Zacks Small-Cap Research

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Jason Napodano, CFA
312-265-9421
jnapodano@zacks.com

scr.zacks.com
111 North Canal Street, Chicago, IL 60606

# Omni Bio Pharma, Inc. (OMBP-OTC)

## *OMBP: Could Omni's FC-AAT Be The Next Blockbuster?*

| | |
|---|---|
| **Current Recommendation** | **Neutral** |
| Prior Recommendation | N/A |
| Date of Last Change | 04/15/2013 |
| Current Price (06/03/13) | $0.35 |
| **Target Price** | **$0.50** |

## INITIATION OF COVERAGE

We are initiating coverage of Omni Bio Pharmaceuticals with a 'Neutral' rating and $0.50 price target. Despite the fact that we see the company as considerably under-valued today given the potential to both sign partnerships around expanded indications of p-AAT and develop a next-generation potential blockbuster in Fc-AAT, the cash position and lack of meaningful catalysts gives us pause. Thanks to a recent financing, Omni Bio is addressing the first of our concerns, the cash position. We think additional cash is required to push forward in development of Fc-AAT. Once this cash is secured, we will have less reservation on the second concern, i.e. a lack of meaningful catalysts to drive the valuation higher.

## SUMMARY DATA

| | |
|---|---|
| **52-Week High** | **$0.39** |
| **52-Week Low** | **$0.25** |
| **One-Year Return (%)** | **N/A** |
| **Beta** | **-0.01** |
| **Average Daily Volume (sh)** | **3,731** |
| **Shares Outstanding (mil)** | **32** |
| **Market Capitalization ($mil)** | **$11** |
| **Short Interest Ratio (days)** | **N/A** |
| **Institutional Ownership (%)** | **5** |
| **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 (Mar) | Q2 (Jun) | Q3 (Sep) | Q4 (Dec) | Year (Dec) |
|---|---|---|---|---|---|
| 2013 | 0 A | 0 A | 0 A | 0 E | 0 E |
| 2014 | 0 E | 0 E | 0 E | 0 E | 0 E |
| 2015 | | | | | 0 E |
| 2016 | | | | | 0 E |

**Earnings per Share**
(EPS is operating earnings)

| | Q1 (Mar) | Q2 (Jun) | Q3 (Sep) | Q4 (Dec) | Year (Dec) |
|---|---|---|---|---|---|
| 2013 | -$0.04 A | -$0.04 A | -$0.07 A | -$0.05 E | -$0.19 E |
| 2014 | -$0.04 E | -$0.04 E | -$0.04 E | -$0.03 E | -$0.14 E |
| 2015 | | | | | -$0.14 E |
| 2016 | | | | | -$0.13 E |

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## INVESTMENT THESIS

**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).

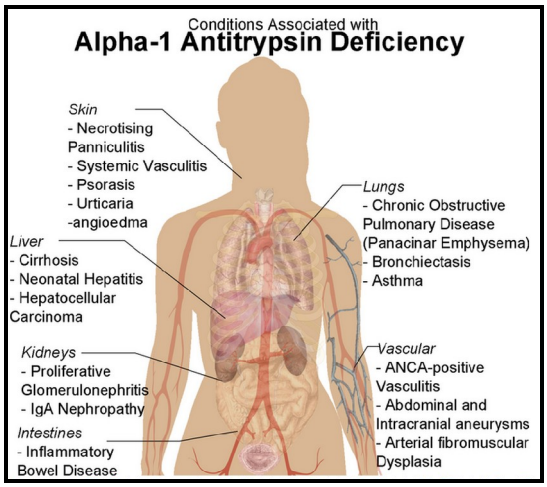
During an acute phase of a disease, the body may increase circulating levels of A1AT to protect tissue, for example in the lungs, liver and pancreas, from inflammatory response. A1AT levels may be increased by more than fourfold, and remain elevated for a week to 10 days (Wewer MD et al., 1987). A1AT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

Prolastin-C: The product is prepared by cold ethanol fractionation from pooled human plasma purified by polyethylene glycol (PEG) precipitation, anion exchange chromatography, and cation exchange chromatography. Two additional steps, a solvent / detergent treatment and 15 nm virus removal nanofiltration are also included in the process to reduce risk of transmission of enveloped and non-enveloped viruses. Pharmacokinetic studies have been completed with Prolastin-C to show increase mean concentrations (Cmax mg/mL) and concentrations over time (AUC0-7 days) post-infusion. Clinical trial experience with Prolastin-C shows a benign adverse event profile, with nausea, urinary tract infection, headache, arthralgia, and importantly, upper respiratory tract infection, occurring at rates less than 1% per infusion. Post-marketing experience with Prolastin-C is suggestive of outstanding safety and tolerability, with an acceptable overall adverse event rate.

Aralast-NP: The product is prepared by cold ethanol fractionation from pooled of human plasma purified by polyethylene glycol (PEG) and zinc chloride precipitations and ion exchange chromatography. To reduce the risk of viral transmission, the manufacturing process includes treatment with a solvent detergent (S/D) mixture (tri-n-butyl phosphate and polysorbate 80) to inactivate enveloped viral agents and a nanofiltration step is incorporated into the manufacturing process to reduce the risk of transmission of enveloped and non-enveloped viral agents. Pharmacokinetic studies with Aralast compared to Prolastin show a similar effect in maintaining target serum A1AT blood levels and clinical effect.

**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).

***…Mechanisms of Action…***

Besides acting as a powerful antioxidant and serum protease inhibitor, p-AAT has a number of interesting molecular targets related to inflammation and binding targets unrelated to protease inhibition. We discuss a number of these mechanisms of action below and propose potential pathways for future development and indications for use.

