Zacks Small-Cap Research

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AmpliPhi Biosciences Corp. (APHB – NYSE MKT)

APHB: Preclinical Data Shows Broad Activity of AB-PA01 Against* P. Aeruginosa *Clinical Isolates; ECC With Intrexon Canceled…

Current Recommendation	**Buy**
Prior Recommendation	Hold
Date of Last Change	12/01/2015
Current Price (04/20/16)	$3.19
Target Price	**$15.00**

UPDATE

On April 12, 2016, AmpliPhi Biosciences Corp. (APHB) presented data on AB-PA01 showing both *in vitro* and *in vivo* activity against almost 88% of *Pseudomonas aeruginosa* clinical isolates from a global population of cystic fibrosis (CF) patients. AB-PA01 was active against both multi-drug resistant and sensitive strains of *P. aeruginosa* and the data presents a strong rationale for moving the drug into clinical testing in CF patients.

On April 14, 2016, AmpliPhi announced that it was terminating the Exclusive Channel Collaboration (ECC) with Intrexon Corp. (XON). This move was undertaken such that the company can partner with other companies for genetic manipulation of phages.

SUMMARY DATA

52-Week High	**$13.95**
52-Week Low	**$2.32**
One-Year Return (%)	**-76.37**
Beta	**1.65**
Average Daily Volume (sh)	**40,929**
Shares Outstanding (mil)	**8**
Market Capitalization ($mil)	**$26**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**38**
Insider Ownership (%)	**1**
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 2015 Estimate	**N/A**
P/E using 2016 Estimate	**N/A**

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

ZACKS ESTIMATES

Revenue
(In millions of $)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2015	0.1 A	0.1 A	0.1 A	0.1 A	0.5 A
2016	0.1 E	0.1 E	0.1 E	0.1 E	0.5 E
2017					0.5 E
2018					0.5 E

Earnings per Share
(EPS is operating earnings before non-recurring items)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2015	-$3.49 A	$1.58 A	-$0.30 A	-$0.40 A	$-1.99 A
2016	-$0.65 E	-$0.53 E	-$0.47 E	-$0.47 E	-$2.04 E
2017					-$1.72 E
2018					-$1.55 E

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AB-PA01 Shows Broad Activity Against *P. Aeruginosa* Clinical Isolates

On April 12, 2016, AmpliPhi Biosciences Corp. (APHB) presented data on AB-PA01 showing both *in vitro* and *in vivo* activity against 87.8% of *Pseudomonas Aeruginosa* clinical isolates from a global population of cystic fibrosis (CF) patients. AB-PA01 was active against both multi-drug resistant and sensitive strains of *P. aeruginosa* and the data presents a strong rationale for moving the drug into clinical testing in CF patients.

Background On Cystic Fibrosis

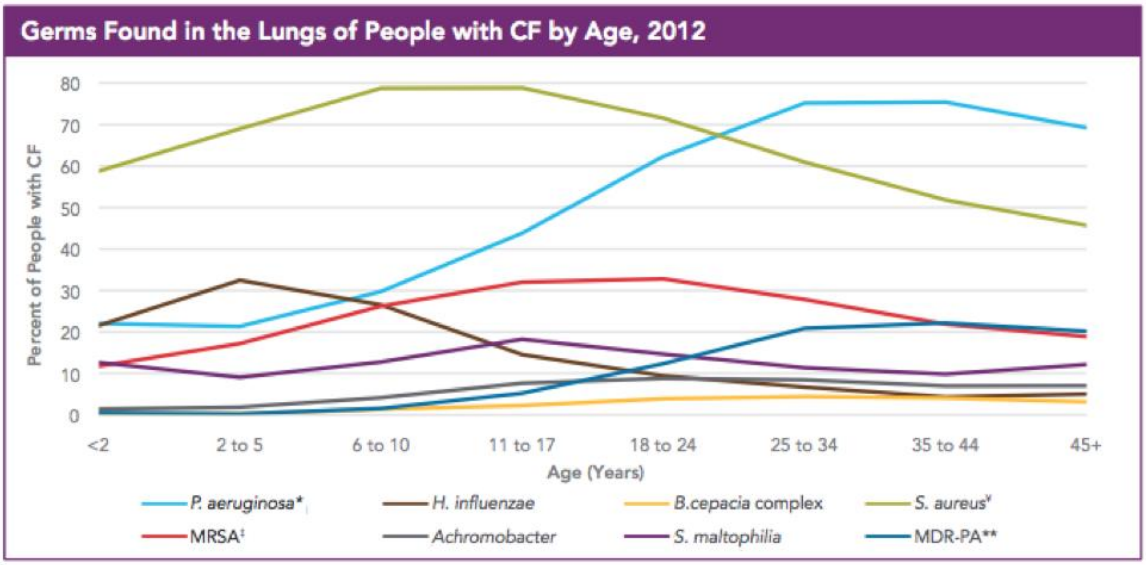
Cystic Fibrosis (CF) is an autosomal recessive genetic disorder that affects close to 30,000 individuals in the U.S. and a total of 70,000 people worldwide. The hallmark of CF is a thick, sticky mucus build up in various organs throughout the body. Typically, mucus is a slippery, water substance produced by tissues that line organs and body cavities, such as the lungs and nose. However, due to abnormal sodium and chloride transport in the lungs, pancreas, liver, and digestive tract, patients suffering from CF have mucus that is thick and sticky and leads to blockages of the airways in the lungs and ducts in the pancreas (Boucher, 2004). The name refers to the characteristic scarring (fibrosis) and cyst formation seen in the pancreas.

