AmpliPhi Biosciences Corp
Form 10-12G/A
November 17, 2014

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

AMENDMENT NO. 4 TO FORM 10

GENERAL FORM FOR REGISTRATION OF SECURITIES

Pursuant to Section 12(b) or (g) of the Securities Exchange Act of 1934

AMPLIPHI BIOSCIENCES CORPORATION

(Exact name of registrant as specified in its charter)

Washington (prior to reincorporation)
Delaware (after reincorporation)

(State or other jurisdiction of incorporation or organization)

91-1549568

(I.R.S. Employer Identification No.)

4870 Sadler Road, Suite 300
Glen Allen, Virginia 23060

(Address of principal executive offices) (Zip Code)

(804) 205-5069

(Registrant s telephone number, including area code)

Securities to be registered pursuant to Section 12(b) of the Act:

Title of each class to be so registered	Name of each exchange on which each class is to be registered
None	Not applicable

Securities to be registered pursuant to Section 12(g) of the Act:

Common Stock, par value $0.01 per share

(Title of class)

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definitions of large accelerated filer, accelerated filer and smaller reporting company in Rule 12b-2 of the Exchange Act.

Large accelerated filer o	Accelerated filer o
Non-accelerated filer o (Do not check if a smaller reporting company)	Smaller reporting company x

TABLE OF CONTENTS

TABLE OF CONTENTS

TABLE OF CONTENTS

EXPLANATORY NOTE REGARDING RESTATEMENT

Unless the context otherwise requires, we use the terms AmpliPhi Biosciences, AmpliPhi, we, us, the Company and our in this report to refer to AmpliPhi Biosciences Corporation and its subsidiaries.

This Registration Statement on Form 10 includes restatement of the following previously filed consolidated financial statements and data (and related disclosures): (1) our consolidated balance sheets as of December 31, 2013, December 31, 2012, and December 31, 2011 and our consolidated statements of operations and comprehensive loss, consolidated statement of stockholders equity (deficit), and consolidated statement of cash flows for the fiscal years ended December 31, 2013, December 31, 2012 and December 31, 2011; (2) our consolidated balance sheet as of June 30, 2014, and our consolidated statements of operations and comprehensive loss, consolidated statement of stockholders equity (deficit), and consolidated statement of cash flows for the six months ended June 30, 2014, (3) our management s discussion and analysis of financial condition and results of operations as of and for our fiscal years ended December 31, 2013, 2012 and 2011, contained in Item 2 of this Registration Statement on Form 10 and (4) our management s discussion and analysis of financial condition and results of operations as of and for the six months ended June 30, 2014 and 2013. All the aforementioned periods are collectively referenced as Affected Periods .

The Company s previously issued December 31, 2013 financial statements have been restated to remove deemed dividends booked on the issuance of preferred shares and to recognize the increase in derivative expense due to adding several features to the valuation model used to measure the compound derivatives and changing from a Black-Scholes valuation model to a Monte Carlo valuation model. Additional paid in capital and accumulated deficit have been reduced by $8,464,000 after removing the deemed dividends. Loss on derivative liabilities increased by $1,755,000 to $42,317,000 due to the change in the valuation model.

The Company also contracted a valuation team to review the purchase price allocation of Biocontrol. As a result, in process research and development (IPR&D) was restated and a new intangible asset, patents, was recognized. For the Biocontrol acquisition, $493,000 of IPR&D was reclassified to patents. In addition, amortization expense for patents of $31,000 was recognized in both 2012 and 2013.

As a result of these corrections, the Company s net loss in 2013 increased $1,787,000 to $57,648,000. The net loss per share decreased by $0.07 per share to $(0.57) per share which also reflects the removal of the deemed dividends.

The Company s previously issued 2012 financial statements have been restated to reclassify the revenue from the sale of assets that was previously reported as part of revenue to a gain on sale of assets from discontinued operations. As a result of this correction, revenue for 2012 was reduced $3,150,000 and a gain on sale of assets from discontinued operations was recorded for $3,150,000. The net loss per share remained the same, but additional disclosures were added to the Consolidated Statements of Operations and Comprehensive Loss for net loss per share from continuing operations and gain from discontinued operations per share.

For the Special Phage Services, $5,161,000 of goodwill was reclassified to IPR&D. The overall purchase price of Special Phage Services was reduced by $299,000 due to a decrease in the valuation of contingent shares reserved for the milestone agreement. This further reduced goodwill by $299,000 and paid-in-capital contingent shares by $299,000.