Protease-Activated Receptors: Besides binding to and inactivating elastase, p-AAT has activity against trypsin and proteinase-3. The presence of excess p-AAT inactivates protease-activated receptors (PARs), creating an intracellular cascade resulting in the diminished inflammatory response. This could play a role in cardiovascular disease (Shah R, 2009), inflammatory gastro-intestinal and mucosal disorders (Dichtl et al, 2000), central nervous system disorders such as multiple sclerosis (Vergnolle et al, 2006), and immune-mediated inflammatory disease such as rheumatoid arthritis (Muroski et al, 2008).

Binding IL-8: A1AT binds to the major neutrophil chemo-attractant IL-8. Scientists believe that blockade of IL-8 may provide benefit during diabetic retinopathy, sickle cell disease, transfusion-related acute lung injury, acute respiratory distress syndrome, renal micro-vasculopathy, acute coronary artery syndrome and stroke (Segal et al, 2011; Al-Omari et al, 2011; Bergin et al, 2010).

Binding Heat Shock Protein: HSPs chaperone proteins for folding inside the cell and function as immune adjuvants and participate in inflammatory responses outside the cell. It has been discovered that elevated levels of HSP70 are present in plasma of patients with type-1 diabetes, but not healthy individuals (Finotti et al, 2004). A1AT has the potential to bind endogenous HSP70 to and preserve islet B-cell biology.

Binding LDL: The role of A1AT in cardiovascular disease is of particular interest given the association with cholesterol levels, particularly low-density lipoprotein apolipoprotein-B. For example, A1AT-LDL complexes have been detected in human atherosclerotic lesions (Mashiba et al, 2001). Potential therapeutic implication for such an association, suggest a protective role of A1AT in atherosclerosis (Talmud et al, 2003).

Binding HIV: Recent research shows that endogenous levels of A1AT prevent infection of HIV-1 (Shapiro et al, 2001) and that adding exogenous human A1AT to latently-infected cell lines reduced production of HIV-1 in vitro (Talmud et al, 2003). Studies also show that HIV-1 infected individuals have reduced serum A1AT concentrations (Bryan et al, 2010).

***…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-1$\beta$ 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).

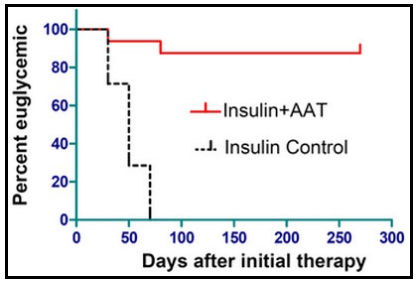


Figure-1

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.<br><br>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.<br><br>Sponsor: Rabin Medical Center, Israel<br>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.<br><br>Sponsor: National Institute of Allergy and Infectious Disease (NIAID)<br>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.<br><br>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.<br><br>Sponsor: University of Colorado: Barbara Davis Center for Childhood Diabetes<br>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).

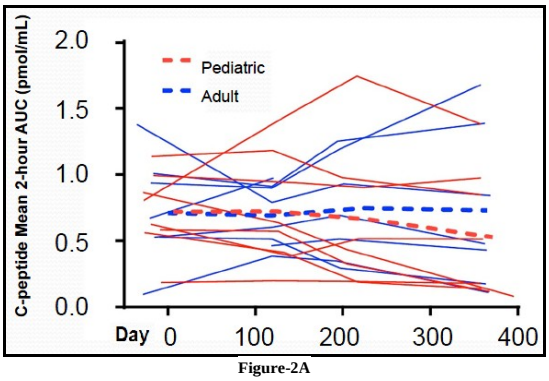


Figure-2A

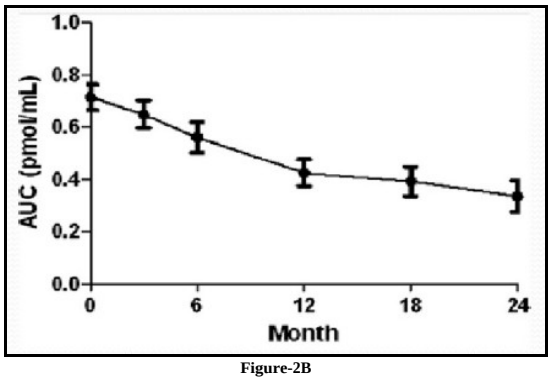


Figure-2B

COPD: Inflammation is a key marker in identifying COPD disease progression (Lewis EC, 2011). Analysis shows that inhaled nonsteroidal anti-inflammatory drugs results in improvement in disease parameters. Preclinical animal studies show inhaled formulations of A1AT confer protection from inflammation and tissue damage caused by cigarette smoke (Pemberton et al, 2006). A logical potential progression for p-AAT development is an inhaled commercial formulation of the drug. The potential for lower doses delivered directly to the lungs may provide for a lower cost vs. the systemic infusion (at around $100,000 per year) required for A1AD or type-1 diabetes.

Cystic Fibrosis: Similar to COPD, inflammation is a key market of disease progression in cystic fibrosis, even in the absence of infection (Sly et al, 2009). Anti-inflammatory agents, such as corticosteroids, are effective in reducing inflammation, but often carry unfavorable tolerability or adverse event profiles. Inhaled agents may provide for a wider therapeutic window given local delivery into the lungs, avoiding systemic metabolism. Preclinical data suggests utility with p-AAT in treating cystic fibrosis (Siekmeier R, 2010). The effect of A1AT on neutrophils, both as an inhibitor of IL-8 function and neutrophil elastase, supports this hypothesis.

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-$\alpha$ and IL-1$\beta$ 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).

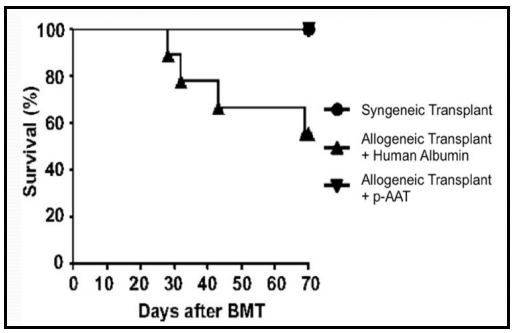


**Figure-3**

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).

