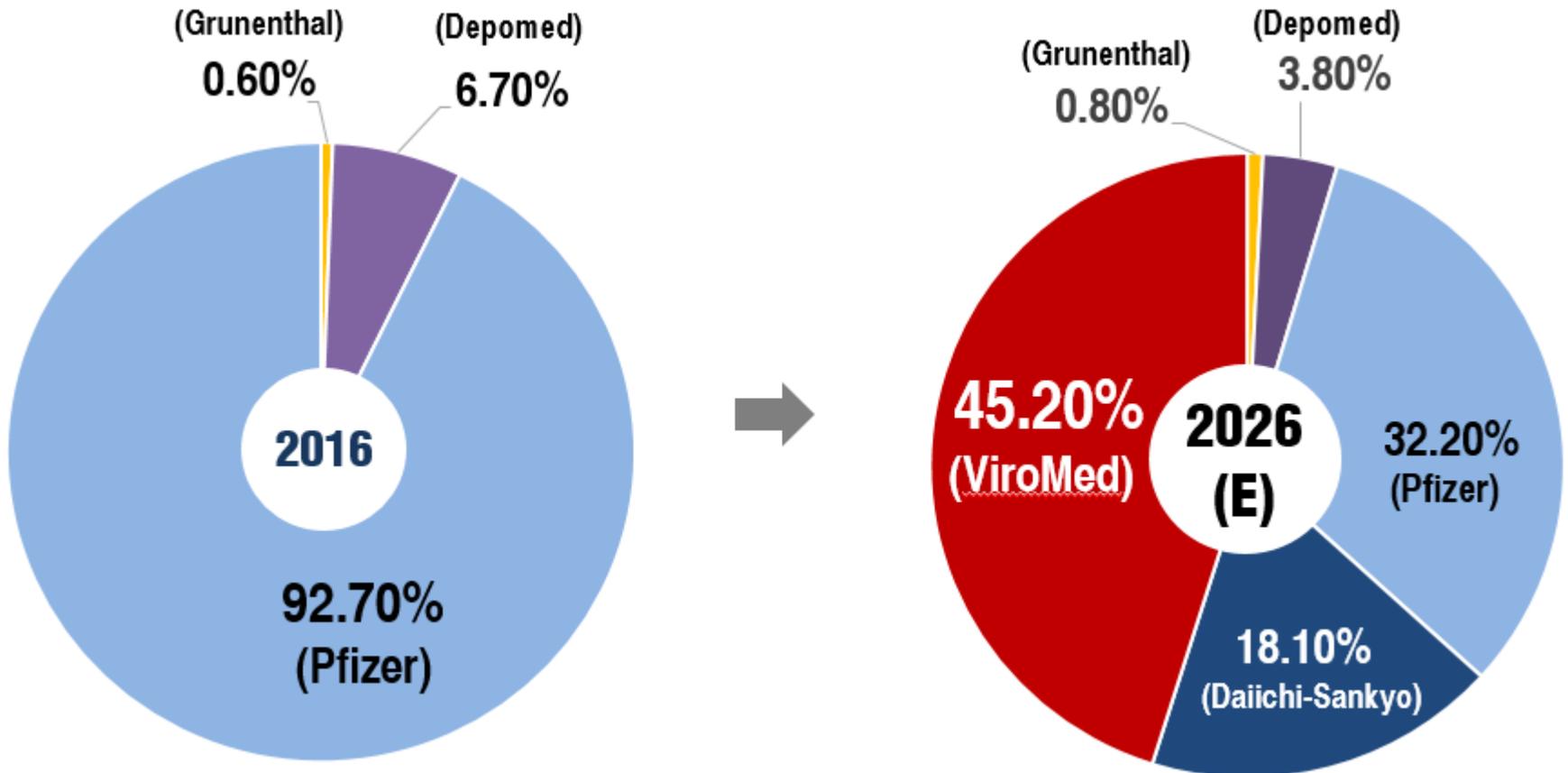
(as of Dec 2017)

