Technology Niche Analysis®

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

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1 Introduction

The following is a generic description of this technology.

<table>
<thead>
<tr>
<th>Description of Technology</th>
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<tr>
<td>The technology is a broad spectrum influenza vaccine that can protect end-users from a wide variety of influenza strains.</td>
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</table>

“Influenza (the flu) is a contagious respiratory disease caused by influenza viruses. It can cause mild to severe illness, and at times can lead to death.”\(^1\) Annually, in the US, 5-20% of the population become infected. Of these, on average 200,000 are hospitalized and 36,000 die.\(^2,3\) Death is more common in children, the elderly, and those with chronic illnesses. About % of deaths attributed to influenza are people age 65 or older.\(^4\) However, during the US 2009-2010 pandemic of the new strain, H1N1, nearly 90% of the approximate 12,000 deaths were younger patients under 65 years of age.\(^5\) The Centers for Disease Control and Prevention (CDC) web site says, “The best way to prevent the flu is to get a flu vaccine each year.”\(^6\) FluVaccine, Inc. has developed a novel influenza vaccine that can provide increased protection from several influenza strains.

What makes this technology a scientific/engineering innovation is: 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, specifically a peptide sequence.

This technology is protected by the following intellectual property package:
- Patents: A provisional application has been submitted, which FluVaccine, Inc. anticipates will be approved and published in the next few months;
- Trade Secret: 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.

FluVaccine, Inc. wishes to find global pharmaceutical development partners and subsequent licensees to commercialize the technology.

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4 Ibid.
6 Ibid.
An application is a potential use for a technology that is based on end-user needs and could provide a feasible market opportunity for a technology. The following table is an option for initial market entry.

<table>
<thead>
<tr>
<th>Viable Application</th>
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<tr>
<td>The global prophylactic and therapeutic influenza market.</td>
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</table>

Due to the great potential market size and significant current unmet end-user needs for a better flu vaccine, the most obvious application worldwide would be in the development of a preventive and/or therapeutic influenza vaccine. There is an opening in the market for such an enhanced vaccine formulation that could possibly be effective not only in the West but also in the developing world via a single, robust, omni-strain dose. This market is well-funded by industry, governments and non-profit, non-governmental organizations (NGOs) due to the highly infectious nature and emerging strains of the flu; this is not a disease of the poor in remote areas, but rather one that can quickly effect everyone, everywhere, including the young and healthy, as was observed in the 2009 Swine flu pandemic. Such a short, novel, 10 amino acid peptide sequence bound to a conserved portion of all influenza viruses could provide a significant and compelling advantage to quickly gain the majority of market share. Such a vaccine can be easily tested in the field and clinic due to the relatively high infection rates in general at any given time and outcomes can be measured and accomplished quickly.

We also identified other potential applications for the technology.

<table>
<thead>
<tr>
<th>Other Applications Identified</th>
<th>Basis for Feasibility</th>
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<tbody>
<tr>
<td>Other Infectious Diseases - Viral</td>
<td>There are numerous viral diseases: Hepatitis, West Nile, Human Papillomavirus (HPV), and chickenpox, among others. While vaccines have been developed for some of these viral diseases, including HPV, chickenpox, H1N1 and Hepatitis B, others still do not have specific vaccines such as West Nile and Hepatitis C. In 2006, there were about 4,269 cases in the US of West Nile. Additionally, about 4 million people in the US have Hepatitis C. Therefore, a novel peptide sequence could be used to help develop vaccines for these viral diseases.</td>
</tr>
<tr>
<td>Cancer</td>
<td>The National Cancer Institute claims that there are only two vaccines certified by the United States Food and Drug Administration (FDA) to prevent viral infections that can...</td>
</tr>
</tbody>
</table>

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lead to cancer. These preventive or prophylactic vaccines are for Hepatitis B and HPV. However, there are currently no therapeutic cancer vaccines on the market. 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 U.S. Food and Drug Administration (FDA) has not approved any cancer vaccine as a standard treatment for any type of cancer. 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, there is a compelling and continual need for new methods of prevention and treatment. A novel peptide sequence could also be used to help develop a vaccine for either cancer prevention or cancer treatment.

2 Methodology Used for this Study

Foresight uses a methodology called Technology Niche Analysis (TNA®). This method filters applications through a series of funnels. Funnels are decision gates in which we eliminate some options, but allow those meeting the decision criteria to pass on for further analysis. Each step assesses potential applications in light of pre-determined criteria. Applications may be eliminated at any step. Eliminated applications are not considered further.

Foresight begins solving the commercialization puzzle by using FluVaccine, Inc.’s definition of the technology’s performance specifications and characteristics. These are used as guides when conducting on-line data searches and interviews with experts to identify applications and markets. We also collect our customer’s preferences for commercializing the technology and use them as a secondary guide.

In today’s rapidly changing global markets, it is unlikely that a single, “best possible” entry strategy exists. Even with the informational resources of the Internet, this remains true, especially for a study such as this that is constrained by budget and time. Of course, budget and time always constrain the data collected and analysis performed for any report. Thus, the findings and recommendations presented here are preliminary. Additional market research may lead to modifications or substantial revisions. Although we strive to describe trends that will be important over a five-year window, market and technology developments are dynamic. Events can overtake the data and analysis presented in this report.

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3 Competitive Opening

End-users are likely to be interested in this technology because of the following advantages it can bring. We have contacted the following experts to gauge their views on the technology’s potential competitive opening. These findings are presented in the table below.

<table>
<thead>
<tr>
<th>Expert on Competitive Opening</th>
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<tbody>
<tr>
<td><strong>Name</strong></td>
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<td><strong>Title</strong></td>
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<td><strong>Organization</strong></td>
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<td><strong>Phone</strong></td>
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<td><strong>E-mail</strong></td>
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**Importance of Need(s) being Addressed**

Tom Doe explained that there is a need for better influenza vaccines. He explained that there is a need for more research to better understand influenza and vaccination methods, as there are a lot of areas that have not been explored. For example, Tom Doe explained that there are 10 or 11 proteins from the influenza genetic sequences and that no one has really looked into the splicing mechanisms that change characteristic proteins.

**Key Specifications and Characteristics to Emphasize for this Niche**

Tom Doe said that efficacy and safety are important. Additionally, clinical trials are very important. Numerous companies have potential influenza vaccines that perform well in animal trials.

**How long will end-users expect a technology like this to be used before it has to be replaced? If consumables are involved, how often are they purchased and in what lot sizes?**

Tom Doe has noticed that vaccine technology has not advanced significantly over the recent decades, e.g., chicken eggs are still used in production. But due to the era of genomics and molecular biology advancements (recombinant DNA, etc.) he said approximately replacement would be in perhaps 5-10 years. Purchasing is not done by his group, therefore he had no comment.

**Price and Pricing Factors for this Niche—Specifically what is a price you would expect to pay for such a technology?**

He did not know the exact prices of influenza vaccines, but said they have been going up. He explained that MedImmune’s FluMist is priced higher than non-active viral vaccines and that it costs around $25 or $30. Tom Doe also said that the Centers for Medicare and Medicaid Services (CMS) publish prices for influenza vaccines.

**Key Competitors**

Tom Doe said that there are five FDA approved influenza vaccines on the market. Companies that have vaccines with the non-active virus include Merck, Novartis, GlaxoSmithKline Biologics, and ID Biomedical Corporation, which is now owned

¹⁷ Tom Doe (Chief of the Relevant Section, Government Agency), XXX-XXX-XXXX, in a telephone conversation with [Analyst’s NAME], July 5, 2007.
by GlaxoSmithKline. The one company with an active virus strain in the vaccine is MedImmune.

**How would you commercialize a technology like this one?**

Tom was not sure about the business of vaccines, as he’s a scientist by training.

**Potential Roadblocks to Commercialization**

Tom said only that if the price is too high for insurers and/or end-users this could preclude successful commercialization.

**Additional Insights**

Tom Doe also spoke about the differences between vaccines developed in eggs versus vaccines developed in tissue. He said that eggs are not a bad thing, but that there are some concerns on the effectiveness of influenza vaccines from eggs. He said that tissue has the potential to more closely mimic the virus and therefore could lead to a better immune response, providing more protection. Additionally, manufacturers are interested in tissue cells because it is easier for them to control the fermentors. They also claim that tissue cells could be faster, but this has not been proven. Next, Tom Doe explained that it is important to have several different manufacturers and several different types of influenza vaccines for back up as there have been shortages in the past such as in 2004.

Also, he spoke about a universal vaccine. Tom Doe said that physicians are interested in a universal vaccine that patients would only have to take once. However, there are several concerns with a universal vaccine. First, vaccines tend to wear off. For example, most people get a measles vaccine when they are one or two years old. However, generally that vaccine wears off before the child reaches college. Additionally, there is the chicken pox vaccine, which does not require a booster because the vaccine is boosted by natural exposure; meaning patients occasionally encounter the chicken pox virus, which helps to boost their immunity. With the flu, people can get it more than once and still be susceptible to it. This means the chicken pox vaccine model is probably not appropriate. Ultimately, this means that more research needs to be done in the area to fully understand the flu.

Finally, he explained that many providers are hesitant to administer the flu vaccine. This is because they purchase so many doses at the beginning of the flu season. However, if the doses come later than expected, then patients start going elsewhere for the vaccine. This means the provider ends up with extra doses at the end of the flu season. Since the flu vaccine formula changes every year, the doses can not be saved for the following year.

Tom Doe said that without data from clinical trials, it is hard to judge the competitiveness of the vaccine. However, he said that a vaccine that decreased the frequency of boosters would be beneficial. Tom Doe said that he is probably not the appropriate person for clinical trials. However, he did say [his] organization is a good place to go for funding.

Both of the experts we spoke with indicated a need for new influenza vaccines. Dave Smith stressed the need for a universal influenza vaccine that would cover all strains and last for numerous years. Meanwhile, Tom Doe explained that there is a need for better influenza vaccines and more manufacturers of influenza vaccines. He also stressed the importance of research to learn more about influenza and develop new vaccines.

Both experts indicated that price will be more important in the future. They explained that patients and physicians have become accustomed to inexpensive flu vaccines. However, new vaccines based on more recent technological advances tend to cost more to recoup R&D
expenditures; this could cause new market dynamics and pressures on the industry in terms of profits and margins.

We have also contacted the following end-users to gauge their views on the technology and the marketplace. In some arenas, the population of end-users is such that these end-users are also the experts. In this case, they were asked to comment from both perspectives in order to gain the necessary information.

