

# 2<sup>nd</sup> Annual Capital Markets Day



**Dr Frank Bedu-Addo**  
CEO, PDS Biotechnology Corporation

Altering the landscape of  
immunotherapy





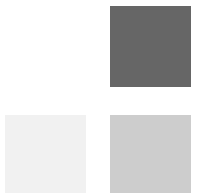
**PDS Biotechnology**

*Protein Delivery Sciences*

## **Next-Generation Cancer Immunotherapies**

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***NetScientific PLC Capital Markets Day - June 14 2016***



## Investment and Partnership Highlights

Innovative immunotherapy platform technology harnessing immune system's power to fight disease

- 1 Immunotherapy Platform**
  - Innovative T-cell activating platform – **Versamune®**
  - Advantages over current approaches already valued in \$billions
- 2 Differentiated Technology/Approach**
  - Simple and differentiated by modes of action
  - ***Developing clinical-stage products across several cancers***
- 3 Big Pharma & National Cancer Inst. Validation**
  - NCI committed to run 3 Phase 2 trials (PDS retains ownership)
  - Merck KGaA partnership; preclinical studies completed
  - Additional partnerships under discussion with notable parties
- 4 Funding**
  - NCI partnership saves > \$40 million in equity capital
  - Considering IPO in UK or private investment to raise \$40-50 million to fund multiple phase 2 clinical programs
- 5 Significant Near-Term Opportunity for Value Inflection**
  - Multiple Phase 2 clinical trials being initiated in 2017-2018
  - Targeting interim Phase 2 clinical trial readouts within 2 years

**Strategy – Maximize opportunity for clinical and commercial success**

## Experienced management team with stellar track record

**Sir Richard Sykes**  
Chairman

**Frank Bedu-Addo, PhD**  
President, CEO

**Gregory Conn, PhD**  
Chief Science Officer

**Robert Shepard, MD**  
Chief Medical Officer

**Michael King, MBA**  
Chief Financial Officer

**Panna Dutta, PhD**  
VP of Development and  
Manufacturing

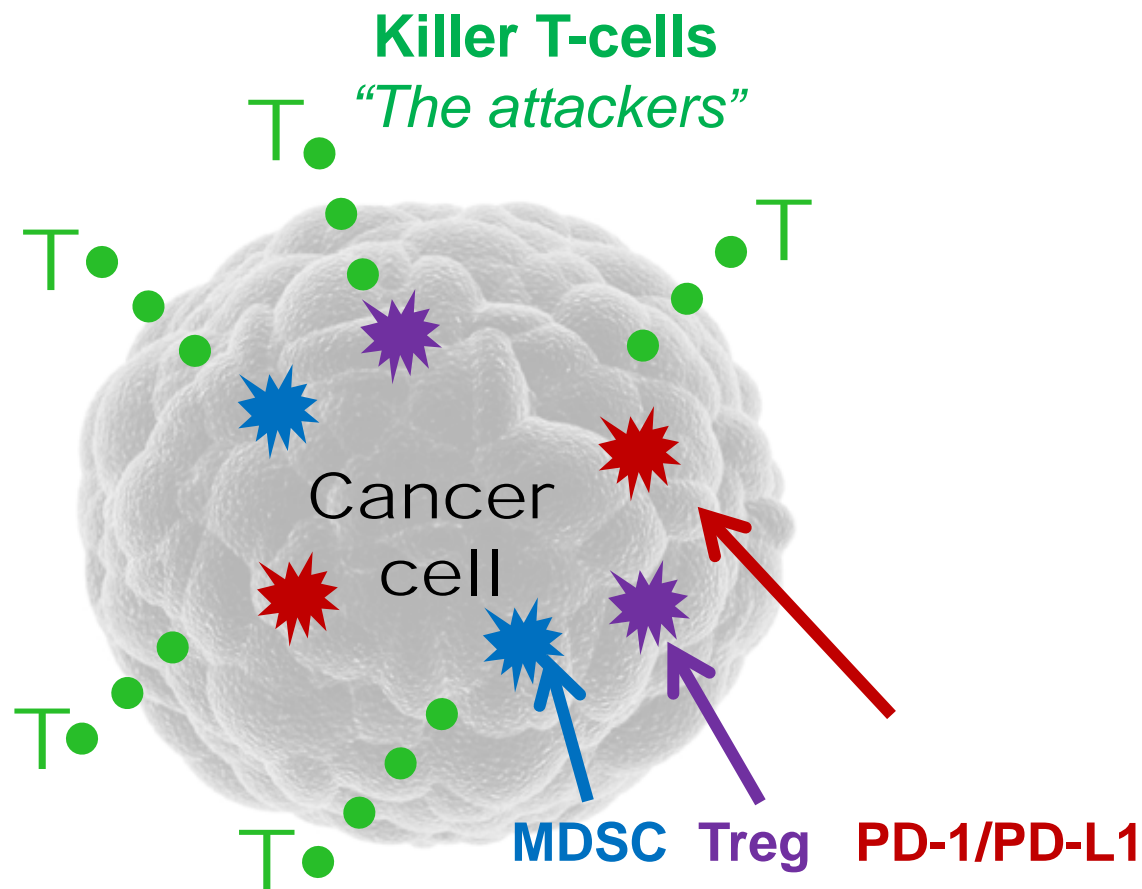
- Chairman and CEO of Glaxo 1995-2000, and GSK until 2002
- Sr. exec.- KBI BioPharma & Cardinal Health
- Development - Abelcet® (Liposome Company/Elan), PEG-Intron® (Schering-Plough/Merck)
- 35+ years of experience - Merck, Regeneron & Covance/Diosynth
- In-depth experience with biotech product dev.
- Former Global Medical Lead for oncology for AstraZeneca/ MedImmune; CMO – Cornerstone
- Former FDA Medical Officer, Cancer Biologics
- Former CBO/CFO of Aprelia Pharmaceuticals; Head US Strategy, Sandoz GmbH; McKinsey
- 25+ years of drug development experience – Pfizer, Baxter, Medicines Co.; led development & successful FDA approval for multiple products



# **Cancer immunotherapy: Significant emerging clinical potential**

# Immunotherapy Goal: Shift balance of “attackers” vs. “defenders” to favor ability of “attackers” to overcome “defenders”

***T-cell induction is critical to the anti-tumor effect***



**Ultimate goal**  
“Enable” a sufficient number of potent or “strong” killer T-cells to overcome and outlast the defenders