Therapeutic class	Pipeline name	Status	Features
<b>Gene therapy</b>	<b>VM202</b> (ViroMed)	<b>Phase III</b>	<ul style="list-style-type: none"> <li>• 1<sup>st</sup> gene therapy</li> <li>• Excellent safety &amp; efficacy profile</li> <li>• Long-term therapeutic effect</li> <li>• Disease-modifying potential</li> </ul>
$\alpha 2\delta$ -1 inhibitor	<b>Mirogabalin Besylate</b> (Daiichi-Sankyo)	<b>Phase III</b>	<ul style="list-style-type: none"> <li>• Improved safety, tolerability and efficacy than pregabalin</li> <li>• Favorable safety profile</li> <li>• Expected to be used as 1<sup>st</sup> line therapy anticonvulsant</li> </ul>
<b>Mu opioid + NOP opioid</b>	<b>Cebranopadol</b> (Grünenthal/ Depomed)	<b>Phase II</b>	<ul style="list-style-type: none"> <li>• Favorable efficacy</li> <li>• Associated with potential abuse and serious AE</li> <li>• Expected to be used as 3<sup>rd</sup> line therapy</li> </ul>
<b>Small molecule</b> NMDA	<b>NYX-2925</b> (Aptinyx)	<b>Phase II</b>	<ul style="list-style-type: none"> <li>• NMDA antagonist</li> <li>• PDPN, fibromyalgia</li> <li>• Expected to be used as 3<sup>rd</sup> line therapy</li> </ul>
<b>Sigma<sub>1</sub></b>	<b>S1A (MR309, E-52862)</b> (Mundipharma/ Purdue Pharma/ Esteve)	<b>Phase II</b>	<ul style="list-style-type: none"> <li>• Sigma 1 antagonist</li> <li>• Neuropathic pain (diabetic neuropathy; post-surgical; nerve injury); acute post-operative pain</li> </ul>
<b>TCA/NMDA antagonist combination</b>	<b>AmiKet</b> (EpiCept/ Immune Pharmaceuticals / Maxim Pharmaceuticals)	<b>Phase II</b>	<ul style="list-style-type: none"> <li>• Amitriptyline &amp; Ketamine</li> <li>• Blocks the ability of peripheral nerve receptors to transmit pain messages</li> <li>• Dual MoA leads to increase in pain relief</li> </ul>