### End-User on Competitive Opening

<table>
<thead>
<tr>
<th>Name</th>
<th>Jamie Yarman¹⁸</th>
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<tbody>
<tr>
<td>Title</td>
<td>Geriatrician, Assistant Professor of Medicine</td>
</tr>
<tr>
<td>Organization</td>
<td>Seniors Health Center and Private School Medical Center, The Private School Department of Medicine</td>
</tr>
<tr>
<td>Phone</td>
<td>XXX-XXX-XXXX</td>
</tr>
<tr>
<td>E-mail</td>
<td><a href="mailto:JamieYarman@privateschool.edu">JamieYarman@privateschool.edu</a></td>
</tr>
<tr>
<td>Importance of Need(s) being Addressed</td>
<td>Jamie Yarman said she thinks current influenza vaccines are relatively adequate, as she does not get a lot of complaints about them.</td>
</tr>
<tr>
<td>Key Specifications and Characteristics to Emphasize for this Niche</td>
<td>She explained that it is important for there to be no side effects, as the only real side effect of current influenza vaccines is a small amount of pain. Next, efficacy should be comparable to current vaccines. Additionally, she said that ease of administration is important. Jamie Yarman said that a pill would be nice, although she did not know of any pill administered vaccines. She also noted that injections are better than a nasal method, explaining that her patients do not like taking anything up the nose.</td>
</tr>
<tr>
<td>How long will end-users expect a technology like this to be used before it has to be replaced? If consumables are involved, how often are they purchased and in what lot sizes?</td>
<td>Jamie estimated that due to the great advances over the last 30 years in molecular biology and genetics, the turnover of technologies will probably be faster; perhaps within 10 years. She does not purchase consumables directly, but surmised that consumables would mimic those needed for current vaccination methods of oral, injectable, and inhalation, and maybe dermal patch now as well. Plastic disposables associated with the above methods of administration are probably ordered in bulk discounts and inventoried in campus-wide stockroom. As per frequency of vaccine purchase, she did say they order several times a year, and patients generally get the shot in September or October. However, she did not know the exact frequency of purchase because the hospital buys the vaccines and then distributes them to the clinic.</td>
</tr>
<tr>
<td>Price and Pricing Factors for this Niche—Specifically what is a price you would expect to pay for such a technology?</td>
<td>Jamie Yarman did not know how much flu vaccinations cost, as the hospital purchases them.</td>
</tr>
<tr>
<td>Key Competitors</td>
<td>Jamie Yarman said there are several companies with injection vaccines on the market, but she did not provide the names of any companies.</td>
</tr>
</tbody>
</table>

¹⁸ Jamie Yarman (Geriatrician, Seniors Health Center and Private School Medical Center), XXX-XXX-XXXX, in a telephone conversation with [Analyst’s Name], July 2, 2007.
How would you commercialize a technology like this one?

She only stated that bringing a vaccine to market would differ depending on country and region in her estimation. However, she is not a business-trained professional.

Potential Roadblocks to Commercialization

Jamie restated her lack of business knowledge, but presumed adverse side effects and too high of a price would be obstacles.

Additional Insights

Additionally, she said they store the vaccines in the office. While liability and insurance coverage is a concern with some vaccines, it tends not to be a problem with the influenza vaccine.

Jamie Yarman said the technology could be competitive if the vaccine only needed to be taken every 5 to 10 years. However, if the vaccine needs to be taken every year or every other year, then it would probably not be very competitive. With a vaccine that needs to be administered every other year, patients will forget which year they need one. With the current system, patients know that in September or October they need to come in for a flu shot. She also said the vaccine would not be competitive if there were side effects associated with it, and she stressed the preference for a pill over an injection by patients.

End-User on Competitive Opening

<table>
<thead>
<tr>
<th>Name</th>
<th>Bonnie Davis, MD¹⁹</th>
</tr>
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<tbody>
<tr>
<td>Title</td>
<td>Professor of Geriatric Medicine</td>
</tr>
<tr>
<td>Organization</td>
<td>Sunny University</td>
</tr>
<tr>
<td>Phone</td>
<td>XXX-XXX-XXXX</td>
</tr>
<tr>
<td>E-mail</td>
<td><a href="mailto:bdavis2@usunny.edu">bdavis2@usunny.edu</a></td>
</tr>
<tr>
<td>Importance of Need(s) being Addressed</td>
<td>She said it is always a struggle to get patients to take their vaccines and so there is an opportunity for another influenza vaccine which does not have to be taken as frequently.</td>
</tr>
<tr>
<td>Key Specifications and Characteristics to Emphasize for this Niche</td>
<td>She explained that important concerns are efficacy and side effects. Additionally, physicians tend to administer the vaccines that are recommended by organizations such as the Advisory Committee on Immunization Practices. Also, the less discomfort the vaccine provides the better. Finally, patients always complain that the vaccine gives them the flu. While the patient does not actually have the flu, the fewer side effects the vaccine has, the better.</td>
</tr>
<tr>
<td>How long will end-users expect a technology like this to be used before it has to be replaced? If consumables are involved, how often are they purchased</td>
<td>She estimated in general that technologies for vaccines may advance more rapidly now in this time of personalized medicine research and genomics; she guessed within 10 years, a new evolutionary vaccine technology would be available. She does not do purchasing, but did add that if consumables become significantly more expensive with a new vaccine, hospitals would probably not buy it unless there was a significant improvement in the efficacy of such. She added that influenza vaccines are purchased from October to February or March.</td>
</tr>
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</table>

¹⁹ Bonnie Davis, MD, (Professor Geriatric Medicine, Sunny University), XXX-XXX-XXXX, in a telephone conversation with Analyst, July 5, 2007.
and in what lot sizes?

<table>
<thead>
<tr>
<th>Price and Pricing Factors for this Niche — Specifically what is a price you would expect to pay for such a technology?</th>
<th>She did not know the exact current prices for influenza vaccinations, as she does not do the direct ordering. However, she indicated that influenza vaccines tend to be among the least expensive per dose than many other vaccines on the market for other diseases.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Key Competitors</td>
<td>She stated two of the major pharma companies: GSK and Roche, and assumed that many other large global companies offered a flu vaccine as well.</td>
</tr>
<tr>
<td>How would you commercialize a technology like this one?</td>
<td>She simply said that clinical trials are needed and price should ultimately be competitive with ones already available.</td>
</tr>
<tr>
<td>Potential Roadblocks to Commercialization</td>
<td>She stressed that she is not trained in business; however, she did state that if the price was too high coupled with an efficacy that was not significantly greater than the vaccine she currently administers, then she and other healthcare providers would probably not order it.</td>
</tr>
<tr>
<td>Additional Insights</td>
<td>She had no further insights.</td>
</tr>
</tbody>
</table>

Bonnie Davis indicated that the vaccine would be competitive if it were taken less frequently, if it provided equivalent efficacy, and if it had no additional side effects. When we inquired how less frequent the vaccine would need to be administered, she explained that any improvement would be beneficial. Taking the vaccine every other year would be better, and taking the vaccine every five years would be even better [than every other year].

### End-User on Competitive Opening

<table>
<thead>
<tr>
<th>Name</th>
<th>Amy Markham, MD²⁰</th>
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<tbody>
<tr>
<td>Title</td>
<td>Pediatrician</td>
</tr>
<tr>
<td>Organization</td>
<td>Medical Practice – Hospital Clinic</td>
</tr>
<tr>
<td>Phone</td>
<td>XXX-XXX-XXXX</td>
</tr>
<tr>
<td>E-mail</td>
<td>Not Provided.</td>
</tr>
<tr>
<td>Importance of Need(s) being Addressed</td>
<td>Dr. Markham explained that there is an opportunity, but not a great need, for an influenza vaccine that would last longer and cover more strains.</td>
</tr>
<tr>
<td>Key Specifications and Characteristics to Emphasize for this Niche</td>
<td>The important characteristics include efficacy, side effects, age group, and administration method. In order to be competitive, the vaccine will need to have an efficacy similar to those on the market. Next, the vaccine should have very few side effects, if any. Also, if younger patients can get the vaccine, then this is better., in terms of being indicated for use in pediatric patients. Finally, nasal spray is preferred over injection. However, the current nasal spray can only be given to patients without asthma, and over 9% (or about 7 million) of children suffer from asthma²¹</td>
</tr>
</tbody>
</table>

²⁰ Amy Markham, MD, (Pediatrician, Medical Practice), XXX-XXX-XXXX, in a telephone conversation with Analyst, June 22, 2007.

<table>
<thead>
<tr>
<th><strong>How long will end-users expect a technology like this to be used before it has to be replaced? If consumables are involved, how often are they purchased and in what lot sizes?</strong></th>
<th>She guessed that vaccines will continue to be relatively slower to evolve as compared to other medicines due to vaccines not being a blockbuster drug that brings in a billion dollars to a drug company. As to purchasing habits, they generally start buying the vaccines in October and then stop doing so in early March. However, she was not sure how frequently they were purchased, because the hospital has a dedicated purchasing department.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Price and Pricing Factors for this Niche — Specifically what is a price you would expect to pay for such a technology?</strong></td>
<td>She explained that insurance companies dictate price as they are the ones that pay doctors for vaccines through reimbursements. Many insurance companies currently do not cover the nasal flu shot and therefore patients will not take it. They will get the injection instead because it is covered by insurance companies. Markham said that they charge about $60 for the nasal version and about $30 for the injection. At hospitals, it costs $12.</td>
</tr>
<tr>
<td><strong>Key Competitors</strong></td>
<td>She explained that there is the nasal version of the flu vaccine by MedImmune Vaccines Inc. One company that sells an injection influenza vaccine is Chiron. They sell Fluvirin.</td>
</tr>
<tr>
<td><strong>How would you commercialize a technology like this one?</strong></td>
<td>She had no ideas other than to keep prices competitive with vaccines on the market.</td>
</tr>
</tbody>
</table>
| **Potential Roadblocks to Commercialization** | She stated insurance as a potential roadblock to successful commercialization if this vaccine is not reimbursed by insurance companies, then its use would be less attractive for organizations to purchase, unless medicinal advantages were greatly significant over another available vaccine. If patients’ insurance carriers did not cover a particular vaccine or if it was not part of a Medicare/Medicaid formulary and available to end-users at a discount, this could slow use.

Amy Markham said there is a concern with patient acceptance. Pediatricians are constantly introducing new vaccines to parents and some parents are hesitant to give their child so many vaccines. Some parents think their child is going to get the flu if they give them the vaccine. Also, patients will complain that they still got sick after getting the vaccine, not realizing that the vaccine only protects against influenza. Finally, there is some concern from pediatricians about storing vaccines in the office and some are very hesitant to do it. This is because there is a storage risk and a reimbursement risk. Markham said that they still keep vaccines in the office, but that their refrigerator has gone out before, destroying all of the vaccines in it. While insurance pays for some of it, they still lose thousands of dollars each time, which is a lot for a pediatrician.