**The best understood immune suppressor cell types - “The defenders”**

## Immunotherapy – Current key approaches and technologies

Current technologies present significant advancements with some limitations

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- **Cancer vaccines**
  - Overview: Prime the immune system to generate tumor specific T-Cells
  - Positioning: Key additions to checkpoint inhibitors as combinations to enhance the tumor destroying capabilities by enhancing T-cell attack
- **CAR-T cells**
  - Overview: T-cells removed and engineered outside the body to target tumors
  - Advantages: Large number of T-cells generated ex-vivo & infused in billions
  - Disadvantages: Sub-optimal safety with deadly “cytokine storms”. Also complex with no ability to impact immune suppression (defenders)
  - Positioning: Terminal cancer patients who have failed existing treatments
- **Check-point inhibitors**
  - Overview: Block the PD-1 and PD-L1 T-cell suppressors
  - Advantages: Allow existing T-cells to perform killing function
  - Disadvantages: Sub-optimal safety potency – No T-cell induction
  - Positioning: Terminal cancer patients who have failed existing treatments

## Immunotherapy: Limitations and opportunities

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- ***Critical Limitations***

- Checkpoint inhibitors and CAR T-cells too unsafe for early stage cancer
- Complexity and cost also prevent application to early stage cancer

***Opportunity: A safe and effective immunotherapy could dominate the larger and potentially more responsive early-stage cancer population - Versamune®***

- ***Combination immuno-oncology – the “next frontier”***

- Combinations of checkpoint inhibitors with other technologies could compound the toxicity of the therapy and even further restrict the patient population
- Combination with other complex approaches could lead to exorbitant and unsustainable cost of treatment

***Opportunity: A safe, cost effective and potent technology that lowers the dose of the checkpoint inhibitors due to potent T-cell activation and reduction of complimentary immune suppressors should result in a superior anti-cancer therapy - Versamune®***



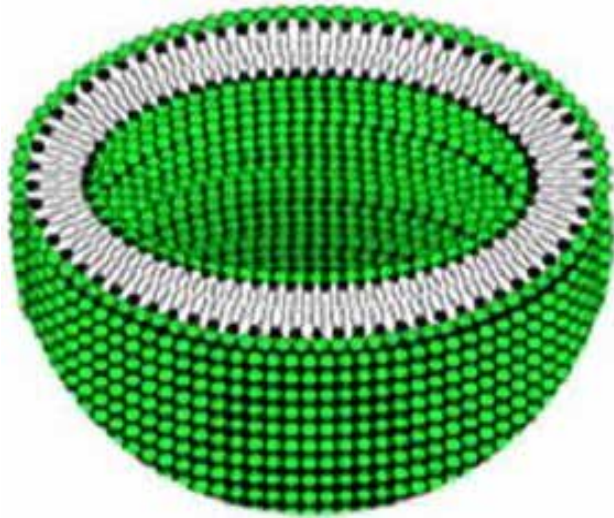
## **The Value Proposition:**

***The first true multi-mechanism platform***

***Overcomes “bottlenecks” and facilitates safer, simpler and more effective immunotherapy***

## Versamune® T-Cell activating platform

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**Cross-section of Versamune®  
Nanoparticles: 100-200nm in size**

**Versamune® is combined with specific  
protein/peptides unique to particular cancers**

**Administered by subQ injection**

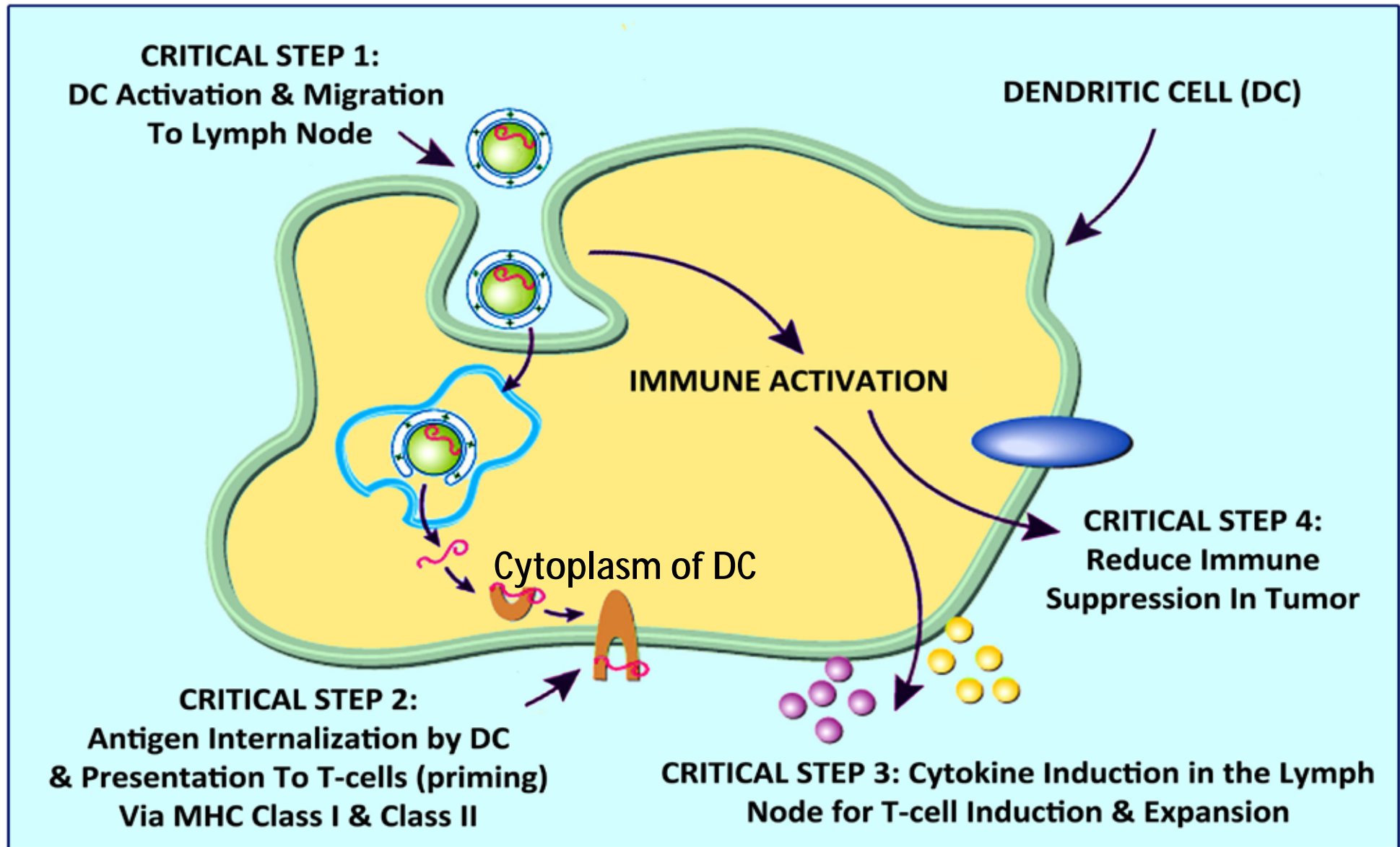
**Ingredient:** A simple positively charged synthetic lipid (fatty acid) called R-DOTAP