# VM202, potential to become the FIRST disease-modifying drug to enter the PDPN market

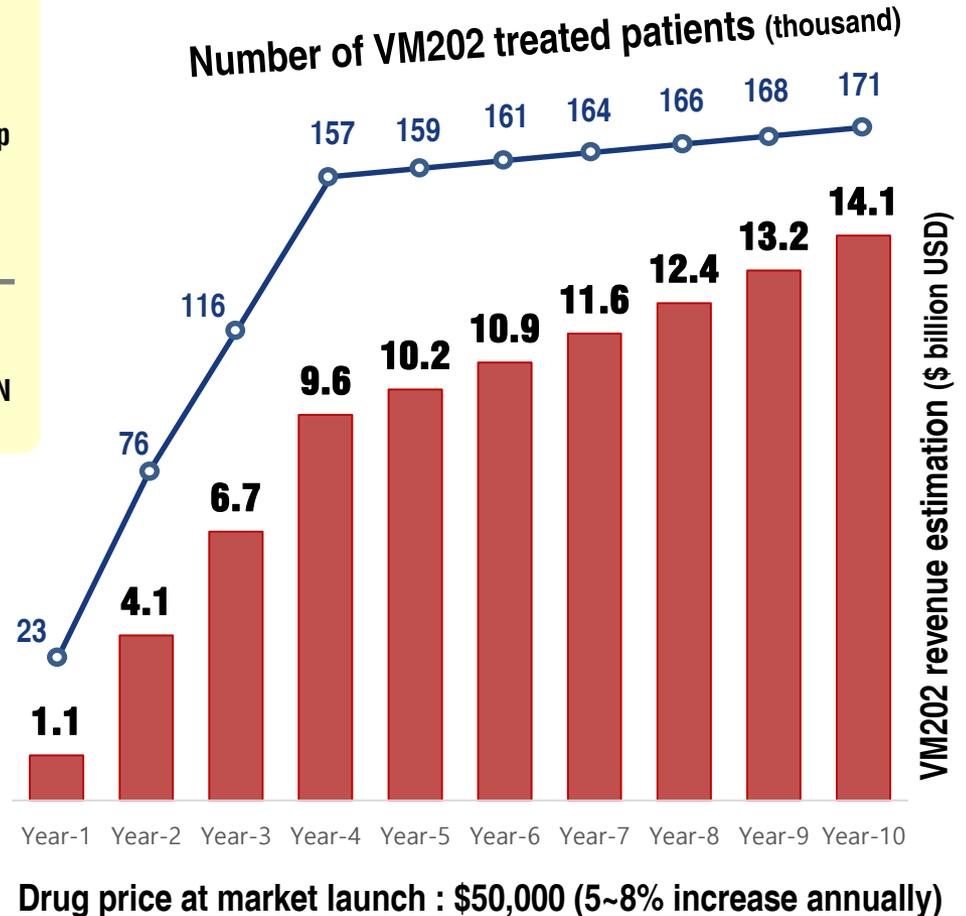
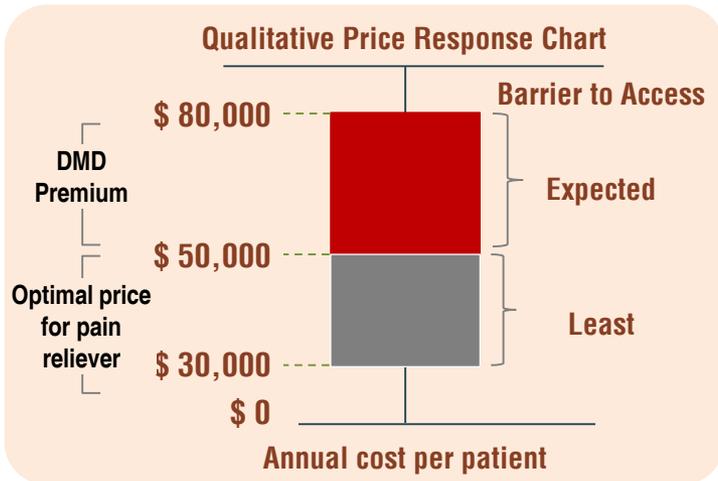
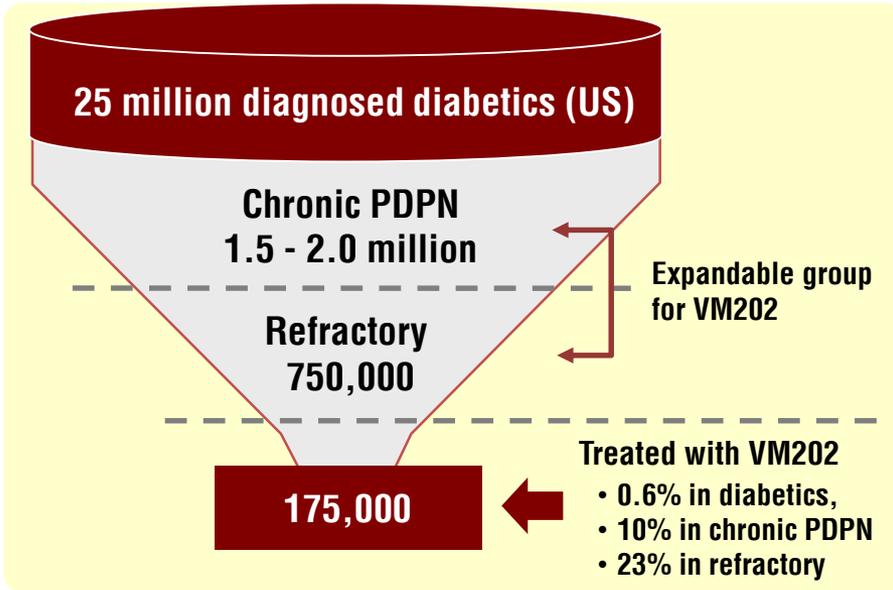
## Geographical distribution of global PDPN sales

