

## Company Report - Hemispherx Biopharma (HEB)

*Hemispherx Biopharma is an exception under the numerous biopharmaceutical companies for it has already a product for sale. It has successfully completed a Phase III clinical trial treating over 230 patients for which the Company plans to file an NDA later this year and it's on the forefront of developing vaccines against Avian Flu and SARS.*



### A. Company Description

Hemispherx Biopharma, based in Philadelphia, is a biopharmaceutical company engaged in the manufacture and clinical development of new drug entities for treatment of viral and immune-based disorders. Hemispherx's flagship products include Alferon N Injection® and the experimental immunotherapeutics/antivirals Ampligen® and Oragens®.

Alferon N Injection® is the company's registered trademark for its injectable formulation of Natural Alpha Interferon, and is approved by the FDA for a category of STD infection. Alferon N Injection® (interferon alfa-n3 human leukocyte derived) is a highly purified, natural source, glycosylated, multispecies alpha interferon product, composed of eight forms of high-purified alpha interferon. Alferon LDO® (Low Dose Oral) is a new experimental drug delivery platform for the Company's highly purified, natural source alpha interferon.

Ampligen® is a synthetic specifically configured double-stranded RNA containing regularly occurring regions of mismatching. Ampligen® and Oragens® experimental nucleic acids are being developed for the potential treatment of globally important viral diseases and disorders of the immune system including HPV, HIV, Chronic Fatigue Syndrome (CFS), Hepatitis and influenza.

Hemispherx's platform technology includes large and small agent components for potential treatment of various viral infections. Hemispherx has in excess of 100 patents comprising its core intellectual property estate covering various forms of double stranded (ds) RNA and their fields of

<b>Symbol:</b>	<b>HEB</b>
<b>Industry:</b>	Biotechnology
<b>Market:</b>	AMEX
<b>Recent Price:</b>	\$2.67
<b>52-Week Price Range:</b>	\$1.26 – \$4.23
<b>Market Cap (mil):</b>	approx 170 million

**Hemispherx Biopharma**  
 One Penn Center, 1617 JFK Boulevard  
 Philadelphia, PA 19103  
 Phone: 215-988-0080  
<http://www.hemispherx.net>

therapeutic application, a fully commercialized product (Alferon N) and a GMP certified manufacturing facilities for its novel pharma products in New Brunswick, New Jersey.

### B. Products

➤ **Alferon N Injection(R)** - Interferons are a group of proteins produced and secreted by cells to combat diseases. Researchers have identified four major classes of human interferon: alpha, beta, gamma and omega. The ALFERON N Injection(R) product contains a multi-species form of alpha interferon. The worldwide market for injectable alpha interferon-based products has experienced rapid growth and various alpha interferon injectable products are approved for many major medical uses worldwide. Alpha interferons are manufactured commercially in three ways: by genetic engineering, by cell culture, and from human white blood cells. All three of these types of alpha interferon are or were approved for commercial sale in the U.S. HEB's natural alpha

interferon is produced from human white blood cells.

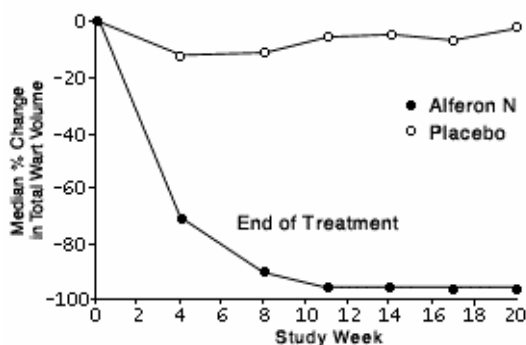


Figure 1. Median Percent Change In Total Wart Volume

Alferon N Injection(R) is approved by the FDA for the treatment of genital warts. Alferon N Injection(R) is also in pre-clinical development for treating Multiple Sclerosis and West Nile Virus ("WNV"). A published report estimates that approximately eight million new and recurrent causes of genital warts occur annually in the United States alone.