For more information regarding the restatement, please refer to Management s Discussion and Analysis of Financial Condition and Results of Operations and Correction of Errors in Note 14 to the Notes to our Consolidated Financial Statements for the Year Ended December 31, 2013 and Note 12 to the Notes to our Consolidated Financial Statements

for the Years Ended December 31, 2012 and 2011.

1

TABLE OF CONTENTS

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This registration statement contains forward-looking statements. The forward-looking statements are contained principally in the sections entitled Risk Factors, Management s Discussion and Analysis of Financial Condition and Results of Operations and Business. These statements relate to future events or to our future financial performance and involve known and unknown risks, uncertainties and other factors which may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. Forward-looking statements include, but are not limited to, statements about:

our ability to manufacture, or otherwise secure the manufacture of, sufficient amounts of our product candidates for our preclinical studies and clinical trials;

our clinical development plans, including planned clinical trials;

our research and development plans, including our plans to initiate at least one new clinical study in 2015;

our ability to select combinations of phages to formulate our product candidates;

the safety and efficacy of our product candidates;

the anticipated regulatory pathways for our product candidates;

our ability to successfully complete preclinical and clinical development of, and obtain regulatory approval of our product candidates and commercialize any approved products on our expected timeframes or at all;

the content and timing of submissions to and decisions made by the FDA and other regulatory agencies;

our ability to leverage the experience of our management team;

our ability to attract and keep management and other key personnel;

the capacities and performance of our suppliers, manufacturers, contract research organizations, or CROs, and other third parties over whom we have limited control;

the actions of our competitors and success of competing drugs that are or may become available;

our expectations with respect to future growth and investments in our infrastructure, and our ability to effectively manage any such growth;

the size and potential growth of the markets for any of our product candidates, and our ability to capture share in or impact the size of those markets;

the benefits of our products and product candidates;

market and industry trends;

the effects of government regulation and regulatory developments, and our ability and the ability of the third parties with whom we engage to comply with applicable regulatory requirements;

our financial performance, including our net revenue, return rates and related estimates, cost of revenue, gross profit and gross margin, operating expenses, utilization of net operating losses, or NOLs, stock-based compensation expense, cash flows, expected uses of anticipated cash flow, funding requirements and market risk;

our expectations regarding future planned expenditures;

our expectations with respect to product pricing;

our ability to effectively remediate any significant deficiencies or material weaknesses in our internal control over financial reporting;

TABLE OF CONTENTS

our ability to achieve and maintain effective internal control over financial reporting in accordance with Section 404 of the Sarbanes-Oxley Act;
our ability to obtain, maintain and successfully enforce adequate patent and other intellectual property protection of any of our products and product candidates;
our ability to operate our business without infringing the intellectual property rights of others; and
our plans to potentially transact business outside the United States.

In some cases, you can identify these statements by terms such as anticipates, believes, could, estimates, expec intends, may, plans, potential, predicts, projects, should, will, would or the negative of those ter expressions. These forward-looking statements reflect our management s beliefs and views with respect to future events and are based on estimates and assumptions as of the date of this registration statement and are subject to risks and uncertainties. We discuss many of these risks in greater detail in the section entitled Risk Factors. Moreover, we operate in a very competitive and rapidly changing environment. New risks emerge from time to time. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. Given these uncertainties, you should not place undue reliance on these forward-looking statements.

You should read this registration statement and the documents that we reference in this registration statement, and have filed as exhibits to this registration statement, completely and with the understanding that our actual future results may be materially different from what we expect. We qualify all of the forward-looking statements in this registration statement by these cautionary statements.

Except as required by law, we assume no obligation to update these forward-looking statements publicly, or to update the reasons actual results could differ materially from those anticipated in these forward-looking statements, even if new information becomes available in the future.

Item 1. Business.

Company History

We were incorporated under the laws of the State of Washington in March 1989 as a wholly owned subsidiary of Immunex Corporation and began operations as an independent company in 1992 as Targeted Genetics Corporation (TGEN). This predecessor company was effectively closed and any remaining technology was licensed or otherwise sold.

In January 2011, we completed the acquisition of Biocontrol Ltd, which we refer to as Biocontrol, an antimicrobial biotechnology company based in the United Kingdom, with the goal of developing their phage therapy programs using funding from the sale of our legacy gene therapy assets. On February 22, 2011, we changed our name to AmpliPhi Biosciences Corporation.

