

Equity Research

March 3, 2014

**Price: \$14.67** (02/28/2014)

**Price Target: \$40.00**

**OUTPERFORM (1)**

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**Key Data**

Symbol **NASDAQ: GNCA**

52-Week Range: **\$16.96 - 10.90**

Market Cap (MM): **\$252.6**

Net Debt (MM): **\$(7.5)**

Cash/Share: **\$38.97**

Dil. Shares Out (MM): **15.5**

Enterprise Value (MM): **\$324.9**

ROIC: **NA**

ROE (LTM): **NA**

BV/Share: **\$(248.44)**

Dividend: **NA**

<b>FY (Dec)</b>	<b>2012A</b>	<b>2013E</b>	<b>2014E</b>
<b>Revenue (MM)</b>			
Year	\$2.0	\$1.0	\$0.0

<b>Earnings Per Share</b>			
Q1	\$0.00	-	\$(0.55)
Q2	\$0.00	-	\$(0.46)
Q3	\$0.00	-	\$(0.53)
Q4	\$0.00	-	\$(0.52)
Year	\$(2.15)	\$(2.12)	\$(2.05)

Initiating Coverage

# *Initiation: The T. Rex Of T Cell Vaccines*

## **The Cowen Insight**

Genocea Biosciences is a leader in the discovery and development of T cell vaccines. Lead candidate GEN-003 for HSV-2 infection has produced strong proof-of-concept Phase II data that our consultants think is "impressive". We estimate a safe and effective HSV-2 therapeutic vaccine would have \$1B+ sales potential. Today we are initiating coverage with an Outperform rating and a \$40 price target.

## **Genocea Has Developed A Proprietary Technology That Allows The Development Of Vaccines Against New Targets.**

Genocea has optimized its ATLAS platform to screen more exhaustively and efficiently than others for epitopes that initiate CD4 (helper T Cells) and CD8 (cytotoxic T Cells) responses. ATLAS is a high throughput approach to antigen identification that allows T Cells from many different patients to be screened and compared to identify not only antigens, but protective antigens.

## **GEN-003 Is A Therapeutic Vaccine Against HSV-2 That Has \$1B+ Potential.**

HSV-2 is the virus that causes herpes and is a big public health problem, infecting 16% of the U.S. population over the age of 14. Currently available antivirals do not completely reduce symptoms, viral shedding, or the risk of infecting a partner. Therefore there remains a need for better or complimentary agents. In a Phase I/IIa proof-of-concept trial a 30mcg dose of GEN-003 was shown to reduce viral shedding by 40-50% and lesion rate by 72%. Our consultants think this data is impressive. Genocea is expected to release 12 month data from the trial in mid-2014. GEN-003 will next enter Ph. II trials to optimize dose and schedule, and is expected to enter Ph. III in 2017. With an estimated 18MM people in the developed world diagnosed with HSV-2, GEN-003's opportunity is large. We project that GEN-003 will achieve \$750MM in revenue by 2025, and our DCF analysis suggests that the GEN-003 opportunity could be worth \$40 per share.

## **Phase I Data From Pneumococcal Candidate Expected Mid-2014.**

*Streptococcus pneumonia* is responsible for more than one million deaths in young children per year worldwide. In the U.S. an estimated 175,000 hospitalizations occur each year due to it, and among those 6,000 deaths result. We estimate the worldwide market for pneumococcal vaccines was \$5.5B in 2013, lead by PFE's Prevnar. While existing vaccines provide important protection against up to 23 serotypes, there are >90 serotypes, the majority of which are not included in current vaccines. The incidence of disease associated with these uncovered strains is believed to be increasing. Genocea's GEN-004 is designed to elicit TH17 responses and therefore be a universal pneumococcal vaccine protecting against all serotypes.

## **Several Vaccines In Preclinical Development.**

Genocea has research programs in Chlamydial and malarial vaccines.

## At A Glance

### Our Investment Thesis

Genocea Biosciences is a clinical stage company developing sophisticated, high value vaccines and in particular is a leader in the discovery and development of T-cell vaccines. Genocea has four visible programs, including two in clinical development. GEN-003 is a therapeutic vaccine for HSV-2, the cause of genital herpes. GEN-003 has produced strong proof-of-concept Phase II data that our consultants have called "impressive". We estimate a safe and effective HSV-2 therapeutic vaccine would have \$1B+ sales potential. Genocea has also advanced a pneumococcal vaccine into early clinical development. Our analysis suggests that Genocea is undervalued just on GEN-003's potential in HSV-2, with no other contribution from Genocea's other programs or value attributed to the ATLAS platform. We expect Genocea to outperform the market over the next 12 – 24 months as GEN-003 and GEN-004 progress through development.

### Forthcoming Catalysts

- 12 month data from GEN-003's Phase I/IIa trial (mid:14)
- Initial data from GEN-004's Phase I trial (mid:14)
- Initiation of GEN-003's Phase II dose titration trial (mid:14)
- Initiation of GEN-004's Phase IIa trial

### Base Case Assumptions

- GEN-003 is successfully developed and generates \$750MM in revenue by 2025
- GEN-004 progresses through development but does not generate substantial revenue before 2020
- Genocea's other vaccine candidates do not create significant shareholder value before 2020

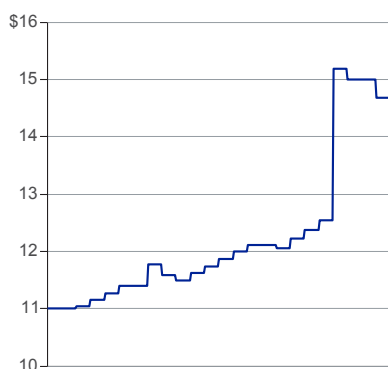
### Upside Scenario

- GEN-003 is successfully developed and generates more than \$750MM in revenue by 2025
- GEN-004 progresses through development and drives significant shareholder value
- Genocea's other vaccine candidates look promising and are attributed much value

### Downside Scenario

- GEN-003 is not successfully developed and/or generates less than \$750MM in revenue by 2025
- GEN-004 does not progress
- Genocea's other vaccine candidates do not create significant shareholder value before 2020
- Genocea's ATLAS technology fails to generate new candidates or partnerships

### Price Performance



Source: Bloomberg

### Company Description

Genocea's key advantages in the competitive field of vaccine discovery and development are novel and proprietary technologies to identify and validate vaccine antigens that generate a strong cellular (T Cell derived) immune response against pathogens that are resistant to conventional antibody-eliciting vaccines. Genocea has optimized its ATLAS platform in order to screen more exhaustively than others for epitopes that initiate CD4 (helper T Cells) and CD8 (cytotoxic T Cells). Genocea has four visible programs, including two in clinical development. GEN-003 is a therapeutic vaccine for HSV-2, the cause of genital herpes. GEN-004 is a pneumococcal vaccine in early clinical development. Genocea has research programs in Chlamydial vaccines and malarial vaccines.

### Analyst Top Picks

	Ticker	Price (02/28/2014)	Price Target	Rating
BioMarin Pharmaceutical	BMRN	\$81.00	\$95.00	Outperform
Gilead Sciences	GILD	\$82.79	\$95.00	Outperform
Neurocrine Biosciences	NBIX	\$17.63	\$20.00	Outperform

## The T. Rex Of T Cell Vaccines

### Investment Thesis

Genocea Biosciences is a clinical stage company developing sophisticated, high value vaccines, and in particular is a leader in the discovery and development of T cell vaccines. Genocea's key advantages in this complex area of drug development are novel and proprietary technologies to identify and validate vaccine antigens that generate a strong cellular (T cell derived) immune responses against pathogens that are resistant to conventional antibody-eliciting vaccines. The company and its founders have a nearly 20-year history of identifying T cell antigens in novel ways. This experience has allowed Genocea to optimize its ATLAS platform in order to screen more rapidly and exhaustively than others for epitopes that initiate CD4 (helper T cells) and/or CD8 (cytotoxic T cells) T cell responses. ATLAS is a high throughput approach to antigen identification that allows T cells from many different patients to be screened and compared to identify not only antigens, but protective antigens. ATLAS also allows Genocea to exploit new advances in immunology - such as rapidly screening for T<sub>H</sub>17 antigens quickly after it was discovered that these newly characterized T cells were a key part of a protective response against pneumococcal disease. Genocea has four visible programs, including two in clinical development. GEN-003 is a therapeutic vaccine for HSV-2, the cause of genital herpes. GEN-003 has produced strong proof-of-concept Phase II data that our consultants have called "impressive." We estimate a safe and effective HSV-2 therapeutic vaccine would have \$1B+ sales potential. Genocea has also advanced a pneumococcal vaccine into early clinical development. In addition, the company has research programs in chlamydial and malarial vaccines. We expect the company to keep collaborating with academic and foundation scientists who wish to apply Genocea's powerful ATLAS technology to new problems in vaccine development. Our analysis suggests that Genocea is undervalued just on GEN-003's potential in HSV-2, with no other contribution from Genocea's other programs or value attributed to the ATLAS platform. We expect Genocea to outperform the market over the next 12-24 months as GEN-003 and GEN-004 progress through development.

### Upcoming Genocea Milestones

Milestone	Timing
12 month data from GEN-003's Ph. I/IIa trial in HSV-2 patients	Mid:2014
Initial data from GEN-004's Phase I trial in healthy volunteers	Mid:2014
Initiation of GEN-003's Phase II dose titration trial	Mid:2014
Initiation of GEN-004's Phase II trial	H2:14
Data from post dose 3 analysis in GEN-003's Phase II dose titration trial	Mid:15
Initiation of GEN-003's Phase II dose regimen trial	H2:15

Source: Cowen and Company

### Vaccines Are a Lucrative Market With Much Opportunity For New Entrants

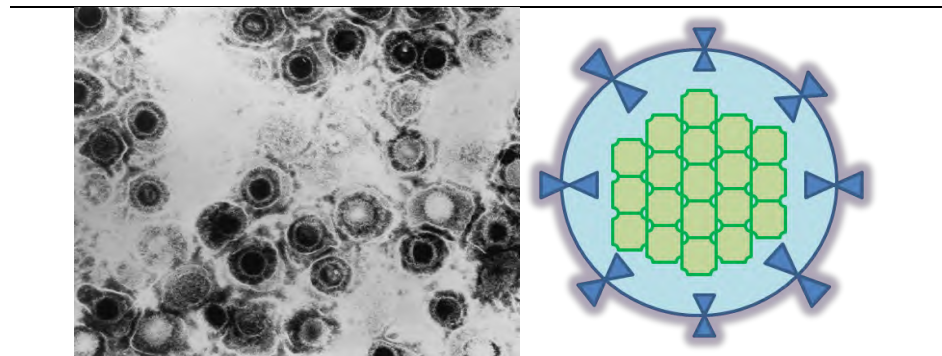
Favorable demographics, the need for primary prevention and/or durable amelioration of symptoms have provided strong underlying demand for vaccines. We estimate the worldwide market for vaccines is \$22B+. Vaccines have traditionally been used for the prevention of bacterial and a limited number of viral infectious diseases. Newer technologies have enabled companies to develop vaccines against previously impossible targets (including Meningococcus B strain and S. aureus), but some

remain elusive (HSV-2). We think the ATLAS technology uniquely enables Genocea to develop vaccines for previously intractable diseases where T cell immunity is particularly important.

### Genocea's Lead Program – A Therapeutic Vaccine for Genital Herpes

Genocea's lead candidate is GEN-003, a therapeutic vaccine for the treatment of herpes simplex virus 2 (HSV-2), the virus that causes genital herpes. This vaccine comprises a viral glycoprotein antigen (HSV-2 G2, designed to elicit an antibody response to the virus) coformulated with a novel T cell antigen (ICP4.2) and a novel adjuvant MM-2. GEN-003 has produced strong data in a Phase I/II proof-of-concept trial. Subsequent Phase II trials will optimize the dose and regimen of GEN-003. Overall, the data to date are exciting and Genocea's technologies impressive. We estimate that a safe and effective HSV-2 therapeutic vaccine could have \$1B+ market potential.