*Alferon is the only natural-source, multi-species alpha interferon currently sold in the U.S. The recombinant DNA derived alpha interferon are now reported to have decreased effectiveness after one year, probably due to antibody formation and other severe toxicities.*

*These detrimental effects have not been reported with the use of Alferon N Injection(R) which could allow this product to assume a much larger market share.*

*It is the Company's belief that the use of Alferon N in combination with Ampligen(R) has the potential to increase the positive therapeutic responses in chronic life threatening viral diseases.*

➤ **Ampligen(R)** is an experimental drug currently undergoing clinical development for the treatment of: Chronic Fatigue Syndrome ("CFS"). In August 2004, Hemispherx completed a Phase III clinical trial ("AMP 516") treating over 230 ME/CFS patients with Ampligen(R) and is presently in the process of preparing a new drug application ("NDA") to be filed with the FDA.

The U.S. FDA has granted Hemispherx orphan drug status for the nucleic acid-derived therapeutics for ME/CFS (Chronic Fatigue Syndrome), HIV, and renal cell carcinoma and malignant melanoma.

*CFS is a debilitating disease that affects between 400,000 and 1,000,000 Americans and*

*an equal number of Europeans. There is currently no effective treatment available in the marketplace. CFS imparts profound deficits in oxygen consumption on its sufferers, which impairs their ability to perform functions necessary to maintain a basic quality of life.*

*According to a report by the Centers for Disease Control and Prevention (CDC), CFS is more serious than multiple sclerosis with respect to medical severity and the overall economic affect that it has on society. This was reported in the CFS Advisory Committee Report dated January 5, 2005.*

**The pre-clinical research indicates that Ampligen can provide cross-protection against avian flu viral mutations as well as boost the effectiveness of Tamiflu and Relenza, the only two drugs formally recognized for combating bird flu, up to 100 times.**

#### CFS Trial Results

The experimental Ampligen® treatment in CFS improved exercise duration up to two times more than approved (or approvable) drugs for their respective chronic disease indications. Ampligen® increased the percentage improvement in endurance (as determined by an "intent to treat" analysis) more than 15% over the placebo group. In the CFS study, maximal oxygen consumption (VO<sub>2</sub>max) increased ten fold with Ampligen vs. Placebo. There was a high correlation between improvement in exercise duration and increase in VO<sub>2</sub> max (p<0.00001). VO<sub>2</sub>max is a measure of oxygen consumption at maximum exertion.

By comparison, analysis of seven (7) recent clinical studies, which resulted in commercial approvals (or "approvable" letters) for various drugs used in these other allied disease categories

(both CHF and AH), showed much lower magnitudes of physical performance improvements due to therapeutic interventions. For example, in CHF: Fosinopril (6.7% improvement), Captopril (6.2%), Ranolazine (6.5%) and Ranolazine (5.7%); in AI, Tracleer (10.6% improvement), Remodulin (8.0%), Remodulin (4.1%) and Remodulin (6.1%). All therapeutic measurements in these seven (7) other studies were determined by exercise treadmill testing (or extent of walking), similar or identical to the therapeutic endpoint used in the CFS study.

These results are complete and have been audited by external researchers.

In conclusion we believe it's safe to say that Ampligen works and has a very high chance of being approved by the FDA.

➤ **Alferon(R) LDO** is an experimental low-dose, oral liquid formulation of Natural Alpha Interferon and like Alferon N Injection(R) should not cause antibody formation, which is a problem with recombinant interferon. It is an experimental immunotherapeutic believed to work by stimulating an immune cascade response in the cells of the mouth and throat, enabling it to bolster an immune response through the entire body orally. Oral interferon would be much more economically feasible for patients and logistically manageable in development programs in third-world countries primarily affected by HIV and other emerging viruses (SARS, Ebola, bird flu, etc.). Oral administration of Alferon(R) N, with its affordability, low toxicity, no production of antibodies, and broad range of potential bio activity, could be a breakthrough treatment for viral diseases.