Next, she noted that patients tend to be hesitant to purchase a vaccine when it first enters the market. Instead they wait to see what side effects other patients are getting. |
| **Additional Insights** | Amy Markham said that about three or four years ago there was a lot of publicity over a few child deaths from influenza. Since then, there has been an increased number of patients being immunized. Additionally, the American Academy of Pediatrics recommends that all children be given an influenza shot. Therefore, they urge immunizations in children under 54 months of age, and strongly recommend it for all of their other patients aged 21 and under. Finally, she indicated that she would be willing to help with clinical trials. |
According to Dr. Markham, if your vaccine can reduce the number of shots a child has to take while maintaining efficacy, then it will be competitive. Additionally, the vaccine must fall within the CPT code for influenza for practitioners to receive insurance reimbursements.

We spoke with two geriatricians and two pediatricians about the influenza vaccine. One geriatrician and one pediatrician said that they are satisfied with current influenza vaccines in terms of performance, and therefore, in this regard, do not see much of a need for a new vaccine. However, shortages in inventory remain a continual and pressing problem worldwide. Meanwhile, the remaining [2] doctors indicated that there is an opportunity for new vaccines that protect against more strains and offer longer vaccine duration. The main characteristics mentioned by physicians were efficacy, side effects, and administration methods. End-users indicated that efficacy should be similar to, or better than, that of current influenza vaccines. Also, there should be few, if any, side effects associated with the vaccine. Finally, the end-users had differing opinions on the appropriate method for administration. Amy Markham indicated that a nasal method is better, while Jamie Yarman said her patients do not like treatments via nasal administration.

Given our own research and the views of these experts and end-users, we anticipate the following parameters will be significant when this technology is evaluated by end-users. It is critical to understand bioengineering requirements for the primary application. If the technology does not meet and/or exceed current requirements for performance, it will be difficult to commercialize.

<table>
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<tr>
<th>Our Current View of End-User Requirements</th>
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<tr>
<td><strong>Engineering Requirement</strong></td>
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<tr>
<td>Efficacy</td>
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End-users also differed in opinion over how much the vaccine would need to increase the length of protection to make it worth purchasing a new vaccine. As mentioned above, Bonnie Davis said that being able to take the vaccine every other year (or less frequently) would be a significant improvement. Moreover, Jamie Yarman said that the vaccine should only have to be taken every 5 to 10 years, explaining that a vaccine administered every other year would only confuse patients.

\(^{22}\) Amy Markham (Pediatrician, Medical Practice) in a telephone conversation with Analyst, June 22, 2007.
Users’ abilities to buy the technologies they want are constrained by relevant federal, state, and local government regulations and by relevant standards and certification requirements. These requirements indicate test and evaluation procedures that can speed market acceptance if incorporated into concurrent engineering.

### Examples of Regulations, Standards, and Certifications

<table>
<thead>
<tr>
<th>Regulatory Requirements</th>
<th>Description</th>
<th>Comments</th>
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<tbody>
<tr>
<td>Food and Drug Administration, Center for Biologics Evaluation and Research (CBER), Office of Vaccines Research and Review, Division of Viral Products</td>
<td>This division is responsible for review, evaluation, and regulation of all viral vaccines and related products. Research programs support this mission and focus on critical issues concerning the development, evaluation, and regulation of viral vaccines and related biological products. It appears that the vaccine approval process is similar to the process of other drugs. First, an Investigational New Drug application (IND) must be submitted to the FDA. Then, the vaccine must pass three phases of clinical trials resulting in the submission of a Biologies License Application (BLA) for approval. Also, many vaccines undergo Phase 4 studies once on the market. Further contact information: Division of Vaccines &amp; Related Products Applications Wellington Sun, MD 301-827-3070 <a href="http://www.fda.gov/AboutFDA/Centersoffices/CBER/ucm123224.htm">http://www.fda.gov/AboutFDA/Centersoffices/CBER/ucm123224.htm</a></td>
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<tr>
<td>National Childhood Vaccine Injury Act of 1986 - FDA and CDC</td>
<td>The National Childhood Vaccine Injury Act established a national system in the United States to track adverse events resulting from vaccine administration in children. This act would be relevant primarily once the vaccine is on the market; at this point, it determines whether or not the vaccine continues to be safe for use in children.</td>
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<tr>
<td>World Health Organization (WHO)</td>
<td>WHO produces guidelines for national governments and manufacturers, addressing general issues and specific products, based upon timely consensus on key regulatory issues. In 2004, WHO published an influenza pandemic preparedness checklist that called for “new procedures and For 50+ years, the WHO International Biological Reference Preparations has helped develop WHO guidelines and recommendations on the production and control of biological products and technologies. These Norms and Standards are based on wide</td>
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26 Ibid.
cooperation among nations in reporting the occurrence of disease, sharing information about outbreaks and acting to prevent a pandemic.” For the 2010 annual update of the International Health Regulations, there are many sources including this on-line article. Additionally, WHO has an influenza surveillance network that includes over 110 laboratories in 82 countries, which constantly monitor the influenza virus. Data from these laboratories are used to make recommendations on the three virus strains to be included in the next season’s influenza vaccine.

The FDA’s Office of International Programs also provides information on the regulatory environment outside the US.

European Commission, the European Medicines Agency (EMEA)

The EMEA provides assistance to EU member states on vaccines. In 2002, the EMEA established the Vaccine Working Group (now the Vaccine Working Party) to provide research and expert advice on vaccines.

The Vaccine Working Group/Party was established and made permanent in response to the fear that negative media attention would significantly reduce the number of people that received vaccines.

Pan America Network of Drug Regulatory Harmonization (PANDRH)

PANDRH operates as a regional office for the WHO to support a unified policy on drugs throughout the Americas. Vaccines are included in their drug promotion group.

Information on the working groups within PANDRH can be found at the European Medicines Agency web site.

Advisory Committee On Immunization Practices (ACIP)

This committee develops written recommendations for the routine administration of vaccines to all individuals in the civilian population; recommendations include age for vaccine administration, number and intervals of doses, and precautions and contraindications. The ACIP is the only entity in the federal government that makes such recommendations.

Foresight Science & Technology
Technology Niche Analysis™ Report

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</tr>
<tr>
<td>The committee consists of 15 experts associated with immunization who develop the recommendations.</td>
<td></td>
</tr>
</tbody>
</table>


34 Ibid.


38 Ibid.
In our search for vaccine regulations, we found that each country appears to have its own regulatory approval process.\(^\text{39}\) The Japan Pharmaceutical Manufacturers Association includes a document in English on regulations in Japan at [http://www.jpma.or.jp/english/parj/1003.html](http://www.jpma.or.jp/english/parj/1003.html). In the US, for example, the Food and Drug Administration (FDA) approves vaccines. In order to gain approval, a vaccine must go through at least three phases of clinical trials and be proven safe and effective. The European Agency for the Evaluation of Medicinal Products (EMEA) provides vaccine approval in the European Union. Similar to the FDA, the EMEA also requires clinical trials.\(^\text{40}\) In addition to the national and pan-national groups in our table, we found that the World Health Organization (WHO) also provides guidance concerning influenza vaccines. As mentioned, we found that the WHO has 110 laboratories, in 82 countries, which constantly monitor influenza viruses. Data from these laboratories are then used to make recommendations on the three virus strains to be included in the next season’s influenza vaccine.\(^\text{41}\)

Also important to note is that end-users indicated that physicians tend to use vaccines recommend by organizations such as the CDC and ACIP.\(^\text{42}\) We suggest contacting these organizations to learn how your vaccine can complete the recommendation process.

Finally, **price** is always a concern for new technology.

<table>
<thead>
<tr>
<th>Price</th>
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<tbody>
<tr>
<td>Data suggest that the price of your technology should be based upon the country in which it is sold. For the US, we recommend US$12 per dose.</td>
</tr>
</tbody>
</table>

We anticipate that your technology will need to be priced similar to current influenza vaccine prices. In our searches, we found the following maximum costs per dose for each of the following adult vaccines on the market: Fluarix®, $10.98;\(^\text{43}\) Fluvirin®, $13.25;\(^\text{44}\) Fluzone®, $13.16;\(^\text{45}\) and FluMist®, $19.70.\(^\text{46}\) Since FluMist® appears to be the most expensive vaccine; we suggest using this price as a ceiling or maximum. This means that your influenza vaccines should be priced at or below $19.70 per dose. Additionally, since your vaccine will be new in the price sensitive, low margin, vaccine market, we suggest pricing your technology on the lower end of the influenza vaccine price spectrum.

\(^\text{42}\) Bonnie Davis (Professor Geriatric Medicine, Sunny University) in a telephone conversation with Analyst, July 5, 2007.
\(^\text{44}\) Ibid.
\(^\text{45}\) Ibid.
\(^\text{46}\) Ibid.
Reimbursement by Medicare and health insurance companies also informed our price recommendation. Federal reimbursement for the influenza vaccine by Medicare began in 1993. Since then, reimbursement for the vaccine has increased. In 2001, about 50 countries had national immunization programs funded by their respective governments, and most of the programs included free influenza vaccines for at-risk patients. In the US, Medicare has been increasing its reimbursement rates for the influenza vaccine. Rates for the administration of the flu vaccine increased from about $3.98 in 2002 to between $16-28 in 2009 (dependent on US state/city). Additionally, reimbursement for the vaccine [product] also increased from about $8.02 in 2002 to a median of $12.54 (average of $13.47) or 95% of the Average Wholesale Price (AWP) when administered outside of a hospital. These considerations, in tandem with our evaluation of the cost of competing products, led us to suggest a price around $12 per dose.

Additionally, we anticipate that the price of your vaccine will need to be even lower in third world countries. As one source noted,

“The natural tendency is to set different prices for different markets, which is called ‘differential pricing.’ Drugs sold for humans generally sell for more than drugs sold for animals. Drugs sold in rich countries are priced higher than drugs sold in poor countries. That’s why a daily dose of the AIDS drug PLC sells for $18 in the United States and $9 in Uganda. In many developing nations, prescription drugs—like most other commodities—are often priced lower than in developed countries.”

4 Competition

There is a range of competitive technologies to consider when comparing this technology to those on the market now, and those that may be available in the next five-years from the date of anticipated market entry. The products, services, and technologies below demonstrate the range of potential substitutes from which customers will be able to choose.

We conducted a search for relevant products, patents, and projects using Google, United States Patent and Trademark Office (USPTO), PubMed, Frost and Sullivan, and Delphion, using the terms “influenza vaccine,” “peptide,” “antigen,” and “increased immunogenicity.”