#### Herpes Simplex Virus 2 (HSV-2)



Source: Cowen and Company

### Herpes Is A Significant Problem

Herpes Simplex Virus 2 (HSV-2) is a dsDNA virus which causes an incurable and chronic infection in humans. Symptoms include painful genital sores in adults and potentially fatal herpes encephalitis in newborns infected via maternal-fetal transmission. At least 500 million people are infected worldwide, making it the most frequent sexually transmitted disease. HSV-2 resides in 16% of the U.S. population aged >14 with higher infection rates within women, minorities and HIV positive patients. The highest infection rate is among men who have sex with men. HSV-2 is estimated to be present in 60% of this group. Because of the stigma associated with herpetic lesions and the risk of infecting sexual partners, many of the sufferers are forced to lead significantly less full lives and/or hide their infected status.

HSV-2 is known for its characteristic lesions, but in fact much of the time HSV-2 infections are latently resting inside the host. It is estimated that through the combination of asymptomatic patients, misdiagnoses (recurrent yeast infections, skin irritation, etc.), and the failure of patients to recognize their symptoms, just 20-25% of the HSV-2 infected population is aware of their status. The average infected patient suffers ~0.5 lesions/year, but the severity of the disease varies widely between patients, with some being completely asymptomatic, others suffering the typical lesion every other year, and some experiencing near-monthly outbreaks. Patients also experience numerous subclinical shedding events. The shedding rate averages 25% of

days surveyed but can range from 2% to 75%. During these periods of viral shedding patients are actively producing infectious virions. In fact, it is believed that 85% of transmission events occur during a period of subclinical shedding.

### Current Genital Herpes Drugs Leave Much Room For Improvement

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Two drugs are approved for HSV-2: acyclovir and valacyclovir (GSK's Valtrex, a prodrug of acyclovir), which are both available generically. Both are nucleoside analogues which inhibit the HSV-2 DNA polymerase. By inhibiting the DNA polymerase, viral replication is halted, and viral shedding becomes severely limited. This blockade prevents to varying degrees 1) the spread of the infection to nearby epithelial cells and a resulting lesion and 2) the shedding of infectious virus into bodily fluids which can be spread to uninfected partners. The CDC recommends daily suppressive therapy for all HSV-2 infected patients. While the antivirals reduce the frequency and duration of genital sores, they have less of an impact on viral shedding and the associated risk of transmission, and have no potential to cure the patient.

Full compliance with the daily therapy regimen results in a ~90% reduction in days with a visible lesion and a ~70% reduction in shedding days. Since viral shedding is not fully prevented, it is unsurprising that in clinical trials daily Valtrex only reduces the risk of transmission by 53%. This translates into an approximately 2% annual risk of transmission for HSV-2 discordant couples despite the use of daily Valtrex.

Moreover, for maximal effectiveness the current antivirals require lifelong daily therapy, something that many patients refuse. Consultants report most patients initially comply with daily suppressive therapy given the stigma associated with HSV-2 and many patients' great concern with transmitting the virus to uninfected partners. But over time >50% fall into an episodic treatment regimen or cease therapy completely. This is due to a combination of the inconvenience of daily therapy, cost, and/or a perception of futility at preventing infection of HSV-2 negative partners. Therefore, the current standard of care leaves much room for improvement.

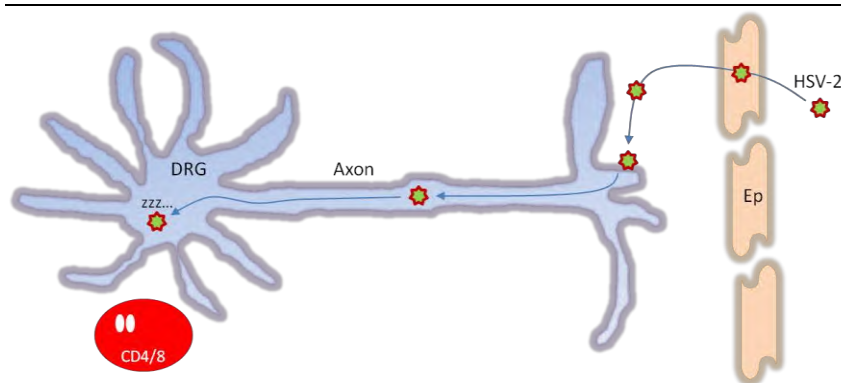
Under an episodic regimen, patients only utilize suppressive therapy when they experience symptoms of active infection such as a lesion. In clinical trials, Valtrex reduced the time to lesion healing from 6 days to 4 days and the time to cessation of viral shedding from 4 days to 2 days. While this approach does shorten the duration of symptoms and shedding once a lesion appears, it does nothing to reduce the frequency of lesions or the risk of transmission during the many subclinical shedding events. Therefore, the combination of treatment burden and incomplete effectiveness leaves much room for improvement from both a patient and public health perspective.

According to our consultants, the combination of current antivirals' incomplete control of shedding and the long-term treatment burden creates a clear clinical need for a therapeutic vaccine with a longer duration. Consultants indicate that while they hope a therapeutic vaccine would at least replicate Valtrex's efficacy they would accept a product that is somewhat inferior from an efficacy perspective (70% reduction in lesions; 50% reduction in shedding) but makes up for it in ease of use and therefore patient compliance. They also see the opportunity for a partially effective vaccine to be used in conjunction with Valtrex to generate more complete control of HSV-2 infections.

## HSV-2 Parties In The Mucosa But Sleeps In Neurons

HSV-2 infections occur most frequently at the genital mucosa, although it is also possible for HSV-2 to infect the oral mucosa or even broken skin. The virus initially infects and replicates within the epithelial/mucosal surface upon which it was deposited. This primary infection may cause a lesion, but often does not. Ultimately, this infection spreads to sensory nerve endings, which allows the virus to migrate up the dorsal root or cranial nerve ganglia where it establishes a long-term dormant/latent infection of the neural cell(s). While residing in neurons, HSV-2 generally only produces a single transcript, the latency associated transcript (LAT). Periodically, through mechanisms which are not entirely known, latent HSV-2 will reactivate. Following reactivation, infectious virions are produced which migrate back down the ganglia to reemerge at the epithelial surface and cause a localized epithelial infection, viral shedding, and/or a lesion.

### HSV-2 Enters Epithelial Cells And Migrates To Sensory Neurons



The virus enters a latent stage in the dorsal root ganglion (DRG) where the immune system may have trouble finding it. Reactivation and return to circulation (shedding) is inhibited by resident T Cells.

Source: Cowen and Company

## The Immune Response Partially Controls HSV-2

During periods of active infection the host immune response plays a vital role in determining the magnitude and severity of both the primary and secondary epithelial infections. During each outbreak of active infection, the innate immune system plays a central role in detecting the viral pathogen, alerting the adaptive immune system of its presence, and producing a range of anti-viral proteins. Central to this communication system are dendritic cells (DCs). Multiple studies have shown that patients with defective DCs suffer severe HSV infections. DCs accomplish their role in controlling HSV-2 infections in multiple ways. First, DCs are important producers of IFN- $\alpha$  and - $\beta$  (via TLR 7/8 mediated recognition of HSV), which have long been known to have potent anti-HSV activity. Second, DC's as well as other innate immune cells combine to present HSV antigens to the adaptive immune system (CD4 T cells, CD8 T cells, etc.), causing its activation.



Activated CD4 cells serve two functions. First, the T<sub>H</sub>2 subset helps stimulate B-cells to produce antibodies. Second, the T<sub>H</sub>1 subset helps activate CD8 T cells after they have been primed by the DCs. Once activated, CD8 T cells are charged with identifying and killing HSV-2 infected cells. This killing is accomplished via multiple mechanisms including the production of IFN- $\gamma$ . Studies in humans have demonstrated an inverse correlation between the presence of CD8 T cells and HSV-2 lesion severity. During the primary infection, this immune cascade serves to clear the active epithelial infection, restricting HSV-2 to the nerve ganglia. The mechanism by which HSV-2 infected nerve ganglia avoid immune mediated destruction is not fully understood. The general lack of HSV-2 protein production in these cells is believed to play a significant role. Additionally, HSV-specific CD8 T cells persistently infiltrate the dorsal root ganglia, indicating some level of immune monitoring is occurring. Periodically, HSV-2 will reactivate and the immune system will respond again. Immune memory allows these secondary responses to be more rapid and/or forceful which causes the viral shedding and lesions to be contained more quickly. HSV-2 specific IFN- $\gamma$  producing cells have been shown to be important for maintaining HSV-2 suppression.

Using synthetic peptides, academic researchers have performed antigen screens. These studies revealed that CD8 T cells are capable of recognizing peptides from throughout the HSV-2 genome. While there are some similarities between patients, for example a dominant response directed towards the HSV tegument, there are also significant variations in the specific antigens recognized by each patient. In immunology it is well established that immune responses directed against one antigen from a pathogen can be protective, while a similar magnitude immune response directed against a different antigen from the same pathogen is not. Therefore, Genocea theorized that it could identify antigens important in the suppression of HSV-2 activation by contrasting the antigens recognized by T cells from patients that successfully contain HSV-2 infection with the antigens recognized by a patient that poorly contains HSV-2.

#### Genocea's ATLAS Identifies ICP4.2

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Genocea utilized its **Antigen Lead Acquisition System (ATLAS)** to compare the T cell response of patients achieving a wide range of HSV-2 control. By interrogating each patient's T-cell response to numerous antigens and their level of HSV-2 control, Genocea was able to identify correlations between the response directed against a subset of antigens and successful control of an HSV-2 infection. This process identified multiple candidate CD4 and/or CD8 specific T cell antigenic regions. A smaller subset of antigens overlapped between both the CD4 and CD8 lists. Among these, ICP4.2 and one other T cell antigen passed a further screening for the protein's ability to 1) be produced *in vitro*, 2) generate an immune response in mice and 3) demonstrate efficacy in a mouse prophylactic vaccine model when combined with the B-cell antigen gD2. The candidate vaccine consisting of the ICP4.2 and gD2 antigens was termed GEN-003 and brought forward for use in guinea pigs, the primary HSV animal model for studying recurrences.

