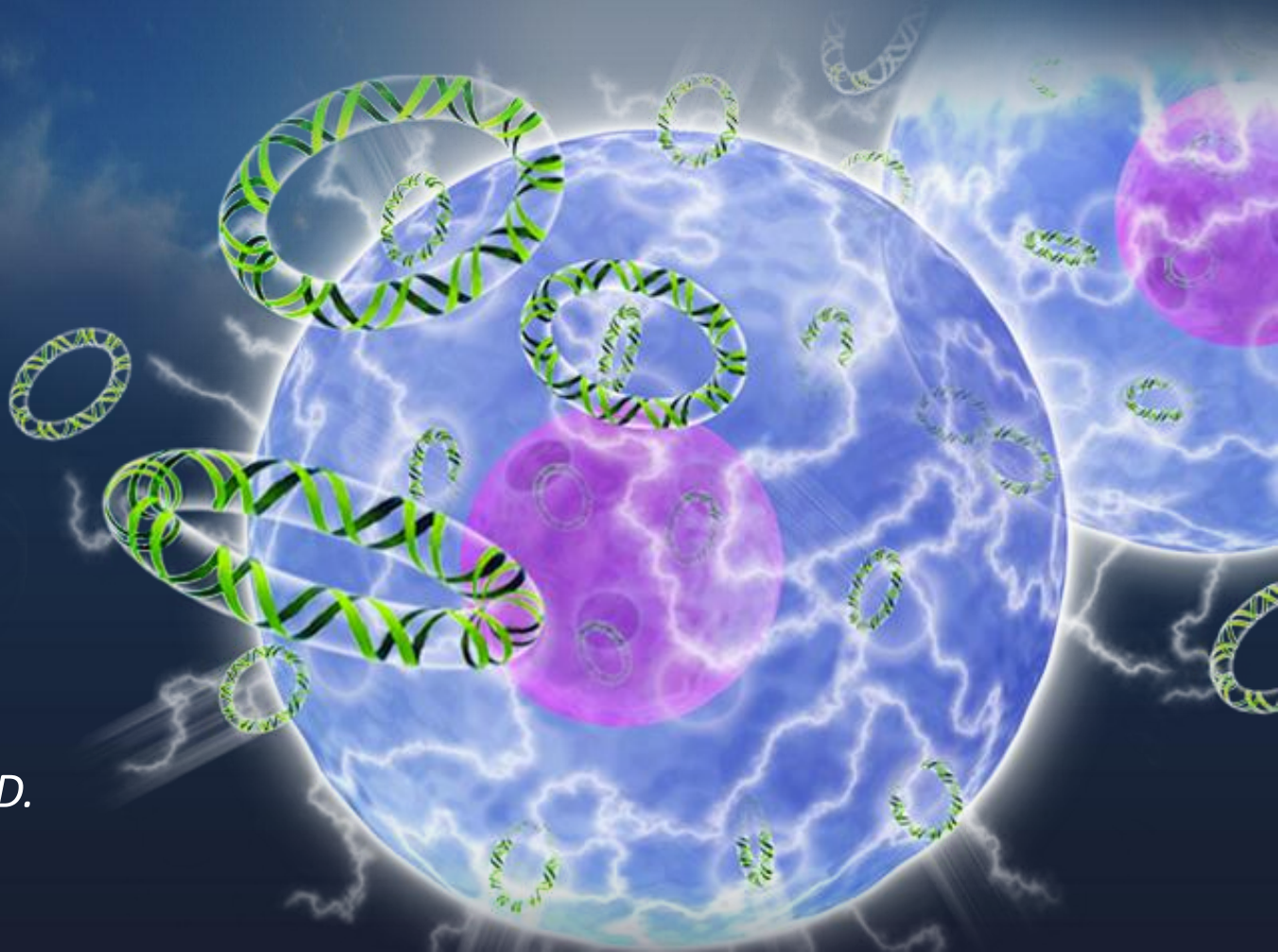
VGX-3100 HPV Specific Immunotherapy for Cervical Intraepithelial Neoplasia: Phase II Efficacy Study Results

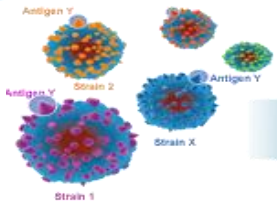


SITC 29th Annual Meeting

November 8th, 2014

Laurent M. Humeau, Ph.D.
Vice President, R&D
Inovio Pharmaceuticals

Inovio combines optimized DNA with safe & effective delivery to generate significant T cells with killing activity

