# A Novel Enantio-Specific Cationic Lipid R-DOTAP + HPV16 E6 & E7 Antigens Induces Potent Antigen-Specific CD8+ T Cell Responses *In-Vivo* in Subjects with CIN and High-Risk Human Papilloma Virus Infection

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**Concurrent Session 209: Virus-Driven Cancers**
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**Oral Presentation (O19), Abstract ID 12533**

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# Disclosures and Forward Looking Statements

The research being reported in this presentation was supported by PDS Biotechnology. The presenting author is an employee of and receives salary and other equity compensation from PDS Biotechnology which is developing products related to the research being reported. This presentation will discuss the investigational use of PDS0101, an immune-activating therapeutic platform targeting HPV-related cancers and pre-cancer.

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Factors that may cause actual results to differ materially from such forward-looking statements include those identified under the caption “Risk Factors” in the documents filed with the Securities and Exchange Commission from time to time, including its Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q and Current Reports on Form 8-K. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date of this presentation. Except to the extent required by applicable law or regulation, PDS undertakes no obligation to update the forward-looking statements included in this presentation to reflect subsequent events or circumstances.

# Properties of The Versamune® Immune-Activating Platform

## Versamune® Composition

- First report of lipid enantiomeric specificity on immunological activation*
- R-DOTAP an enantiomerically pure cationic lipid designed to form liposomal nanoparticles 100-200nm to maximize dendritic cell uptake

## Immunologic Activity

When combined with antigen(s), Versamune® promotes**

- Efficient dendritic cell antigen uptake, processing and presentation by MHC class 1 and class II pathways
  - Robust antigen cross presentation with activation and expansion of antigen-specific CD8+ T cells with a Granzyme-B functional cytolytic profile
- Specific induction of Type 1 interferons and related chemokines within lymph nodes, resulting in a localized immune response with limited systemic exposure
- Regression of tumors and induction of memory T cells



* *Cancer Immunology, Immunotherapy,* 2011; 60(5): 629-638 DOI: 10.1007/s00262-011-0970-1
** *J Immunology* 2019, 202(12): 3524-3536 DOI: https://doi.org/10.4049/jimmunol.1801634

# PDS0101 Phase I Clinical Study

**An Open-Label, Phase I, Escalating Dose Study to Evaluate the Safety, Tolerability and Pharmacodynamics of PDS0101 (ImmunoMAPK-RDOTAP/HPV-16 E6 & E7 Peptides) in Subjects with Cervical Intraepithelial Neoplasia (CIN) and High-Risk Human Papillomavirus (HPV) Infection**

**ClinicalTrials.gov Identifier:** NCT02065973

**Study Sites:** Suffolk Obstetrics and Gynecology, Port Jefferson, NY
Montefiore Medical Center, Bronx, NY
Augusta University, Augusta, GA

# Phase I Study Summary

**PDS0101 Investigational Product:** R-DOTAP [R-enantiomer of 1,2-dioleoyl-3trimethylammonium-propane chloride] and multi-epitope HPV16 E6 & E7 peptides [HPVmix]

**Study Design:** Modified 3 + 3 dose escalation design

| | Cohort 1 | Cohort 2 | Cohort 3 |
|---|---|---|---|
| **R-DOTAP Dose** | 1.0 mg | 3.0 mg | 10.0 mg |
| **HPV16 peptide mix** | 2.4 mg | 2.4 mg | 2.4 mg |
| **Number of Subjects** | 3-6 | 3-6 | 6 |

**PDS0101 Dosing:** Three total doses, administered subcutaneously every 3 weeks, on Days 1, 22 and 43

**Study Objectives:**

- ➤ Safety and tolerability of multiple escalating doses of PDS0101
- ➤ T-cell immunogenicity assessed by HPV16-specific Granzyme-B and IFN-γ ELISPOT pre-treatment and on Days 15, 36, 57 and 133 (± 5 days)