Rheumatoid Arthritis: Biologics block TNF-$\alpha$, IL-1$\beta$, and IL-6 are clinically effective in slowing and reversing rheumatoid arthritis (RA) disease progression. Given the mechanism of action of A1AT in inhibiting these cytokines, treatment with p-AAT may be an effective new treatment option for RA. Specifically, inhibition of neutrophil elastase has been sown to interfere with disease progression in respective animal models (Kakimoto et al, 1995). Additionally, new data in mice show that p-AAT can delay arthritis development (Grimstein et al, 2010, 2011). We think p-AAT may offer improve tolerability versus blockbuster biologics such as Remicade, Enbrel and Humira that inhibit TNF- $\alpha$.

Multiple Sclerosis: Inflammation as a therapeutic target in neurologic disorders such as multiple sclerosis (MS) represents and interesting potential indication for p-AAT. Animal studies suggest circulating A1AT may protect from disease progression and initial signs of pathology (Subramanian et al, 2011).

IBD: Although several studies suggest an imbalance of protease activities during inflammatory bowel disease (IBD), correlation appears to exist between A1AT deficiency and IBD only in populations with a severe type of genetic A1AD (Folwaczny et al, 1998; Kotlowski et al, 2008). Nevertheless, considering that intestinal paneth cells are potent producers of inducible AAT (Molmenti et al, 1993), its involvement in IBD as being produced extra-hepatically may be relevant.

Ischemic Heart Disease: Significant interest exists in seeking to reduce inflammatory response during and following an acute myocardial injury. Data shows that p-AAT may play a role in preserving tissue integrity and reducing scar formation thanks to its potent anti-inflammatory characteristic (124). Evidence also shows protection from ischemia reperfusion injury in renal mouse models by p-AAT (Daemen et al, 2000).

Work published in the Journal of Molecular Cell Cardiology shows the effects of exogenously administered p-AAT on caspase-1 activity and on the outcome of ischemia-reperfusion injury in a mouse model of acute myocardial infarction. Mice underwent 30 min of coronary artery ligation followed by reperfusion and were randomly assigned to receive clinical-grade A1AT or albumin at reperfusion. Infarct size was evaluated after 1 and 7 days. A1AT-treated mice had significantly smaller infarct sizes (-30% day 1 and -55% day 7) compared with mice treated with albumin (Figure-4). AAT-treated mice also exhibited a >90% smaller increase in left ventricular end-diastolic diameter and end-systolic diameter, and smaller reduction in ejection fraction. The authors conclude that exogenous administration of clinical grade A1AT reduces caspase-1 activity in the ischemic myocardium leading to preservation of viable myocardium and prevention of adverse cardiac remodeling (Toldo S et al, 2011).

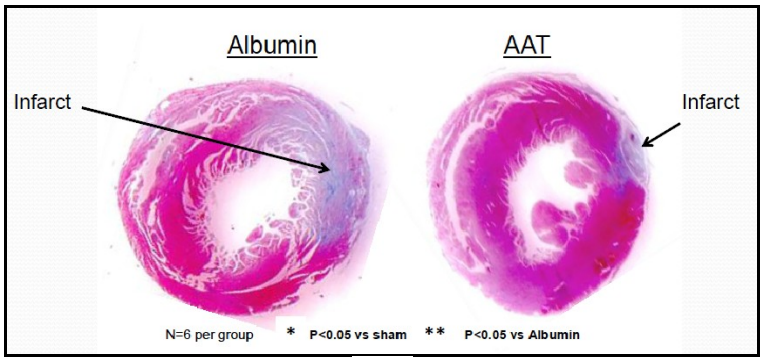



**Figure-4**

Anti-Infections: A1AT belongs to the Serpin superfamily, a class with well-documented antibacterial function (Sallenave JM, 2002). Data show the ability of A1AT to inhibit bacterial expansion through independent mechanisms from protease inhibition. For example, data shows IL-1 blockage by A1AT may interfere with bacterial growth (Lewis EC, 2011). Clinical studies indicate that augmentation therapy with p-AAT for genetically deficient patients effectively attenuates microbial colonization, as well as the frequency and severity of acute COPD exacerbations (Lieberman J, 2000). Moreover, the fact that cystic fibrosis patients benefit from p-AAT inhalation, even when introduced during active lung infections such as *Staphylococcus* and *Pseudomonas* (Griese et al, 2007), further supports the claim that host defenses are enforced in the presence of elevated A1AT levels.

Nitric Oxide (NO) Biomarker For Disease: A recent paper published in the Journal of Leukocyte Biology (JLB) in December 2012 (Chan et al, 2012) explores an interesting characteristic of A1AT. Nitric oxide (NO) is an endogenously produced gas that regulates inflammation, vascular tone, neurotransmission, and immunity. NO production can be increased by exposing cells to several endogenous and exogenous pro-inflammatory mediators, including IFN-gamma, TNF-$\alpha$, IL-1$\beta$, and LPS. Many illnesses are associated with increased NO synthesis, including septic shock, asthma, COPD, lung diseases, type 1 diabetes, inflammatory arthritides, and myocardial reperfusion injury.

Serine protease activity appears to enhance NO production whereas, A1AT has been shown to inhibit NO production *in vitro*. Thus, the authors hypothesized that A1AT might operating under a similar mechanism *in vivo*. After all, A1AT has been shown to inhibit cell activation and suppress cytokine production associated with pro-inflammatory stimulation.

The authors tested this hypothesis on nine healthy volunteers (controls) and five volunteers with genetic abnormalities resulting from reduced circulating A1AT levels. The results show that A1AT concentrations significantly inhibited combined LPS- and IFN-γ-induced NO synthesis, and NO synthesis inhibition was associated with decreased expression of intracellular isoenzymes that produce NO.

