Zacks Small-Cap Research

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Omni Bio Pharma, Inc. (OMBP-OTCQB)

OMBP: Patent Granted for Fc-ATT, Omni's Proprietary Antitrypsin Molecule

Current Recommendation	**Neutral**
Prior Recommendation	N/A
Date of Last Change	04/15/2013
Current Price (11/18/13)	$0.19
Target Price	**$0.25**

UPDATE

On November 14, 2013, Omni Bio Pharmaceuticals reported their Q2 FY 2014 results. Notable events in the current quarter include the granting of a U.S. patent for the company's proprietary Fc-AAT molecule, which is expected to provide a commercially important advantage over existing human plasma-derived AAT in posing less of a risk of transmitting infections and increasing the interval between inconvenient IV administrations. The company's net loss for the quarter was $0.64 million, including expenditures of $0.1 million on R&D and $0.54 million on G&A. Cash burn was $0.48 million. Cash on hand on September 30, 2013 was $0.78 million, which management believes will be sufficient to fund operations through March 2014.

SUMMARY DATA

52-Week High	**$0.39**
52-Week Low	**$0.13**
One-Year Return (%)	**N/A**
Beta	**N/A**
Average Daily Volume (sh)	**67,988**
Shares Outstanding (mil)	**38**
Market Capitalization ($mil)	**$7**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**0**
Insider Ownership (%)	**N/A**
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	**High**
Type of Stock	**Small-Growth**
Industry	**Med-Biomed/Gene**

ZACKS ESTIMATES

Revenue
(In millions of $)

	Q1 (Jun)	Q2 (Sep)	Q3 (Dec)	Q4 (Mar)	Year (Mar)
2013	0 A	0 A	0 A	0 A	0 A
2014	0 E	0 A	0 E	0 E	0 E
2015					0 E
2016					0 E

Earnings per Share
(EPS is operating earnings)

	Q1 (Jun)	Q2 (Sep)	Q3 (Dec)	Q4 (Mar)	Year (Mar)
2013	-$0.04 A	-$0.04 A	-$0.07 A	-$0.09 A	-$0.23 A
2014	-$0.02 A	-$0.02 A	-$0.05 E	-$0.04 E	-$0.13 E
2015					-$0.15 E
2016					-$0.15 E

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WHAT'S NEW

Patent Granted for Fc-AAT

On November 14, 2013, Omni Bio Pharmaceuticals filed form 10-Q for the second quarter of its 2014 financial year. Key events this quarter include the grant of a U.S. patent for the company's proprietary recombinant alpha-1 antitrypsin molecule ATT-Fc. As described in our previous reports, Fc-ATT is being developed as an extended half-life version of alpha-1 antitrypsin (A1AT). This technology has previously been used successfully in the development of:

- Zaltrap, Regeneron's Fc conjugated soluble endothelial growth factor receptor, approved in 2012 for the treatment of colorectal cancer
- Alprolix (Fc conjugated Factor IX) and Eloctate (Fc-conjugated Factor VIII), for which Biogen-Idec has submitted Biological License Applications to the U.S. FDA. In clinical trials. Alprolix has demonstrated a serum half-life approximately three times longer than unconjugated Factor IX
- Dulaglutide, an Fc conjugated version of glucagon-like peptide, for which Eli Lilly has filed an New Drug Application. In clinical trials, Dulaglutide was administered weekly. Other GLP-1 analogs are administered with frequencies ranging from twice daily to once-weekly.

This is a positive result as existing formulations of A1AT are administered by IV infusion once weekly. Given the inconvenience of the mode of administration, a product requiring less frequent dosing would have an obvious commercial advantage in this $650 million dollar market. Furthermore, preclinical studies have suggested that Fc-AAT is more potent than A1AT and can potentially be self-administered by the subcutaneous route. Fc-ATT is a recombinant protein produced in CHO cells. This gives it the additional advantages of low cost-of-goods and reduced risk of contamination with adventitious pathogens relative to current alpha-1 antitrypsin products, which are produced from pooled donor plasma.

Financial Update

Financial results for the quarter ending September 30, 2013 were as follows: The company's net loss for the quarter was $0.64 million, vs. $1.33 million for the corresponding quarter of FY 2013. Operating expenses of $0.64 million included $0.10 million in R&D expense and $0.54 million in G&A expenses. These compare to $0.13 million in R&D expenses and $1.10 million in G&A expenses in the corresponding quarter of FY 2013. Non-cash expenses (stock-based compensation) were $0.17 million in the quarter ending September 30, 2013 and $0.86 million in the corresponding quarter of FY 2013. Cash operating expenditures increased by $0.13 million, due to increases in officer salaries and related taxes; consulting fees; investor relations expenses, and royalty payments.

Non-operating expenses decreased from $0.98 million in the second quarter of FY 2013 to $0.002 million in the corresponding quarter of FY 2014. This decrease largely reflects a decrease in expense related to equity loss from BioMimetix, which was fully written off in March 2013.

Cash used in operations in the first six months of FY 2014 was $0.92 million. This includes G&A cash expenditures of $0.67 million, R&D cash expenditures of $0.13 million, and a $0.1 million decrease in accrued expenses due to a settlement agreement for a sponsored research agreement. Other uses of cash included a reduction in accounts payable, a reduction in accrued liabilities, an increase in prepaid expenses, and an increase in accrued interest associated with the Convertible Notes. This was offset by $1.36 million raised in an offering of common stock and warrants in the first quarter of FY 2014, leading to a net increase in cash of $0.44 million relative to the end of FY 2013. The company's cash position on September 30, 2013 was $0.78 million, and amount that management believes is sufficient to fund operations through March 2014.

INVESTMENT OVERVIEW

An Introduction To A1AT

Alpha-1 Antitrypsin (A1AT) is a protease inhibitor belonging to the serpin family. A1AT is a single-chain 52-kDa / 394 amino acid glycoprotein produced by the liver with a circulating reference range in blood between 1.0 and 3.5 mg/mL. A1AT acts as a serum trypsin inhibitor, inhibiting a wide variety of proteases, protecting tissue from enzymes of inflammatory cells, especially neutrophil elastase. Research shows that A1AT modifies dendritic cell maturation and promotes T-cell differentiation. Specifically, A1AT decreases the production of important inflammatory cytokines such as tumor necrosis factor (TNF)-α and interleukin (IL)-1β, two prototypical upstream mediators of inflammation. A1AT also lowers the levels of the chemokines and monocyte chemotactic protein (MCP)-1, two major chemokines in the trafficking of inflammatory cells (Lewis EC, 2011).

