Zacks Small-Cap Research

scr.zacks.com

February 22, 2016
David Bautz, PhD
312-265-9471
dbautz@zacks.com

10 S. Riverside Plaza, Suite 1600, Chicago, IL 60606

BiondVax Pharmaceuticals, Ltd. (BVXV - NASDAQ)

BVXV: Initiating Coverage of BiondVax Pharmaceuticals, Ltd.; Developing a Universal Influenza Vaccine…

Current Recommendation	**Buy**
Prior Recommendation	N/A
Date of Last Change	02/22/2016
Current Price (02/22/16)	$3.51
Target Price	**$17.00**

INITIATION

We are initiating coverage of BiondVax Pharmaceuticals, Ltd. with a Buy rating and a $17.00 price target.

BiondVax is an advanced clinical stage biopharmaceutical company developing immunomodulation therapies for infectious diseases. The company's lead product candidate, M-001, is a universal influenza vaccine composed of peptide antigens. Unlike currently existing influenza vaccines, which offer only limited protection against a limited number of specific strains, M-001 is designed to provide long-lasting and increased protection against *all* existing and future seasonal and pandemic influenza strains. To date, the company has successfully completed five clinical trials in 480 young and elderly adults. The two phase 1/2 and three phase 2 studies showed the vaccine to be well tolerated with incitement of both cellular and humoral immune responses. Two additional phase 2 trials are ongoing: in Europe (funded by the EU) and in the U.S. (funded by the NIH/NIAID). We believe M-001 is highly differentiated from currently available influenza vaccines and could lead to the first effective universal preventative for influenza infection, build significant herd immunity, and potentially lead to the eradication of influenza in humans.

SUMMARY DATA

52-Week High	**$5.39**
52-Week Low	**$3.39**
One-Year Return (%)	**N/A**
Beta	**N/A**
Average Daily Volume (sh)	**5,657**
Shares Outstanding (mil)	**3.38**
Market Capitalization ($mil)	**$12**
Short Interest Ratio (days)	**9.37**
Institutional Ownership (%)	**1**
Insider Ownership (%)	**3**
Annual Cash Dividend	**$0.00**
Dividend Yield (%)	**0.00**
5-Yr. Historical Growth Rates	
Sales (%)	**N/A**
Earnings Per Share (%)	**N/A**
Dividend (%)	**N/A**
P/E using TTM EPS	**N/A**
P/E using 2013 Estimate	**N/A**
P/E using 2014 Estimate	**N/A**

Risk Level	**Above Average**
Type of Stock	**Small-Growth**
Industry	**Med-Biomed/Gene**

ZACKS ESTIMATES

Revenue

(In millions of $)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2014	0.0 A	0.0 A	0.0 A	0.0 A	0.3 A
2015	0.0 A	0.0 A	0.0 A	0.0 E	0.0 E
2016					0.0 E
2017					0.0 E

Earnings per Share

(EPS is operating earnings before non-recurring items)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2014	- A	- A	- A	- A	-$0.04 A
2015	-$0.01 A	-$0.02 A	-$0.00 A	-$0.01 E	-$0.03 E
2016					-$0.02 E
2017					-$0.02 E

© Copyright 2016, Zacks Investment Research. All Rights Reserved.

WHAT'S NEW

Initiating Coverage

We are initiating coverage of BiondVax Pharmaceuticals, Ltd. (BVXV) with a Buy rating and a $17.00 price target. BiondVax is an advanced clinical stage biopharmaceutical company developing immunomodulation therapies for infectious diseases. The company's lead product candidate, M-001, is a peptide-based vaccine that offers long-lasting protection against multiple strains of both seasonal and pandemic influenza virus, in contrast to the currently available influenza vaccines that must be administered yearly and only offer protection against a limited range of specifically targeted influenza strains.

M-001 is composed of nine conserved and common peptides sequentially joined in one protein product that work to activate both arms of the immune system: the humoral response (generation of antibodies) and a cellular response (generation of virus-specific T-cells to destroy the virus infected cells) to prevent the spread of the virus and lessen the duration and severity of illness. The selected peptides are from the hemagglutinin (HA), nucleoprotein (NP), and matrix protein (M_1) of both influenza Type A and Type B viruses. Each peptide is comprised of 8 to 18 amino acids. The peptides are common to the vast majority of the approximately 40,000 known influenza strains, thus the universality of the M-001 vaccine.

There are a number of advantages that M-001 possesses which make an investment in BiondVax a compelling opportunity:

- **Broad Coverage of Influenza Strains**: BiondVax has accumulated data to show that immunization with M-001 offers broad coverage of different type A and B seasonal and pandemic influenza strains. This means that unlike the current influenza vaccine solution, a new vaccine containing new strains will not need to be developed each year prior to each influenza season. In addition, only M-001 needs to be included in pandemic influenza stockpiles, rather than today's multiple vaccine stockpiles for each particular potential pandemic influenza strain.
- **Long-Lasting Protection**: Since the M-001 vaccine is designed to activate both arms of the immune system, i.e. antibodies and other specific white blood cells, if will be effective against many existing influenza strains and will also provide longer acting protection against future influenza strains.
- **Continual Sales Cycle / Year Round Vaccination**: The currently offered influenza vaccine, which protects against only three or four past influenza strains, is primarily sold in the Northern Hemisphere between September and November each year. Due to the fact that M-001 is made of conserved and common influenza elements (peptides), there is no need to reformulate the vaccine every season or for every new pandemic. Therefore, the vaccine could be sold throughout the year, independent of influenza seasons.
- **Short Production Times / Year Round Production & Stockpiling**: The currently offered influenza vaccines all require 16-24 weeks to be produced, while M-001 has a production time of only 6-8 weeks. This short timeframe could prove to be a valuable characteristic in the event of a pandemic outbreak that would necessitate a large order of vaccine produced in a limited amount of time. M-001's unique and unchanging formulation enables year-round, flexible production and stockpiling according to market demands.
- **No Egg Allergy Concerns**: Most current influenza vaccines are produced in chicken eggs, which can result in an allergic reaction when administered to those with egg allergies. An epidemiological study in 2011 concluded that eggs are one of the most common allergens in Europe, however since M-001 is produced in bacterial cells, and not produced in eggs there is no concern in administering the vaccine to those with egg allergies.

With a market cap of only around $12 million and about $10 million in net cash, with an approximate $250K monthly burn rate, solid clinical data, and broad IP coverage, we see BiondVax as a highly undiscovered opportunity for investors. The seasonal influenza vaccine market is currently valued at over $3.2 billion worldwide every year and is expected to continue growing at approximately 5.7% annually. The advantages shown above lead us to believe that M-001 could become the new "gold standard" for influenza vaccines, and that an investment at this juncture could lead to significant returns for investors.

INVESTMENT THESIS

Influenza

Influenza is one of the most common infectious diseases and is caused by the influenza virus. It is an airborne virus that is highly contagious and tends to occur in seasonal outbreaks during winter months. There are a variety of symptoms associated with the disease, with almost all infected developing a fever along with cough, nasal congestion, runny nose, body aches, fatigue, and headache. Complications of influenza can be serious and include pneumonia, sinus infections, and exacerbation of underlying morbidities such as heart disease and asthma. The disease can be fatal, particularly in those with weaker immune systems such as the very young and the elderly.

There are three types of influenza viruses that infect humans: Influenza type A, with many subtypes and responsible for about 80% of influenza illness; Influenza type B, with many fewer subtypes and responsible for about 20% of flu illness in human; and Influenza type C, which only rarely and mildly infects humans. The influenza virus spreads easily from person to person through contact as well as through airborne droplets from coughs and sneezes. Inhalation of infected aerosols leads to viral binding and uptake by cells of the respiratory tract. Once inside the cell, the virus takes over the cellular machinery to replicate, produce many multiple additional copies of itself, and release viral progeny.

The incubation period for influenza ranges from one to four days with aerosol transmission occurring up to one day before symptoms begin (Gu *et al*., 2011). Viral shedding then continues for an additional five to seven days, though in young children and immuno-compromised patients this may continue for longer.

Influenza outbreaks occur at different times of the year depending upon the location. In areas near the equator, influenza occurs year-round. In the Northern Hemisphere, influenza infections typically begin in early fall, peaks in February, and then ends in late spring. The World Health Organization (WHO) estimates that annually around the world, 5-10% of adults and 20-30% of children will contract influenza, with three to five million severe cases, and approximately 250,000 to 500,000 deaths (WHO factsheet N°211). The U.S. Centers for Disease Control (CDC) estimates influenza-associated deaths ranged from 3000-49,000 annually between 1976 and 2006 in the U.S., with an average of 23,000 American dying from influenza and its complications each year, 21,000 of them elderly.

Influenza Viruses

The influenza viruses belong to the family Orthomyxoviridae, have a single-stranded RNA genome (that is separated into eight segments), and typically are of a spherical shape (Hay *et al*., 2001). There are three genera of influenza virus:

- Influenza A: infects birds, mammals, and humans
- Influenza B: infects seals, ferrets, and humans
- Influenza C: infects pigs, dogs, and rarely humans

Influenza A: Wild aquatic birds are the natural host for most influenza A viruses, which have been the cause of all influenza pandemic outbreaks in humans. Different influenza A serotypes are classified according to the two most prominent surface antigens, hemagglutinin (HA or H) and neuramidase (NA or N). Thus far, 18 HA serotypes and nine NA serotypes have been identified with the varying combinations yielding 162 potential subtypes of influenza. The HA and NA variants are used to identify different subtypes of the virus (e.g., subtype H1N1 expresses hemagglutinin 1 and neuramidase 1). The most common subtypes of influenza A contain hemagglutinins 1, 2, and 3 and neuramidases 1 and 2. The H1N1 serotype caused the infamous 1918 “Spanish flu” at the end of World War I, which killed an estimated 20-100 million people worldwide.