Versamune® nanoparticles form spontaneously in aqueous environment

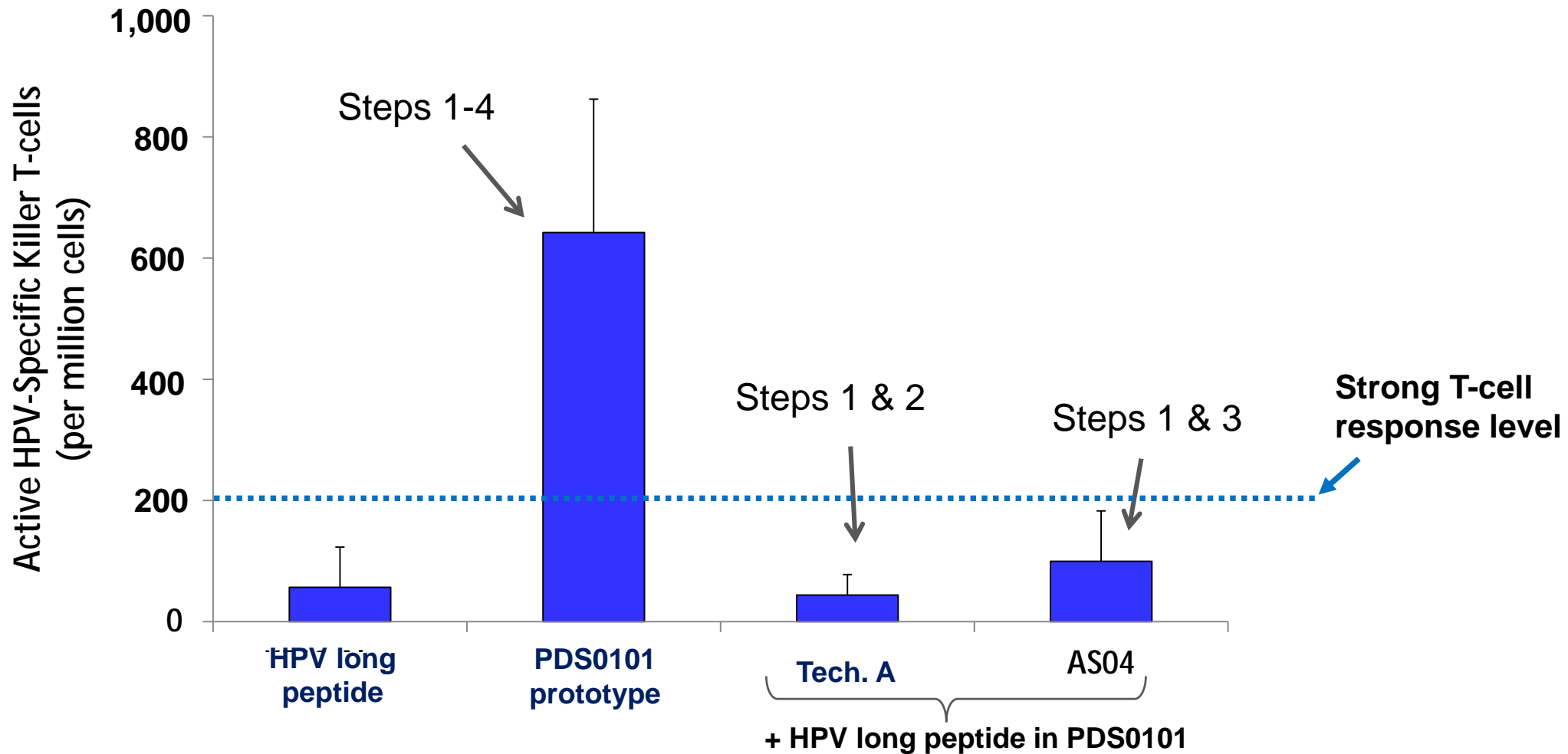
Developed at Univ. of Pittsburgh School of Medicine and acquired by PDS

Versamune® patent portfolio: *8 patents* cover composition and use of any cationic lipid to induce an immune response and/or reduce immune suppressors

## Critical steps required for full therapeutic T-cell mediated immune response (*Versamune*<sup>®</sup> is the only proven to facilitate all four)



## Versamune®: Activation of all critical pathways leads to superior induction of active killer T-cells (*ELISPOT study – HPV cancer*)



**AS04:** GSK adjuvant

**Tech. A:** Positively charged delivery system that activates step 1 (uptake) only

## **Clinical data**

***Human Proof-of-Principle  
Human HPV-specific T-cell Induction  
(PDS product # 1 - PDS0101)***

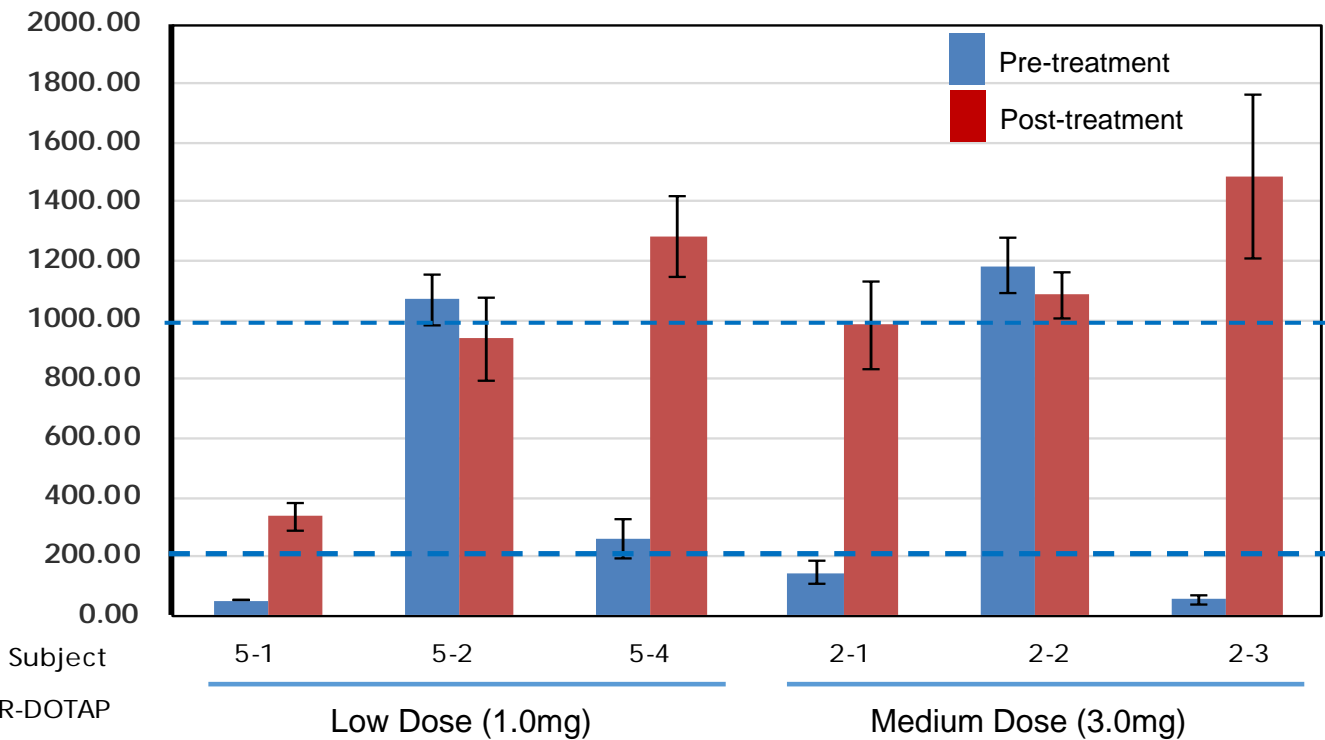
# Phase 1 human trial - 100% T-cell induction efficacy in small patient population