(by GlobalData PDPN market forecast, 2018)



# PDPN & VM202 Market Estimation

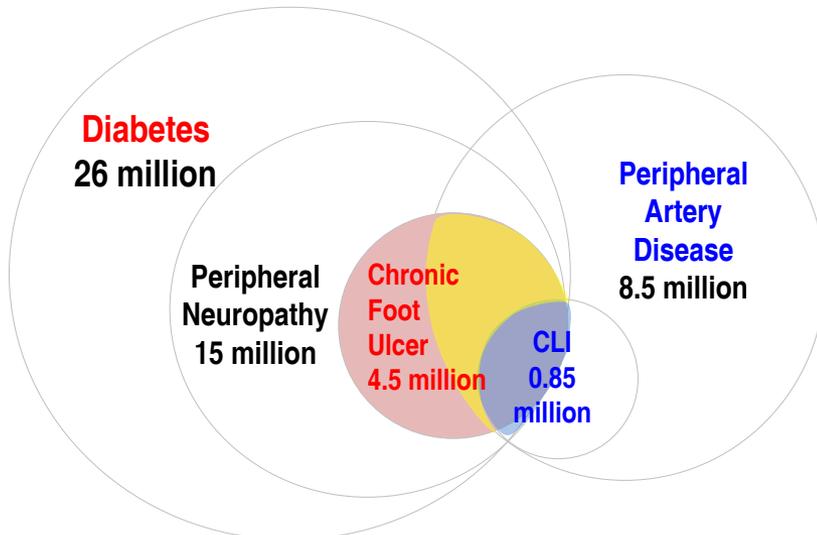
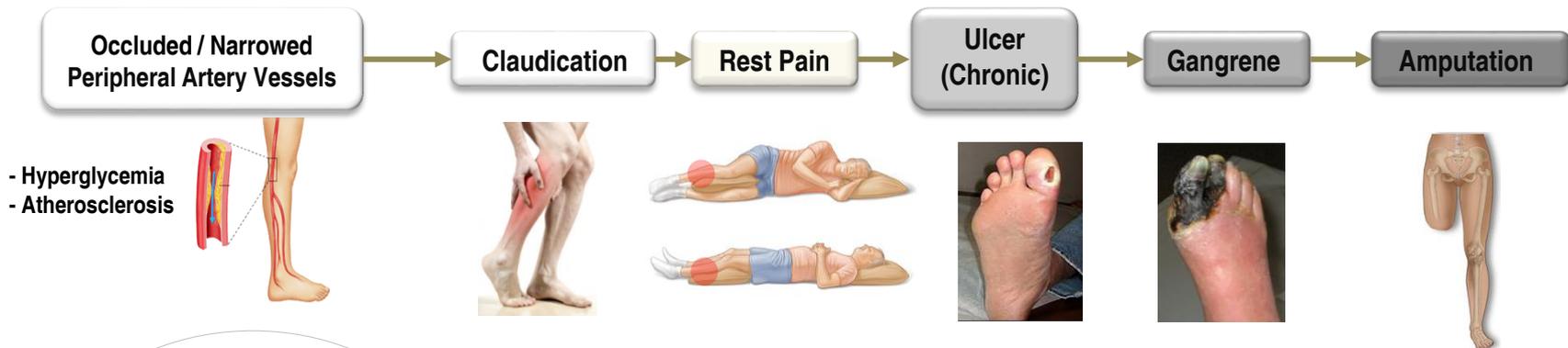
(by Viewpoint (NYC, US), Nov. 2017)



## 2<sup>nd</sup> Target Disease of VM202

# Chronic Diabetic Foot Ulcers with Peripheral Artery Problems

- Foot ulcers with PAD result from narrowing or blockage of peripheral arteries in the legs.
- Many diabetes patients suffer from chronic, non-healing foot ulcer.

