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.viromed21.com

ViroMed (San Diego, California)
Genopis Inc.

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

Present
Product Portfolio

Biologics

- Gene Therapy
  - DNA
  - CAR-T
- Protein
  - Antibody
  - Cytokine

Phytotherapeutics

- Prescription Drugs
- Nutraceuticals with Health Claim

- Thrombocytopenia
  - Phase III (China)

- Hematological tumors
- Solid tumors

- 1E4

- Osteoarthritis
- ADHD

- Allergic disease
- Memory improvement
- Joint Health

- Prostate health
- Respiratory health
- Insomnia

- Diabetic Peripheral Neuropathy
- Diabetic Non-Healing Foot Ulcer
- Lou Gehrig’s Disease
- Ischemic Heart Disease
- Neurovascular Diseases
- Neuromuscular Diseases
**Leadership Highlights**

**Proprietary gene therapy platform technologies**
Can lead to development of multiple products for various human diseases with high unmet medical needs

**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

**Manufacturing capability**
Manufacturing capability for go-to-market: facility 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

**Leadership Team**
- **William Schmidt, Ph.D.**
  Vice President, Global Clinical Development
- **Seungshin Yu, Ph.D.**
  Managing Director, Research & Business Development
- **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
- **Keith Hall**
  COO, GENOPIS in San Diego
- **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 -

\[ \text{ColE1} \rightarrow \text{Kan}^r \rightarrow \text{HGF-X7} \rightarrow \text{pA} \]

 menjiske

Exon number

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18

Alternative splicing

Freeze Dried DNA

**Special Features**

- **Therapeutic Gene:** HGF
- **Two isoforms:** HGF\(_{723}\) + HGF\(_{728}\)
- **Expression Level:** Promoter, UTR, Intron
- **Formulation**: Freeze Dried DNA

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**
- Formation of New Blood Vessels

**2. Reduction in the level of pain factors**
- (CSF-1, IL-6, α2δ1, 5-HTT, etc.)

**3. Regeneration of damaged nerves**
- Damaged Nerve → Repaired Nerve
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
- Spinal Cord
- Motor neuron
- Muscle
- Diabetic Peripheral Neuropathy
  - Painful Diabetic Peripheral Neuropathy
  - Phase III (US) ongoing
1st 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

Painful diabetic peripheral neuropathy

Blood vessel damage

Nerves shrivel when blood vessels disappear

Normal Blood vessel Nerve

Throbbing, Burning, Stabbing, Tingling
Currently Used Medicines for Painful DPN

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

- **Anticonvulsants:** Pregabalin (Lyrica®, Pfizer)
  $ ~5.1 B (2014), Neuropathic pain market: 30-50%
  Gabapentin (Neurontin®, Pfizer)
  $ ~ 210 M (2014)

- **Antidepressants:** Duloxetine (Cymbalta®, Eli Lilly)
  $ 5 B (2013), Neuropathic pain market > $1 B

- **NSAIDs**

- **Opioids:** Tapentadol (Nucynta® ER, Depomed)
  $ 281 Million (US, 2016)

**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

**Improvement Needed in**

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

All Subjects
(n=84)

High long-term pain-relieving effects

Changes in severity from baseline

Months after first injection

[*p<0.05, vs. placebo, ‡p<0.05, vs. baseline, Δ VM202 16mg – Placebo]

Subjects NOT on Lyrica and/or Neurontin
(n=49)

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

Changes in severity from baseline

Months after first injection

[*p<0.05, vs. placebo, ‡p<0.05, vs. baseline, Δ VM202 16mg – Placebo]

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
• 25 geographically-distributed sites in the USA
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)

<table>
<thead>
<tr>
<th>Therapeutic class</th>
<th>Pipeline name</th>
<th>Status</th>
<th>Features</th>
</tr>
</thead>
</table>
| Gene therapy      | VM202 (ViroMed) | Phase III | • 1st gene therapy  
|                   |               |         | • Excellent safety & efficacy profile  
|                   |               |         | • Long-term therapeutic effect  
|                   |               |         | • Disease-modifying potential  |
| \(\alpha_2\delta-1\) inhibitor | Mirogabalin Besylate (Daiichi-Sankyo) | Phase III | • Improved safety, tolerability and efficacy than pregabalin  
| Mu opioid + NOP opioid | Cebranopadol (Grüenthal/ Depomed) | Phase II | • Favorable efficacy  
|                   |               |         | • Associated with potential abuse and serious AE  
|                   |               |         | • Expected to be used as 1st line therapy anticonvulsant  |
| NMDA              | NYX-2925 (Apitinyx) | Phase II | • NMDA antagonist  
|                   |               |         | • PDPN, fibromyalgia  
|                   |               |         | • Expected to be used as 3rd line therapy  |
| Sigma\(_1\)       | S1A (MR309, E-52862) (Mundipharma/ Purdue Pharma/ Esteve) | Phase II | • Sigma 1 antagonist  
|                   |               |         | • Neuropathic pain (diabetic neuropathy; post-surgical; nerve injury); acute post-operative pain  |
| TCA/NMDA antagonist combination | AmiKet (EpiCept/ Immune Pharmaceuticals / Maxim Pharmaceuticals) | Phase II | • Amitriptyline & Ketamine  
|                   |               |         | • Blocks the ability of peripheral nerve receptors to transmit pain messages  
|                   |               |         | • Dual MoA leads to increase in pain relief  |
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)