Below is a representation of exhaled NO concentration for healthy subjects (control, n=9), subjects with smoking-associate COPD (COPD, n=15), and individuals with A1AD (AAT-deficient, n=5) (Figure-5A). The graph shows patients with A1AH have a statistically significant greater concentration of NO than the control or the smoking-associate COPD population. The addition of A1AT at various concentrations (0.1, 1, 2, 3mg/mL) reduced the volume of NO metabolite, $NO_2^-$, when stimulated with pro-inflammatory cytokines, LPS and IFN-gamma (Figure-5B). All data and graphs are from the Chan et al, 2012 paper published in JBP, December 2012.

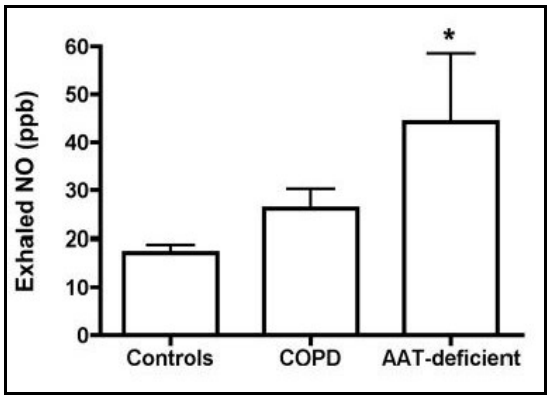



Figure-5A

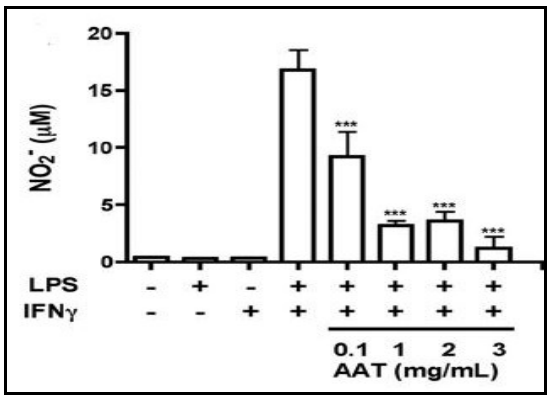



Figure-5B

***…Omni Bio's Business Model…***

Omni Bio Pharmaceuticals was formed around intellectual property claiming method of use rights for p-AAT in the treatment of a broad spectrum of inflammatory and auto-immune diseases, as well as viral and bacterial diseases. The company holds licenses to patents issued in the U.S. for the treatment of diabetes, and certain bacterial and viral indications. Patent applications are pending in several other areas, including GvHD related to bone marrow transplantation rejection, radioprotection, inflammatory bowel disease (IBD) and cardiac remodeling following myocardial infarction.

Omni Bio is currently engaging in business development activities, with a goal to license the rights to these expanded indications to the leading manufacturers of p-AAT such as Grifols, Baxter, CSL Behring, and Kamada, Ltd. We believe for these companies it's a matter of timing and potentially expanding the indications of use for their respective p-AAT products, versus supply. For Omni Bio, we believe licensing these rights could provide non-dilutive cash in terms of upfront and royalty payments to fund operations and the advancement of the company's next-generation Fc-AAT molecule, which we discuss in greater detail below.

Omni Bio has licensed the rights to these applications from independent institutions and will owe sub-license and sub-royalty payments on deals it signs with p-AAT manufacturers. In September 2008, the company entered into a licensing agreement with Bio Holding, Inc. for the patent applications relating to the use of p-AAT for the treatment of diabetes. This patent was issued to Bio Holding in December 2011 for the methods for treating diabetes by administering p-AAT. Bio Holding is majority-owned by Dr. Leland Shapiro, who is the inventor on the patent and an Associate Professor of Medicine at the University of Colorado, Denver. Omni will owe Bio Holding a 4% royalty on sales of p-AAT in diabetes and 30% of any sub-license payments it may receive for sub-licensing the rights to the patent to a p-AAT manufacturer such as Grifols or Baxter.

All other applications with p-AAT, such as bacterial disorders, viral disorders, and transplant rejection are licensed from Reagents University of Colorado (RUC). Omni will owe RUC a 3% royalty on sales of p-AAT into these indications and 20% of any sub-license payments it receives for sub-licensing these rights to a p-AAT manufacturer.

The challenge for Omni Bio in this regard is getting A1AT manufacturers to shell out upfront cash and promise backend milestone and royalty payments on a drug with limited supply and no pivotal registration data yet in hand. Baxter markets Aralast-NP for A1AD. To market for indications such as diabetes or GvHD, larger phase 2/3 trials will need to be conducted.

Omni Bio's patents stop Baxter and Grifols from marketing Aralast-NP and Prolastin-C in indications outside of A1AD, but physicians are not bound by patents when using the drug off-label. We suspect that all four manufacturers, Grifols, Baxter, CSL Behring, and Kamada would love to market their products for these larger indications, but none of them want to pay for it. Positive data from any p-AAT drug will surely help drive sales of the other three competing products.

**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.

***…Alternative Sources & Ideas…***

According to Lewis EC, 2011, attempts to utilize transgenic sheep for producing human A1AT and other methods for A1AT mass production have been met with limited success. Sheep can be genetically altered to product human A1AT under the control of mammary gland promoter. Biologically active human A1AT has been generated in milk and purified and introduced to humans by intravenous infusion (Niemann et al, 2003). In fact, a population of 4,500 sheep is capable of providing 5,000 kg human A1AT. That would be enough to treat 1,600 of the confirmed 5,000 A1AD patients in the U.S. each year.

Unfortunately, when human A1AT produced by transgenic sheep was infused into human subjects, a reaction of rapid onset of fever due to the mounting of human anti-sheep antibodies against residual sheep alpha-1 antichymotrypsin. Thus, efforts in this endeavor have been discontinued.