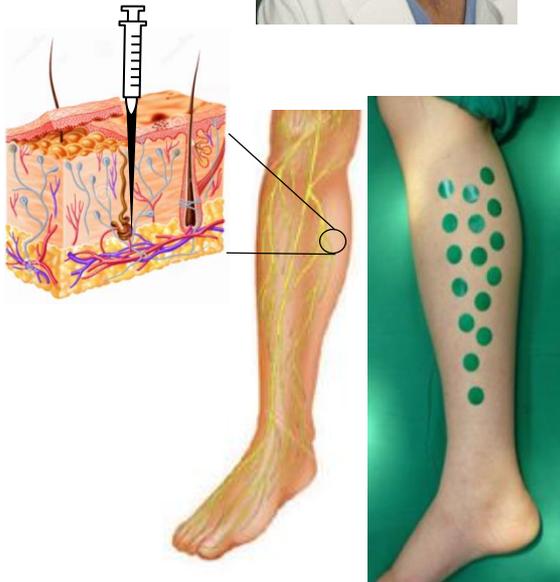


	<b>Chronic Foot Ulcer</b>	<b>CLI</b> Critical Limb Ischemia
<b>Total Number</b>	~ 4.5 Million	~ 0.85 Million
<b>Amputation</b>	82,000	200,000
<b>Medical Costs</b>	\$ 9-13 Billion	~ \$ 8 Billion

# Phase II Trial for CLI as a POC model

A Double-Blind, Randomized, Placebo-Controlled, Multicenter Study (US, Korea)

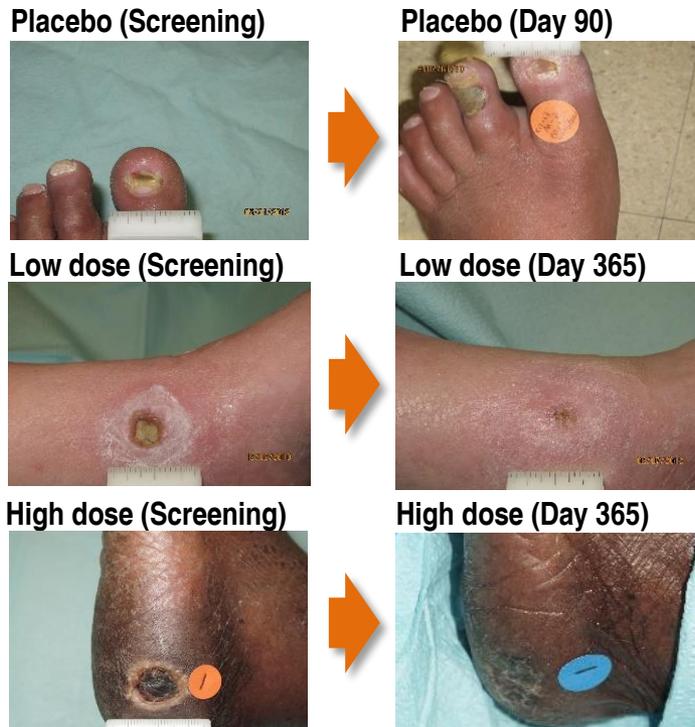
Principal Investigator  
EMERSON C. PERIN, M.D.  
(Texas Heart Institute)



- 1. Indication:** Critical Limb Ischemia (Rutherford class 4 and 5)
- 2. Total administered subjects: 52**
  - Placebo (0.9% normal saline): 11 subjects
  - Low dose of VM202 (2 mg/visit): 21 subjects
  - High dose of VM202 (4 mg/visit): 20 subjects

※ 30/52 (57.6%) subjects had diabetes.
- 3. Injection scheme:** 4 injection cycles along the calf line  
(days 0, 14, 28, & 42), unilateral IM injection
- 4. Follow-up period:** 12 months
- 5. Efficacy**
- 6. Safety**

# Substantial Healing Effects Observed in Ulcers



Group (Number of ulcers)	Completely healed	Improved <sup>1)</sup>
Placebo (n = 9)	11% (1/9)	11% (1/9)
Low dose (n = 27)	52% (14/27)	70%* (19/27)
<b>High dose (n = 13)</b>	<b>62%* (8/13)</b>	<b>69%* (9/13)</b>

(Kibbe *et al.*, *Gene Therapy* (2016) 1-7)

<sup>1)</sup> Reduction of ulcer area > 50%

[\*  $p < 0.05$ , vs. placebo (Fischer Exact Test)]

- >60% of ulcers were **completely healed** in the high dose group during 12-month follow-up period.
- Improvements ABI, Tcpo2 and VAS for pain were also observed.

