Foresight
science & technology

JumpStart™ Assessment Report

Broad Spectrum Influenza Vaccine

SAMPLE

Developer's NAIC: 325414 Biological Product (except Diagnostic) Manufacturing
Science/Technology Fields: Vaccine, Influenza
Arena NAIC: 325414 Biological Product (except Diagnostic) Manufacturing
Technology Type: Product
Supply Chain: Design and Development
International Patent Classification: A61K 39/00
Geographic Region: Global

Prepared by

Foresight Science & Technology, Inc.
401-273-4844

sales@ForesightST.com

Foresight Science & Technology, Inc. 34 Hayden Rowe St., Suite 300, Hopkinton, MA 01748
Voice: 401-273-4844; Fax: 401-354-1301; Web: http://www.foresightst.com/

1 Executive Summary

The function of the JumpStart™ is to determine if there are markets worth pursuing for a technology. Our findings are based on an examination of the material provided by the client and Web searching/ subscriptions.

The key findings are:

Innovation Being Commercialized: The key scientific innovation is a novel vaccine with the ability to protect against multiple viral strains, for a longer duration, and with greater immunogenicity. This is achieved through the creation of a proprietary enhancing agent, a peptide sequence.

Intellectual Property: This vaccine technology is protected by the following intellectual property package: Patent(s): an application has been submitted, which the client anticipates will clear in the next few months; Trade Secret(s): All present know-how and knowledge are protected via strict confidentiality. All employees and contractors working with the firm have signed non-disclosure agreements (NDAs) before being allowed to work with the technology.

Niches that may be Feasible: We found three feasible market niches in which to commercialize this technology. The first is the global prophylactic and therapeutic influenza vaccine market. This disease area, as with the overall vaccine market for all diseases, has continuing double-digit growth, increased investment, and unmet technological and medical needs concerning formulation, efficacy, and supply availability.[1] The threat of avian flu and other pandemics that may mutate into multiple strains has revived interest, R&D efforts and funding to develop a universal flu vaccine to protect against most/all human flu strains.[2]

A second niche is the global infectious disease market in the Third World. Infectious diseases, including HIV, influenza, hepatitis A,B,C, among many others, are indeed more debilitating in poorer and often more remote regions of the world. Many diseases do not have specific vaccines available such as HIV, West Nile, hepatitis C. For example, HIV is greatest in sub Saharan Africa with upwards of 28% of the population infected; highest incidence is in the poorer regions of this continent.[3] That said, in our globalized world, infections left untreated can have epidemiological implications worldwide.

The third market niche is that of global cancer vaccines. This market is generally an adult vaccine marketplace that may be able to command higher prices and is wide open in terms of competitors and products due to very few approved to-date.[4] This is also a more recent area of

[1] Jocelyn Kaiser, "A One-Size-Fits-All Flu Vaccine?" American Association for the Advancement of Science 312: no. 5772 (April 2006) AAAS web site, http://www.sciencemag.org/cgi/content/full/312/5772/380?etoc (accessed August 16, 2010).
[2] Ibid.
[3] "HIV/AIDS: Global epidemic data and statistics," World Health Organization web site, http://www.who.int/hiv/data/global_data/en/index.html (accessed August 12, 2010).
[4] "Global Vaccines Market," December 7, 2009, Frost & Sullivan web site, http://www.frost.com/ Subscription required (accessed August 12, 2010).

renewed pharma R&D interest. Currently, only two FDA-approved prophylactic vaccines exist and no therapeutic cancer vaccines are on the market.[5] With a US cancer prevalence (2006) of over 11 million people, cancer deaths (2009) at 562,340, and new cases (2009) about 1.5 million resulting in a 43% death rate, there is a continuing and compelling need for new methods of prevention and treatment.[6,7]

Major Substitutable Products and Technology That Already Exist: There are several well-known and established vaccines on the market; examples include vaccines for Influenza, Pneumococcal infections, and HPV-cancer, respectively: MedImmune's FluMist®, Prevnar 7® and now 13® by Pfizer, and Gardasil® by Merck. Some of these vaccines are based on more conventional methods, while others incorporate advanced molecular biology and genetics techniques such as recombinant DNA and sequencing technologies and platforms.[8]

Commercialization Strategy Considerations: There is continual and growing R&D in the area of new vaccines among not only big pharma but also a plethora of start-ups, virtual companies and medium-sized companies worldwide, who may form mergers / partnerships [with each other]. Intellectual property (IP) in the form of patent protection is important to generate value for potential licensees and/or to attract investors, if you attempt to incubate and spinout a company around this technology. Because vaccine development is relatively expensive in terms of creating a production facility, global supply chain and marketing franchise, we recommend a more simple and straightforward license of your [IP] technology to a large, well-established industry partner, who can provide the necessary financial, supply chain and marketing-sales resources to bring your vaccine to market timely. This industry partner can also be an integral part (manufacturing) of an alliance with a non-profit such as the Global Alliance for Vaccine Immunisations (GAVI).

Examples of Potential Targets: Any one of the top tier global vaccine manufacturers represents a potential and primary pool of licensees and collaborators: Pfizer, GlaxoSmithKline (GSK), Novartis, Sanofi Pasteur (Aventis), MedImmune LLC. Secondarily, you may consider medium-sized industry players, Solvay (http://www.solvay.com), but most likely not startups that are cash- and resource-strapped. Also to consider are big players in large, developing and emerging markets, such as China: National Vaccine & Serum Institute (NVSI), Sinovac Biotech, Ltd., and/or Shanghai Institute of Biological Products (SIBP), among others[9], or India: Serum Institute of India, Ltd. (http://www.seruminstitute.com), among others.[10]

---

[5] "Cancer Vaccine Fact Sheet," National Cancer Institute web site, http://www.cancer.gov/cancertopics/factsheet/cancervaccine (accessed August 5, 2010).
[6] "Learn About Cancer: Cancer Basics," American Cancer Society web site, http://www.cancer.org/Cancer/CancerBasics/cancer-prevalence (accessed August 5, 2010).
[7] "Cancer Statistics 2007," American Cancer Society web site, http://www.cancer.org/Cancer/news/News/cancer-death-rate-steadily-declining (accessed August 5, 2010).
[8] As per respective company websites: http://www.roche.com, http://www.merck.com, http://www.pfizer.com, http://www.medimmune.com (accessed August 16, 2010).
[9] "China Today: Vaccine Development in China," April 2007, BioPharm International web site, http://www.bioplanassociates.com/publications/articles/VACCINES_China_Zhou_Apr07_ChinaB.pdf (accessed August 16, 2010).
[10] ExportersIndia web site, http://www.exportersindia.com/indian-manufacturers/vaccines.htm (accessed August 16, 2010).

Value Proposition: The value proposition of this broad spectrum vaccine technology is to bring a superior vaccine to market in terms of multi-strain and longer-lasting protection, greater efficacy, with fewer side effects, ease-of-use, and at an affordable price.

The following individual has been designated as a point of contact in the company, Dr. Smart N. Clever, VP – R&D, xxx-xxx-xxxx, xxx@xxxx.com.

2 Description of Technology

Description of Technology
This technology is a novel vaccine with the ability to protect against multiple viral strains, for a longer duration, and with greater immunogenicity.

This vaccine innovation is achieved through the creation of a proprietary enhancing agent, a peptide sequence. A proprietary peptide sequence can be modified and fine-tuned to more tightly bind to a specific target strain (in this case multiple strains simultaneously) of the influenza virus. Hence, this significantly increases specificity and immunogenicity. With tighter binding, the immune response or affect is lengthened providing a longer period of protection against influenza. This also has potential implications for dosing by requiring fewer – single vaccination - and less frequent doses over one's lifetime. This peptide is incorporated into the vaccine formulation. Moreover, this vaccine peptide technology can be adapted to be used against a myriad of other diseases either as a prophylactic or therapeutic.

2.1 Supplemental Proprietary Description of Technology

The proprietary peptide sequence has a molecular weight of 900MW and a length of 10 amino acids with sequence:

N-Terminus Lys – Tyr – Asp – Glu – Phe – Val – Leu – His – Try – Gly C-Terminus

The DNA (sequence) codons are:

AAA – TAT – GAC – GAG – TTC – GTG – CTA – CAT – TGG – GGG
with stop codons: TAG

The peptide structure is a(n) α-helix that binds to the influenza viral DNA/RNA at ….. –XXX.

3 Major Substitutable Products and Technologies Identified

We conducted a search for relevant products using Google, Frost and Sullivan, and the US Food and Drug Administration (FDA) website using the terms "vaccine," "cancer vaccine," "influenza vaccine," and "vaccine AND peptide."