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### Examples of Relevant Products/Services Identified

<table>
<thead>
<tr>
<th>Product Name</th>
<th>Manufacturer</th>
<th>Relevance</th>
<th>Web site/Phone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluarix® – Influenza Virus Vaccine</td>
<td>GlaxoSmithKline Biologics</td>
<td>FLUARIX®, an influenza virus vaccine for intramuscular use, is a sterile suspension prepared from influenza viruses produced in chicken eggs. Side effects include pain at the injection site, muscle aches, fatigue, and headache. Finally, the adult vaccine appears to cost $8.90 for the CDC and $10.98 for the private sector per dose.</td>
<td><a href="http://www.fluarix.com/">http://www.fluarix.com/</a> 888-825-5249</td>
</tr>
<tr>
<td>FluLaval® – Influenza Virus Vaccine</td>
<td>Manufactured by ID Biomedical Corporation of Quebec, (a GSK Group Company. Distributed by GlaxoSmithKline)</td>
<td>FLULAVAL® is an influenza vaccine indicated for active immunization of adults 18 years of age and older against influenza caused by virus subtypes A and B. Adverse reactions appear to be pain, redness, or swelling at the site of injection, headache, fatigue, myalgia, low grade fever, and malaise.</td>
<td><a href="http://us.gsk.com/products/assets/us_flulaval.pdf">http://us.gsk.com/products/assets/us_flulaval.pdf</a> 32-2-656-9831</td>
</tr>
<tr>
<td>Fluvirin®</td>
<td>Novartis Vaccines and Diagnostics (prior Chiron Vaccines)</td>
<td>FLUVIRIN® is a vaccine for influenza subtypes A and B. It is in a liquid form for intramuscular injection and is produced in chicken eggs. For adults, the cost per dose is up to $12.75 for the CDC, and $13.25 for private companies.</td>
<td><a href="http://www.novartisvaccines.com/products-diseases/influenza-products/index.shtml">http://www.novartisvaccines.com/products-diseases/influenza-products/index.shtml</a> 800-244-7668</td>
</tr>
<tr>
<td>Fluzone®</td>
<td>Sanofi Pasteur Inc.</td>
<td>This vaccine contains three inactivated flu viruses and is injected into the muscle. Subtypes protected are A H1N1, type A H3N2, and type B. The vaccine is grown in chicken eggs, and must</td>
<td><a href="http://www.fluzone.com/">http://www.fluzone.com/</a> 570-839-7187</td>
</tr>
</tbody>
</table>

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be stored at a refrigerator temperature – not to be frozen.60 The price per dose is $9.06 for the CDC, and $12.41 for the private sector.61

| FluMist®       | MedImmune, LLC.       | FluMist® is indicated for virus subtypes A and B in healthy individuals from 2-49 years of age.62 This is a live attenuated virus vaccine that is administered nasally.63 The cost per dose (adult) is $15.70 for the CDC, and $19.70 for the private sector.64 | http://www.flumist.com/ 877-633-4411 |

There are two types of influenza vaccines on the market that could provide competition. The most frequently used type appears to be vaccines made with inactivated (also known as killed or dead) influenza virus and is known as a Trivalent Inactivated Influenza Vaccine (TIV). TIV is injected into the muscle. Companies selling this type include GlaxoSmithKline Biologics, Novartis, CSL Biotherapies-US, and Sanofi Pasteur Inc. among others. The second major vaccine type includes active (also known as live or attenuated) virus and is called a Live Intranasal Influenza Vaccine (LAIV). The only company we found selling this type of vaccine appears to be MedImmune, LLC. In the US, eight vaccines were approved for the 2010-2011 flu season; these include all of the above competitors plus Afluria® (CSL Limited) and Agriflu® (Novartis).65 One should note, for example, that Novartis sells six influenza vaccine brands worldwide; some may be the same formulation, but simply be marketed under a different [brand] name depending on culture, country or region where approved and sold.66

We search the following data sets: INPADOC, which contains patent family documents from 71 world patent signatories and legal status information from 42 patent offices; WIPO PCT Publications, which contains abstracts, full document images, and full text from over a hundred member countries of the Patent Cooperation Treaty; European Patents and Applications from the European Patent Office; and US Patents and Applications from the U.S. Patent and Trademark

Office. Searching these data sets simultaneously often does lead to multiple counts of the same patent, as both the application and patent may be retrieved or the item can show up in multiple databases. This procedure highlights applicants who file, pursue the patent, and protect it in multiple jurisdictions and the presumption is a patent protected in multiple jurisdictions is more important to its owners than one which is not.

Given this procedure, the following assignees appear to be among the major patent holders of technology found using the following search string “influenza vaccine”: Novartis AG with 21; MedImmune, LLC with 11; Novartis Vaccines and Diagnostics SRL with 11; GlaxoSmithKline Biologicals SA with 9; Merial Limited with 8; Becton Dickinson and Company with 7; Juridical Foundation The Chemo- Sero- Therapeutic Research Institute with 7; Protein Sciences Corporation with 7; Saechsisches Serumwerk Dresden with 7.

We identify these assignees by looking at the ultimate company (parent) of the assignee as identified with the aid of Delphion. Overall, the string produced 1,388 hits. However, for this 2010 update, the further search string of “universal influenza vaccine” yielded 6 hits; some of the most recent and relevant are included in the table below. Additionally, a search with string “influenza vaccine AND peptide” presented 335 hits with more recent patents (2008-2010) represented from a greater percentage of small to medium size bio-pharma companies, which may, in turn, be in a co-development and commercial partnership with a large pharmaceutical company for entry into market.

The following patents and patent applications indicate kinds and range of technology that show up in the patent literature. We emphasize that we look at patents from the standpoint of market competition. We have no opinion on the patentability of your technology. Please consult with qualified legal counsel for opinions on FluVaccine, Inc.’s freedom to operate and extent of intellectual property protection. Material in quotes is from the patent abstract unless otherwise indicated.

<table>
<thead>
<tr>
<th>Patent or Patent Application Number</th>
<th>Patent Title</th>
<th>Date</th>
<th>Relevance</th>
<th>Assignee</th>
</tr>
</thead>
<tbody>
<tr>
<td>US7763450</td>
<td>Functional influenza virus-like particles (VLPs)</td>
<td>July 27, 2010</td>
<td>This patent refers to 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.</td>
<td>Novavax, Inc., MD, USA</td>
</tr>
<tr>
<td>EP2204187A1</td>
<td>Human flu vaccine containing four influenza peptides</td>
<td>July 7, 2010</td>
<td>Four different (peptide) epitopes of flu virus comprise this synthetic vaccine expressed in a Salmonella bacteria cell culture. Epitopes represented can bind to the most prevalent HLA molecules</td>
<td>Yeda Research and Development Company, Ltd., Israel</td>
</tr>
<tr>
<td>Patent Number</td>
<td>Title</td>
<td>Date</td>
<td>Description</td>
<td>Inventor/Institution</td>
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</tr>
<tr>
<td>US7736642</td>
<td>Yeast-based Vaccine for inducing an immune response</td>
<td>June 15, 2010</td>
<td>This work refers to a yeast-derived vaccine whereby an intracellular fusion protein is created from influenza virus and proprietary protein (amino acid) sequence that enables the fine-tuning of the immune response either humoral or cell-mediated.</td>
<td>GlobeImmune, Inc., CO, USA</td>
</tr>
<tr>
<td>US7732130</td>
<td>Immunoprotective influenza antigen and its use in vaccination</td>
<td>June 8, 2010</td>
<td>This document refers to 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.</td>
<td>Vlaams Interuniversitair Instituut Voor Biotechnologie, Belgium</td>
</tr>
<tr>
<td>US20100098721A1</td>
<td>Methods and compositions for preparing a universal influenza vaccine</td>
<td>April 22, 2010</td>
<td>This patent refers to a multivalent vaccine technology that provides protection against multiple strains in a population composed of one or more vector proteins or antigenic portions that can recognize 4 or more viral strains to elicit an immune response.</td>
<td>St. Jude Children’s Research Hospital, TN, USA</td>
</tr>
<tr>
<td>EP2168987A1</td>
<td>Multifunctional linker protein containing an antibody against hemagglutinin, a conserved influenza antigen and an immunostimulating carrier binding domain</td>
<td>March 31, 2010</td>
<td>This work is a trivalent human vaccine with an HA binding domain that can bind to multiple HA subtypes, a conserved influenza protein, and an IBD.</td>
<td>Mucosis, BV, Netherlands</td>
</tr>
<tr>
<td>CN11353375A</td>
<td>Method for producing influenza hemagglutinin multivalent vaccine</td>
<td>January 28, 2009</td>
<td>This is a recombinant DNA vaccine technology toward hemagglutinin, produced in an insect viral-vector expression system (cell-based), for potential polyvalent vaccine for both flu subtypes A and B.</td>
<td>MG PMC Co Ltd, USA</td>
</tr>
<tr>
<td>EP2003198A2</td>
<td>Peptide for inhibition of influenza infection, inhibitor of influenza infection, liposome, and prophylactic/therapeutic agent for influenza</td>
<td>December 17, 2008</td>
<td>This patent refers to a proprietary peptide (amino acid sequence)-based vaccine, whereby the sequence can be modified to have both high affinity of binding to hemagglutinin and inhibitory effects on flu virus, and therefore have use as a prophylactic or therapeutic vaccine potentially.</td>
<td>Keio University, Japan</td>
</tr>
<tr>
<td>WO07066334A1</td>
<td>Improved Influenza Vaccine</td>
<td>June 14, 2007</td>
<td>This application refers to a human and animal vaccine that has a longer duration of effect and multi-strain</td>
<td>Yeda Research and Development Co. Ltd. at the</td>
</tr>
</tbody>
</table>
It appears that there is a growing trend associated with the production of vaccine in various cell lines/cultures and the utilization of newer recombinant DNA methods to sequence peptide epitopes that may potentially bind more than one strain of influenza or virus subtype, across populations and with stronger immunogenicity. In fact, for example, Roche Pharmaceuticals has a recent patent with the University of Texas–Austin for cell culture methods of influenza vaccine production and several other recent patents, related to search string “roche AND influenza vaccine,” within the last five years. While there seems to be overlap among the patents and applications in our table above, two inventions appear to offer similar advantages to your vaccine: EP2204187A1 (2010) and WO07066334A1 (2007), both from Yeda Research and Development. Together, these patents and applications involve long term, multi-epitope, cross-strain protection, and therefore, could represent competition. However, since all patents and applications above are indeed associated with influenza vaccines, we anticipate that all could result in eventual market competition. It seems that vaccines produced in cell line-culture methods and with advanced molecular cell biology and genetics techniques could possibly provide more immediate and rigorous competition by eliminating the time disadvantages associated with the use of chicken eggs in the manufacturing process.

Various organizations below, among many others, are continuing to research and develop technologies that may become a competitive threat within the next five years.