---

**Positive results in the ongoing clinical studies would potentially make Alferon LDO the first orally active interferon drug candidate and would open an opportunity leading to a wide range of potential new indications.**

---

A clinical study to evaluate the use of Alferon(R) LDO in HIV infected volunteers was initiated during the second quarter 2005 in Philadelphia, PA. The study is currently being conducted at Drexel University and Philadelphia FIGHT, a comprehensive AIDS service organization providing primary care, consumer education, advocacy and research on potential treatments and vaccines. The study is designed to determine whether Alferon(R) LDO can resuscitate the broad-spectrum antiviral and immunostimulatory genes. As of December 31, 2005, seven patients have enrolled and completed dosing. We are currently receiving data from this study and we are in the process of analyzing the results. The trial methodology may have implications for treating other emerging viruses such as avian influenza (bird flu).

### Avian Flu

With the threat of an avian influenza pandemic rising and health officials warning that the virus could develop resistance to current flu treatments, the pursuit of a cost-effective and capable co-administered immunotherapeutic to existing antivirals and vaccines has become critical. This combination may permit the use of lower dosages and fewer injections of the antivirals and vaccines used to combat avian flu, thereby decreasing the cost of both immunization programs and treatment programs for the full-blown disease.



Avian Flu normally only infects birds or pigs.

Recently, at the fourth annual Biodefense Research Meeting of the American Society of Microbiology held in Washington, D.C., HEB presented results of laboratory testing that showed that Ampligen(R) and Alferon(R), are potentially useful against H5N1, or avian flu, virus.

## C. Valuation

Investing in small biotech companies is speculative in nature. However, there are methods with which you can determine the potential value of a new drug. For obvious reasons we are only taking the CFS trial into account. The other trials are still a reasonable time away from potential approval.

Determining the potential value of Ampligen® in the CFS marketplace is a very important, if not the most important, factor to consider before making an investment in this Company.

We take three steps in determining the potential value:

- **Identifying the population.** The first step in forecasting future sales is to narrow down the population that the drug will serve as much as possible. For example, it is not sufficient to say that a drug will be used in the treatment of psoriasis. Psoriasis has a range of severity, and patients with mild forms of the disease are treated with different types of drugs than patients with severe forms. Many diseases are stratified in this manner, where different drugs are used to treat patients in the different niches. It is important to identify, with as much precision as possible, the exact patient population, because a failure to put the drug in the correct niche will lead to an inappropriate sales estimate.
  - In Hemispherx' case, estimates of ME/CFS patient numbers in the United States alone range from a low of 500,000 (1995-Centers for Disease Control, Atlanta, GA) to a high of 1,000,000 (1999-DePaul University study). For further calculations we will use the lowest number in the range.
  - 20% of those 500,000 patients (or 100,000) have serious to severe symptoms. Those are the patients that Hemispherx is targeting.
  - We will be very conservative and use only 20% of that group.
  - This means about 20,000 patients could be treated with Ampligen annually.

- **Market share.** The market-share estimate is probably the single biggest source of error in this process. It's very difficult to know if a drug will have 5% or 30% market share in the future. Therefore, it is our feeling that it is best to be conservative in the estimate.

- In Hemispherx' case this is the easiest of them all, since there is NO OTHER drug on the market for ME/CFS, nor in the pipeline.

- **Drug-pricing.** The annual cost of therapy is the last piece of the puzzle.

If there are comparable drugs already on the market, it is certainly reasonable to make the assumption that the drug will be priced in line with the competitors, give or take a bit. If the drug has superior efficacy or fewer side effects against the competition, a pricing premium is likely, and should figure into the estimate. On the other hand, if the drug is entering a market with an entrenched competitor, a lower price may come into play to encourage uptake and accelerate sales volume.

