

AmpliPhi Biosciences Corp
Form 424B5
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The information in this preliminary prospectus supplement is not complete and may be changed. A registration statement relating to these securities has been declared effective by the Securities and Exchange Commission. This preliminary prospectus supplement and the accompanying prospectus are not an offer to sell these securities, and we are not soliciting offers to buy these securities, in any state or other jurisdiction where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED JANUARY 9, 2018

PRELIMINARY PROSPECTUS SUPPLEMENT

(To Prospectus dated May 13, 2016)

Shares

Common Stock

We are offering _____ shares of our common stock pursuant to this prospectus supplement and the accompanying prospectus. The final public offering price will be determined through negotiation between us and the investors in the offering and the recent market price used throughout this prospectus supplement may not be indicative of the final offering price.

Our common stock is traded on the NYSE American under the symbol "APHB." On January 8, 2018, the last reported sale price of our common stock as reported on the NYSE American was \$1.87 per share.

We have retained H.C. Wainwright & Co., LLC to act as our exclusive placement agent (“placement agent”) in connection with the shares of common stock offered by this prospectus supplement. The placement agent has agreed to use its reasonable best efforts to arrange for the sale of the common stock offered by this prospectus supplement. The placement agent is not purchasing or selling any of the shares of common stock we are offering and the placement agent is not required to arrange the purchase or sale of any specific number of shares or dollar amount. We have agreed to pay to the placement agent the placement agent fees set forth in the table below, which assumes that we sell all of the common stock offered by this prospectus supplement. See “Plan of Distribution” on page S-10 of this prospectus supplement for more information regarding these arrangements.

As of the date of this prospectus supplement, the aggregate market value of our outstanding common stock held by non-affiliates, or public float, was approximately \$17.3 million, based on 9,271,504 shares of outstanding common stock held by non-affiliates as of the date of this prospectus supplement, at a price of \$1.87 per share, which was the last reported sale price of our common stock on the NYSE American on January 8, 2018. Pursuant to General Instruction I.B.6 of Form S-3, in no event will we sell securities registered on the registration statement of which this prospectus supplement is a part in a primary offering with a value exceeding more than one-third of our public float in any 12-month period so long as our public float remains below \$75.0 million. Other than the securities offered by this prospectus supplement, we have not offered any securities pursuant to General Instruction I.B.6 of Form S-3 during the 12 calendar months prior to and including the date of this prospectus supplement.

Investing in our common stock involves a high degree of risk. See “Risk Factors” beginning on page S-5 of this prospectus supplement.

	Per Share	Total
Public offering price	\$	\$
Placement agent’s fees ⁽¹⁾	\$	\$
Proceeds, before expenses, to us	\$	\$

(1) We have also agreed to reimburse the placement agent for certain offering-related expenses. See “Plan of Distribution.”

We have agreed to pay the placement agent a placement agent fee in an amount equal to 6.0% of the aggregate gross proceeds in this offering. Because there is no minimum offering amount required as a condition to closing in this offering, the actual public offering amount, placement agent fees, and proceeds to us, if any, are not presently determinable and may be substantially less than the total maximum offering amounts set forth above. See “Plan of Distribution” for more information on this offering and the placement agent arrangements.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus supplement or the accompanying prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

Delivery of the shares of common stock is expected to be made on or about January , 2018, subject to customary closing conditions.

H.C. Wainwright & Co.

The date of this prospectus supplement is January , 2018.

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We have not, and the placement agent has not, authorized anyone to provide you with information that is different from that which is contained in or incorporated by reference in this prospectus supplement, the accompanying prospectus and in any free writing prospectus that we have authorized for use in connection with this offering. We are not, and the placement agent is not, making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus supplement, the accompanying prospectus, the documents incorporated by reference in this prospectus supplement and the accompanying prospectus, and in any free writing prospectus that we have authorized for use in connection with this offering, is accurate only as of the date of those respective documents. Our business, financial condition, results of operations and prospects may have changed since those dates. You should read this prospectus supplement, the accompanying prospectus, the documents incorporated by reference in this prospectus supplement and the accompanying prospectus, and any free writing prospectus that we have authorized for use in connection with this offering, in their entirety before making an investment decision. You should also read and consider the information in the documents to which we have referred you in the sections of this prospectus supplement entitled “Where You Can Find More Information” and “Incorporation of Certain Information by Reference.”

ABOUT THIS PROSPECTUS SUPPLEMENT

This document is in two parts. The first part is the prospectus supplement, which describes the specific terms of the common stock being offered by us, and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference. The second part, the accompanying prospectus, including the documents incorporated by reference therein, provides more general information, some of which may not apply to this offering of common stock. Generally, when we refer to this prospectus, we are referring to both parts of this document combined. To the extent there is a conflict between the information contained in this prospectus supplement, on the one hand, and the information contained in the accompanying prospectus or in any document incorporated by reference that was filed with the Securities and Exchange Commission, or SEC, before the date of this prospectus supplement, on the other hand, you should rely on the information in this prospectus supplement. If any statement in one of these documents is inconsistent with a statement in another document having a later date — for example, a document incorporated by reference in the accompanying prospectus — the statement in the document having the later date modifies or supersedes the earlier statement.