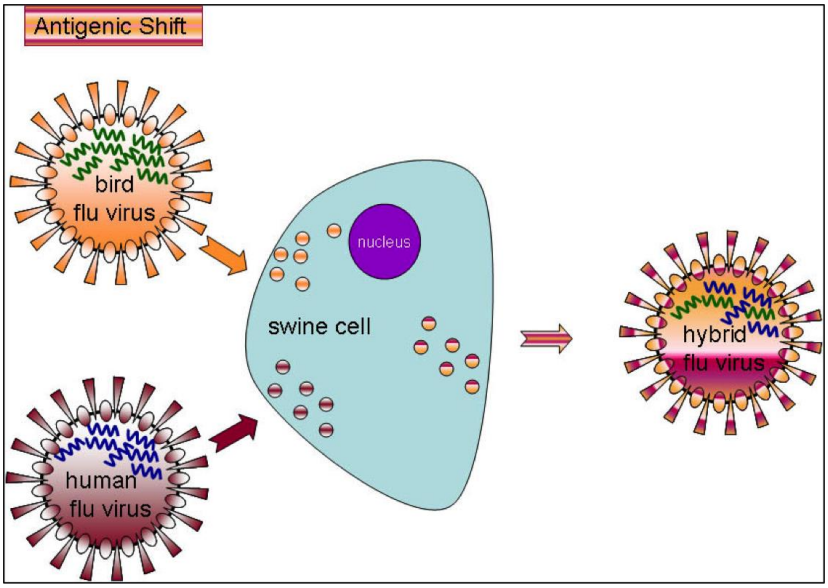
Influenza B: This virus is less common than influenza A and only infects humans, seals (Osterhaus *et al*., 2000), and ferrets (Jakeman *et al*., 1994). There are only two lineages – Yamagata and Victoria – of influenza B, and it is known to mutate at a much slower rate than influenza A (Nobusawa *et al*., 2006). The slow mutation rate and the limited number of potential host species means that pandemics of influenza B do not occur (Zambon, 1999).

Influenza C: This is the least common of the three genera. It infects pigs, dogs, and humans, and is typically

associated with the least severe symptoms, including in children (Matsuzaki *et al*., 2006). However, it is possible for local outbreaks of the virus that can result in severe disease (Matsuzaki *et al*., 2002). There is no vaccine currently available for influenza C.

The seasonal outbreaks that occur each year are typically caused by different serotypes of the influenza virus, as the viruses are constantly mutating and evolving. Due to the absence of RNA-proofreading enzymes in the host cell machinery, it is estimated that there is one error in the genome each time the influenza genome is replicated (Drake, 1993). Mutations resulting in changes to the amino acid sequence of HA or NA on the surface of the virus results in antigenic drift, which is a slow process by which novel strains of the influenza virus are produced until one evolves that can infect people by evading their immune system. This new strain then spreads rapidly through the population, replacing the previous strain of the virus that had been circulating, and often causing an epidemic (Wolf *et al*., 2006). However, since the new serotype is still similar to the prior serotype in circulation a large percentage of the population will still be immune.

In contrast to the yearly epidemics, when influenza viruses that normally infect two different species reassort, a novel strain is produced with entirely new antigens that very few if any members of a population will have immunity to in a process called antigenic shift. A novel strain produced through antigenic shift has the potential to produce a pandemic and spread uncontrolled through the population (Parrish *et al*., 2005). While antigenic drift occurs in all influenza genera, antigenic shift only occurs in influenza A, since it infects so many different species of animals. An example of antigenic shift would be if a human and avian influenza virus both infected the same cell, with the host cell then forming new viral particles that combine parts of each of the original strains. The recent pandemic outbreak of H1N1 in 2009 was the result of antigenic shift that occurred through the reassortment of human, avian, and swine viruses (Smith *et al*., 2009). The following figure shows what occurs during antigenic shift.



Source: www.saylor.org

Influenza Vaccines

The influenza vaccine is a yearly inoculation given to protect against influenza. There are currently three types of influenza vaccine available:

1. Inactivated Influenza Vaccine (IIV), which include whole virus vaccines, split virus vaccines (where the virus has been disrupted by a detergent), and subunit vaccines (where HA and NA have been further purified from other viral components). These are administered intramuscularly or intradermally;
2. Live Attenuated Influenza Vaccine (LAIV), which are based on temperature-sensitive variant vaccine strains that replicate well in the nasopharynx but poorly in the lower respiratory tract. These are administered intranasally;
3. Recombinant Influenza Vaccine (RIV), which uses recombinant HA proteins produced in insect cells. These are administered intramuscularly.

A new version of the vaccine is produced each year due to antigenic drift that results in novel strains of the influenza virus circulating through the human population each year. Each year, three strains are chosen by the

WHO Global Influenza Surveillance and Response System for inclusion in the yearly vaccine, with a fourth strain identified for use in the quadrivalent vaccine. The chosen strains are serotypes of H1N1, H3N2, and a Type-B strain that is forecasted to be most prevalent during the next influenza season. A second Type-B strain is added for the quadrivalent vaccine. It is noted that the random unpredictable mutations (drifts) are typically different in the different parts of the northern hemisphere but still the same vaccine strain composition is used for a specific season, often resulting in mismatch with actual circulating flu strains and therefore poor vaccine effectiveness.

The Global Influenza Surveillance and Response System (GISRS) was established in 1952 and is comprised of a number of different institutions in 133 countries around the world. The primary purpose for these institutions is to monitor disease outbreaks as well as perform primary virus isolation and preliminary antigenic characterization. The samples are then sent back to the WHO for further antigenic and genetic analysis, with the results being the basis for the WHO's recommendation for the next influenza vaccine. Since the Group's recommendation is based on its best estimate for which strains will predominate in the next year's influenza season (around 9 months later), it is tantamount to an "educated guess" and is susceptible to a mismatch between the vaccine and the circulating strains, thus the poor vaccine effectiveness of current strain-dependent influenza vaccines.

There are currently three methods through which influenza vaccines are produced:

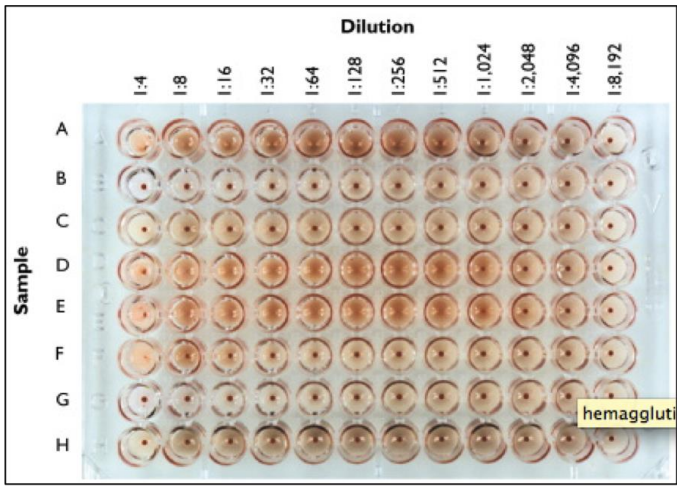
Egg-Based: This is still the most common method for producing influenza vaccines and has been in use for more than 70 years. Egg-based vaccine manufacturing is used to produce both "inactivated" vaccine (delivered through an injection) as well as "attenuated" vaccine (delivered through a nasal spray). The process begins with the CDC delivering vaccine viruses (serotypes of which were chosen for that upcoming influenza season's vaccine by the GISRS) grown in eggs to the drug manufacturers. The vaccine viruses are then injected into fertilized chicken egg's embryos and incubated for several days to allow for viral replication to take place. The virus-containing fluid is then harvested from the eggs and the virus is inactivated and viral fragments are filtered for use in a vaccine. This production technique requires a very large quantity of eggs and takes the longest amount of time to produce vaccine, typically six months. The yields in the egg-based production technology are variable and depend on the strains. In general, for one seasonal influenza vaccine dose, one to two eggs are required. The yields for pandemic strains, and in particular avian strains (i.e., H5 and H7), are much lower because the avian strains kill the chicken embryo. Therefore, approximately 3 eggs are needed for one pandemic vaccine dose. Alternatively, an adjuvant (typically added to vaccines to boost immune response) is added to the vaccine since it contains less pandemic influenza antigen.

Cell-Based: First approved in 2012, the cell-based method uses the same egg-grown vaccine viruses supplied by the CDC, which are then mixed with cultured mammalian cells and allowed to incubate for several days. The virus-containing fluid is then collected and the viral proteins are filtered or purified for use in the vaccine. There is currently one FDA approved cell-based influenza vaccine available in the U.S (Flucelvax®). Although yields of the cell-based production are higher than those achieved in egg-based production, costs of production in cell-based are higher than the egg-based due to the expensive growth media used for the cell cultures. The advantage of this technology is the reduction of the production cycle to four months in comparison to the six months needed for the egg-based technology. Another advantage is that mammalian cells are not as sensitive to the avian influenza strains as the chicken embryos.

Recombinant-Based: This process does not require the use of eggs or the influenza virus during any step of vaccine production. Instead, the vaccine is composed of the HA proteins from the selected influenza strains that are produced through recombinant DNA technology. There is currently one FDA approved recombinant-based influenza vaccine available in the U.S. (FluBlok®), which was first approved in 2013, and is approximately double the cost of the other vaccines.