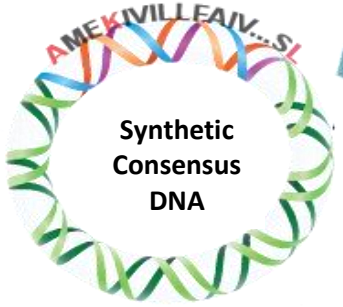


Diverse strains/variants of a target virus/cancer

Assess gene sequence of selected antigen from chosen strains/variants of the virus/cancer

Sequence 1	EMEKIVLLFAIV...SL
Sequence 2	AMESIVLLFAIV...SL
Sequence X	AMEKIVILLFAIV...SK
Consensus	AMEKIVILLFAIV...SL

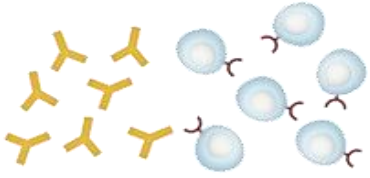
Synthetically create optimal consensus gene sequence for the selected antigen



Insert synthetic consensus gene sequence for selected antigen into DNA plasmid

Manufacture DNA vaccine

Deliver vaccine into muscle or skin tissue using electroporation



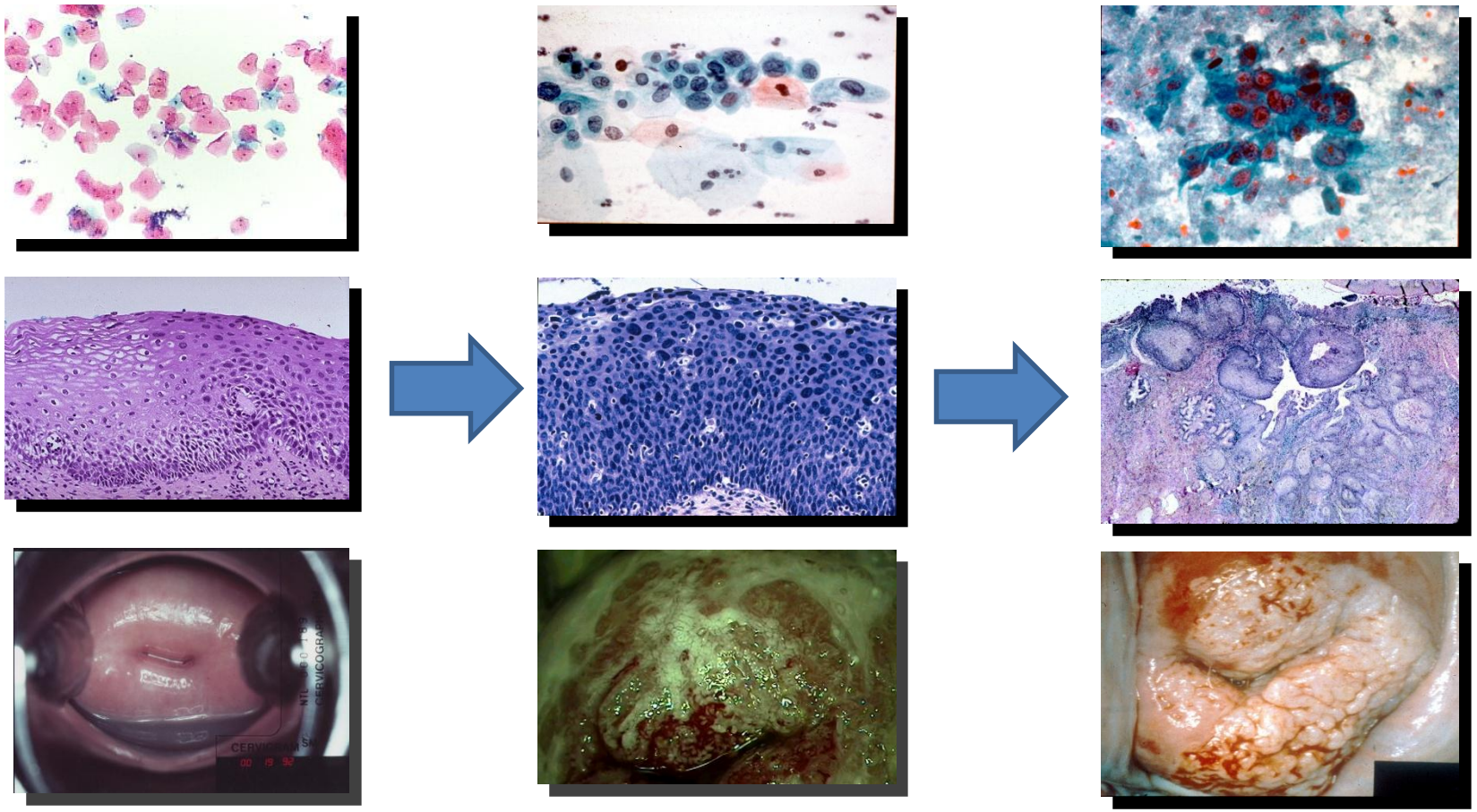
Protective universal antibodies and killerT-cells produced by immune system against diverse strains of a virus