# Study Outline of Phase III for DFU

Double-Blind, Randomized, Placebo-Controlled, Multicenter

- 1. Indication:** Chronic non-healing foot ulcers in diabetic patients with concomitant PAD
  - Ulcer(s) on or around the foot area that are unresponsive to standard therapies and persist despite 4 weeks of appropriate care
- 2. Total administered subjects: 300**
  - 16 mg VM202 + Standard Care: 200 subjects
  - Placebo (VM202 vehicle) + Standard Care: 100 subjects
  - 78 subjects enrolled, 16 subjects randomized (as of 18 Jul, 2018)
- 3. Injection scheme:**
  - 4 unilateral injection cycles in the ipsilateral calf of the affected foot (day 0, 14, 28, and 42)
- 4. Follow-up:** 7 months
- 5. Efficacy endpoints:**
  - Primary: **Complete wound closure, 4 months**
- 6. Safety endpoints**



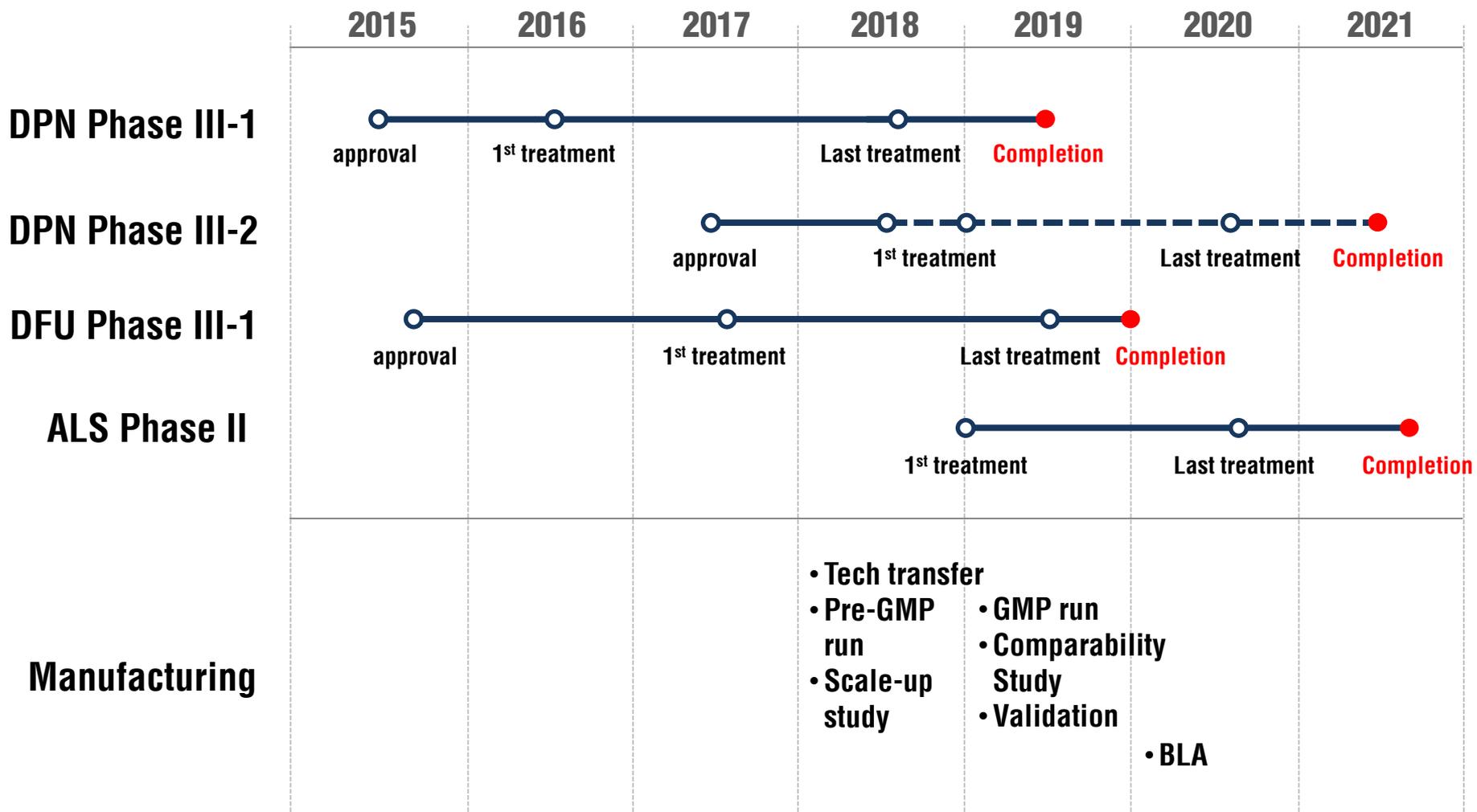
▲ SilhouetteStar  
Ulcer size is measured using 3D camera to determine ulcer depth or volume

