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 -

※ Pioneer and global leader in plasmid DNA-based gene therapy, with a particular emphasis on diseases associated with neurological, muscular or ischemic problems

- Listed on KOSDAQ (084990)
- Seoul (HQ, R & D): 90+ people in Seoul
- San Diego (Clinical Development, Production): 30+ people in San Diego
- Flagship Product VM202 -

Plasmid DNA designed to simultaneously express two isoforms of HGF

ViroMed has a strong patent position with VM202, covering DNA constructs, indications, formulation, and manufacturing, among others
- Biological Outcomes of IM Injections of VM202 -

1. Regeneration of damaged nerves
2. Angiogenesis
3. Reduction in the level of pain factors (CSF-1, IL-6, α2δ1, 5-HTT, etc.)
4. Amelioration of muscle atrophy

DPN
DFU

[Cardiac Muscle]

CAD

[Upper and Lower Limbs]

[Upper and Lower Limbs]

[Cardial Muscle]
- Target Indications under Clinical Studies -

* Amyotrophic Lateral Sclerosis
  (Lou Gehrig’s disease)
  - Phase II
  - Planned in US

* Acute Myocardial Infarction
  - Phase II
  - Planned in Korea

* Painful Diabetic Peripheral Neuropathy
  - Phase III
  - Ongoing in US

* Diabetic Foot Ulcer
  - Phase III
  - Ongoing in US
Most Advanced Indication - Painful Diabetic Peripheral Neuropathy (PDPN)

- US -

| DM | 30.3 M (1.5 M new cases/year) |
| DPN | 28.5% in DM |
| Painful DPN | 40-50% of DPN |
| Refractory PDPN | 30% of PDPN |

- Patients suffer from burning, tingling, throbbing, and stabbing pain

- PDPN market size (2017) ~5 billion
- US DPN market accounts for 71% among 7 MM

[Currently Used Medicines]

- Pregabalin (Lyrica®, Pfizer), Gabapentin (Neurotin, Pfizer) (Anticonvulsants)
- Duloxetine (Cymbalta®, Eli Lilly), (Antidepressant)
- Tapentadol (Nucynta® ER, Depomed), (Opioid)
- Capsaicin (Qutenza, Averitas Pharma), (Topical patch)

1 2015, ADA
2 A Boulton et al, Management of diabetic peripheral neuropathy; Clinical diabetes 2005 Jan; 23(1): 9-15
3 MJ Young et al, A multicenter study of the prevalence of diabetic peripheral neuropathy in the United Kingdom hospital clinic population
4 PDPN market research, The Dominion Group 2018
5 Painful diabetic neuropathy drugs market by drug type-growth, future prospects & competitive analysis, 2018-2026, Credence Research, May 2018
6 Painful Diabetic Neuropathy, GlobalData 2018
- High Unmet Medical Needs in PDPN -

- Average number of Rx medications used for PDPN in the preceding week\(^2\): 3.8 (NSAIDs, SAO & LAO, anticonvulsants, antidepressant, etc.)

- Modest treatment benefits

- Current treatments provide pain relief only without any disease modifying capability

- Safety and tolerability profile minimize compliance

- About 40% PDPN patients remain untreated\(^3\)

- 76% of patients take opioids 6 mon before and/or 1 year after taking pregabalin\(^1\)

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**Market size expected to grow to $ 11 billion by 2026**

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1 Kozma CM et al, Opioid before and after initiation of pregabalin in patients with diabetic peripheral neuropathy, Curr Med Res Opin. 2012 Sep;28(9):1485-96


3 MJ Snyder et al., Treating painful diabetic peripheral neuropathy: An update, Am Fam Physician. 2016 Aug 1;94(3):227-34

** Global neuropathic pain management market, Persistence market research 2018
- Opioid Usage in PDPN (Opioid Crisis in US) -

68% of 70,200 drug overdose deaths in 2017 involved an opioid¹

![Percentage of Opioid Utilization among DPN Patients] (chart showing 48.7%, 82.7%, and 88.4% for DPN, Painful DPN, and Severe Painful DPN respectively)

- Among treated DPN patients, 33% use opioid as first line treatment³ because there is no other option to manage pain
- 62% of PDPN patients have chronic use of short-acting-opioid⁴

¹ Opioid overdose, Understanding the Epidemic, CDC
⁴ Pesa J et al., Opioid utilization patterns among medicare patients with diabetic peripheral neuropathy, Am Health Drug Benefits. 2013 May;6(4):188-96
- Study Outline of VM202-DPN Phase II -

A Double-Blind, Randomized, Placebo-Controlled, Multicenter Study

1. **Indication**
   Painful Diabetic Peripheral Neuropathy

2. **Treatment groups** (Total: 102 subjects)
   - 16 mg VM202 (8mg/leg): 39 subjects
   - 32 mg VM202 (16mg/leg): 42 subjects
   - Placebo (0.9% normal saline): 21 subjects

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, and PGIC* among others

6. **Safety**
- Safety -

- No deaths or drug related serious adverse events
  - A total of 202 AEs in 69 out of 102 subjects: None related to study drug
  - A total of 13 SAEs in 10 out of 102 subjects: None related to study drug

