Developing T cell vaccines for HSV-2 Infection

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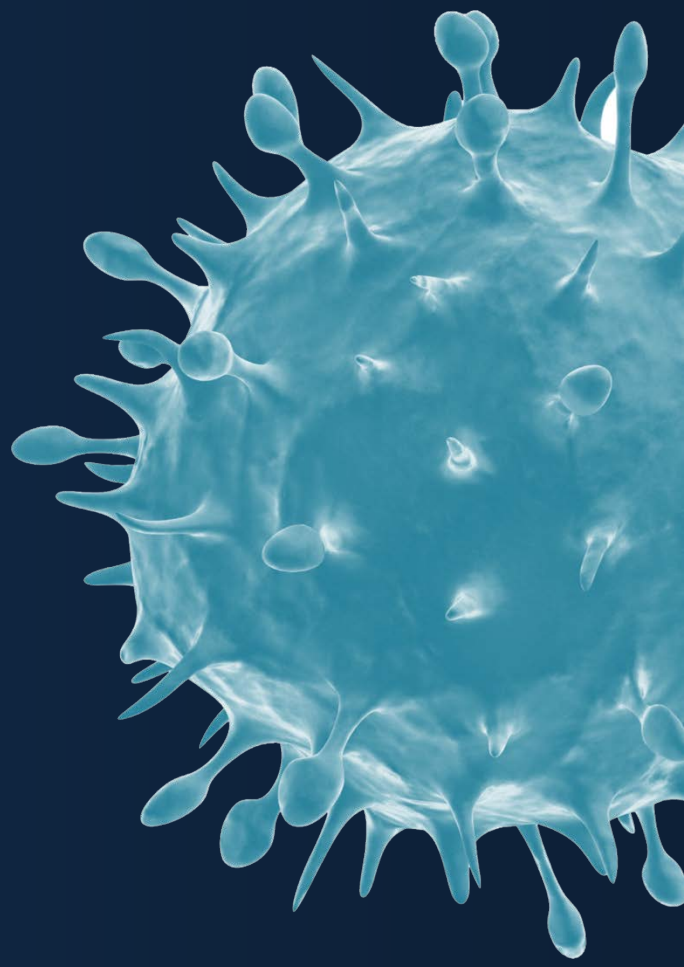
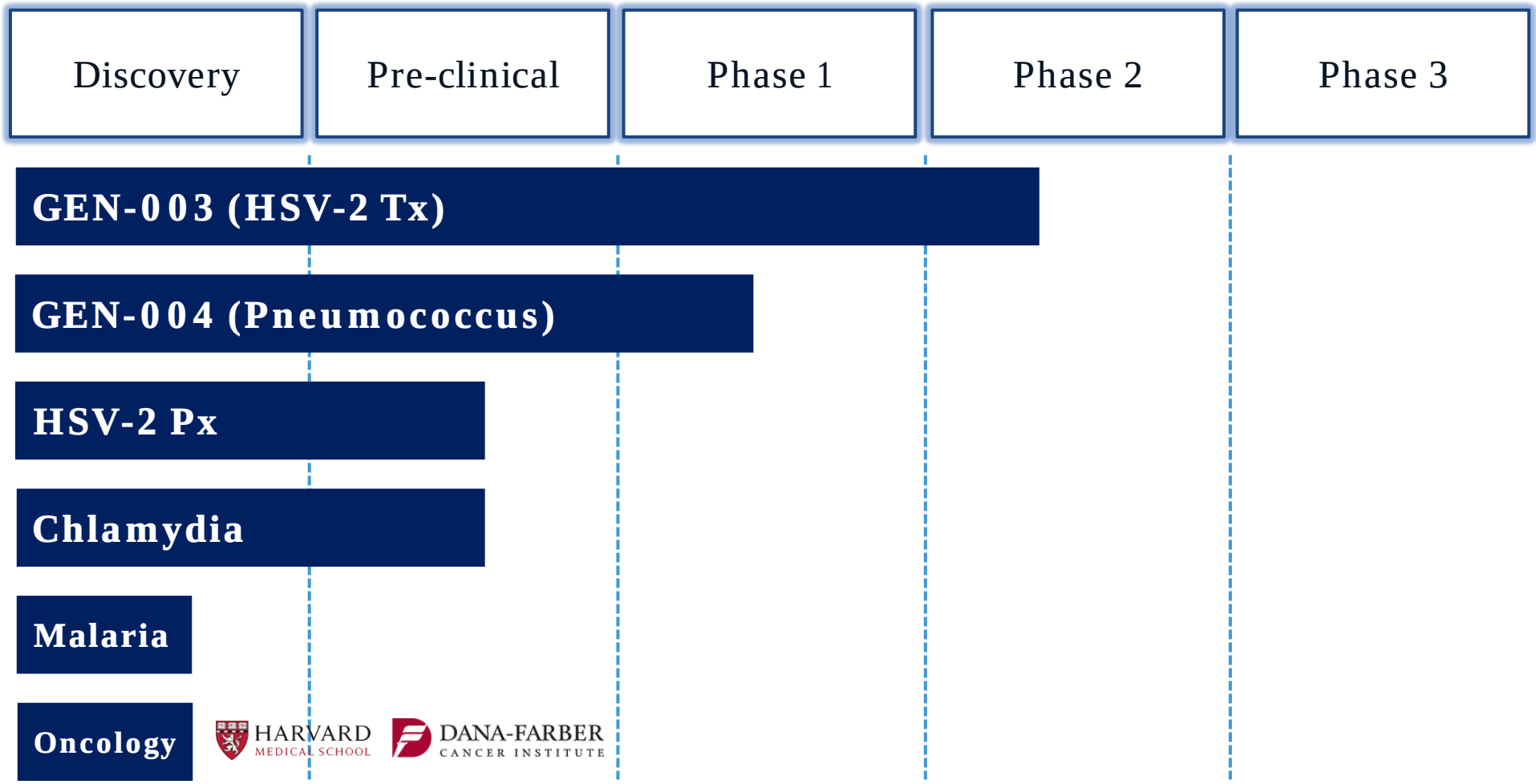
World Vaccine Congress
24-26 March, 2014