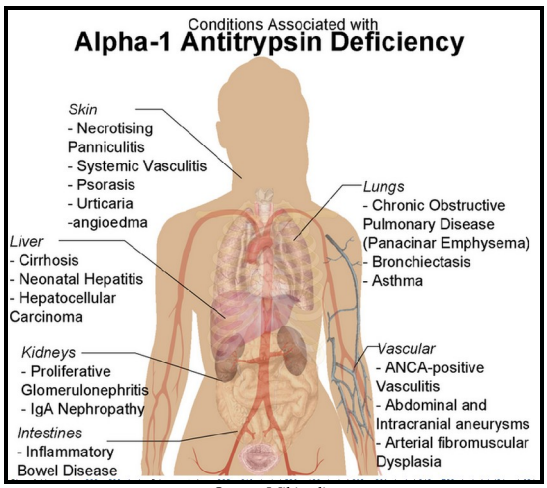
During an acute phase of a disease, the body may increase circulating levels of A1AT to protect tissue, for example in the lungs, liver and pancreas, from inflammatory response. A1AT levels may be increased by more than fourfold, and remain elevated for a week to 10 days (Wewer MD et al., 1987). A1AT production also increases during pregnancy (Larsson et al, 2008).

…A1AT Deficiency…

In the absence or low levels of circulating A1AT, proteases such as neutrophil elastase are free to break down the connective tissue fiber elastin, which contributes to the elasticity of the lungs, resulting in respiratory complications such as emphysema or chronic obstructive pulmonary disease (COPD) in adults and hepatic cirrhosis in children. Genetic disorders that result in low levels of A1AT allow for the degradation of lung tissue that leads to the characteristic manifestation of pulmonary emphysema (Tuder et al, 2010).

Alpha-1 Antitrypsin deficiency (A1AD) is a generic disorder that causes the defective production of A1AT, characterized by circulating A1AT levels below 0.5 mg/mL. Low levels of A1AT in the blood and lungs cause panacinar emphysema or COPD, as well as liver disease in young children. In fact, A1AT deficiency represents the most common inherited condition that leads to liver failure and the need for transplants in infants and children (Perlmutter DH, 2011).

A1AD is most common in Caucasian individuals of Northern European and Middle Eastern origin. In the U.S., an estimated 25 million Americans are carriers of an abnormal gene for the production of A1AT (heterozygous). Luckily, to develop A1AD, both parents must be carriers, thus giving birth to a homozygous offspring. There are an estimated 100,000 homozygous A1AD patients in the U.S. (de Serres FJ, 2003).



Source: Wikipedia

Diagnosis for A1AD remains a significant challenge. Of the roughly 100,000 or so Americans with A1AD, only around 5,000 are confirmed (Campos et al, 2005). Symptoms of A1AD include shortness of breath, wheezing, rhonchi, and rales. Patients with A1AD may also be subject to recurrent respiratory infections or asthma that do not respond to treatment. Often these symptoms do not appear until the age of 30, although smoking can accelerate disease progression (Anthonisen N, 2008). Thus, the disease is often miss-diagnosed as emphysema, asthma, COPD, or chronic bronchitis for years before A1AD is confirmed.

Patients with suspected A1AD disease must be tested to confirm A1AD and rule out other forms of lung diseases such as emphysema, asthma, or COPD. Diagnostic tests to confirm A1AD include both genetic tests looking for the faulty A1AT gene and blood tests designed to check the circulating levels of A1AT. Lung tests also exist that utilize high-resolution computer tomography (CT) scanning or x-rays and lung function testing that involves measuring how much air you can breathe in an out, how fast you can breathe air out, and how well the lungs deliver oxygen to the blood (NIH-NHLBI guidelines).

…A1AD Treatment…

A1AD has no cure. Instead, physicians attempt to manage the symptoms of the disease, either by treating the related lung or liver conditions or augmenting circulating A1AT levels with weekly infusions of plasma-derived A1AT (p-AAT). Managing the symptoms may include use of bronchodilators and inhaled steroids to help open the airways and make breathing easier. Patients with severe breathing impairment may require supplemental oxygen or a lung transplant. It is also recommended that A1AD patients obtain flu and pneumococcal vaccines to protect from illness than could exacerbate the condition.

Augmentation by weekly infusions of p-AAT is recommended only for patients with severe A1AD. Data suggests that weekly infusions of p-AAT can help reduce pulmonary exacerbations and the rate of progression of emphysema, although statistics from adequately powered, randomized clinical trials is lacking. The intended theoretical goal is to provide protection to the lower respiratory tract by correcting the imbalance between neutrophil elastase and protease inhibitors through the intravenous infusions of p-AAT at doses of approximately 60 mg/kg body weight. This dosing level results in significantly increased levels of circulating A1AT representative of anti-neutrophil elastase activity, with a mean Cmax between 1.5 mg/mL and 3.0 mg/mL. The half-life of p-AAT is roughly 3 to 5 days.

There are four manufacturers of p-AAT worldwide, Grifols, Baxter, CSL Behring, and Kamada. The two largest products we found are Grifols' Prolastin-C, with sales at an estimated $500 million and Baxter's Aralast-NP with sales at an estimated $60 million. Management at Omni Bio Pharma estimated the total global market for p-AAT is around $600-700 million. The average cost of therapy is around $2,000 per 60 mg/kg weekly infusion, or around $100,000 per year. The infusion process typically takes about 2 hours at infusion clinic centers.

Expanding Indications For p-AAT

Both products above are indicated for chronic augmentation therapy in patients having congenital deficiency of Alpha-1 Antitrypsin with clinically evident emphysema. However, there is significant interest from the academic and medical community in using p-AAT in non-deficient individuals suffering from inflammatory or immune-mediated diseases. These include type-1 and type-2 diabetes, acute myocardial infarction, rheumatoid arthritis, inflammatory bowel disease, cystic fibrosis, gout, transplant rejection, graft versus host disease (GvHD) and multiple sclerosis. Evidence exists that p-AAT may also act as an antibacterial and an inhibitor of viral infections, such as influenza and human immunodeficiency virus (HIV).