Measuring Immune Response to Vaccines

The hemagglutinin inhibition (HAI) assay is used to determine the immune response to seasonal influenza vaccines. However, this assay's efficacy applies only to the strains included in the vaccine, which may not be relevant to the vaccine effectiveness against the unpredicted circulating strains in the upcoming flu season. HA binds to erythrocytes (red blood cells) and causes the formation of a lattice structure, a process called hemagluttination. The hemagglutinin assay involves mixing two-fold serial dilutions of virus with a fixed amount of red blood cells to the wells of a plastic tray to determine the titer of virus that will cause hemagglutination. The red blood cells that are not bound by the virus sink to the bottom of the well, which can be visualized as a dark red dot. The following image shows the results of a hemagglutinin assay involving different viruses (A-H) and their corresponding dilutions (1:4 – 1:8,192).



Source: www.virology.ws

In the preceding figure, Sample A causes hemagglutination up to a dilution of 1:256, while Sample B has no detectable virus. In order to perform the HAI assay, a fixed amount of virus that causes hemagglutination is utilized along with two-fold dilutions of patient sera to determine the dilution at which the antibodies in the sera will still prevent hemagglutination, which is referred to as the HA antibody titer. Typical outcomes for immunogenicity include:

- ✓ The proportion of subjects with seroconversion, which is defined as A) going from a pre-immunization HA titer of ≤ 1:10 to post-vaccination HA titer of ≥1:40, *or* B) a significant increase (at least a four-fold increase from a pre-vaccination HA titer of ≥1:10)
- ✓ Geometric Mean Titer (GMT) increase of vaccination-specific antibodies of >2.5
- ✓ The proportion of patients with post-vaccination HA antibody titer ≥1:40

Regulatory authorities utilize the immunogenicity of the each season's influenza vaccine as a surrogate marker for approval. While specific antibody titers post-vaccination have not been correlated with protection from influenza, some clinical trials have shown that antibody titers ≥1:40 have been associated with protection from influenza illness in up to 50% of subjects (Hannoun *et al*., 2004).

Influenza Vaccine Market

The following vaccines were available for sale in the U.S. for the 2015-2016 influenza season (CDC):

Trade Name	Manufacturer	Age Indication	Route of Administration
Inactivated influenza vaccine, quadrivalent (IIV4), standard dose			
Fluarix Quadrivalent	GlaxoSmithKline	≥3 yrs	IM
FluLaval Quadrivalent	ID Biomedical Corp. of Quebec (distributed by GlaxoSmithKline)	≥3 yrs	IM
Fluzone Quadrivalent	Sanofi Pasteur	≥6 mos	IM
Fluzone Intradermal Quadrivalent	Sanofi Pasteur	18–64 yrs	ID
Inactivated influenza vaccine, trivalent (IIV3), standard dose			
Afluria	bioCSL	≥9 yrs via needle 18-64 years via jet injector	IM
Fluvirin	Novartis Vaccines and Diagnostics	≥4 yrs	IM
Fluzone	Sanofi Pasteur	≥6 mos	IM
Inactivated influenza vaccine, cell-culture-based (ccIIV3), standard dose			
Flucelvax	Novartis Vaccines and Diagnostics	≥18 yrs	IM
Inactivated influenza vaccine, trivalent (IIV3), high dose			
Fluzone High-Dose	Sanofi Pasteur	≥65 yrs	IM
Recombinant influenza vaccine, trivalent (RIV3), standard dose			
FluBlok	Protein Sciences	≥18 yrs	IM
Live attenuated influenza vaccine, quadrivalent (LAIV4)			
FluMist Quadrivalent	MedImmune	2–49 yrs	IN

Abbreviations: ID = intradermal; IM = intramuscular; IN = intranasal
Source: Centers for Disease Control / Zacks SCR

According to PharmaPoint, the seasonal influenza vaccine market was valued at approximately $3.2 billion in 2013 and is expected to grow to over $5 billion in 2021. Approximately 135 million doses of the seasonal flu vaccine are sold annually in the U.S. each year, with a total of 500 million doses sold worldwide. In 2009-2010, sales of the pandemic swine flu (H1N1) vaccine by Novartis, Sanofi, and GlaxoSmithKline totaled $6.4 billion worldwide.

The U.S. government has a goal to stockpile enough influenza vaccine to cover 20 million individuals in the critical workforce (for example the emergency services as well as medical and Government workers). At an average of $12 per dose (the CDC adult vaccine price), that is a potential $240 million opportunity.

As shown in the table above, the influenza vaccine market is currently served by a limited number of companies. Each of the vaccines offered by those companies are identical in terms of which influenza strains are targeted, with the only differences being how the vaccines are produced, what other components are in the vaccine (e.g., if the vaccine contains thimeorsal as a preservative), and the mode of delivery. Sales figures for the top-selling influenza vaccines are given below:

Product	Company	2014 Sales ($Millions)	Product	Company	2014 Sales ($Millions)
FluLaval/Fluarix	GlaxoSmithKline	$354	Fluvirin	CSL/Novartis	$359
Fluzone	Sanofi	$1,724	Flucelvax	CSL/Novartis	$118
Afluria	CSL	$134	FluMist	AstraZeneca	$295

Source: EvaluatePharma / Zacks SCR

Influenza Vaccine Efficacy/Effectiveness

How well vaccines perform in preventing the disease for which they are developed is a function of the vaccines *efficacy* and *effectiveness*, two related terms that have distinct epidemiological meanings. The formula to calculate a vaccine's efficacy is over 100 years old and was first proposed in 1915 in a study on whole cell cholera and typhoid vaccines (Greenwood *et al*., 1915). Using results from a randomized, double blind, placebo controlled clinical trial, vaccine efficacy is calculated using the relative risk (RR) of disease between unvaccinated (UVac) and vaccinated (Vac) patients as follows:

$$Efficacy = \frac{Uvac - Vac}{Uvac}\ x\ 100$$

and

$$Efficacy = (1 - RR)\ x\ 100$$

For example, the efficacy of FluBlok® was evaluated in a randomized, double blind, placebo controlled clinical trial of 4,648 adults (Treanor *et al*., 2011). Patients were evaluated for CDC-defined influenza-like illness (CDC-ILI) and any patients with an episode of CDC-ILI had throat and nasal swab samples evaluated for the presence of influenza virus. The results showed that out of 2,344 patients immunized with FluBlock®, 44 (1.9%) exhibited ILI and tested positive for any influenza strain, compared to 78 (3.4%) of 2,304 patients administered placebo. Flublok's® efficacy was calculated as 44.6% in preventing culture-confirmed CDC-ILI.

$$Efficacy = \frac{\left(\frac{78}{2304}\right) - \left(\frac{44}{2344}\right)}{\left(\frac{78}{2304}\right)} x\ 100 = 44.6\%$$

In contrast to efficacy, which is calculated for a vaccine under ideal circumstances and 100% vaccine uptake, a vaccine's effectiveness measures how well a vaccine performs when it is used in normal circumstances in a community. It can also measure the net benefits compared to adverse effects of a vaccination program. A vaccine's effectiveness is proportional to vaccine efficacy, but is also affected by vaccine uptake in a target population and nonvaccine-related factors such as hospitalization rates, ambulatory visits, and costs.

The CDC Vaccine Effectiveness (VE) Network is composed of five study sites across the U.S. that work together to conduct studies to measure the effectiveness of seasonal influenza vaccination each year. These prospective case-control studies include patients with acute respiratory illness and cough and utilize a highly accurate laboratory test to confirm influenza infection, with the cases being those that test positive for influenza virus and the controls being

those that test negative. Each patient's vaccination status is then confirmed by self reporting and medical records. VE estimates are calculated as a rate difference using the odds ratio (OR) for developing infection despite vaccination (e.g., the odds of vaccination among outpatients with acute respiratory illness and laboratory-confirmed influenza infection compared to the odds of vaccination among outpatients with acute respiratory illness who test negative for influenza infection).

$$VE = (1 - OR)\ x\ 100$$

The CDC has conducted VE studies for the seasonal influenza vaccine since the 2004-2005 influenza season, with the results shown in the following table.

Influenza Season	Study Site(s)	No. of Patients	Adjusted Overall VE
2004-05	WI	762	10%
2005-06	WI	346	21%
2006-07	WI	871	52%
2007-08	WI	1914	37%
2009-10	WI, MI, NY, TN	6757	56%
2010-11	WI, MI, NY, TN	4757	60%
2011-12	WI, MI, PA, TX, WA	4771	47%
2012-13	WI, MI, PA, TX, WA	6452	49%
2013-14	WI, MI, PA, TX, WA	5990	51%
2014-15	WI, MI, PA, TX, WA	9329	23%

Source: Centers for Disease Control / Zacks SCR

The VE numbers shown above point to one of the main problems with the currently available seasonal vaccine, which is that if the vaccine is not matched up well with the strain of influenza that circulates the following season there is a very low effectiveness (e.g., in last year's 2014-2015 influenza season, the VE was only 23%). If a poor match is determined between the vaccine and the circulating strain there is nothing that can be done since it takes approximately six months to produce sufficient quantities of the vaccine and begin dispensing them.

Influenza and the Elderly

While influenza can be a serious disease for people of all ages, those that are age 65 and older are the most vulnerable to developing complications from influenza, including death. Mortality associated with seasonal influenza disproportionately affects elderly persons as 90% of influenza-related deaths occur in persons aged 65 years or older (Thompson *et al*., 2003). This is due in part to the fact that the seasonal influenza vaccine is not as effective in the elderly, with VE rates as low as 9% in this population (WHO). Complicating matters is the fact that 80% of elderly individuals suffer from some type of chronic illness (National Council on Aging), and influenza is known to worsen outcomes in those with chronic diseases. The total economic impact of influenza in the elderly population is estimated at approximately $56 billion (Molinari *et al*., 2007).