<table>
<thead>
<tr>
<th>Project Title</th>
<th>Performing Institution</th>
<th>Performance Period</th>
<th>Relevance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flu Cell Culture Technology: The Next Frontier</td>
<td>Novartis Vaccines</td>
<td>This research appears to be ongoing.</td>
<td>Cell lines (culture methods) have been used to develop vaccines for many years. However, these methods seem to be the primary focus of Novartis’ future vaccine endeavors for several reasons associated with the disadvantages of producing vaccines in chicken eggs: egg protein allergies, egg availability, contamination and/or other chemicals, lead time and time to manufacture issues. These production challenges make rapid response time in the case of a sudden flu outbreak more difficult to achieve. In contrast, cell culture production methods enable flexible and faster production with more controlled...</td>
</tr>
</tbody>
</table>

variables and the ability to modify for flu strains more easily. Currently, Novartis has eight clinical trials ongoing in the area of influenza vaccines.69

| Next Generation Flu Vaccine | GlaxoSmithKline | Several R&D sources that speak to GSK's ongoing and future vaccine focus from 2006-2010. | GSK has a proprietary novel adjuvant system to enhance the immune response in patients aged 65 years and older; this adjuvant (or enhancer) helps yield similar protection typically observed in younger adults.70 In general, adjuvants seem to be a focus at GSK for H1N1 - for example. 71,72,73,74 Currently, GSK has about 20 ongoing studies in clinical trials involving influenza vaccines at various stages.75

| Development of adenoviral-vector-based pandemic influenza vaccine against antigenically distinct human H5N1 strains in mice | Purdue University | The research appears to go from April 2005 to March 2010. | This research is trying to develop adenoviral vectors expressing hemagglutinin, nucleoprotein, or matrix protein 2 from H5N1 or hemagglutinin from H7N7 or H9N2. The vectors will then be evaluated on their ability to induce humoral and cell-mediated immunity in mice. The goal of the research is to eventually develop a long-lasting adenoviral, vector-based influenza vaccine.76

| Rapid cloning of high affinity human monoclonal | University of Oklahoma Health Sciences Center | April 2008 | The overall goal of this research was to develop influenza vaccines with a higher efficacy. To do this, the researchers planned to maximize induction of the neutralizing antibodies against the vaccine strain while also decreasing the response to denatured glycoproteins.

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antibodies against influenza virus and internal proteins. To develop these vaccines, researchers decided to first examine the antibodies present in serum after several flu vaccinations or infections. Then, the researchers examined the antigenic regions, and finally developed a vaccine that optimizes production of neutralizing antibodies.77

| TechnoVax reports on a VLP vaccine designed to protect against the devastating 1918 pandemic influenza as well as a novel bivalent virus-like particle (VLP) vaccine candidate | Technovax Inc. | The research appears to go from May 2005 to April 2007. | The goal of this research was to develop a cell-based system that can create influenza virus-like-particle (VLP) vaccines. Vaccine candidates came from harvested, purified insect cells that had been infected with one of four quadruple baculovirus recombinants. Then the candidates were evaluated in mice and ferrets.78 |

We searched PubMed under “influenza vaccine,” which provided 15,818 hits. The large number of relevant projects indicates that there is a significant amount of research in the arena. Next we refined our searched to “influenza vaccine AND increased immunogenicity,” which provided 138 hits; “influenza vaccine AND antiviral,” which provided 1,121 hits; and “influenza vaccine AND peptide sequence,” which provided 283 hits. Finally, we concluded with a Google search.

There appears to be a significant amount of research in the arena, and therefore, it is important to note that the projects listed above are only a small sampling of relevant projects that could lead to competition within the next five years. For example, Novartis is developing a cell culture-derived influenza vaccine, and GlaxoSmithKline (GSK) has 25 vaccines in clinical development and expects to have 5 major product launches within the next 5 years.79 GSK specializes in adjuvant technologies that enhance immune response when acting in concert with the drug and are part of the drug formulation.

Furthermore, other companies of varying size are developing influenza vaccines such as Technovax Inc of Tarrytown, NY, USA. According to the Technovax Inc. web site, this


company has proprietary technology using influenza virus-like particles (VLPs) for a vaccine that will go into development potentially within 18 months. Technovax’s vaccine seems to address similar parameters [as FluVaccine, Inc. ‘s technology] of mono/poly-valence, immunogenicity, and advanced cell-based production. Additional companies trying to compete in the vaccine R&D space include, but are not limited to, Mucosis and Novavax. Fifteen other “vaccine” technology organizations, with three of these in the “flu vaccine” arena exist locally on the Massachusetts Biotechnology Council web site alone. There appear to be 34 global vaccine manufacturers; some may or may not be actively pursuing R&D or may have partners that do so.

Searching the global clinical trials database (http://www.clinicaltrials.gov), sponsored by the NIH, with the search string “influenza vaccine,” we find a total of 117 on-going, active trials with sponsors encompassing academia, government and industry labs. At this web site, with the same search string, we see that MedImmune, LLC has 47 studies listed with 1 on-going, Protein Sciences Corporation has completed 6 studies, and Novavax has 5 recruiting currently, among others. Also, a search of “anti-infectives AND influenza vaccine” yields 14 studies with 4 actively recruiting.

Finally, we also list some projects by universities. Purdue University, for example, is developing influenza vaccines based on adenoviral vectors, while the University of Oklahoma Health Sciences Center is developing an influenza vaccine with a higher efficacy for the elderly. Since all of these projects could lead to influenza vaccines, we anticipate that they all could provide competition. Moreover, a significant number of academic and clinical research is funded through collaboration with larger pharmaceutical companies, as illustrated through the Roche and University of Texas-Austin clinical trial example.

<table>
<thead>
<tr>
<th>Competitive Landscape</th>
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<tbody>
<tr>
<td>We found that the US and Canada together are the largest purchasers of influenza vaccines. In the US, for the 2010-2011 flu season, it appears that the following vaccines have been FDA-approved: Fluvirin® by Novartis Vaccines, Fluarix® by GlaxoSmithKline Biologics, FluLaval® by ID Biomedical Corporation, FluMist® by MedImmune, LLC., Fluzone® by Sanofi Pasteur, and Afluria® by CSL Limited. Important differences between the vaccines are that Fluvirin®, Fluarix®, FluLaval®, and Fluzone® use inactivated influenza viruses and are administered by injection, while FluMist® uses active virus and is administered through the nasal passage. Additionally, we note that, until 2005, the US vaccine market was mainly split between Chiron (now Novartis</td>
</tr>
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Vaccines) and Sanofi Pasteur. However, after vaccine shortages during the 2004-2005 flu season, the market opened up to new players.86

We examined the general global vaccine market. We found that the top five vaccine manufacturers – or tier 1 – accounting for almost 90% of the market, are GlaxoSmithKline with 30 vaccines on the market, Sanofi Pasteur, Pfizer, Merck & Co. Inc., and Novartis.87,88 These companies may have large partnerships or joint ventures with production facilities in India and China, thereby expanding their market reach and penetration. We also found that North America represented about 47.5% of the global vaccine market in 2005, while Europe represented about 32% of the market. This means the rest of the world contains about 20.5% of the global vaccine market; these percentages have not changed significantly since then.89

There appears to be a significant amount of research in the arena for vaccines and vaccine production platforms. Experts indicated that the two major areas of research focus are on developing influenza vaccines using cell cultures and developing “universal” flu vaccines, possibly through DNA techniques, that will protect against most strains, and therefore, will not need to be modified each year.90

5 Market

While market sizes are hard to estimate, the following provides an example of how to figure out the total addressable market for this technology. While we seek to be as accurate as feasible in the estimate below, it is budget constrained and thus preliminary. We estimate the total market size, at saturation, for the World, and for all competitors, to be approximately:

<table>
<thead>
<tr>
<th>Market Niche Size</th>
<th>Market Size in Dollars</th>
<th>Growth Rate</th>
<th>Base Year</th>
<th>Detailed Basis for Estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$7 billion</td>
<td>12.1%</td>
<td>2008-2015</td>
<td>The influenza vaccine market is forecasted to be US$7 billion for 2010. The total global vaccine market is growing at an average rate of 12.1%.91 Therefore, it is possible and reasonable that the influenza vaccine market is growing at about this rate, due to market drivers.</td>
</tr>
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</table>

The market size and growth rate is a function of the number of people in the market and the anticipated rate of buying. As markets transition between emerging, growth, shakeout, mature, and declining, the basis for competition and the number of competitors usually changes, along

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89 Ibid.
90 Dave Smith (Professor, Epidemiology, Big School) in a telephone conversation with Analyst, July 3, 2007.
with the factors influencing adoption of innovation. The number of and growth rate for customers suggests how many units might be sold.\textsuperscript{92}

| **Our Current View on the Phase of the Market** |
|----------------|-----------------|
| **Today**         | **Trend**        |
| Growth            | Growth          |

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 5 years ago.\textsuperscript{93} However, a 2006 report by Frost & Sullivan stated that the North American vaccine market was about to enter a “new era of growth,” \textsuperscript{94} 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.\textsuperscript{95}

Markets can also be described in terms of the basis for competition (best technological performance; best value or the price/performance tradeoff that best matches the end-users’ preferences; lowest price; or best availability or the ability to get the product quickly). This dimension helps to define the context in which a commercialization strategy must be developed.

| **Our Current View of the Basis for Competition in the Arena** |
|----------------|-----------------|
| **Today**         | **Trend**        |
| Best Value        | Best Value      |

It appears that flu vaccines are based on a best value scenario, meaning that both price and performance are important. The importance of price could be seen when FluMist\textsuperscript{\textregistered} was marketed as a premium product at a price of $70. While the vaccine could be easily purchased at a pharmacy and offered a simple nasal spray administration method, revenues in 2003 were well below projections. Instead of selling an estimated 4 to 6 million doses, a mere 80,000 doses were sold.\textsuperscript{96,97}


\textsuperscript{95} Dave Smith (Professor, Epidemiology, Big School) in a telephone conversation with Analyst, July 3, 2007.


End-users indicated that performance is also important, indicating that the vaccine can not have major side effects and should have a high efficacy. These two factors combined led us to a best value conclusion, and we do not anticipate the trend to be different.

Entry barriers are obstacles that remove customer segments from the market for some period of time. They limit the size of the addressable market in general or the market share that can be captured. These barriers must be overcome or avoided to have a successful market entry. Our work to-date suggests the following entry barriers may prevent customer segments from buying FluVaccine, Inc.’s technology for some period of time.