# Study Population Baseline Characteristics

| | |
|---|---|
| **Total Subjects:** | N = 12 |
| **Age (median):** | 33 years (range 24-51) |
| **Ethnicity/Race:** | |
| Hispanic | N = 4 (33%) |
| Not Hispanic, Black | N = 2 (17%) |
| Not Hispanic, White | N = 6 (50%) |

| | |
|---|---|
| **Cohort Distribution:** | |
| Cohort 1 (1.0mg) | N = 3 |
| Cohort 2 (3.0mg) | N = 3 |
| Cohort 3 (10.0mg) | N = 6 |

**Key Protocol Inclusion Criteria:**

- Pathologically confirmed CIN1
- Confirmed high risk HPV DNA infection

**High Risk HPV Genotypes**

**HPV 16 vs nonHPV16 Genotypes**

| | |
|---|---|
| **HPV16 Infected** | **N = 4 (33%)** |
| **nonHPV16 infected** | **N = 8 (67%)** |

**Number of High Risk HPV Genotypes Per Patient**

| | |
|---|---|
| **Single Genotype** | **N = 4 (33.3%)** |
| **Multiple Genotypes** | **N = 8 (66.7%)** |
| Two Genotypes | N = 3 |
| Three Genotypes | N = 3 |
| Four Genotypes | N = 0 |
| ≥ Five Genotypes | N = 2 |

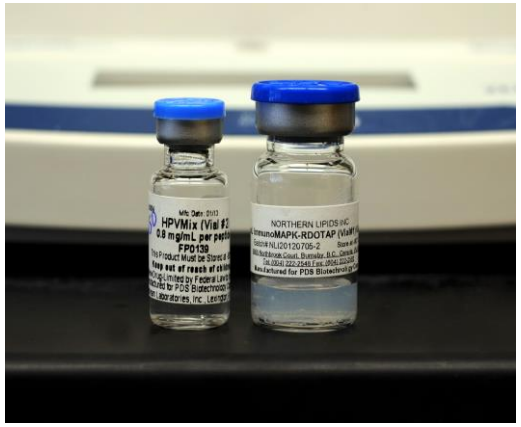
**HPV DNA Genotype Representation:**

**30 *total* HPV genotypes among 12 subjects (mean 2.5/subject)**

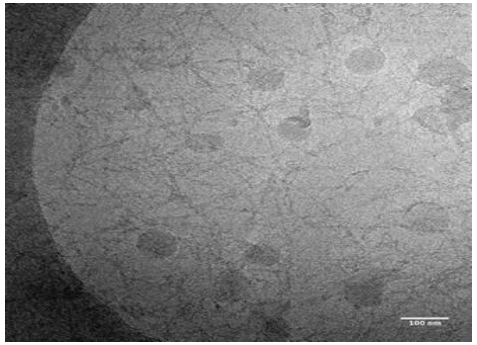
**15 *different* HPV genotypes represented**

# PDS0101: R-DOTAP (Versamune®)
# HPVmix Cationic Liposomal Formulation

Vial of
HPV Peptides



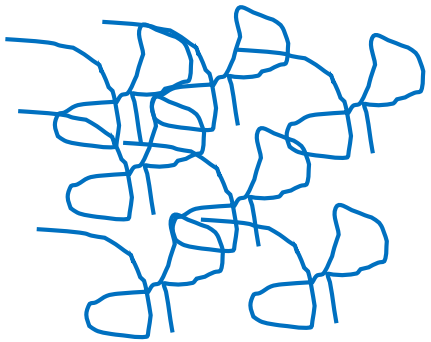
Vial of
Versamune®



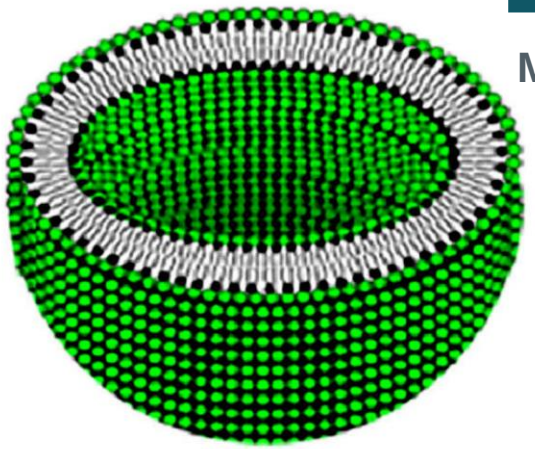
PDS0101 Formulation
By Electron Microscopy