From 1989 to 1997, the influenza vaccination rate for persons aged 65 and older in the U.S. increased from 30% to 67%, however mortality and hospitalization rates continued to increase rather than decline as would be expected (Glezen *et al*., 2006). Part of the reason for this could be due to declining immunological function and frailty that are experienced by elderly patients. For this reason, a new high-dose seasonal influenza vaccine has been formulated (Fluzone® High Dose) that was reported to have relative efficacy of 24.2% compared to the standard dose vaccination in elderly patients (DiazGranados *et al*., 2014). While encouraging, these results were obtained during influenza seasons where there was a relatively good match between the seasonal vaccine and circulating strains, and different results could possibly be seen in years where the relatedness between the vaccine and circulating strains differed materially.

The Need for a Better Influenza Vaccine

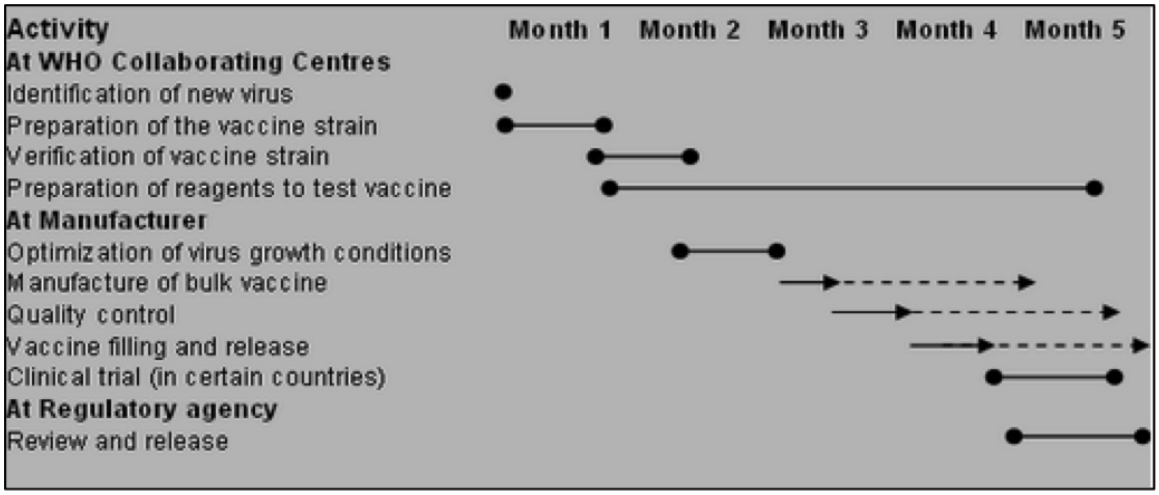
The preceding discussion on currently available influenza vaccines identifies a number of deficiencies, including:

- **Strain Specificity**: The current seasonal influenza vaccine is only formulated against three or four specific past strains of the influenza virus, which are identified based upon worldwide laboratory monitoring and identification of the most likely strains to be circulating through the population during the next influenza

season. In a pandemic situation, by the time that the industry formulates the pandemic strain-specific vaccine, approximately six months after the outbreak and identification of the pandemic flu strain, different drifted pandemic strains will circulate that will result in mismatch and a reduced pandemic vaccine effectiveness.

- **New Vaccine Required Every Year**: Due to antigenic drift, a seasonal influenza vaccine only offers (limited) protection for one season, and must be reformulated and re-administered every year.

- **Long Production Cycle**: The seasonal influenza vaccine takes approximately five to six months to be produced from the initial identification of a new viral strain to being reviewed and approved by regulatory authorities. The timetable shown below is from the WHO.



Source: WHO

- **Limited Immunological Response**: The seasonal influenza vaccines elicit a humoral response from the immune system which results in the production of antibodies directed against the influenza virus (specifically against HA). However, there is little if any generation of influenza virus-specific T-cells, which are the primary means through which the body eliminates virally-infected cells in the body.

- **Egg Allergies**: The majority of seasonal and pandemic influenza vaccines are produced in fertilized hen eggs, thus they cannot be administered to individuals with egg allergies.

Clearly, based upon the aforementioned shortcomings, there is a significant unmet need for a more effective influenza vaccine that can overcome these deficiencies. In particular, there is a need for a more robust vaccine to overcome the most significant challenge of the seasonal influenza vaccine, which is strain-specificity brought about by the sometimes inaccurate forecasting of which influenza strains to target.

M-001

BiondVax has developed the M-001 vaccine, a synthetic peptide-based protein that targets both existing and future seasonal and pandemic strains of the influenza virus. The vaccine targets conserved regions of Type A and B influenza viruses such that M-001 could be considered a “universal” influenza vaccine, capable of offering immunological protection against all strains of the influenza virus.

The company is planning to seek regulatory approval through a two-part strategy:

1. As a “Universal Primer” to be used before any HA-based flu vaccine. BiondVax targets two indications for its universal primer: i) seasonal primer for influenza vaccine in the elderly, and ii) pandemic primer for national stockpile.
2. As a stand-alone independent “universal” vaccine against influenza.

Many infectious diseases have been eradicated over the past century, for example polio and smallpox, thanks to vaccination. In order to eradicate an infectious disease, a community (or herd) immunity must be achieved. Three conditions are required to achieve community immunity:

1. An effective vaccine,
2. Broad coverage and unchanging vaccine formulation, and
3. Enough people to be vaccinated.

With a universal flu vaccine such as BiondVax's M-001, it appears theoretically possible, for the first time in history, to achieve the goal of influenza eradication.

M-001 Composition

M-001 is composed of nine peptides that are believed to be common to most known influenza strains in existence, in part because these peptides seem to be critical for the virus' ability to infect a host cell. They are derived from hemagglutinin (HA), matrix 1 (M1) and nucleoprotein (NP) viral proteins and are arranged as triplicates into a single recombinant protein easily manufactured in bacteria. As discussed above, HA is an antigenic glycoprotein found on the surface of influenza viruses and is also the main constituent for a number of seasonal influenza vaccines. However, the peptides from HA in M-001 are derived from the inner parts of the protein where little to no variability between strains exists. M1 is a matrix protein that forms a layer under the patches of the viral cell membrane that contain HA, NA, and M2 proteins, and is responsible for mediating the encapsulation of RNA-nucleoprotein complexes into the membrane envelope (Sha *et al*., 1997). NP is a structural protein that encapsidates the viral RNA inside the virus. The sequence of each of the peptides is shown below, along with the order in which the peptides are arranged in the full-length recombinant protein.

Peptide	Amino Acids Sequence
Hemagglutinin (HA) epitope 1	PKYVKQNTLKLAT
Hemagglutinin (HA) epitope 2	SKAYSNCYPYDVPDYASL
Hemagglutinin (HA) epitope 3	WLTGKNGLYP
Hemagglutinin (HA) epitope 4	WTGVTQN
Hemagglutinin (HA) epitope 5	PAKLLKERGFFGAIAGFLE
Nucleoprotein (NP) epitope 6	FWRGENGRKTRSAYERMCNILKGK
Nucleoprotein (NP) epitope 7	SAAFEDLRVLSFIRGY
Nucleoprotein (NP) epitope 8	ELRSRYWAIRTRSG
Matrix (M) epitope 9	SLLTEVETYVP

(HA epitope 1) - (HA epitope 2) - (M1 epitope 9) - (HA epitope 3) - (HA epitope 4) - (NP epitope 6) - (HA epitope 5) - (NP epitope 7) - (NP epitope 8).

Source: Atsmon *et al*., 2012

The peptides were selected based upon their ability to elicit either a B- or T-cell immune response and each of them has the ability to bind to a wide array of human leukocyte antigen (HLA) proteins (both Class I and Class II), which are responsible for presenting peptides to the immune system. Some may question the use of peptides from proteins located inside the virus, however there is a strong rationale for their use. It has long been known that a mild influenza infection in animals provides protection against a subsequent, more severe challenge with a virus harboring different HA and NA (Yetter *et al*., 1980). This effect appears to be mediated by both CD4+ and CD8+ T-cells that recognize conserved regions on viral proteins (Furuya *et al*., 2010). The CD4+ T-cells that are specific for conserved internal viral antigens also potentiate antibody responses to the HA of subsequently encountered viruses (Scherle *et al*., 1986). The end result is that immunizing with conserved internal viral antigens results in an increased immunological response to infection following subsequent exposure to influenza viruses.

