

May 5, 2016

Greffex Has the Zika Vaccine Candidate Ready!

Greffex has developed a Zika vaccine candidate ready for immediate testing. Our vaccine is based on our highly successful GreVac[®] platform employed in the development of the Greffex Avian Flu and MERS Co-V vaccine candidates.

If you are wondering why there is no Zika vaccine “ready to go,” you need to understand vaccine development writ large. It is not quite as easy as going to your local pharmacy or health care provider for a new or novel vaccine.

First a vaccine developer must create a candidate vaccine. Then the vaccine has to be tested. If the disease newly arises, testing agents may not exist and will have to be developed. Once these reagents are provided and the candidate vaccine is tested, studies to determine safety and efficacy in animals must be completed. A vaccine candidate then goes through human clinical trials; if these first steps are successful then human clinical trials lead to approval and to the manufacturing process. Manufacturing and distribution are no easy tasks. All of these tests, trials and development can take many years. Unless there is a pandemic, the steps from inception to inoculation cannot be abbreviated.

Vaccine developers like Greffex argue that the speed to creation of vaccines on their extraordinary platform make their vaccine candidate(s) more accessible to the public. Governments must decide what kind of “universal platform,” (the way to repeat creating a vaccine candidate for every emerging disease rather than reinventing a vaccine candidate each time a disease rears its ugly head) and to date, that evaluative process has been slow and methodical. Everything costs money. Money to develop, to test, to manufacture and to distribute. Small companies rely on investors and the government to provide needed capital. Larger pharmaceutical companies rely on existing technology exploitation, and in many cases governmental assistance to advance their technology. Small vaccine companies hope their technology has the feel of a Tesla[®] and pray that it isn't like a DeLorean[®].

Private investors are the life-blood of good technology companies. Government assistance in paying for certain development strategies and in offering to buy the vaccines along the development trail allows biotech companies to remain valuable. There is a valid conversation to be had regarding the insertion of government funding into private companies. The argument can also be made that small biotechnology companies and university science teams, whom I call “garage band technologists[®],” create more innovative science. The counter argument is that the

major pharmaceutical companies such as Sanofi or GSK have the depth of experience to better understand the development cycle.

An irrefutable fact is that the funding process of governments is political and not often financially driven in the outcomes. If it were otherwise, major pharmaceutical companies that receive government funding for the development of any vaccine or drug would be required to return the government contribution and be required to pay a royalty or investment fee to the government. This does not happen. "Garage band technologists®" argue that by funding major pharmaceutical companies, available capital is crowded out to them and innovation is stifled. Government must also look at the likelihood of success of receiving a needed vaccine and of the long-term sustainability of vaccine development programs and ask whether pharmaceutical companies can better provide them that outcome. Greffex believes otherwise.

Since capital drives success in biotechnology, what role does Wall Street play in the development of vaccines? In fact, very little. Wall Street investment houses are not long term "players," nor are they technically savvy enough to determine which vaccine is best. They invest where they believe they will get the greatest return most quickly. They rely on each other to provide direction and rely on outside evidence to give them relative assurance. Frankly, one of the reasons that "garage band technologists®" compete so mightily for governmental funding is that governments evaluate technologies without prejudice. Therefore technology approval, while not assuring success, leads third parties to view the validity of technology somewhere between cachet and credible.

What does all this have to do with a Zika vaccine? It takes money to develop one. Wall Street can't provide it. The government can but has many competing voices for the limited amount of capital available. Foundations such as the Bill & Melinda Gates Foundation or the Wellcome Trust are just fingers in the dike. There will be need for more vaccines than those charitable trusts could ever provide.

There is some good news: Greffex is in very early stage discussions with The National Institute of Health (NIH) and the National Institute of Allergy and Infectious Diseases (NIAID) for testing of our candidate Zika vaccine through its Pre-Clinical Testing Services. It is our hope that funds will be provided for the advancement of a Zika vaccine by us and others laboring in this endeavor.