#### Patient Pools Utilized to Identify T-cell Antigens

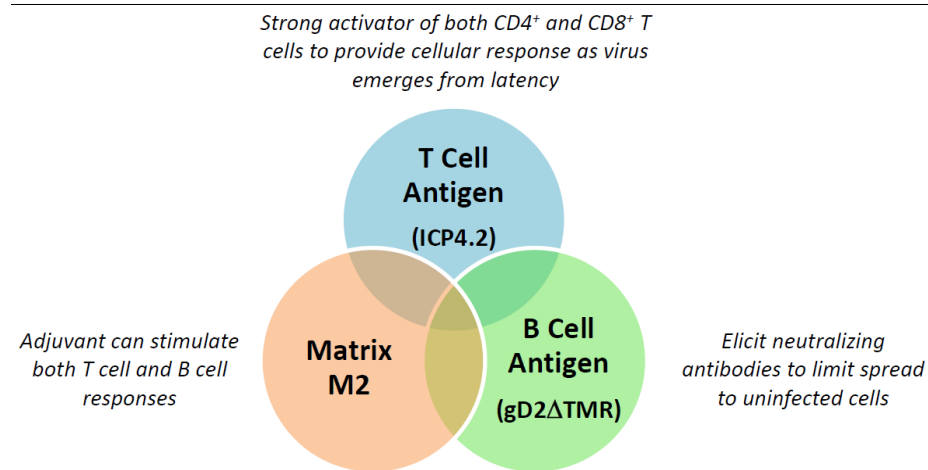
	Cohort	Presence of HSV-2 Antibody	Description	Number of Subjects
Increased Protection ↑	Exposed / Sterilizing Immunity	—	In a sexual relationship with a HSV-2 <sup>+</sup> partner but no infection	43
	Asymptomatic	+	No clinical genital outbreak since initial diagnosis	41
	Infrequent Recurrer	+	1-3 clinical outbreaks/year	47
	Frequent Recurrer	+	≥4 clinical outbreaks/year	43
	HSV-1 Positive	—	Genital outbreaks	11
	Presumed Naïve	—	No known exposure to the virus	10

Source: Genocea

#### GEN-003 Reduces The Recurrence Of Lesions In Guinea Pigs

GEN-003 couples a well-known viral surface glycoprotein antigen (D2ΔMTR340-363, gD2) with a proprietary fragment of infected cell polypeptide 4 (ICP4 383-766, ICP4.2). These two antigens are formulated with Matrix M-2 adjuvant (from NovaVax, MM-2). Genocea believes the T cell response will limit HSV-2 infection by killing infected cells before they can spread the virus, while gD2 antibodies will help prevent the spread of the infection by any free virions which manage to escape from infected cells.

#### GEN-003 Design Rationale



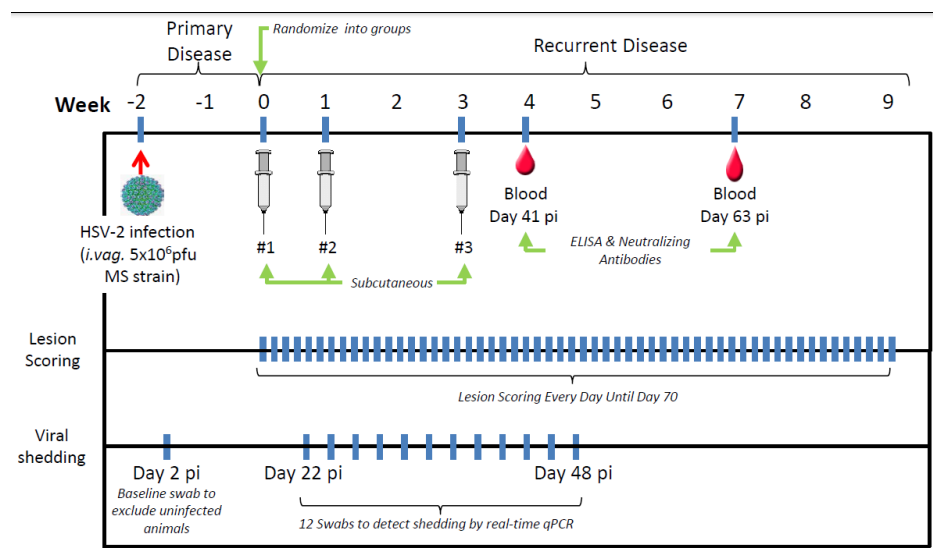
Source: Genocea

Mice become latently infected with HSV-2 but do not experience spontaneous recurrences; this limits the applicability of mouse studies to humans. Like humans,



guinea pigs suffer from spontaneous recurrences of lesions and viral shedding. As a result, guinea pigs are the primary model organism for assessing the potential of therapeutic interventions like GEN-003. Genocea conducted an experiment whereby female guinea pigs were infected intravaginally with HSV-2. Two-weeks post-infection (day 0), the guinea pigs began an immunization protocol with GEN-003±MM-2, or placebo/PBS. Guinea pigs were immunized via subcutaneous administration at days 0, 7, and 22. Guinea pigs were then scored for the presence/severity of lesions and swabbed to assess the level of viral shedding.

#### Guinea Pig Immunization Protocol

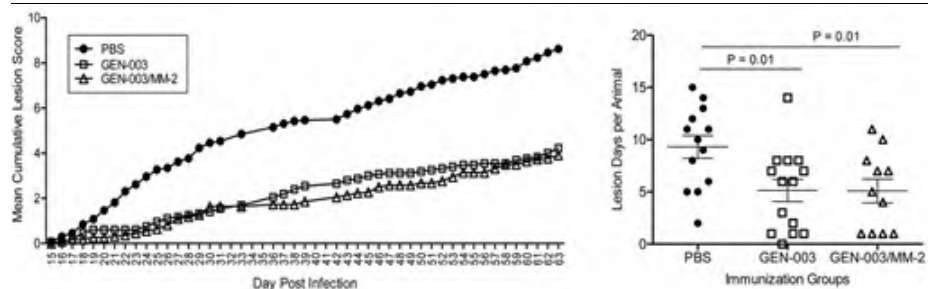


Source: Genocea

#### GEN-003 Efficacy Signal

GEN-003 without MM-2 was found to reduce the cumulative lesion score 51% ( $p < 0.05$ ) compared to placebo guinea pigs. GEN-003 with MM-2 reduced the cumulative score 55% ( $p < 0.05$ ) compared to placebo. Similarly, the frequency of days with lesions present declined approximately 45% in both the GEN-003 ± MM-2 groups ( $p = 0.01$ ). Viral shedding was assessed by PCR. This analysis revealed the presence of HSV-2 DNA in 15.1% of all swabs from the placebo group, compared to 14% for the GEN-003 without MM-2 group and 12.8% for the GEN-003 with MM-2 group. Swabs obtained only after the second vaccine dose had been administered were 10.0%, 8.6%, and 8.6% HSV-2 positive, respectively. Samples obtained following the third vaccine dose were 4.4%, 2.6%, and 0.0% HSV-2 DNA positive. Notably, these data demonstrate an elimination of shedding following three doses of Gen-003 with MM-2. The significant effect on the presence of lesions, along with the elimination of shedding after the third dose, motivated Genocea to bring GEN-003 forward for human trials.

### GEN-003 Vaccination of Guinea Pigs Reduced HSV-2 Lesions



Source: Genocea; Skoberne M et al. 2013

### Phase I/II Trial Establishes Proof Of Concept For GEN-003 In Patients

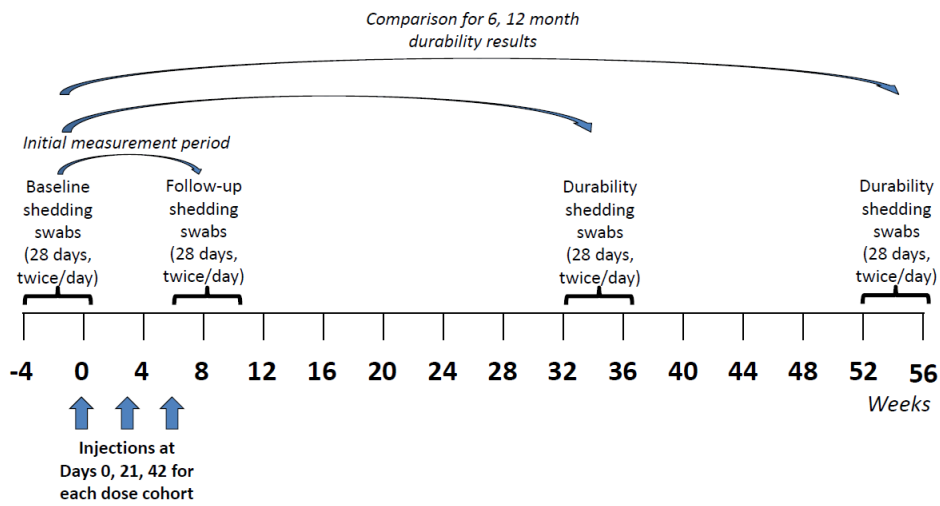
Genocea released data from GEN-003's Phase I/II human proof-of-concept trial during 2013. GEN-003 has been tested in almost 150 patients with HSV-2 infections where it resulted in decreases in both viral shedding and the number of days with genital sores. In our opinion, GEN-003's patient data are quite positive and robust. Our consultants think these data have provided proof-of-concept for GEN-003 and that it will be a commercially viable vaccine should subsequent studies be consistent with the early data. Nonetheless, they think it possible that GEN-003's efficacy could be improved by subsequent dose -optimization studies.

#### GEN003-001 Trial Design

The primary objective of GEN-003's Phase I/II "therapeutic" trial was to assess the safety of three doses of the vaccine in HSV-2 seropositive patients. Secondary endpoints included the effects of vaccination on HSV-2 shedding and the antibody and cellular immune responses elicited by the complete vaccine (including adjuvant) and by the proteins alone (without adjuvant). A final exploratory aim (due to trial size) of this trial was to measure effects of vaccination on the clinical recurrences of genital sores in this population.

The GEN003-001 trial enrolled 143 patients in five arms (Table 1). Three different antigen doses (10µg, 30µg, and 100µg) were tested along with a no adjuvant arm and a placebo arm. Patients were 18-50 years of age, HSV-2 seropositive and had displayed documented genital infections for >1 year. Vaccine was dosed three times on weeks 0, 3 and 6. Patients were monitored for levels of HSV-2 viral shedding during weeks -4 to 0 in order to establish patient baselines and during weeks 6-10 to measure treatment effects of GEN001/MM2. Shedding was monitored via BID genital swabbing over the 28 days. Immune responses were measured at weeks 0, 4, 8 and 32.

GEN-003 Phase I/IIa Trial Design

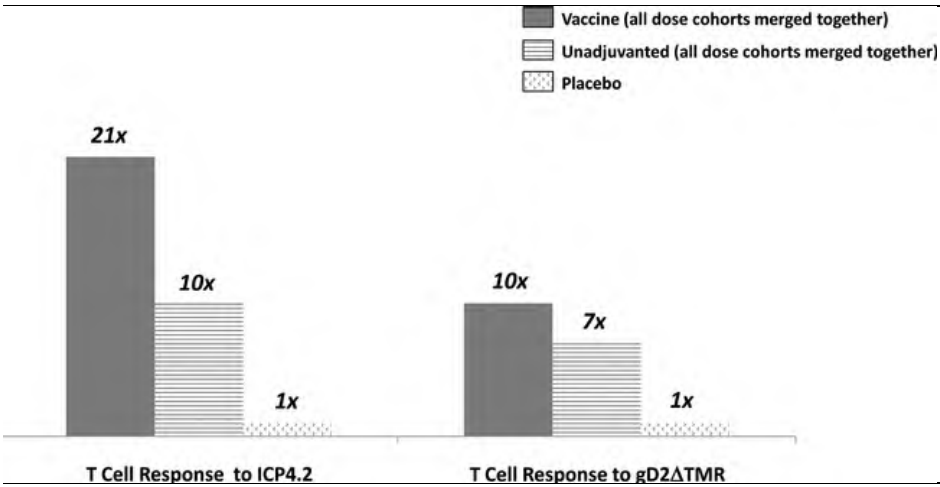


Source: Genocea

GEN-003 Induces a Significant Increase In T cell Responses

Following vaccination, Genocea examined the ability of patients' T cells to respond to the antigens included in GEN003. T cell responses were measured by IFN- $\gamma$  ELISPOT. In this assay, the ability of T cells to respond to the gD2 antigen increased 7X when the patients were treated with the antigens alone. When the MM-2 adjuvant was added, this increase intensified to 10X. Since ICP4.2 was developed as a T-cell antigen it is unsurprising that the induced T cell response was even stronger for ICP4.2. Following vaccination the presence of IFN- $\gamma$  producing T cells increased 10X in the absence of adjuvant, and 21X when MM-2 was present. Therefore, GEN-003 is operating as expected and generating a robust T cell response.