CF is caused by a mutation in the cystic fibrosis transmembrane conductance regulator (CFTR), a gene found on chromosome #7. The typical protein produced by the CFTR gene contains 1,480 amino acids, however in 70% of CF patients worldwide, and 90% of patients in the U.S., there is a loss of the amino acid phenylalanine at the 508th position on the protein (Bobadilla *et al*., 2002). This mutation, termed ΔF508 (Δ meaning deletion), causes the protein to fold improperly thus resulting in its degradation.

The CFTR protein is a chloride ion channel that is involved in creating sweat, digestive juices, and mucus. When the protein is either not present or not functioning properly, there is a buildup of chloride ions inside the cells in the airway. While no one knows exactly how this leads to a buildup of thick mucus, one theory suggests that the malfunctioning CFTR protein leads to a paradoxical increase in sodium and chloride uptake, which in turn leads to increased water reabsorption, creating dehydrated and thick mucus.

The most serious complication associated with the disease is difficulty in breathing due to recurrent lung infections. Lung disease in patients with CF results from airway blockage and resulting inflammation. The build up of mucus is an ideal environment for bacteria to grow, and the inflammation and repeated infections result in injury and structural changes to the lungs. Early stages of the disease are characterized by excessive coughing, phlegm production, and shortness of breath. These symptoms are exacerbated when the overgrowth of bacteria leads to pneumonia. *Staphylococcus aureus*, *Haemophilus influenza*, and *Pseudomonas aeruginosa* are the three most common organisms that cause lung infections in CF patients.

The lungs of CF patients are colonized by bacteria starting at a very young age. The combination of bacterial growth and thick mucus leads to the production of bacterial microenvironments known as biofilms, which are an aggregate of microorganisms in which cells stick to each other and are embedded within a self-produced matrix of extracellular polymeric substance. Biofilms are difficult both for the immune system and for antibiotics to penetrate, thus leading to reduced treatment efficacy. Early in life, *S. aureus* and *H. influenzae* are the most common bacterial strains found in CF patients lungs. However, by the age of 18, 70% of CF patients will harbor *P. aeruginosa* (CFF 2012 Patient Registry Report). The spread of bacteria between CF patients is so common that they are routinely isolated from one another in a healthcare setting.



