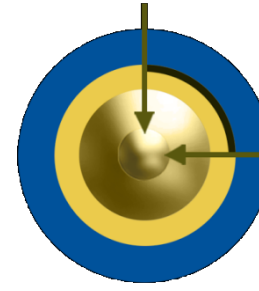


# Nanoviricides Prevent Varicella Zoster Virus Infection in Human Skin



**UPSTATE**  
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**NanoViricides**  
Incorporated

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## Background

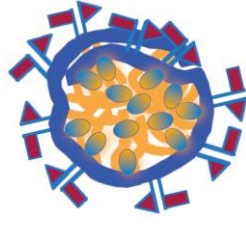
### Disease application

- Varicella zoster virus causes infections in the skin and eyes
- Therapy is needed to prevent virus spread and reduce contagiousness

### Nanoviricide® mechanism and activity

- Designed to act like a decoy of a human cell
- It binds to virions and infected cells, inactivating them
- A VZV-specific ligand was designed for this series of test agents
- NV-118 is effective in cells (EC<sub>50</sub> 16 µg/mL)

## Nanoparticle Structure & Evaluation



### Structure

Covalent conjugate of a virus-specific ligand and a PEG-based polymer

### Purpose

- Evaluate NV-118 and derivatives as a topical treatment for VZV
- Test in the Skin Organ Culture Model
- Identify lead compounds for NanoViricides, Inc.

## Results

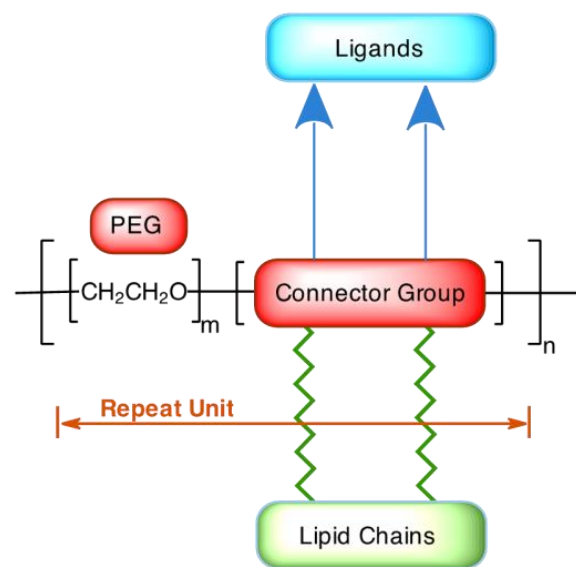
### Anti-VZV Nanoparticles are:

- Effective in ARPE-19 cells
- Not cytotoxic
- Effective in human skin organ culture
- Tolerated in human skin

*Lead compounds were identified*  
*Optimal vehicle for topical treatment was selected*

## Nanoparticle synthesis

### Nanoparticle subunit



### Polymer

Functionalize PEG with Connector Group

Polymerize PEG-Connector to n-degree

Covalently bind Pendant Lipid to polymer PEG-Connector-Lipid (n)

Synthesize Nanoviricide® by covalently binding ligands to PEG-Connector-Lipid polymer  
Purify at each step