Strongly activated T-cells in the 4 of 6 patients who had low pre-treatment T-cells (Cohorts 1 & 2)

**Excellent T-Cell responses\* in Phase I clinical trial:  
Max peak responses 2 weeks after administration**

**Versamune®  
Created Highly  
Potent Immune  
Responses**

T-Cells Recognizing Cancer Protein\*  
SFC per million cells



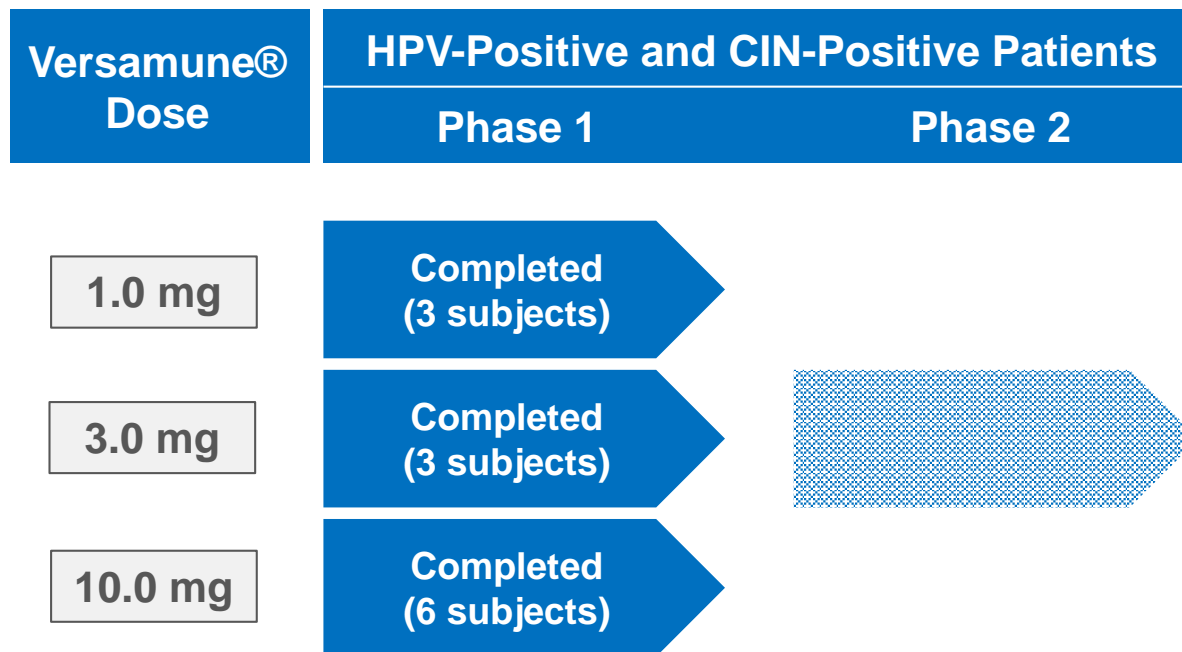
**Versamune®  
Response –  
4 – 7X “Strong”  
(200 spots)**

High T-cell induction also seen in all 6 high-dose patients (10.0mg dose)

\* *IFN-γ ELISPOT –SFC/10<sup>6</sup> Cells. Most commonly reported measure of T-cell efficacy  
Measurement: all T-cells recognizing HPV (induced IFN-γ levels)*

## Versamune® demonstrated excellent safety profile in Phase 1 clinical trial

PDS0101 clinical trial data: No safety issues, even at the highest doses



- **SAFE:** Organ function / blood chemistry
- **SAFE:** Systemic / inflammation (fevers etc.) / immunology
- **SAFE:** Transient injection site reactions only (immune response)
- **SAFE:** Maximum tolerated dose – None / Safe at all tested doses

Safety profile is a result of:

1. High uptake from injection site by immune system & minimal blood presence
2. Biodegradable nanoparticles – broken down into fatty acids & excreted