Examples of Relevant Products/Services Identified			
Product	***Manufacturer***	***Relevance***	***Web site/***

Name			***Phone #***
Fluarix® – Influenza Vaccine	GlaxoSmithKline Biologics	FLUARIX®, an active influenza vaccine for intramuscular injection, is a sterile suspension prepared from influenza viruses produced in chicken eggs.[11,12] The drug is for adults 18+ years of age and protects against influenza caused by virus subtypes A and B.[13] Side effects include pain at injection site, muscle aches, fatigue, and headache.[14] The adult vaccine appears to cost $8.90 (CDC cost) and $10.98 per dose for private sector.[15]	http://www.fluarix.com/ 888-825-5249
Fluzone® - Influenza Vaccine	Sanofi Pasteur Inc.	This vaccine contains three inactivated flu viruses and is injected into the muscle in individuals six months and older.[16] Subtypes protected are A H1N1, type A H3N2, and type B. The vaccine is grown in chicken eggs[17] and must be stored at a refrigerator temperature (not frozen).[18] The price per dose is $9.06 for the CDC, and $12.41 for the private sector.[19]	http://www.fluzone.com/ 570-839-7187
FluMist® - Influenza Vaccine	MedImmune, LLC.	FluMist® is indicated for virus subtypes A and B in healthy individuals from 2-49 years of age.[20] This is a live attenuated virus vaccine that is administered nasally with surface proteins for HA and NA and contains three viruses. The cost per dose (adult) is $15.70 for the CDC, and $19.70 for the private sector.[21,22]	http://www.flumist.com/ 877-633-4411
An unnamed [HIV] gel - a proprietary mix comprised of tenofovir disoproxil	Gilead Sciences, Inc. (USA)	This product is in late-stage clinical trials as a new, colorless and odorless gel prophylactic (non-vaccine) applied to skin indicated for use in women to prevent transmission of the AIDS and genital herpes viruses. Transmission has been reduced by 39% and 51% respectively – in South Africa. This	http://www.gilead.com/ 650-574-3000 800445-3235

[11] "Influenza Virus Vaccine Fluarix®," GlaxoSmithKline web site, http://us.gsk.com/products/assets/us_fluarix.pdf (accessed August 4, 2010).
[12] "Fluarix," RxList – The Internet Drug Index, founded by pharmacists and owned and operated by WebMD, web site, http://www.rxlist.com/fluarix-drug.htm (accessed August 13, 2010).
[13] "Product Approval Information," U.S. Food and Drug Administration web site, http://www.fda.gov/cber/efoi/approve.htm#flu (accessed August 4, 2010).
[14] "Get the Facts on the Flu & Fluarix," GlaxoSmithKline web site, http://www.fluarix.com/dtc/index.htm#isi (accessed August 4, 2010).
[15] "CDC Vaccine Price List: Adult Influenza Vaccine Price List," Centers for Disease Control and Prevention web site, http://www.cdc.gov/vaccines/programs/vfc/cdc-vac-price-list.htm, (accessed August 5, 2010).
[16] "Fluzone," RxList web site, http://www.rxlist.com/fluzone-drug.htm (accessed August 13, 2010).
[17] "Fluzone," Sanofi Pasteur web site, http://www.fluzone.com/?fa=protect/fluzone/about/character (accessed August 4, 2010).
[18] "Fluzone," Sanofi Pasteur web site, http://www.fluzone.com/?fa=protect/fluzone/about/storage (accessed August 4, 2010).
[19] "CDC Vaccine Price List: Adult Influenza Vaccine Price List," Centers for Disease Control and Prevention web site, http://www.cdc.gov/vaccines/programs/vfc/cdc-vac-price-list.htm, (accessed August 5, 2010).
[20] "Flu Protection for Your Family Starts Here," MedImmune, LLC web site, http://www.flumist.com/ (accessed August 5, 2010).
[21] "CDC Vaccine Price List: Adult Influenza Vaccine Price List," Centers for Disease Control and Prevention web site, http://www.cdc.gov/vaccines/programs/vfc/cdc-vac-price-list.htm, (accessed August 5, 2010).
[22] "FluMist," RxList web site, http://www.rxlist.com/flumist-drug.htm (accessed August 13, 2010).

fumarate, an antiretroviral and other molecules. (Viread® brand name of tenofovir in US market, or Apropovir®)		gel is subsidized at a price per dose of US$0.32 – with potential for being offered at a penny per dose through economies of scale – by Clinton Health Access Initiative, Gilead Foundation and US Agency for International Development.[23] Viread® is also approved for hepatitis B. One ingredient in this vaccine, tenofovir, is a nucleotide analogue reverse transcriptase inhibitor (nRTIs) with the formula $C_9H_{14}N_5O_4P$[24]	
Atripla® - a antiretroviral combination pill: tenofovir + emtricitabine + efavirenz[25]	Gilead Sciences, Inc. (USA)	This combination antiviral HIV drug (non-vaccine) formulation is efavirenz 600 mg/emtricitabine 200 mg/ tenofovir disoproxil fumarate 300 mg. It represents the 1st single-tablet therapeutic regimen for HIV.	http://www.gilead.com/ 650-574-3000 800445-3235
Prevnar 13® - Pneumococcal Vaccine	Pfizer (USA)	A vaccine indicated for pneumonia and meningitis (pneumococcal) that protects against multiple [13] strains. In the West, the price will be US$108 per dose.[26] This is the top seller globally.[27]	http://www.pfizer.com 212-733-2323
Fuzeon® - HIV Vaccine (other names include: Enfuvirtide, Envelope polyprotein GP160 precursor with exterior membrane glycoprotein GP120, and transmembrane glycoprotein GP41[28])	Roche (Switzerland)	A peptide anti-viral therapeutic (and possible prophylactic) indicated for HIV. This anti-viral drug is an injectable powder in solution with about a 4 hour half-life. A linear 36-amino acid [synthetic] peptide – inhibitor – with formula: $C_{204}H_{301}N_{51}O_{64.}$ Fuzeon® may be combined with a protease inhibitor such as darunavir for enhanced efficacy.[29] The synthetic peptide inhibits the fusion of CD4 cells and HIV-1 The peptide has an acetylated N-terminal and a carboxamide C-terminal.[30] Protein sequence: YTSLIHSLIEESQNQQEKNEQELLELDKWASL WNWF.[31,32]	http://www.roche.com 973-235-5000

[23] "New Gel Cuts Risk of HIV Infection," July 20, 2010, *The Wall Street Journal*: *Health* web site, http://online.wsj.com/article/SB10001424052748704720004575377140651050822.html?KEYWORDS=vaccine+price+third+world (accessed August 13, 2010).
[24] "Tenofovir," DrugBank, a database supported by the University of Alberta, Canada and the non-profits Genome Alberta and Genome Canada, both funded by the Canadian Government, and GenomeQuest, Inc., a genomic information company web site, http://www.drugbank.ca/drugs/DB00300 (accessed August 13, 2010).
[25] "Atripla," DrugBank web site, http://www.drugbank.ca/search/search?query=atripla (accessed August 13, 2010).
[26] Jonathan D. Rockoff, "Approval of New Version of Prevnar Lifts Pfizer," February 25, 2010, *The Wall Street Journal* web site, http://online.wsj.com/article/NA_WSJ_PUB:SB10001424052748704240004575085423525747254.html (accessed August 13, 2010).
[27] "Global Vaccine Market," Frost and Sullivan web site, http://www.frost.com Subscription required (accessed August 13, 2010).
[28] "Fuzeon," DrugBank, a database supported by the University of Alberta, Canada and the non-profits Genome Alberta and Genome Canada, both funded by the Canadian Government, and GenomeQuest, Inc., a genomic information company web site, http://www.drugbank.ca/drugs/DB00109 (accessed August 13, 2010).
[29] "Investor Update: Fuzeon," June 26, 2006, Roche web site, http://www.roche.com/investors/ir_update/inv-update-2006-06-26.htm= (accessed August 13, 2010).
[30] "Fuzeon," DrugBank web site, http://www.drugbank.ca/drugs/DB00109 (accessed August 13, 2010).

Gardasil® - Cancer / HPV Vaccine	Merck (USA)	The first vaccine (quadrivalent specifically against 4 types of HPV) developed and on the market as a prophylactic for HPV and cervical cancer and is FDA approved for women between the ages of 9-26 years of age. There is a three dose regimen that costs approximately US$360 total.[33] The injected vaccine is a recombinant, VLP-based vaccine.[34]	http://www.merck.comm http://www.gardasil.com 908-423-1000
OncoVAX® - Colon Cancer Vaccine	Vaccinogen, Inc. (USA)	In late-stage Phase IIIa clinical trials, this patient-specific injected vaccine is the first commercially available for colon cancer recurrence niche post-surgery; it has been approved for market in Europe in 2008. The technology involves mixing in a lab, the patient's autologous tumor cells - stage II -with a bacterial adjuvant to create an "active specific immunotherapy" (ASI). A series of injections yields a delayed-type hypersensitive response indicating that T-cells will respond to the tumor antigens or essentially stimulates the patient's immune system to attack the cancer that it would not have recognized.[35]	http://www.vaccinogeninc.com 301-668-8400
Provenge® - Prostate Cancer Vaccine	Dendreon Corp. (USA)	The new FDA-approved niche vaccine used not as a cure but as a last line treatment for non-responders of hormone therapy in cancer patients. A few transient side effects include chills, fever, headache, fatigue, nausea, joint aches and back pain. The vaccine is composed of a patient's [own] white blood cells that are exposed *in vivo* to a prostate cancer cell protein. The drug is expected to be expensive and it may / may not be covered by insurers.[36]	http://www.dendreon.com/ 877-256-4545