Vials

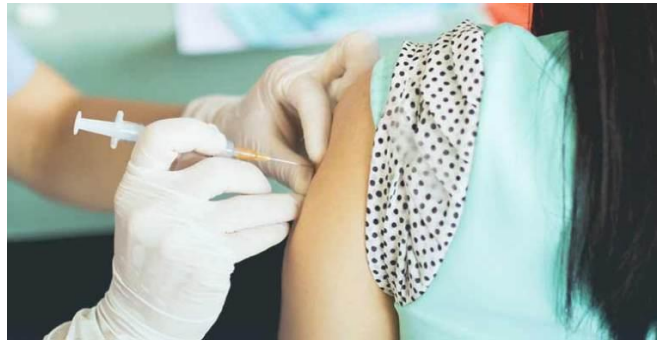
Mixed Bedside



Proprietary HPV
Peptide Antigens

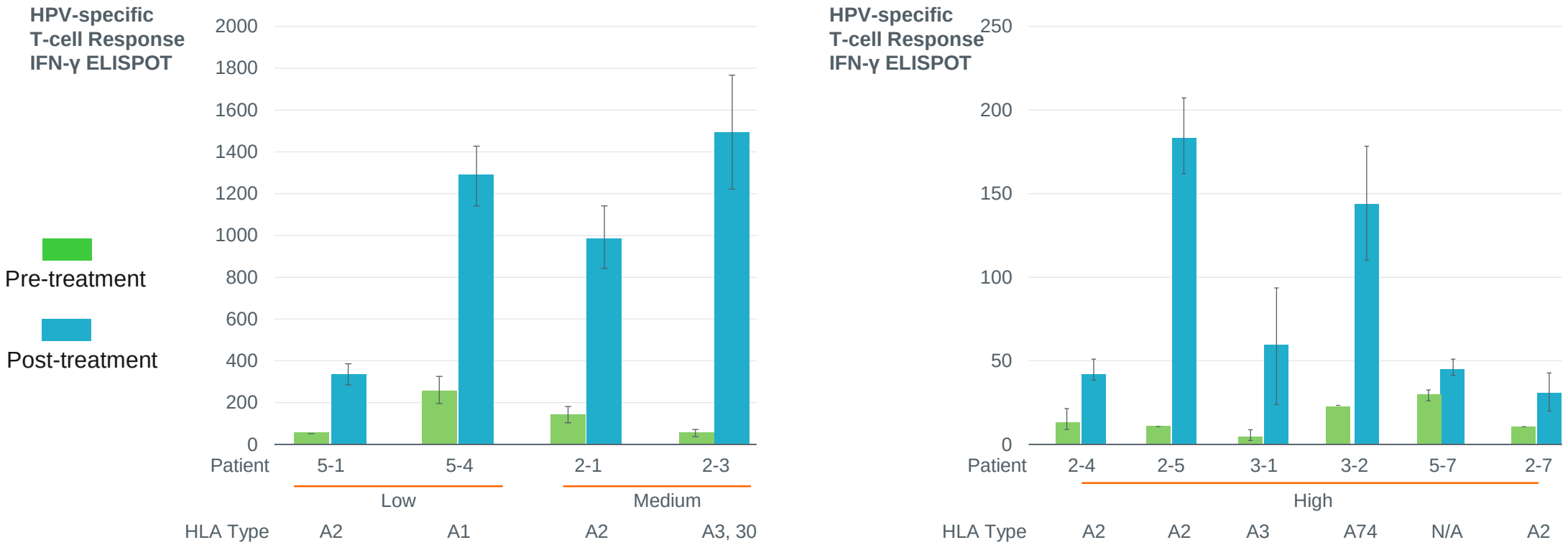


Versamune®