- 25 million diagnosed diabetics (US)
  - Chronic PDPN: 1.5 - 2.0 million
  - Refractory: 750,000
  - Expandable group for VM202

- Treated with VM202:
  - 0.6% in diabetics,
  - 10% in chronic PDPN,
  - 23% in refractory

- 175,000

- Qualitative Price Response Chart
  - DMD Premium
  - Optimal price for pain reliever

- VM202 revenue estimation ($ billion USD)
  - Year-1: $164
  - Year-2: $166
  - Year-3: $168
  - Year-4: $171

- Drug price at market launch: $50,000 (5-8% increase annually)

Number of VM202 treated patients (thousand)
- Year-1: 157
- Year-2: 159
- Year-3: 161
- Year-4: 164
- Year-5: 166
- Year-6: 168
- Year-7: 171
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.

- Hyperglycemia
- Atherosclerosis

### 2nd Target Disease of VM202

**Chronic Diabetic Foot Ulcers with Peripheral Artery Problems**

- Diabetes: 26 million
  - Peripheral Neuropathy: 15 million
  - Chronic Foot Ulcer Disease: 8.5 million
    - Chronic Foot Ulcer: 4.5 million
    - CLI: 0.85 million

<table>
<thead>
<tr>
<th></th>
<th>Chronic Foot Ulcer</th>
<th>CLI Critical Limb Ischemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Number</td>
<td>~ 4.5 Million</td>
<td>~ 0.85 Million</td>
</tr>
<tr>
<td>Amputation</td>
<td>82,000</td>
<td>200,000</td>
</tr>
<tr>
<td>Medical Costs</td>
<td>$ 9-13 Billion</td>
<td>~ $ 8 Billion</td>
</tr>
</tbody>
</table>
Phase II Trial for CLI as a POC model
A Double-Blind, Randomized, Placebo-Controlled, Multicenter Study (US, Korea)

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

- >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.

<table>
<thead>
<tr>
<th>Group</th>
<th>Completely healed</th>
<th>Improved ¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo (n = 9)</td>
<td>11% (1/9)</td>
<td>11% (1/9)</td>
</tr>
<tr>
<td>Low dose (n = 27)</td>
<td>52% (14/27)</td>
<td>70% * (19/27)</td>
</tr>
<tr>
<td>High dose (n = 13)</td>
<td>62% ★ (8/13)</td>
<td>69% ★ (9/13)</td>
</tr>
</tbody>
</table>

(Kibbe et al., *Gene Therapy* (2016) 1-7) ¹Reduction of ulcer area > 50%

[* p < 0.05, vs. placebo (Fischer Exact Test)]
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**
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 ft²)

- 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

<table>
<thead>
<tr>
<th>Phase</th>
<th>Year 1</th>
<th>Year 2</th>
<th>Year 3</th>
<th>Year 4</th>
<th>Year 5</th>
<th>Year 6</th>
<th>Year 7</th>
</tr>
</thead>
<tbody>
<tr>
<td>DPN Phase III-1</td>
<td>approval</td>
<td>1st treatment</td>
<td>Last treatment</td>
<td>Completion</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DPN Phase III-2</td>
<td>approval</td>
<td>1st treatment</td>
<td>Last treatment</td>
<td>Completion</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DFU Phase III-1</td>
<td>approval</td>
<td>1st treatment</td>
<td>Last treatment</td>
<td>Completion</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ALS Phase II</td>
<td>1st treatment</td>
<td>Last treatment</td>
<td>Completion</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Manufacturing**
- Tech transfer
- Pre-GMP run
- Scale-up study
- GMP run
- Comparability Study
- Validation
- BLA
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.

Expression Platform
(pCK, pTx, pQx)

Therapeutic Gene

HGF

VM202
• DPN
• DFU
• ALS
• CAD

Her2/neu

VM206
• Breast cancer

SNI

pIKO
• Neuro-ischemic diseases

RTS

pMUN
• Neuro-muscular diseases

X + Y

Research
• Cancers
• Allergic diseases
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
  - VM 801
  - VM 802
- Cell processing
  - VM 803
  - VM 804

**GMP**
- Cell processing

**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.)