Recombinant A1AT has been derived from plants, yeast, fungi, animals, insect cells, bacteria and mammalian cells. Efforts have been made to manipulate humanized systems to product A1AT and conjugate with polyethylene glycol (PEG) to prolong half-life and circulation. Conjugating with PEG is an attempt to avoid antibody-mediated inactivation of after dosing. Formulations of inhaled recombinant A1AT exist, and have even been shown to ameliorate cigarette smoke-induced emphysema in mice (Pemberton et al, 2006). Nevertheless, none of the above approaches appear at superior to human pooled p-AAT for patients with A1AD.

Attempt to use gene therapy to correct the defective coding for the A1AT protein in patients with A1AT has also been met with limited success. Experimental genetic manipulations may surpass the requirement of purification of p-AAT and reduce exposure to infectious material, but gene therapy still holds the downside of the inability to control circulating A1AT levels once introduced.

**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. While Omni Bio is pursing patent applications for its lead Fc-AAT molecule, 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-6A) 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-6B).

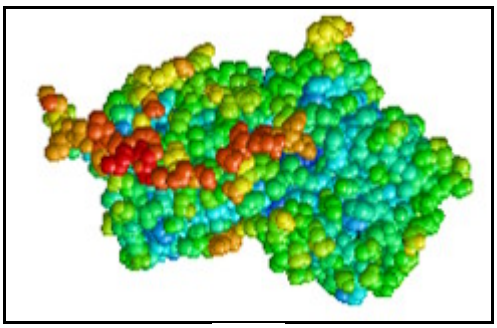


Figure-6A

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

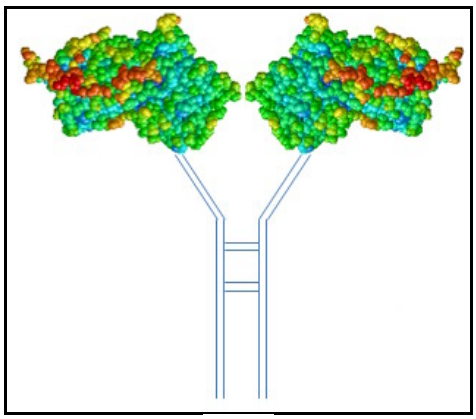


Figure-6B

Omni Bio believes the technology used to construct Fc-AAT is similar to that already used to create highly successful drugs for human application, such as Amgen / Pfizer's Enbrel. Enbrel was jointly developed by Immunex (acquired by Amgen) and Wyeth (acquired by Pfizer). Omni Bio's CEO, Dr. Bruce Schneider, was a senior R&D executive at Wyeth and was intimately involved in the development of Enbrel. Through our conversations with Dr. Schneider, he tells us that many of the experiences with Enbrel are transferable to the development of Omni Bio's Fc-AAT molecule.

We are encouraged by the fact that Fc-AAT is following the development path of a highly successful drug in Enbrel, and that Dr. Schneider brings significant experience to table in this regard. 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 4$^{th}$ 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-1$\beta$ and IL-6 in a dose-dependent manner (Figure-7A). Data also show Fc-AAT was at least 40x more potent than p-AAT (Figure-7B).

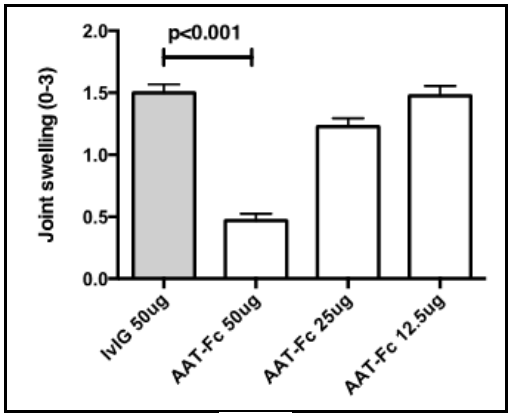



Figure-7A

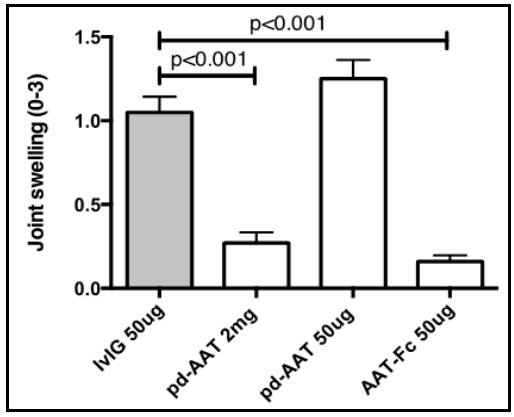



Figure-7B

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.

***…Development Time Lines…***

Omni Bio exited its third quarter (ended December 31, 2012) with $0.789 million in cash and equivalents. We model the company burned roughly $0.450 million in the fourth quarter 2013 (ended March 31, 2013), meaning the company will report around $0.350 million when it files fiscal year end 2013 financials in late June 2013.

In late May 2013, the company raised approximately $1.540 million ($1.369 million net) through the sale of 6.1 million shares of stock at $0.25 per share. Management remains active in seeking additional capital. We expect the company to secure another $1-2 million over the next few weeks. Besides operations, we believe the company requires cash to push forward with the necessary scale-up synthesis and safety and toxicity studies on Fc-AAT required prior to filing the investigation new drug (IND) application. We estimate the company requires $5 to $6 million to complete these studies over the next two years; that's on top of an estimated $3 to $4 million in overhead operating burn. Therefore, we believe the company still requires, from today, roughly $8 million to execute on it's business plan.