M-001 Clinical Trial Results

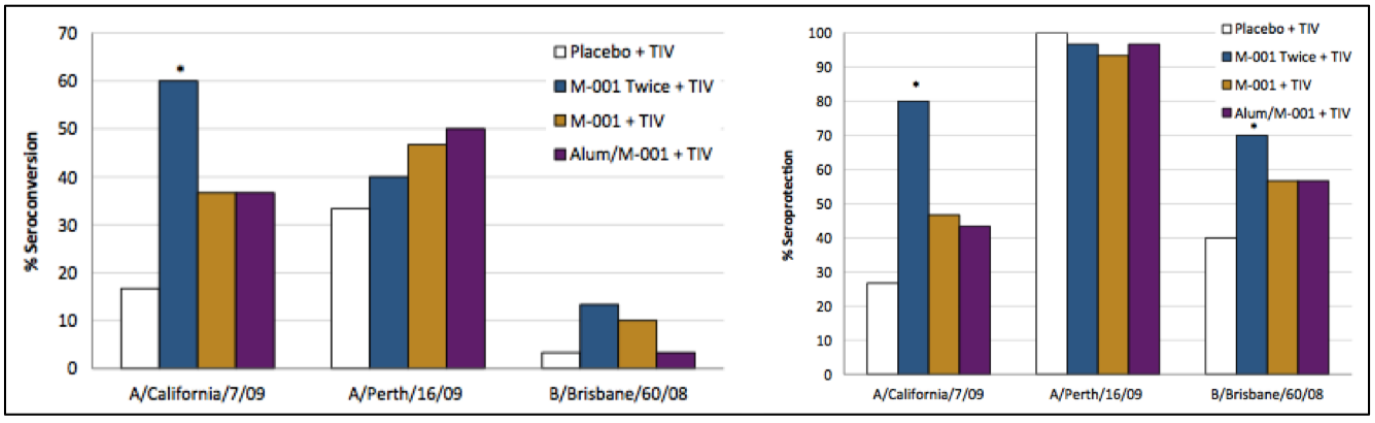
Thus far, M-001 has been tested in 479 participants through five different clinical trials, with the details presented in the following chart. In each of the trials, the vaccine was shown to be safe and able to induce a robust immune response. Due to the fact that M-001 does not target the variable region of HA, the HAI assay cannot be employed as a surrogate endpoint for determining vaccine efficacy when M-001 is administered on its own. Thus, the company has developed additional immunological assays to determine immunogenicity. In addition, in its first stage in bringing M-001 to market, the company is pursuing a "prime-boost" strategy, where M-001 is given prior to immunization with the traditional seasonal influenza vaccine, in which case the HAI assay can be utilized to compare immunogenicity to currently available influenza vaccines. The results from some of those trials are presented below.

Study	ClinicalTrials.gov Identifier	Phase	Year	# Pts	Ages
BVX-002	NCT00877448	1/2	2009	63	18-49
BVX-003	NCT01010737	1/2	2010	60	55-75
BVX-004	NCT01146119	2	2011	200	18-49
BVX-005	NCT01419925	2	2012	120	65+
BVX-006	NCT02293317	2	2015	36	50-65

Source: BiondVax Pharmaceuticals Ltd. / Zacks SCR

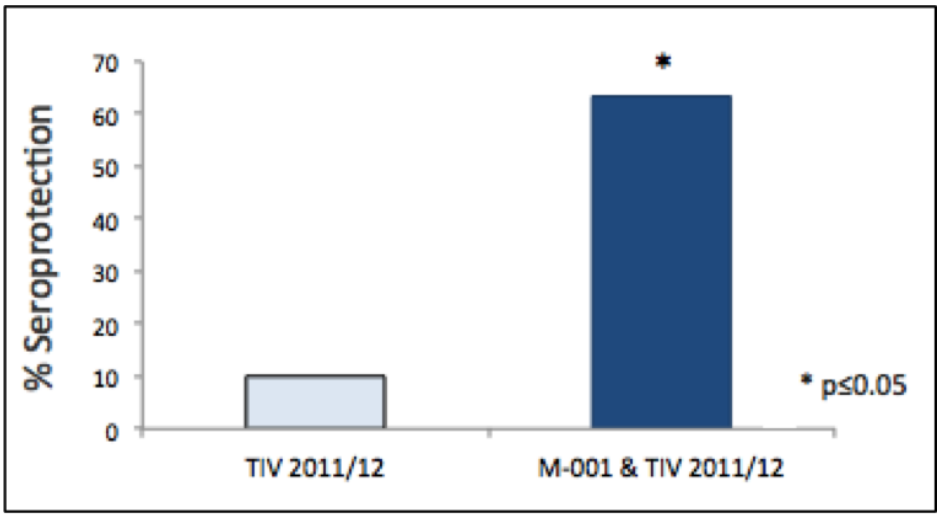
BVX-002 (Atsmon *et al*., 2012): This was a single-center, randomized, placebo controlled, single blind first-in-human study to examine the safety and immunological response to M-001 in healthy adults age 18-49. For safety purposes, three subjects were dosed once with 0.125 mg of M-001 and monitored for 7-9 days before the rest of the patients were administered the planned doses. There were four dosing cohorts, and within each cohort subjects were randomized in a 2:1 fashion to receive either 0.25 mg or 0.5 mg M-001 (n=10) or placebo (n=5), with or without adjuvant. The results showed that M-001 was well tolerated with only mild and moderate adverse events (AEs), with no significant difference between vaccine and placebo recipients for AEs. A robust humoral (antibodies to M-001) and cellular (PBMC proliferation to viral peptides) immune response was noted for participants immunized with M-001, and while there were greater humoral responses in patients immunized with M-001 plus adjuvant, there did not appear to be a difference in cellular response between subjects dosed with adjuvant and those without.

BVX-005 (Atsmon *et al*., 2014): This was a two-center, randomized, placebo controlled study in a total of 120 elderly volunteers (age 65+). The subjects were randomized 1:1:1:1 into four parallel groups to receive either 1) two sequential non-adjuvanted 0.5 mg M-001, or 2) a single non-adjuvanted 0.5 mg M-001, or 3) a single adjuvanted IM injection of 0.5 mg M-001, or 4) one placebo injection. All participants subsequently received the seasonal trivalent influenza vaccine (TIV) three weeks following the last M-001 or placebo injection. The primary outcome measures were safety, tolerability, and tolerance of M-001 with secondary outcomes being humoral and cellular immune responses. The results showed that priming with M-001 enhanced seroconversion towards all three strains in that season's influenza vaccine (denoted on the y-axis in the figure below). The following figure shows the percentage of patients that tested positive for seroconversion (defined as a mean fold increase in anti-HA antibody levels of ≥ four-fold from levels detected in sera collected on day 0, and reaching a level of ≥1:40 post-immunization) and seroprotection (defined as the number of participants per cohort expressing anti-HA antibody levels of ≥1:40 post-immunization). Addition of an adjuvant did not appear to offer any additional immunostimulatory effect.



Source: Atsmon *et al*., 2014

In 2015, a new 'Swiss' epidemic influenza strain (H3N2: A/Switzerland/9715293/13) emerged that did not exist in 2011, which was when the BVX-005 trial took place and the participants in the trial were immunized with M-001. Blood serum samples from the participants in the BVX-005 trial were exposed to the 'Swiss' influenza strain, with results showing that greater than 60% of the M-001 vaccinated group had seroprotection against this new Swiss strain, compared to only 10% of those immunized with just the seasonal vaccine. This suggests that M-001 may offer a broader, long-lasting immune response not just to strains currently in existence, but to future strains that do not even exist yet!



Source: BiondVax Pharmaceuticals, Ltd.

Final Phase 2 Clinical Trials for M-001

BiondVax has initiated two Phase 2 clinical trials that will involve a total of 372 participants; one that is ongoing in Europe (BVX-007) and one that will soon start admitting participants in the U.S. (BVX-008). The BVX-007 trial is currently taking place in Hungary, with support by the European UNISEC Consortium, with enrollment ongoing. The BVX-008 trial is taking place in the U.S. and is being fully funded by the National Institutes of Health (NIH) and conducted by the National Institute of Allergy and Infectious Diseases (NIAID).

BVX-007: This is a Phase 2b clinical trial that is expected to enroll 222 adults (age 18-60). The study will evaluate the safety and immunogenicity of M-001 when used as a primer to the H5N1 avian influenza vaccine. The H5N1 avian influenza vaccine will be given once, at a sub-optimal dose, in order to test whether M-001 can enhance its immunogenicity. If successful, this trial could show the dose sparing potential of M-001, which in the case of a pandemic situation could allow for the available doses of pandemic vaccine to be administered to more subjects. The trial is being funded through a grant from the European Union and is being conducted in conjunction with the European UNISEC Consortium, which is a group of three academic partners, five National Health Institutes, and three companies with the objective to identify, develop, and clinically test the most promising leads for a universal influenza vaccine. We anticipate results from this trial to be reported in the fourth quarter of 2016.

BVX-008: This will be a Phase 2 clinical trial being conducted by the NIAID, which is part of the NIH. The double blind, multicenter, randomized, placebo controlled trial is expected to enroll 150 adults (18-45) and will examine the use of M-001 as a primer vaccine to be given several weeks before the H7N9 avian pandemic vaccine. The primary outcome will be safety and tolerability with secondary endpoints examining humoral and cellular immune responses. We anticipate this trial will begin during the second quarter with results from this trial in late 2016 or early 2017.

BiondVax Regulatory Strategy and Opportunity

BiondVax is pursuing a two-part strategy for the development of M-001 that involves first attaining approval for the vaccine as a “universal” primer for use before any seasonal influenza vaccine in the elderly and before any pandemic influenza vaccine as part of preparing for any pandemic outbreak using a national stockpile of M-001. The company will then continue development of M-001 as a stand-alone independent universal influenza vaccine.

Following the successful completion of the company’s ongoing Phase 2 clinical trials, BiondVax’s management anticipates an end of Phase 2 meeting being held with the FDA in the 2017/18 timeframe such that an Investigational New Drug (IND) application can be filed for Phase 3 clinical trials for M-001. In order to fund the Phase 3 trials, we believe the company is pursuing non-dilutive financial sources either via grants, from royalty bearing regional manufacturing and distribution agreements with down payments, or in collaborations with larger pharmaceutical companies. We believe the Phase 3 program could cost between $25-50 million. The following chart gives additional details about the planned Phase 3 clinical trials.

Indication	Participants in Phase 3 clinical trials	Administration to Control Group	Expected Results
Universal Standalone Indication	Adults	Placebo	Statistically, a higher level of antibodies found in experimental group
Universal Seasonal Primer for Elderly Indication	Elderly population with co-Morbidity	Placebo instead of Primer, seasonal influenza vaccine as Boost.	Statistically, a higher level of antibodies found in experimental group
Universal Pandemic Primer Indication	Adults	Placebo instead of Primer, pandemic influenza vaccine as Boost.	Statistically, a higher level of antibodies found in experimental group

Source: BiondVax Pharmaceuticals, Ltd.