<table>
<thead>
<tr>
<th>Generally Applicable Market Entry Barriers</th>
<th>Description/Why</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Competition from Large Companies</strong></td>
<td>It appears that the top five vaccine manufactures are GlaxoSmithKline, Pfizer, Merck &amp; Co., Inc., Sanofi-Pasteur Inc., and Novartis Vaccines. These companies represent about % 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. Supporting this, another source stated that there are high entry barriers to the flu vaccine market, such as biological manufacturing know-how and expense and established, complex industry and public relationships and network; thus, the established players face little competition.</td>
</tr>
<tr>
<td><strong>Negative Publicity from Anti-Vaccine Groups</strong></td>
<td>It appears that anti-vaccine groups persist in trying to give vaccines a negative reputation, although their influence wanes during recent pandemics. Examples of these groups include the Committee Against Compulsory Vaccinations, the Vaccination Risk Awareness Network, and the PutChildrenFirst.Org organization. However, these general opponents can also take the form of loosely tied parent organizations as well as religious groups both. The PutChildrenFirst.Org organization, for example, has tried to increase the awareness of the dangers of mercury in flu vaccines. Frost &amp; Sullivan explains that the negative publicity and inappropriate information generated by these anti-vaccination groups has negatively affected vaccine manufacturers.</td>
</tr>
</tbody>
</table>

98 Jamie Yarman (Geriatrician, Seniors Health Center and Private School Medical Center) in a telephone conversation with Analyst, July 2, 2007.
| Lack of Health Structures in Third World Countries | Frost & Sullivan indicates that many Third World countries lack structured health care systems and the infrastructure to administer immunization programs. This means there are problems concerning vaccine storage, vaccine supply, immunization records, booster administration, transportation, and sourcing skilled labor. While 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.105 |
| Vaccine Administration Method | Earlier in this report, we noted that ease of use may be hampered by choosing one particular method of administering the vaccine injection. One source indicated research concerning needle aversion that may keep about 30% of the general population from getting vaccinated.106 |
| Regulatory Barriers | Numerous countries appear to have vaccine approval processes that a vaccine must go through before being 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.107 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.108 Therefore, we anticipate that regulations could be a barrier to market entry. |
| End-User Needs Changing or Unstable | These needs vary from year-to-year depending on number of infections during flu season, the changing global climate and associated epidemiology, and emerging strains, e.g., H1N1, H3N1. Demand often surpasses supply.109 |
| Basis of Competition in Market Does Not Favor Introduction of New Technology | At current relatively low pricing of competitor vaccines, the introduction of yet another [vaccine] may present challenges in capturing market share. Competitors are primarily large pharma with significant name recognition, funds and resources for sales, marketing, and advertising, as well as established global supply chains, networks and locations.110 |
| Many Substitutable Products Available or Will Be | For select strains of influenza, there are vaccines currently available and competitors continue to enter this market or expand their market share.111,112 |
| Materials or Supplies May be Difficult to Obtain | This is relevant in terms of a potential market demand outpacing the supply of vaccine, which has happened from time-to-time in this market. Additionally, it may be an issue with a remote customer (end-user) in a developing country, where infrastructure is lacking or nonexistent.113 |

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105 Ibid.
108 Ibid.
110 Ibid.
111 Ibid.
## No or Poor Distribution Channels
This will be the case primarily for small companies that are selling the vaccine, due to the lack of a professional sales organization or distributor network established. In terms of reaching customers geographically, this will most likely be an obstacle to overcome in developing or underdeveloped countries and other remote areas.  

## Lack of Control Over Factors of Production Makes it Hard to Plan Costs and/or Production
Any biologic drug may have unexpected manufacturing issues due to the fact that biological material and processes are involved in producing vaccine. However, this is a daily challenge shared by all biologic companies.

## Difficult to Attain Economies of Scale, Scope, or Network Economies
This may be a barrier for smaller companies who are distributing and selling the vaccine due to the lack of a sales force or global network most likely. As per the manufacturing process, again, when biologic processes are involved, there can be unforeseen delays, i.e., contamination of product during the production process.

## Low Profitability of Targeted Customers or Potential Partners
This 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 in poorer regions of the world where there is significant unmet vaccine needs.

## Potential Partners Have Competing Technology or Just Not Interested
This will be an obstacle if a vaccine does not offer significant improvement(s) over what is currently available in the market. For a potential competing partner with vaccine sales, there would be no incentive to commercialize this new vaccine, thereby cannibalizing their established business, unless the new technology offered a compelling improvement over other competitor’s vaccines. Other potential [pharma] partners may make a strategic decision to focus on other disease areas.

## Competitor Goodwill (loyalty of customers or targets)
This is a common barrier in any market and will be probably remain, unless there is a compelling, significant reason for customers to change. Customer inertia is always present; health benefits need to be great enough to provide incentive to change.

## Business Cycles and/or Poor Economic Conditions in Targeted Market
As mentioned prior, poverty and under-developed countries will be market obstacles in getting vaccine to those in need in remote areas and at a price that sustains business. As per business cycles, manufacturing and production capacity challenges remain to meet unexpected influenza outbreaks and seasonal fluctuations, due to orders being placed erratically and not always on a regular basis. If a new vaccine enters the market during a season when there are few flu cases or a non-pandemic situation, this could create less demand.

It is also important to note that there appears to be a lot of research towards developing new influenza vaccines, occurring within industry and at academic universities. We anticipate that

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114 Ibid.
115 Ibid.
116 Ibid.
117 Ibid.
118 Ibid.
121 Dave Smith (Professor, Epidemiology, Big School) in a telephone conversation with [Analyst], July 3, 2007.
this research could lead to more competition in the industry, potentially restricting your market share. This potential competition could be due to not only the strength of the top 5 global vaccine manufacturers, but also to the plethora of smaller industry players, with proprietary technologies, which are independent or in partnership with a big pharma, e.g., ID Biomedical and GSK. We strongly recommend you consider the regulatory and health structures of the countries you plan to enter. In summary, as the table above attempts to convey, there are many potential barriers to market entry pertaining to large, well-established competitors, political, geographic and cultural issues, regulatory hurdles, investment intensive production, historical market inertia, pricing and profitability, manufacturing and access challenges, and seasonal disease – business cycles. All of these barriers could apply to this vaccine technology; however, pricing and profitability stand out as particularly salient for a new vaccine along with the seasonal business cycles that may need to be considered.

The likelihood of buying at any given point of time is a function of a number of individual decisions. Therefore, there is a distribution, or wave, of possible outcomes, which reflects the probability of individual buying decisions. The market drivers identified below are statistical tendencies that will influence buying by accelerating or retarding it to a greater or lesser extent.

Market drivers are forces that strengthen or weaken the importance of end-user needs over time. Practice level drivers are micro-economic; they affect the end-user directly. They influence the selection of substitutable goods and thus affect market share. Arena level drivers affect the organizations and industrial sectors in which the end-users work. They influence the overall demand for goods, like this technology and its substitutes. They affect when and how much of the total addressable market is actually going to be in the market and buying.

<table>
<thead>
<tr>
<th>Drivers Identified as Important</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Level</strong></td>
</tr>
<tr>
<td><strong>Affecting Market Size</strong></td>
</tr>
</tbody>
</table>


influenza 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.\(^{125}\)

Physician trends concerning the administration of influenza vaccines also affect the use of vaccines. One survey found that 80% of physicians administered the influenza vaccine for 3 to 5 months. However, only 27% of surveyed physicians administered the vaccine after the national peak of influenza activity. Additionally, 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 telephone to contact high-risk patients and remind them about obtaining a vaccine.\(^{126}\)

Many developing countries have increasing influenza vaccine use, with higher levels of influenza vaccine administrations than developed countries. One source indicated that about one third of all influenza vaccinations occur outside of North America, western Europe, Australia, and New Zealand.\(^{127}\) Finally, another source noted that influenza vaccine use in children, in particular, is expected to increase in the future.\(^{128}\)

Affecting Market Share

The main driver appears to be the threat of influenza. While the number of cases of the flu varies widely each year, it is estimated that about 10 to 15% of the global population is affected.\(^{129}\)

Federal reimbursement for the influenza vaccine by Medicare began in 1993.\(^{144}\) Since then, reimbursement for the vaccine has increased, with most/all human flu strains.\(^{131}\) However, the WHO believes that such a vaccine is still downstream, and might not be available in within the next 5-10 years.\(^{132}\)

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population gets influenza each year. However, during epidemics, numbers can be as high as 50%. Additionally, the European Influenza Surveillance Scheme notes that influenza outbreaks continue to be substantial. In the US, about 200,000 people are hospitalized each year as a result of the flu and about 36,000 die from the flu. Frost & Sullivan explains that the threat of influenza has led countries to stockpile influenza vaccines and should result in increased supply. Meanwhile another source notes that recently 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. Influenza vaccines have been a catalyst due to pandemic fears. This trend is expected to continue, although flu vaccine revenues will depend on meeting ambitious coverage targets.

There also appears to be a lack of awareness about the flu vaccine and is common among adults aged 65 years, with high-risk conditions, such as diabetes or asthma. For example, 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. Frost & Sullivan explains that 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. At a recent National Influenza Vaccine Summit, organizers measured awareness in the record pre-booking of Sanofi Pasteur’s planned doses of influenza vaccine as well as the expectation of the availability of 120 million flu

has increased. In 2001, about 50 countries had national immunization programs funded by the government and most of the programs included free influenza vaccines for at risk patients. Therefore, this shows a continuing and increasing trend in government funding and reimbursement programs for a flu vaccine.

In western countries, there has been an increased emphasis placed on preventative medicine. This emphasis has created a greater demand for vaccines. Additionally, one source explained that the influenza vaccine market sector will continue to offer the most market potential – over other segments.

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.

The anticipated rise in influenza vaccine research may be pegged in part on to the fear of another flu pandemic.

vaccine doses - the greatest number in US history - for the 2006-2007 season.\textsuperscript{140}

Efforts to expand the use of vaccines extend globally. In particular, the World Health Organization, the Bill & Melinda Gates Foundation, and the Global Alliance for Vaccines and Immunization (GAVI) Alliance have help lead the effort. For example, the Bill & Melinda Gates Foundation gave $2.7 million to a nonprofit research organization to develop a novel vaccine technology which would increase the cost-effective production of influenza vaccines.\textsuperscript{141} Meanwhile, the GAVI Alliance focuses on increasing children’s access to vaccines in poor countries.\textsuperscript{142} 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 influenza vaccines.\textsuperscript{143}

At the arena level, there appears to be a demand from manufacturers for better methods of producing the influenza vaccine. This appears to include factors such as a shorter manufacturing process and the ability to rapidly scale up production. We anticipate that this driver would support your vaccine if it provides a better production method, meaning a shorter manufacturing process and the ability to rapidly and reliably scale-up production. Additionally, there appears to be a demand for a universal vaccine that would protect against all strains of influenza and would not require boosters. This driver may also support your technology, as your vaccine appears to increase the number of strains covered by the vaccine and also the length of time between boosters.