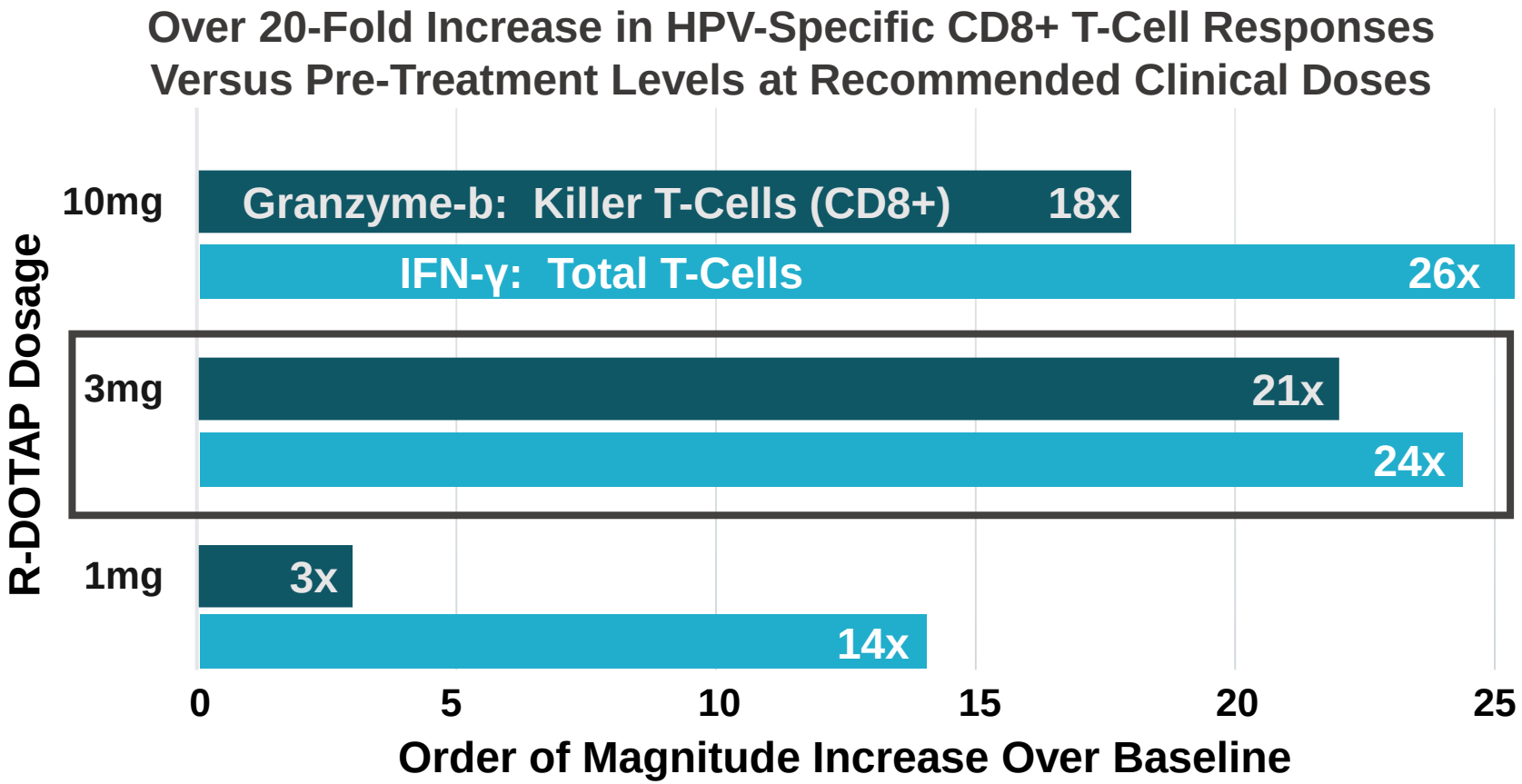
# Human Clinical Results: PDS0101 Induced Strong *In-Vivo* HPV16 T-Cell Responses Independent of Patient Genetic Sub-Type

