AmpliPhi Biosciences Corp
Form 10-K
March 25, 2019

**UNITED STATES**

**SECURITIES AND EXCHANGE COMMISSION**

**Washington, D.C. 20549**

**FORM 10-K**

(Mark One)

x **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
**For the fiscal year ended December 31, 2018**

**or**

.. **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
**For the transition period from to**

**Commission File Number 001-37544**

**AMPLIPHI BIOSCIENCES CORPORATION**

(Exact name of registrant as specified in its charter)

| **Washington** | **91-1549568** |
|---|---|

(State or other jurisdiction of incorporation and organization) (I.R.S. Employer Identification No.)

**3579 Valley Centre Drive, Suite 100**

**San Diego, California 92130**

(Address of principal executive offices, including zip code)

**(858) 829-0829**

(Registrant's telephone number, including area code)

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

| Title of each class | Name of each exchange on which registered |
|---|---|
| Common Stock, par value $0.01 per share | NYSE American |

Securities registered pursuant to Section 12(g) of the Act: **None**

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ¨ No x

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Exchange Act. Yes ¨ No x

Indicate by check mark whether the Registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the Registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes x No ¨

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes x No ¨

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of Registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. x

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

| | | | |
|---|---|---|---|
| Large accelerated filer | ¨ | Accelerated filer | ¨ |
| Non-accelerated filer | x | Smaller reporting company | x |
| | | Emerging growth company | x |

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. x

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act).
Yes ¨ No x

As of June 29, 2018, the aggregate market value of voting stock held by non-affiliates of the Registrant, based on the closing price of the Common Stock on June 29, 2018 (the last business day of the Registrant's most recently completed second quarter) as quoted on the NYSE American, was approximately $18.6 million.

As of March 8, 2019, 32,294,008 shares of the Registrant's Common Stock were outstanding.

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**AMPLIPHI BIOSCIENCES CORPORATION**

**SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS**

This report and certain information incorporated herein by reference contain forward-looking statements, which are provided under the "safe harbor" protection of the Private Securities Litigation Reform Act of 1995. These statements relate to future events, results or to our future financial performance and involve known and unknown risks, uncertainties and other factors which may cause our actual results, performance or events to be materially different from any future results, performance or events expressed or implied by the forward-looking statements. Forward-looking statements in this report include, but are not limited to, statements regarding:

- our estimates regarding anticipated operating losses, capital requirements and needs for additional funds;
- 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 clinical development plans;
- 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 U.S. Food and Drug Administration, or 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 or other therapies 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 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;
- the accuracy of our estimates regarding future expenses, revenues, capital requirements and need for additional financing;
- our expectations regarding future planned expenditures;
- our ability to achieve and maintain effective internal control over financial reporting in accordance with Section 404 of the Sarbanes-Oxley Act;
- whether and when the proposed merger with C3J Therapeutics, Inc. will be consummated, including the likelihood of the satisfaction of certain conditions to the completion of the proposed merger;
- whether and when the proposed $10.0 million private placement to be completed immediately following the closing of the proposed merger with C3J Therapeutics, Inc. will be consummated;

- our expected benefits of and the potential value to be created by the consummation of the proposed merger with C3J Therapeutics, Inc.;
- our ability to obtain, maintain and successfully enforce adequate patent and other intellectual property protection of any of our products and product candidates; and
- our ability to operate our business without infringing the intellectual property rights of others.

In some cases, you can identify these statements by terms such as “anticipate,” “believe,” “could,” “estimate,” “expect,” “inten “may,” “plan,” “potential,” “predict,” “project,” “should,” “will,” “would” or the negative of those terms, and similar expressio 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 report 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. In addition, statements that “we believe” and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this report, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain. Given these uncertainties, you should not place undue reliance on any of the forward-looking statements included in this report. In addition, this report also contains estimates, projections and other information concerning our industry, our business, and the markets for our product candidates, as well as data regarding market research, estimates and forecasts prepared by our management. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances reflected in this information. These statements are based upon information available to us as of the date of this report, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information.

This report includes trademarks and registered trademarks of AmpliPhi Biosciences Corporation. Products or service names of other companies mentioned in this report may be trademarks or registered trademarks of their respective owners.

As used in this report, unless the context requires otherwise, the “Company,” “we,” “us” and “our” refer to AmpliPhi Biosciences Corporation and its wholly owned subsidiaries.

**PART I**

**Item 1. BUSINESS**

**Company Overview**

We are a biotechnology company pioneering the development of therapies for antibiotic-resistant infections using bacteriophage-based technology. Phages have powerful and highly selective mechanisms of action that permit them to bind to and kill specific bacteria. We believe that phages represent a promising means to treat bacterial infections, especially those that have developed resistance to current therapies, including the so-called multi-drug-resistant or "superbug" strains of bacteria.