…Disease Applications…

Type-2 Diabetes: Type-2 diabetes is associated with the failure of insulin to communicate intracellular signals upon engagement with its receptor. The current therapeutic approach primarily centers on diet and exercise, along with manipulation of liver cells to halt endogenous glucose production and attempts to enhance insulin sensitivity and insulin release (Lewis EC, 2011). New research suggests that blocking the inflammatory pathway could improve insulin signaling and reduce insulin resistance. The hypothesis is backed by knowledge that high glucose, fatty acid, and IL-1β levels exert direct toxic effects on B-cells.

Given its protective mechanism of action, some scientists believe that high levels of A1AT may confer protection on the islet B-cells. We know that low circulating A1AT levels are common in patients with type-2 diabetes (Sandstörm et al, 2008). Studies must now be conducted to test whether or not systemic glucose control can be improved by adding A1AT, or whether or not A1AT can ameliorate B-cell injury in the presence of chronic elevated glucose or high fatty acid levels.

Type-1 Diabetes: Type-1 diabetes is an autoimmune disorder resulting in the destruction of insulin-producing B-cells of the pancreas. The lack of insulin leads to increased blood and urine glucose. Type-1 diabetes must be treated by injection (or inhalation) of insulin. Protection of the islet cells is the obvious target for new therapeutic methods of treatment, and new clinical studies are focusing on stopping the T-cell-mediated autoimmune attack. Anti-inflammatory agents, such as anti-CD3 antibodies, have shown encouraging signs of efficacy. Data show that blockage of the inflammatory molecule IL-1, a direct B-cell toxic agent, results in reduced insulin dependence when tested on children with early-stage disease (Sumpter et al, 2011).

Research on non-obese diabetic (NOD) mice show that inflammatory mechanisms trigger insulitis, insulin resistance, faulty insulin signaling, and the loss of immune tolerance to islets. The data demonstrate that treatment with p-AAT, an agent that dampens inflammation, does not directly inhibit T cell activation, ablates invasive insulitis, and restores euglycemia (normal blood glucose levels), immune tolerance to B cells, normal insulin signaling, and insulin responsiveness in NOD mice with recent-onset type-1 diabetes through favorable changes in the inflammation cascade (Figure-1) (Koulmanda et al., 2008).

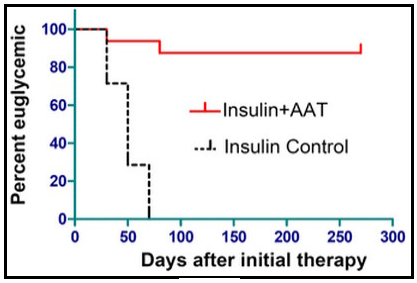


Figure-1

There are essentially three key points that lead us to believe p-AAT may have therapeutic utility in type-1 diabetes.

- ✓ Firstly, non-functional circulating A1AT has been shown to exist in most individuals with type-1 diabetes (Yaghmaei et al, 2009), suggesting that A1AT levels may play a role in disease progression.
- ✓ Secondly, multiple preclinical animal models also show consistent benefit of A1AT on protection of insulin producing islet B-cells (Kamada, Ltd., November 2012; Koulmanda et al., 2008).
- ✓ Thirdly, A1AT is endogenously produced under inflammatory stimuli by human islet cells (Bosco et al, 2005). These three conclusions strengthen the case for testing p-AAT in human clinical trials in children recently diagnosed with type-1 diabetes.

We found five clinical trials listed on clinicaltrials.gov testing p-AAT in children and young adults with type-1 diabetes. These include:

Identifier No.	Stage	Design / Comments	Status
NCT01304537	Phase 1/2	Tolerability and efficacy of three doses (40, 60, 80 mg/kg) p-AAT (Glassia®) in patients (n=24) with type-1 diabetes over 4, 8, and 12 weeks. Results (November 2012) suggest Glassia may halt the progression of diabetes, enabling the pancreas beta cells to continue excreting insulin and thus providing better glucose balance and control. Data show stabilization in c-peptide levels. Sponsor: Kamada, Ltd.	Completed
NCT01661192	Phase 2	Open-label extension study to evaluate the long-term treatment effects and safety, tolerability, and efficacy of p-AAT (Glassia®) in patients (n=24) with type-1 diabetes over 36 months. Data expected January 2017. Sponsor: Rabin Medical Center, Israel Collaborator: Kamada, Ltd.	Active, Recruiting
NCT01183468	Phase 2-A	RETAIN-1: Safety and dose-level (45-90 mg/kg) study of p-AAT (Aralast-NP) to assess the effects of intravenous infusions on preserving B-cell function in patients (n=16) with new onset type-1 diabetes. Results in October 2012 are discussed below. Sponsor: National Institute of Allergy and Infectious Disease (NIAID) Collaborator: Immune Tolerance Network (ITN) & Juvenile Diabetes Research Foundation (JDRF).	Active, Not Recruiting
NCT01183455	Phase 2-B	RETAIN-2: Randomized, two-arm, double-blind, placebo-controlled assessment of 90 mg/kg p-AAT (Aralast-NP) infused once a week in patients (n=66) with new onset type-1 diabetes over 12 weeks. Data expected November 2014. Sponsor: NIAID Collaborator: ITN & JDRF	Not Yet Recruiting
NCT01319331	Phase 1	Safety and feasibility of p-AAT (Aralast-NP) infused once a week in patients (n=15) with recent onset (<5 years) type-1 diabetes over an 8 week. Data expected September 2013. Sponsor: University of Colorado: Barbara Davis Center for Childhood Diabetes Collaborator: Omni Bio Pharmaceuticals, Inc.	Active, Recruiting

The phase 1 trial sponsored by the University of Colorado, Barbara Davis Center for Childhood Diabetes is the one that Omni Bio Pharmaceuticals is in collaborated on. Omni Bio tells us that data from the ongoing phase 1 study will be submitted for publication in the near future. Patent applications relating to the findings will also be filed in 2013.