Using M-001 as a universal primer vaccine to be used before any seasonal and pandemic vaccines is a wise strategy, as it allows BiondVax to leverage the existing approved regulatory marker (HAI) for influenza vaccines, and therefore to conduct smaller clinical trials, providing a faster time to market than could be achieved for M-001 as a stand-alone independent vaccine.

We believe that for the seasonal primer for the elderly indication, a post marketing Phase 4 clinical trial with clinical efficacy as an endpoint may be required for obtaining permanent marketing authorization, similar to what was required for the approval of Fluzone HD. The clinical efficacy endpoint is defined as reduction of illness rate and severity, and will require significantly more participants than for the primer indications. The stand-alone indication will also require a clinical efficacy endpoint, however that will be part of the Phase 3 progam.

The company has already shown that M-001 enhances the immunogenicity of the seasonal vaccine in young adults and elderly participants, including to the pandemic H1N1 swine flu strain that is included in the seasonal flu vaccines since 2010. Currently the company, together with the UNISEC consortium (EU) and the NIH/NIAID (US), is testing the ability of the vaccine to be used as a universal pandemic primer vaccine. Both of these indications are potentially quite lucrative.

There were approximately 135 million doses of the influenza vaccine administered last year with approximately 20% of those administered to the elderly. Assuming a 33% penetration rate which will use M-001 as part of prime-boost vaccine, then at approximately $20 per dose (based on a midpoint between the Fluzone HD geared to the elderly price of $28 and the standard Fluzone price of $8 per dose) it is a potential $200 million opportunity just in the U.S.

Another market is the pandemic primer for national stockpile. The critical workforce in the U.S. is approximately 15% of the population (20 million people), and 1/3rd of the stockpile is replaced annually (given a shelf-life of three years). At $12 per dose that represents another $240 million opportunity. The total influenza vaccine market is expected to be over $5 billion by 2021, so even with only a 10% penetration rate, that is a potential $500 million annual opportunity.

Other Universal Influenza Vaccines Under Development

There are a number of other companies developing universal influenza vaccines, however BiondVax appears to be the furthest ahead in development.

- **SEEK**: Seek is developing a universal influenza vaccine based on six unique peptides that induce a cellular response by the immune system. The vaccine, Flu-v, has been tested in 80 individuals in a Phase 1 and a Phase 2 clinical trial. Results from those studies showed that vaccinated subjects had significantly lower symptom scores and viral titer levels compared with non-vaccinated subjects. In addition, blood from vaccinated subjects showed a cross-reactive immunity to both Type-A and Type-B influenza viruses.

- **Inovio**: Inovio is developing synthetic DNA vaccines against both seasonal and pandemic strains of the influenza virus. The company has conducted two Phase 1 open label studies to evaluate the safety, tolerability, and immune responses against multiple combinations of Type A influenza subtypes. Both studies showed the vaccine to be safe and well tolerated as well as capable of generating a robust immune response.

- **FluGen**: FluGen is developing a vaccine made from a genetically engineered influenza virus, M2SR, that has a specific deletion in the viral genome. This deletion allows for only a single replication of the vaccine

virus within the host cell, which results in long-lasting, cross-protective immunity against multiple viral subtypes without the generation of progeny virions. The company recently raised $12 million in order to perform a Phase 1 clinical trial.

Financials and Capital Structure

BiondVax is well capitalized and has a very lean structure with minimal cash burn each quarter.

As of September 30, 2015, the company had $10.4 million in cash and cash equivalents due to a U.S. initial public offering in May 2015 of 1.9 million American Depository Shares (ADSs), with each ADS representing 40 of the company's common shares, which are listed on the Tel Aviv Stock Exchange. The ADSs were sold for $5 per ADS, gaining investors one share and one warrant (convertible at $6.25 to 1 share). This netted the company gross proceeds of $9.6 million. In June 2015, the company closed an additional and partial exercise of the over-allotment option granted to the underwriters, who purchased 110,000 additional ADSs for $5 per ADS. Total gross proceeds to BiondVax from the offering were approximately $10.1 million. The company is currently burning approximately $250,000 per month. It is noted that its two ongoing clinical trials (BVX-007 and BVX-008) are being funded primarily by third parties. We estimate there is sufficient capital to fund operations until mid-2018, and if the warrants are converted to shares, it will provide additional funds (of up to $13.3 million). In addition, there is no debt on the balance sheet.

BiondVax's common shares are traded on the Tel-Aviv Stock Exchange while the company's ADSs are traded on the Nasdaq. There are currently 135 million shares outstanding (listed in Tel Aviv), or 3.4 million ADSs (listed on Nasdaq), and when factoring in the options and warrants the company has a fully diluted share count of approximately 251 million shares, or 6.3 million ADSs.

The following table breaks down the company's capital structure.

Sep 30, 2015	Shares Outstanding	ADS Equivalent	%	Exercise price NIS ($)	ADS Equivalent	Expiration Date
	ADS-Shares 1:40 ratio					
Ordinary shares	**135,097,367**	**3,377,434**	**53.76%**			
Options	13,215,367	330,384	5.26%	NIS 0.70 ($ 0.18)	$ 7.20	Employees Variable
Options (Series 3)	5,650,000	141,250	2.25%	NIS 1.80 ($ 0.46)	$ 18.40	Nov 6, 2016
Options (Series 4)	5,685,000	142,125	2.26%	NIS 1.50 ($ 0.39)	$ 15.60	Feb 27, 2017
Options (Series 5)	6,302,000	157,550	2.51%	NIS 1.50 ($ 0.39)	$ 15.60	Oct 29, 2017
ADS Warrants	81,520,000	2,038,000	32.44%	$ 6.25		May 5 , 2022
Warrants issued to underwriters	3,820,000	95,500	1.52%	$ 6.25		May 11, 2022
Fully Diluted Shares Outstanding	**251,289,734**	**6,282,243**	**100.00%**			

Source: BiondVax Pharmaceuticals, Inc.

Intellectual Property

BiondVax has an exclusive worldwide license agreement to two patent families from Yeda Research and Development Company Ltd., which is an affiliate of the Weizmann Institute of Science in Israel, along with patents that are assigned and/or filed by the company. The patents, along with their expiration dates, are shown below and give strong IP protection covering:

- The conserved peptides used in BiondVax's universal flu vaccines;
- Their preparation; and
- Their use for protection against influenza;

Patent applications where filed in major countries in the world have tentative expiration dates until 2035. In some countries (e.g., the U.S.) patent term extension of up to five additional years may be granted upon receiving drug approval.

Title	International Publication	Subject Matter	Priority & Assignee	Status	Expiry
Peptide-Based Vaccine for Influenza	WO 00/032228	Vaccine comprising different epitopes of the virus	11/30/1998 Yeda R&D licensed to BiondVax	**Granted:** USA, Israel, Australia, Korea, Mexico, New Zealand, Canada, Hong Kong, Austria, Belgium, France, Germany, Italy, Netherlands, Sweden, Spain, Switzerland, UK	Nov 2019 (Aug 2020 for US-1)
Improved Influenza Vaccine	WO 2007/066334	Wide–range vaccines – broad strain and extended protection	12/6/2005 Yeda R&D licensed to BiondVax	**Granted:** USA, Australia, Austria, Belgium, Canada, Denmark, France, Germany, Greece, Ireland, Israel, Italy, Luxembourg, Netherlands, Portugal, Sweden, Spain, Switzerland, UK	Dec 2026 (Jan 2017 for US)
Multimeric Multi-Epitope Influenza Vaccines	WO 2009/016639	Vaccines comprising multiple copies of several epitopes – current product	8/2/2007 BiondVax	**Granted:** US, Mexico, Russia, Australia, China, Hong Kong, Japan, Austria, Belgium, Croatia, Czech Republic, Denmark, Finland, France, Germany, Hungary, Ireland, Italy, Luxembourg, Netherlands, Poland, Portugal, Romania, Spain, Sweden, Switzerland, Turkey, UK, Korea **Filed:** Brazil **Under Examination:** Israel, Canada, India	Aug 2028 (Aug 2031 for US)
Multimeric Multi-Epitope Polypeptides in Improved Seasonal and Pandemic Influenza Vaccines	WO 2012/114323	Use of Multimeric as a primer to conventional vaccines	BiondVax	**Filed:** Australia, Canada **Under Examination:** USA	Feb 2031
Vaccine Compositions of Multimeric Multi-epitope Influenza Polypeptides and their Production	WO 2015/151103	Production & formulation	4/3/2014 BiondVax	**International application filed** : April 2015	April 2035

Source: BiondVax Pharmaceuticals Ltd.

Risks to Consider

Additional Capital Will Be Necessary to Fund Phase 3 Trials: The company currently does not have enough cash to conduct the Phase 3 trials that will be necessary to seek FDA approval for M-001 as a universal primer for the seasonal influenza vaccine in the elderly and as a universal primer for pandemic strain-specific vaccines. Raising additional capital from the capital markets could result in significant dilution to current shareholders. If the company enters into strategic collaborations or partnerships in order to fund the Phase 3 program, it may be necessary to relinquish some rights of the company's technologies and products as a result of royalty bearing regional manufacturing and distribution agreements with down payments in selected territories.

M-001 May Not Be Successful in Future Clinical Trials: While M-001 has shown to been safe and well tolerated in the clinical trials that have been conducted thus far, there is no guarantee that the compound will show efficacy or meet end-points in Phase 3 clinical trials that involve thousands of patients. In addition, it is possible that safety signals not seen in earlier clinical trials could arise when M-001 is tested in a much larger cohort of subjects.