The extensive use of antibiotics since the beginning of the modern antibiotics era in the 1940s has resulted in drug resistance among many disease-causing bacteria. According to the U.S. Centers for Disease Control and Prevention, or CDC, resistance to antibiotics threatens to reverse many of the key medical advances of the last half-century. Examples of clinically important microbes that are rapidly developing resistance to available antimicrobials, many of which are included on the World Health Organization Priority Pathogens List published in February 2017, include bacteria that cause skin, bone, lung and bloodstream infections (e.g., *Staphylococcus aureus,* or *S. aureus*, and methicillin-resistant *S. aureus*, or MRSA), pneumonia and lung infections in both community and hospital settings and cystic fibrosis, or CF, patients (e.g., *S. aureus*, *Acinetobacter baumannii*, or *A. baumanii, Pseudomonas aeruginosa*, or *P. aeruginosa,* and *Klebsiella pneumonia*, or *K. pneumoniae*), meningitis (e.g., *Streptococcus pneumonia*, or *S. pneumonia*), urinary tract and gastrointestinal infections (e.g., *P. aeruginosa, E. coli* and *Clostridium difficile*, or *C. difficile*). As phages kill bacteria in ways entirely unlike the mechanisms used by traditional antibiotics, we believe that most multi-drug resistant, or MDR, bacteria will be susceptible to phage therapy. We believe bacteriophage therapeutics could also have the potential for the treatment of inflammatory diseases based on selective modulation of the microbiome and for the treatment of bacterial-driven cancers.

Our goal is to be a leading developer of phage therapeutics. We are combining our expertise in the manufacture of drug-quality bacteriophages and our proprietary approach and expertise in identifying, characterizing and developing naturally occurring bacteriophages with that of collaboration partners in bacteriophage biology, synthetic biology and manufacturing, to develop state-of-the-art bacteriophage products. We are developing phage products to combat multi- or pan-drug-resistant bacterial pathogens, leveraging advances in sequencing and molecular biology. We have developed certain phage combinations that we believe maximize efficacy and minimize phage resistance. We currently have product candidates in clinical and preclinical development for the treatment of *S. aureus* infections, including MRSA and *P. aeruginosa* infections. We intend to develop these product candidates for the treatment of serious or life-threatening, MDR infections.

We believe our bacteriophage technology may have unique application in the area of targeted medicine, and in May 2017, we announced a new strategic emphasis on targeted therapies for serious or life-threatening antibiotic-resistant infections. In particular, we believe our bacteriophage technology can be used to develop precisely targeted therapies for patients who suffer from serious or life-threatening antibiotic-resistant bacterial infections and who have limited or no other satisfactory treatment options. Moreover, we believe our ability to target phage therapies for antibiotic-resistant infections, combined with the ability of bacteriophage to re-sensitize drug-resistant populations to antibiotics, represents what could be a powerful tool against the growing challenge of antibiotic-resistant infections.

Under existing single-patient expanded access guidelines (also referred to as “compassionate use”), established by U.S. and Australia regulatory agencies, we began to provide targeted phage therapies to patients suffering from severe antibiotic-resistant infections who have failed prior antibiotic therapies. We believe this strategic approach will not only provide potential benefit to patients to whom we are able to provide targeted phage therapies, but also provide the clinical and microbiological data from these cases that we expect to support the potential validation of the clinical utility of phage therapy, identify the most promising indications for further clinical development of our AB-SA01 and AB-PA01 product candidates for *S. aureus* and *P. aeruginosa*, define optimal treatment regimens, and inform our future discussions with the FDA and other regulatory agencies on defining a potential path to market approval. We are initially making targeted phage therapies available under the appropriate expanded access guidelines in the United States and in Australia, where we collaborate with select leading hospitals and key opinion leaders to identify and select eligible patients. We believe that the United States and Australia have a favorable regulatory framework and clinical expertise with respect to treating patients under single-patient expanded access guidelines.

Our emphasis on targeted therapies builds upon our prior successes using tailored bacteriophage therapies under emergency investigational new drug applications to treat individual patients battling life-threatening, MDR bacterial pathogens who had exhausted their treatment options. In March 2016, we collaborated with several academic institutions and a U.S. Navy laboratory to produce a targeted bacteriophage therapy that successfully treated a critically ill, comatose patient with an MDR *A. baumannii* infection. Shortly after phage therapy was initiated, the patient emerged from the coma and continued to improve under an ongoing combination of phage and antibiotic therapies until the infection was cleared. To date, the infection has not returned.

In May 2017, we initiated an expanded access program to provide investigational bacteriophage therapies AB-SA01 and AB-PA01 to patients suffering from serious and life-threatening infections in the United States and Australia.

In January 2018, we announced interim, topline results for the first seven patients treated with our investigational bacteriophage product candidates, AB-SA01 and AB-PA01, under our ongoing single-patient expanded access program. The patients in this program were severely ill and unresponsive to antibiotic treatment at the time of enrollment and were treated under emergency investigational new drug applications in the United States or under the Special Access Scheme in Australia.