Data from the RETAIN-1 phase 2a study sponsored by the NIAID-NIH and collaborated with the ITN and JDRF indicate stabilization of c-peptide levels (Figure-2A). C-peptide is a measure of insulin-producing pancreatic B-cell function. These data are consistent with the findings from the Kamada, Ltd phase 1/2 studies. The literature notes the rate of anticipated decline in C-peptide levels during the first 12 months following diagnosis is 0.3 pmol/mL (15-20%), and may be even faster in children and adolescents (Figure-2B) (Greenbaum et al, 2012).

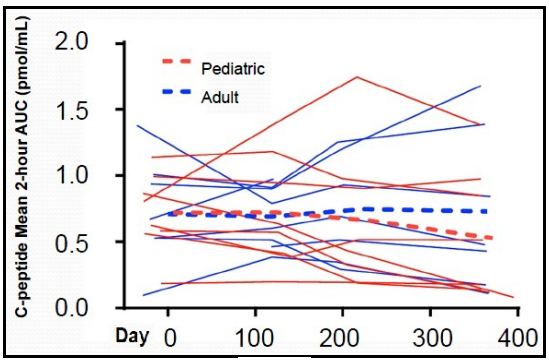


Figure-2A

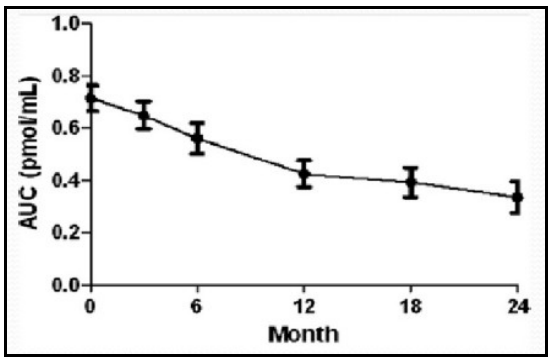


Figure-2B

GvHD: Graft-versus-host disease is a common complication following allogeneic (genetically-mismatched) tissue transplant, most often associated with stem cell or bone marrow transplant. Symptoms in both acute and chronic GvHD range from mild to severe, and usually show up within the first three months after a transplant. Common treatment options for patients post allogenic stem cell transplant includes drugs that suppress the T cell mediated immune onslaught on the host tissues, including glucocorticoids such as prednisone. These drugs often have poor tolerability, may illicit harmful side effects on the kidneys and liver, and create risk of infection of cancer relapse. Despite treatment with high-dose prednisone, 40% to 50% of unrelated allogeneic tissue transplant patients will develop GvHD. Thus, there exists a significant unmet medical need to develop a new immune modulating agent that can allow the T cell mediated graft-versus-leukemia response while sparing the recipient from an injurious inflammatory and immunological assault (Lewis EC, 2011). Along with its potent anti-inflammatory profile, research shows that A1AT has the ability to modify dendritic cells toward a tolerogenic phenotype (Subramanian et al, 2011; Lewis et al, 2008).

Data published in the Proceedings of the National Academy of Sciences (PNAS) shows that administration of p-AAT early after bone marrow transplant decreased mortality in three models of GvHD and reduced serum levels of pro-inflammatory cytokines such as TNF-α and IL-1β in the allogeneic recipients compared with the control (Figure-3). Furthermore, p-AAT treatment reduced the expansion of alloreactive T effector cells but enhanced the recovery of T regulatory T cells, thus reducing the pathological harmful response. Treatment with p-AAT also resulting in increased production of anti-inflammatory cytokines, IL-10 (Tawara I et al, 2012).

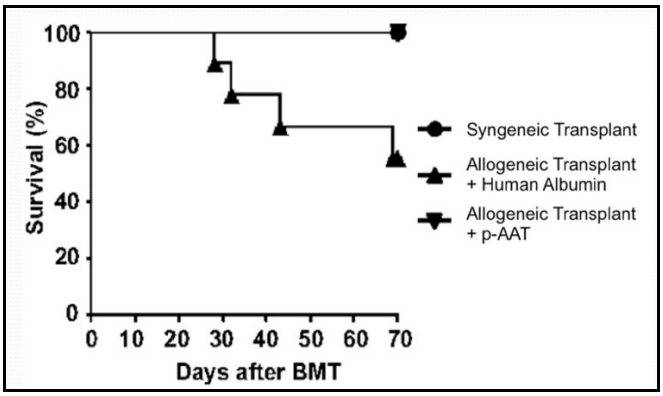


Figure-3

Similar to type-1 diabetes, we see a number of key points and preclinical findings that support the utility of p-AAT in the treatment and prevention of GvHD:

- ✓ Data shows a loss of A1AT during intestinal GvHD in children (Hagen et al, 2011).
- ✓ Significant scientific evidence exists to support the involvement of IL-1 during the progression of GvHD, and treatment with IL-1 receptor antagonists have been shown to slow progression and reduce disease severity (Dinarello CA, 2011; Antin et al, 1994).
- ✓ Animal model data shows p-AAT provides a clear benefit to immune profile, body weight, and survival (Marcondes et al, 2011; Tawara et al, 2012).

On July 10, 2013, Omni Bio announced it will be collaborating with the University of Michigan Cancer Center (UMCC) and Leukemia and Lymphoma Society (LLS) to study plasma-derived alpha-1 antitrypsin (p-AAT) for the treatment of complications following bone marrow transplantation, or as it's more commonly referred to, GvHD. The Phase 2 multicenter pilot study (ClinicalTrials.gov # NCT01700036) will be funded almost entirely by UMCC and LLS. Omni Bio will supply logistical support and drug will be supplied by CSL Behring.

The principal investigator of the study is Dr. Ravan R. Reddy, MD, co-Director of the Bone Marrow Transplantation and Hematological Malignancy Program, and Associate Professor of Internal Medicine at the University of Michigan. ClinicalTrials.gov lists the study as multicenter, so we are expecting additional sites to come online shortly.

The multicenter Phase 2 study will be open-label design, and is expected to enroll up to 40 patients with acute steroid-refractory GvHD. We remind investors that for patients who don't respond to steroid therapy, GvHD can be fatal, either from organ damage or opportunistic infection as a consequence of high dose steroid treatments. There is currently no known effective therapy for patients with acute graft vs. host disease that's refractory (non-responsive) to steroid therapy. Six month mortality rates in this population exceed 50%.