M-001 is Currently the Company's Only Product Under Development: BiondVax is solely focused on the development of M-001 as it is the only product currently in the company's pipeline. Thus, the company's success relies solely on the ability to commercialize M-001.

MANAGEMENT PROFILES

Ron Babecoff, DVM – President and CEO
Dr. Babecoff has led the company as its President and CEO since its inception. He has guided the company through 5 successful clinical trials (Phase 1/2 and 2), and two ongoing Phase 2 trials in collaboration with the E.U. and the U.S. NIH towards the Phase 3 development of M-001. Prior to founding BiondVax, Dr. Babecoff worked for 10 years in marketing and business development in the pharmaceutical industry. As Marketing Manager at Omrix Biopharmaceuticals Ltd., he was responsible for marketing, sales training, public relations, and new product development. His professional experience ranges from identifying West Nile Fever treatments, building cooperation with the NIH, to forming alliances with leading international pharmaceutical companies. Dr. Babecoff holds a D.V.M. degree from the University of Liège (ULg), Belgium and a Master of Entrepreneurship and Innovation (MEI) from the Swinburne University of Technology of Melbourne, Australia.

Tamar Ben-Yedidia, PhD – Chief Scientific Officer
Dr. Ben-Yedidia has more than 15 years of experience in the field of Immunology, with specific expertise in the development of vaccines. She started her career with Biotechnology General Ltd, BTG (Rehovot), working on the development of a recombinant Hepatitis-B vaccine. She joined the Weizmann Institute of Science in 1994, and under the auspices of Prof. Ruth Arnon in the Department of Immunology, worked on the design of a peptide-based vaccine against several pathogens and focused on influenza. She continued this work when she left the Weizmann Institute in 2004 to join BiondVax. Dr. Ben-Yedidia was involved in two European Consortium projects related to evaluation of different approaches for vaccination in which leading laboratories in the field participated. Dr. Ben-Yedidia is widely published, with numerous refereed articles and invited reviews in various renowned scientific journals. She received her Ph.D. from the Weizmann Institute after completion of her doctoral thesis entitled *"A Peptide-Based Vaccine Against Influenza"*.

Shimon Hassin, PhD – Chief Operating Officer
Dr. Hassin has over 10 years of experience in biotechnology, with specific expertise in the development of biopharmaceuticals. Prior to joining the company, Dr. Hassin was co-founder and CEO of Kadimastem, an embryonic stem cell company developing an artificial pancreas for curing Juvenile Diabetes. Before joining BiondVax, he worked at InSight Biopharmaceuticals, a leading Israeli biotechnology company active in the area of Biogenerics. In his capacity as Head of Process Development he was responsible for the manufacturing of a variety of Biogenerics such as therapeutic antibodies, cytokines and hormones. Dr. Hassin holds a Ph.D. in Biotechnology from the University of Maryland Biotechnology Institute and was a post-doctoral associate at the University of Bergen Center of Marine Biotechnology.

Uri Ben-Or – Chief Financial Officer
Mr. Ben-Or brings over a decade of broad experience in corporate finance, accounting, M&A transactions, IPO's and operations. He provides his services to BiondVax through CFO Direct, a company that he founded and is the Chief Executive Officer. Prior to founding CFO Direct he served as the VP Finance of Glycominds, a leading biotechnology company, and as CFO of a spin-off from Telrad Networks, where he led all the corporate finance activities, fund raising, and legal aspects of the company. He also served as a Corporate Controller at Menorah Capital Markets and as an Auditor at PriceWaterhouseCoopers. Mr. Ben-Or holds a BA degree in Business from the College of Administration, and a MBA degree from the Bar Ilan University. He is a Certified Public Accountant.

VALUATION AND RECOMMENDATION

We are initiating coverage of BiondVax Pharmaceuticals Ltd. (Nasdaq: BVXV) with a Buy rating and a price target of $17.00. BiondVax is an advanced clinical stage biopharmaceutical company developing immunomodulation therapies for infectious diseases. The company's lead product candidate, M-001, is a peptide-based vaccine that offers long-lasting protection against multiple strains of both seasonal and pandemic influenza virus, in contrast to the currently available influenza vaccines that must be administered yearly and only offer protection against a limited range of specifically targeted influenza strains.

M-001

The company's lead compound is M-001, a synthetic peptide-based protein vaccine that targets both existing and future seasonal and pandemic strains of the influenza virus. M-001 is composed of nine peptides that are believed to be common to most known influenza strains in existence, in part because these peptides seem to be critical for the virus' ability to infect a host cell. They are derived from hemagglutinin (HA), matrix 1 (M1) and nucleoprotein (NP) viral proteins and are arranged as triplicates into a single recombinant protein easily manufactured in bacteria. The peptides were selected based upon their ability to elicit either a B- or T-cell immune response and each of them has the ability to bind to a wide array of human leukocyte antigen (HLA) proteins (both Class I and Class II), which are responsible for presenting peptides to the immune system.

Thus far, M-001 has been tested in 479 participants through five different clinical trials. In each of the trials, the vaccine was shown to be safe and able to induce a robust immune response. BiondVax has initiated two final Phase 2 clinical trials that will involve a total of 372 participants; one that is ongoing in Europe (BVX-007) and one that will soon start admitting participants in the U.S. (BVX-008). The BVX-007 trial is currently taking place in Hungary, with support by the European UNISEC Consortium, with enrollment ongoing. The BVX-008 trial is taking place in the U.S. and is being fully funded by the National Institutes of Health (NIH) and conducted by the National Institute of Allergy and Infectious Diseases (NIAID).

The company is planning to seek regulatory approval through a two-part strategy:

1. As a "Universal Primer" to be used before any HA-based flu vaccine. BiondVax targets two indications for its universal primer: i) seasonal primer for influenza vaccine in the elderly, and ii) pandemic primer for national stockpile.
2. As a stand-alone independent "universal" vaccine against influenza.

Following the successful completion of the company's ongoing Phase 2 clinical trials, BiondVax's management anticipates an end of Phase 2 meeting being held with the FDA in the 2017/18 timeframe such that an Investigational New Drug (IND) application can be filed for Phase 3 clinical trials for M-001. We believe the Phase 3 clinical trials will cost between $25-50 million, and anticipate the company will pursue non-dilutive financing either via grants, from royalty bearing regional manufacturing and distribution agreements with down payments, or in collaborations with larger pharmaceutical companies.

Valuation Methodology

We value BiondVax using a probability adjusted discounted cash flow model that takes into account potential revenues from the sale of M-001 as 1) a seasonal primer for influenza vaccine in the elderly; 2) a pandemic primer for a national stockpile; and 3) a stand-alone independent universal influenza vaccine. At this point, we are assuming that the company will enter into one or more partnerships with larger pharmaceutical companies that will result in BiondVax receiving royalties (we model 15% for all indications) on the sale of M-001.

As a primer for both the seasonal vaccine in the elderly and a pandemic stockpile, we model for the current Phase 2 clinical trials to be completed by the first half of 2017. This will allow for an end-of-Phase 2 meeting with the FDA and initiation of a Phase 3 program in 2018, regulatory filings in 2020, and approval in 2021.

In the U.S., there were approximately 135 million doses of the influenza vaccine administered last year with approximately 20% of those administered to the elderly. Assuming a 33% penetration rate which will use M-001 as part of prime-boost vaccine, then at approximately $20 per dose (based on a midpoint between the Fluzone HD

geared to the elderly price of $28 and the standard Fluzone price of $8 per dose) it is a potential $200 million opportunity just in the U.S. We believe the rest of the world represents a potential $300 million peak opportunity. We apply an 18% discount rate and a 50% probability of approval to arrive at a net present value for M-001 as a primer for seasonal vaccination in the elderly of $41 million.

Another market is the pandemic primer for national stockpile. The critical workforce in the U.S. is approximately 15% of the population (20 million people), and 1/3rd of the stockpile is replaced annually (given a shelf-life of three years). At $12 per dose that represents another $240 million annual opportunity. We apply an 18% discount rate and a 50% probability of approval to arrive at a net present value for M-001 as a primer for a pandemic vaccine of $34 million.

As a stand-along universal vaccine, we anticipate Phase 3 trials initiating in 2019 with a regulatory filing in 2021 and approval in 2022. By that time we model for approximately 140 million doses of the influenza vaccine being administered in the U.S., and with a peak market share of 25%, we model for peak revenues of over $700 million. We apply an 18% discount rate and a 33% probability of approval to arrive at a net present value for M-001 as a stand-along universal vaccine of $36 million.

Combining the net present value for each of the company's development programs along with the company's cash total as of September 30, 2015 ($9.4 million) and expected operating burn of $15 million, we arrive at a net present value for the company of approximately $106 million. Dividing this by the company's fully diluted share count of 6.3 million ADSs leads to a fair value of approximately $17 per share, and we are assigning a 'Buy' rating to the stock.