The goal following FDA approval of the IND application is to secure a development and commercialization partnership with a larger pharmaceutical company – one that sees and agrees with management's optimistic belief on the potential for Fc-AAT. Thus, a deal could potentially get done in 2015 or 2016. This remains the single biggest catalyst for shareholders going forward. We see the pathway for GvHD as potentially the quickest route to market, moving from phase 1 right into registration studies given the high unmet medical need. Indications in diabetes or gout would require a full clinical program of the standard phase 1, 2, and 3 trials.

## MANAGEMENT & BOARD PROFILES

**BRUCE SCHNEIDER, PH.D. - CHIEF EXECUTIVE OFFICER**

Dr. Schneider has served as the company's CEO and a member of the Board of Directors since January 1, 2013. Since 2010, he has provided R&D executive advisory and business development services to several large and small pharmaceutical companies, including an extensive role with Pfizer where he was engaged to facilitate strategic planning and decision-making for its early drug development pipeline. From 2009 to 2010, he was employed by Pfizer as Executive Vice President & R&D Integration Lead. From 1972-2009, he was employed by Wyeth Research, which was acquired by Pfizer in 2009, where he held numerous senior-level R&D positions, including Executive Vice President & Chief of Operations (2002 to 2009), Senior Vice President, Research Operations & Planning (1992-2002) and Vice President, Worldwide Clinical Operations (1987-1992). Dr. Schneider holds a Ph.D. in Applied Statistics from Temple University and a Sc.B in Applied Mathematics from Brown University.

**CHARLES DINARELLO - CHIEF SCIENTIFIC OFFICER**

Charles Dinarello, MD has served as the company's Chief Scientific Officer and Director of Medical Affairs since February 2011. He also serves on the company's Scientific Advisory Board. From March 2009 to February 2011, he served as Acting Chief Executive Officer and a member of the Board of Directors. Previously Professor of Medicine at Tufts University in Boston, since 1996, he is Professor of Medicine and Immunology at the University of Colorado Denver. Dr. Dinarello has published over 700 original research articles on cytokines, particularly interleukin-1 (IL-1) and tumor necrosis factor, and is considered a "founding father" of cytokine biology. He is also a member of the editorial board of the Proceedings of the National Academy of Sciences.

**ROBERT OGDEN - CHIEF FINANCIAL OFFICER**

Robert Ogden has served as the company's Chief Financial Officer, Treasurer and Secretary since May 2009. From 2007 to 2009, Mr. Ogden was a financial consultant, primarily providing services to public companies, including Fortune 500 and micro-cap entities. From May 2004 to June 2007, Mr. Ogden served as Chief Financial Officer, Treasurer and Secretary of SAN Holdings, Inc., a publicly-traded data storage solutions provider and software company, where he was responsible for all administrative and finance functions. From 2000 to May 2004, he was a multi-industry financial consultant providing financial controller and reporting services to both private and public companies. His prior experience includes financial executive positions with two NASDAQ companies. Mr. Ogden began his career as a public accountant with PricewaterhouseCoopers LLP. Mr. Ogden received a BS in Commerce from the University of Virginia and is a CPA.

**MICHAEL KAMARCK – BOARD MEMBER**

Michael Kamarck has served as a member of the Board of Directors since January 2013. From 2010 to 2012, Dr. Kamarck was employed by Merck as President of Merck BioVentures and SVP of Vaccines and Biologics Manufacturing. From 2001 to 2009, he was employed by Wyeth, where he held various senior executive positions, including President, Technical Operations and Product Supply and was responsible for global technical operations for all of the Wyeth businesses. Dr. Kamarck also served as a member of the Wyeth Management Committee. Prior to Wyeth, he was employed by Bayer AG for 17 years in a variety of technical and leadership capacities. Dr. Kamarck received his B.A. from Oberlin College, his Ph.D. from MIT and was a Leukemia Society Fellow at Yale University.

**VICKI BARONE – BOARD CHAIRPERSON**

Vicki Barone has served as the Chairperson of the Board of Directors since March 2009 and is the Chair of the Audit Committee. From March 2008 until March 2009, she was the Chairperson of the Board of Directors of Apro Bio Pharmaceutical Corporation, Omni Bio's predecessor operating company. Since 1996, Ms. Barone has served as the Chief Financial and Compliance Officer for GVC Capital LLC, where she is also a Senior Managing Partner and a member of the Commitment Committee, and actively manages the corporate finance projects of the firm. Since 2010, she has served on the board of the National Investment Banking Association, which she also served on from 2005 to 2007, including serving as the Chairperson in 2007 and Secretary and Treasurer in 2006. She is a CPA and a Certified Financial Planner and received a BS in Finance and MS in Accounting from the University of Colorado.

**STEVEN BATHGATE – BOARD MEMBER**

Steven Bathgate has served as a member of the Board of Directors since March 2009. From August 31, 2012 to December 31, 2012, he served as Interim Chief Executive Officer. From March 2008 until March 2009, he was a director of Apro Bio Pharmaceutical Corporation, Omni Bio's predecessor operating company. Since 1996, Mr. Bathgate has served as a Senior Managing Partner of GVC Capital., and is its founder. Prior to starting GVC Capital, he was Chairman and Chief Executive Officer of Cohig & Associates, Inc. Mr. Bathgate currently serves on the board of directors of Creston Resources, Inc. (OTC: CSTJ) and formerly served on the board of directors of Birner Dental Management Services, Inc. (Nasdaq: BDMS). He received a BS degree in Finance from the University of Colorado.