### Ligand

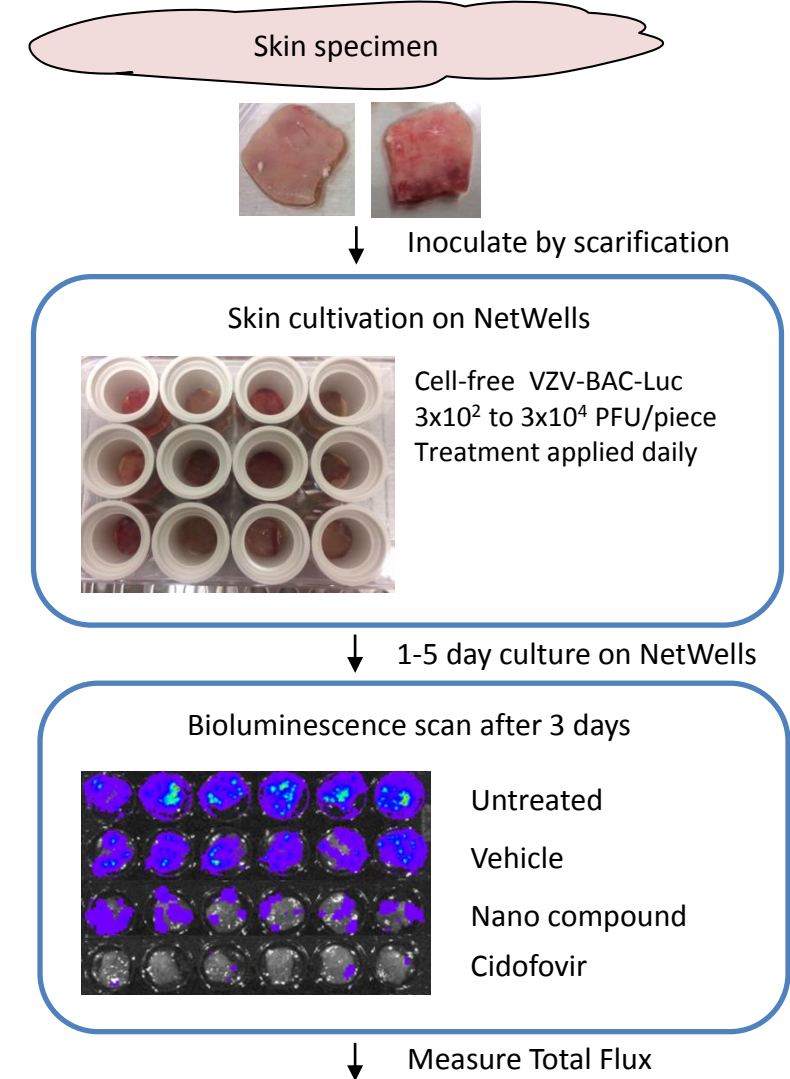
Ligands designed to mimic cellular receptors that bind virus coat protein

Synthesize, screen and select ligands for activity

Synthesize selected ligands for incorporation into nanoparticles

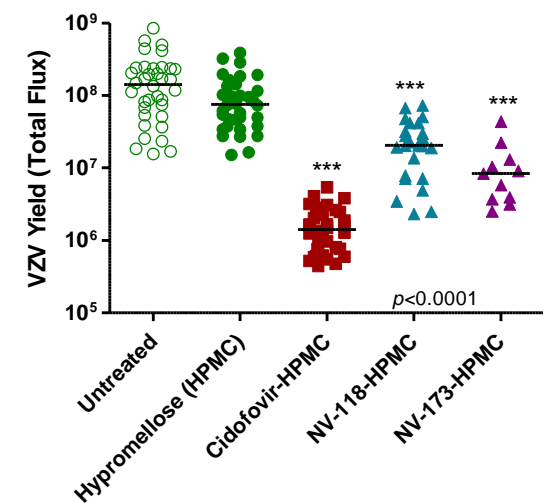
## Evaluation in Skin Organ Culture

### Skin Organ Culture System

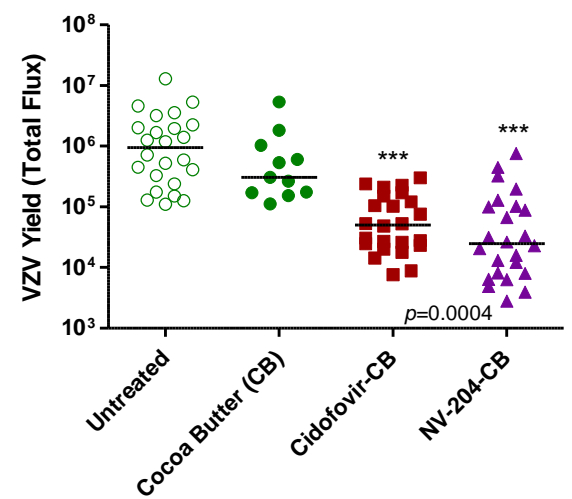


### Skin Organ Culture Assays

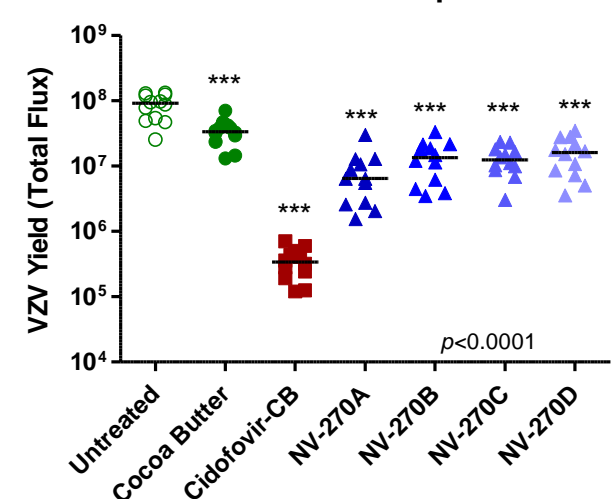
#### NV-118 and NV-173 are effective in skin