PROJECTED FINANCIALS

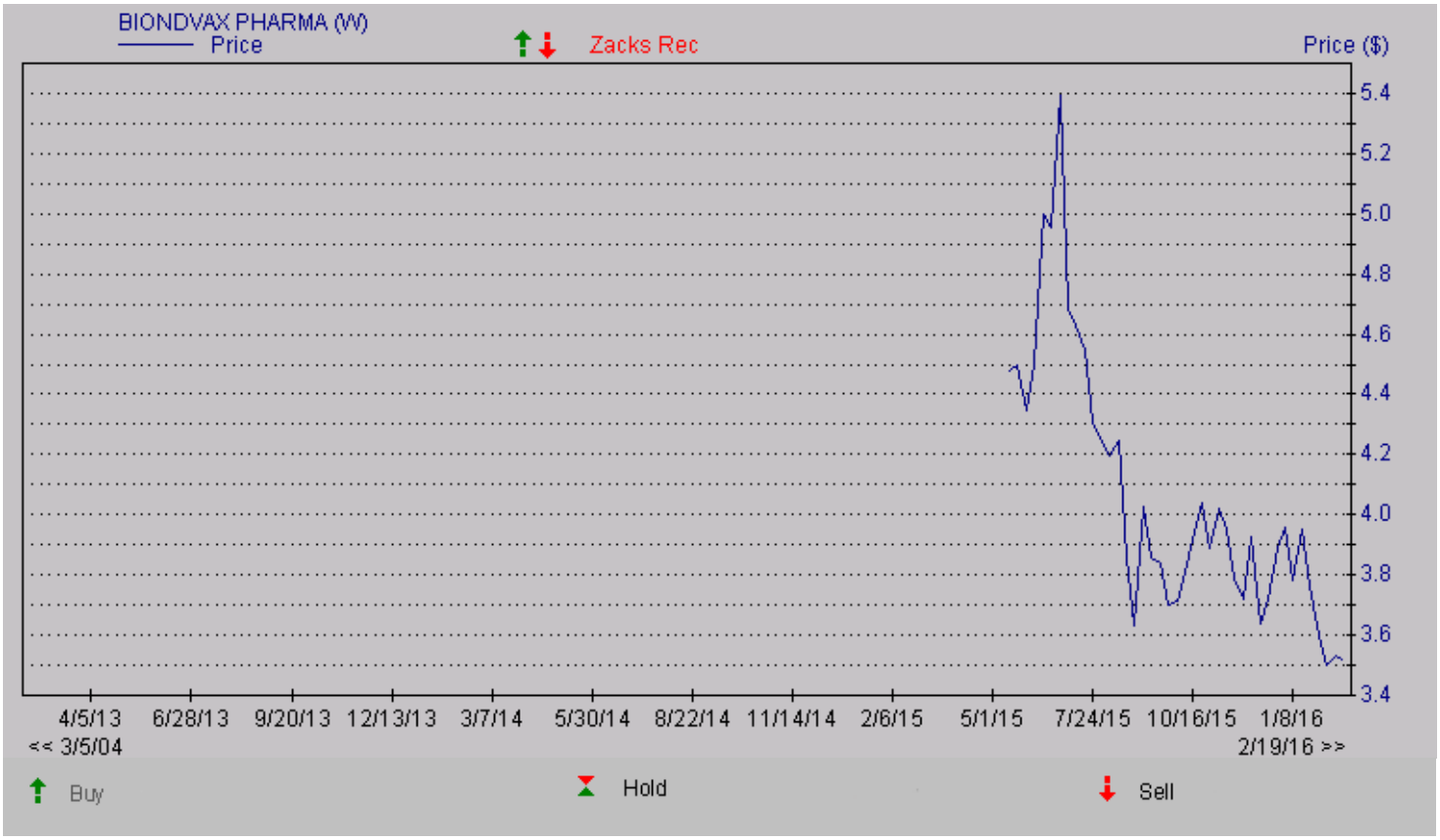
BiondVax Pharmaceuticals, Ltd.
Income Statement

BiondVax Therapeutics, Ltd.	2014 A	Q1 A	Q2 A	Q3 A	Q4 E	2015 E	2016 E	2017 E
M-001 (Elderly Primer)	$0	$0	$0	$0	$0	$0	$0	$0
YOY Growth	-	-	-	-	-	-	-	
M-001 (Pandemic Primer)	$0	$0	$0	$0	$0	$0	$0	$0
YOY Growth	-	-	-	-	-	-	-	
M-001 (Universal Vaccine)	$0	$0	$0	$0	$0	$0	$0	$0
YOY Growth	-	-	-	-	-	-	-	
Grants & Collaborative Revenue	$0	$0	$0	$0	$0	$0	$0	$0
YOY Growth	-	-	-	-	-	-	-	
Total Revenues	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**
YOY Growth	-	-	-	-	-	-	-	
Cost of Sales	$0	$0	$0	$0	$0	$0	$0	$0
Product Gross Margin	-	-	-	-	-	-	-	
Research & Development	$1.4	$0.3	$0.7	$0.3	$0.4	$1.7	$15.0	$18.0
General & Administrative	$0.7	$0.2	$0.2	$0.2	$0.3	$0.8	$12.0	$14.0
Other Expenses	$0	$0	$0	$0	$0	$0	$0	$0
Operating Income	($2.1)	($0.5)	($0.8)	($0.6)	($0.7)	($2.5)	($27.0)	($32.0)
Operating Margin	-	-	-	-	-	-	-	
Non-Operating Expenses (Net)	$0.1	($0.0)	($0.5)	$0.5	($0.1)	($0.1)	($0.1)	($0.1)
Pre-Tax Income	($2.0)	($0.5)	($1.4)	($0.1)	($0.8)	($2.6)	($27.1)	($32.1)
Income Taxes Paid	$0	$0	$0	$0	$0	$0	$0	$0
Tax Rate	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*
Net Income	**($2.0)**	**($0.5)**	**($1.4)**	**($0.1)**	**($0.8)**	**($2.6)**	**($27.1)**	**($32.1)**
Net Margin	-	-	-	-	-	-	-	
Reported EPS	**($0.04)**	**($0.01)**	**($0.02)**	**($0.00)**	**($0.01)**	**($0.03)**	**($0.19)**	**($0.20)**
YOY Growth	-	-	-	-	-	-	-	
Basic Shares Outstanding	54.3	54.3	75.3	95.5	136.0	90.3	145.0	160.0
Basic ADS Outstanding			1.9	2.4	3.4	2.3	3.6	4.0

Source: Zacks Investment Research, Inc. *David Bautz, PhD*

© Copyright 2016, Zacks Investment Research. All Rights Reserved.

HISTORICAL ZACKS RECOMMENDATIONS



© Copyright 2016, Zacks Investment Research. All Rights Reserved.

DISCLOSURES

The following disclosures relate to relationships between Zacks Small-Cap Research ("Zacks SCR"), a division of Zacks Investment Research ("ZIR"), and the issuers covered by the Zacks SCR Analysts in the Small-Cap Universe.

ANALYST DISCLOSURES

I, David Bautz, PhD, hereby certify that the view expressed in this research report accurately reflect my personal views about the subject securities and issuers. I also certify that no part of my compensation was, is, or will be, directly or indirectly, related to the recommendations or views expressed in this research report. I believe the information used for the creation of this report has been obtained from sources I considered to be reliable, but I can neither guarantee nor represent the completeness or accuracy of the information herewith. Such information and the opinions expressed are subject to change without notice.

INVESMENT BANKING, REFERRALS, AND FEES FOR SERVICE

Zacks SCR does not provide nor has received compensation for investment banking services on the securities covered in this report. Zacks SCR does not expect to receive compensation for investment banking services on the Small-Cap Universe. Zacks SCR may seek to provide referrals for a fee to investment banks. Zacks & Co., a separate legal entity from ZIR, is, among others, one of these investment banks. Referrals may include securities and issuers noted in this report. Zacks & Co. may have paid referral fees to Zacks SCR related to some of the securities and issuers noted in this report. From time to time, Zacks SCR pays investment banks, including Zacks & Co., a referral fee for research coverage.

Zacks SCR has received compensation for non-investment banking services on the Small-Cap Universe, and expects to receive additional compensation for non-investment banking services on the Small-Cap Universe, paid by issuers of securities covered by Zacks SCR Analysts. Non-investment banking services include investor relations services and software, financial database analysis, advertising services, brokerage services, advisory services, investment research, investment management, non-deal road shows, and attendance fees for conferences sponsored or co-sponsored by Zacks SCR. The fees for these services vary on a per client basis and are subject to the number of services contracted. Fees typically range between ten thousand and fifty thousand per annum.

POLICY DISCLOSURES

Zacks SCR Analysts are restricted from holding or trading securities in the issuers which they cover. ZIR and Zacks SCR do not make a market in any security nor do they act as dealers in securities. Each Zacks SCR Analyst has full discretion on the rating and price target based on his or her own due diligence. Analysts are paid in part based on the overall profitability of Zacks SCR. Such profitability is derived from a variety of sources and includes payments received from issuers of securities covered by Zacks SCR for services described above. No part of analyst compensation was, is or will be, directly or indirectly, related to the specific recommendations or views expressed in any report or article.

ADDITIONAL INFORMATION

Additional information is available upon request. Zacks SCR reports are based on data obtained from sources we believe to be reliable, but are not guaranteed as to be accurate nor do we purport to be complete. Because of individual objectives, this report should not be construed as advice designed to meet the particular investment needs of any investor. Any opinions expressed by Zacks SCR Analysts are subject to change without notice. Reports are not to be construed as an offer or solicitation of an offer to buy or sell the securities herein mentioned.

ZACKS RATING & RECOMMENDATION

ZIR uses the following rating system for the 1242 companies whose securities it covers, including securities covered by Zacks SCR:
Buy/Outperform: The analyst expects that the subject company will outperform the broader U.S. equity market over the next one to two quarters.
Hold/Neutral: The analyst expects that the company will perform in line with the broader U.S. equity market over the next one to two quarters.
Sell/Underperform: The analyst expects the company will underperform the broader U.S. Equity market over the next one to two quarters.

The current distribution is as follows: Buy/Outperform- 24.2%, Hold/Neutral- 53.1%, Sell/Underperform – 17.0%. Data is as of midnight on the business day immediately prior to this publication.