In mid-2018, we compiled the treatment results from our single-patient access program data from 2017 and 2018 and we submitted to the FDA suggested clinical trial designs for continued development of our bacteriophage programs. In September 2018, we announced that we had received the official minutes from our August 2018 Type B Pre-IND meeting with the FDA regarding our proposed clinical development of AB-SA01 for the treatment of *S. aureus* bacteremia infections as well as patients with a hip or knee prosthetic joint infection due to *S. aureus*. The FDA expressed general agreement with our proposed clinical trial designs and, based on the current FDA feedback, no additional clinical or nonclinical data are required to proceed with two proposed randomized clinical trials. The first such clinical trial would be a Phase 1/2 randomized, controlled clinical trial to evaluate the safety and efficacy of AB-SA01, administered intravenously with the best available antibiotic therapy, compared to placebo plus best available antibiotic therapy, in approximately 100 patients with *S. aureus* bacteremia. The second such clinical trial would be a Phase 1/2 randomized, controlled clinical trial to evaluate the safety and efficacy of AB-SA01, administered by intra-articular injection and then intravenously with the best available antibiotic therapy, compared to placebo plus the best available antibiotic therapy, in approximately 100 patients with a hip or knee prosthetic joint infection due to *S. aureus* as an adjunct to surgical treatment. We expect that we would produce our proprietary bacteriophage therapeutics for these clinical trials at our wholly owned manufacturing facility, which is good manufacturing practices (GMP) certified by the governmental authorities in the jurisdiction in which it operates. We believe our GMP-facility has the capacity to produce our proprietary bacteriophage therapeutics for these clinical trials through a potential filing of a biologics license application and potential approval.

In September 2018, we also received positive feedback from the FDA regarding our clinical development plans for AB-PA01 for the treatment of *P. aeruginosa* infections. Resistant *P. aeruginosa* is designated as ‘Priority 1: Critical’ pathogen on the World Health Organization’s Priority Pathogens List and as ‘Serious Threat’ by the U.S. Centers for Disease Control and Prevention. The FDA expressed general agreement with our proposed clinical trial designs and, based on the current FDA feedback, no additional clinical or nonclinical data are required to proceed with two proposed randomized clinical trials. The first such clinical trial would be a Phase 1/2 randomized, controlled clinical trial to evaluate the safety and efficacy of AB-PA01, administered intravenously with the best available antibiotic therapy, compared to placebo plus best available antibiotic therapy, in approximately 100 patients with hospital-acquired and ventilator-associated pneumonia due to *P. aeruginosa*. The second clinical trial would be a Phase 1/2 randomized, controlled clinical trial to evaluate the safety and efficacy of AB-PA01, administered intravenously with the best available antibiotic therapy, compared to placebo plus best available antibiotic therapy, in approximately 100 patients with P. aeruginosa bacteremia. We intend to seek non-dilutive financing and explore other opportunities to conduct these clinical trials.

In addition, in September 2018 we provided updated topline clinical results for our ongoing single-patient expanded access program. 84% of patients achieved treatment success (physician’s assessment) at the end of bacteriophage therapy, defined as complete resolution or significant improvement of baseline signs and symptoms. We have now received clinical outcome results for 21 of the patients provided with our investigational bacteriophage therapeutics, across seven hospitals, and with serious or life-threatening infections not responding to antibiotic therapy. See the detailed clinical results in the paragraphs below.

Following the announcement of the positive FDA feedback and updated topline data results, we raised capital On October 16, 2018, from an underwritten public offering in which we sold 14,875,000 shares of common stock and 2,125,000 pre-funded warrants to purchase common stock, and common warrants to purchase 17,500,000 shares of common stock. Aggregate net proceeds from the offering were $5.8 million. Beginning in December of 2017, we engaged Ladenburg Thalmann to perform a strategic review of alternatives including a merger or sale. With the recent FDA feedback and known existing and sources of capital, we continued to believe that a strategic transaction would be an option to continue to advance the bacteriophage technology of the Company.

On January 3, 2019, we entered into an Agreement and Plan of Merger and Reorganization with C3J Therapeutics Inc. ("C3J"), a private clinical stage biotechnology company focused on the development of novel targeted antimicrobials, which included the proposed business combination ("Merger") of the C3J and Ceres Merger Sub, Inc, a wholly owned subsidiary of ours, with C3J as the surviving company, subject to shareholder approval.

At the effective time of the Merger, we anticipate that each share of C3J common stock outstanding immediately prior to the effective time of the Merger will be converted into the right to receive approximately 0.6892 shares of AmpliPhi common stock, subject to adjustment to account for a reverse split of AmpliPhi common stock at a reverse split ratio of between1-for-3 and 1-for-20, inclusive, to be determined by AmpliPhi's board of directors and to be implemented prior to the consummation of the Merger.

Immediately following the Merger, the former C3J security holders will own approximately 70% of the aggregate number of shares of AmpliPhi common stock and the security holders of AmpliPhi as of immediately prior to the Merger will own approximately 30% of the aggregate number of shares of AmpliPhi common stock on a fully diluted basis.