At the practice level, the main driver supporting influenza vaccines appears to be the threat of the flu or a flu pandemic. Additionally, there appears to be large effort to distribute vaccines globally, increasing the global immunized population. We anticipate that both of the drivers will support your technology. Finally, there appears to be a low but increasing awareness of the

\begin{itemize}
\item\textsuperscript{146} “Global Vaccines Markets,” 2006, Frost & Sullivan web site, \url{http://www.frost.com} Subscription required (accessed August 4, 2010).
\item\textsuperscript{147} “United States Influenza Pharmaceutical Markets,” 2000, Frost & Sullivan web site, \url{http://www.frost.com} Subscription required (accessed August 4, 2010).
\item\textsuperscript{142} “About the GAVI Alliance,” Global Alliance for Vaccines and Immunization (GAVI) web site, \url{http://www.gavialliance.org/General_Information/About_alliance/index.php} (accessed August 4, 2010).
\end{itemize}
influenza vaccine worldwide, depending on the region. While select low awareness among certain populations and anti-vaccine organizations many hinder sales, the ever-increasing awareness could help support your technology.

The window of opportunity is that time period when a market can be entered successfully. In light of the above discussion, we currently see the window of opportunity for this application roughly in this range.

<table>
<thead>
<tr>
<th>Likely Window of Opportunity</th>
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<tbody>
<tr>
<td>We anticipate that the window of opportunity is currently open and will remain open for the next five years.</td>
</tr>
</tbody>
</table>

Since experts indicated a need for new influenza vaccines, we anticipate that the window of opportunity is currently open.148 However, it is also important to note that there appears to be a significant amount of research in the arena. Should a new influenza vaccine be developed that provides a better performance at a lower cost, then we anticipate that the window of opportunity may close. Yet, one source indicated that an ideal influenza vaccine will probably not be available for the next five to ten years.149

The following venues can be used for additional market intelligence gathering and communication with potential end-users and targets.

<table>
<thead>
<tr>
<th>Examples of Organizations, Meetings, and Publications to Use for Networking, Promotion, and Competitive Intelligence</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Organization</strong></td>
</tr>
<tr>
<td>Vaccine Journal</td>
</tr>
<tr>
<td>Vaccine Weekly</td>
</tr>
</tbody>
</table>

148 Dave Smith (Professor, Epidemiology, Big School) in a telephone conversation with Analyst, July 3, 2007.
<table>
<thead>
<tr>
<th>Event</th>
<th>Description</th>
<th>Contact Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>World's Only Vaccine Newsweekly,“World's Only Vaccine Newsweekly,”</td>
<td>The website is an expansion of the prior “Clinical and Diagnostic Laboratory Immunology”. CVI publishes articles on topics related to basic and clinical immunology, pathophysiology, and vaccine research, including new animal models for understanding immunology. 152</td>
<td>Susan F. Plaeger Editor-in-Chief Government Agency 301-496-0637 <a href="mailto:splaeger@niaid.nih.gov">splaeger@niaid.nih.gov</a> <a href="http://cvi.asm.org/">http://cvi.asm.org/</a></td>
</tr>
<tr>
<td>Clinical and Vaccine Immunology (CVI)</td>
<td>The conference is run by the European Scientific Working Group (Party) on Influenza aims to raise awareness on the impact of influenza.</td>
<td>David De Pooter, ESWI Management Link Inc. 32-3-232-93-42 <a href="mailto:info@link.inc.be">info@link.inc.be</a> <a href="http://www.eswiconference.org/">http://www.eswiconference.org/</a></td>
</tr>
<tr>
<td>Third European Influenza Conference 11-14 September, 2011, in Malta</td>
<td>The NFID is a non-profit dedicated to educating the public about the causes, treatments and prevention of infectious diseases. 153</td>
<td>Dr. Lorne Babiuk Director 301-656-0003 <a href="mailto:info@nfid.org">info@nfid.org</a> <a href="http://www.nfid.org/conferences">http://www.nfid.org/conferences</a></td>
</tr>
<tr>
<td>National Foundation for Infectious Diseases (NFID)</td>
<td>At this conference, experts in the field of infectious diseases present their recent research in vaccine development and policy. 154,155</td>
<td>Jennifer Corrigan 732-382-8898 <a href="http://www.nfid.org/conferences/">http://www.nfid.org/conferences/</a></td>
</tr>
<tr>
<td>Conference on Vaccine Research</td>
<td>This major global conference occurs yearly in a different location and is one of the premier scientific and industry forums for all those involved in vaccine registration and further information. 156</td>
<td>Sarah Pegden Conference registration and further information +44 (0) 207 242 1508 in the UK <a href="http://www.terrapinn.com/2010/wvcl/">http://www.terrapinn.com/2010/wvcl/</a></td>
</tr>
<tr>
<td>12th Annual World Vaccine Congress, 4-7 October 2010, Lyon,</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


6 Entry Strategy

Using the data we have collected, we now turn to the question of how to accomplish market entry in order to sell the technology to end-users.

6.1 Objectives

FluVaccine, Inc. aims to collaborate with a large pharmaceutical company to enable their product to reach end-users. FluVaccine, Inc. did not indicate a specific deal type, as they would like the relationship with a partner or partners to evolve with the continued development of the vaccine. At present, they would be looking to have the pharmaceutical aid in conducting clinical trials. Assuming these are successful, they aim to have that company obtain FDA and other regulatory approval for their vaccine, then market and distribute the vaccine to hospitals and other centers.

6.2 Advantages

From FluVaccine, Inc.’s end, their advantages lie with their product and market-driven opportunities. From our conversations with end-users, we found the product aligns to end-users’ needs for a vaccine that covers more strains and provides longer vaccine duration. Having completed animal trials is an important step.

FluVaccine, Inc. is likely to benefit from the increased R&D and business interest in vaccine development and commercialization, particularly flu vaccines. While the market for vaccines is still generally considered low margin, influenza vaccines appear at the forefront of a double-digit growth trend. Further, we anticipate the continued emphasis on preventative medicine in Western/developed nations will provide significant pull-through potential. This high volume pull-through can generate significant revenues and profits based on sheer volume of vaccine doses ordered.

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6.3 Obstacles

From the market standpoint, we found several major threats. Our project search revealed a great deal of research in the arena. For example, companies such as Pfizer and Cytos Biotechnology (http://www.cytos.com) continue to work towards developing a universal flu vaccine.159,160,161 There are also high entry barriers to the influenza vaccine market, such as biological manufacturing know-how and established industry relationships and networks with big pharma and large vaccine manufacturers globally. Lastly, the nature of regulations raises timing and financial concerns. The process is known for being resource intensive, requiring relatively high financial investment, labor and time commitments, whether one is utilizing conventional chicken egg or newer cell culture production methods. Also, end-users do prefer a more mature drug that has advanced significantly through clinical trials. In the United States, in particular, the Food and Drug Administration requires manufacturers to pass through a stringent approval process that includes three phases of clinical trials and sometimes a post-market fourth phase.

6.4 Strategy

Since you have completed animal trials, we now suggest beginning the human clinical trials Process - Phase 1. To initiate such, we recommend contacting the FDA for further direction and information concerning Good Clinical Practices (GCPs) and Human Subject Protection (HSP) requirements: http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/ucm155713.htm#FDARegulations.

Also, we suggest you call the office that monitors GCPs for vaccines: Bioresearch Monitoring Branch Office of Compliance and Biologics Quality (CBER), at 301-827-6221.

When conducting trials, it is important to partner with well-respected medical centers that have a large population of patients at risk for influenza. These are likely to serve as good first steps, particularly as they can link you to other well-respected centers. To get the word out about your results, we recommend publishing your results in relevant journals such as Vaccine Weekly. The most effective articles are likely to be written and submitted by your clinical partner, as they can speak to your end-users. Thus, we suggest getting your clinical partner to publish timing clinical results. These results should, in particular, reveal that you have increased the number of strains that your vaccine protects against and increased the length of time between boosters – if appropriately supported. At present, immunizations last for one year, as these must keep pace with the annual evolution and transmission of influenza virus strains. Each year that you can add increases the value of your vaccine to the end-user. We advise annual follow-ups to validate

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vaccine duration lasting for five years, during your ongoing research and after initial clinical trials. This will provide the most value to end-users, and correspondingly, enable your technology to look best in comparison with the competition.

Pricing will also aid in overcoming competition. We suggest pricing your technology just below the competition. Therefore, we recommend a price of around $12 per dose. Should your technology protect against fewer strains than potential competition, consider lowering your vaccine price.

While conducting clinical trials, it is important to network through conferences and organizations as these are good places to meet potential partners, end-users, and key opinion leaders in the field. Three examples of relevant conferences include the Third European Influenza Conference, the Conference on Vaccine Research, and the World Vaccine Congress, among others.

Finally, we suggest considering a partnership with a large pharmaceutical company, as these companies have the resources and reputation in place to manufacture and commercialize the vaccine. They also have the resources and infrastructure to help with clinical trials. Importantly, these large and well-established players have the name [and brand] recognition you may need for end-users to purchase the product. Examples of potential targets are LargePharma Inc. and BigPharma Company. Another potential target with financial backing worth considering may be LargeNon-Profit; we have provided such a contact in this report.

7 Targets

The target is the organization that will partner with FluVaccine, Inc. to commercialize this technology. There are feasible and viable targets. Feasible targets have relevant product lines and appear to have an established presence in the market. In short, they are probably worth checking out to see if they make good candidates for partnering. We seek viable targets that appear to be in good financial health, are established in the market with a relevant product line, can provide capabilities that are relevant for commercializing this technology, and possess good absorptive capacity. Viable targets, unless otherwise noted, are those that still appear to be good candidates after we have spoken to them on the phone to confirm their potential interest in this technology.

We cold called several targets to assess interest in this intellectual asset package. We presented this technology’s attractiveness as follows: This technology is an influenza vaccine that increases the immunogenicity of a given antigen. Additionally, the vaccine can protect patients from more strains of the influenza virus and can last longer.

We begin with examples of viable targets and then provide a way to find other likely feasible targets. The following tables summarize key information on viable targets.

