

## EMERGING COMPANY PROFILE

# X-Vax: Bucking dogma in HSV vaccine development

BY SANDI WONG, STAFF WRITER

Veering from the field's focus on neutralizing antibodies, X-Vax is developing vaccines that elicit non-neutralizing antibodies that direct the immune system to kill infected cells. Its lead candidate is in preclinical development to prevent HSV infection.

X-Vax Technology Inc. COO Andreas Eggert told BioCentury that HSV vaccine R&D has centered on eliciting neutralizing antibodies (nAbs) against glycoprotein D, a protein required for the virus to enter cells. Glycoprotein D also attracts the lion's share of the immune response.

None of those programs have yielded an approved HSV vaccine, however, suggesting that use of anti-glycoprotein D nAbs to block viral entry into host cells is insufficient to confer protection.

X-Vax believes the key to immunity against HSV is to prevent new virion production and release by killing infected cells. Its lead vaccine,  $\Delta$ gD-2, elicits non-neutralizing antibodies that trigger antibody-dependent cellular cytotoxicity (ADCC).

Founded in 2015 by serial entrepreneur Isaac Blech and William Haseltine, the company exclusively licensed IP covering the vaccine from Albert Einstein College of Medicine. Blech co-founded Celgene Corp. (NASDAQ:CELG) and ICOS Corp. among other companies; and Haseltine was a Harvard Medical School professor and chairman and CEO of Human Genome Sciences Inc.

The vaccine, created by X-Vax SAB members and Albert Einstein professors William Jacobs and Betsy Herold, comprises HSV-2 lacking the gene for glycoprotein D to prevent active infection. Because ADCC requires cells to display viral proteins, the vaccine is produced in glycoprotein D-expressing cells, which enables it to enter host cells upon immunization and undergo a single replication cycle.

Jacobs and Herold had created  $\Delta$ gD-2 as a tool to investigate whether and how glycoprotein D prevents the immune system from mounting an effective response. Glycoprotein D could mask epitopes that elicit protective antibodies or trigger the wrong type

### X-VAX TECHNOLOGY INC.

Jupiter, Fla.

**Technology:** Herpes vaccine eliciting non-neutralizing antibodies

**Disease focus:** Infectious

**Clinical status:** Preclinical

**Founded:** 2015 by Isaac Blech and William Haseltine

**University collaborators:** Albert Einstein College of Medicine

**Corporate partners:** N/A

**Number of employees:** 6

**Funds raised:** \$60 million

**Investors:** Johnson & Johnson Innovation - JJDC Inc., Adjuvant Capital, Serum Institute of India, Alexandria Venture Investments, Founders Fund

**CEO:** Ulf Wiinberg

**Patents:** 2 issued covering the  $\Delta$ gD-2 HSV vaccine and its use to elicit an immune response

of immune response. According to Eggert, Jacobs and Herold serendipitously found the vaccine protected mice against the virus.

The researchers' early work, published in a 2015 *eLife* paper and a 2016 *JCI Insight* paper, showed  $\Delta$ gD-2 induced ADCC. The NK cell-mediated response, activated by antibody-Fc interactions, prevented the virus from going latent in spinal nerves following intravaginal and skin challenges that are lethal to untreated mice.

Eggert said the vaccine protects against HSV-1 and HSV-2 infection, and that while X-Vax has focused its efforts in preventative settings, it believes  $\Delta$ gD-2 could also be used as therapeutic vaccine for herpes flare-ups following HSV reactivation.

He said the company has preliminary preclinical data suggesting the vaccine doesn't induce ADCC against latently infected neurons.

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The company is working on CMC for ΔgD-2 and hopes to have it clinical testing in the prevention setting within two years.

It expects its July \$56 million series A to last at least three years and enable it to complete a Phase I study. Eggert said X-Vax may run Phase II testing on its own but foresees either partnering with a pharma company to complete development or selling the asset.

He added that because glycoprotein D is a large gene, taking it out of the virus creates room to add other genes. The company is evaluating whether it can expand its platform by using the mutated HSV as a vector to deliver antigens associated with other pathogens such as flu, tuberculosis and HIV.

Xenova Group plc and GlaxoSmithKline (LSE:GSK; NYSE:GSK) discontinued development in 2001 of TA-HSV, a therapeutic vaccine similar to ΔgD-2 in that it comprises HSV with genetic deletion of

glycoprotein H, which interacts with glycoprotein D to mediate viral entry to cells. TA-HSV was ineffective in Phase II for genital herpes patients.

According to Eggert, unlike ΔgD-2, TA-HSV “elicited primarily neutralizing antibody responses.”

In addition to X-Vax, at least two companies are developing HSV vaccines. Sanofi (Euronext:SAN; NASDAQ:SNY) has a preclinical vaccine combining live attenuated HSV with adjuvanted recombinant antigens, which will be given in a prime-boost protocol. A spokesperson for Sanofi said the pharma will begin clinical testing in the coming year of different formulations of the components for the prime dose.

Rational Vaccines Inc.’s lead candidate, a genital herpes therapeutic vaccine, also is in preclinical development. ■

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