Source: CFF, 2012 Patient Registry Report

AB-PA01 is Active Against Multiple* P. aeruginosa *Isolates

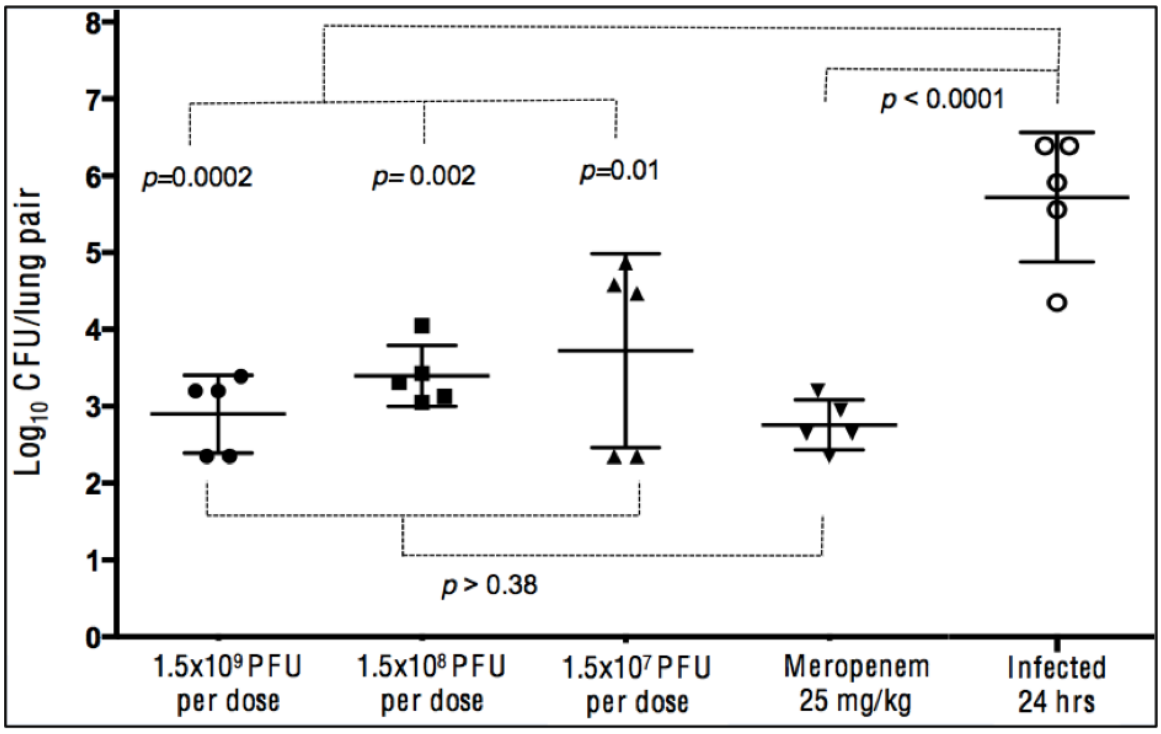
AB-PA01 is a mixture of four bacteriophages that specifically target *P. aeruginosa*. To develop this product, AmpliPhi created a global "diversity" panel of relevant *P. aeruginosa* clinical isolates from CF clinics around the globe. Clinical isolates are bacteria cultured from infected patients. This diversity panel was screened against the company's bacteriophage library that was isolated and characterized according to their proprietary discovery and development platform. The bacteriophage mix was selected to exhibit a high degree of "complementation," defined as the number of bacteria targeted by more than one bacteriophage in the product. High complementation is an important factor in preventing bacteria from developing resistance to bacteriophage products.

To test the activity of AB-PA01, 10^8 PFU/mL was spotted onto different strains of *P. aeurigonsa* cultures. Each strain was considered sensitive if more than 20 plaques (areas of bacterial cell death) were observed. The following table shows the percentage of *P. aeruginosa* isolates that were sensitive to treatment with AB-PA01. Complementation was shown by the high percentage of *P. aeruginosa* isolates that were sensitive to two or more of the phages in AB-PA01.

Number of Isolates	Area (Year of Isolation)	Type	AB-PA01 % of Activity	% of isolates sensitive to ≥2 phages in mix
67*	UK/AU/USA (2012-13)	CF	95.5%	87.5%
120	UK (2012-13)	CF	85.0%	95.0%
60	AU (2007-2013)	CF	93.3%	98.2%
40	USA (2014)	CF	87.5%	91.4%
82	UK (2015)	CF	81.7%	92.5%
60	USA/EU/AU (2013)	Non-CF	83.3%	80.0%
369	Total CF Isolates		87.8%	93.2%
429	Total isolates (CF + Non-CF)		87.2%	91.4%

Source: Lehman *et al.*, 2016

The *in vivo* activity of AB-PA01 was tested in immunocompetent CD-1 mice infected with 6.26 $\log_{10}$ CFU of *P. aeruginosa*. Two hours after infecting the mice, three different doses of AB-PA01 ($7.5x10^9$/mL, $7.5x10^8$/mL, or $7.5x10^7$/mL) were administered intranasally to three different dosage groups (n=5). A second dose of phage was administered four hours later. Meropenem, a broad spectrum antibiotic, was administered to a fourth group of animals subcutaneously two and six hours post infection, while a fifth group of animals received phage diluent as a control. The mice were euthanized 24 hours after infection and the CFU/lung pair was determined. The following graph shows that all three doses of phage resulted in a statistically significant decrease in bacterial load compared to the control group. There was also a dose response seen with higher doses of AB-PA01 resulting in decreased bacterial load. Lastly, AB-PA01 showed similar efficacy to meropenem.