T Cell Responses to GEN-003's Constituent Antigens

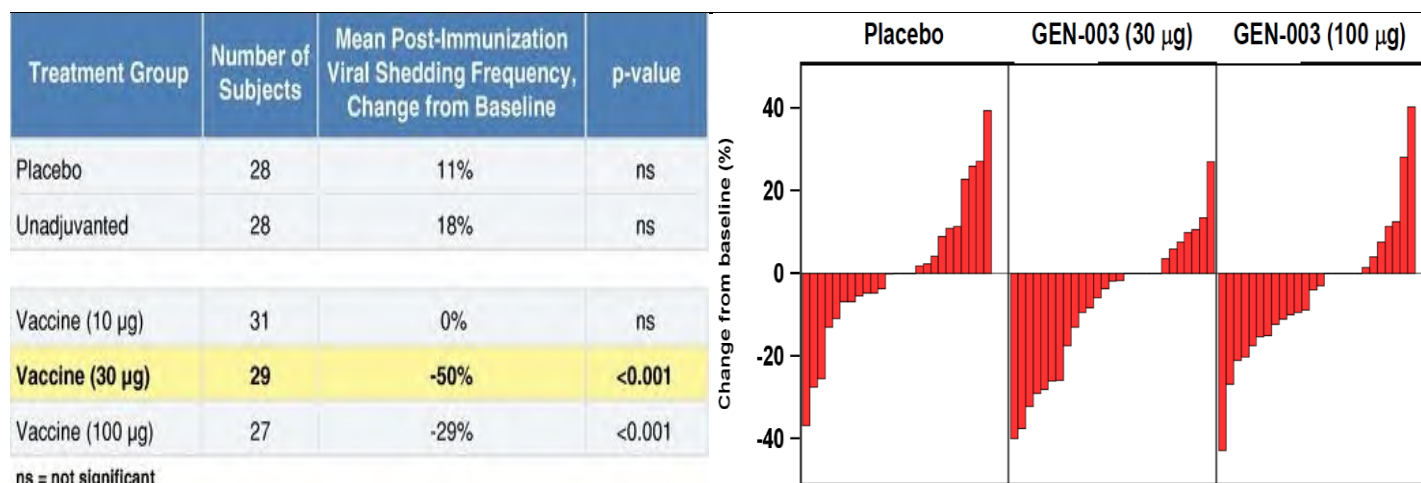


Source: Genocea

### Reduction in HSV-2 Shedding Observed Following Immunization...

Following the third immunization (at week 6) patients were assessed for viral shedding by twice-daily genital swabs. PCRs of these swabs revealed a significant difference in the change in shedding frequency from baseline. Patients in the placebo and unadjuvanted vaccination groups experienced shedding frequency changes of +12% and +17%, respectively. The increase in shedding is indicative of the natural variation in HSV-2 disease. Conversely, patients vaccinated with antigens+MM-2 experienced changes in shedding frequency from baseline of -0%, -50% ( $p<0.001$ ), and -29% ( $p<0.001$ ) for the 10, 30, and 100 $\mu$ g groups. On an individual patient basis, just three placebo patients experienced a >20% reduction in shedding rate from baseline, whereas seven 30 $\mu$ g patients experienced this level of shedding reduction. Similarly, four placebo patients experienced a >20% increase in shedding rate compared to just one 30 $\mu$ g patient. In the below chart, group wide (left panel) and patient specific (right panel) changes in viral shedding are presented.

#### GEN-003 Reduces Shedding Immediately Following Vaccination in Phase I/IIa



Source: Genocea

Genocea reports that GEN-003 appeared safe and well tolerated for a therapeutic vaccine. Within the first week post-vaccination the most frequent AEs were fatigue, myalgia, pain, tenderness, and induration. These are consistent with many vaccines and generally resolved within a few days. The AE rate appeared highest in the 10 $\mu$ g cohort; no reason for this effect is known. Beyond day 7 post-vaccination, AEs were similar in nature to the initial week, although lacked the treatment effect. Only two patients discontinued further vaccinations, one from the combination of myalgia, fatigue, and pain/tenderness at the injection site, the other patient withdrew following injection site pain. Both of these patients were in the 10 $\mu$ g cohort.

Following the positive results from the period immediately after immunization, management extended the trial to assess the status of patients' HSV-2 infection at 6 months and 12 months post-vaccination. Unfortunately, by the time this decision was made, a portion of patients had already surpassed 6 months post-vaccination. Consequently, these patients were excluded from the 6-month analysis. These patients are expected to be included in the 12-month analysis (expected mid-2014).

### ...And At 6-months

Six months after vaccination patients' HSV-2 symptoms were assessed for another 4-week period. At this time patients that received placebo and non-adjuvanted vaccine experienced changes in viral shedding from baseline of +32% ( $p < 0.003$ ) and +14%. The patient groups that received GEN-003 with adjuvant experienced shedding changes of +54%, -40% ( $p < 0.001$ ), and -18% respectively.

Twelve month data from the Phase I/IIa are expected in mid-2014.

#### Phase I/IIa 6 Month Durability Data

Treatment Group	Number of Subjects	Mean 6 Month Viral Shedding Frequency, Change from Baseline	p-value
<b>Placebo</b>	23	+32%	<0.003
<b>Unadjuvanted</b>	22	+14%	ns
<b>Vaccine (10 µg)</b>	26	+54%	ns
<b>Vaccine (30 µg)</b>	19	-40%	<0.001
<b>Vaccine (100 µg)</b>	24	-18%	ns

**ns = not significant**

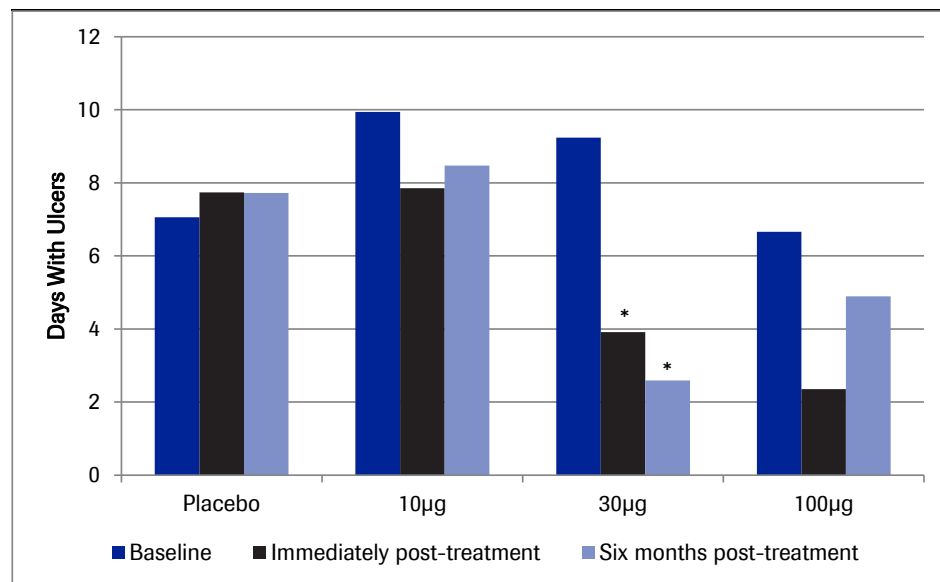
Source: Genocea

#### GEN-003 Also Reduces The Frequency And Severity of Lesions

Genocea believes shedding may be important for GEN003's commercial adoption and public health utility, but the FDA will likely be unwilling to approve an HSV-2 vaccine on the ability to alter shedding. Instead, management expects measures of clinical symptoms/lesion activity will need to show statistically significant improvement in pivotal Phase III registration studies.

Genocea collected data on the impact of GEN-003 on lesions in the Phase I/IIa. By counting the total number of days with a lesion, both the frequency of lesions and the lesion(s) duration is captured. In February 2014, Genocea released lesion data from the first six months following vaccination in the Phase I/IIa. This analysis demonstrated that the 30µg dosage of GEN-003 is capable of reducing the number of days on which patients self-report the presence of lesions. In the four weeks leading up to vaccination this group experienced an average of 9.24 days with a lesion, compared to 3.91 ( $p < 0.001$ ) and 2.59 ( $p < 0.001$ ) in the four-week periods immediately following vaccination and 6 months after vaccination, respectively. This implies a reduction of 58% in lesion rate immediately following the vaccination, and of 72% in lesion rate six months after the vaccination.

#### Self-Reported Days With Ulcers Over a Four-Week Period



Source: Cowen and Company; Genocea Free Writing Prospectus

#### Genocea Will Next Conduct Phase II Trials To Optimize Dose And Schedule

Genocea is planning a Phase II program to optimize GEN-003's dose and administration schedule. These trials will explore additional protein and adjuvant dosages, as well as different dosing intervals. The first Phase II trial will be a dose titration trial. This study is expected to begin in mid-2014, enroll about 300 patients, and complete in 2015. The MM-2 adjuvant has previously been administered at 50mg; management intends to also test 25mg and 75mg in Phase II. In Phase I/II, the 30µg antigen dose has performed best with doses above (100µg) and below (10µg) looking inferior. Management reports this resembles a "U" shaped curve observed in guinea pigs. Therefore, in addition to maintaining the 30µg antigen dose, management also intends to test an antigen dose between 10 and 30µg, as well as a dose between 30µg and 100µg. As in the Phase I/IIa trial, endpoints will include viral shedding as well as clinical symptoms (% of patients symptom free at 6 and 12 months, recurrence rate, time to next recurrence).

After the completion of the dose titration trial, in 2015 Genocea expects to begin a second Phase II trial testing various dosing regimens. This trial is expected to complete in 2017, and support the initiation of a pivotal program.

Genocea anticipates that GEN-003's pivotal program will consist of 3 trials, a trial in the U.S., one in the EU, and a third safety study. Genocea expects the efficacy trials will have herpes symptoms as their primary endpoints. Genocea expects to generate an overall safety database of 3-5K people prior to 2019 regulatory filings.

While a 3-5K patient database is smaller than required for most vaccines, Genocea thinks this will be sufficient since GEN-003 is a therapeutic vaccine. Most vaccines are prophylactic, and therefore will only actually benefit the small portion of people who are later exposed to the pathogen. This generates a large safety hurdle which often requires a safety database that can be over 10K people. Since, GEN-003 is being developed as a therapeutic vaccine, every patient receiving GEN-003 has the potential

to see a benefit. Based upon initial FDA discussions, management anticipates a total safety database of 3-5K patients should be sufficient.

### Consultants Think GEN-003 Is Promising And The Leading Candidate

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Our consultants think that a T cell mediated vaccine is a promising approach for the treatment of HSV-2. They think the administration profile of a vaccine – an initial course followed by periodic boosters – would appeal to many patients. Moreover, as B cell based vaccines have proven ineffective, they think a T cell based approach is justified. They think it likely that vaccines that harness cell-mediated immune responses will prove more able to control shedding and outbreaks.

Our consultants think that the design of GEN-003 is rational. In particular, they are intrigued by the inclusion of the T Cell antigen ICP4.2. They find the preclinical data suggesting that a T cell response to ICP4.2 helps individuals better control an HSV-2 infection powerful. They find the preclinical data persuasive, and it made them optimistic that GEN-003 would show efficacy in clinical trials.

Our consultants found GEN-003's clinical data "impressive." They think that the 40% decrease in shedding is of sufficient magnitude to result in long-term clinical benefits. Although admittedly not as large of a decrease in shedding as produced by the small molecules, our consultants think it is sufficiently large to translate to reduction in the risk of transmission and better control of outbreaks. Moreover, they think that the safety profile generated thus far looks good.

Based on the clinical profile generated thus far, the physicians think patients will be willing to use GEN-003. They expect that it will appeal to those patients who want some control of their HSV-2 but are unwilling to take a daily medication. They also think it will appeal to patients who are adherent with their daily Valtrex but want to further reduce their chances of an outbreak, or of infecting a partner.