If untreated, moderate/severe cervical dysplasia (CIN2/3) may progress to invasive cancer

Cervical Intraepithelial Neoplasia (CIN3)

Normal

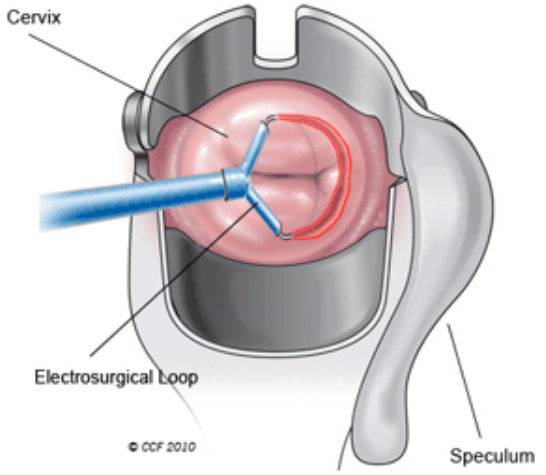
Invasive Cancer



LEEP is perceived to be highly effective, but there is concern of poor longer-term reproductive outcomes

- Loop Electrosurgical Excision Procedure (LEEP) is the surgical procedure for treating abnormal, pre-cancerous cells on the cervix (cervical dysplasia)

- Although most women do not have any serious side effects after LEEP, risks include:
  - Heavy vaginal bleeding
  - Premature birth and having a low birth weight baby
  - Infertility/difficulty becoming pregnant
  - Menstrual problems



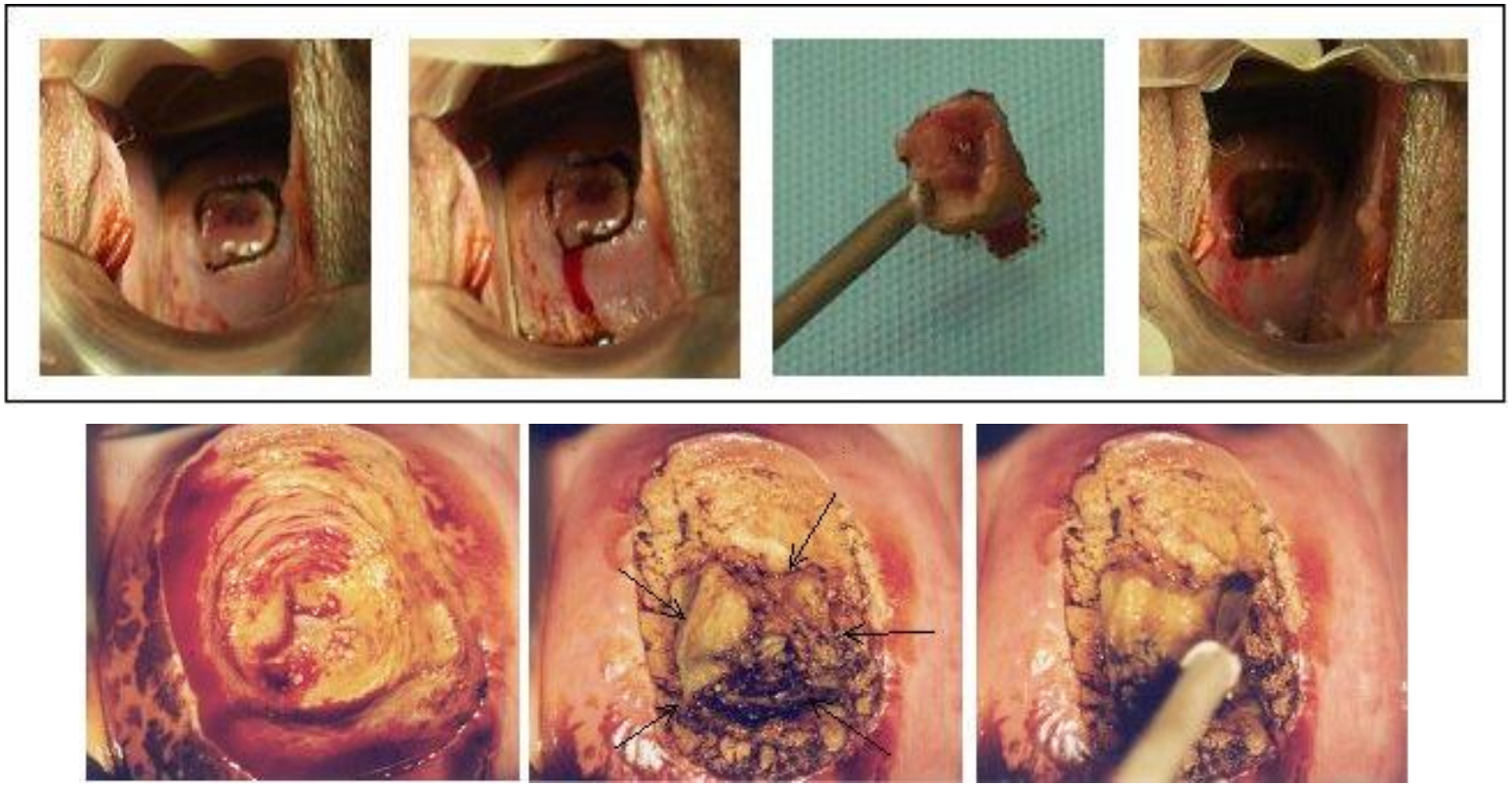
- Additionally, avoiding surgery is a powerful motivator even among women not considering childbirth