Source: Lehman *et al*., 2016

AmpliPhi is developing AB-PA01 in collaboration with the Royal Brompton Hospital in London, England. The company is continuing formulation work on AB-PA01 through the rest of 2016, and we anticipate a Clinical Trial Application (CTA) being submitted to the Medicines and Healthcare Products Regulatory Authority (MHRA) in the UK in the first half of 2017, with the first clinical trial likely to commence shortly thereafter. The MHRA has agreed with the company's plans to conduct a first-in-man dose ranging clinical trial in CF patients, thus bypassing the need to test AB-PA01 first in healthy volunteers.

AmpliPhi Cancels ECC With Intrexon

On April 14, 2016, AmpliPhi announced that it had provided written notice to Intrexon Corp (XON) to cancel the Exclusive Channel Collaboration (ECC) between the two companies. The ECC agreement was directed towards the research, development, and commercialization of the company's *P. aeruginosa* and *Clostridium difficile* programs. AmpliPhi decided to terminate the agreement due to the belief that meaningful progress had not been made under the collaboration program and the desire to avoid any further fiduciary responsibility under the agreement. In addition, this allows the company to pursue collaborations for genetic modification of phage products with other companies.

Conclusion

The data presented by AmpliPhi on AB-PA01 are very encouraging in both the activity toward such a high percentage of clinical isolates of *P. aeruginosa* as well as *in vivo* activity that matches the effects of a broad spectrum antibiotic. There are approximately 30,000 patients with CF in the U.S. and another 40,000 in the rest of the world. With 70% of CF adults harboring *P. aeruginosa* infections, most of which are resistant to antibiotics due to the development of biofilms or acquired resistance, this represents a sizeable market opportunity for the company. We anticipate Phase 1 dose-ranging studies beginning in CF patients in 2017.

As a reminder, AmpliPhi is currently conducting a Phase 1 study of AB-SA01 in patients with chronic rhinosinusitis. We anticipate results from this study being released in the second half of 2016. While this study is primarily a safety study, that does not mean additional information won't be gained from it in regards to patient outcomes. We are looking forward to reviewing the data when it is released, and note that a positive trend toward improving patients' symptoms could be a catalyst for the stock. We continue to remain positive on the AmpliPhi story. Our target price is $15, and we are maintaining a 'Buy' rating.

PROJECTED INCOME STATEMENT

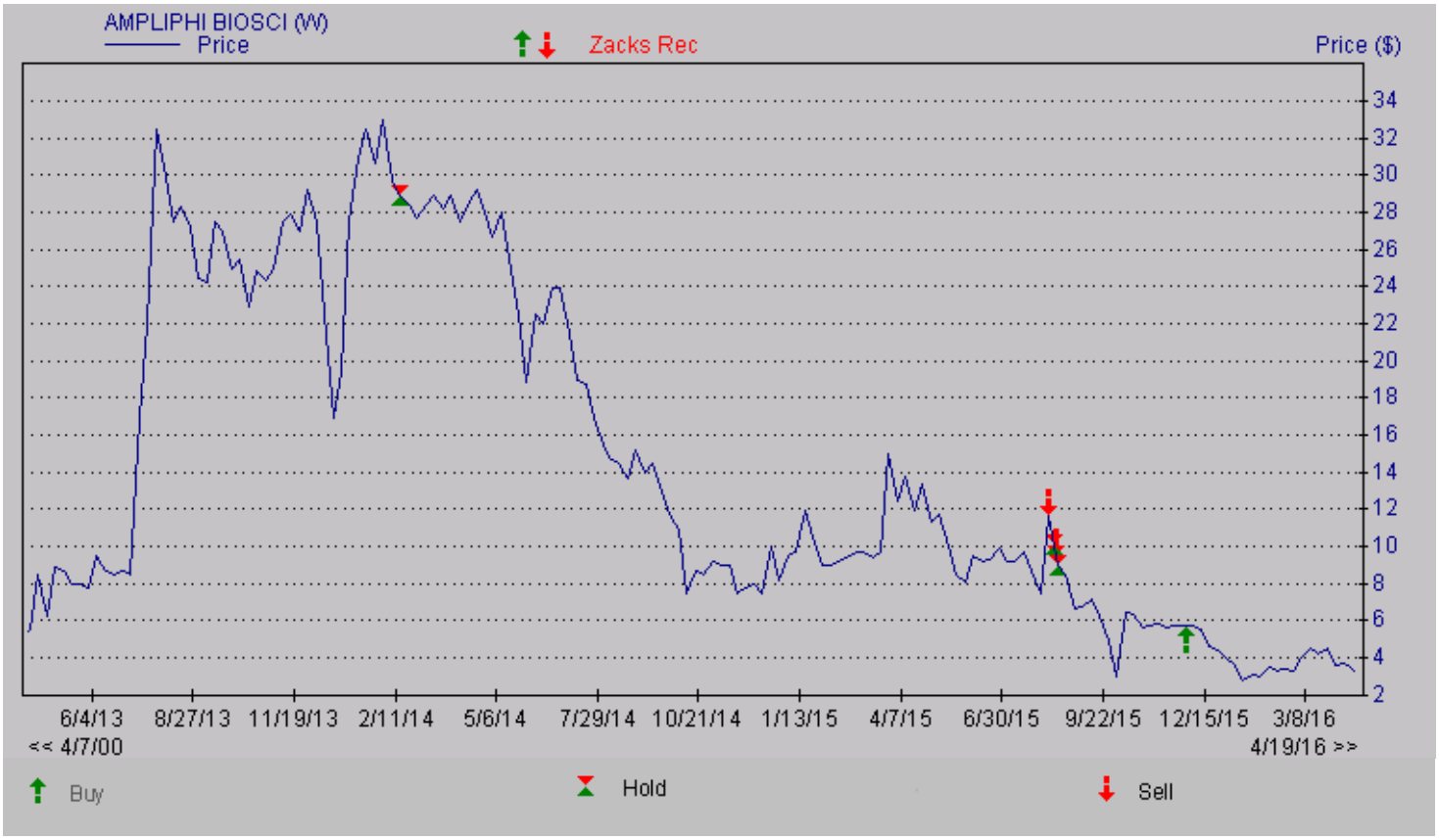
AmpliPhi Biosciences Corporation
Income Statement