While our consultants think GEN-003 is viable if future studies simply replicate the clinical profile seen in Phase I/II, they think there is a chance that Genocea could improve the vaccine further. They suggest that GEN-003's efficacy could possibly be increased by varying the dose levels and intervals, as well as the addition of annual booster shots. Genocea plans to explore all of these options in subsequent Phase II trials. Consultants say that maximizing the efficacy of any vaccine involves a bit of "alchemy" as it is nearly impossible to predict how such factors will impact efficacy, and therefore there is a decent chance a different dose and schedule could reduce viral shedding by an even greater magnitude. They think a 70% reduction in viral shedding would be a "home run" as this would put GEN-003's potency on par with that of daily antiviral therapy. However, they think that patients would be much more willing to take a vaccine course than a daily pill, and therefore if GEN-003 were to simply match the efficacy of Valtrex, GEN-003 could replace it as standard of care.

### GEN-003 Intellectual Property

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GEN-003 is protected by a number of patents and patent application families. GEN-003's composition of matter patent has been allowed and will expire in 2031. Genocea has 2 additional patent application families on file. Genocea also has an exclusive license to the Matrix-M2 adjuvant from Novavax for HSV-2. The Matrix-M2 adjuvant is protected by issued patents that expire in 2023-2024.



## Some Competition In HSV-2 Vaccine Space, But We Think Genocea Is The Clear Leader

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### Vical

Vical has moved a herpes simplex virus type 2 (HSV-2) vaccine candidate into the clinic. Vical is investigating both a prophylactic and therapeutic vaccine approach. Several versions of the plasmid DNA-based vaccine, encoding different combinations of viral proteins and formulated with Vaxfectin, have demonstrated efficacy in preclinical guinea pig and murine models. In guinea pig prophylactic studies, Vical has shown complete protection from primary and recurrent disease ( $p < 0.001$ ) and significant reduction of viral replication at both primary and latent infection sites. In guinea pig therapeutic studies, Vical has shown significant reduction in both the frequency of genital lesion outbreaks and the frequency of genital virus shedding (both  $p < 0.05$ ). Similarly, in murine experiments, therapeutic treatment reduced vaginal and dorsal root ganglion HSV-2 copies, while prophylactic treatment reduced mortality resulting from a 500 x LD50 viral challenge from 100% to 20%.

An initial Phase I/II proof-of-concept trial for the therapeutic vaccine was initiated in December 2013. The trial will enroll 150 HSV-2 patients who experience 2-9 recurrences/year. Baseline shedding will be assessed for 60 days, followed by 3 monthly vaccinations, and finally another 60 days of shedding assessment will occur. The primary endpoint will be safety. A secondary endpoint of reduction in shedding days will also be assessed. Based upon an assumption of 20-30% of baseline shedding positive patient days, the secondary endpoint is powered to detect a 30% reduction in shedding. Vical expects that a safety database in the thousands of patients would be required to support an NDA.

### Agenus

Agenus also has an HSV-2 vaccine candidate. In November 2013, Agenus completed a Phase II trial of 80 patients, 70 of which received vaccine, which demonstrated a 15% reduction in viral shedding. Our consultants suggest that a 15% reduction in viral shedding is not likely to meaningfully impact the frequency or severity of herpes symptoms, and therefore we suspect that Agenus will need to improve the potency in order for it to be commercially viable.

### Sanofi

Finally, Sanofi is collaborating with the NIH to conduct a Phase I trial of a replication-defective vaccine. This trial was initiated in November 2013 and is expected to be completed in October 2016.

## We Estimate That A Safe And Effective HSV-2 Therapeutic Vaccine Has \$1B+ Revenue Potential

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The CDC estimates that 16% of the U.S. population aged >14 has been infected with HSV-2. Therefore, we model 43MM potentially treatable Americans. Consultants estimate that just 20-25% of infected people are aware of their status. Therefore we conservatively estimate the population of patients capable of seeking care at 9M people. 90% of patients experience at least one lesion breakout per year and therefore are most amenable to treatment. We also assume that just 67% of these patients will actually seek out care for their HSV-2 infection in a given year for a population of 5.2MM under active care for HSV-2 in the U.S. This leaves 2.6MM diagnosed Americans refusing care due to a combination of the burden and/or cost of antivirals.

We project a 2020 launch and that GEN-003 will penetrate 23% of treated HSV-2 patients by 2025. We also expect a portion of the patients currently not receiving care will seek therapy due to the convenience of GEN-003. As a result, we model a ramp to 9% penetration within currently untreated patients by 2025. In total, this brings GEN-003's user base to 1.4MM people in the U.S. Management has suggested a price of ~\$300/vaccine course or booster shot. Therefore, we model U.S. sales of \$15MM in 2020 increasing to \$550MM in 2025. We assume a similar number of people outside of the U.S. are treated and would have access to GEN-003. WHO estimates of HSV-2 prevalence place Western Europe and Japan's infected populations on par with North America (17.8 vs. 17.9M). We model ex-U.S. launches beginning in 2021. Our model assumes an average price of about \$150/course at the time of launch, and that about 1MM people are on GEN-003 outside of the U.S. by 2025. Our 2025 ex-U.S. sales estimate is \$200MM, and our worldwide estimate \$750MM.

Our model assumes adoption of GEN-003 in the U.S., Western Europe, and Japan. However, infected populations in Eastern Europe and Latin America are much larger than those of the western world. We do not model sales in these regions as it is unclear who will have access to, and be able to afford, GEN-003. Nonetheless, sales outside of the U.S., EU and Japan may provide a source of upside relative to our model.

Genocea reports that the antigens contained in GEN-003 are highly conserved between HSV-2 and HSV-1 (oral herpes). Therefore, management believes efficacy in HSV-2 may translate into efficacy against HSV-1 as well. HSV-1 is generally less severe, but it is estimated that 58% of the U.S. population aged 14-49 is infected with HSV-1. Our model does not assume any off-label sales to HSV-1 infected individuals, though this population may represent an additional source of upside.

## GEN-003 Revenue Model

	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E
<b>U.S. HSV-2 Market</b>								
Number of People Infected With HSV-2 In The United States (MM)	43	43	43	43	43	43	43	43
<i>% Diagnosed</i>	20%	20%	20%	20%	20%	20%	20%	20%
Number of People Diagnosed With HSV-2 Infection In The U.S. (MM)	9	9	9	9	9	9	9	9
<i>% Diagnosed Who Have Annual Outbreaks</i>	90%	90%	90%	90%	90%	90%	90%	90%
Number Of People With Symptomatic HSV-2 Infection (MM)	7.8	7.8	7.8	7.8	7.8	7.8	7.8	7.8
<i>% Of Symptomatic People Who Seek Treatment</i>	67%	67%	67%	67%	67%	67%	67%	67%
Number Of People With Symptomatic HSV-2 Who Seek Treatment (MM)	5.2	5.2	5.2	5.2	5.2	5.2	5.2	5.2
<i>GEN-003 Share (%)</i>	0%	0%	1%	5%	10%	15%	20%	23%
Number Of Current Treaters Who Go On GEN-003 (MM)	0.0	0.0	0.1	0.3	0.5	0.8	1.0	1.2
<i>% Of Symptomatic People Who Do Not Seek Treatment</i>	33%	33%	33%	33%	33%	33%	33%	33%
Number Of People With Symptomatic HSV-2 Who Do Not Seek Treatment (MM)	2.6	2.6	2.6	2.6	2.6	2.6	2.6	2.6
<i>GEN-003 Share (%)</i>	0%	0%	0%	0%	1%	3%	5%	9%
Number Of Current Non-Treaters Who Go On GEN-003 (MM)	0.0	0.0	0.0	0.0	0.0	0.1	0.1	0.2
Total Number of People On GEN-003 In U.S. (MM)	0.0	0.0	0.1	0.3	0.5	0.9	1.2	1.4
Average Cost per Patient (\$)	300	300	300	315	331	347	365	383
<b>GEN-003 Revenue From U.S. Adults (\$MM)</b>	<b>0.0</b>	<b>0.0</b>	<b>15.0</b>	<b>85.0</b>	<b>180.0</b>	<b>300.0</b>	<b>425.0</b>	<b>550.0</b>
<i>Y/Y Growth (%)</i>				467%	112%	67%	42%	29%
<b>ROW HSV-2 Market</b>								
Number of People Infected With HSV-2 ROW Who Have Access To Care (MM)	43	43	43	43	43	43	43	43
<i>% Diagnosed</i>	20%	20%	20%	20%	20%	20%	20%	20%
Number of People Diagnosed With HSV-2 Infection ROW (MM)	9	9	9	9	9	9	9	9
<i>% Diagnosed Who Have Annual Outbreaks</i>	90%	90%	90%	90%	90%	90%	90%	90%
Number Of People With Symptomatic HSV-2 Infection (MM)	7.8	7.8	7.8	7.8	7.8	7.8	7.8	7.8
<i>% Of Symptomatic People Who Seek Treatment</i>	67%	67%	67%	67%	67%	67%	67%	67%
Number Of People With Symptomatic HSV-2 Who Seek Treatment (MM)	5.2	5.2	5.2	5.2	5.2	5.2	5.2	5.2
<i>GEN-003 Share (%)</i>	0%	0%	0%	1%	5%	10%	13%	16%
Number Of Current Treaters Who Go On GEN-003 (MM)	0.0	0.0	0.0	0.0	0.3	0.5	0.7	0.8
<i>% Of Symptomatic People Who Do Not Seek Treatment</i>	33%	33%	33%	33%	33%	33%	33%	33%
Number Of People With Symptomatic HSV-2 Who Do Not Seek Treatment (MM)	2.6	2.6	2.6	2.6	2.6	2.6	2.6	2.6
<i>GEN-003 Share (%)</i>	0%	0%	0%	0%	1%	3%	5%	8%
Number Of Current Non-Treaters Who Go On GEN-003 (MM)	0.0	0.0	0.0	0.0	0.0	0.1	0.1	0.2
Total Number of People On GEN-003 ROW (MM)	0.0	0.0	0.0	0.0	0.3	0.6	0.8	1.0
Average Cost per Patient (\$)	150	150	150	157.5	165	174	182	191
<b>GEN-003 Revenue From ROW Adults (\$MM)</b>	<b>0.0</b>	<b>0.0</b>	<b>0.0</b>	<b>5.0</b>	<b>50.0</b>	<b>100.0</b>	<b>150.0</b>	<b>200.0</b>
<i>Y/Y Growth (%)</i>					900%	100%	50%	33%
<b>Worldwide GEN-003 Revenue (\$MM)</b>	<b>0.0</b>	<b>0.0</b>	<b>15.0</b>	<b>90.0</b>	<b>230.0</b>	<b>400.0</b>	<b>575.0</b>	<b>750.0</b>
<i>Y/Y Growth (%)</i>				500%	156%	74%	44%	30%

Source: Cowen and Company

## Genocea's Second Program: An Improved Pneumococcal Vaccine

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Genocea's second wholly owned clinical program, GEN-004, is a potential universal pneumococcal vaccine that entered Phase I trials in late 2013. GEN-004 is focused on eliciting T<sub>H</sub>17 cells which have been shown to be capable of directing a sterilizing immune response in the absence of antibodies in mice and be produced in larger numbers by adult humans who are generally considered "protected" from pneumococcal disease. Current pneumococcal vaccines are directed at generating antibodies to surface proteins. These antibodies are specific for just a fraction of circulating serotypes. Nonetheless, pneumococcal vaccines currently sell >\$5.5B worldwide. GEN-004's antigens are highly conserved across all serotypes. As a result, if GEN-004 is successful it is likely to protect against most if not all pneumococcal strains. Therefore, we believe GEN-004 has the potential to capture a significant share of this massive market.