This product table represents a range of competitive vaccines – all potential consumer substitutes - to consider when comparing this vaccine technology to others on the market in the three potential market niches. The first three are a sampling of well-established influenza vaccine brands sold by large, global pharmaceutical companies with highly-developed, commercial networks and significant market share.[37,38] The next four technologies represent a range of current and [potentially] forthcoming products available for various infectious disease

---

[31] "Fuzeon," DrugBank web site, http://www.drugbank.ca/drugs/DB00109 (accessed August 13, 2010).
[32] "Drigs A-Z: Professional: Fuzeon," RxList – The Internet Drug Index web site, http://www.rxlist.com/fuzeon-drug.htm (accessed August 13, 2010).
[33] "Sexually Transmitted Diseases: HPV Vaccine Information for Clinicians," Centers for Disease Control and Prevention web site, http://www.cdc.gov/std/HPV/STDFact-HPV-vaccine-hcp.htm#overview (accessed August 13, 2010).
[34] "Gardasil," RxList web site, http://www.rxlist.com/gardasil-drug.htm (accessed August 13, 2010).
[35] "What is OncoVAX®?," Vaccinogen, Inc. web site, http://www.vaccinogeninc.com/vaccinogen/about-vaccinogen/what-is-oncovax/ (accessed August 13, 2010).
[36] "News: FDA Approves Prostate Cancer Vaccine," April 29, 2010, American Cancer Society web site, http://www.cancer.org/Cancer/news/News/fda-approves-prostate-cancer-vaccine (accessed August 13, 2010).
[37],"World Adult infectious Diseases Vaccines Market," December 3, 2001, Frost & Sullivan web site, http://www.frost.com/ Subscription required (accessed August 11, 2010).
[38], "Global Vaccines Markets," December 7, 2009, Frost & Sullivan web site, http://www.frost.com/ Subscription required (accessed August 11, 2010).

indications, such as meningitis, pneumonia, and HIV that are prevalent worldwide, but with increased mortality rates in under- / developing geographies.[39] Gilead has 2 non-vaccine HIV drugs – one therapeutic on the market and one prophylactic in late-stage clinical trials that could preclude the need for a vaccine. Pfizer has a global top seller with Prevnar 13® that is polyvalent for 13 strains of pneumococcal, and Roche sells a well-known peptide vaccine for HIV. Prices are significantly discounted in the Third World marketplace due to subsidies by governments, international non-profits such as the Global Alliance for Vaccines and Immunisation (GAVI), Bill and Melinda Gates Foundation and UNICEF, and partnerships with industry. For example, vaccines for pneumococcal diseases (indications: pneumonia, meningitis), Prevnar 13® (Pfizer) and Synflorix® (GSK) cost between US$54-$108 per dose in the West, but will be offered at between US$3.50-$7.00 per dose in poorer regions.[40] Generally, medicines are sold in developing countries at about one tenth of western prices.[41] The last three drugs listed in our table above are vaccines indicated for a range of cancers – cervical, colon, prostate – to provide a cross-section of potential competitive products in the overall global vaccine market. Gardasil® is a blockbuster polyvalent vaccine; OncoVAX® is in late-stage clinical trials; Provenge® is a recent FDA approval for prostate cancer.

We conducted a search for relevant patents using the terms "vaccine," "influenza vaccine AND peptide," "cancer vaccine," and "peptide vaccine" on the United States Patent and Trademark Office (USPTO) web site and with Delphion. Material in quotes is from the patent abstract unless otherwise noted.

Examples of Relevant Patents and Patent Applications Identified

Patent or Patent Application #	***Patent Title***	***Date***	***Relevance***	***Assignee***
US7763450	Functional influenza virus-like particles (VLPs)	July 27, 2010	This work involves a type of vaccine, whereby, recombinant DNA technology produces virus proteins to HA, NA, M1 in a cell culture expression system. Each structural protein is from a different influenza strain and mimics the binding ability of the virus, yet neutralizes the epitope.	Novavax, Inc., MD, USA
US20100098721 A1	Methods and compositions for preparing a universal influenza vaccine	April 22, 2010	This is for a multivalent vaccine technology that provides protection against multiple strains in a population composed of one or more vector proteins - or antigenic portions	St. Jude Children's Research Hospital, TN, USA

[39] "HIV/AIDS: Global epidemic data and statistics," World Health Organization web site, http://www.who.int/hiv/data/global_data/en/index.html (accessed August 13, 2010).
[40] Andrew Pollack, "Deal Provides Vaccines to Poor Nations at Lower Cost," March 23, 2010, *The New York Times, Global Business* web site, http://www.nytimes.com/2010/03/24/business/global/24vaccine.html (accessed August 13, 2010).
[41] "Global Vaccine Market – Industry Challenges," December 7, 2009, Frost and Sullivan web site, http://www.frost.com Subscription required (accessed August 13, 2010).

			- that can recognize 4+ viral strains to elicit an immune response.	
US7732130	Immunoprotective influenza antigen and its use in vaccination	June 8, 2010	This work involves a fusion protein vaccine technology, whereby, the proprietary antigen is comprised of an extracellular membrane portion of influenza virus, a protein (amino acid) sequence that can recognize a heterologous carrier - either polypeptide ligands or non-peptide molecules.	Vlaams Interuniversitair Instituut Voor Biotechnologoie, Belgium
US20100196394 A1	Anti-Cancer Vaccine Composition	August 5, 2010	This patent involves cancer vaccines or treatment of autoimmune and infectious diseases: transfection *in vitro* of autoimmune T-cells with construct to express a CD223 coding sequence.	The Johns Hopkins University, USA
EP2206720A1	Albumin fusion proteins	July 14, 2010	This is a fusion protein composed of a therapeutic protein and albumin for the treatment of various cancers, HIV or other infections, with a proprietary nucleic acid sequence – along with vectors and methods - codes for the albumin fusion proteins.	Human Genome Sciences, Inc., USA
EP2186896A1	Cancer antigen peptides derived from WT1	May 19, 2010	This work is a novel peptide sequence directed toward HLA-A26 cancer antigens from tumor cells (WT1) for a potential vaccine to induce cytotoxic T-cells.	International Institute of Cancer Immunology, Inc., Osaka, Japan
US20100189641 A1	Novel Strategies for Improved Cancer Vaccines	July 29, 2010	This patent involves a dimer, anti-cancer vaccine complex antibody that recognizes dendritic cells via a proprietary peptide sequence with anchoring domain and a xenoantigen bound to a DDD. Apoptosis is induced.	ImmunoMedics, Inc., USA

Above, we have provided a sampling of the latest patents that may potentially compete with your technology in the areas of influenza, cancer, and other infectious diseases. These patents seem to cover technologies and methods that may be transferable across diseases to prevent and/or treat such. The patents appear to involve sequencing novel proteins as part of a vaccine complex that can be specifically directed to recognize cancer cells by sequencing a gene (protein) of interest.

A search of PubMed was conducted using the terms “vaccine,” “influenza vaccine AND peptide,” “influenza vaccine AND universal,” “cancer vaccine,” and “vaccine AND peptide”. We also examined the literature for R&D and practices via a Web search.

Examples of Relevant Projects Identified			
Project Title	***Performing Institution***	***Performance Period***	***Relevance***
Glycosylation at 158N of	MedImmune,	July 2010	This molecular animal study compares a 9

the hemagglutinin protein and receptor binding specificity synergistically affect the antigenicity and immunogenicity of a live attenuated H5N1 A/Vietnam/1203/2004 vaccine virus in ferrets	LLC. USA		amino acid difference in the H5 HA1 proteins of, and its affect on, the immune response between, a Vietnam H5N1 flu strain (VN04ca) and the Hong Kong strain (HK03ca) and their binding characteristics to alpha2,3-linked and/or alpha2,6-linked sialosides. Masking antigenic epitopes by 158N glycosylation of the HA globular head and binding preferences of VN04ca for alpha2,3SAL affected viral replication, antigenicity and subsequent diminished Ab response.[42]
Innate and adaptive immune correlates of vaccine and adjuvant-induced control of mucosal transmission of SIV in macaques	National Cancer Institute and National Institute of Allergy and Infectious Disease, NIH, USA	May 25, 2010	This study involves molecular adjuvants for inducing protection in HIV and SIV to better protect in the mucosal layer. The vaccine used was a peptide/poxvirus HIV/SIV mucosal vaccine in macaques along with Toll-like receptor agonists and IL-15 adjuvants.[43]
A vesicular stomatitis virus-based hepatitis B virus vaccine vector provides protection against challenge in a single dose	Yale University School of Medicine, USA	August 2010	A study involving the globally pervasive HBV virus. Here, a recombinant VSV-based vaccine was used to study the effectiveness of a single therapeutic dose. A middle envelope surface protein from the HBV virus was used in mice to generate a strong antibody HBs-specific response. A VSV-MS single dose did elicit a stronger and broader CD8 T-cell activation with a single vaccination over current vaccine vectors - including recombinant protein.[44]
WT1 peptide immunotherapy for cancer in children and young adults	Osaka University Graduate School of Medicine, Japan	August 2010	Clinical study whereby the WT1 tumor gene was overexpressed to evaluate vaccine efficacy in children for potential therapeutic against solid tumors or leukemia. The patient cohort was HLA-A*2402 +.[45]
Concomitant tumor and autoantigen vaccination supports renal cell carcinoma rejection.	University of Heidelberg, Germany	June 14,, 2010	This study explores the efficacy of a dendritic cell vaccine with a covaccine to strengthen immune response in renal cancer. Concomitant induction involving tumor antigen and an autoantigen supported CTL activation (e.g., CD4+. CD8+) and expression