http://www.hopkinsmedicine.org

Jin et al. Obstet Gyn (2014), Hienonen et al. Obstet Gyn (2013)

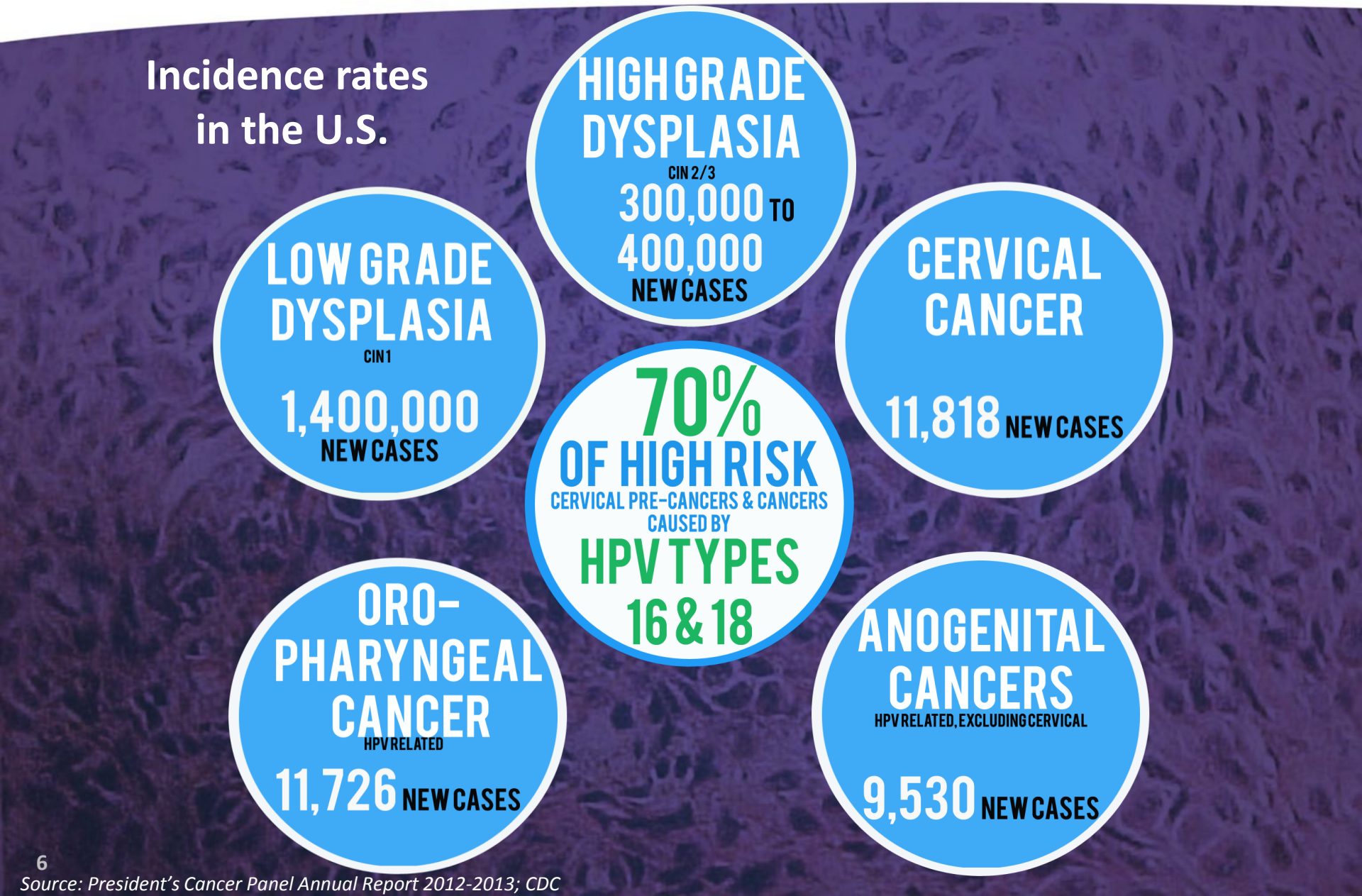
LEEP is the surgical standard-of-care for the treatment of cervical dysplasia