In November 2012, we completed the acquisition of Special Phage Holdings Pty Ltd, a company based in Australia, which we refer to as SPH, pursuant to our offer to acquire all outstanding shares of SPH from its shareholders under the terms of a Shareholder Sale Agreement and a Managers Warranty Deed. SPH was formed in 2004 to address the rapidly escalating problem of antibiotic resistance through the development of a series of bacteriophage-based treatments.

We intend to reincorporate as AmpliPhi Biosciences Corporation in the State of Delaware.

Our principal executive offices are located at 4870 Sadler Road, Suite 300, Glen Allen, VA 23060. The telephone number at our principal executive office is (804) 205-5069. Our website address is *http://www.ampliphibio.com*. Our website and the information contained on, or that can be accessed through, our website will not be deemed to be incorporated by reference in, and are not considered part of, this registration statement. You should not rely on our website or any such information in making your decision whether to purchase our common stock.

TABLE OF CONTENTS

Implications of Being an Emerging Growth Company

We are an emerging growth company, as defined in the Jumpstart Our Business Startups Act of 2012. We will remain an emerging growth company until the earliest of (1) the last day of the first fiscal year(a) following the fifth anniversary of the completion of an initial public offering, (b) in which we have total annual gross revenue of at least $1.0 billion or (c) in which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeded $700.0 million as of the prior June 30th; or (2) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three-year period. We refer to the Jumpstart Our Business Startups Act of 2012 herein as the JOBS Act and references herein to emerging growth company shall have the meaning associated with it in the JOBS Act.

As an emerging growth company, we intend to take advantage of specified reduced disclosure and other requirements that are otherwise applicable generally to public companies. These provisions include:

only two years of audited consolidated financial statements in addition to any required unaudited interim financial statements with correspondingly reduced Management s Discussion and Analysis of Financial Conditions and Results of Operations disclosure;

reduced disclosure about our executive compensation arrangements;

no requirement that we hold non-binding advisory votes on executive compensation or golden parachute arrangements; and

exemption from the auditor attestation requirement in the assessment of our internal control over financial reporting.

Under the JOBS Act, emerging growth companies can delay adopting new or revised accounting standards issued subsequent to the enactment of the JOBS Act until such time as those standards apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards, and, therefore, will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

We also qualify as a smaller reporting company, as defined by Regulation S-K under the Securities Act of 1933, as amended, which we refer to as the Securities Act. As such, we also are exempt from the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act and also are subject to less extensive disclosure requirements regarding executive compensation in our periodic reports and proxy statements, and to exemptions from the requirements to hold a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved. We will continue to be deemed a smaller reporting company until our public float exceeds $75 million on the last day of our second fiscal quarter in any fiscal year.

As used in this registration statement, unless the context requires otherwise, the Company, we, us and our refer t AmpliPhi Biosciences Corporation, a Washington corporation, or, where appropriate, Targeted Genetics Corporation or AmpliPhi Biosciences Corporation, a Delaware corporation to be formed in connection with the Company s planned reincorporation.

Company Overview

We are a biotechnology company focused on the discovery, development and commercialization of novel phage therapeutics. Our proprietary pipeline is based on the use of bacteriophages, a family of viruses that infect only bacteria. Phages have powerful and highly selective mechanisms of action that permit them to target and kill specific bacterial pathogens, including the so-called multi-drug-resistant (MDR) or Superbug strains.

We believe that we are a leading developer of phage-based therapeutics. We are combining our proprietary approach and expertise in identifying, characterizing and developing naturally occurring bacteriophages with that of our collaboration partners in bacteriophage biology, drug engineering, development

TABLE OF CONTENTS

and manufacturing, to develop second-generation bacteriophage products. We believe that phages represent a promising means to treat bacterial infections, especially those that have developed resistance to current medicines.