[42] Weijia Wang et al, "Glycosylation at 158N of the hemagglutinin protein and receptor binding specificity synergistically affect the antigenicity and immunogenicity of a live attenuated H5N1 A/Vietnam/1203/2004 vaccine virus in ferrets," July 2010, *Journal of Virology*, American Society for Microbiology web site, http://jvi.asm.org/cgi/content/abstract/84/13/6570 (accessed September 14, 2010).
[43] Y. Sui et al, "Innate and adaptive immune correlates of vaccine and adjuvant-induced control of mucosal transmission of SIV in macaques," May 25, 2010, *Proceedings of the National Academy of Sciences USA*, PubMed web site, http://www.ncbi.nlm.nih.gov/pubmed/20457926 (accessed September 14, 2010).
[44] M.A. Cobleigh et al, "A vesicular stomatitis virus-based hepatitis B virus vaccine vector provides protection against challenge in a single dose," August 2010, *Journal of Virology*, PubMed web site, http://www.ncbi.nlm.nih.gov/pubmed/20504927 (accessed September 14, 2010).
[45] Y. Hashii et al, "WT1 peptide immunotherapy for cancer in children and young adults," August 2010, *Pediatric Blood Cancer*, PubMed web site, http://www.ncbi.nlm.nih.gov/pubmed/20582983 (accessed September 14, 2010).

			of associated cytokines (i.e., IL-12, IFN-γ) thereby supporting the eradication of tumor cells. Cells involved: renal cell carcinoma antigens MAGE9 and G250 and GOLGA4 autoantigen. The study was conducted in BALBc mice.[46]
Adjuvant engineering for cancer immunotherapy: Development of a synthetic TLR2 ligand with increased cell adhesion	Osaka Medical Center for Cancer and Cardiovascular Diseases, Japan	July 2010	This paper involves adjuvant engineering or synthesizing an adjuvant molecule based on the structure of MALP-2 peptide, a type of TLR-2 protein. A functional motif was sequenced and linked to a macrophage-activating lipoprotein to generate a novel molecule that binds to integrins, which are expressed on dendritic cells, among other immune cell types, that can inhibit the growth of tumors.[47]

The literature cited above represents some recent studies and projects, globally, that may potentially compete with your technology. These appear to focus on molecular-based techniques, such as sequencing/modifying, in an attempt to further refine the immune response – efficacy, binding specificity, strength, and required dosage - in some way and across several disease areas, in this case influenza, cancers/HBV and HIV. Novel vaccine adjuvants appear to be a recurring theme. Note the Osaka University study that also involves a peptide – here, WT1 -, and the Yale University project that is looking to decrease vaccine dosages.

4 Markets That May Be Feasible

[46] Nicolas Herbert et al, "Concomitant tumor and autoantigen vaccination supports renal cell carcinoma rejection," June 14, 2010, *The Journal of Immunology* web site, http://www.jimmunol.org/cgi/content/abstract/185/2/902 (accessed September 14, 2010).
[47] T. Akazawa et al, "Adjuvant engineering for cancer immunotherapy: Development of a synthetic TLR2 ligand with increased cell adhesion," July 2010, *Cancer Science*, PubMed web site, http://www.ncbi.nlm.nih.gov/pubmed/20507323 (accessed September 14, 2010).

Market Niche Summary	
Name	Global Influenza Vaccine Market – Prophylactic &/ Therapeutic
Basis for Feasibility in Niche	There are unmet medical and disease needs and lack of access worldwide.[48] There is room for significant improvement in available influenza vaccines, formulations, administration, drug half-life, efficacy, and specificity.[49] The threat of avian flu and other pandemics that may mutate into multiple strains has revived interest, R&D efforts and funding to develop a universal flu vaccine to protect against most/all human flu strains.[50]
Likely Market Driver(s)	Relevant market forces exist in manufacturing and administration. All flu vaccines are produced in chicken eggs, which suffer from supply and scale-up issues, low yields, and lengthy manufacturing processes (on average six months). These issues have contributed to vaccine shortages in five of six recent flu seasons.[51] To reach the 30[52] to 40[53] million most vulnerable people, public health officials could use a vaccine manufactured in a more streamlined manner. While several segments of the population are indicated, the elderly are the hardest hit by flu outbreaks. In fact, 85-90% of influenza deaths are in patients over 65. An effective antiviral will help reduce the rate of hospitalizations and deaths attributed to the flu virus especially as the US population ages.[54] Physician trends concerning administration of influenza vaccines affect vaccine use. One survey found that 80% of physicians administered the flu vaccine for 3-5 months. However, only 27% of those surveyed administered the vaccine after the national peak of flu activity. Only about half of physicians said their practices are able to generate lists of patients with chronic illnesses, who are at high risk for flu complications, and only about 25% had used mail or phone reminders to contact high-risk patients about obtaining a vaccine.[55] Many developing countries have increased use of flu vaccine - higher

[48] "Global Alert and Response (GAR): Global Pandemic Influenza Action Plan to Increase Vaccine Supply," World Health Organization web site, http://www.who.int/csr/resources/publications/influenza/CDS_EPR_GIP_2006_1.pdf (accessed August 11, 2010).
[49],"World Adult infectious Diseases Vaccines Market," December 3, 2001, Frost & Sullivan web site, http://www.frost.com/ Subscription required (accessed August 11, 2010).
[50] Jocelyn Kaiser, "A One-Size-Fits-All Flu Vaccine?" American Association for the Advancement of Science 312: no. 5772 (April 2006), AAAS web site, http://www.sciencemag.org/cgi/content/full/312/5772/380?etoc (accessed August 11, 2010).
[51] Anthony B. Iton, MD, JD, MPH, "Rationing Influenza Vaccine: Legal Strategies and Considerations for Local Health Officials," *Journal of Public Health Management & Practice*, vol. 12 no. 4, July/August 2006, PubMed web site, http://www.ncbi.nlm.nih.gov/pubmed/16775532?ordinalpos=1&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVAbstractPlus (accessed August 4, 2010).
[52] "Vaccine Plan for Flu Pandemic Drafted," Associated Press/AP Online, October 22, 2007, HighBeam Research web site, http://www.highbeam.com Subscription required (accessed August 10, 2010).
[53] Steve Inskeep, "Analysis: Details released on US flu pandemic strategy," Morning Edition (NPR), November 2, 2005, HighBeam Research web site, http://www.highbeam.com subscription required (accessed August 10, 2010).
[54] "United States Influenza Pharmaceutical Markets," 2000, Frost & Sullivan web site, http://www.frost.com subscription required (accessed August 4, 2010).
[55] Matthew M Davis et al., "A National Survey of Physician Practices Regarding Influenza Vaccine," *Journal of General Internal Medicine*, September 17, 2002, 17(9) 670-676, PubMed web site, http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=1495108 (accessed August 4, 2010).

	vaccination levels - than developed countries. One source indicated that about one third of all flu vaccinations occur outside of North America, Western Europe, Australia, and New Zealand.[56] Another source noted that flu vaccine use in children, in particular, is expected to increase in the future.[57] Another significant driver appears to be the threat of influenza pandemics. While the number of flu cases varies widely each year, it is estimated that about 10 -15% of the global population gets influenza each year. However, during epidemics, numbers can be as high as 50%.[58] In the US, about 200,000 people are hospitalized each year as a result of the flu and about 36,000 die.[59] Meanwhile, another source notes, in the recent past, there has been a renewed interest in the general vaccines market, even though historically this market has been a relatively low-margin business with high barriers to entry. This trend is expected to continue, although flu vaccine revenues will depend on meeting ambitious coverage targets.[60] There also appears to be a lack of awareness about the flu vaccine, and this is common among adults aged 65 years, with high-risk conditions, such as diabetes or asthma. In a 2003 source, it was indicated that 75% of unvaccinated persons aged 18-64 with diabetes were unaware that they should get a flu vaccine.[61] Despite the efforts of anti-vaccination groups such as the Committee Against Compulsory Vaccinations and the Vaccination Risk Awareness Network, there has been an increased awareness about vaccines and immunization programs.[62] At a 2008 National Influenza Vaccine Summit, organizers had measured awareness in the record pre-booking of Sanofi Pasteur's planned doses of flu vaccine and the expectation of the availability of 120 million doses - the greatest number in US history - for the 2006-2007 season.[63] Efforts to expand the use of vaccines extend globally. In particular, the

[56] G.A. van Essen et al., "Influenza vaccination in 2000: recommendations and vaccine use in 50 developed and rapidly developing countries, *Vaccine* May 1, 2003 21(16) 1780-5, PubMed web site, http://www.ncbi.nlm.nih.gov/sites/entrez?cmd=Retrieve&db=PubMed&list_uids=12686094 (accessed August 4, 2010).