### Prevnar-13 is Good But Better Is Required

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*Streptococcus pneumonia* is responsible for more than one million deaths in young children per year. In fact, The Gates Foundation estimates it kills more children under age five globally than any other organism. Pneumococcal disease's associated morbidity is typically manifested as otitis media, but less commonly as pneumonia, bacteremia, and meningitis. An estimated 175,000 hospitalizations occur each year in the U.S. due to *S. pneumonia*; among those 6,000 deaths result. The incidence of invasive disease jumps from 3.8 for those aged 18-34 to 36.4 in those 65 and older.

The development of pneumococcal vaccines against a representative subset of serotypes of *Streptococcus pneumoniae* was a landmark achievement of the biopharmaceutical industry. We estimate that the worldwide pneumococcal vaccine market generated over \$5.5B in revenue in 2013. The first vaccine of this type – PFE's Prevnar-7, was approved in 2000 for the protection of children 2-23 months of age. This vaccine consisted of seven of the 90 or so capsular polysaccharides from representative serotypes all conjugated to a bacterial protein for increased immunogenicity. The vaccine was "updated" in 2010 to Prevnar-13 with six more antigens. Prevnar-13 (PFE) is the next-generation 13 valent version (PCV-13) which is replacing Prevnar and was granted accelerated FDA approval based upon immunogenicity. Synflorix (GSK) is a 10 valent conjugated vaccine and is only available in the EU. Pneumovax (MRK) is a 23 valent polysaccharide vaccine (PPSV-23) which had been the dominant vaccine in the adult market for the past 20 years.

The CDC currently recommends the conjugated pneumococcal vaccine Prevnar-13 for all children 6 weeks to 5 years old, for vaccine naïve children 6-17 y.o., for children age 6-18 y.o with immunocompromising conditions (off label use), and for adults 50 and older. The CDC recommends the polysaccharide vaccine (Pneumovax) for all adults age 65 and older, high-risk adults age 19-64, adults living in nursing/long term care homes, and adults who smoke. However, other groups including the JCVI only recommend Pneumovax for risk groups rather than the entire age 65 and older population. ACIP recommends use of Prevnar-13 in immunocompromised adults, but this recommendation is not, at present, consistent with other medical groups. As part of its commitment from Prevnar-13's accelerated approval, Pfizer initiated the CAPiTA trial to evaluate Prevnar-13's efficacy in preventing community acquired pneumonia. Positive top-line results from the trial were released in February 2014 and we expect these results will provide a platform for expanded use of Prevnar-13 in adults.

We expect a broad recommendation for use in adults 50 years and older will be considered following the positive CAPiTA data. Our consultants suggest whether or not Prevnar-13 garners an ACIP recommendation will depend on how ACIP views the relevance of CAPiTA (done in the Netherlands) and Prevnar-13's price (3x that of Pneumovax). The Prevnar family generated \$1.12B in U.S. and \$3.89B in WW sales during 2013. We estimate Prevnar-13 WW sales of \$4.06B in 2014, \$4.48B in 2016, and \$4.83B in 2018.

While existing vaccines provide important protection against up to 23 serotypes, there are >90 serotypes, the majority of which are not included in current vaccines. The incidence of disease associated with these uncovered strains is believed to be increasing, filling the void left by vaccine strains which are becoming increasingly rare. Consequently, Pfizer is already working on additional follow-on products to Prevnar-13 which contain yet more strains. Genocea believes there are technical and manufacturing limitations to how many strains can be contained in a Prevnar-like vaccine. Therefore, a universal pneumococcal vaccine has tremendous potential.

#### Comparison Of Approved Pneumococcal Vaccines

	Prevnar	Synflorix	Prevnar 13
Company	Pfizer	Glaxo	Pfizer
Approved	WW	Ex-U.S.	WW
Serotypes	4	<b>1</b>	<b>1</b>
	6B	4	<u>3</u>
	9V	<b>5</b>	4
	14	6B	<b>5</b>
	18C	<b>7F</b>	<u>6A</u>
	19F	9V	6B
	23F	14	<b>7F</b>
		18C	9V
		19F	14
		23F	18C
			<u>19A</u>
			19F
			23F
Carrier protein	CRM197	Non-typeable <i>H. influenza</i>	CRM 197

Bold = additional serotypes vs. Prevnar

Underlined= additional serotypes vs. Prevnar and Synflorix

Source: Cowen and Company

#### T<sub>H</sub>17 Cells May Be The Answer

The major source of diversity between pneumococcal strains is the exterior surface. This is also the only portion of the pneumococcus which is accessible to antibodies, and all existing vaccines are dependent upon antibody production for efficacy. As a result, the solution to the universal vaccine problem is to generate an immune response specific to internal antigens which are conserved across strains. These antigens are generally only targetable by T cells.

In the mid-late 2000s a new CD4 helper T cell subset was described which primarily resides at mucosal surfaces and predominantly expressed IL-17. This subset was given the moniker T<sub>H</sub>17 cells. IL-17 causes a strong pro-inflammatory signal in the body that can lead to tissue injury within autoimmune disorders, but also makes T<sub>H</sub>17 cells particularly important in recruiting and activating other immune cells to fight off

pathogens at mucosal barriers before they enter the body. Recent academic studies have revealed that a  $T_H17$  response, elicited by a killed whole cell antigen vaccine, allows mice to fight off *S. pneumoniae* in the complete absence of antibodies. Additional studies indicate that humans mount a  $T_H17$  response when naturally confronted with live pneumococcus. Therefore, Genocea believes a  $T_H17$  focused vaccine directed against conserved antigens could serve as the much-needed universal pneumococcal vaccine.

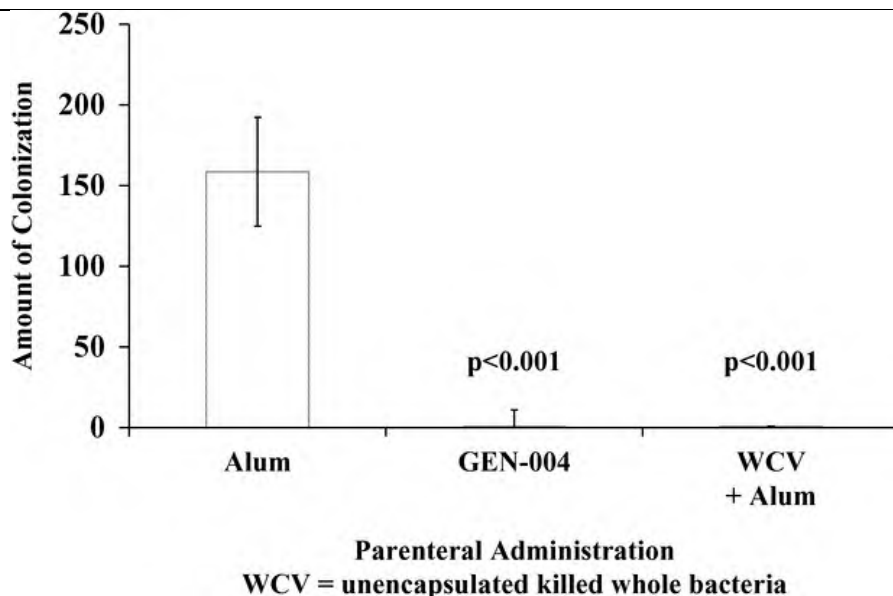
### Genocea Has Identified Conserved Antigens Eliciting $T_H17$ Responses

Genocea adapted its ATLAS technology to screen for IL-17 production rather than IFN- $\gamma$ . Using a library spanning the more than 2,200 proteins in the pneumococcus proteome, Genocea then identified antigens which generated large  $T_H17$  responses in adults (who are considered protected against pneumococcal disease). Given the desire to generate a universal pneumococcal vaccine, Genocea also checked antigens ATLAS selected for conservation across known pneumococcal serotypes. This process identified three novel T cell antigens (SP0148, SP1912, and SP2108) which elicit  $T_H17$  responses and are highly conserved across pneumococcal serotypes.

### GEN-004 Prevents Colonization In Mice

Genocea has combined the SP0148, SP1912, and SP2108 antigens with an alhydrogel adjuvant to make GEN-004. Using a mouse model of nasal colonization, GEN-004 has demonstrated the ability to protect mice from pneumococcal acquisition. In this experiment mice are immunized with GEN-004, then exposed intranasally with live pneumococci. Following a 10-day incubation period, the nasal cavities of the mice are washed with saline. The saline is then assayed for the presence of pneumococci. As shown below, control immunization with just alum allows the colonization of the nasal cavity to occur. Conversely, immunization with either the previously described whole cell antigen vaccine (WCV) or GEN-004 prevents the colonization of the nasal cavity ( $p < 0.001$ ).

#### Pneumococcal Colonization of Mouse Nasal Cavities Is Prevented By GEN-004



Source: Genocea

## GEN-004 Has Begun Phase I

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In December 2013, Genocea initiated a randomized, double-blind Phase I trial of GEN-004 in 90 healthy adult volunteers aged 18-50. Genocea plans to enroll 18 patients in each of 5 treatment groups: placebo, proteins only, GEN-004 containing 10µg of protein, GEN-004 containing 30µg of protein, and GEN-004 containing 100µg of protein. Patients will be dosed three times at 1-month intervals. In addition to safety, the generation of IL-17 producing T cells and antibodies against the vaccine will be assessed. As of January 28, 2014 [clinicaltrials.gov](http://clinicaltrials.gov) indicates that Genocea has fully enrolled the trial. Genocea expects to release results by mid-2014.

## Additional Opportunities - Vaccine Candidates for Chlamydial Disease and Malaria

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In addition to the two clinical programs described in the preceding sections, Genocea has also disclosed two earlier stage programs. Both are consistent with Genocea's discovery capabilities and represent opportunities where complex vaccines, if efficacious, would represent huge healthcare advances.

### Chlamydia - Another T Cell Vaccine Candidate

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Chlamydia is the most common communicable disease in North America and Europe, with an estimated 90 million cases worldwide. In the U.S., the disease is mainly seen in adolescents and young adults resulting in an estimated \$2 billion in healthcare costs. Beyond financial considerations, the disease has long-term health consequences including blindness, chronic pelvic pain, ectopic pregnancy (fetal development outside uterus) and infertility. Chlamydial infection also increases the chance of HIV and HPV infection. The causative agent, *Chlamydia trachomatis*, is an obligate intracellular pathogen that causes an asymptomatic infection in up to 90% of cases. While chlamydia can be easily cured with antibiotics, asymptomatic infection prevents many people from seeking treatment. Importantly, asymptomatic infections can spontaneously transition to symptomatic infections and are infectious. As a result, chlamydia incidence continues to rise (5% per year according to the FDA).

Chlamydia's intracellular nature largely masks it from the activity of antibodies. In fact, animal studies have shown that the adoptive transfer of T<sub>H</sub>1 CD4 T Cells (which primarily stimulate cytotoxic CD8 T Cells) can be curative while the adoptive transfer of T<sub>H</sub>2 CD4 T Cells (which primarily stimulate the production of neutralizing antibodies) is not. Therefore, the medical and scientific communities believe a T-cell vaccine (possibly with a complementary antibody response) is required for immunity to be generated. Whole-cell preparations of chlamydia have been successfully developed as vaccines in the veterinary setting. When this approach was tried in humans, it actually heightened disease. Chlamydia simultaneously expresses surface proteins that both stimulate and suppress the immune system. It is believed the Chlamydia whole cell preparations failed because of an imbalance between immune-stimulation and immune-suppression. Consequently, the field hopes that by selecting specific T cell antigens rather than a crude whole cell lysate the proper balance can be achieved.