In addition, on February 5, 2019, certain existing C3J shareholders executed a Share Purchase Agreement with us pursuant to which the shareholders agreed, subject to the satisfaction of customary closing condition, to purchase $10.0 million in common stock of the combined company upon the closing of the Merger at a price per share equal to (i) $40.0 million, divided by (ii) the total number of shares of our common stock outstanding on a fully diluted, as-converted basis, assuming the conversion, exercise or settlement of all outstanding options, warrants, and restricted stock units as of immediately after the effective time of the Merger, but excluding (A) any shares of common stock issuable pursuant to the Share Purchase Agreement and (B) any shares of our common stock reserved for issuance under any equity incentive plan, stock option plan or similar arrangement but for which awards have not yet been granted as of the effective time of the Merger and (C) any shares of common stock issuable in connection with out-of-the-money options and out-of-the-money warrants. Based on our and C3J's respective current capitalizations, we expect the purchase price per share to be approximately $0.36.

**Clinical Results for Expanded Access Program**

On September 17, 2018, we announced updated topline clinical results for our ongoing single-patient expanded access program. 84% of patients achieved treatment success (physician's assessment) at the end of bacteriophage therapy, defined as complete resolution or significant improvement of baseline signs and symptoms.

We have now received clinical outcome results for 21 of the patents to whom we have provided our investigational bacteriophage therapeutics, at seven hospitals, with serious or life-threatening infections not responding to antibiotic therapy. Of the 21 patients, 57% were male and 43% were female, and the mean age was 57 years old with patients ranging from 16 years old to 96 years old. These patients were treated with AB-SA01 or AB-PA01, along with antibiotics, under single-patient expanded access programs in the United States (Emergency INDs, per the FDA) or Australia (Special Access Scheme, per the Australian Therapeutic Goods Administration).

Through our expanded access program, 15 patients with serious *S. aureus* infections were treated with AB-SA01 and six patients with serious *P. aeruginosa* infections were treated with AB-PA01. The treated patients' infections included bacteremia and septicemia, native and prosthetic valve endocarditis, recurrent pneumonia (cystic fibrosis, post-transplant, VAPB), ventilator-associated pneumonia, prosthetic joint infection, ventricular assist device infection, septicemia due to burns, chronic rhinosinusitis and others. Over 1,000 bacteriophage doses were administered as part of the expanded access program including, over 400 doses of AB-SA01, of which over 300 doses were administered intravenously. Treatment of AB-SA01 was well-tolerated in all patients with no treatment-related serious adverse events, or SAEs. Over 600 doses of AB-PA01 were administered, including over 400 doses administered intravenously. Treatment of AB-PA01 was well-tolerated in five patients. One patient discontinued treatment of AB-PA01 due to Grade 1 and 2 adverse events, which resolved within 18 hours. There were no treatment-related SAEs.

Of the patients in the modified intent-to-treat population, or mITT, 84% (16 out of 19) achieved treatment success at the end of therapy. Treatment success, as determined by the treating physician, was defined as a complete resolution or significant improvement of baseline signs and symptoms. mITT population was defined as all patients who met the criteria for clinical diagnosis, whose bacterial isolate was susceptible to phage and who received at least one dose of phage.

The following chart shows the safety and tolerability results of our expanded access program:

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The following chart shows the clinical outcomes at the end of therapy of our expanded access program:

The following chart shows the patient disposition from our expanded access program:

**AB-SA01 (*S. Aureus*) Clinical Development Plan**

We conducted meetings with the FDA in February 2017 and August 2018 regarding our proposed clinical development of AB-SA01. During the February 2017 meeting with the FDA, we received feedback on our previously submitted detailed development proposal to commence a Phase 2 trial with AB-SA01 for the treatment of antibiotic-resistant *S. aureus* infections in patients with chronic rhinosinusitis. In the official minutes from that meeting, the FDA acknowledged that phage therapy is an exciting approach for treatment of multi-drug-resistant organisms and expressed a commitment to addressing the unique regulatory challenges that might arise during product development. In addition, the FDA Center for Biologics Evaluation and Research stated that the clinical safety and effectiveness data collected during development, including from emergency case studies, could inform future discussions for clinical development and ultimately, the regulatory pathway to approval. During the August 2018 meeting with the FDA, which was a Type B pre-IND meeting, we shared the clinical and microbiological results for patients treated with AB-SA01 under our single-patient expanded access program in 2017 and 2018 and the proposed design of randomized controlled clinical trials that we developed based on input from key infectious disease physician opinion leaders, in order to establish a Phase 2 development plan for multiple indications, including bacteremia and prosthetic joint infection.