[57] K.M. Zangwill and R.B. Belshe, "Safety and efficacy of trivalent inactivated influenza vaccine in young children: a summary for the new era of routine vaccination,",*Journal of Pediatric Infectious Disease*, March 23, 2004, PubMed web site, http://www.ncbi.nlm.nih.gov/sites/entrez?cmd=Retrieve&db=PubMed&list_uids=15014289&dopt=Citation (accessed August 4, 2010).

[58] "Health Topics: Influenza," World Health Organization web site, http://www.who.int/topics/influenza/en/ (accessed August 9, 2010).

[59] "Key Facts about Influenza and the Influenza Vaccine," Centers for Disease Control and Prevention web site, http://www.cdc.gov/flu/keyfacts.htm (accessed August 4, 2010).

[60] "Pandemic Threat Reignites Influenza Vaccine Market," April 20, 2006,Pharmaceutical Business Review web site, http://www.pharmaceutical-business-review.com/article_feature.asp?guid=C4410902-FB92-4ADE-89F0-26BADA77D453 (accessed August 4, 2010).

[61] B.H. Bardenheier, "Influenza and Pneumococcal Vaccination Coverage Amount Persons Aged ≥65 Years and Persons Aged 18-64 Years with Diabetes or Asthma-United States, 2003," *The Journal of the American Medical Association* 292: no. 22 (December 8, 2004). *JAMA* web site, http://jama.ama-assn.org/cgi/content/full/292/22/2715 (accessed August 4, 2010).

[62] "Global Vaccines Markets," December 7, 2009, Frost & Sullivan web site, http://www.frost.com/ subscription required (accessed August 4, 2010).

[63] "National Influenza Vaccine Summit Comments on Status of Prebooked Influenza Vaccine for 2006-2007," *Business Wire*, February 7, 2006, HighBeam Research web site, http://www.highbeam.com/ subscription required (accessed August 4, 2010).

	World Health Organization, the Bill & Melinda Gates Foundation, and the Global Alliance for Vaccines and Immunization (GAVI) Alliance have helped lead the effort. The Bill & Melinda Gates Foundation gave $2.7 million to a nonprofit research organization to develop a novel vaccine technology that would increase the cost-effective production of flu vaccines.[64] GAVI focuses on increasing children's access to vaccines in poor countries.[65] Additionally, the US contributed $10 million to support flu vaccine development in other countries in 2006, after a World Health Organization report suggested increasing the supply of flu vaccines.[66]
Anticipated End-User Criteria	End-users indicate that performance, efficacy and lack of major side effects are important in a vaccine, and these parameters must be sufficient.[67] End-users would like to have a universal vaccine that could protect against multiple existing and emerging strains in a single dose. Demand often surpasses supply.[68] Therefore, end-users need a ready supply in inventory for potential outbreaks.
Initial Impression of Adequacy of Current Technology to Address those Needs	The threat of avian flu and other influenza pandemics involving mutated and/or multiple strains has revived interest, R&D efforts and funding to develop a universal flu vaccine to protect against most/all human flu strains.[69] Currently, on the market, there exist adequate individual vaccines for a particular strain and/or vaccine combinations - taken in concert - to protect against 2-3 subtypes; however, there is no universal vaccine that can protect against all/most strains in a single dose. Additionally, supply-demand issues persist due to manufacturing constraints.
Anticipated Barriers to Entry	Competition from large companies is a primary barrier. It appears that the top five vaccine manufacturers are GlaxoSmithKline, Pfizer, Merck & Co., Inc., Sanofi-Pasteur Inc., and Novartis Vaccines. These companies represent about 90% of the global vaccine market. These large companies have significant resources that allow for a high level of innovation and strong research and development pipelines. Since the cost of developing a vaccine is very high, the resources of these large companies are more readily able to meet the financial requirements; whereas, it is difficult for smaller companies to compete in such a market.[70] Supporting this, another source stated that there are high entry

[64] "Bill & Melinda Gates Foundation Fund Influenza Vaccine Research," December 20, 2006, PNNOnline (for non-profit news) web site http://pnnonline.org/article.php?sid=7170 (accessed August 4, 2010).
[65] "About the GAVI Alliance," Global Alliance for Vaccines and Immunization web site, http://www.gavialliance.org/General_Information/About_alliance/index.php (accessed August 4, 2010).
[66] Cheryl Pellerin, "United States Gives $10 Million to Develop Global Flu Vaccine," International Information Programs USINFO.STATE.Gov, October 23, 2006, web site, http://usinfo.state.gov/xarchives/display.html?p=washfile-english&y=2006&m=October&x=20061023130051lcnirellep0.7225916 (accessed August 4, 2010).
[67] "Global Alert and Response (GAR): Global Pandemic Influenza Action Plan to Increase Vaccine Supply," World Health Organization web site, http://www.who.int/csr/resources/publications/influenza/CDS_EPR_GIP_2006_1.pdf (accessed August 11, 2010).
[68] "Global Alert and Response (GAR): Global Pandemic Influenza Action Plan to Increase Vaccine Supply," World Health Organization web site, http://www.who.int/csr/resources/publications/influenza/CDS_EPR_GIP_2006_1.pdf (accessed August 11, 2010).
[69] Jocelyn Kaiser, "A One-Size-Fits-All Flu Vaccine?" American Association for the Advancement of Science 312: no. 5772 (April 2006) AAAS, *Science* web site, http://www.sciencemag.org/cgi/content/full/312/5772/380?etoc (accessed August 4, 2010).
[70] "Global Vaccines Markets," December 7, 2009, Frost & Sullivan web site, http://www.frost.com/ Subscription required (accessed August 4, 2010).

	barriers to the flu vaccine market, such as biological manufacturing know-how, expense and established, complex industry and public relationships and networks, thus, the established players face little competition. Formidable regulatory barriers exist. Numerous countries appear to have vaccine approval processes in place that need to be completed successfully before a vaccine is allowed into the market. In the US, the Food and Drug Administration requires at least three phases of clinical trials to be conducted before approving a vaccine.[71] Not only do these clinical trials require significant funding, but also, safety has been a high priority, meaning that clinical outcomes data thresholds are very rigorous.[72]
Cost or Price of Current Technology	In our searches, we found the following maximum costs per dose for each of the following adult vaccines on the US market: Fluarix®, $10.98;[73] Fluvirin®, $13.25;[74] Fluzone®, $13.16;[75] FluMist®, $19.70.[76]
Market Niche Size and Growth Rate	The influenza vaccine market is forecasted to be US$7billion for 2010. The total global vaccine market is growing at an average rate of 12.1%.[77] Therefore, it is possible and reasonable that the influenza vaccine market is growing at about this rate, due to market drivers.
Product Opportunities	The development of potent influenza vaccines is critical for protection from future pandemics. The hot spots for product entry seem to be outlined in various roadmaps as: targeting the development of new tools for the diagnosis and prevention of influenza outbreaks. [78] In particular "A Strategic Framework for Reducing Risks of Infectious Diseases at the Animal–Human–Ecosystems Interface," emphasizes the importance of the development of new tools for the diagnosis and prevention of the broad spectrum of existing and emerging infectious diseases.[79]

The flu market has traditionally been seasonal; however, with the advent of climate change and increased population movement, the global market is becoming year-round. Also, with the emergence of new strains (H5N1, H1N1), it appears that the vaccine market will continue to grow or at least have new potential markets. This market is well-funded with end-users and buyers including governments, non-profits, patients, and private insurers in developed and Third World countries alike.

[71] "Vaccine Product Approval Process," US Food and Drug Administration web site, http://www.fda.gov/cber/vaccine/vacappr.htm (accessed August 4, 2010).
[72] "Global Vaccines Markets," December 7, 2009, Frost & Sullivan web site, http://www.frost.com/ Subscription required (accessed August 4, 2010).
[73] "CDC Vaccine Price List: Adult Influenza Vaccine Price List," Centers for Disease Control and Prevention web site, http://www.cdc.gov/vaccines/programs/vfc/cdc-vac-price-list.htm, (accessed August 5, 2010).
[74] Ibid.
[75] "CDC Vaccine Price List: Adult Influenza Vaccine Price List," Centers for Disease Control and Prevention web site, http://www.cdc.gov/vaccines/programs/vfc/cdc-vac-price-list.htm, (accessed August 5, 2010).
[76] Ibid.
[77] "Global Vaccines Markets: Global Market Overview," December 7, 2009, Frost & Sullivan web site, http://www.frost.com/ subscription required (accessed August 10, 2010).
[78] "A Strategic Framework for Reducing Risks of Infectious Diseases at the Animal–Human–Ecosystems Interface" Food and Agriculture Organization web site ftp://ftp.fao.org/docrep/fao/011/aj137e/aj137e00.pdf (accessed August 11, 2010)
[79] Ibid.