The extensive use of antibiotics, since their discovery in the 1940s, has resulted in drug resistance among many disease-causing bacteria. Resistance to antibiotics, according to the Centers for Disease Control (CDC), threatens to reverse the medical advances of the last half-century. Examples of clinically important microbes that are rapidly developing resistance to available antimicrobials include bacteria that cause skin, bone, lung and bloodstream infections (e.g., *S. aureus* and MRSA), pneumonia and lung infections in the community, hospital and cystic fibrosis (e.g., *A. baumanii*, *P. aeruginosa*, and *K. pneumoniae*), meningitis (e.g., *S. pneumonia*), urinary tract and gastrointestinal infections (e.g., *E. coli* and *C. difficile*). As a phage kills bacteria in ways entirely unlike the mechanisms used by antibiotics, multi-drug resistant bacteria are not resistant to a phage in the same manner. Furthermore, as new resistant bacteria emerge, it should be possible to identify new phages that will still have efficacy.

Our lead program is AmpliPhage-002, for the treatment of *S. aureus* infections (including methicillin-resistant MRSA). We also have two other product candidates in development: AmpliPhage-001 for the treatment of *P. aeruginosa* lung infections in CF patients, and AmpliPhage-004 for the treatment of *C. difficile* infections.

We are developing these phage product candidates using our proprietary discovery and development platform, which is designed for rapid identification, characterization and manufacturing of multiple phage therapies. Each product candidate combines several carefully chosen phages which target a specific disease-causing bacterial pathogen such as MRSA, *P. aeruginosa* and *C. difficile*. We believe that our understanding of unique regulatory and development requirements of bacteriophage biology combined with the clinical and scientific expertise of our collaboration partners will enable the rapid advancement of phage treatments through the clinic and eventually to the market.

In March 2013, we entered into an Exclusive Channel Collaboration (ECC) with Intrexon Corporation, which we refer to as Intrexon, directed towards the research, development and commercialization of new bacteriophage-based therapies to target specific antibiotic-resistant infections, including for use in the treatment of bacterial infections associated with acute and chronic wounds, the treatment of acute and chronic *P. aeruginosa* lung infections, and the treatment of infections of *C. difficile*.

In April 2013, we entered into a collaboration agreement, which we refer to as the April Collaboration Agreement, and on September 5, 2013, we entered into a license agreement, which we refer to as the Leicester License Agreement, with the University of Leicester to develop a phage therapy that targets and kills all toxin types of *C. difficile*. Pursuant to the Leicester License Agreement, we may be obligated to pay the University of Leicester a percentage royalty in the single digits and an aggregate of up to £575,000 in milestone payments. We also entered into a collaboration agreement on August 1, 2013, which we refer to as the August Collaboration Agreement, with the University of Leicester and the University of Glasgow, whereby the University of Glasgow will carry out certain animal model development work. Pursuant to the August Collaboration Agreement, we may be obligated to pay up to a total of approximately £205,000 in milestone payments.

In June 2013, we entered a Cooperative Research and Development Agreement (CRADA) with the United States Army Reserve Medical Corps (USAMRMC) and the Walter Reed Army Institute of Research (WRAIR) focusing on developing bacteriophage therapeutics to treat *S. aureus*, *E. coli* and *P. aeruginosa* infections.

We plan to initiate a clinical trial in 2015 in collaboration with the U.S. Army that will support the development of a treatment for *S. Aureus* infections for wound and skin infections.

In October 2014, we entered into a collaboration agreement, effect as of November 9, 2014, with the University of Leicester to develop phage therapies targeting *C. difficile*.

TABLE OF CONTENTS

The Need for New Anti-Infective Therapies

The rapid and continuous emergence of antibiotic-resistant bacteria has become a global crisis. While the numbers of novel anti-infective therapies in development are at historically low levels, antibiotic-resistant infections have dramatically increased. The CDC estimates that more than two million people in the United States acquire an antibiotic-resistant infection each year and more than 23,000 of these prove fatal. It is estimated that 50 70% of hospital-acquired infections are resistant to first-line anti-infective therapies. The cumulative annual cost for treating resistant bacterial infections in the United States alone is estimated to be $20 billion, while the global antibiotics market opportunity is estimated to be $40.3 billion by 2015.

The CDC s latest report on the matter, *Antibiotic Resistance Threats in the United States, 2013*, notes that there are potentially catastrophic consequences of inaction and ranks *C. difficile* as belonging to the highest tier of threat, Urgent Threats. Despite the potential market opportunity, only two new antibacterial drug applications were approved between 2010 and 2012 compared to eighteen in the period between 1980 and 1984. One of the primary CDC recommendations is the development of new antibiotics to diversify treatment options.