In September 2018, we received the official minutes from our August 2018 Type B pre-IND meeting. The FDA expressed general agreement with our proposed clinical trial designs and, based on the current FDA feedback, no additional clinical or nonclinical data are required to proceed with two proposed randomized clinical trials. The first such clinical trial would be a Phase 1/2 randomized, controlled clinical trial to evaluate the safety and efficacy of AB-SA01, administered intravenously with the best available antibiotic therapy, compared to placebo plus best available antibiotic therapy, in approximately 100 patients with *S. aureus* bacteremia. The second such clinical trial would be a Phase 1/2 randomized, controlled clinical trial to evaluate the safety and efficacy of AB-SA01, administered by intra-articular injection and then intravenously with the best available antibiotic therapy, compared to placebo plus the best available antibiotic therapy, in approximately 100 patients with a hip or knee prosthetic joint infection due to *S. aureus* as an adjunct to surgical treatment. We are actively seeking and intend to continue to seek non-dilutive financing and explore other opportunities to conduct these clinical trials of AB-SA01. We may also choose to conduct one or more smaller-scale clinical trials of similar design as an alternative to conducting the

approximately 100 patient clinical trials described above in an effort to reduce clinical trial expenditures. It is possible that results from such smaller-scale clinical trials may not be viewed by the FDA or other regulatory agencies as sufficient for the advancement of AB-SA01 into Phase 2 trials, including potentially registrational Phase 2 trials, due to the smaller trial populations even if the trial results are otherwise positive, which in turn could result in the FDA or other regulatory agencies requiring us to conduct additional studies beyond those that would have been required if we had conducted trials of approximately 100 patients as proposed in our August 2018 Type B pre-IND meeting. We expect that we would produce our proprietary bacteriophage therapeutics for these clinical trials at our wholly owned manufacturing facility, which is good manufacturing practices (GMP) certified by the governmental authorities in the jurisdiction in which it operates. We believe our GMP-facility has the capacity to produce our proprietary bacteriophage therapeutics for these clinical trials through a potential biologics license application filing and potential approval.

Furthermore, we continue to investigate whether AB-SA01 may be eligible for Fast Track Designation and for approval under the Limited Population pathway, or LPAD pathway, which is intended to facilitate development of therapeutics to treat serious or life-threatening infections in a limited population of patients with unmet need. Products eligible for approval under the LPAD pathway may follow streamlined approaches for clinical development, which may involve smaller, shorter, or fewer clinical trials to help reduce the overall product development timeline.

**AB-PA01 (*P. aeruginosa*) Clinical Development Plan**

In September 2018, we received positive feedback, via written response, from the FDA regarding our development plans for AB-PA01, without the need for a Type B pre-IND meeting. The FDA expressed general agreement with our proposed clinical trial designs and, based on the current FDA feedback, no additional clinical or nonclinical data are required to proceed with two proposed randomized clinical trials. The first such clinical trial would be a Phase 1/2 randomized, controlled clinical trial to evaluate the safety and efficacy of AB-PA01, administered intravenously with the best available antibiotic therapy, compared to placebo plus best available antibiotic therapy, in approximately 100 patients with hospital-acquired and ventilator-associated pneumonia (HAP/VAP) due to *P. aeruginosa*. The second clinical trial would be a Phase 1/2 randomized, controlled clinical trial to evaluate the safety and efficacy of AB-PA01, administered intravenously with the best available antibiotic therapy, compared to placebo plus best available antibiotic therapy, in approximately 100 patients with *P. aeruginosa* bacteremia.

We considered the clinical development timelines for both the AB-SA01 and AB-PA01 development programs. We concluded in the fourth quarter of 2018 that since the AB-SA01 program is further advanced in the development process, the AB-SA01 program will continue to be advanced and the AB-PA01 program will not be pursued in the near term. As we are not actively pursuing the AB-PA01 program, we have recorded an impairment charge of approximately $1.9 million within operating expenses of the consolidated statement of operations in the fourth quarter of 2018.

**Our Pipeline**

Our development pipeline of product candidates is as follows:

AB-SA01 covers approximately 95% of *S. aureus* strains, including multi-drug-resistant infections, and AB-PA01 covers approximately 80% of *P. aeruginosa* strains, including multi-drug-resistant infections.

**The Need for New Anti-Infective Therapies**

The rapid and continuous emergence of antibiotic-resistant bacteria has become a global crisis. Despite this crisis, the number of novel anti-infective therapies currently in development is at historically-low levels. Based on our market research, we estimate that there are more than 300,000 serious *S. aureus* infections in the United States each year, including approximately 150,000 cases of *S. aureus* bacteremia each year that lead to approximately 30,000 deaths each year.

The Centers for Disease Control and Prevention estimates that 1.5 million people in the United States develop bacteremia each year and approximately 250,000 deaths occur as a direct result of infection. It is estimated that one in three patients who die in the hospital have bacteremia. Bacteremia is the most expensive condition treated at U.S. hospitals, costing approximately $24 billion annually. *S. aureus* is the second most common pathogen associated with bacteremia, causing approximately 150,000 cases each year and approximately 30,000 deaths.