Market Niche Summary	
Name	Third World Vaccines Market – Prophylactic &/ Therapeutic
Basis for Feasibility in Niche	There are numerous viral, infectious diseases: hepatitis (A,B,C), West Nile, Human Papillomavirus (HPV), and chickenpox, among others that affect different populations globally to varying degrees. While vaccines have been developed for some of these viral diseases, including HPV, chickenpox, H1N1[80] and hepatitis B,[81] others still do not have specific vaccines such as HIV, West Nile, and hepatitis C. For example, adult prevalence of HIV is greatest in sub Saharan Africa with upwards of 28% of the population infected – the incidence is greatest in the poorer regions of this continent as well. [82]
Likely Market Driver(s)	A main driver appears to be the threat and high mortality rates of emerging (mutated) strains that can spread rapidly through populations – around the globe – especially where cultural norms differ and sanitation issues contribute to such, i.e., Third World countries, Africa. A source notes, in the recent past there has been a renewed interest in the general vaccines market, even though historically this market has been a relatively low-margin business with high barriers to entry. This trend is expected to continue, although flu vaccine revenues will depend on meeting ambitious coverage targets.[83] Western countries have seen an increased emphasis placed on preventative medicine due to our globalized world. This emphasis has created a greater demand for vaccines, overall. For example, studies in Africa, Mexico, and Thailand have described a high level of demand (>75%) for an HIV vaccine, even if people would have to pay for it themselves, at a reasonable price point. [84, 85] Positive advertising makes the public more amenable to being vaccinated. Increases in public advertisements and media coverage are expected to greatly increase the growth of the vaccination development market in the next 1–4 years. This trend is expected to boost the development of vaccine clinics.[86]
Anticipated End-User Criteria	End-users indicate that performance, efficacy and lack of major side effects are important in a vaccine, and these parameters must be sufficient (adequate) to affect a comprehensive immune response.
Initial Impression of Adequacy	There are many infectious diseases without a vaccine prophylactic or

[80] "2009 H1N1 Flu," Centers for Disease Control and Prevention web site, http://www.cdc.gov/h1n1flu/ (accessed August 5, 2010).
[81] "Hepatitis B," World Health Organization web site, http://www.who.int/immunization/topics/hepatitis_b/en/index.html (accessed August 5, 2010).
[82] "HIV/AIDS: Global epidemic data and statistics," World Health Organization web site, http://www.who.int/hiv/data/global_data/en/index.html (accessed August 12, 2010).
[83] "Global Vaccines Markets," December 7, 2009, Frost & Sullivan web site, http://www.frost.com/ subscription required (accessed August 11, 2010).

[84] Hecht, et al. "Estimating the Demand for a Preventive HIV Vaccine: Why We Need to Do Better," Public Library of Science (PLoS) Medicine, 2006 Sept 3(10):e398, web site, http://medicine.plosjournals.org/perlserv/?request=get-document&doi=10.1371%2Fjournal.pmed.0030398 (accessed August 12, 2010).

[85] "Media Center: Sixty-third World Health Assembly," World Health Organization web site, http://www.who.int/mediacentre/events/2010/wha63/en/ (accessed August 12, 2010).
[86] "Global Vaccines Markets," 2009, Frost & Sullivan web site, http://www.frost.com subscription required (accessed August 11, 2010).

of Current Technology to Address those Needs	therapeutic available on the market, so there is an inadequacy in current technology to address these unmet needs.[87] That said, vaccines that are on the market can continue to be improved vis-à-vis formulation, efficacy and production. Furthermore, the present vaccines simply have not been sufficiently available in poorer regions for many reasons.[88]
Anticipated Barriers to Entry	R&D competition from large companies: It appears that the top five vaccine manufacturers are GlaxoSmithKline (GSK), Pfizer, Merck, Sanofi-Pasteur, and Novartis [Vaccines]. These companies represent about 90% of the global vaccine market. Additionally, these large companies have significant resources that allow a high level of innovation and strong research and development pipelines. Since the cost of developing a vaccine is very high, the resources of these large companies have made it difficult for smaller companies to compete in the market.[89] Price may present a barrier depending on pricing, customer, geography, and company that is selling the vaccine. The vaccine market has historically been a lower profit business due to pricing, seasonal sales, production issues, and lack of affordability – ability to pay higher prices – in poorer regions of the world where there is significant unmet vaccine needs.[90] Substantial pressure exists on vaccine manufacturers to keep vaccine prices low and even to provide the vaccine free of charge in developing nations, hence the formation of GAVI and other vaccine alliances between philanthropic organizations and industry.[91] Negative Publicity from Anti-Vaccine Groups / Governments / Culture Norms: It appears that there are several anti-vaccine groups giving vaccines a negative reputation. Examples of these groups include the Committee Against Compulsory Vaccinations, the Vaccination Risk Awareness Network, [92] and the PutChildrenFirst.Org organization. The PutChildrenFirst.Org organization, for example, has tried to increase the awareness of the dangers of mercury in flu vaccines.[93] Negative publicity and inappropriate information generated by these anti-vaccination groups has negatively affected vaccine manufacturers and persists to varying degrees.[94] Lack of health structures in Third World countries: Many Third World countries lack structured health care systems, infrastructure and budgets to administer immunization programs. This means there are problems concerning vaccine storage, vaccine supply, immunization records, booster administration, transportation, and sourcing skilled labor. While

[87] "GAVI: Innovative Funding," Global Alliance for Vaccines and Immunisation web site, Ghttp://www.gavialliance.org/about/in_finance/index.php (accessed August 12, 2010).
[88] "Advances in Nanotechnology for Healthcare in Developing Countries (Technical Insights)," December 31, 2009, Frost & Sullivan web site, http://www.frost.com subscription required (accessed August 12, 2010).
[89] "Global Vaccines Markets," December 7, 2009, Frost & Sullivan web site, http://www.frost.com/ subscription required (accessed August 11, 2010).
[90] Ibid.
[91] "GAVI: Innovative Funding," Global Alliance for Vaccines and Immunisation web site, http://www.gavialliance.org/about/in_finance/index.php (accessed August 12, 2010).

[92] "About VRAN: INDEX," http://www.vran.org/philosophy/philosophy-index.htm (accessed August 11, 2010).
[93] Manny Alvarez, "Anti-Vaccine Group Challenges CDC's Flu Shot Guidelines for Infants," Fox News, November 14, 2006, http://www.foxnews.com/story/0,2933,229156,00.html (accessed August 11, 2010).
[94] Frost & Sullivan, "Global Vaccines Markets," December 7, 2009, http://www.frost.com/ Subscription required (accessed August 4, 2010).

	organizations such as the GAVI alliance are trying to help reduce these hurdles, the lack of structure creates a barrier when trying to market in third world countries.[95,96,97] Formidable regulations: numerous countries appear to have vaccine approval processes that need to be completed successfully before a vaccine is allowed into the market. Not only do these clinical trials require significant funding, but also, safety has been a high priority, meaning that clinical outcomes data thresholds are rigorous.[98,99, 100]
Cost or Price of Current Technology	Through GAVIs partners, i.e., GSK, Pneumococcal vaccine can be offered in the Third World for $3.50 per dose.[101] Gilead Sciences (CA, USA) HIV gel is $0.32 per dose in Africa, subsidized by Clinton Health Access Initiative and Gilead.[102]
Market Niche Size and Growth Rate	The total global vaccine market is forecasted to grow annually at an average rate of 12.1%[103] from 2008-2015, with continued growth expected in emerging markets as well.[104] The market size via revenues has been stated at about US$ 27bil for 2009.[105]
Product Opportunities	The efficiency of vaccination in the developing world is often compromised by the necessity to store the vaccine in cold environment.[106] According to some reports about 50% of vaccines fail in Africa due to the breakdown in the cold chain.[107] New technologies should focus on improved thermostability making vaccine transportation and delivery in the warm climate convenient and inexpensive.[108]

[95] Ibid.
[96] "Africa: Clusters and Programmes: Health System and Service: Essential Medicines," http://www.afro.who.int/en/divisions-a-programmes/dsd/essential-medicines.html (accessed August 12, 2010).
[97] "GAVI features: Interactive guide to GAVI's support for the pentavalent vaccine," Global Alliance for Vaccines and Immunisation, http://www.gavialliance.org/media_centre/features/2009_05_15_pentavalent_guide_diseases.php (accessed August 12, 2010).
[98] Frost & Sullivan, "Global Vaccines Markets," December 7, 2009, http://www.frost.com/ Subscription required (accessed August 4, 2010).
[99] "Africa: Clusters and Programmes: Health System and Service: Essential Medicines," http://www.afro.who.int/en/divisions-a-programmes/dsd/essential-medicines.html (accessed August 12, 2010).
[100] "GAVI: Innovative Funding," Global Alliance for Vaccines and Immunisation, http://www.gavialliance.org/about/in_finance/index.php, (accessed August 12, 2010).
[101] "Ibid
[102] "New Gel Cuts Risk of HIV Infection," *The Wall Street Journal*: Health, July 20, 2010, http://online.wsj.com/article/SB10001424052748704720004575377140651050822.html?KEYWORDS=vaccine+price+third+world (accessed August 12, 2010).
[103] Frost & Sullivan, "Global Vaccines Markets: Global Market Overview," December 7, 2009, http://www.frost.com/ Subscription required (accessed August 10, 2010).
[104] "Global Vaccines Markets," December 7, 2009, Frost & Sullivan web site, http://www.frost.com/ subscription required (accessed August 12, 2010).
[105] "Revenues from global vaccine market register UD$27 billion," March 26, 2010, Vaccine Truth web site, http://vactruth.com/2010/03/26/revenues-from-global-vaccine-market-register-ud27-billion/ (accessed September 14, 2010).
[106] "Immunization service delivery," World Health Organization web site. http://www.who.int/immunization_delivery/systems_policy/optimize/en/index.html (accessed August 10, 2010).
[107] "New vaccine delivery company starts with $15 million investment" The University of Queensland web site http://www.aibn.uq.edu.au/vaxxas-established (accessed August 10, 2010)
[108] Ibid.