- Antibody to HGF: None

- No change in the serum level of HGF
  - HGF protein in general population: 0.26 - 1.26 ng/mL
  - VM202 subjects showed HGF protein level relatively stable at all time points (mostly 1 - 2 ng/mL range)

※ VM202 showed an excellent safety profile
- Effect on Pain Severity (Daily Pain Diary) -

**Changes in severity from baseline**

- 3-month: -1.53
- 6-month: -1.59 (Δ=-1.19)
- 9-month: -1.95 (Δ=-1.03)

**Efficacy population (n=84)**

- **VM202**: -3.03 (Δ=-1.5)
- **Lyrica**: -2.78 (Δ=-1.03)
- **Neurontin**: -2.98
- **Cymbalta**: -1.59
- **Nucynta**: -1.53

**Long-term, high pain-relieving effects observed**

Δ (Drug-Placebo): -1.5 VM202 -1.2* Lyrica -1.1* Neurontin -1.3* Cymbalta -1.4* Nucynta

* Data of other pain killers were taken from public sources.

Significant improvements were achieved particularly in the area of activity, mood, walking ability, ability to work, relationship with other people, sleep, and overall enjoyment of life, resulting in improved QoL.

* Brief Pain Inventory

** Patient's Global Impression of Change

1. **Excellent safety profile**
   - No antibody to HGF, no changes in HGF serum level
   - No drug-related AEs or SAEs except Grade I

2. **Significant improvements in all pain measurements for a long period of time.**
   (Daily pain diary, BPI-DPN, VAS, PGIC)

3. **Disease-modifying potential**
   Monofilament tests suggested that VM202 might aid sensory functions recovery and have the potential to be disease-modifying.
DPN Phase III Study Outline

- Double-Blind, Randomized, Placebo-Controlled, Multicenter Center

1. Target indication: Painful DPN
2. Treatment arms: 477 (Placebo: 159, VM202: 318)
3. Sites: Geographically well distributed 25 sites in the US
4. Injection scheme: 2 treatments in 9 months
   - 16 mg + 16 mg (Days 0, 14) (Days 90, 104)
5. Follow-up: 9 months
6. Primary endpoint: Daily pain diary at 3 month
   - ≥ 50% responder at 3 month
7. Secondary endpoint: Daily pain diary at 6 month
   - ≥ 50% responder at 6 month
- DPN Phase III Current Status -

✓ **Enrollment as of 24 Dec, 2018:**
  - 507 randomized
  - 493 completed day 0 treatment
  - 308 completed study to full 9 months

✓ **Dropouts:** 51 discontinued study (10.1%, much lower than other trials)

✓ **Concomitant DPN medications as of 24 Dec, 2018:**
  
  of 507 subjects in total:
  - Receiving Lyrica (36) or Neurontin (212) or Both (4) = 252
  - Not receiving Lyrica and Neurontin = 255
- Genopis Inc -
Manufacturing Facility (San Diego)

✓ **Plasmid DNA production facility**
  - GMP ready production facility
  - with successful experience in regulatory due diligence
  - In partnership with a private equity investment firm
  - 68,400 sq ft plant
  - 500 L fermenter, cell culture lab and QC test lab, etc.
  - Extra space for future expansion (> 174,000 ft²)
  - 27 workers highly experienced in large scale production of plasmid DNA

✓ **Strategic benefits for ViroMed**
  - High quality, reliable in-house production capability for both clinical and commercial drug supply
  - Less reliance on third-party manufacturers
  - Likely the first commercial plasmid DNA manufacturing facility
- Status of VM202 Studies for Other Indications -

**Diabetic Foot Ulcer**

- Phase III ongoing in the US for chronic non-healing foot ulcers in diabetic patients with concomitant peripheral artery disease
- Total administered subjects: 300 - As of Dec 2018, 37 randomized, 10 completed
- Follow-up: 7 months
- Efficacy endpoint: complete wound closure at 4 months

**ALS**

- 18 subjects I/II in the US completed
- Evaluation measures include ALSFRS-R scale, FVC, muscle strength (MRC)
- Positive trend observed in slow down of disease progression at 2-3 months
- Phase IIa to be initiated in 2019 in the US

**Chronic Foot Ulcer**

- Total Number: ~ 4.5 Million
- Amputation: 82,000 / year
- Medical Costs: $ 9-13 Billion
ViroMed’s Goal Through 2025 in Gene Therapy

1. To be a global leader in plasmid DNA-based gene therapy
   - By becoming world’s first company commercializing plasmid DNA (VM202) as a medicine for human
   - By continuously introducing new products:
     Already planning to initiate 3 new phase I studies in the US by 2021

2. To be the most prominent biotech in gene therapy, both in science and business
   (Basis: list of current phase IIs)
Partnering Opportunities with ViroMed

- **Partnering opportunity**
  - After phase 3 readout around June, 2019
  - After each BLA approval
  - Regional rights

- **Investment in Genopis Inc (San Diego)**
  - Likely to become world’s first commercial production site for plasmid DNA
  - Primary commercial production site for VM202
  - CMO business