AmpliPhi Bio	2015 A	Q1 E	Q2 E	Q3 E	Q4 E	2016 E	2017 E	2018 E
AB-PA01 (*P. aeruginosa*)	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**
YOY Growth								
AB-SA01 (*S. aureus*)	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**
YOY Growth								
AB-CD01 (*C. difficile*)	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**
YOY Growth	-	-	-	-	-	-	-	-
Licensing & Royalties	**$0.5**	**$0.1**	**$0.1**	**$0.1**	**$0.1**	**$0.5**	**$0.5**	**$0.5**
YOY Growth	-	-	-	-	-	-	-	-
Total Revenues	**$0.5**	**$0.1**	**$0.1**	**$0.1**	**$0.1**	**$0.5**	**$0.5**	**$0.5**
YOY Growth	-	-	-	-	-	-	-	-
Cost of Sales	$0	$0	$0	$0	$0	$0	$0	$0
Product Gross Margin	-	-	-	-	-	-	-	-
General & Administration	$6.4	$2.0	$2.0	$2.1	$2.2	$8.3	$9.0	$10.0
Research & Development	$4.0	$1.1	$1.1	$1.2	$1.2	$4.6	$5.0	$5.5
Other Operating Expenses	$0.3	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Operating Income	($10.2)	($3.0)	($3.0)	($3.2)	($3.3)	($12.4)	($13.5)	($15.0)
Operating Margin	-	-	-	-	-	-	-	-
Non-Operating Expenses (Net)	$9.6	($0.5)	($0.5)	($0.5)	($0.5)	($2.0)	($2.0)	($2.0)
Pre-Tax Income	($0.6)	($3.5)	($3.5)	($3.7)	($3.8)	($14.4)	($15.5)	($17.0)
Income Taxes Paid	($0)	$0	$0	$0	$0	$0	$0	$0
Tax Rate	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*
Deemed Dividends	$10	$0	$0	$0	$0	$0	$0	$0
Net Income	($10.8)	($3.8)	($3.5)	($3.7)	($3.8)	($14.4)	($15.5)	($17.0)
Net Margin	-	-	-	-	-	-	-	-
Reported EPS	**($1.99)**	**($0.65)**	**($0.53)**	**($0.47)**	**($0.47)**	**($2.04)**	**($1.72)**	**($1.55)**
YOY Growth	*-134%*	-	-	-	-	*2%*	*-16%*	*-10%*
Basic Shares Outstanding	5.4	5.9	6.5	7.8	8.0	7.1	9.0	11.0

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

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Sell/Underperform: The analyst expects the company will underperform the broader U.S. Equity market over the next one to two quarters.

The current distribution is as follows: Buy/Outperform- 28.7%, Hold/Neutral- 49.5%, Sell/Underperform – 14.9%. Data is as of midnight on the business day immediately prior to this publication.