**MICHAEL ISEMAN – BOARD MEMBER**

Michael Iseman, MD has served as a member of the Board of Directors since March 2009 and is the Chairman of the Scientific Advisory Board. From August 2008 until March 2009, Dr. Iseman was a director of Apro Bio Pharmaceutical. Since 1980, he has been a Professor of Medicine at the University of Colorado Denver with appointments in both the Division of Pulmonary Medicine and Infectious Diseases. Since 1983, he has also been a physician with the National Jewish Medical and Research Center in Denver and currently serves as its Chief of Clinical Mycobacterial Disease Service. Dr. Iseman received his undergraduate degree with honors from Princeton University and his MD from Columbia University's College of Physicians and Surgeons**.**

**MICHAEL WORT – BOARD MEMBER**

Michael Wort has served as a member of the Board of Directors since March 2009, and is a founder of Apro Bio Pharmaceutical Corporation. From October 2008 until March 2009, he was a director of Apro Bio Pharmaceutical Corporation and from October 2008 through December 2008, he served as its Interim Chief Executive Officer. Since 2007, Mr. Wort has served as the Managing Director of De Facto Communications, a subsidiary of Chime Communications, which is listed on the London Stock Exchange. In 2004, Mr. Wort founded MC BioCommunications, an investor and public relations firm specializing in emerging bioscience companies. He is also a founder and director of BeckPharma Limited, a technology transfer company, and PharmScape, a biotechnology consultancy company, both of which were founded in 2003. Mr. Wort's other prior experience includes various sales, marketing and general management positions with GlaxoSmithKline plc. Additionally, he has served as an advisor and consultant on fund raising for more than 15 small-cap, biotechnology companies. Mr. Wort received his BSC in Applied Biology and is a Chartered Graduate Biologist in Industrial Microbiology.

**ALBERT KRAMER – BOARD MEMBER**

Albert Kramer has served as a member of the Board of Directors since March 2009. From April 2008 until March 2009, he was a director of Apro Bio Pharmaceutical Corporation. Since 1993, Mr. Kramer has served as an attorney with the Kramer Law Firm. From 1993 to 2005, Mr. Kramer served as Special Counsel to Syratech Corporation. From 2004 to 2008, he served as Chief Counsel to Travelers Marketing, LLC. From 1975 to 1992, Mr. Kramer served as a District Court Judge for the Massachusetts Trial Court. He received his undergraduate and law degrees from Boston University.

## VALUATION & RECOMMENDATION

**Initiating Coverage**

We are initiating coverage of Omni Bio Pharmaceuticals with a 'Neutral' rating and $0.50 price target. Despite the fact that we see the company as considerably under-valued today given the potential to both sign partnerships around expanded indications of p-AAT and develop a next-generation potential blockbuster in Fc-AAT, the cash position and lack of meaningful catalysts gives us pause. Thanks to a recent financing, Omni Bio is addressing the first of our concerns, the cash position. We think additional cash is required to push forward in development of Fc-AAT. Once this cash is secured, we will have less reservation on the second concern, i.e. a lack of meaningful catalysts to drive the valuation higher.

***...Summary Recommendation…***

Alpha-1 Antitrypsin (A1AT) is a protease inhibitor belonging to the serpin family. A1AT acts as a serum trypsin inhibitor, inhibiting a wide variety of proteases, protecting tissue from enzymes of inflammatory cells, especially neutrophil elastase. 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.

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. 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

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). 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. We 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 clinical centers.

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. However, 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. 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. 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.

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). Omni Bio's lead Fc-AAT molecule, which they refer to internally as Fc-AAT-2, is a fusion protein that combines human A1AT 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. Omni Bio believes the technology used to construct Fc-AAT is similar to that already used to create highly successful drugs for human application, such as Enbrel. Omni Bio's CEO, Dr. Bruce Schneider, was a senior R&D executive at Wyeth and was intimately involved in the development of Enbrel. Through our conversations with Dr. Schneider, he tells us that many of the experiences with Enbrel are transferable to the development of Omni Bio's Fc-AAT molecule.

We are encouraged by the fact that Fc-AAT is following the development path of a highly successful drug in Enbrel, and that Dr. Schneider brings significant experience to table in this regard. 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.

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.

If successfully commercialized, we see the opportunity for Fc-AAT eclipsing $1 billion given potential indications in type-1 diabetes, GvHD, and gout. We have built heavily discounted financial projections in an attempt to value this opportunity. Below is a representation of these projections, which yield a fair-value in the area of $30 million, or $0.50 per share. This represents attractive upside given the current stock price at only $0.35 per share.

However, the company just recently raised cash to the tune of $1.54 million at the end of May 2013 at $0.25 per share. We estimate the company will report around $0.350 million in cash when they report year-end 2013 financials (period ending March 31, 2013). Adding in a net of $1.369 million from the raise and subtracting out around $0.400 million in operating burn for the first quarter fiscal 2014 (period ending June 30, 2013), we forecast the cash position to be around $1.325 million on June 30, 2013.

The company notes being in active discussions to raise an additional $4.5 million in cash, with similar terms to the financial just completed in late May 2013 (straight stock at $0.25 per share with no warrants). Despite the fact that we like the story and the potential for Fc-AAT, we hesitate to tell people to buy the stock today at $0.35 knowing future offerings are likely at $0.25. Our two primary concerns at this stage are:

1) The need for cash and future dilutive offerings, and
2) The lack of meaningful catalysts on the clinical development front.

We are pleased to see the company addressing the first issue by raising $1.54 million in late May 2013. As noted above, more is coming by the end of June 2013 – potentially as much as $4.5 million more. Just how successful the company is over the next month in pulling in more cash at $0.25 per share should give investors a sense of the interest and upside in the stock. Take note, if the company can close an additional $4.5 million, the floor in the stock will be $0.25, and that might be a great entry-price for new investors.

The second issue, a lack of catalysts, stems from the fact that the company does not have enough cash to push forward with the necessary scale-up synthesis and safety and toxicity studies on Fc-AAT required prior to filing the investigation new drug (IND) application. Essentially, concern No. 2 listed above is a direct result of concern No. 1. Therefore, as the company addresses concern No. 1, which they are doing now, concern No. 2 disappears.

Thus, we are initiating coverage today so that investors can better familiarize themselves with the story, perhaps even establish long-term positions, but more importantly put Omni Bio on their radar as the company completes its financing and pushes forward with a potential blockbuster drug in Fc-AAT.