# Manufacturing Facility in San Diego

- **Acquisition of a plasmid DNA production facility** (July 2018) in the form of a JV (*GENOPIS*) in partnership with a private equity investment firm
  - 68,400 square foot plant, research laboratory and office space
  - 500 L fermenter, cell culture lab and QC test lab, etc.
  - Extra space for future expansion (> 174,000 ft<sup>2</sup>)
- **Strategic benefits for ViroMed**
  - High quality, reliable in-house production capability for both clinical and commercial drug supply
  - Likely the first commercial plasmid DNA manufacturing facility
  - Less reliance on third-party manufacturers



# VM202 5-Year Timeline

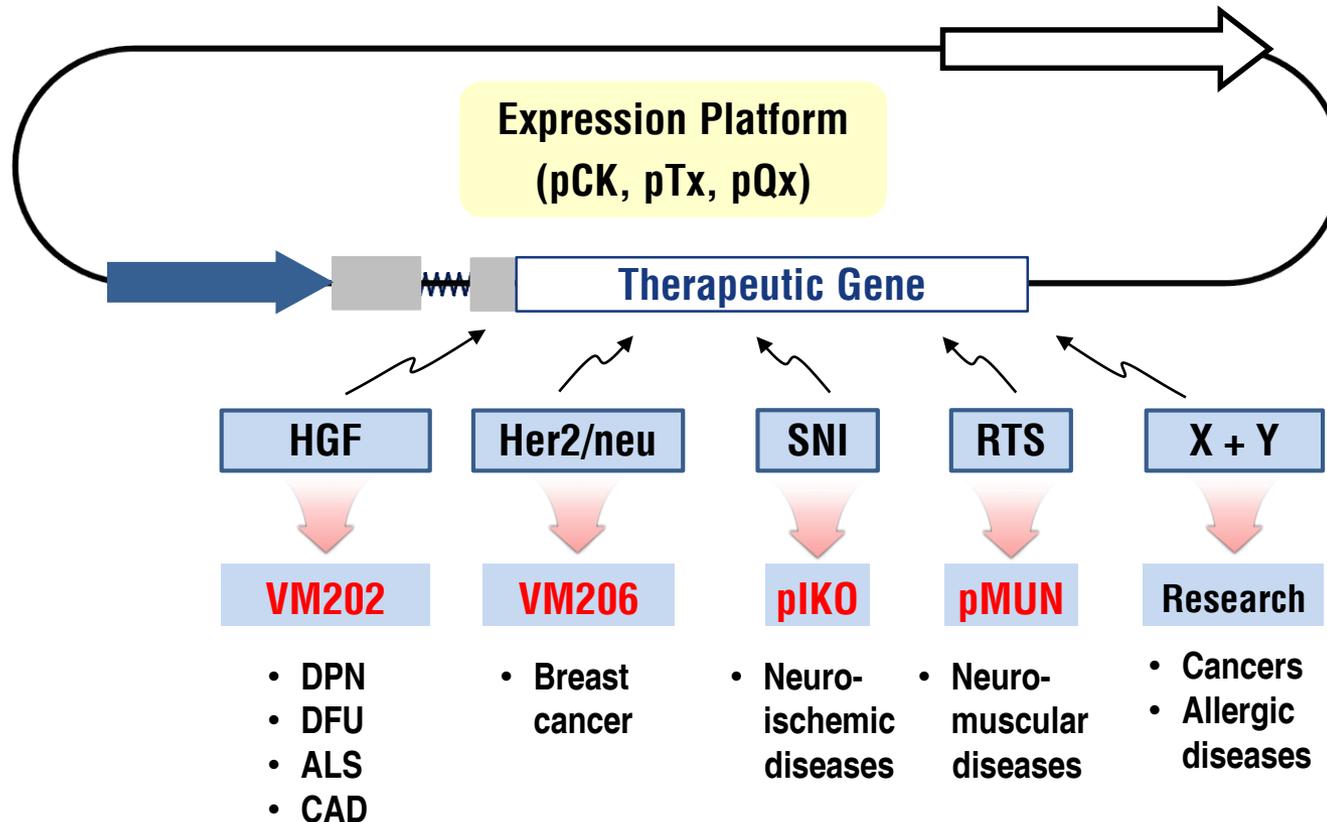


# ViroMed's Position in Gene Therapy

1. **FIRST** gene therapy in phase III for neuropathic pain
  - Potential to be the first disease modifying drug for pain
2. **FIRST** gene therapy in phase III for diabetic foot ulcer
  - Potential to be the first regenerative medicine in foot ulcer
3. Potential to be the **FIRST** in commercializing DNA as a drug for humans  **Opening up a new era in drug development**
4. Targeting highly prevalent diseases with high unmet medical needs
  -  **Great commercial potential**
5. Aiming to be **THE global leader** in plasmid DNA gene therapy