**Versamune® safety profile is unusually good in immunotherapy**

# **Drug Development Strategy and Pipeline**

## **PDS0101 Target Markets**

**Head-to-head comparisons with top competitors**



## PDS pipeline selection strategy

Focus on maximizing opportunities for clinical and commercial success

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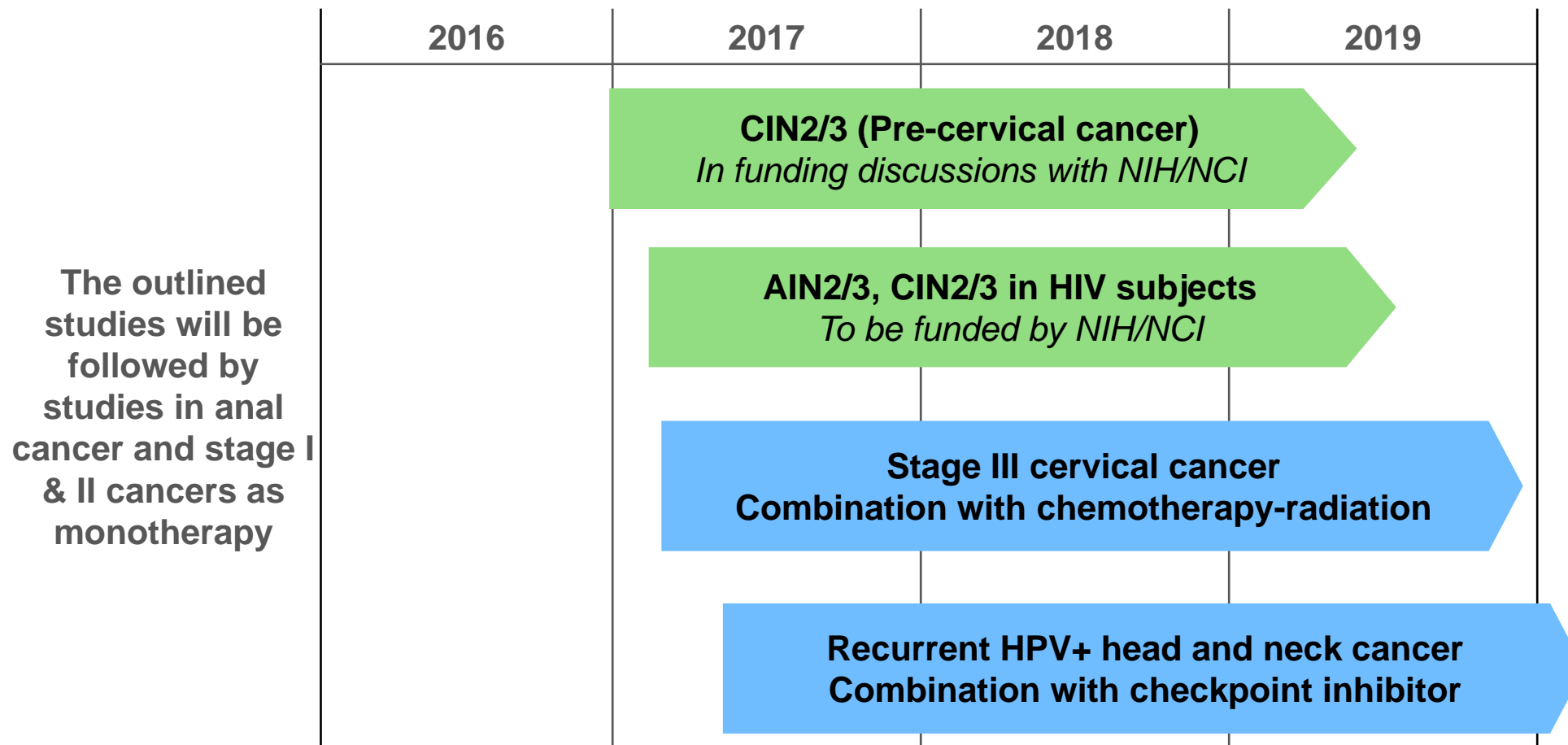
- Select indications and targets where the cancer proteins (antigens) and immune response to the disease or cancer is well understood
  - Relevant preclinical models
  - Highly expressed antigens on the tumors
  - Antigens highly compatible with the platform that can be efficiently presented to the immune system for T-cell priming
- Select indications where the target has been well validated and convincing clinical data demonstrated with other competitive products
  - Demonstrate superior efficacy to top “successful” programs in preclinical and early clinical studies
  - Demonstrate superiority in at least one clinically relevant characteristic that will enable the product to be highly competitive

***PDS has developed and selected a clinical pipeline with high probability for clinical success based on the above principles***

## PDS Drug Development Pipeline: Phase 2 clinical trials in HPV cancers

PDS0101: Broad application in HPV related cancers and pre-cancers

Current projected timetable, subject to change:

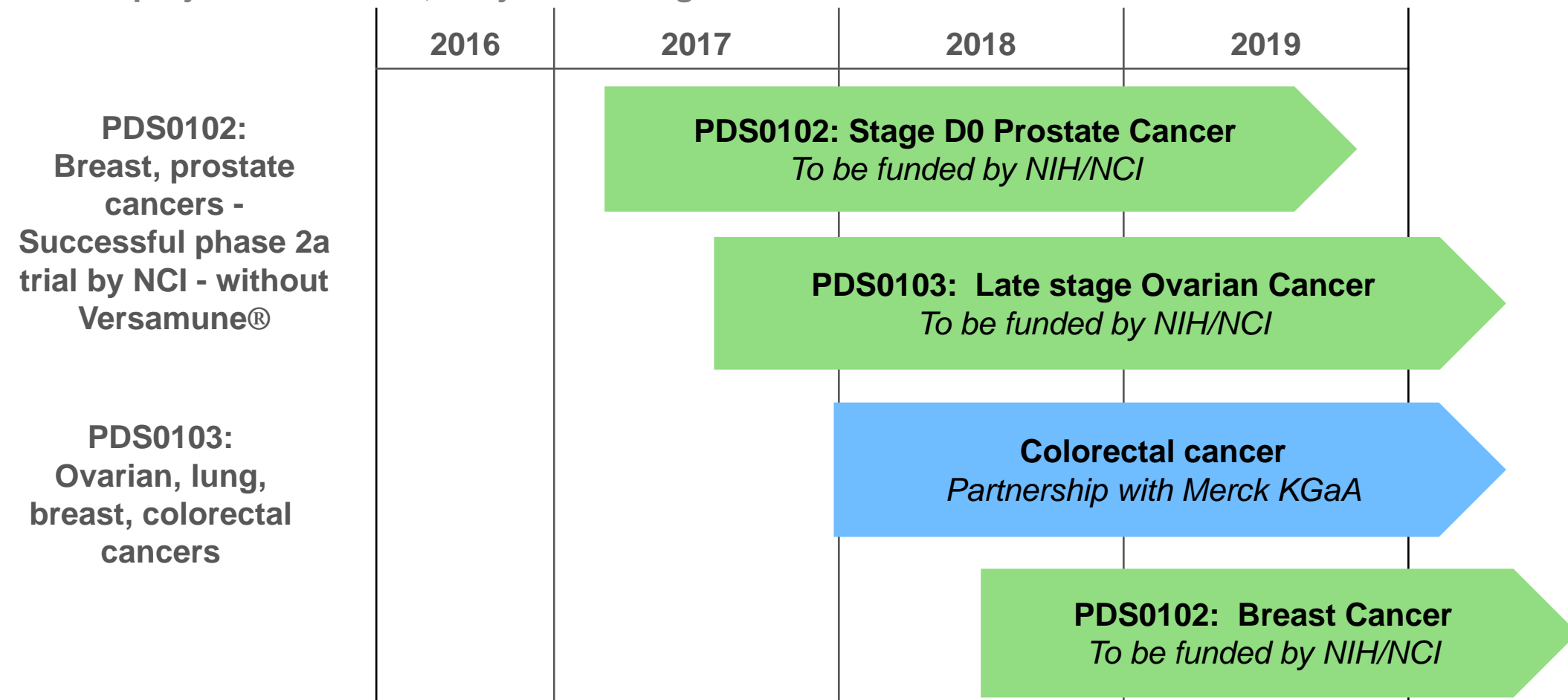


**NCI collaboration substantially increases upside valuation leverage**

## PDS Drug Development Pipeline: Phase 2 Trials in Non-viral Cancers

Phase 2 clinical trials to be funded by partners – Annual revenues for each > \$1 B