genocea
BIOSCIENCES

Deep Pipeline of T Cell-Enabled Vaccine Candidates

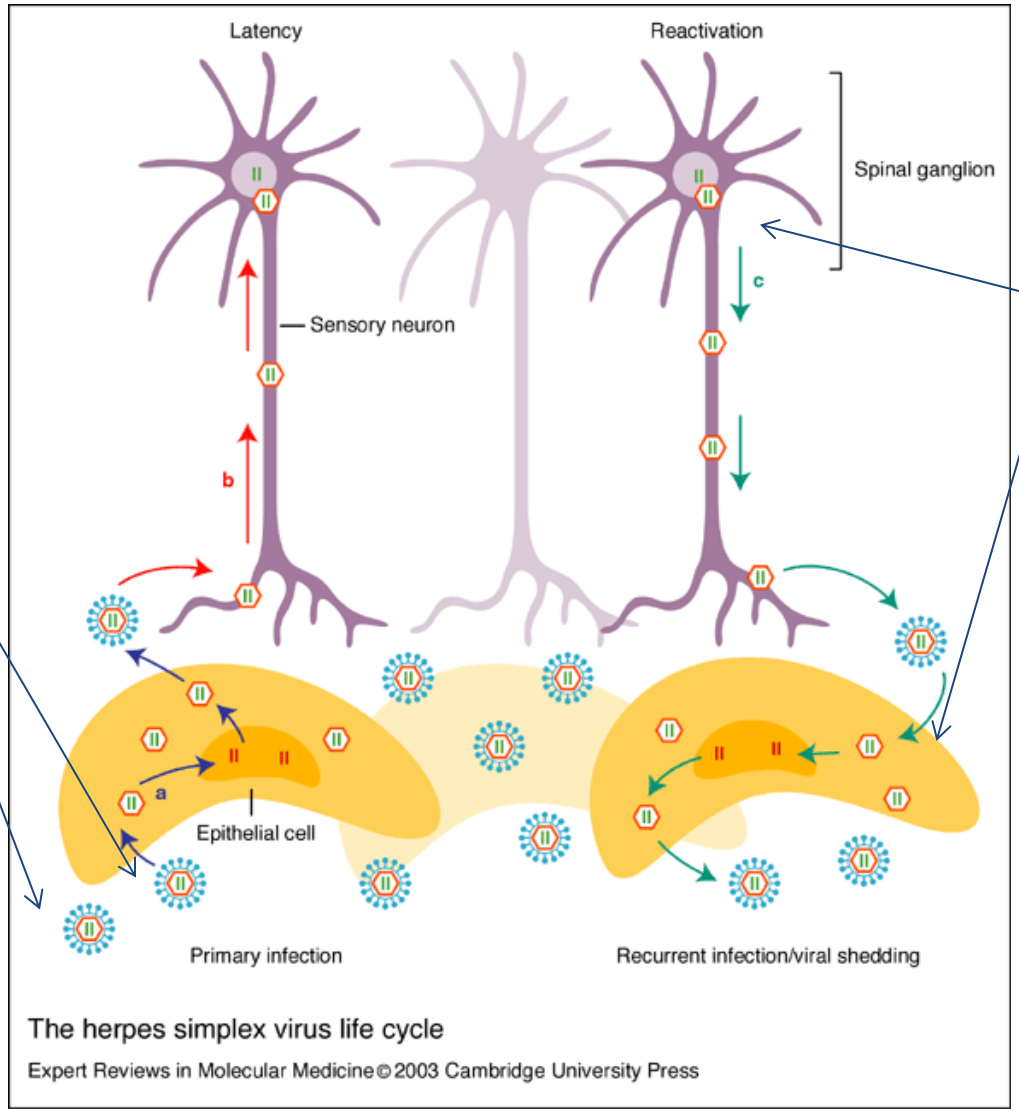


Epidemiology and Therapy of HSV-2

- **Incurable STD**
- **Public health epidemic**
  - 500 million people infected worldwide
  - Increased risk of HIV-1
  - Serious complications of neonatal transmission
- **Oral anti-viral drugs**
  - Incomplete symptom control
  - Continued transmission risk
  - Daily dosing for optimal effect

The Unique Life Cycle of HSV-2 Has Made it Refractory to Vaccine Development

Antibodies[1]



T cells[2,3]

[1]Muggeridge (2000) *J Gen Virol*
[2]Koelle *et al.*, (1998) *JCI*
[3]Knickelbein *et al.*, (2008) *Science*