Product Candidates

AmpliPhage-002: Wound and Skin Infections Caused by S. aureus

In conjunction with our CRADA with the USAMRMC, we are developing a phage product that is intended to effectively treat acute and chronic wound and skin infections caused by S. aureus, including infections caused by methicillin-resistant (MRSA) strains of the same bacterium. MRSA infections are one of the most common causes of hospital-acquired (nosocomial) infections and Global Data estimates the MRSA market for infections alone was more than $2.7 billion in 2007. This market is forecast to grow to more than $3.5 billion by 2019.

By screening our proprietary library of phage samples against a panel of S. aureus bacterium, we have selected a phage product mix that has demonstrated in in vitro studies greater than 85% efficacy with high overlap against a global diversity panel that includes some of the most virulent isolates of S. aureus, including MRSA identified by the U.S. Army.

We plan to initiate a clinical trial in 2015 in collaboration with the U.S. Army that will support the development of a treatment for *S. Aureus* infections for wound and skin infections.

After extensive financial and capability evaluation and a global search we have elected to proceed with cGMP manufacturing at a wholly owned facility that has been constructed in Ljubljana, Slovenia. We have been able to access and hire highly skilled process development and phage manufacturing expertise and believe that we now have control of our proprietary platform from phage identification through final product fill and finish. Our facility inclusive of laboratory and office space is approximately 4,000 sq. ft. and is expected to produce cGMP product for our currently planned and future studies. We believe that this facility should be sufficient to meet our product needs through Phase 3 and initial commercialization. Our current formulation for AmpliPhage -002 is intended for nasal and/or topical delivery via a small spray device. We plan to further formulate our product for delivery to patients with wound and skin infections.

AmpliPhage-001: Lung Infections in Cystic Fibrosis (CF) Patients Caused by *P. aeruginosa*

According to Global Data in April 2013, the market for CF therapeutics was $1.2 billion in 2012 and forecasted to grow to $4.6 billion in 2017, with 65% of this market in the United States. One of our lead programs targets *P. aeruginosa*, the most prevalent bacterial infection that leads to the highest mortality in patients with CF with approximately 440 deaths per year in the United States. To develop our products, we have created a global diversity panel of relevant *P. aeruginosa* clinical isolates from CF clinics around the globe. Clinical isolates are bacteria isolated from patients. This diversity panel has been screened against our phage library that was isolated and characterized according to our proprietary discovery and development platform. We have demonstrated *in vitro* that we are able to effectively kill the targeted bacteria with a mixture of a few phages propagated in carefully selected bacterial hosts. Furthermore, our phage mix was selected to exhibit a high degree of overlap, defined as the number of bacteria targeted by more than one phage in the product. We believe that high overlap is an important factor in preventing bacteria from developing resistance to our phage products.

TABLE OF CONTENTS

In collaboration with Institut Pasteur (Paris, France) and Brompton Clinic, Imperial College (London, United Kingdom), we have demonstrated in the preclinical studies described below that phages can effectively treat infections in animal models of acute *P. aeruginosa* lung infections. The graphic below shows the three groups from a study conducted at the Institute Pasteur. Each group consisted of eight mice. Group 1 was treated with Placebo, or PBS, Group 2 was treated with an antibiotic (note the model was optimized for this antibiotic) and Group 3 was treated with an AmpliPhi phage mix. The colored regions, measured by light intensity, or luminescence, demonstrate where the *P. aeruginosa* infection is active and the bacteria are actively replicating. By the 24th hour, the surviving untreated animals (Group 1) are sacrificed as the infection has spread and in some cases has already proved lethal whereas the two treatment groups (Group 2, antibiotic and Group 3, phage) demonstrate effective reduction of the active infection.

TABLE OF CONTENTS

Average luminescence for each group is shown below:

Bacterial counts and the number of bacteriophage infection units detected by assay, or phage titers, were measured in these animals after 24 hours, and the results demonstrated that our phage mix effectively lowered the bacterial counts, or CFU, in the mouse lung to levels comparable to antibiotic treatment (PBS vs. antibiotic, p=0.0003; PBS vs. bacteriophage, p=0.0003). Furthermore, it was evident that phage replicated to high levels in the infected lung. These results are shown in the graphics below.