- Loop Electrosurgical Excision Procedure (LEEP) uses a high-voltage electrical arc at 100^{o}C to vaporize a plane through the cervix
- Followed by fulguration using a cautery



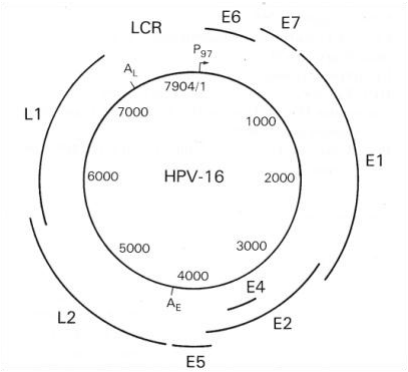
IARC Monograph 2003: Edited by J.W. Sellors and R. Sankaranarayanan

HPV is responsible for nearly 300,000 annual cases of high-grade cervical dysplasia (CIN2/3) in the US

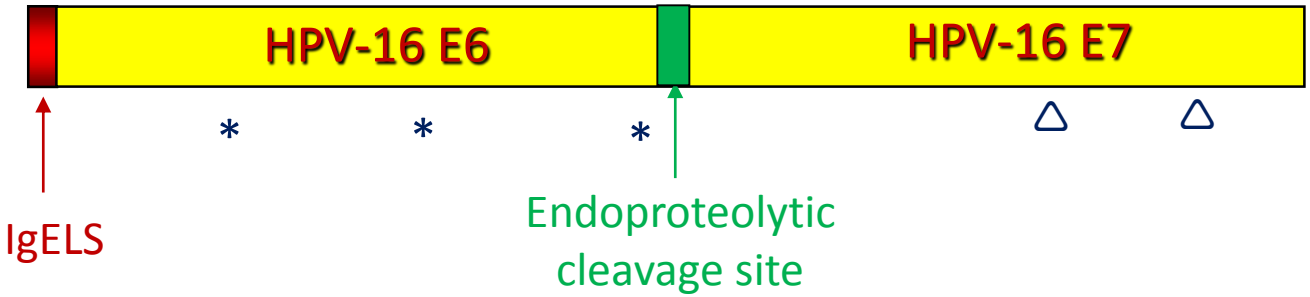


Source: President's Cancer Panel Annual Report 2012-2013; CDC

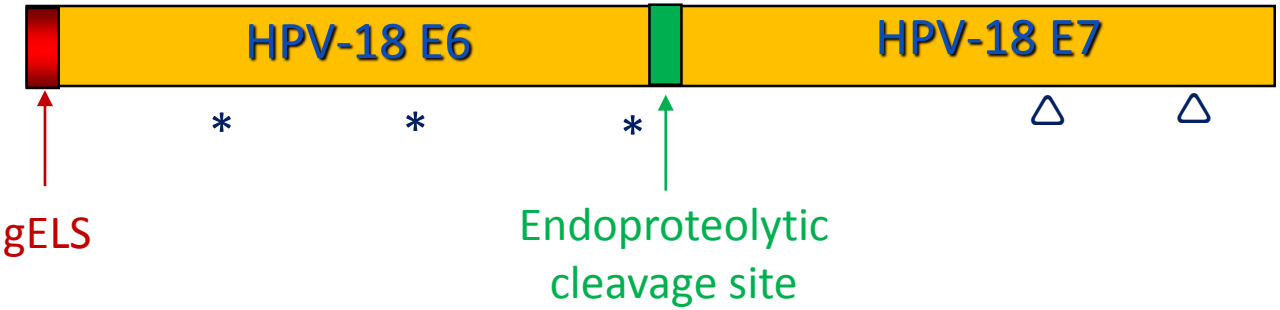
VGX-3100: HPV16,18 E6/E7 Immunotherapy



pCon16E6E7



pCon18E6E7



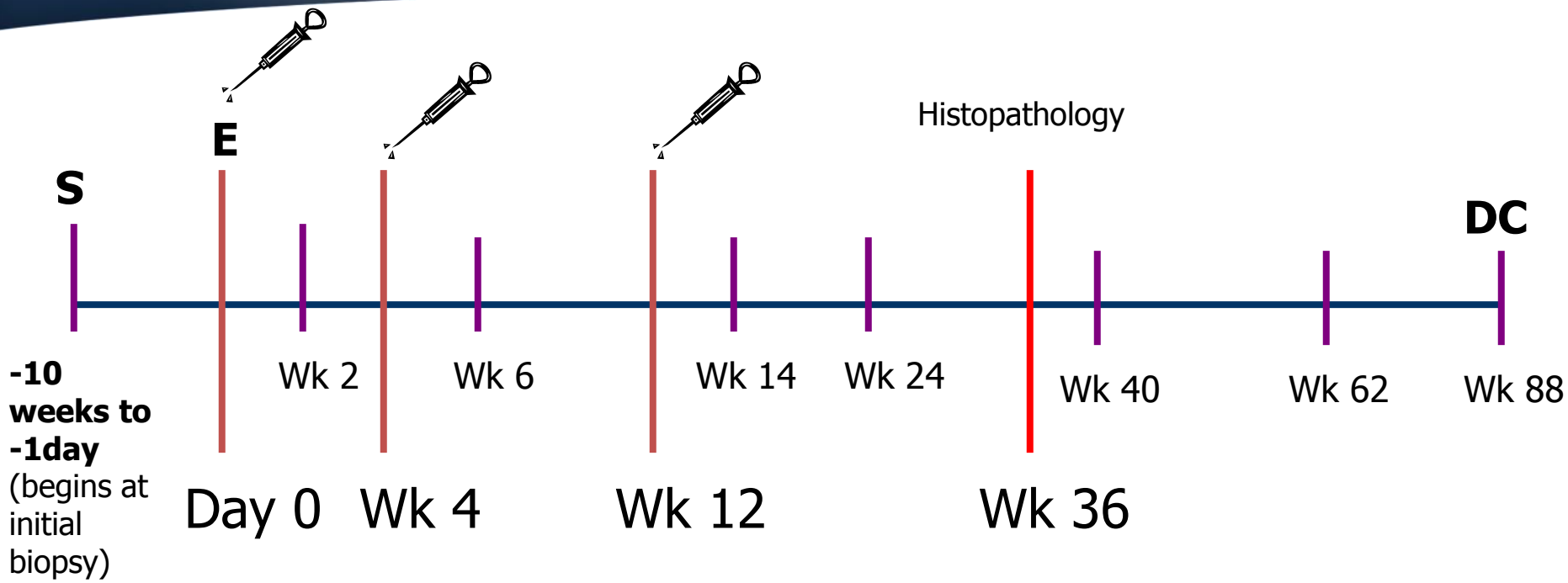
*Deletions or mutations important for p53 binding and degradation