Prosthetic joint infection is a difficult to treat and costly condition. There are more than one million knee and hip joint replacements performed in the U.S. each year, which is projected to increase to over four million each year by 2030. There are approximately 50,000 prosthetic joint infections each year, with approximately 20% caused by *S. aureus*. Prosthetic joint infection is costly with the annual inpatient costs exceeding $1 billion and rapidly rising.

The historical and projected number of infected total hip arthroplasty and total knee arthroplasty in the United States are as follows:

(3) Kurtz S et al. 2012. The Journal of Arthroplasty; 27(8): S1.

Prosthetic joint infection is difficult to treat because biofilm formation increases bacterial resistance to antibiotics. The current standard of care is a combination of surgery and antibiotics, with significant patient morbidity, high costs and up to 30% failure rate. The current standard of care includes a two-stage revision: surgery to remove the infected joint, four to six weeks of intravenous antibiotics, surgery to implant a new joint, followed by six weeks of antibiotics.

**Anti-Infective Treatments with Bacteriophages**

***Background***

The dramatic rise in antibiotic resistance, the appearance of an increasing number of new “superbugs” and the lack of new antibiotics in the pipeline has prompted calls to action from many of the world’s major health bodies such as the CDC and the WHO, who warn of an “antibiotic cliff” and a “post-antibiotic era.” In 2009, the European Antimicrobial Resistance Surveillance System concluded that “the loss of effective antimicrobial therapy increasingly threatens the delivery of crucial health services in hospitals and in the community.” This conclusion was reinforced by The Antimicrobial Availability Task Force of the Infectious Diseases Society of America and the European Centre for Disease Prevention and Control in conjunction with the European Medicine Agency, or EMA. We therefore believe there is a pressing need to find alternative antibacterial therapies.

Bacteriophage therapy has the potential to be an alternative method of treating bacterial infection. Phages are ubiquitous environmental viruses that grow only within bacteria, but are among the most abundant and diverse

organisms on the planet. The name “bacteriophage” translates as “eaters of bacteria” and reflects the fact that as they grow, phages kill the bacterial host by multiplying inside and then bursting through the cell membrane in order to release the next generation of phages. Phages can differ substantially in morphology and each phage is active against a specific range of a given bacterial species. Phages were first discovered in 1915 at the Institut Pasteur and were shown to kill bacteria taken from patients suffering from dysentery. Furthermore, it was noted that phage numbers rose as patients recovered from infection, suggesting a direct association.

***Life Cycle of a Bacteriophage***

Until the discovery of effective antibiotics, phages were used as an effective means of combating bacterial infection. When broad-spectrum antibiotics came into common use in the early 1940s, phages were considered unnecessary, with antibiotics being seen for many years as the answer to bacterial disease. This attitude persisted until the development of the wide-ranging, and in some cases total, resistance to antibiotics seen within the last 10 years.

Phages have the potential to provide both an alternative to, and a synergistic approach with, antibiotic therapy. Since they use different mechanisms of action, phages are unaffected by resistance to conventional antibiotics. Phages containing certain enzymes also have the ability to disrupt bacterial biofilms, thus potentiating the effect of chemical antibiotics when used in combination with them.

**Strategic Alliances and Research Agreements**

***Global R&D Agreement with U.S. Army***

In June 2013, we entered into a Research and Development Agreement with the U.S. Army Medical Research and Materiel Command. The Research and Development Agreement focuses on developing bacteriophage therapeutics to treat *S. aureus*, *E. coli* and *P. aeruginosa* infections, with the initial therapeutic development focus being wounds and skin infections from *S. aureus*, which is the leading pathogen in healthcare-associated infections in the United States as a whole, accounting for 30.4% of surgical site infections.

We retain global regulatory ownership and commercial rights to all products developed by us under the Research and Development Agreement. The U.S. Army Medical Research and Materiel Command will have the right to retain a non-exclusive license to use any products developed by or on behalf of the U.S. Government for non-commercial uses. We also have the rights to exclusively license any intellectual property developed by the U.S. Army Medical Research and Materiel Command under the collaboration on terms to be agreed upon.

The Research and Development Agreement will expire in June 2020 and can be terminated by either the U.S. Army Medical Research and Materiel Command or us upon 60 days' written notice to the other party at any time.

***License Agreement with United Kingdom Secretary of State for the Department of Health***

In January 2011, upon completion of our acquisition of Biocontrol Ltd., we assumed a license agreement entered into in March 2007 between Biocontrol Ltd. and the Health Protection Agency, Centre for Emergency Preparedness and Response, to use certain intellectual property rights to develop treatments for bacterial biofilm infections. The agreement was subsequently assigned to the United Kingdom Secretary of State for the Department of Health, or DoH.

Under the license agreement, we have obtained exclusive rights to a patent portfolio related to the use of bacteriophages combined with biofilm-disrupting agents in treating biofilm infections. In consideration for the exclusive license, we may be required to pay to the DoH certain milestone payments in the aggregate of up to £10,000 per product, as well as single digit percentage royalty on net sales of products incorporating licensed intellectual property.