The primary outcome of the study is the proportion of patients who respond to p-AAT at a dose of 60 mg/kg twice weekly for 8 doses (4 weeks). Under uncontrolled circumstances, we would expect this population to be less than 50%. Therefore, any improvement to 50% or better in response would be a clear sign of efficacy in our view for p-ATT. Secondary outcome measures include:

- ✓ Complete response to treatment at four weeks.
- ✓ The rate of infection at four weeks.
- ✓ Overall survival at six months (we would expect untreated patients would have an OS below 50% at six months).
- ✓ Analysis of six plasma cytokine (IL1Rα, TNFR1, HGF, IL8, elafin, and reg3α) levels.
- ✓ Analysis of plasma levels for Alpha-1-Antitrypsin levels.

Assuming a smooth enrollment and an additional one or two centers coming online in the next few weeks, we would expect to see data from this study by the end of the year.

…Omni Bio's Business Model…

We see GvHD as a potential enormous opportunity for Omni Bio. According to data from the Center for International Blood and Marrow Transplant, the incidence of acute GvHD ranges from 26% to 34% in recipients of full matched sibling donor grafts, to 42% to 52% in recipients of matched unrelated donor grafts. The incidence is directly related to the degree of human leukocyte antigens (HLA) disparity. The median onset of acute GvHD is typically 21 to 25 days after transplantation. Chronic GvHD ranges in incidence from 30% in recipients of fully histocompatible transplants to 60% to 70% in recipients of mismatched hematopoietic cells or hematopoietic cells from an unrelated donor. The median time of diagnosis of chronic GvHD is 4.5 months after HLA-identical sibling transplantation and four months after unrelated donor transplantation.

GvHD is listed as a "rare disease" by the Office of Rare Diseases (ORD) of the NIH. Given the number of Americans that undergo a transplant per year, we estimate there are approximately 7,500 cases of acute GvHD per year in the U.S. According to data from the NIH, 30% to 50% of patients respond to high doses of corticosteroids, such as methylprednisolone. This would place the refractory-treatment population in the U.S. at approximately 4,000 patients per year. Including Europe and the rest of the developed world, Omni Bio is probably looking at an addressable patient population of approximately 10,000 individuals.

This represents a very attractive label expansion opportunity for the four big manufacturers of p-AAT noted above: Grifols, Baxter, CSL Behring, and Kamada. It essentially doubles the market from the $600-700 million now with A1AD. With positive proof-of-concept data, we think Omni Bio can strike a deal with one of these major players. A deal with Grifols, the market leader, makes sense from a defensive standpoint. Grifols could acquire the rights to use p-AAT in GvHD from Omni Bio to protect its market-leading position. A deal with Baxter, CSL Behring, or Kamada makes sense if one of these smaller players wants to make an offensive move on the market leader.

Challenges of Existing p-AAT Treatments

As noted above, p-AAT is currently manufactured by only four companies. The supply of p-AAT is limited because it is a plasma protein and must be purified from plasma obtained from human blood. Management at Omni Bio Pharma estimated the total global market for p-AAT is around $600-700 million. The average cost of therapy is around $2,000 per 60 mg/kg weekly infusion, or around $100,000 per year. The infusion process typically takes about 2 hours at infusion clinic centers. Under these economics, supplying enough p-AAT to tap new markets such as diabetes, GvHD, gout, or myocardial infarction seems a significant challenge.

FC-AAT – The Solution

Providing adequate supply of p-AAT for a diseases and disorders outside of A1AD, such as type 1 or type 2 diabetes, GvHD, gout, and myocardial infarction, seems a significant challenge, especially considering varying requirements of duration of therapies. Thus, it seems logical to pursue development of a novel alternative to plasma-derived A1AT; perhaps in the form of a synthetic analog.

In the second half of 2011, Omni Bio began to look at the opportunity to develop a novel synthetic form of A1AT. The company filed provisional patent applications directed to compositions, methods and uses for the synthetically manufactured A1AT referred to as “recombinant AAT” or “AAT fusion molecules." Management believes the successful characterization and development of a synthetic A1AT molecule would provide for a patentable composition that could be introduced into new and larger markets, protecting the molecule in major markets for al least 10-12 years after market introduction via patent life and / or market exclusivity law. As discussed above, potential clinical uses include treatment of inflammatory diseases and other conditions such as type 1 diabetes, bone marrow transplantation, gout, and myocardial infarction. We believe a synthetic A1AT molecule, with reduced cost and time to manufacture compared to the currently available plasma-derived products, would be a potential blockbuster opportunity for the company.

In January 2012, Omni Bio announced its intention to commence research and development on a synthetic form of A1AT, where a synthetic fusion protein involving A1AT is linked to an Fc fragment of immunoglobulin (IgG1). In March 2012, management entered into research agreement with the Reagents University of Colorado (RUC) to advance the development of Fc-AAT. The work is being supervised by Omni Bio’s chief scientific officer, Dr. Charles Dinarello, and is being conducted at several research facilities including the University of Colorado Denver Anschutz Medical Campus (UCD) and Konkuk University in South Korea. Omni was recently granted a U.S. patent for its lead Fc-AAT molecule, and it also has an exclusive licensing arrangement with UCD and Kontuk University for a class of follow on Fc-AAT molecules with differing constructions related to the lead molecule. Worldwide patent applications have also been filed for this follow-on series of molecules.

Omni Bio’s lead Fc-AAT molecule, which they refer to internally as Fc-AAT-2, is a fusion protein that combines human A1AT (Figure-4A) with an Fc fragment of human IgG1 immunoglobulin molecule. This fusion protein spontaneously binds together to form a dimer. Each dimer contains two A1AT molecules and two Fc molecules connected by molecular bonds (Figure-4B).