## PROJECTED FINANCIALS

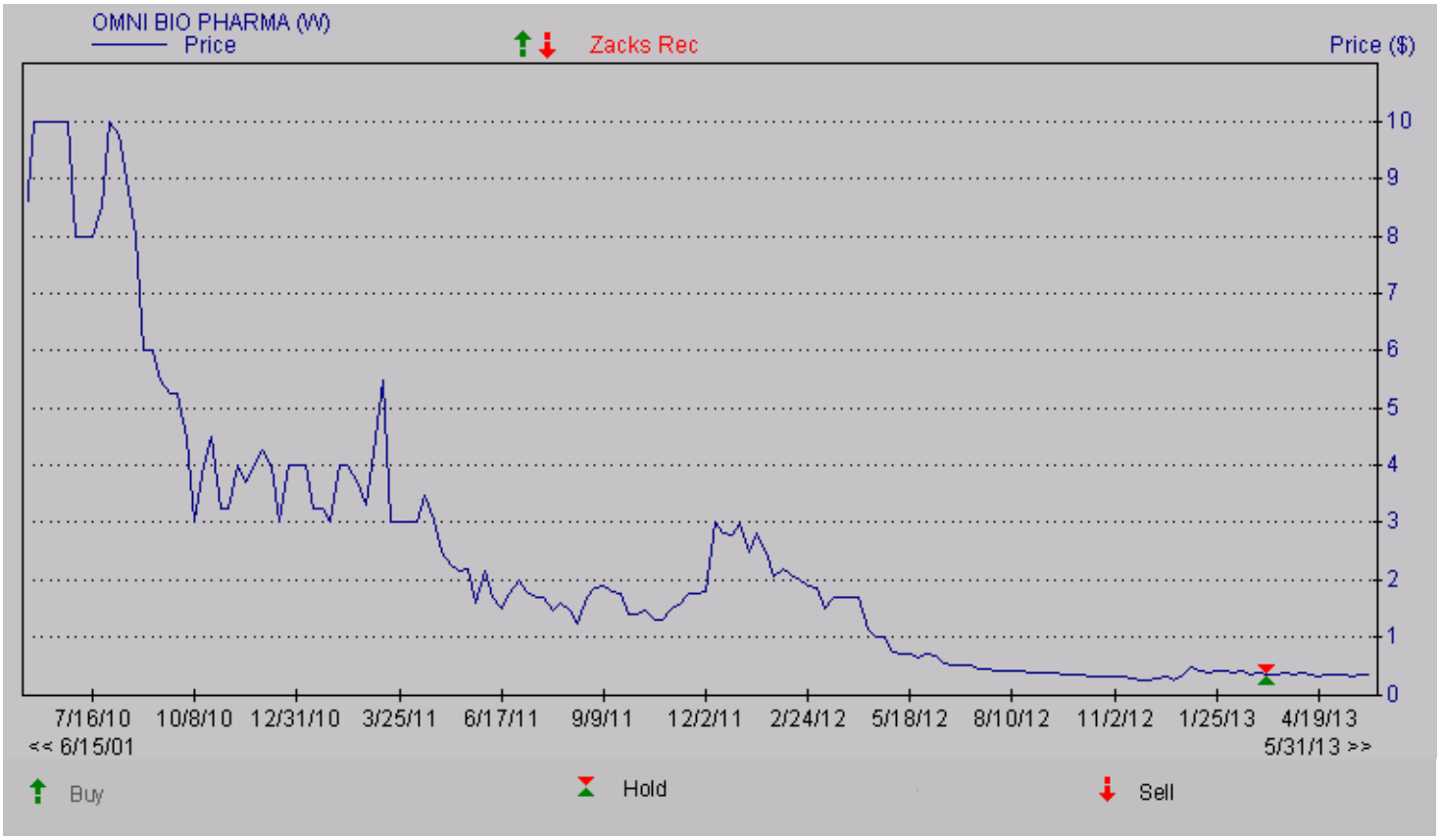
**Omni Bio Pharmaceuticals, Inc.**
Income Statement

| | FY'12 A | June-12A | Sept-12A | Dec-12A | Mar-13E | FY'13E | 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 | $0.022 | $0.128 | $0.073 | $0.100 | $0.322 | $0.500 | $0.750 | $1.000 |
| *% R&D* | - | - | - | - | - | - | - | - | - |
| SG&A | $4.237 | $1.120 | $1.104 | $1.747 | $1.400 | $5.372 | $5.500 | $6.000 | $6.500 |
| *% SG&A* | - | - | - | - | - | - | - | - | - |
| Operating Income | **($4.635)** | **($1.143)** | **($1.232)** | **($1.819)** | **($1.500)** | **($5.694)** | **($6.000)** | **($6.750)** | **($7.500)** |
| *Operating Margin* | - | - | - | - | - | - | - | - | - |
| Interest & Other Income | ($0.760) | $0.011 | ($0.098) | ($0.352) | ($0.100) | ($0.540) | ($0.350) | ($0.250) | ($0.250) |
| Pre-Tax Income | ($5.395) | ($1.132) | ($1.330) | ($2.172) | ($1.600) | ($6.234) | ($6.350) | ($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) | ($1.132) | ($1.330) | ($2.172) | ($1.600) | ($6.234) | ($6.350) | ($7.000) | ($7.750) |
| *Net Margin* | - | - | - | - | - | - | - | - | - |
| **Reported EPS** | **($0.17)** | **($0.04)** | **($0.04)** | **($0.07)** | **($0.05)** | **($0.19)** | **($0.14)** | **($0.14)** | **($0.13)** |
| *YOY Growth* | - | - | - | - | - | - | - | - | - |
| Basic Shares Outstanding | 31.4 | 32.0 | 32.0 | 32.0 | 35.0 | 32.8 | 44.5 | 50.0 | 60.0 |

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

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