Many T cell antigens have been proposed in academic literature, but none have been brought into the clinic in more than 50 years. Genocea has deployed ATLAS in an effort to identify a chlamydia protective antigen(s). The company employed T cells from multiple classes of patients including those who suffered from infertility as a result of chlamydia infection (suggesting no protective T cells) and patients that



spontaneously cleared their disease (suggesting the presence of protective T cell clones). By screening large numbers of patients' T cells against the *C. trachomatis* proteome, the company has identified 22 proteins associated with a protective immune response. Management reports that a combination of three of these proteins and the MM-2 adjuvant significantly reduced chlamydial infections in an animal model.

### Malaria And The Gates Foundation

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Malaria, primarily mosquito-borne, is one of the most prevalent infectious diseases in the world with over 3.3 billion people living in at-risk areas, primarily tropics and sub-tropics. The World Health Organization estimates that there are roughly 220MM infections each year and 660,000 deaths (in 2010), mostly of children in Africa. The infection is caused by a single-cell parasite from the genus *Plasmodium*, of which four types commonly infect humans with *Plasmodium falciparum* responsible for most deaths. The malaria parasite is primarily transmitted by the *Anopheles* mosquito, although it can also be transmitted through transfusions, organ transplants, or shared needle use involving contaminated blood.

There are effective treatments (Malarone, Coartem, Quinine, Mefloquine) which are also commonly used prophylactically by travelers to high-risk areas. However, the use of drug therapy in most-impacted areas is not an option due to both cost and need for chronic use. There is currently no vaccine available, although GSK's RTS,S vaccine has been shown to reduce infections by 46% in Phase III trials. While less than ideal, this has been hailed as one of the most important advances in the history of global health research. GSK intends to file an MAA in 2014. If approved, GSK has promised to price RTS,S at cost+5% with the 5% margin being exclusively used for further malaria research.

The Navy and Bill and Melinda Gates foundation have contracted with Genocea to deploy ATLAS to the pursuit of alternative malaria antigens, which may result in improved efficacy. The advancement of this program is likely to be entirely dependent upon the availability of outside funding.

### Vaccines 101

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In the 1700's, after learning that dairy workers rarely suffered the full effects of smallpox, Edward Jenner decided to try inoculating an 8-year old boy first with cowpox and then six weeks later with smallpox. This and subsequent studies revealed that infection with the less dangerous cowpox virus generated an immune response that in turn protected a person from the closely related and deadly smallpox virus. Ultimately another closely related virus, vaccinia, was widely adopted and the resulting vaccine eradicated smallpox in 1980. In the 250 years since Edward Jenner's observation many more vaccines have been successfully developed using a number of approaches.

- 1) Live attenuated vaccines: Pathogens which have been grown repeatedly in cell culture or animals so that they become adapted to the new environment. In doing this the pathogen loses the ability to cause serious disease yet retains important immunity producing features when it is returned to humans. Examples include the yellow fever, oral (Sabin) polio, and oral typhoid vaccines.
- 2) Killed vaccines: A pathogen is killed in a laboratory via chemical or environmental methods. Thus, it does not spread and cause disease but may retain important

immunity generating features on its surface. Examples include most flu, the inactivated (Salk) polio and rabies vaccines.

- 3) Subunit vaccines: A small portion (protein, virus like particle, etc.) of a pathogen which is capable of generating a protective immune response (an antigen) is identified, manufactured at scale and introduced into a patient. A variation on this approach includes linking multiple polysaccharides from a pathogen together into a “conjugate” vaccine. Examples include the hepatitis B, HPV, and pneumococcus vaccines.

Live attenuated vaccines are generally considered the best at generating an immune response. This is because they replicate inside the body, are processed by all of the normal immune mechanisms, and therefore generate responses from throughout the immune system including both T and B cells. Unfortunately, the ability to replicate also presents a safety problem. There is a fine line between retaining the ability to replicate enough to generate an immune response and retaining sufficient ability to cause disease. As a result, live attenuated vaccines are particularly dangerous in immunosuppressed patients. In addition, it is possible for the vaccine strain to evolve so that it reacquires characteristics of the pathogenic strain which cause disease in healthy individuals. This has been observed to occur on rare occasion with the oral polio vaccine.

As a result of these safety concerns, researchers developed the killed, subunit and conjugate vaccine approaches. These approaches are safer as they can neither replicate nor cause disease. However, these approaches do have their drawbacks. Since no replication occurs, all of the antigen needed to stimulate the immune system must be delivered at once rather than allowing the pathogen to build more antigen inside the body. Depending upon the dosages required this can be difficult to achieve or may require repeated exposures to smaller dosages. In addition, since these vaccines are not processed through all the normal immune generating methods, only a partial immune response is triggered.

Antibodies tend to be directed against antigens on the surface of pathogens. These portions of pathogens are the primary drivers of immune responses in killed vaccines, and can be easily harvested in crude subunit preparations. In addition, B cell (antibody) responses have historically been easier to isolate and characterize than T cell responses (cell-mediated response). As a result of a combination of all these factors, non-attenuated vaccines have tended to focus on eliciting B cell centric responses and their resulting neutralizing antibodies.

While the biopharmaceutical industry has been successful at generating vaccines against numerous pathogens, many pathogens have remained refractory to traditional approaches. It is believed many of these pathogens have been intractable as a result of insufficient stimulation of T cell responses. While it has been possible to map T cell responses to particular regions of a proteome, this process has been extremely labor intensive and could take months to accomplish for just a few patient samples. This has made the development of rationally designed T cell centric vaccines largely impractical. Genocea's ATLAS platform alters this dynamic. Consequently, ATLAS is an engine which could fuel a rapid expansion into a largely empty T cell vaccine space.

### Genocea's ATLAS Technology

Genocea employs an elegant methodology termed ATLAS (AnTigen Lead Acquisition System) to identify T cell antigens. ATLAS addresses many of the known issues with the identification of T cell antigens and is quite systematic. At its core, ATLAS is a

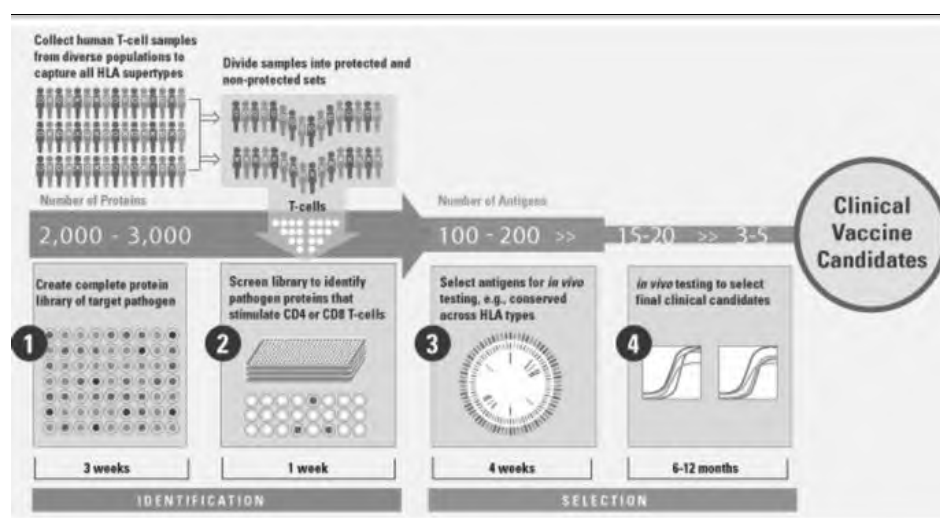
“Reverse Vaccinology” approach. Meaning, it seeks to identify immune responses present in the population which provide protection and then identify the antigen which generates the response, rather than simply putting “forward” candidate antigens and then testing for the generation of protective immune responses.

Before ATLAS can begin, Genocea identifies a pool of patients who have:

- 1) Either been exposed to or infected with a pathogen of interest
- 2) Possess immune responses ranging from fully protected to fully ineffective

Once identified, Genocea obtains blood samples from these patients for use in ATLAS. Separately, Genocea generates a library of recombinant bacteria expressing the entire proteome of the pathogen of interest. This library is then put in a high-throughput screening protocol whereby each protein in the proteome library is incubated with patient antigen presenting cells (APCs) and T cells. Mimicking what occurs in the body, the patient’s APCs take up the pathogen’s protein, process it into epitopes, and then presents those epitopes to the same patient’s T cells. If a patient’s T cells recognize the protein, cytokines and/or effector molecules it will mount a response which includes the secretion of cytokines such as IFN- $\gamma$  into the cell culture media. Genocea can then harvest the media and test it for the presence of a cytokine(s) of interest using ELISAs, multiplexed arrays, etc. Genocea is then able to identify candidate antigens/epitopes by correlating the presence/absence of a T cell response with patients’ immune protection status. The high throughput nature of ATLAS condenses a process which has traditionally taken immunologists years to complete into an 8 week process. The ATLAS platform is protected by 3 patent families (4 issued and 2 pending patents) that expire in 2018-2030.

#### Genocea's High Throughput Cross Presentation Platform



Source: Cowen and Company

ATLAS was originally developed to detect IFN- $\gamma$  responses. Traditionally, IFN- $\gamma$  has been one of the most important cytokines in the immune response. However, additional cytokines have been shown to be important in developing strong immunity, for example IL-17 in pneumococcus, MIP-1 $\beta$  in HIV, and many others. Due to ATLAS’ modular nature, Genocea can quickly adapt the platform to emerging science

describing the ideal cytokine production profile for fighting off a pathogen of interest. This flexibility will allow Genocea to rapidly expand its vaccine pipeline either internally or via collaborations.

We expect that Genocea will constantly be on the watch for additional opportunities to apply the ATLAS technology and its antigen discovery expertise. T-cell vaccines are thought to have potential utility in a wide range of infectious diseases, and potentially even cancer. Genocea has suggested it will explore a wide range of diseases and conditions in order to find the best opportunities for development.

#### **DCF Analysis Suggests That Genocea Is Undervalued On The Potential Of GEN-003, With Little Contribution From The Rest Of The Pipeline**

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We have incorporated our GEN-003 and Genocea expense estimates into a DCF. Briefly, we assume GEN-003 is launched in 2020 and achieves \$750MM in revenue by 2025. We assume it grows to \$1.8B in 2032, and declines following the expiration of its patents. We assume that Genocea's R&D expense grows from \$25MM in 2014 to \$75MM in 2020, and that its SG&A increases from \$10MM in 2014 to \$115MM by 2020. Our model assumes that Genocea breaks into profitability in 2023 after the launch of GEN-003, and does not project any revenue from GEN-004. We apply a 12% discount rate, and a -20% terminal growth rate. Our analysis suggests that GEN-003 is worth \$40/share, with no contribution from GEN-004 or the rest of GNCA's pipeline.