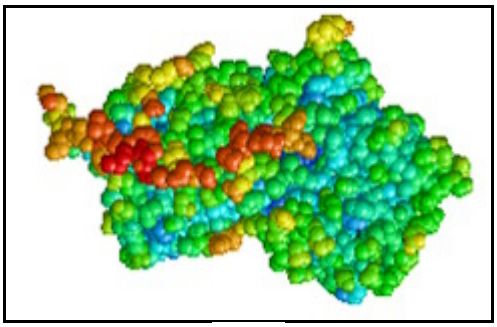


Figure-4A

Plasma-Derived A1AT (p-AAT) = 52 kDa
Recombinant Fc-AAT-2 = 174 kDa

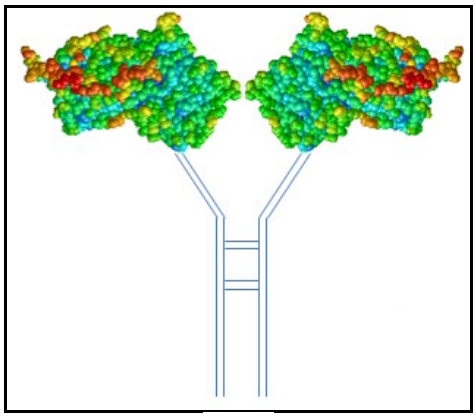


Figure-4B

Fc-AAT is being developed in a standard cell line (Chinese hamster ovary) that is frequently used for producing recombinant proteins, including a number of proteins that are now FDA approved drugs. Additionally, Fc fusion proteins have a remarkable safety record that is recognized by the FDA; as does p-AAT. Of course there is always development risk, but at this stage we think there concept of Fc-AAT makes excellent sense from a development standpoint.

Another attractive feature of Fc molecules is that they are inherently designed to extend duration of action. Omni Bio has generated preclinical data indicating that Fc-AAT has 100x more potency *in vitro* than p-AAT. Animal studies show Fc-AAT may be 40-50x more potent than p-AAT and also have a longer duration of effect. For example, Fc-AAT in models of gout and myocardial infarction that show good dose response and also that a 50ug dose of Fc-AAT performed at least as well as a 2mg dose of p-AAT.

Data on the effects of Fc-AAT were recently presented at the 4th European Workshop on Crystals in Human Diseases on March 8, 2013. The data show Fc-AAT to be highly effective in mouse models of gouty arthritis. Treatment yielded an 85% reduction in pro-inflammatory response as measured by cell influx, joint swelling, IL-1β and IL-6 in a dose-dependent manner (Figure-5A). Data also show Fc-AAT was at least 40x more potent than p-AAT (Figure-5B).

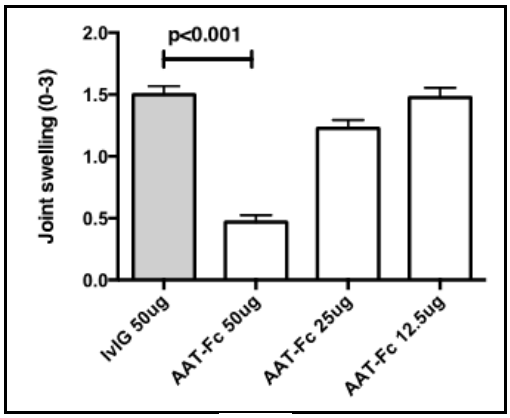


Figure-5A

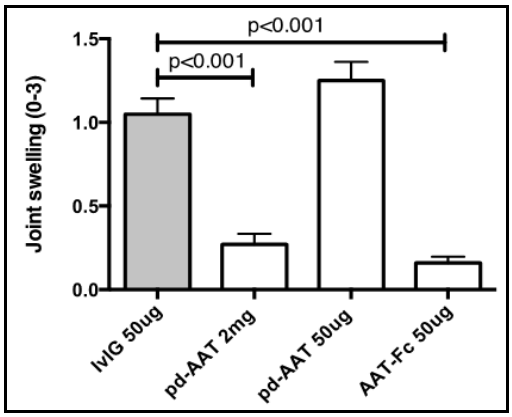


Figure-5B

This significant reduction in dose facilitates the potential for self-administered subcutaneous dosing of Fc-AAT – a huge advantage compared to the 2 hour intravenous infusions currently required with p-AAT. Omni Bio has submitted this preclinical data for publication to the Proceedings of the National Academy of Sciences.

Omni Bio is currently pursuing a strategic partner to help with drug scale-up and formulation activities. It is expected that manufacturing of CHO cells systems will enable Fc-AAT to be produced at substantially lower cost and in greater volumes than can be accomplished by purifying A1AT from the limited human plasma resources. This has the potential to reduce the yearly cost of treatment with A1AT from roughly $100,000 for p-AAT to $15,000 for Fc-AAT, thereby opening the potential to use in new and larger indications, such as diabetes, GvHD, and treatment refractory gout.

…Market Opportunity…

Omni Bio's investor presentation from February 2013 lists three lead indications for Fc-AAT: Type-1 diabetes, GvHD, and treatment refractory gout. Secondary indications include RA, IBD, COPD, and cardiac remodeling. Also all of these potential indications offer a market opportunity in excess of $1 billion worldwide.

Lead Indications Under Consideration

Disease	Market Size (US/EU)
Type 1 Diabetes (Early Onset)	>$1B
Graft vs Host Disease	~$500M
Gout (Treatment Refractory)	>$1B

Options For Life Cycle Management

Disease	Market Size (US/EU)
Rheumatoid Arthritis	>$1B
Inflammatory Bowel Disease (Crohn's Disease, Ulcerative Colitis)	>$1B
Chronic Obstructive Pulmonary Disease	>$1B
Cardiac Remodeling	>$1B

Under terms of its agreement with the Reagents of the University of Colorado (RUC), Omni Bio would owe between 2.5% and 4% net royalty on sales of Fc-AAT but are otherwise free to sub-license the molecule to a larger pharma player should they decide to do so.

Type-1 Diabetes: According to epidemiology data published in a 2010 NIH Public Access manuscript (Maahs et al, 2010), approximately 1 in 300 Americans below the age of 18 have type-1 diabetes, growing at a rate between 2% and 5% per year. That equates to roughly 240,000 individuals. Statistics from the U.S. Center for Disease Control pegs 26 million Americans with diabetes, of which around 19 million have been diagnosed and 7 million are undiagnosed. The CDC estimated approximately 5% of the cases are type-1 diabetes, or around 1.3 million Americans.

Data from the Harvard Medical School estimates the global diabetes population at approximately 350 million, growing at an astonishing rate of 6% to 8% per year. Assuming similar breakdown globally to the U.S., puts an estimated 20+ million type-1 diabetics worldwide.