- For an Ampligen treatment of 1 year we estimate the cost at approximately \$15,000. (Which is relatively cheap compared with other chronic diseases).
- Again we will be very conservative, and assume that Hemispherx will only receive 50% of the drug's retail price. (= \$7,500)

- **Putting it all together.** If we put all this together, we should be able to get a fair conservative estimate of the potential annual revenue for Ampligen in the treatment of ME/CFS.

20,000 patients treated annually, multiplied by an annual cost of treatment of \$7,500 makes \$150 million revenue annually.

**This is approximately \$2.45 annual revenue per share for Ampligen in the United States alone!**

## D. Conclusion

**Commercial sales.** Hemispherx Biopharma is an exception under the numerous young biopharmaceutical companies for it has already a product for sale. The FDA approved Alferon N Injection ® for the treatment of recurring external genital warts, a sexually transmitted disease. A published report estimates that approximately eight million new and recurrent causes of genital warts occur annually in the United States alone.

**Addressing large markets with major medical needs.** Ampligen ® is the Company's future star product. It successfully completed a Phase III clinical trial treating over 230 ME/CFS (Chronic Fatigue Syndrome) patients. The Company is in the process of preparing a new drug application (NDA) to be filed with the FDA. Recently announced results give strong hope for a positive outcome. The experimental Ampligen® treatment in CFS improved exercise duration up to two times more than approved (or approvable) drugs for their respective chronic disease indications. Analysis of seven (7) recent clinical studies, which resulted in commercial approvals (or "approvable" letters) for various drugs used in other allied disease categories, showed much lower magnitudes of physical performance improvements.

**No competition.** Currently there is NO OTHER drug on the market for ME/CFS, nor in the pipeline. Furthermore the U.S. FDA has granted Hemispherx orphan drug status<sup>1</sup> for ME/CFS. This status grants the Company protection against competition for a period of seven years following FDA approval, as well as certain federal tax incentives, and other regulatory benefits.

**A GMP (good manufacturing practice) certified manufacturing facility.** Hemispherx wholly owns a 43,000 sq. ft. facility in New Brunswick, New Jersey, which meets all necessary GMP standards. This facility is currently used by the Company to manufacture Alferon N. Hemispherx is making the necessary arrangements in order to produce Ampligen ® at these same facilities.

**Patents.** Hemispherx' technology is protected by several hundred patents. Many more are currently pending in various international markets. Ampligen ® alone is protected by more than 170 patents worldwide with 14 additional patent applications pending to provide further proprietary protection.

**In-house control.** Unlike many other biotech companies, HEB still owns all the rights to all of its products. It hasn't closed any deals yet with major pharmaceutical companies. This means that when revenues start coming in, they won't be pruned away by distributors and others.

**Cash position.** The Company sits on a nice pile of cash. It's cash burn rate is relatively low and is certainly much lower than similar early-stage biopharmaceutical companies.

**Conclusion.** Based on these facts and the valuation on page 4, we believe that Hemispherx Biopharma is one of the most undervalued biopharmaceutical companies on the market today.

The Smallcaps.us staff.

Comments & suggestions: [editor@smallcaps.us](mailto:editor@smallcaps.us)

*Through hard work, patience, a bit of common sense and some good fortune fine returns can be achieved. But all readers are advised that they should not assume that current or future recommendations will be profitable or equal the performance of past recommendations. All stock investments carry some degree of risk. The portfolios of smallcaps.us and/or its employees may include securities mentioned on Smallcaps.us. Smallcaps.us has NOT been compensated in any way for writing, publishing and distributing this report. Information contained on Smallcaps.us was derived from sources believed to be reliable. However its accuracy and completeness is not guaranteed. Always do your own due diligence.*

© 2003 - 2006 Smallcaps.us. All rights reserved.