Harnessing T Cells to Enable Vaccine Development

Collect PBMC* from exposed humans

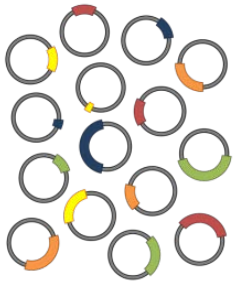
Uninfected, exposed

Infected, asymptomatic

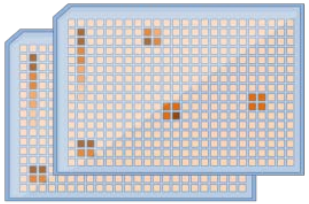
Infected, ≤ 3 outbreaks/yr

Infected, >3 outbreaks/yr

HSV-2 proteome



T cell response, by subject, by cohort



Bioinformatics

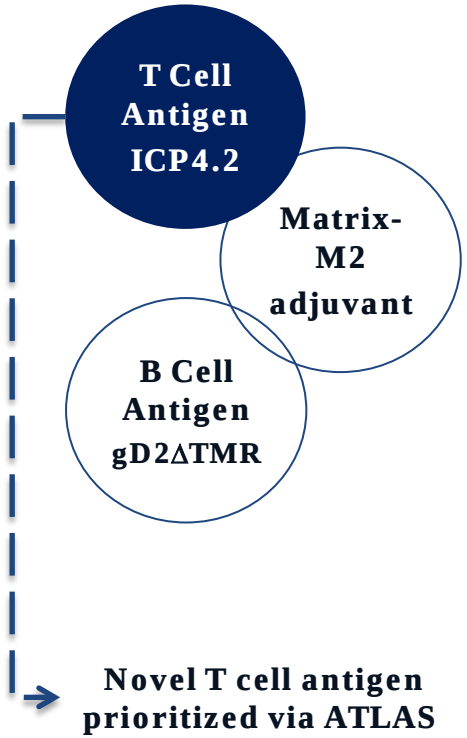
GEN-003

ATLAS™: high-throughput, comprehensive, T cell antigen discovery