Current projected timetable, subject to change:



**NCI collaboration substantially increases upside valuation leverage**

## PDS0101: Excellent probability for clinical & commercial success

PDS0101 unique combination of safety, potency low COGs presents excellent opportunity

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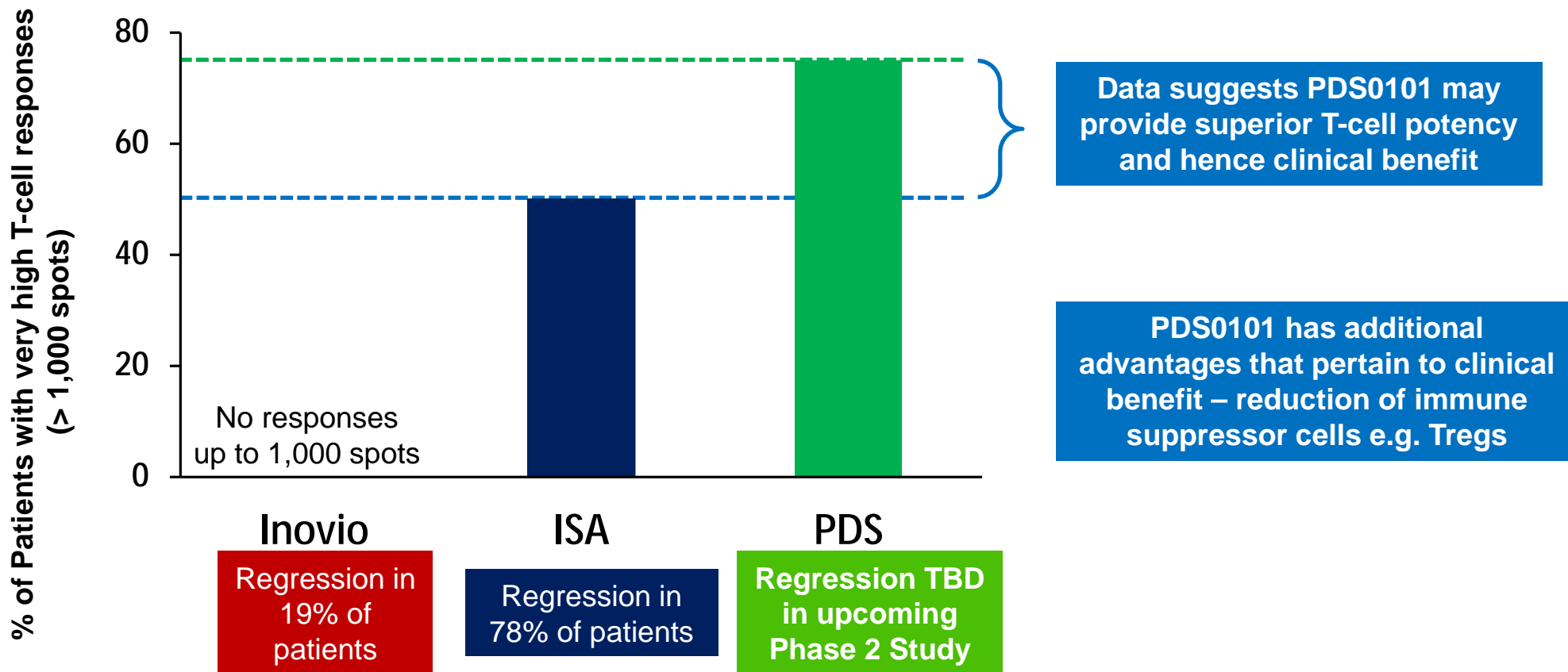
- No approved therapy to treat the HPV induced pre-cancer (neoplasia)
- High-grade neoplasia is treated by surgery – over 80% effective
  - Severe side effects e.g. infertility, pre-term labor, cervical stenosis in ~15%
    - Precludes surgery in low-grade neoplasia
  - Risk of recurrence and progression after surgery could be as high as 20%
- PDS0101 immunotherapy presents excellent potential to treat pre-cancer & cancer
  - ISA Pharma - >70% regression in high-grade vulvar neoplasia (Phase 2)
  - Advaxis – Best results to date in recurrent cervical cancer (Phase 2)
  - ***PDS0101 is significantly superior in potency and safety to both products***
- ***Significant opportunity for PDS0101***
  - Potency – PDS0101 significantly superior to Advaxis, ISA and Inovio
  - Safety – Only PDS0101 has safety profile for high and low grade neoplasias
  - Simplicity and cost of goods – Only PDS0101 can replace surgery

# PDS0101 Phase 1 study – Suggests superiority to best human HPV T-cell data

PDS “Best in Class” advantages in T-cell potency, safety and overcoming immune suppression

## Comparison of HPV-Specific T-Cell Induction – Max. responses

PDS0101 vs. ISA Pharma & Inovio (Previous “Successful” Phase II HPV Programs)