The license agreement will remain in effect until the expiration of the last patent exclusively licensed under the license agreement. If we default on any milestone or royalty payments, or upon breach by us of certain other terms of the license agreement, the DoH may either terminate the license agreement immediately upon written notice or modify the license to be non-exclusive upon 30 days' written notice.

**Intellectual Property**

***General***

Our goal is to obtain, maintain and enforce patent protection for our product candidates, formulations, processes, methods and any other proprietary technologies, preserve our trade secrets and operate without infringing on the proprietary rights of other parties, both in the United States and in other countries. Our policy is to actively seek to obtain, where appropriate, the broadest intellectual property protection possible for our current product candidates and any future product candidates, proprietary information and proprietary technology through a combination of contractual arrangements and patents, both in the United States and abroad. However, patent protection may not afford us with complete protection against competitors who seek to circumvent our patents.

We also depend upon the skills, knowledge, experience and know-how of our management and research and development personnel, as well as that of our advisors, consultants and other contractors. To help protect our proprietary know-how, which is not patentable, and for inventions for which patents may be difficult to enforce, we currently and will in the future rely on trade secret protection and contractual obligations with third parties to protect our interests. To this end, we require all of our employees, consultants, advisors and other contractors to enter into agreements with contractual obligations that prohibit the disclosure of confidential information and, where applicable, require disclosure and assignment to us of the ideas, developments, discoveries and inventions important to our business.

As of December 31, 2018, we owned or had exclusive license rights to a total of 68 patents and applications: 7 U.S. patents, 4 U.S. non-provisional patent applications, 8 U. S. provisional patent applications, 1 pending Patent Cooperation Treaty (PCT) application, 41 foreign patents, and 7 foreign patent applications, with nominal expiration on various dates between 2024 and 2039. We believe these patents and applications cover our lead phage-therapeutic programs and use thereof, beneficial effects of bacteriophage treatment, bacteriophage combinations, the sequential use of bacteriophages in combination with conventional antibiotics, genetic sequence variations, biofilm disrupting agents, methods to reduce antibiotic resistance, methods to design therapeutic combination panels of bacteriophage, disinfection methods using bacteriophages, and bacteriophage mutants having increased bacterial host spectra.

Our success in preserving market exclusivity for our product candidates relies on patent protection, including extensions to this where appropriate, and on data exclusivity relating to an approved biologic. This may be extended by orphan drug and/or pediatric use protection where appropriate. Once any regulatory period of data exclusivity expires, depending on the status of our patent coverage, we may not be able to prevent others from marketing and selling biosimilar versions of our product candidates. We are also dependent upon the diligence of our appointed agents in national jurisdictions, acting for and on our behalf, which manage the prosecution of pending domestic and foreign patent applications and maintain granted domestic and foreign patents.

**Competition**

We operate in highly competitive segments of the biotechnology and biopharmaceutical markets. We face competition from many different sources, including commercial pharmaceutical and biotechnology enterprises, academic institutions, government agencies and private and public research institutions all seeking to develop novel treatment modalities for bacterial infections. Many of our competitors have significantly greater financial, product development, manufacturing and marketing resources than us. Large pharmaceutical companies have extensive experience in clinical development and obtaining regulatory approval for drug products. In addition, many universities and private and public research institutes are active in antibacterial research, some in direct competition with us. We also may compete with these organizations to recruit scientists and clinical development personnel.

There are a handful of small biotechnology companies developing bacteriophage products to treat human diseases. To our knowledge, several biotechnology companies, including C3J Therapeutics, Adaptive Phage Therapeutics, Pherecydes Pharma, BiomX, Epibiome, Intralytix, iNtRON, PhageLux, EnBiotix, Fixed-Phage, Locus Biosciences, Phagomed, Phi Therapeutics, TechnoPhage and LytPhage, Inc., as well as academic institutions, have discovery stage or clinical programs utilizing naturally occurring phages or synthetic biology approaches to genetically modify bacteriophages to remove or input genes to improve therapeutic properties such as increases to the bacterial host range to infect a larger number of bacterial strains and decrease the need for using multiple phages in a product.

A related approach to treating *Staphylococcus* infections is being pursued by Contrafect Corporation using a bacteriophage lysin (a hydrolytic enzyme produced by bacteriophages) to treat *S. aureus* bacteremia (infection in the blood). In 2018, Contrafect completed a Phase 2 clinical trial of its lysin product candidate in patients with *S. aureus* bacteremia.

Our bacteriophage programs may compete with or be synergistic with currently approved antibiotics, and experimental approaches such as novel antibiotics, antimicrobial peptides, antimicrobial vaccines, metals, antisense, monoclonal antibodies and possibly microbiome manipulation.

**Manufacturing and Supply**

We have developed our own manufacturing capabilities at a facility in Ljubljana, Slovenia that is leased by our wholly owned subsidiary, AmpliPhi, Biotehnološke Raziskave in Razvoj, d.o.o. We believe that our facility complies with applicable cGMP regulations, which require, among other things, quality control and quality assurance as well as the corresponding maintenance of records and documentation. Pharmaceutical product manufacturers and other entities involved in the manufacture and distribution of approved pharmaceutical products are required to register their establishments with the FDA, and certain state agencies, including the applicable government agency where the facility is located, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP and other laws.

