Genocea's Herpes Vaccine Update: An Interview With Chip Clark, CEO

By Josh Bloom — May 26, 2017

Chip Clark, Genocea’s CEO, kindly agreed to answer my questions about the company’s GEN-003 herpes vaccine, and provide an update on the vaccine's progress. I would like to thank Chip for taking a considerable amount of time to speak with me. The interview below should answer some of the many questions that readers have been writing and calling about.

JB: Can you update us on Genocea’s current plans and timelines. If all goes well, can you estimate when the Biologics License Application (BLA) might be granted? (1)

CC: Genocea is currently finishing up its Phase II program on GEN-003, and recently had a successful end of Phase II meeting with the FDA. In the middle of the year, we expect to announce the 12-month placebo-controlled clinical results from the Phase IIb trial that uses the Phase III-ready formulation of GEN-003 at the expected Phase III dose. If all continues to go well, Genocea plans to have GEN-003 ready for Phase III by the end of 2017. We expect the clinical trials to take approximately two years from initiation to data and could, therefore, be in a position to file our BLA in 2020, with the potential for approval in 2021.

JB: Is it possible for people to enroll in any of these trials?

CC: At this time, our ongoing Phase II clinical trials are fully enrolled. The next enrollment opportunity will be in our Phase III program, the full details of which will appear on clinicaltrials.gov when the protocol is finalized and the trial(s) open.

JB: People are very interested in 003, both for therapy and prevention. It is, of course, more
difficult to run a trial for prevention. Do you plan to do so, and if so, when?

CC: GEN-003 is being developed as an immunotherapy/therapeutic vaccine in patients already infected with HSV. Theoretically, GEN-003 could be used in uninfected patients to help prevent infections, but we have no plans to conduct such a trial before an approval as a therapeutic.

JB: HSV-1 is now the most common cause of genital herpes in young women. Rumor has it that 003 is not expected to work against HSV-1. Is this correct? If so, do you think this will be problematic since so many genital herpes cases are caused by HSV-1?

CC: This is not correct. The antigens identified and chosen for GEN-003 are highly conserved across HSV types 1 and 2. Thus far, we have only studied GEN-003 in patients with HSV-2, but, given the biology, we believe that GEN-003 could work in patients with either HSV-1 or 2. We intend to include both HSV-2 and HSV-1 patients in the Phase 3 program and to seek approval for the treatment of genital herpes infections irrespective of serotype.

JB: Subunit (synthetic) vaccines have a poor track record. Why do you expect 003 to work when many others have failed?

CC: Simply put, we think that other vaccines have failed because they have used the wrong antigens, and have therefore failed to effectively direct T cell responses to attack the virus.

We selected the GEN-003 antigens using our ATLAS (2) platform, which comprehensively profiled the T cell immune responses of approximately 200 people to HSV-2 and associated those T cell response signatures with clinical outcomes. We found that a handful of HSV-2 antigens were associated with protective T cell responses and, from that small number of antigen candidates, we selected the two protein components of our vaccine.

We have shown now in three trials that GEN-003 reduces the genital lesion rate, reduces viral shedding, and drives strong and antigen-specific T and B cell responses.

JB: Is 003 intended to be a stand-alone treatment, or will it be necessary to also use an antiviral such as Valtrex.

A: We have recently shown that GEN-003 can reduce the genital lesion rate vs. placebo by 50% at six months post-dosing. Whether a patient chooses to use GEN-003 alone or together with an antiviral drug may ultimately come down to patient choice. We know from our market research that patients hate taking a pill every day and for this reason, about two-thirds of patients who take antivirals only take them when they have a lesion recurrence.

This represents a significant unmet medical need because taking antivirals in this way does nothing to reduce the frequency of recurrences and provides no reduction in viral shedding when they are not taking the pills (increasing transmission risk). We do plan to study GEN-003 in combination with daily Valtrex in the future to see if there is an additive benefit of taking both together.

Our market research suggests that the prospect of GEN-003’s significant and sustained efficacy from a single course of injections would cause many patients currently taking antivirals to switch. You can also imagine a scenario where GEN-003 could be the cornerstone therapy for a patient,
who could preserve antiviral use to treat outbreaks if they occur.

**JB:** Do you expect to see an enhanced immune response during dose finding Phase IIb studies? Do you expect the Phase IIb results to be superior to those of Phase IIa?

**A:** We have already shown consistent clinical and virologic efficacy and immune response results between our prior Phase II trial and our ongoing Phase IIb trial.

**JB:** Can you briefly compare 003 with vaccines from Theravax, NanoBio, and U Penn, especially with regard to immune response, efficacy (when available), safety, and your estimate of the chance of success of all four.

**A:** No. Our point of unique differentiation is how we selected the antigens for GEN-003 using ATLAS. Without ATLAS, we believe you are guessing.

**JB:** I have called your Phase IIa data unimpressive. Is this fair? If not, why?

**A:** No. I don't think this is a fair statement. We have now shown statistically significant clinical efficacy and viral shedding results across three separate clinical trials. Our most recent data — here [1] — from the previous Phase II trial shows that we continue to reduce genital lesion rate and viral shedding rate vs. baseline by up to 77% for at least two years after dosing. Moreover, in our ongoing Phase IIb trial, we announced median genital lesion rate reductions vs. placebo of 52% over the six-month period post dosing (this is expected to be our primary Phase III endpoint).

Our market research (involving hundreds of patients and physicians) has been conducted on the basis of our actual clinical trial results, not an aspirational profile, and consistently supports our assertion that GEN-003’s demonstrated levels of efficacy in its trials to date are highly attractive to patients and physicians who have been starved of innovation and new treatments for this serious disease for more than 20 years.

**JB:** Are other papers about 003 being written? If so, when do you think they might be published?

**A:** We have an active publication calendar. You can view previous publications on our website at www.genocea.com [2]. We’ve had a number of abstracts just accepted to the IHW meeting this summer in Belgium as posters and one oral presentation, and we also expect to be presenting data at the IDWeek conference in October in San Diego. We have manuscript drafts in the works as well, and plan to submit these to peer-reviewed journals for publication when completed.

**Notes:**

(1) A Biologics License Application (BLA) is like the New Drug Application (NDA) that must be granted by the FDA for approval. The difference is that the BLA includes biologics, such as vaccines, and antibodies, while the NDA is for small molecule drugs (pills).

(2) ATLAS is Genocea's proprietary rapid antigen identification screening system that is designed to find targets of protective T cell responses.