\* ELISPOT study: IFN- $\gamma$  levels/10<sup>6</sup> PBMCs

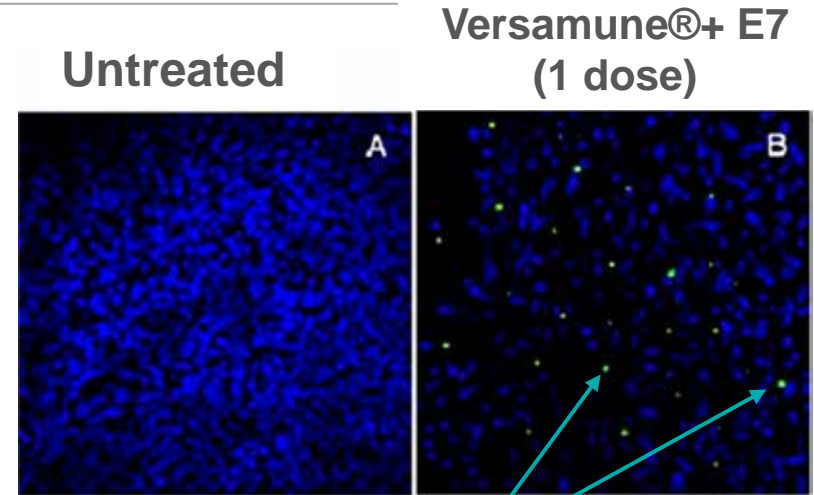
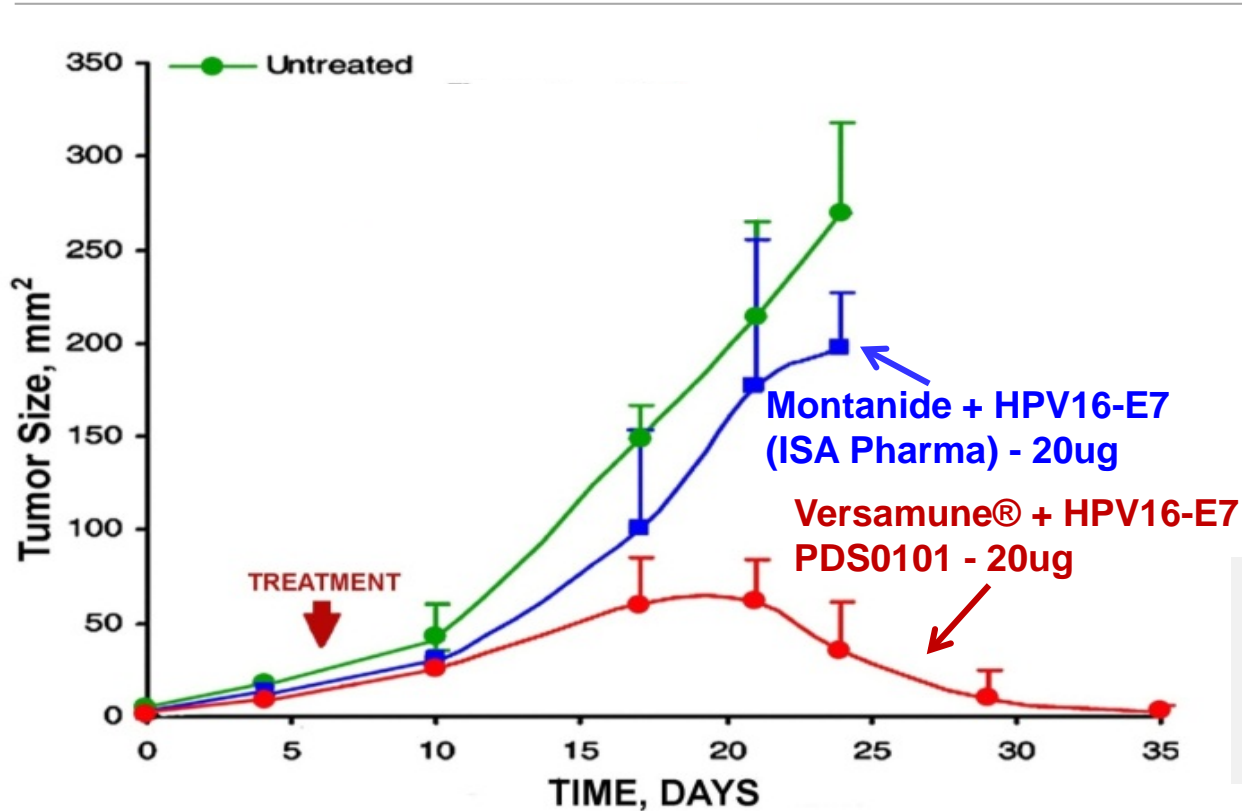
PDS0101: Combined low and medium Phase I doses (expected Phase II dose)

ISA: Data extract from Clin. Cancer Res 2008; 169 14(1) & NEJM 2009, 361, 1838-47 (ISA – ISA5 most potent group)

Inovio: Data extract from The Lancet 2015, 386, 2078

## Versamune®: Multi-action mechanism leads to superior cancer treatment

Superior pre-clinical HPV tumor regression vs. ISA Pharma and leading T-Cell activators



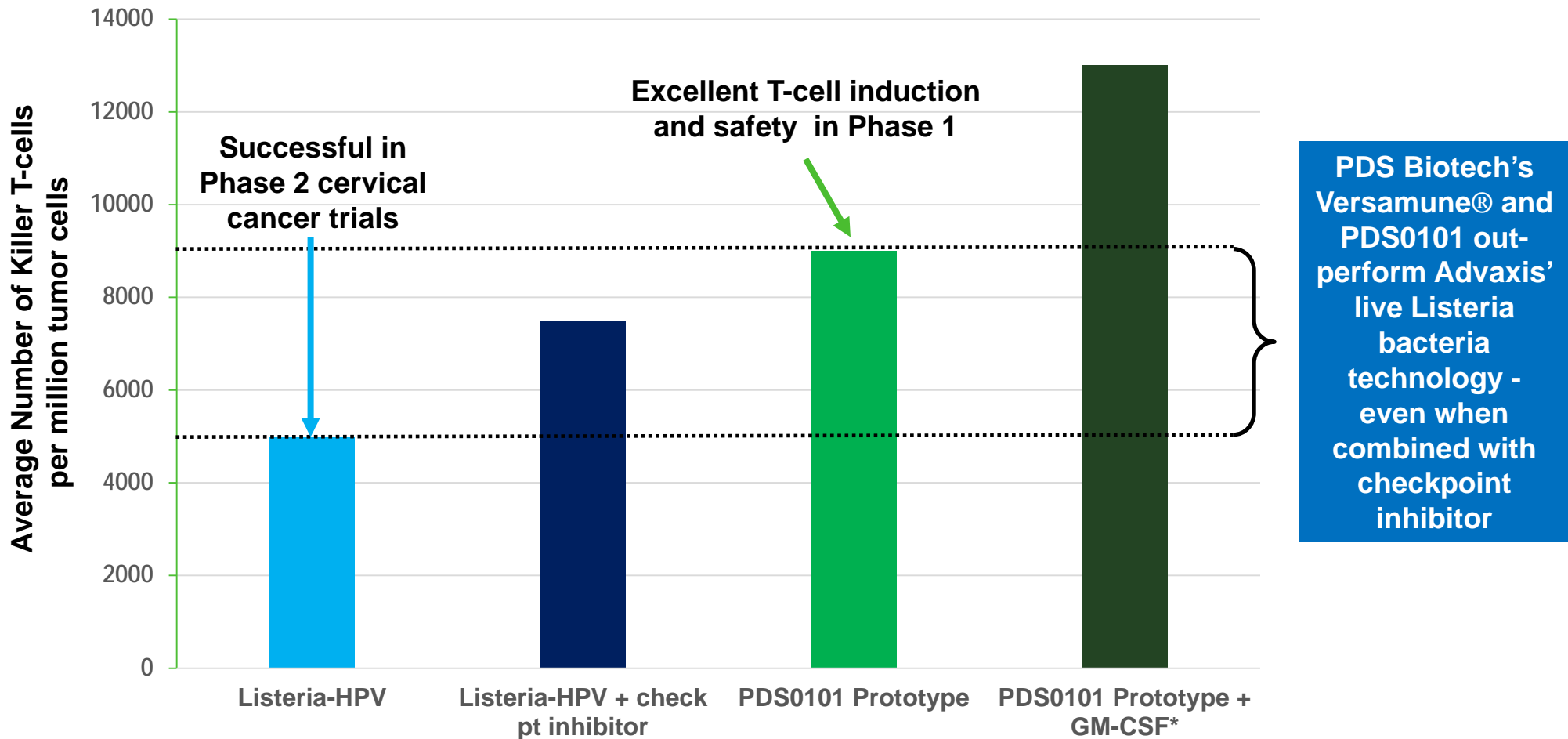
- CD8+ (killer) T-cells infiltrate tumors
- Studies show induction of cell death
- Evaluations 7 days after treatment