*PBMC = peripheral blood mononuclear cells

GEN-003: A Novel Therapeutic Vaccine Candidate

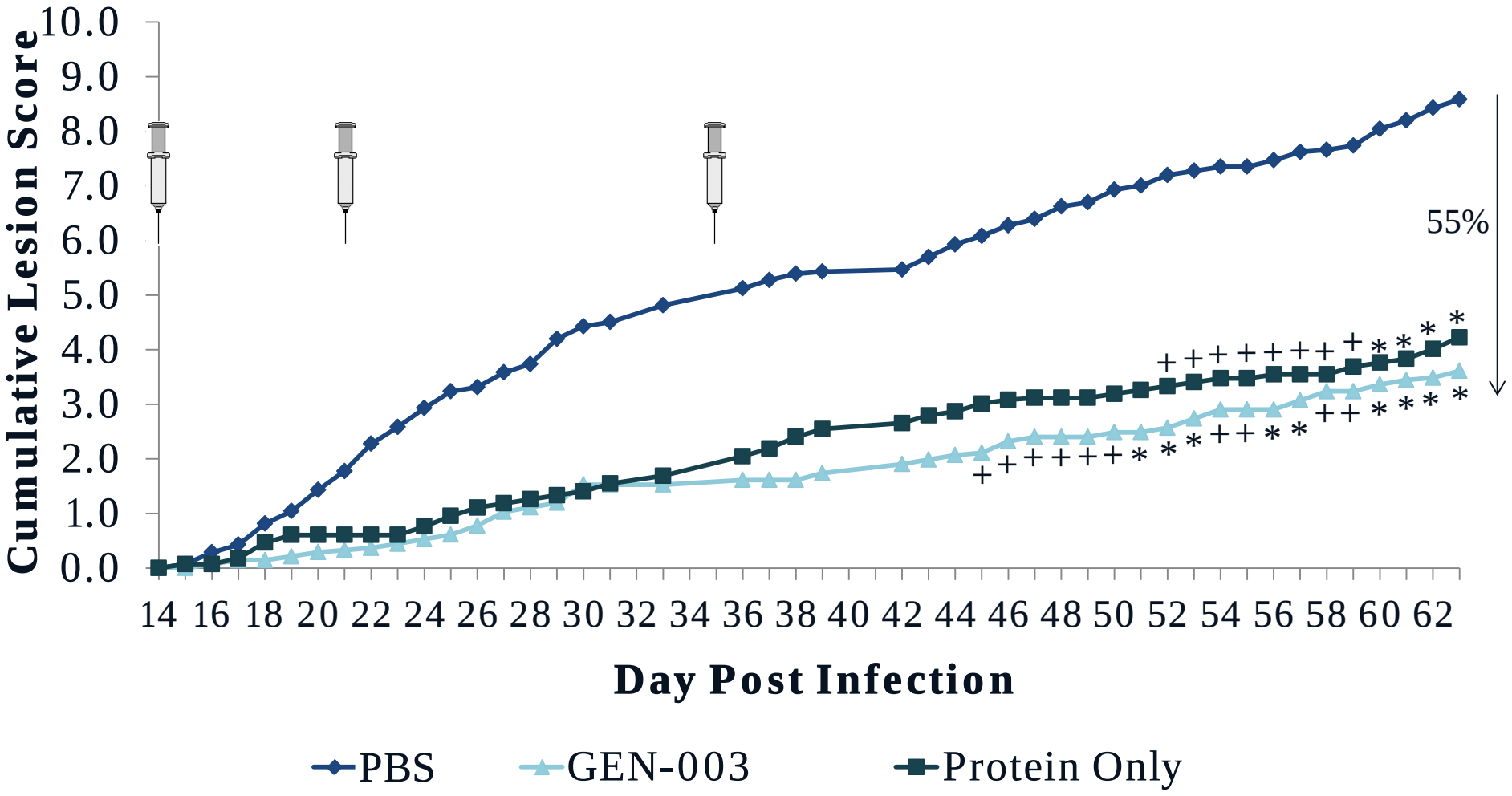
GEN-003



GEN-003 Proposition

- Reduce viral shedding and transmission risk
- Ameliorate symptoms
- Convenient dosing regimen
- Novel mechanism of action

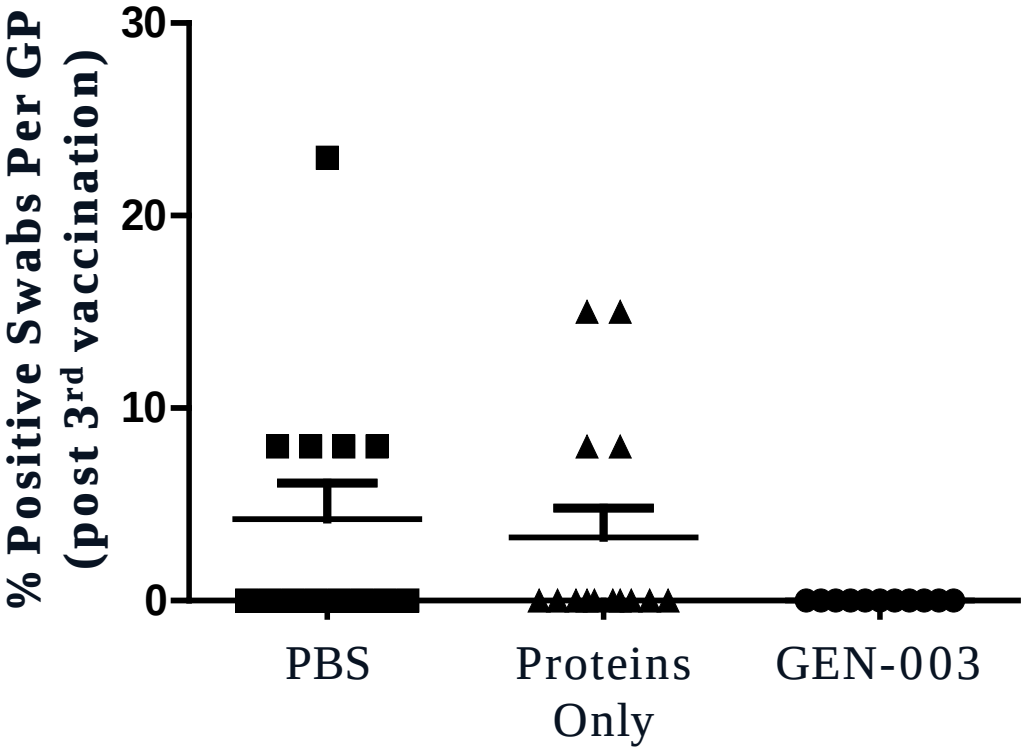
GEN-003 Significantly Reduces Symptoms in Guinea Pig Therapeutic Model