Genoea DCF Analysis

Financial Year End	12/31/2013
Valuation Date	2/27/2014
Discount Rate	12.0%
Terminal Growth Rate	-20.0%

GENOECA: DCF Valuation																			
\$MM	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032
GEN-003 <i>Growth (%)</i>	0	0	0	0	0	0	15	90 <i>500%</i>	230 <i>156%</i>	400 <i>74%</i>	575 <i>44%</i>	750 <i>30%</i>	937 <i>25%</i>	1,125 <i>20%</i>	1,294 <i>15%</i>	1,423 <i>10%</i>	1,585 <i>10%</i>	1,722 <i>10%</i>	1,808 <i>5%</i>
GEN-004 <i>Growth (%)</i>	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Contract, Grant Revenue And Other <i>Growth (%)</i>	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Total Revenues <i>Growth (%)</i>	0	0	0	0	0	0	15	90 <i>156%</i>	230 <i>74%</i>	400 <i>44%</i>	575 <i>30%</i>	750 <i>25%</i>	937 <i>20%</i>	1125 <i>15%</i>	1294 <i>10%</i>	1423 <i>10%</i>	1585 <i>10%</i>	1722 <i>10%</i>	1808 <i>5%</i>
COGS <i>COGS as a % of sales</i>	0	0	0	0	0	0	2	7 <i>8%</i>	18 <i>8%</i>	32 <i>8%</i>	46 <i>8%</i>	60 <i>8%</i>	75 <i>8%</i>	90 <i>8%</i>	104 <i>8%</i>	114 <i>8%</i>	125 <i>8%</i>	138 <i>8%</i>	145 <i>8%</i>
R&D <i>R&amp;D as a % of Revenues</i>	25	28	30	45	55	65	75	90 <i>100%</i>	115 <i>50%</i>	140 <i>35%</i>	144 <i>25%</i>	150 <i>20%</i>	188 <i>20%</i>	225 <i>20%</i>	259 <i>20%</i>	213 <i>15%</i>	157 <i>10%</i>	172 <i>10%</i>	181 <i>10%</i>
SG&A <i>SG&amp;A as a % of Revenues</i>	10	11	12	15	25	50	115	115 <i>128%</i>	115 <i>50%</i>	120 <i>30%</i>	129 <i>23%</i>	135 <i>18%</i>	169 <i>18%</i>	203 <i>18%</i>	233 <i>18%</i>	256 <i>18%</i>	235 <i>15%</i>	207 <i>12%</i>	217 <i>12%</i>
Operating Income	-35	-39	-42	-60	-80	-115	-177	-122	-18	108	256	405	506	608	699	840	1049	1205	1266
Tax <i>Tax rate</i>	0 <i>0%</i>	0 <i>0%</i>	0 <i>0%</i>	0 <i>0%</i>	0 <i>0%</i>	0 <i>0%</i>	0 <i>0%</i>	0 <i>0%</i>	0 <i>0%</i>	0 <i>0%</i>	0 <i>0%</i>	81 <i>20%</i>	152 <i>30%</i>	182 <i>30%</i>	210 <i>30%</i>	252 <i>30%</i>	315 <i>30%</i>	362 <i>30%</i>	380 <i>30%</i>
NOL/Tax Assets Utilized <i>Tax rate</i>																			
Taxes Paid	0	0	0	0	0	0	0	0	0	0	0	81	152	182	210	252	315	362	380
Approx Free Cash Flow	(35)	(39)	(42)	(60)	(80)	(115)	(177)	(122)	(18)	108	256	324	354	425	489	588	734	844	886
Years	0.84	1.84	2.84	3.84	4.84	5.84	6.84	7.84	8.84	9.84	10.84	11.84	12.84	13.84	14.84	15.84	16.84	17.84	18.84
Discount Factor	0.91	0.81	0.72	0.65	0.58	0.52	0.46	0.41	0.37	0.33	0.29	0.26	0.23	0.21	0.19	0.17	0.15	0.13	0.12
NPV of Cash flows	(32)	(31)	(30)	(39)	(48)	(59)	(81)	(50)	(7)	35	75	85	83	89	91	98	109	112	105

Terminal Value Calculation	
Final year FCF	886
Perpetual Growth Rate	-20.0%
Terminal Value	2215
Discount Factor	0.12
Present Value of Terminal Value	262
Present Value of Cash Flows	399
Enterprise Value	661
Add: Net cash	65
Market Value	726
Fully Diluted Shares Outstanding	18.0
Value per Fully Diluted Share	\$40.33

Source: Cowen and Company.

Genocea Quarterly P&L (\$MM)

	2012A	2013E	Q1:14E	Q2:14E	Q3:14E	Q4:14E	2014E
GEN-003			-				
GEN-004			-				
Contract, Grant Revenue And Other	2.0	1.0					
Total Revenue	2.0	1.0	-	-	-	-	-
COGS			-	-	-	-	-
<i>Gross Margin</i>							
R&D	11.2	14.5	5.5	5.5	7.0	7.0	25.0
SG&A	3.7	4.5	2.8	2.5	2.5	2.5	10.3
Other							
Operating Expenses	14.9	19.0	8.3	8.0	9.5	9.5	35.3
Operating Income / (Loss)	(13.0)	(18.0)	(8.3)	(8.0)	(9.5)	(9.5)	(35.3)
Interest Income, net	(0.5)	(0.7)	(0.2)	(0.2)	(0.2)	(0.2)	(0.8)
Other Income	0.1	(0.2)					
Pretax net income	(13.4)	(18.9)	(8.5)	(8.2)	(9.7)	(9.7)	(36.1)
Accretion of redeemable convertible preferred stock	(1.8)	(1.2)					
Taxes			-	-	-	-	-
<i>Tax Rate</i>			0%	0%	0%	0%	0%
GAAP Net Income	(15.1)	(20.1)	(8.5)	(8.2)	(9.7)	(9.7)	(36.1)
<b>GAAP EPS</b>	<b>\$ (2.15)</b>	<b>\$ (2.12)</b>	<b>\$ (0.55)</b>	<b>\$ (0.46)</b>	<b>\$ (0.53)</b>	<b>\$ (0.52)</b>	<b>\$ (2.05)</b>
Diluted Shares Outstanding (MM)	7.1	9.5	15.5	18.0	18.2	18.6	17.6

Source: Cowen and Company

Genocea Annual P&L (\$MM)

	2012A	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E
GEN-003	-	-	-	-	-	-	-	-	15.0
GEN-004	-	-	-	-	-	-	-	-	-
Contract, Grant Revenue And Other	2.0	1.0	-	-	-	-	-	-	-
Total Revenue	2.0	1.0	-	-	-	-	-	-	15.0
COGS	-	-	-	-	-	-	-	-	1.5
<i>Gross Margin</i>			0%	0%	0%	0%	0%	0%	90%
R&D	11.2	14.5	25.0	27.5	30.0	45.0	55.0	65.0	75.0
SG&A	3.7	4.5	10.3	11.0	12.0	15.0	25.0	50.0	115.0
Other	-	-	-	-	-	-	-	-	-
Operating Expenses	14.9	19.0	35.3	38.5	42.0	60.0	80.0	115.0	191.5
Operating Income / (Loss)	(13.0)	(18.0)	(35.3)	(38.5)	(42.0)	(60.0)	(80.0)	(115.0)	(176.5)
Interest Income, net	(0.5)	(0.7)	(0.8)	(1.0)	(1.0)	-	2.0	6.0	8.0
Other Income	0.1								
Pretax net income	(13.4)	(18.9)	(36.1)	(39.5)	(43.0)	(60.0)	(78.0)	(109.0)	(168.5)
Accretion of redeemable convertible preferred stock	(1.8)								
Taxes	-	-	-	-	-	-	-	-	-
<i>Tax Rate</i>			0%	0%	0%	0%	0%	0%	0%
GAAP Net Income	(15.1)	(20.1)	(36.1)	(39.5)	(43.0)	(60.0)	(78.0)	(109.0)	(168.5)
<b>GAAP EPS</b>	<b>(2.15)</b>	<b>(2.12)</b>	<b>(2.05)</b>	<b>(2.05)</b>	<b>(1.70)</b>	<b>(2.35)</b>	<b>(3.00)</b>	<b>(3.10)</b>	<b>(4.10)</b>
Diluted Shares Outstanding (MM)	7.1	9.5	17.6	19.3	25.3	25.5	26.0	35.2	41.1

Source: Cowen and Company

# *Valuation Methodology And Risks*

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## **Valuation Methodology**

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### **Biotechnology:**

In calculating our 12-month target price, we employ one or more valuation methodologies, which include a discounted earnings analysis, discounted cash flow analysis, net present value analysis and/or a comparable company analysis. These analyses may or may not require the use of objective measures such as price-to-earnings or price-to-sales multiples as well as subjective measures such as discount rates.

We make investment recommendations on early stage (pre-commercial) biotechnology companies based upon an assessment of their technology, the probability of pipeline success, and the potential market opportunity in the event of success. However, because these companies lack traditional financial metrics, we do not believe there are any good methodologies for assigning a specific target price to such stocks.

## **Investment Risks**

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### **Biotechnology:**

There are multiple risks that are inherent with an investment in the biotechnology sector. Beyond systemic risk, there is also clinical, regulatory, and commercial risk. Additionally, biotechnology companies require significant amounts of capital in order to develop their clinical programs. The capital-raising environment is always changing and there is risk that necessary capital to complete development may not be readily available.

## **Risks To The Price Target**

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Much of Genocea's valuation rests on the value of its ATLAS vaccine discovery technology platform, and the revenue potential of its pipeline programs. Determining the value of a technology platform is difficult. Many factors could alter the value, including competition from newer technology platforms, the success or failure of Genocea's candidate vaccines, and the attractiveness of vaccine development more generally. Projecting future sales for any product is difficult, and this is particularly the case for candidates that have yet to be approved. Genocea's stock could be impacted by changes in the regulatory, commercial, or competitive environment for its candidate vaccines or for vaccines more generally. Moreover, the market exclusivity of Genocea's vaccines is largely dependent on their patents, which could be subject to challenge.



# Addendum

## Stocks Mentioned In Important Disclosures

Ticker	Company Name
BMRN	BioMarin Pharmaceutical
GNCA	Genocea Biosciences
GILD	Gilead Sciences
NBIX	Neurocrine Biosciences

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Genocea Biosciences and Neurocrine Biosciences have been client(s) of Cowen and Company, LLC in the past 12 months.

Cowen and Company, LLC and/or its affiliates expect to receive, or intend to seek, compensation for investment banking services in the next 3 months from Genocea Biosciences and Neurocrine Biosciences.

Genocea Biosciences and Neurocrine Biosciences is or was in the past 12 months a client of Cowen and Company, LLC; during the past 12 months, Cowen and Company, LLC provided IB services.

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**Outperform (1):** The stock is expected to achieve a total positive return of at least 15% over the next 12 months

**Market Perform (2):** The stock is expected to have a total return that falls between the parameters of an Outperform and Underperform over the next 12 months

**Underperform (3):** Stock is expected to achieve a total negative return of at least 10% over the next 12 months

**Assumption:** The expected total return calculation includes anticipated dividend yield

#### Cowen and Company Rating System until May 25, 2013

**Outperform (1):** Stock expected to outperform the S&P 500

**Neutral (2):** Stock expected to perform in line with the S&P 500

**Underperform (3):** Stock expected to underperform the S&P 500

**Assumptions:** Time horizon is 12 months; S&P 500 is flat over forecast period

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**Hold** – The fundamentals/valuations of the subject company are neither improving nor deteriorating and the investment return is expected to be in line with the general market return

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Rating	Count	Ratings Distribution	Count	IB Services/Past 12 Months
Buy (a)	415	59.20%	68	16.39%
Hold (b)	270	38.52%	4	1.48%
Sell (c)	16	2.28%	1	6.25%

(a) Corresponds to "Outperform" rated stocks as defined in Cowen and Company, LLC's rating definitions. (b) Corresponds to "Market Perform" as defined in Cowen and Company, LLC's ratings definitions. (c) Corresponds to "Underperform" as defined in Cowen and Company, LLC's ratings definitions.

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### Genoclea Biosciences Rating History as of 02/28/2014

powered by: BlueMatrix



— Closing Price — Target Price

### BioMarin Pharmaceutical Rating History as of 02/28/2014

powered by: BlueMatrix



### Gilead Sciences Rating History as of 02/28/2014

powered by: BlueMatrix



### Neurocrine Biosciences Rating History as of 02/28/2014

powered by: BlueMatrix



#### Legend for Price Chart:

I = Initiation | 1 = Outperform | 2 = Market Perform | 3 = Underperform | UR = Price Target Under Review | T = Terminated Coverage | \$xx = Price Target | NA = Not Available

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