Type-1 diabetics are insulin dependent. Individuals with type-1 diabetes may be on either rapid-acting or long-acting insulin, or a combination of both. Diabetics may also be on high blood pressure and cholesterol-lowering drugs. The CDC estimates the direct and indirect cost of diabetes in American is over $200 billion. Omni Bio's Fc-AAT has the potential to be a disease modifying agent for type-1 diabetes in preserving the beta cell function in the pancreas. Safety from the phase 2a RETAIN-1 trial showed excellent safety and clear sign of biomarker improvement and disease stabilization. There are not drugs on the market today that could claim that sort of profile.

With a 10% market share of the 240,000 or so American's below the age of 18 on Fc-AAT, with a yearly cost of around $15,000, Omni Bio is looking at a potential $360 million opportunity. Including Europe, with disease prevalence dynamics similar to the U.S., and the opportunity grows to over $750 million. Additionally, with the potential for a subcutaneous administration, we can envision market share gains beyond 10%, which leads us to believe that Fc-AAT has billion-dollar potential in this indication alone.

GvHD: According to data from the Center for International Blood and Marrow Transplant, the incidence of acute GVHD ranges from 26% to 34% in recipients of full matched sibling donor grafts, to 42% to 52% in recipients of matched unrelated donor grafts. The incidence is directly related to the degree of human leukocyte antigens (HLA) disparity. The median onset of acute GvHD is typically 21 to 25 days after transplantation. Chronic GvHD ranges in incidence from 30% in recipients of fully histocompatible transplants to 60% to 70% in recipients of mismatched hematopoietic cells or hematopoietic cells from an unrelated donor. The median time of diagnosis of chronic GvHD is 4.5 months after HLA-identical sibling transplantation and 4 months after unrelated donor transplantation.

GvHD is listed as a "rare disease" by the Office of Rare Diseases (ORD) of the NIH. Given the number of American's that under a transplant per year, we estimate there are approximately 7,500 cases of acute GvHD per year in the U.S. According to data from the NIH, 30% to 50% of patients respond to high doses of corticosteroids, such as methylprednisolone. This would place the refractory-treatment population in the U.S. at approximately 4,000 patients per year. Including Europe and the rest of the developed world, Omni Bio is probably looking at an addressable patient population of approximately 10,000 individuals. We suspect that the price of Fc-AAT for treatment-refractory GvHD will be around $10,000 to $15,000 per course of treatment, putting the potential peak global market opportunity $125 million.

A potentially larger opportunity for Fc-AAT in GvHD exists if the drug can show utility as a prophylactic therapy. This would allow management to target not only the entire GvHD population of an estimated 20,000 or so between the U.S. and Europe, but the entire bone marrow transplant population. According to the U.S. Department of Health and Human Services, there are approximately 18,000 bone marrow transplants in the U.S. each year. Between the U.S. and Europe, the number is roughly 40,000. And this does not include the 65,000 solid organ transplants done between the two continents. Such a development could expand the market opportunity to $500 million or higher for Omni Bio and Fc-AAT.

Gout: Gout is a rheumatic disease resulting from deposition of uric acid crystals (monosodium urate) in tissues and fluids within the body. This process is caused by an overproduction or under excretion of uric acid. Gout can range from asymptomatic, to acute flare-ups, to chronic states of sore aching joints and arthritis.

Data from the CDC pegs the U.S. incidence rate of gout at around 50 cases per 100,000, or around 8 to 10 million adult Americans. The American College of Rheumatology estimates that 8.3 million Americans had gout in 2012, with another 30+ million Americans reporting hyperuricemia (high uric acid levels). Prevalence of gout increases for men over the age of 65. A study of managed care enrollees over the age of 65 estimated prevalence at around 20%. ACR studies also show greater incidence in patients with obesity and metabolic syndrome.

Treatment options for gout include a combination of corticosteroids and over-the-counter non-steroidal anti-inflammatory drugs such as ibuprofen and naproxen during flare-ups. Uricosuric agents such as probenecid are used to increase elimination of uric acid by the kidneys and xanthine oxidase inhibitors such as allopurinol and febuxostat are used to decrease production of uric acid by the body. Omni Bio would be targeting development of gout in patients who are refractory or non-responsive to existing treatments. We estimate that as many as 30% of all gout patients fall into this category and would be amenable to treatment with Fc-AAT. GBI Research estimates the U.S. chronic gout market is approximately $550 million, growing at an estimated 7%. Takeda's Uloric (febuxostat) did $202 million in sales in 2012, but the competitive could be dramatically changed by a biologic medication with disease modifying effects. We think the dynamics of the gout market could change post Fc-AAT approval similar to how the RA market changed with the approval of Remicade and Enbrel. Steroids and febuxostat remain first-line and cheap, whereas the refractory population shifts to Fc-AAT.

On a global basis, we conservatively forecast Fc-AAT could have peak sales in this indication ranging from $250 to $500 million depending on the level of safety and efficacy compared to allopurinol and febuxostat. However, with impressive clinical data that shows a disease modifying effect and the ability to treat patients that are refractory to steroids or other non-biologic medications, Fc-AAT could be a $500 million or bigger opportunity.

VALUATION & RECOMMENDATION

The news on the funding for a Phase 2 trial with p-AAT in GvHD is very encouraging for Omni Bio investors. Back in early June 2013, we initiated coverage of Omni Bio Pharmaceuticals with a 'Neutral' rating. Despite our favorable view on the potential for expanding indications with p-AAT and development of a next-generation Fc-AAT, our two biggest concerns in early June were financing and a lack of clinical catalysts.

Two positive events that have occurred since that time include the news on funding for a Phase 2 trial with p-AAT in GvHD and the recent issuance of a patent for the company's proprietary Fc-AAT conjugate molecule.

We note that the company recently completed a financing and is in the process of closing add-on financing for additional funding. Once complete, this alleviates one of our major concerns. The initiation of a Phase 2 program in GvHD, with potential data coming in the fourth quarter 2013, potentially alleviates a second concern in a lack of catalysts. We encourage investors to keep in an eye on the Omni Bio story. This is a $10 million company that is potentially sitting on a multi-hundred million dollar product; and this management team seems astutely focused on striking a deal or selling the company in the not-so-distant future.