+=p<0.05
*=p<0.01
2-way ANOVA with Bonferroni post-test

GEN-003 Significantly Reduces Viral Shedding in Guinea Pig Therapeutic Model

Shedding Frequency



Mean Titer*

	Days 15-21	Days 22-36	Days 37-63
PBS	4.33	4.58	3.06
Proteins Only	4.18	3.51	2.48
GEN-003	3.73	3.38	–
Log Reduction in Titer for GEN-003	**0.6**	**1.2**	**3.1**

** Expressed in Log10 copies/mL; calculated only from animals that are shedding*

Robust Phase 1/2a Trial Design

- **Patients: 143 with HSV-2 infections**
  - Moderate-to-severe infections (3-9 outbreaks/year)

- **Design:**
  - Double-blind, placebo-controlled
  - ~30 subjects in each of 5 groups:
    - Placebo
    - Proteins only
    - GEN-003 (10 µg per protein + 50 µg adjuvant)
    - GEN-003 (30 µg per protein + 50 µg adjuvant)
    - GEN-003 (100 µg per protein + 50 µg adjuvant)
  - 3 immunizations at 21 day intervals

- **Endpoints:**
  - Safety, tolerability, immune response
  - Impact on viral shedding
  - Impact on symptoms (exploratory)

Viral Shedding as an Indicator of Anti-Viral Effect

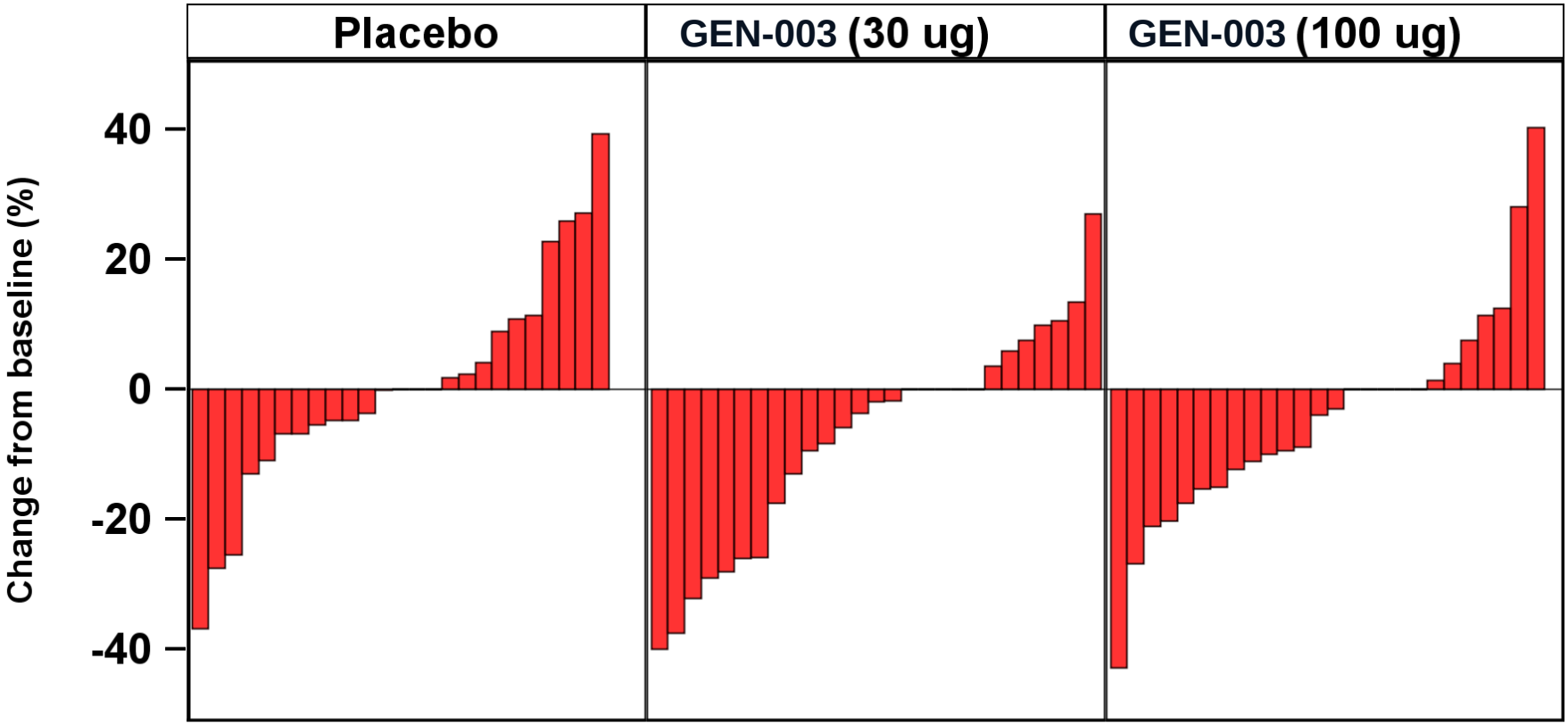
- **Defined as the % of days with HSV-2 detected on the skin/mucous membranes**
- **Measured over defined intervals (28 days or more)**
- **Repeated measures before and after immunotherapy**