The deadline has passed for Congress to allocate the nearly \$1.9 billion requested by President Obama to combat the Zika virus. The money would have been used to provide barriers against carrier mosquitoes, to pay for developing and developed vaccines, and to produce better testing. This is disappointing although not unexpected. A partial allocation of funds was to be: \$828 million to the Centers for Disease Control and Prevention; \$246 million to the Centers for Medicare and Medicaid Services; \$130 million to the National Institutes of Health (NIH); and \$10 million to the Food and Drug Administration (FDA). Less than 10% of the allocation

requested will go to develop a Zika vaccine. While it is true that \$600 million of the Ebola program will be shifted to Zika, it remains to be seen exactly how much money will actually get into the hands of vaccine developers. As frustrating as it is to those of us trying to get a Zika vaccine into the world population, it is at least equally frustrating to the U.S. government agencies (Health and Human Services and its agencies and departments such as Preparedness and Response, National Institutes of Health and the National Institute for Allergy and Infectious Diseases) to be challenged with advancing a needed vaccine without needed resources *and* coupled with the public perception of unlimited funding availability.

The absence of a Zika vaccine candidate is not the fault of the Department of Health and Human Services (HHS), BARDA, NIH, NIAID, CDC, FDA and a host of alphabet soup agencies charged with getting one out the door. The fault is with Congress. Not Democrats and not Republicans. Congress in total. If Congress wants a Zika vaccine, this country's scientists can give them one. It is that simple!

Finally, I would be remiss if I did not provide you with a list of science companies working on Zika. Greffex absolutely believes when the Greffex Zika vaccine is developed it will be the very best vaccine available based on the test results of our other vaccine candidates. Because we are pushing towards the clinic with our H5N1 Avian Flu vaccine, we might not cross the finish line before other companies do. We believe that a Zika vaccine may ultimately be a long-term childhood vaccine. While the need is great today, it may be greater later. We remain committed to making a Zika vaccine. If not today, then tomorrow. (If there is money available.)

In my next communication, I will offer some potential solutions for accelerating vaccine development and some ideas about funding. Thank you for taking the time to read this letter.

I invite readers to contact me with questions about Zika and the Greffex vaccine platform. You may reach me at jprice@greffex.com

With best regards,

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Zika vaccine pipeline- May 2016

Institution	Technology	Status & Timelines	Collaboration
Bharat	Inactivated purified virus as priority project ; VLP with pRME protein	Preclinical work ongoing, GMP lots 3Q-2016	
Butantan	Live dengue recombinant ; inactivated purified	Work initiated	Collaboration with US NIH
Bio-Manguinhos / Fiocruz	Inactivated purified ; YF17DD chimeric ; VLP ; DNA	Work initiated	Under consideration
US CDC	DNA plasmid expressing VLP ; live recombinant adenovirus	Work initiated	
Hawaii Biotech	Insect cell line produced recombinant proteins plus Alhydrogel or proprietary adjuvant fom collaborator	Work initiated. GMP lots 4Q-2016	Under discussion
InOvivo/GeneOne	DNA – electroporation; work initiated	Preclinical work initiated	
Institut Pasteur	Lentivirus-vectored, measles vectored	Work initiated	Measles vectored work in collaboration with Themis
NewLink	Purified Inactivated virus	Work initiated, clinical evaluation 2018	
US NIH	Zika targeted mutation live attenuated (longer-term), DNA, live VSV recombinant	Work initiated	Various
Novavax	E protein – nanoparticles	Preclinical work initiated	
Replikin	Synthetic replilink peptides	Preclinical work initiated	
Sanofi	ChimeriVax (YF17D) ; other undisclosed technologies	Work initiated	Under consideration
Themis Bioscience	Measles vaccine virus vector (live)	Work initiated	Institut Pasteur
Valneva	Purified inactivated virus	Work initiated	
CureVac	mRNA to express protein	? (no timeline on website)	
Geovax	Modified Vaccinia Virus Ankara- VLP	In development	University of Georgia
GSK	adjuvanted purified inactivated (based on Dengue vax)	10-15 years	
Pasteur	purified inactivated/ YF-17D expressing envelope protein	working	
Johnson & Johnson	Crucell- whole inactivated	evaluating technologies	
Merck	adjuvanted recombinant envelope protein (based on Dengue)	evaluating technologies	
Oxford	Simian adenoviral vector (seems to be ChAdOx1)	hopeful for June pre-clinical	
PaxVax	adenoviral-based vaccine	Early finding moving into early animal testing	
Pfizer	evaluating technologies	n/a	
Profectus Biosciences	replication-competent vesiculoviruses	n/a	
Protein Science	Protiens made in insect cells	Early stages, "6 to 8 weeks to testing"	
Sementis	Based on Chikungunya	launched a project to develop a vaccine	The University of South Australia
Sinergium	Everything in spanish	Can't find any good sources	
Takeda	Tooing into current technology	Looking for money first, then will reseach	