△Mutations in Rb binding site

Phase II: Study Design

- Placebo-controlled, randomized, double blind
  - 148+ subjects: Females 18-55 years old
  - Histologically confirmed HPV16 or 18-associated CIN 2/3 or 3
  - 3:1 VGX-3100/electroporation vs. placebo/electroporation
  - Two plasmids: Type 16 and Type 18, each encoded for E6/E7 antigens; 3 mg/ml per plasmid; treatment at months 0, 1, 3
- Primary endpoint (Month 9)
  - Regression of CIN 2/3 to CIN 1 or no disease
- Secondary endpoints
  - Regression plus clearance of HPV 16 or 18 genotype detected during screening (Week 36)
  - Immunogenicity
  - Safety

Phase II: Study Timeline



Legend: S–Screening E–Enrollment Wk–Week DC-Discharge

- 18 month Protocol
  - 3 month (0, 4, 12 week) regimen
  - +6 months to primary endpoint
  - + 9 months long term follow-up

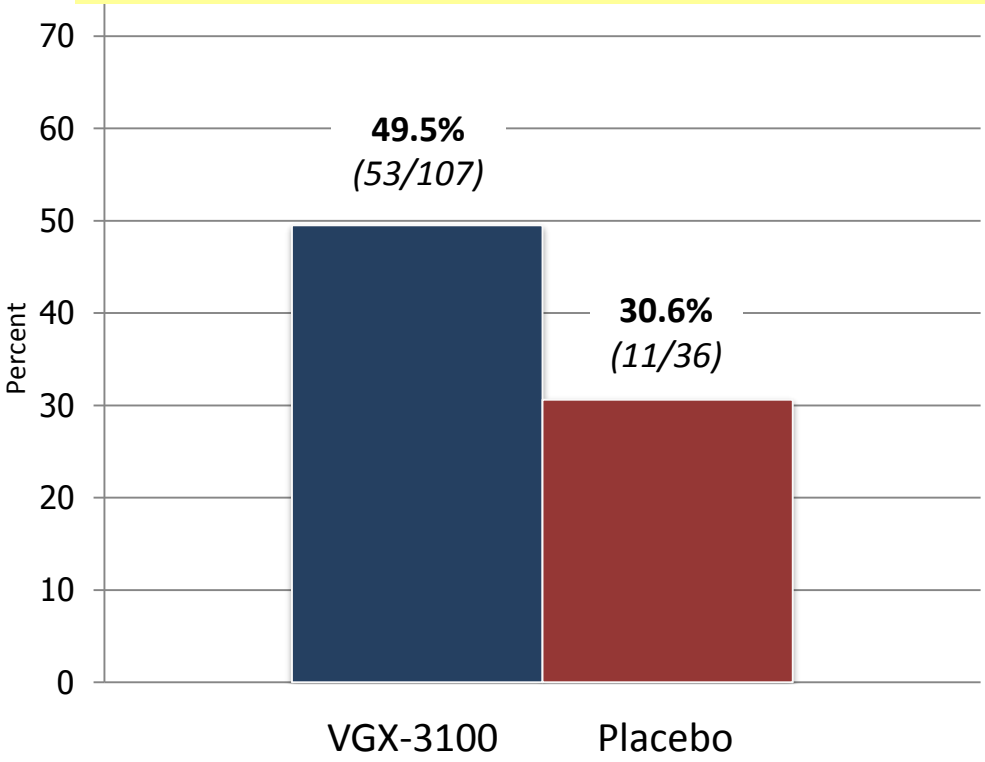
Phase II: Efficacy Assessment and Monitoring

- Subjects monitored for clinical progression of disease by
  - Mandatory Pap smear and HPV PCR on cervical samples (Weeks 14, 62 and 88)
  - Mandatory colposcopy with biopsy if clinically indicated (Week 24)
- Colposcopy and/or biopsy can be performed at any time based upon suspicion of disease progression
- Surgical excision of cervical lesions at Week 36
- All biopsy and excised tissue sent to Pathology Adjudication Panel
- Overall subjects are followed for safety for one year after surgical excision (Week 88)

CIN2/3 resolved to CIN1 or normal in a higher percentage of VGX-3100-treated patients vs. placebo-treated patients

Overall Histopathologic Regression Incidence
Per-Protocol* Population (N=143)

Difference between VGX-3100 and placebo is statistically significant (p=0.017, strata-adjusted)