After conducting a global search, we elected to proceed with establishing a wholly owned cGMP compliant manufacturing facility in Ljubljana, Slovenia, and we plan to manufacture each of our product candidates in this facility. We have been able to access and hire highly skilled process development and phage manufacturing expertise and believe that we have control of our proprietary platform from phage identification through final product fill and finish. Our facility is comprised of approximately 5,300 sq. ft. of laboratory and office space, where we produce cGMP clinical trial supplies in our 40-liter bioreactor for our current and planned clinical trials. We believe this facility will be sufficient to meet our manufacturing needs through initial Phase 3 clinical trials. Our current formulation for AB-SA01 is intended for intravenous, inhaled, sino-nasal or topical delivery. We may further optimize future formulations of our product candidates.

Our facility in Ljubljana, Slovenia is subject to inspection and regulation by JAZMP, the Slovenian agency that regulates and supervises pharmaceutical products in Slovenia. Discovery of problems with a product after approval may result in restrictions on a product, manufacturer or holder of an approved New Drug Application/Biologics License Application, including withdrawal of the product from the market. In addition, changes to the manufacturing process generally require prior regulatory approval before being implemented and other types of changes to the approved product, such as adding new indications and additional labeling claims, are also subject to further regulatory review and approval, including approval by the FDA.

In 2017, our manufacturing facility successfully completed a periodic regulatory GMP inspection by JAZMP, and our GMP certification was renewed. We believe that we have the world’s only GMP-certified facility dedicated to manufacturing bacteriophage therapeutic candidates for human use.

**Commercialization and Marketing**

We have full worldwide commercial rights to all of our phage-based product candidates to treat drug-resistant bacterial infections, including our product candidates: AB-SA01, for the treatment of *S. aureus* infections, and AB-PA01 for the treatment of *P. aeruginosa* infections. We believe we can maximize the value of our company by retaining substantial global commercialization rights to these product candidates and, where appropriate, entering into partnerships to develop and commercialize these product candidates.

We have not yet established a sales, marketing or product distribution infrastructure because our lead candidates are still in early clinical development. Subject to receiving marketing approvals, we intend to explore building the necessary marketing and sales infrastructure to market and sell our current product candidates. We also intend to explore the use of a variety of distribution agreements and commercial partnerships in those territories where we do not establish a sales force for any of our product candidates that obtain marketing approval.

**Government Regulation and Product Approval**

Government authorities in the United States, at the federal, state and local level, and other countries extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring and reporting, marketing and export and import of products such as those we are developing.

***United States Product Development Process***

In the United States, the FDA regulates biological products under the Federal Food, Drug and Cosmetic Act, or FDCA, and the Public Health Service Act, or the PHS Act, and related regulations. Biological products are also subject to other federal, state and local statutes and regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources. Failure to comply with the applicable United States requirements at any time during the product development process or approval process, or after approval, may subject an applicant to administrative or judicial sanctions. FDA sanctions could include refusal to approve pending applications, withdrawal of an approval, a clinical hold, warning letters, product recalls, product seizures, total or partial suspension of production or distribution injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us. The process required by the FDA before a biological product may be marketed in the United States generally includes the following:

- completion of preclinical laboratory tests, animal studies and formulation studies according to good laboratory practice requirements, or GLP, or other applicable regulations;

- submission to the FDA of an IND, which must become effective before human clinical trials may begin in the United States;

- performance of adequate and well-controlled human clinical trials according to the FDA's regulations commonly referred to as good clinical practices, or GCPs, and any additional requirements for the protection of human research subjects and their health information, to establish the safety and effectiveness of the proposed biological product for its intended use or uses;

- submission to the FDA of a Biologics License Application, or BLA, for a new biological product;

- satisfactory completion of an FDA inspection of the manufacturing facility or facilities where the biological product is produced to assess compliance with the FDA's cGMP regulations, to assure that the facilities, methods and controls are adequate to preserve the biological product's identity, strength, quality and purity;

- potential FDA audit of the nonclinical study sites and clinical trial sites that generated the data in support of the BLA; and

- FDA review and approval, or licensure, of the BLA which must occur before a biological product can be marketed or sold.

The lengthy process of seeking required approvals and the continuing need for compliance with applicable statutes and regulations require the expenditure of substantial resources even when approvals are inherently uncertain.

The strategies, nature, and technologies of bacteriophage products are different from the conventional antibiotic therapy products. From the regulatory requirements established to ensure the safety, efficacy and quality of bacteriophage preparations, there are several major points to consider during the development, manufacturing, characterization, preclinical study and clinical trial of bacteriophage. The major issues include:

- bacteriophage preparation design (single agent versus phage mixes and wild-type phage versus genetically engineered phage);