TABLE OF CONTENTS

In a separate *in vivo* study of acute *P. aeruginosa* infection of the mouse lung conducted at the Brompton Clinic, results demonstrated that our phage mix reduced CFU levels upon simultaneous intranasal administration (six mice in each of the treatment and control groups) and also when administered 24 hours post-bacterial infection (seven mice in the treatment group and eight mice in the control group) using Pa01, a standard strain of *P. aeruginosa*. These results are depicted in the graphics below.

Importantly, a preclinical study conducted at the Institut Pasteur in mice (12 mice in each of the treatment and control groups) demonstrated the ability of our phage mix to reach the lung within two hours of being delivered by oral administration. The phage levels increased between two and six hours post-treatment, and the results were statistically significant (p-value <0.001). A p-value is a statistical measure of the probability that the difference in two values could have occurred by chance. The smaller the p-value, the greater the confidence that the results are significant. These results demonstrate that when orally administered in mice, phages not only reached the lungs but were also able to infect and multiply in target bacteria.

We were granted an advisory meeting with United Kingdom Medicines and Healthcare products Regulatory Agency (MHRA) in the first quarter of 2014 to discuss our plans and intent to move the CF program into additional preclinical testing in preparation for a Phase 1/2 study in CF patients. We also sought advice and comment that our planned Chemistry Manufacturing Controls (CMC) plans were acceptable to the MRHA. The MRHA concurred with our approach and plans as presented, including a first in man dose ranging clinical study in CF patients. Subject to the availability of adequate financing, we expect to continue product selection and formulation work. Upon final product selection, we plan to manufacture the AmpliPhage-001 product in our facility in Ljubljana, Slovenia.

We believe that successful proof of concept in this lung indication could lead to other acute and chronic lung infection markets, such as Ventilator Associated Bacterial Pneumonia (VABP) and Chronic Obstructive Pulmonary Disease (COPD). The bacteria we are currently targeting are predominant pathogens in both of these indications.

TABLE OF CONTENTS

AmpliPhage-004: Gastrointestinal (GI) Infection Caused by *C. difficile Infection (CDI)*

From 2000 through 2007, deaths in the United States from *C. difficile* infection increased over 400%. Over 90% of such deaths occur in hospitalized or confined patients over the age of 65. Global Data estimates that the major European Union and United States markets for CDI therapies grew to more than $314 million in 2011 and they are expected to grow to more than $500 million by 2019.

According to the CDC, almost 250,000 people each year require hospitalization for *C.difficile* infections, and at least 14,000 people die each year in the United States from *C. difficile* infections. From 2000 through 2007, deaths in the United States from *C. difficile* infections increased over 400%. We are actively working with researchers at the University of Leicester and the University of Glasgow to develop a phage therapy that targets and kills all toxin types of *C. difficile*. We believe that orally delivered phages are well suited to treat CDI. Within this collaboration, researchers at the University of Leicester have discovered phages that have been shown to be effective against clinically-relevant strains of *C. difficile* isolated from around the world. Since current therapies against *C. difficile* are considered less than optimal, we believe that there is a significant market opportunity for our product in treating this disease.

Prior Clinical Development

In 2010, the Company s wholly owned subsidiary, Biocontrol, reported a double-blind placebo-controlled, randomized Phase 1/2 clinical trial targeting chronic ear infections (otitis) caused by antibiotic-resistant *P. aeruginosa*. This was the first, and to date, we believe the only, regulated efficacy trial of bacteriophage therapy in humans that has been reported. Positive results were reported demonstrating decreasing levels of *P. aeruginosa* in the ear and improvement of clinical condition with a single input dose of 2.4 nanograms of bacteriophage preparation. While this was a small trial (n=24), changes from baseline at the end of the trial in the test group (n=12) were statistically significant for both clinical condition (p=0.001) and bacterial load (p=0.016). No significant changes were seen in the control group (n=12) compared to baseline at the end of the trial. Difference between test and control groups was statistically significant by analysis by covariance (ANCOVA) on day 21 for bacterial count (p=0.0365). These results will need to be validated in larger well-controlled trials.

Anti-Infective Therapeutics Market

The market opportunity for antibiotics is extremely large, with the market estimated to reach $40.3 billion in annual sales globally in 2015.

Almost one in every five deaths worldwide occurs as a result of infection and, according to the World Health Organization, or WHO, many bacterial infections will become difficult or impossible to cure as the efficacy of current antibiotic drugs wanes. Despite the advances in antimicrobial and vaccine development, infectious diseases still remain as the third-leading cause of death in the United States and the second-leading cause of death worldwide.