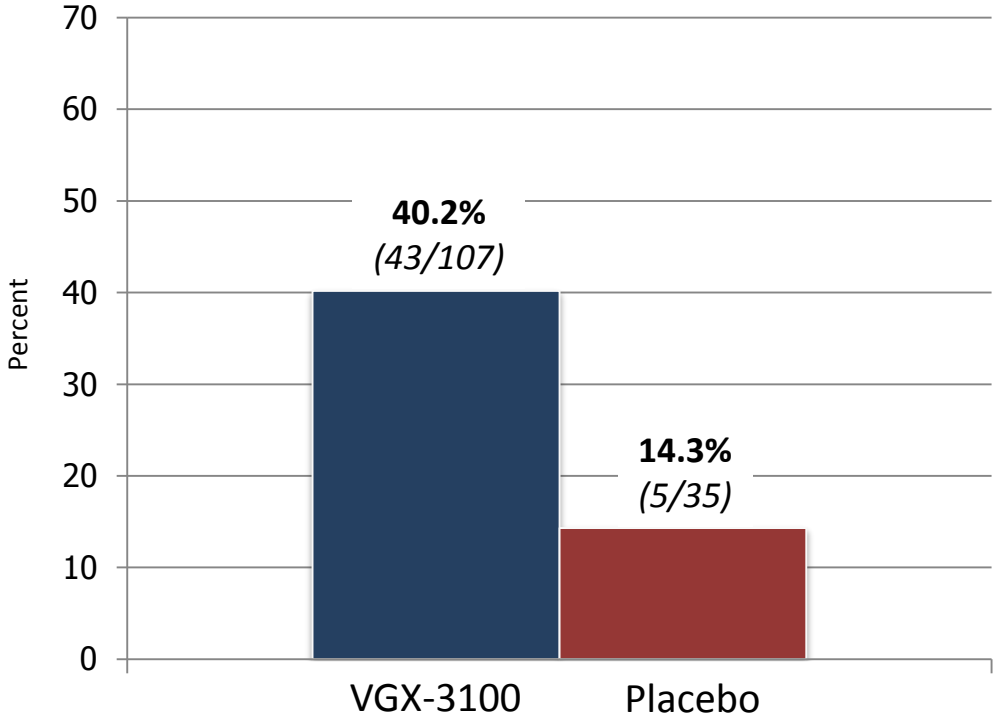
*Per-protocol population (PPP) includes subjects given 3 doses / EP who were biopsied or had surgical excision at any time starting from 14 days prior to the protocol-specified target date of Week 36

PPP also includes subjects with suspected disease progression who underwent early intervention prior to this time frame or discontinued the study; these subjects are treated as non-regressors

CIN2/3 resolved to CIN1 or normal with virological clearance of HPV 16 and/or 18 in a higher % of VGX-3100- vs. placebo-treated patients

Overall Histopathologic Regression* and Virological (HPV Type 16 or 18) Clearance Incidence Per-Protocol** Population (N=142)

Difference between VGX-3100 and placebo is statistically significant (p=0.001, strata adjusted)



*Defined as overall biopsy diagnosis or overall definitive therapy diagnosis as either CIN 1 or No Significant Pathological Change

**Per-protocol population (PPP) includes subjects given 3 doses / EP who were biopsied or had surgical excision at any time starting from 14 days prior to the protocol-specified target date of Week 36

PPP also includes subjects with suspected disease progression who underwent early intervention prior to this time frame or discontinued the study; these subjects are treated as non-regressors

SUMMARY: VGX-3100 has the potential to address a high unmet medical need in the treatment of HPV-driven cervical dysplasia

- HPV 16 and 18 are responsible for nearly 300,000 cases of high-grade cervical dysplasia in the US annually
- There is a high unmet need for a non-surgical option that preserves a woman's reproductive health
- VGX-3100 is generally well-tolerated with only administration site redness occurring significantly more frequently in the VGX-3100 group vs. placebo group
- **Immunization with VGX-3100 results in regression of CIN2/3 to CIN1 or normal and virological clearance of HPV 16 and/or 18**
  - **49.5% regression to CIN1 or less, 40.2% regression to CIN1 or less in the context of complete elimination of HPV 16/18 infection**

VGX-3100: Next Steps

ANALYSIS of PHASE II DATA IN PROGRESS

- Additional immunological and histological data in progress
- Manuscript in preparation

PHASE III in PLANNING UNDERWAY

- Clinical and Regulatory
- Commercial EP Device Development
- Quantitative Market Research
- Supply Chain Strategy
- Pricing & Reimbursement

EXPANSION of HPV PROGRAM to RELATED INDICATIONS

- Cervical Cancer
- Head & Neck
- Anogenital Cancers
- VIN, PIN

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