## PDS0101 PRECLINICAL T-CELL RESPONSES REPLICATED IN HUMAN PATIENTS IN PHASE 1 CLINICAL TRIAL ON DAY 14-19




Two subjects (one in Cohort 1 and one in Cohort 2) had high pre-existing HPV-specific responses

# Human Clinical Results: Induction of HPV16 CD8+ T-Cell Responses at All Doses




## Immunogenicity at Day 14

10 subjects with low, baseline HPV-16 T cell responses:

- **9 of 10 (90%) had IFN-γ responses**
- **6 of 9 (67%) had Granzyme-B responses** (1 additional subject had insufficient specimen for testing)

- Strong & Measurable *In-Vivo* Induction of HPV-Specific Killer T-cells 14 Days Post Treatment
- Defined Dose for Phase 2 Studies

# Human Clinical Results: Safety, Tolerability, and Additional Clinical Outcomes

## Safety and Tolerability

- No DLTs observed
- Most common TRAEs were local injection site reactions that generally resolved within several days
- More intense ISRs were observed with higher doses of R-DOTAP

## Additional Data on Clinical Outcomes

- Documented high levels of circulating Granzyme-B CD8+ T-cells prompted an IRB-approved retrospective evaluation of clinical outcomes for 24 months following the 3$^{rd}$ dose of PDS0101
- Limited follow-up clinical data was available from 11 of 12 patients, with confirmatory review by PDS of reported source data for all but two patients (both in 10mg dose group, and whose data were reported by correspondence from the investigator)
- Clinical responses (reported regression / elimination of CIN) determined by cytology and/or colposcopy as available, and were observed in 60% of evaluable patients across the three tested doses

# Human Clinical Results: Regression of CIN Lesions

| Dose Cohort | Evaluable Patients* | Clearance of CIN 12 Months Post Treatment** | |
|---|---|---|---|
| | N = | N = | % of Evaluable |
| **1 mg** | 3 of 3 | 2 | 67% |
| **3 mg** | 2 of 3 | 1 | 50% |
| **10 mg** | 5 of 6 | 3 | 60% |
| **Total** | 10 | 6 | 60% |

* Two of twelve patients were not evaluable: one patient, who demonstrated a strong immune response (high dose cohort), was lost to follow up and another received standard of care LEEP excision therapy at 4 months (mid dose cohort)

** Two of ten evaluable patients who had clearance of CIN by cytology were not considered as clinical responders: one patient regressed from CIN to atypical squamous cells of undetermined significance (ASCUS) with detectable virus, and the other showed consistent disease elimination by cytology, but showed residual disease by colposcopy

# SUMMARY:
# PDS0101 [R-DOTAP (Versamune®)/HPVmix]

- PDS0101 was immunologically active at all three doses studied:
  - Mean 3- to 26-fold increases were seen in circulating HPV16-specific CD8 T-cells
  - HPV16 T cell responses observed in 10/10 subjects with low baseline HPV responses
- PDS0101 was safe, well tolerated, and associated with local injection site reactions of limited duration, without observed DLTs
- Retrospective evaluation of clinical outcomes documented:
  - CIN regression by cytology and/or colposcopy in 6 of 10 evaluable patients
  - Timing of these responses seen as early as 1 to 3 months in some patients
- PDS0101 Phase 1 human data is consistent with preclinical data demonstrating the ability of R-DOTAP with HPV antigens to induce potent cytolytic HPV16-specific T cell responses
- **3.0 mg dose of Versamune® has been selected as the defined dose moving forward**
  - **Phase 2 studies in combination with KETYRUDA® in treatment of HPV16+ HNSCC, and**
  - **In combination with other I-O agents and chemoradiation in treatment of HPV-related cancers**

# Acknowledgements

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