PROJECTED FINANCIALS

Omni Bio Pharmaceuticals, Inc.
Income Statement

	FY'12 A	FY'13A	June-13A	Sept-13A	Dec-13E	Mar-14E	FY'14E	FY'15E	FY'16E
Product Sales (Fc-AAT)	$0	$0	$0	$0	$0	$0	$0	$0	$0
YOY Growth	-	-	-	-	-	-	-	-	-
Licensing & Collaborative Payments	$0	$0	$0	$0	$0	$0	$0	$0	$0
YOY Growth	-	-	-	-	-	-	-	-	-
Total Revenues	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**
YOY Growth	*100.0%*	-					-	-	-
CoGS	$0	$0	$0	$0	$0	$0	$0	$0	$0.0
Product Gross Margin	-	-					-	-	-
R&D	$0.398	$0.297	$0.028	$0.099	$0.200	$0.250	$0.577	$0.750	$1.000
% R&D	-	-	-	-	-	-	-	-	-
SG&A	$4.237	$5.423	$0.503	$0.540	$1.400	$1.450	$3.893	$6.000	$6.500
% SG&A	-	-	-	-	-	-	-	-	-
Operating Income	**($4.635)**	**($5.720)**	**($0.531)**	**($0.638)**	**($1.600)**	**($1.700)**	**($4.469)**	**($6.750)**	**($7.500)**
Operating Margin	-	-	-	-	-	-	-	-	-
Interest & Other Income	($0.760)	($1.734)	($0.150)	($0.002)	($0.352)	($0.100)	($0.604)	($0.250)	($0.250)
Pre-Tax Income	($5.395)	($7.454)	($0.681)	($0.640)	($1.952)	($1.800)	($5.074)	($7.000)	($7.750)
Taxes & Other	$0	$0	$0	$0	$0	$0	$0	$0	$0
Tax Rate	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*
Net Income	($5.395)	($7.454)	($0.681)	($0.640)	($1.952)	($1.800)	($5.074)	($7.000)	($7.750)
Net Margin	-	-					-	-	-
Reported EPS	**($0.17)**	**($0.23)**	**($0.02)**	**($0.02)**	**($0.05)**	**($0.04)**	**($0.13)**	**($0.15)**	**($0.15)**
YOY Growth	-	-	-	-	-	-	-	-	-
Basic Shares Outstanding	31.4	32.0	34.1	38.2	42.0	46.0	40.1	48.0	52.0

Source: Zacks Investment Research, Inc. *Jason Napodano, CFA*

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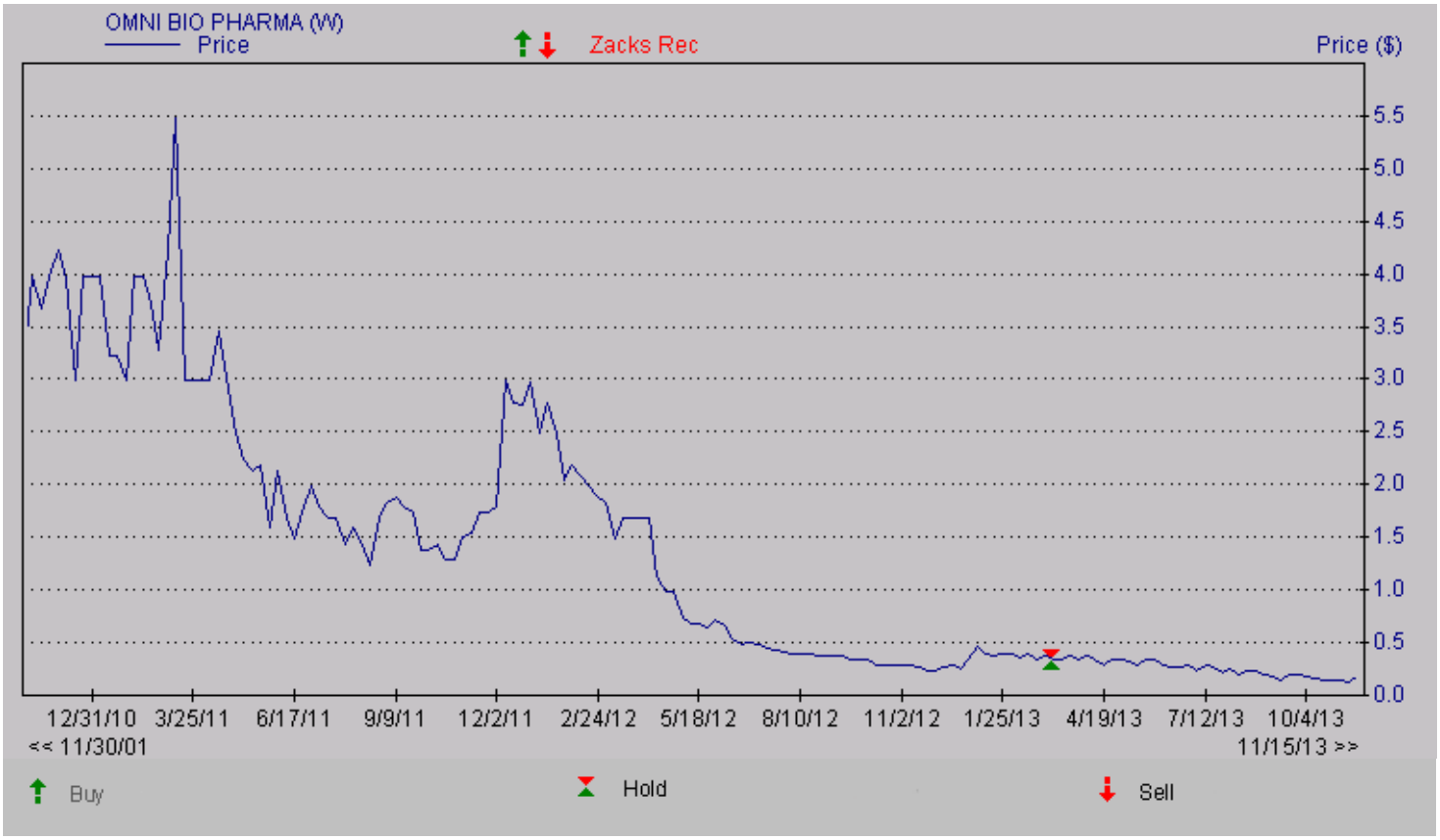

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