Statistically Significant, Durable Reduction in Viral Shedding

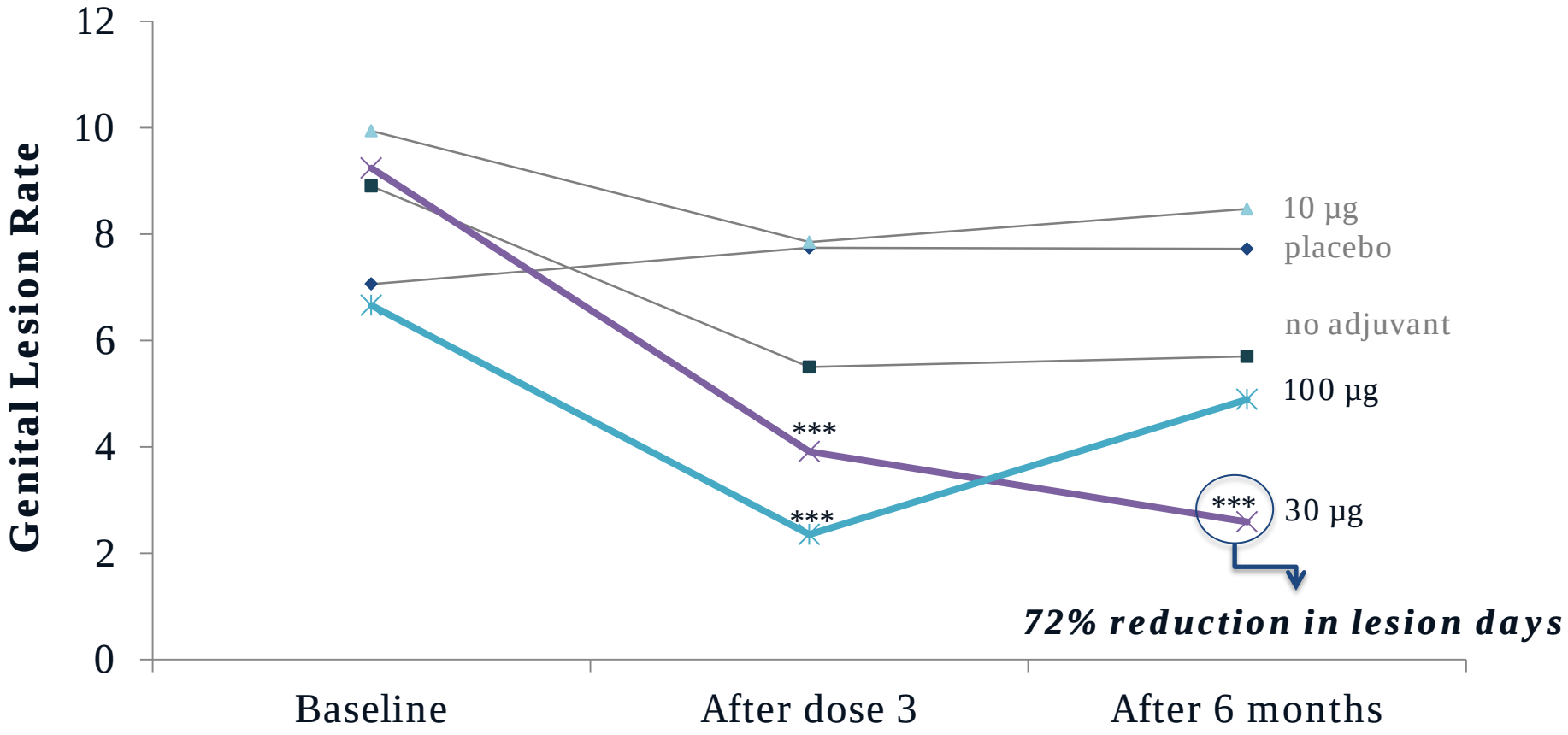
Treatment Group	# of Subjects	(Post Dose 3) Mean Viral Shedding Frequency: Change from Baseline	p-value	# of Subjects	(After 6 Months) Mean Viral Shedding Frequency: Change from Baseline	p-value
Placebo	28	+11%	NS	23	+32%	<0.003
No adjuvant	28	+18%	NS	22	+14%	NS
GEN-003 (10 µg)	31	0%	NS	26	+54%	<0.001
GEN-003 (30 µg)	**29**	**-50%**	**<0.001**	**19**	**-40%**	**<0.001**
GEN-003 (100 µg)	**27**	**-29%**	**<0.001**	24	-18%	NS