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163 Absorptive capacity measures the degree to which the potential partner’s staff has the scientific and engineering education and know-how to help commercialize this technology without having to “come up to speed” on generic technical issues.
<table>
<thead>
<tr>
<th><strong>Target Profile</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Name of Target and Relevant Unit</strong></td>
<td>Big Pharma</td>
</tr>
</tbody>
</table>
| **Address of Unit** | Street  
City, ST Zip |
| **Point of Contact in Target with Position** | Sally Jenkins\(^{164}\)  
Senior Director of Licensing |
| **Phone of Point of Contact** | XXX-XXX-XXXX |
| **E-Mail of Point of Contact** | jenkins@BigPharma.com |
| **Current Customer Base** | BigPharma is a global pharmaceutical company that develops vaccines for patients around the world.\(^{165}\) |
| **Target’s Reason for Interest** | BigPharma is constantly doing research and development with other companies or partnerships if they believe that the new technology from the outside party is impressive. Sally Jenkins said that BigPharma usually gets their vaccines from outside sources. Their scientists are always interested at looking at new technologies related to vaccines, especially from small companies or universities. |
| **Example of Prior Acquisition of Technology from the Outside, if Relevant** | Sally Jenkins provided numerous examples of prior acquisitions of vaccine technology. She said that last year alone they probably had at least 50 deals made with outside parties. |
| **Criteria Likely to be Used to Evaluate This Technology** | She said that the scientists in the labs determine if they like the technology or not. If it is something that they have been waiting for 20 years, then they will probably jump right into it. If the technology is something BigPharma is already working on, then BigPharma will not pursue it. They also examine the market and the competition in the field. |
| **Likely Information Desired** | She would like the non-propriety information. She said to email her all non-confidential information. |
| **Anticipated Time to Decision from Initial Expression of Serious Interest** | She said they generally they will get back to an outside company in less than a month. |
| **Name, Title, Phone, and E-mail of Likely Champion for Technology in Target if One can be Suggested** | Sally Jenkins  
Her contact information is provided above. |
| **Likely Preferred Legal Structure for Deal** | She said that at BigPharma they look for deals that work on both ends. Usually with partnerships or LLCs, they begin by mapping out a path of what they want to accomplish. They would then structure an agreement if you give them an exclusive license. |
| **At What Stage in Maturity does the Target Prefer to Obtain Technology** | She said they work with a lot of small companies and universities and so they understand that sometimes the technology might not yet be in a mature state. She said that she can not answer at what stage of maturity the technology needs to be, as she is not a scientist. However, if the scientists are interested in the vaccine, then they will... |

\(^{164}\) Sally Jenkins (Senior Director of Licensing, BigPharma), XXX-XXX-XXXX, in a telephone conversation with [Analyst], July 19, 2007.

start research and development at a very early stage. She said it all depends on the science of the technology.

| **Will the Target Participate in Concurrent Engineering or Test and Evaluation** | She is not the decision maker, as scientists initiate any participation; however, they have worked with other companies in this way. |
|**Who is the Ultimate Decision-Maker(s)** | She said the scientists make the decision. |
|**What Kinds of Assets or Capabilities will the Target Contribute to the Commercialization Effort, Both Before and After a Formal Deal is Signed** | Sally Jenkins said that BigPharma is very willing to contribute and use their assets when it comes to commercialization, research, and development. She explained that at BigPharma they are willing to commercialize a product and conduct market research. They like to make sure that both parties get what they want. |

Sally Jenkins explained that her organization is committed to improving human and animal health, and that they understand the need to bring in outside technology to do this. As a result, they work with several small companies and universities, and actually get most of their vaccine technology from other companies. She explained that she wants to know the market needs for the technology, and how this vaccine is unique. We suggest contacting Sally Jenkins to further evaluate her as a potential partner.

We recommend that you contact the targets listed above as soon as possible. Even if you feel that your technology is not mature enough at this time to pursue partnerships, it is important to establish lines of communication and keep them open. In this way, you may not lose out on an opportunity to partner.

We have also contacted the following companies.

<table>
<thead>
<tr>
<th><strong>Name of Company or Unit</strong></th>
<th><strong>Address, Web site</strong></th>
<th><strong>Reason for Recommending</strong></th>
<th><strong>Name, Title, Phone, and E-mail of Point of Contact</strong></th>
<th><strong>Number of Times Contacted</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>BigWigPharma</td>
<td>Street City, ST Zip <a href="http://www.bigwig.com/">http://www.bigwig.com/</a></td>
<td>BigWigPharma is a global pharmaceutical company that develops vaccines for patients around the world.</td>
<td>Madam Lady Executive Director, Corporate Licensing XXX-XXX-XXXX</td>
<td>Lady was on vacation over the week we called. We recommend contacting her in the next few days.</td>
</tr>
<tr>
<td>RespectedPharma</td>
<td>Street City, ST Zip <a href="http://www.rpharma.com/">http://www.rpharma.com/</a></td>
<td>This is a large pharmaceutical company.</td>
<td>Doctor Doctor, Ph.D. Associate Director, Vaccine Development, XXX-XXX-XXXX</td>
<td>He did not reply to repeated phone calls by Foresight.</td>
</tr>
<tr>
<td>Well-Known Pharma</td>
<td>Street City, ST Zip</td>
<td>Well-Known Pharma is involved</td>
<td>Dr. Person, Vice President of</td>
<td>Dr. Person was unavailable each</td>
</tr>
</tbody>
</table>

As noted in the table above, we have contacted all the companies listed two or more times and were not able to get positive responses in the time allotted for this report.

The three companies listed above round out the companies we contacted in an effort to find a partner for FluVaccine, Inc. As we did not have the chance to chat with any of the contacts listed above, we cannot say whether or not they will have an interest in your technology.

We recommend developing a preliminary plan for deal-making before meeting with targets. This plan should be openly discussed with the target and a consensus one developed if they are interested to explore being an investor/partner/licensee after meeting with FluVaccine, Inc.

8 Revenue Projection

Market and revenue projections are always an educated guess based on the relevant information available. Because markets are changing and technology is constantly advancing, it is not possible to make a definitive projection, yet it is possible to make a well-informed estimate. In our projections, all revenues are derived from sales because, as Foresight Chairman of the Board David Speser says, “Nothing happens without a sale.”

For TNAs™, Foresight employs two widely used methods to estimate total addressable market and potential revenues: Bottom Up and Top Down. We then calculate a growth rate and market share. If we cannot get the data we need, we try to do a Threshold Analysis. How each of these works is described below. What is important to realize is that our estimates are like tossing darts. An experienced player can make a better toss than a novice, but there is always a margin of error. As our budget and time is limited, what is important is to see how we constructed the estimates and use this information to inform subsequent estimates. These estimates should not be taken as definitive. They are merely preliminary.

**Bottom Up Approach:** In this method, we arrive at the potential revenues by estimating the number of units that can be sold. The estimated number of units is a product of how many buyers are likely to be in the market and how many units each one will purchase in the time frame of interest. In difficult cases, where a single unit is combined within a platform or system technology, which in turn, is then integrated into a more complex product or system, we calculate the total number of units by multiplying out to the final application. For instance, a

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microwave electronic pressure sensor might be integrated into a component system, which is then used in the production of a more complex device, which might incorporate multiple component systems into the end product. In this example, it is necessary to multiply the number of units not only by the number of end products sold over a given time frame, but by the number of units used in each component or subsystem of the end product. The resulting number times the price gives us the potential revenues.

**Top Down Approach:** In this approach, we look at a larger market and slice it down to arrive at the total addressable market for this technology. The slice represents the percentage of the larger market that is the total addressable market for this technology. This percent is determined by using data obtained from market research reports, interviews with experts, historical data from equivalent technology in the market niche of interest, and other sources. Once the total addressable market is determined, the market share can be calculated as above.

**Growth Rates:** Once we develop a baseline for the estimated potential revenues, we factor in a growth rate. We look at such growth rates in light of the phase of the market. This is because market phase influences the slope for product sales, which directly affects the sales growth potential for the technology. Other points of consideration that are common across both approaches for revenue projections include the overall competitive advantage of this technology, how much education and awareness building will be required to allow buyers to appreciate these advantages, and the potential for stakeholders and others to create pull-through by advocating this technology.

**Market Share:** Unless clear market data is available, we typically estimate market share by beginning with the total addressable market in any given year. We then consider the current phase of the market (which influences what percentage of the total addressable market might be buying), barriers to entry (which eliminate potential customer segments), drivers (which skew buying forward or backward in time and affect what the buyer might seek in new technology), and the competitive landscape (which influences how the buyers might be divided up among competing offerings). Once we obtain a suitable estimate for the number of buyers and the number of units that each will purchase, we can easily calculate an estimate for the total number of units that can be sold. Multiplying this number by the unit price (as mentioned in the Price Table above) gives a revenue projection that was built from the bottom up. Dividing the revenues by the market size gives a potential market share, which should be taken as a sales goal or objective for this technology.

**Threshold Analysis:** Sometimes, despite our best efforts, we cannot find data to support a market size or market share estimate. In that case, we try to do a threshold analysis. In this approach, we see how many sales we feel might occur, based on expert and end-user feedback and other data. If that looks sufficient to justify moving forward with commercialization, we say the threshold is passed.

Again, these are the methodologies we use to compile the revenue projections in our TNA™ assessments. More sophisticated methods may be used for valuations and other services. The projections here should serve as a starting point for making a more detailed and definitive estimate of the potential revenues for this technology.
There is no set standard for calculating market share. In the end, it is important to be conservative because something can always go wrong or influencing factors can be missed.

The text below uses this methodology to compile the revenue projections for this technology. Again, these revenues projections should serve as a starting point for deeper discussions about the issue of revenue. The methodology described above should serve as a guide for future projects.

Potential investors/partners/licensees will want to know how much money they can make with this technology. Given the analysis to date, we can make a very preliminary projection of gross revenues the technology could generate using US$12 as the price per unit.

1) Year One: $36 million based on 3 million
2) Year Two: $60 million based on 5 million
3) Year Three: $108 million based on 9 million
4) Year Four: $240 million based on 20 million
5) Year Five: $600 million based on 50 million

First, we obtained the price per unit from the price section. Then we estimated the number of units that you might sell each year. To make these estimations, we first examined the number of units each company sells each year. For example, we found that MedImmune planned to sell about four or five million doses of FluMist® during its first year on the market. Additionally, we found that in 2004, Fluzone® by Sanofi Pasteur Inc. had 46% of the global market, Chiron (now Novartis) flu vaccines had 12% of the market, Influvac® by Solvay had 11% of the market, Fluarix® had 7% of the market, Inflexal® V by Crucell had 4 percent of the market, FluMist® had 3% of the market, Fluviral® by GSK had 2% of the market, and other influenza vaccines represented the remaining 15% of the market. Since about 300 million doses are sold each year in recent years, we anticipate that 2% of the market represents about 6 million doses.

Next, since patients tend to be hesitant to use immunizations during first year on the market, we anticipate your sales will represent about 1% of the market or 3 million doses. However, since your technology protects against several strains, we anticipate that the number of doses sold each year will indeed increase.

By taking the total market gross revenues and each year’s preliminary revenue estimate, we can derive a preliminary market share goal that begins at less than 1% and ends at 4.32% after five years from the date of market entry.

We calculated the market by using the [forecasted] 2010 base market size of $7 billion and then increasing the market size each year using the growth rate of 12.1%. Then, we obtained the

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revenue goals from the revenue in the table above. Finally, we divided the revenue goals by the market size to get the market share goals.