	In-pharmacy or non-clinical administration of vaccine seems to be important, globally.[109] This may be particularly relevant to third-world countries, where skilled people (i.e. Registered Nurse Immuniser) may not be readily available.

The overall infectious disease market in developing countries, our second potential market, is subsidized again by governments and major non-profits such as GAVI. Quantity of vaccine sold can potentially make up for a lower price point. Infectious diseases – HIV for one – continue to mutate and offer new and continuing opportunities for vaccine revenues.

[109] "Community Pharmacy Roadmap Program Development Template," The Pharmacy Guild of Australia web site. http://www.guild.org.au/iwov-resources/documents/The_Guild/tab-The_Guild/Strategic_Direction/C6%20Vaccine%20Administration%20%28Final%29.pdf (accessed August 11, 2010).

Market Niche Summary	
Name	Global Cancer Market – Prophylactic &/ Therapeutic
Basis for Feasibility in Niche	The National Cancer Institute claims that there are only two vaccines certified by the US Food and Drug Administration (FDA) to prevent viral infections that can lead to cancer. These preventive or prophylactic vaccines protect against hepatitis B and HPV. However, there are currently no therapeutic cancer vaccines (cures) on the market.[110] As one source noted, cancer vaccines are primarily in the experimental phase, as an emerging biologic. At this time, several clinical trials are being conducted for vaccines against various cancer types. The FDA has not approved any cancer vaccine as a standard treatment or cure for cancer; Provenge®, a vaccine for late-stage prostate cancer was recently approved as a last line treatment.[111] With a US cancer prevalence (2006) of over 11 million people, cancer deaths (2009) at 562,340, and new cases (2009) about 1.5 million resulting in a 43% death rate, there is an urgent and continual need for new methods of prevention and treatment.[112,113] From another perspective, in the US, approximately 20 million people are infected with genital human papillomavirus (HPV) and about half of those infected are from 15-24 years of age. Some of the HPV types are oncogenic; about 12,000 women (US) are diagnosed annually with associated cervical cancer and a third will die.[114]
Likely Market Driver(s)	Economic growth correlates with adequate vaccination programs.[115] The need for new cancer therapeutics is great due to high mortality rates among cancers currently. Overall survival has not improved.[116] R&D and healthcare costs continue to be daunting for cancer therapeutics overall and understanding the complex, underlying biology of the disease has been elusive.[117] Big pharma is changing business model and vaccines are becoming potentially significant revenue streams due to adult therapeutic market vs traditional pediatric vaccination market.[118]

[110] "Cancer Vaccine Fact Sheet," National Cancer Institute web site, http://www.cancer.gov/cancertopics/factsheet/cancervaccine (accessed August 5, 2010).
[111] "Treating and Preventing Cancer with Vaccines," National Cancer Institute web site, http://www.cancer.gov/clinicaltrials/learning/cancervaccines (accessed January 4, 2016).
[112] "Learn About Cancer: Cancer Basics," American Cancer Society web site, http://www.cancer.org/Cancer/CancerBasics/cancer-prevalence (accessed August 5, 2010).
[113] "Cancer Statistics 2007," American Cancer Society web site, http://www.cancer.org/Cancer/news/News/cancer-death-rate-steadily-declining (accessed August 5, 2010).
[114] "Sexually Transmitted Diseases: HPV Vaccine Information for Clinicians," Centers for Disease Control and Prevention web site, http://www.cdc.gov/std/HPV/STDFact-HPV-vaccine-hcp.htm#overview (accessed August 13, 2010).
[115] "Global Vaccines Market," December 7, 2009, Frost & Sullivan web site, http://www.frost.com/ subscription required (accessed August 12, 2010).
[116] "Vaccines, Blood & Biologics: Development of Safe and Effective Tumor Vaccines and Gene Therapy Products," Raj K. Puri, MD, PhD, US Food and Drug Administration web site, http://www.fda.gov/BiologicsBloodVaccines/ScienceResearch/BiologicsResearchAreas/ucm127167.htm (accessed August 12, 2010).
[117] "Advances Come in War on Cancer," June 7, 2010, *The Wall Street Journal – Business: Health*, web site http://online.wsj.com/article/SB10001424052748704002104575291103764336126.html?KEYWORDS=cancer+vaccine (accessed August 12, 2010).

	Manufacturing, platform, delivery and formulation innovations are driving this new paradigm of a potentially more lucrative vaccine business[119] via new revenue streams due to untapped markets created by new technologies.[120]
Anticipated End-User Criteria	End-users want a vaccine to be safe, effective as per efficacy, increased immunogenicity, and have few if any adverse side effects or what is known as a low profile for side effects. Overall, performance and safety should be improved over exiting cancer therapies to be attractive and the vaccine should be easy to administer and priced fairly.
Initial Impression of Adequacy of Current Technology to Address those Needs	Currently, there are only a couple of marketed cancer vaccines – using different technological advances – with several in the pipelines of various biopharma companies worldwide. However, only Gardasil® is available for the niche of cervical cancer and has only been approved for use in young women up to 26 years of age. Therefore, current pipeline technologies will be market tested over the next 10 years – effectiveness is yet to be determined. It appears to be an open field. [121]
Anticipated Barriers to Entry	The primary market barriers include those for other vaccine markets such as a fragmented, disparate global market landscape that presents a manufacturing challenge, and the significant financial investment required to produce vaccines. Also, developing markets tend to be more unpredictable when it comes to growth historically, and as a corollary, infrastructure issues and poverty persist, thereby limiting sales in these less developed regions.[122] Regulatory requirements need to be met as with other types of vaccines.
Cost or Price of Current Technology	As a benchmark, current cancer drugs (not vaccines) cost between US$2000-$4000 per month and is approximately $100-$2000 per dose depending on brand and number of doses required. Gardasil®, an HPV vaccine for 4 types, costs $120 per dose with a requirement of 3 doses to be effective.
Market Niche Size and Growth Rate	Cancer vaccines are considered an untapped and potentially very large market with conservative market research estimates to be about US$1.3billion by 2018.[123] The total global vaccine market is expected to continue to grow at an average rate of 12.1%[124] annually from 2008-2015. Gardasil®, Merck's HPV vaccine to prevent cervical cancer in young woman, contributed to more than doubling the global overall vaccine market (2005-2007) from US$9.9billion to approx. US$21.3billion. Therefore, we can estimate the cancer vaccine global market to be worth over $10billion alone in 2007.[125]
Product Opportunities	With over 230 cancer vaccines in clinical development, lung cancer

[118] "Global Vaccines Market," December 7, 2009, Frost & Sullivan web site, http://www.frost.com/ subscription required (accessed August 12, 2010).
[119] Ibid.
[120] Ibid.
[121] Ibid.
[122] Ibid.
[123] "Pipeline Insight: Therapeutic Cancer Vaccines – Prospect of first approval set to reinvigorate interest from major companies," December 11, 2009, Datamonitor Press Release, Fiercebiotech web site, http://www.fiercebiotech.com/research/pipeline-insight-therapeutic-cancer-vaccines-prospect-first-approval-set-reinvigorate-inter (accessed August 12, 2010).
[124] "Global Vaccines Market," December 7, 2009, Frost & Sullivan web site, http://www.frost.com/ subscription required (accessed August 12, 2010).
[125] Ibid.

	seems to have more late-stage vaccine candidates than other cancers, such as pancreas, breast, multiple myeloma and kidney cancers. The real opportunity for early stage vaccines seem to lie with melanoma, prostate, brain leukemia, NHL, Hodgkin lymphoma, cervix and bladder cancers.[126]

The third potential market is that of cancer vaccines. This market has great untapped potential due to the lack of vaccines developed thus far and therefore in the market. The field appears to be wide open, and the adult vaccine market is becoming more lucrative than the historical pediatric inoculation programs, i.e., Gardasil® launch; however, this fact is true of the influenza and other infectious disease markets as well.[127] As we experienced with the swine flu, healthy younger adults were significantly affected as the patient population; this age group is also vulnerable to cancer.