NS = not significant

Shedding Rate Changes from Baseline by Treatment Arm



GEN-003 Decreases the Frequency of Days with Ulcers Present



*** $p<0.001$

Summary and Next Steps

- **Rationally designed vaccine using ATLAS™**
- **Compelling first-in-class profile in Phase 1/2a**
  - 50% reduction in viral shedding
  - 72% reduction in symptomatic disease
  - Durable for at least six months
  - Well-tolerated
  - Reporting 12-month data in mid-year
- **Planned Phase 2 trials**
  - Adjuvant dose titration
  - Dose number and interval

Acknowledgements

- **All the patients who participated in the study**
- **University of Washington**
  - Anna Wald MD, Phd
  - Amalia Margaret, PhD
  - Emma Robinson
- **Westover Heights Clinic**
  - Terri Warren RN, ANP
  - Basak Gokcora
- **Indiana University School of Medicine**
  - Kenneth Fife MD
  - Elisha Eppes NP
- **Center for Clinical Studies, Houston TX**
  - Stephen Tyring MD
  - Farhan Khan MD, MBA
- **Center for Clinical Studies, Webster TX**
  - Patricia Lee MD
  - Deborah Yetman
- **IND2Results**
  - Amy Morris
- **University of Alabama Birmingham**
  - Nick Van Wagoner MD
  - Aeryn Peck
- **Cincinnati Children's Medical Center**
  - David Bernstein MD
  - Tara Foltz RN
  - Rhonda Cardin, PhD
- **Rho, Inc.**
  - Karen Kessler, PhD
  - Patricia Stephenson, PhD
- **Genocea Biosciences**
  - Seth Hetherington MD
  - Alexander Lee
  - Deborah Long, PhD
  - Shane Larson
  - Veronica Clemens
  - Lena Kien
  - Amy Baccari
  - Omar Magid
  - Danielle Garvie
  - Bruno Piqani
  - Bharat Dixit, PhD