The number of new antibiotics approved by the FDA and other global regulatory authorities has declined consistently over the last two decades. According to the Infectious Diseases Society of America, as of early 2013, only two new antibiotics have been approved by the FDA since 2009 and only seven new antibiotics targeting multi-drug-resistant Gram-negative bacilli were in either Phase 2 or Phase 3 trials. This dramatic decrease in productivity is evidenced by only two classes of antibiotics oxazolidinones and cyclic lipopeptides having been developed and launched in the last 30 years. At the same time, the evolution of antibiotic-resistant bacteria has led to an increasing number of infections for which there are no current treatments available.

Hospital-acquired (nosocomial) infections are a major healthcare problem throughout the world, affecting developed countries as well as resource-poor countries. The WHO reports that hospital-acquired infections are among the major causes of death and increased morbidity among hospitalized patients and estimates that more than 1.4 million people per year worldwide suffer from infectious complications from a hospital stay.

A recent CDC report also cites that in the United States, between 5 and 10% of all patients admitted to a hospital will be affected by a hospital-aquired infection during their stay, typically requiring extended stays and additional care. There is also a significant risk of death from such infections. In the United States, the

TABLE OF CONTENTS

CDC estimates that approximately 99,000 people die from hospital-acquired infections each year. The Cystic Fibrosis Foundation estimates that *P. aeruginosa* accounts for 10% of all hospital-acquired infections.

Infections also occur in connection with Cystic Fibrosis (CF), which is a genetic disease affecting primarily Caucasians of northern European descent. According to the Cystic Fibrosis Foundation, there are approximately 50,000 cases of CF in North America and Europe. *P. aeruginosa* opportunistically infects the mucous membranes, primarily the lungs, of CF patients and quickly grows out of control, resulting in pneumonia. *P. aeruginosa* infections are notoriously resistant to known antibiotics, and treatment may be further complicated by the formation of biofilms. Biofilms are organized structures of microorganisms growing on solid surfaces (such as lung tissue) and often limit access of antibiotics to the covered tissues. Since phages attack bacteria in a manner independent of chemical antibiotic resistance mechanisms and can infect bacteria growing in biofilms, we believe that *P. aeruginosa* infection among CF patients represents a compelling indication to pursue. The availability of *Pseudomonas* specific phages along with validated animal models of *P. aeruginosa* lung infections has contributed to the development of our bacteriophage program in CF.

Compounding the above situations is the alarming and continuing rise in the prevalence of antibiotic-resistant bacterial infections. This, coupled with the lack of new antibiotics in current discovery and development pipelines, has generated a significant clinical management problem worldwide, leading to increases in morbidity and mortality due to these antibiotic-resistant bacteria as well as increases in healthcare costs.

The first of these antibiotic-resistant infections to reach epidemic proportions was caused by the Gram-positive bacterium *S. aureus*. *S. aureus* resistance to a broad range of antibiotics has necessitated the use of expensive and potentially toxic drugs of last resort , most notably vancomycin. Antibiotic-resistant forms of *S. aureus*, usually termed MRSA (methicillin-resistant *S. aureus*), VISA (vancomycin-intermediate *S. aureus*), or VRSA (vancomycin-resistant *S. aureus*), can be extremely challenging to treat. Although several antibiotics targeting *S. aureus* have been developed, rapidly developing bacterial resistance has been noted for all of these including linezolid, daptomycin and tigecycline. On the basis of historical evidence, resistance to these existing products is likely to increase over time, and this picture is further complicated by the reduced efficacy of conventional antibiotics against *Staphylococcus* biofilms.

Typically *S. aureus* infection causes a variety of suppurative (pus-forming) infections and toxinoses in humans. It causes superficial skin lesions such as boils, styes and furuncles; more serious infections such as pneumonia, mastitis, phlebitis, meningitis and urinary tract infections; and deep-seated infections, such as osteomyelitis and endocarditis. *S. aureus* is the leading cause of wound infections, in particular, hospital-acquired (nosocomial) infection of surgical wounds and infections associated with indwelling medical devices. *S. aureus* is the leading pathogen in healthcare-associated infections in the United States as a whole, accounting for 30.4% of surgical site infections (SSI), and 15.6% of such infections overall.

Anti-Infective Treatments with Bacteriophages

Background

The dramatic rise in antibiotic resistance, the appearance of an increasing number of new superbugs&#148