5 Commercialization Considerations

Overall the characteristics of the vaccine marketplace include a forecasted double-digit growth until 2015, with the influenza market alone estimated to be worth US$7billion by the end of this year 2010. The vaccine market recently went through a stage of consolidation, with over a dozen companies manufacturing flu vaccines 30 years ago to only four companies manufacturing vaccines about five years ago.[128] However, a 2006 report by Frost & Sullivan stated that the North American vaccine market was about to enter a "new era of growth," [129] and indeed now there are about 34 global vaccine manufacturers. This was supported by experts who indicated that a tremendous amount of research is occurring in large, small and start-up companies to develop new influenza vaccines,[130] which may also translate to more competing technologies and products ultimately.

Concerning other infectious disease vaccines for the developing world, while organizations such as the GAVI alliance are trying to help reduce the hurdles of a lack of health care systems and infrastructure to administer immunization programs: vaccine storage, vaccine supply, immunization records, booster administration, transportation, and sourcing skilled labor; these barriers persist when trying to market in Third World countries.[131]

As for cancer vaccines, there are very few on the market; this is a nascent industry with more recent R&D efforts coming to fruition. The market has much potential and opportunity due to this lack of available vaccines. If we use the benchmark of Gardasil® (HPV/Cervical Cancer), this vaccine – with about $10billion sales in 2007 - helped to double the [total] global vaccine market in only two years from about US$10 billion to over $21billion.

---

[126] "Game Plan for Therapeutic Cancer Vaccines: Status of Cancer Vaccine Research," CliniPace. http://www.slideshare.net/david.levin/game-planfortherapeuticcancervaccines (accessed August 10, 2010).
[127] Ibid.
[128] David Brown, "How U.S. Got Down to Two Makers of Flu Vaccine," *Washington Post* web site, http://www.washingtonpost.com/ac2/wp-dyn/A38776-2004Oct16?language=printer (accessed August 4, 2010).
[129] "Global Vaccines Markets," January 16, 2006, Frost & Sullivan web site, http://www.frost.com/ subscription required (accessed August 4, 2010).
[130] Dave Smith (Professor, Epidemiology, Big School) in a telephone conversation with Analyst, July 3, 2007.
[131] "Global Vaccines Markets," January 16, 2007, Frost & Sullivan web site, http://www.frost.com/ subscription required (accessed August 4, 2010).

It appears that the top five vaccine manufacturers are GSK, Pfizer, Merck, Sanofi-Pasteur and Novartis. These companies represent about 90% of the global vaccine market. These big pharma have significant resources. Since the cost of developing a vaccine is very high, the resources of these large companies have made it difficult for smaller companies to compete in the market.[132]

Another unique characteristic of the vaccine market is negative publicity and inappropriate information generated by anti-vaccination groups and governments that have negatively affected vaccine manufacturers.[133] As a corollary, needle aversion may also keep about 30% of the general population from getting vaccinated. [134]

Government regulations with clinical trials require significant funding, and safety has been a high priority, meaning that clinical outcomes, data thresholds, are very rigorous.[135]

There are significant and compelling unmet medical and disease needs and lack of access worldwide.[136] Overall end-user requirements suggest that there is room for great improvement in available vaccines: formulations, administration, drug half-life, efficacy, and specificity. Basically, a vaccine must be safe, effective and easy to use.

The primary advantages of this technology are the potential for a universal vaccine or at least a vaccine that can protect against most strains – current and emerging – with fewer doses that last longer and with greater immunogenicity.

This technology holds promise for commercialization; however, it will be crucial to partner with a company / organization having significant resources to cover the high financial and labor intensive development costs associated with bringing a vaccine through the clinic to market. Finding a partner to subsidize remaining proof-of-concept/validation preclinical studies and development milestones is the challenge.

If we think in terms of potential value of the technology, we can look at some market comparables in the area of existing influenza vaccines, such as FluMist® and Fluarix®, et al which sells within a range of approximately US$10-$20 per dose/regimen, and at Gardasil® that involves an infectious disease (HPV) with cancer implication and sells for US$360 per regimen (or $120 / dose). Other non-vaccine cancer therapeutics can cost thousands of dollars per month - Avastin for Breast Cancer – in the developed world. Sheer quantities can be profitable in developing countries with populations of 1 billion or more (China, India), even if the price is

---

[132] Ibid.
[133] Ibid.
[134] Elizabeth Olson, "An Option for the Needle-Shy: Spray Flue Vaccine," November 4, 2003, *The New York Times* web site, http://query.nytimes.com/gst/fullpage.html?sec=health&res=9504EEDF1E30F937A35752C1A9659C8B63 (accessed August 4, 2010).
[135] "Global Vaccines Markets," January 16, 2007, Frost & Sullivan web site, http://www.frost.com/ subscription required (accessed August 4, 2010).
[136] "Global Alert and Response (GAR): Global Pandemic Influenza Action Plan to Increase Vaccine Supply," World Health Organization web site, http://www.who.int/csr/resources/publications/influenza/CDS_EPR_GIP_2006_1.pdf (accessed August 11, 2010).

relatively lower, and with government and other philanthropic subsidies, especially if one considers that there were 300 million doses of flu vaccine alone ordered in 2005.[137]

Possible deal types for development and commercialization include partnerships with a global big pharma, such as Pfizer, GSK, Novartis, etc., who would contribute financial and other resources to accomplish laboratory and clinical development milestones with an option to license at a specified time point (i.e., after phase II) if positive results and clinical data points are met. Such a license deal could be globally exclusive with one partner or could be non-exclusive, whereby, one licenses to multiple partners according to, for example, geographic region (North America only or China) or scope (disease area / application). In this case, the big pharma would most likely be both the manufacturer and marketer – but not necessarily – of your vaccine technology via a commercial license.

Another permutation is to similarly partner through a licensing agreement with a non-profit such as GAVI to market in underdeveloped countries, while a license with big pharma to manufacture for GAVI and market in developed regions could be in place.

One could also create a company, incubate the technology with the help of investors and spinoff such to then manufacture and sell as a new biopharma company, or additionally and subsequently license to a big pharma to scale up as your business grows.

The end-user value proposition is to obtain a better vaccine than what is currently – if at all - available on the market; an affordable vaccine that offers rigorous and broader protection in fewer doses. The value proposition for a big pharma target is to be able to generate revenue that exceeds their costs of development and commercialization. Simply, GAVI as a non-profit will need to break even with their operating costs while bringing important and affordable medicines to those most vulnerable and in need.

6 Potential Targets

Potential targets for commercialization partners may include:

Examples of Potential Targets			
Target	***Reason for Inclusion***	***Web site***	***Point of Contact with Phone or E-mail***
Pfizer	Big pharma and top vaccine manufacturer - #1 by some sources - with money, resources globally.	www.pfizer.com	212-733-2323 (NY, USA) www.pfizer.com Go to 'Research and Development' – 'Partnering with Pfizer' – 'Submit an Inquiry' or 'Venture Investments': Barbara Dalton, VP Elaine Jones, Exec Director

[137] "Global Pandemic Influenza Action Plan to Increase Vaccine Supply: Progress Report 2008," World Health Organization web site, http://www.who.int/vaccine_research/Global_Pandemic_Influenza.pdf (accessed August 16, 2010).

			ventureinvestments@pfizer.com
Global Alliance for Vaccine Immunisation (GAVI)	Global, non-profit funded by industry and major philanthropic organizations, i.e., Gates Foundation, WHO, UNICEF, among others with innovative funding schemes.	www.gavialliance.org	+41 22 909 6500 (Geneva, Switzerland) External Relations office: info@gavialliance.org At the Bill & Melinda Gates Foundation, USA: www.gatesfoundation.org info@gatesfoundation.org 206-709-3100 (Seattle) Dr. Stefano Bertozzi, Director, HIV Global Health Program. Dr. Regina Rabinovich, Director, Infectious Diseases Global Health Program. Dr. Rajeev Venkayya, Director, Global Health Vaccine Delivery, Global Health Program.
GlaxoSmithKline (GSK)	Big pharma with several vaccines on the market and money, resources globally.	www.gsk.com	+44 (0) 20 8047 5000 (UK) 888-825-5249 (USA) Infectious Disease Scientific Licensing: Leslie Boyd, VP Leslie.2.boyd@gsk.com Oncology Scientific Licensing: Paul B. Bolno, VP Oncology R&D Business Development Paul.b.bolno@gsk.com Biopharmaceutical Business Development: Jon H. Ellis, VP Biopharm R&D Business Development Jon.h.ellis@gsk.com Platforms & Enabling Technology: Austin K. Doyle, Manager, Biopharm R&D Austin.k.doyle@gsk.com

Names of other potential targets may be found at the following web sites.

Internet Sites Linking to Other Potential Targets	
Web site	***Reason for Listing***
www.gavi.org	Global Alliance for Vaccines and Immunisation (GAVI) non-profit that is funded by Gates Foundation, big pharma such as GSK, among other global partners with innovative funding strategies.
http://www.ifpma.org/	International Federation of Pharmaceutical Manufacturers and Associations – source of potential industry partners.
http://www.evm-vaccines.org/	European Vaccine Manufactures Association – source of potential industry partners.
http://www.serumindustry.org/advocacy.htm	International Serum Industry Association – source of potential industry partners.