P–34; **DELIVERY OF HPV ANTIGENS USING A MODIFIED HSV-2 VECTOR: DEVELOPMENT OF A COMBINED VACCINE FOR HPV AND HSV-2**

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Background: Herpes simplex virus (HSV) infects antigen-presenting cells very efficiently indicating its potential as an efficient antigen delivery platform for vaccine purposes. HSV encodes various proteins to block a potent immune response. These proteins include ICP47 (blocks MHC loading); vhs (blocks DC activation); ICP34.5 (blocks interferon-mediated responses); US5 (inhibits apoptosis in infected cells); and UL43 (reduces immunogenicity by an unknown means).

Materials and Methods: We have produced an HSV-2 vaccine (ImmunoVEX^{HSV-2}) in which these genes are deleted, the first immune evasion function-deleted HSV vaccine candidate to be produced. Unlike wild-type HSV, this non-pathogenic, replication impaired virus significantly activates DC enhancing its immunogenicity.

Results: We have previously reported that ImmunoVEX^{HSV-2} gave 100% efficacy as a prophylactic vaccine in the female guinea pig model of genital herpes. The vaccine was shown to generate specific and neutralising anti-HSV antibodies in this model and to reduce the level of latent infection in DRG following challenge. We have also shown that ImmunoVEX^{HSV-2} induces HSV-specific antibody and T-cell responses in mice and rats. Pre-clinical studies have shown that ImmunoVEX^{HSV-2} does not induce any macroscopic or microscopic toxicological findings following repeat subcutaneous dosing with clinically relevant doses in guinea pigs or rats. In contrast to wild type HSV-2, ImmunoVEX^{HSV-2} does not induce inflammation or PNS/CNS disease following intranasal or intracranial administration in mice. In addition, ImmunoVEX^{HSV-2} does not establish latent infections following intranasal or subcutaneous administration in mice as measured by qPCR. A clinical trial with this stand-alone HSV vaccine candidate is planned to begin during 2008.

Conclusions: It is our belief that a combined vaccine for HSV-2/HPV is scientifically and commercially attractive. To this end, we have used the ImmunoVEX^{HSV-2} platform to develop two combined vaccines where codon-optimised versions of HPV-16 E2/L1/L2, or E2/E6/E7 have been expressed from the ImmunoVEX^{HSV-2} backbone in place of ICP34.5 and vhs. These combination vaccines for HSV-2 and HPV are currently in pre-clinical testing.