# ViroMed's DNA Platform Technology

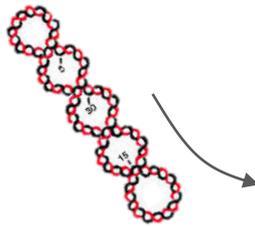
※ By inserting different genes, a variety of drugs are developed.



# Other Gene Therapy Products: Plasmid DNA- and CART-Based Gene Medicines

## Plasmid DNA

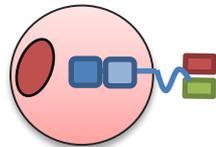
- New expression platform
  - pTx, pQx
- Disease platform (Muscle/Vascular/Neurological)
- Gene discovery & optimization
- Efficacy research technology



- pIKO
- pMUN

## CAR-T

- CAR optimization
- Vector production
- Cell processing

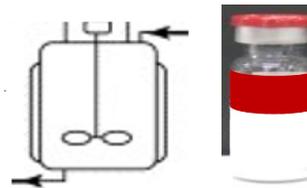


- VM 801
- VM 802
- VM 803
- VM 804

## GMP



- Cell processing



- DNA production (GENOPIS) in San Diego



Clinical trial  
PI → PII → PIII



- US
- Korea

Armed with hands-on experience and extensive global network for Muscle / Vascular / Neurological disorders

# **ViroMed's Goal through 2025 in the Area of Gene Therapy**

- 1. To be the biotech company with **world's largest revenue** from **gene therapy products**.  
(Basis: list of current phase IIIs)**
- 2. To maintain a global leader position in plasmid DNA-based gene therapy.**
- 3. To be conducting phase IIIs for 2-3 additional gene medicines with blockbuster potential similar to VM202.  
(Current status: Prototypes of 2 new candidate products are 90 percent ready for consideration of clinical trials in the US.)**