### Single Dose Study (Established HPV-Positive Tumors)

- T-cell activators (adjuvants) e.g. Montanide (ISA Pharma), CpG fail to induce tumor regression
- Versamune® mediates potent tumor regression with a single SubQ dose
- Data generated in several hundred animals to date

# NCI studies suggest PDS0101 is superior to Advaxis “successful” product

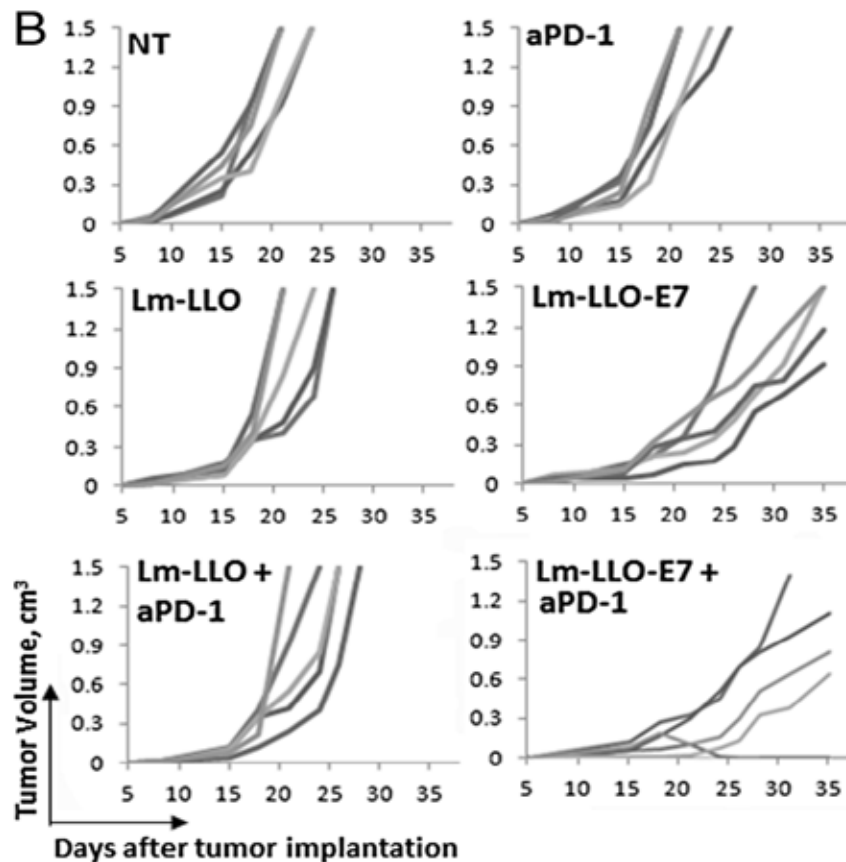
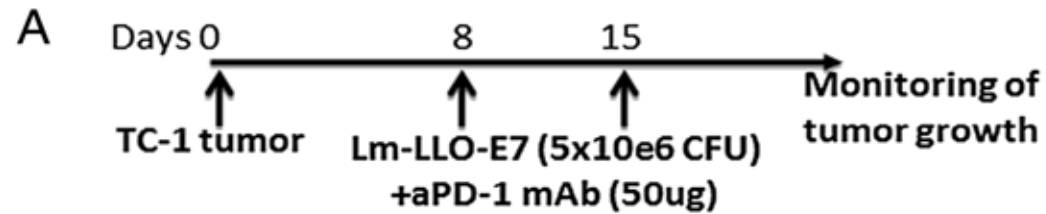
Significantly superior pre-clinical T-cell induction by PDS0101 (Independent study)



\*PDS0101 + GM-CSF Not yet tested in humans – reduces population of MDSC immune suppressor cells  
 All studies done by the same investigators at the NIH’s National Cancer Institute, Cancer Vaccine Division

## Regression of established TC-1 HPV-positive tumors (mouse model)

### Advaxis Listeria bacteria T-cell activating immunotherapy





## PDS0101 market size and projected revenues (excluding licensing)

Year 5 peak sales revenues for US, EU and Japan could be \$2-5 billion

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High grade neoplasia  
US, EU, JP  
Target size = 950,000  
\$1.1 billion

Low grade neoplasia  
US, EU, JP  
Target size = 9,500,000  
\$3.2 billion

Cancer markets  
US, EU, JP  
Target size = 31,500  
\$940 million

Estimated worldwide low-grade, high grade  
and cancer markets at 30% market  
penetration – approx. \$7 billion

- Market Analysis by F. Potter Consulting – Oct 2015 (incorporates effect of current Merck and GSK preventive HPV vaccines)
- Pre-cancer revenues based on US pricing of CIN2/3 procedures: \$1,634 in 2010; \$2,721 in 2023
- 40% market penetration assumed for high grade, 30% for low grade pricing: US - \$3,750; EU - \$2,500; Japan - \$3,125
- Cancer revenues based on pricing: US - \$37,500; EU - \$25,000; Japan - \$31,250

## Results of PDS0101 human clinical trials and comparative analysis

Human data was accurately predicted by preclinical studies

- 1 Safety**
  - First effective cancer immunotherapy with a safety profile suitable to address early stage cancer & pre-cancer
- 2 Potency**
  - Significantly superior T-cell potency to all competitors - Human studies & head-to-head pre-clinical comparisons
- 3 Synthetic, low COGs**
  - Possibly the simplest immunotherapy to date
  - Synthetic nanotechnology platform + peptides

### Positioning

- Only immunotherapy with simplicity (cost), safety and potency to replace surgery as first-line treatment for pre- and early-stage cancers
- First capable of true “reduced risk” combination with checkpoint inhibitors. Opportunity for improved safety and potency (expanding existing market)

**Superiority to “successful clinical” products projects excellent success probability  
A true “disruptive” approach to immunotherapy and cancer treatment/prevention**

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## Questions?

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