#### NV-204 in cocoa butter is effective



#### NV-270-CB is dose dependent

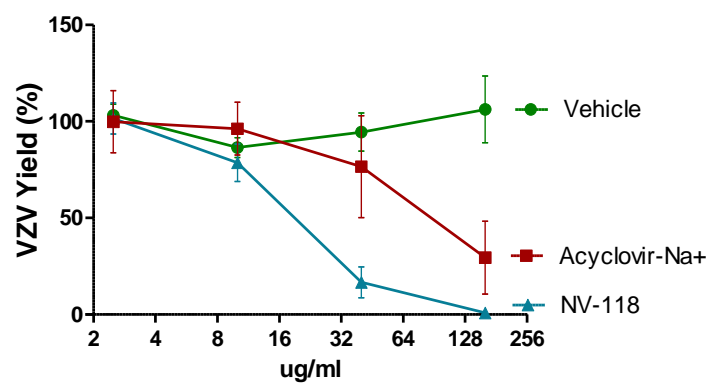


### Statistical Analysis

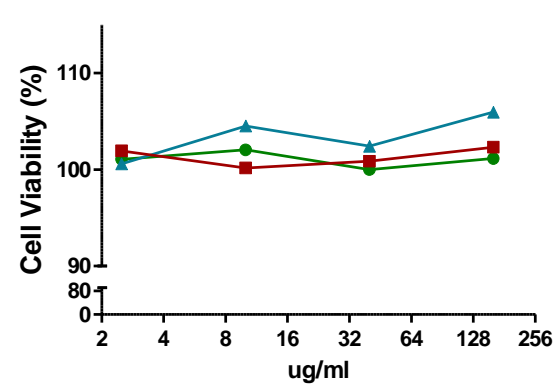
- Each symbol represents one piece of skin
- Bars are the median
- 1-way ANOVA with Dunnett post hoc test
- Data are combined from 1-3 separate experiments

## Evaluation in Cells

#### NV-118 is effective in ARPE-19 cells



#### NV-118 is not cytotoxic

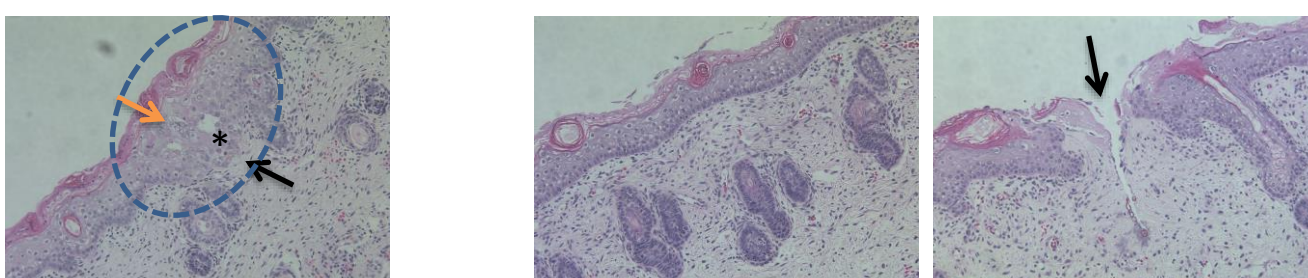


- VZV was pre-incubated with the compounds or vehicle for 1 h
- Then added to ARPE-19 cells and cultured for 6 days
- VZV-infected cells were detected by immunocytochemistry and measured by ELISA
- Each point is the mean ± SD, N=6 replicates

Cytotoxicity measured by MTT assay

## Histopathology in Human Skin

### H&E Stained Skin Sections



### Untreated skin

- VZV lesion in the epidermis (circled)
- Multinucleated giant cells (orange arrow)
- Breach of the basal cell layer (black arrow)
- Vesicle forming in lesion (\*)

### Skin treated with NV-118

- No VZV lesions were observed
- Normal epidermis and dermis
- Hair follicles were abundant
- Needle track where VZV was inoculated