This prospectus contains references to our trademarks and to trademarks and trade names belonging to other entities. Solely for convenience, trademarks and trade names referred to in this prospectus, including logos, artwork and other visual displays, may appear without the ® or ™ symbols, but such references are not intended to indicate, in any way, that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto. We do not intend our use or display of other companies' trade names or trademarks to imply a relationship with, or endorsement or sponsorship of us by, any other companies.

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights information contained in other parts of this prospectus supplement or incorporated by reference into this prospectus supplement from our filings with the SEC listed in the section of the prospectus supplement entitled “Incorporation of Certain Information by Reference.” Because it is only a summary, it does not contain all of the information that you should consider before purchasing our shares of common stock in this offering and it is qualified in its entirety by, and should be read in conjunction with, the more detailed information appearing elsewhere or incorporated by reference into this prospectus supplement. You should read the entire prospectus supplement, the registration statement of which this prospectus supplement is a part, and the information incorporated by reference herein in their entirety, including the “Risk Factors” and our financial statements and the related notes incorporated by reference into this prospectus supplement, before purchasing our shares of common stock in this offering. Unless the context requires otherwise, references in this prospectus supplement to “AmpliPhi,” “we,” “us” and “our” refer to AmpliPhi Biosciences Corporation together with its wholly owned subsidiaries.

Our Company

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. baumannii*, *Pseudomonas aeruginosa*, or *P. aeruginosa*, and *Klebsiella pneumoniae*, or *K. pneumoniae*), meningitis (e.g., *Streptococcus pneumoniae*, or *S. pneumoniae*), 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 bacteria will be susceptible to phage therapy. Furthermore, should resistant bacteria emerge or evolve, we believe it will remain possible to identify phages that can effectively kill these resistant bacteria.

Our goal is to be the 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, multi-drug resistant, or MDR, infections. We also intend to seek to advance our chronic rhinosinusitis, or CRS, program and preclinical CF program through partnerships, arrangements and/or with additional outside funding. In April 2017, the U.S. Food and Drug Administration, or FDA, provided positive feedback on our previously submitted detailed development proposal to commence a Phase 2 trial with our proprietary bacteriophage cocktail AB-SA01 for the treatment of antibiotic-resistant *S. aureus* infections in patients with CRS, which feedback followed a Type B telephonic meeting held with us on February 21, 2017. In the official minutes from the meeting, the FDA acknowledged that phage therapy is an exciting approach to treatment of multi-drug-resistant organisms and expressed a commitment to addressing the unique regulatory challenges that might arise during product development.

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 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 the regulatory agencies, we have begun to provide targeted phage therapies to patients suffering from severe MDR infections who have failed prior 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 in 2018 or later 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. Additionally, in December 2007 our wholly owned subsidiary, Special Phage Services, was instrumental in developing a targeted phage therapy that, together with a course of antibiotics, eliminated a previously antibiotic-resistant *P. aeruginosa* infection in the bladder of a female cancer patient.

We are implementing the targeted therapy strategy and, through the date of this prospectus supplement have provided bacteriophage investigational therapies AB-SA01 and AB-PA01 for seven patients suffering from serious and life-threatening infections under emergency investigational new drug applications, or INDs, in the United States or Special Access Scheme Category A in Australia.

On January 3, 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.

Of the seven patients treated, four patients received AB-SA01, administered intravenously, for treatment of *Staphylococcus aureus* infection, and three patients received AB-PA01, administered intravenously or in some cases by nebulizer, for treatment of *Pseudomonas aeruginosa* infection. The bacteriophage therapy was administered along with the treating physician's choice of best available antibiotic therapy. Treated patients suffered from bacteremia, endocarditis and lung infections, and both AB-SA01 and AB-PA01 were well tolerated in all patients with no treatment-related serious adverse events reported.

Treatment success, defined as complete resolution or significant improvement of baseline signs and symptoms, was reported in six of the seven patients (86%) by physician's assessment. One patient was determined to be a treatment failure due to death, which occurred during surgery after three days of bacteriophage treatment. The treating physician determined that the death was unrelated to treatment with bacteriophage therapy. The 28-day all-cause mortality rate was 14%. No additional deaths occurred within 90 days following initiation of therapy, and patient follow-up is continuing. Based on the APACHE II scores (a validated critical care scoring system predictive of mortality) of the seven patients prior to initiation of bacteriophage therapy, the predicted mortality rate for this patient group was 46%.

No bacterial isolates resistant to the bacteriophage therapeutics were detected during the bacteriophage treatment course. Additional analyses of these data are ongoing, and presentations or publications of the detailed results are planned.

Certain Preliminary Financial Results

As of December 31, 2017, we had approximately \$5.1 million of cash and cash equivalents. This amount is unaudited and preliminary, is subject to completion of financial closing procedures that could result in changes to the amount, and does not present all information necessary for an understanding of our financial condition as of December 31, 2017.

Corporate and Other Information

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.

In January 2011, we completed the acquisition of Biocontrol Ltd, 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.

In February 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, with the goal of combining SPH’s research on addressing the rapidly escalating problem of antibiotic resistance through the development of a series of bacteriophage-based treatments into our own development programs.

In August 2015, we effected a 1-for-50 reverse split of our common stock. The share and per share information described in this prospectus that occurred prior to the reverse split have been adjusted to give retrospective effect to

the reverse split.

In April 2017, we effected a 1-for-10 reverse split of our common stock. The share and per share information described in this prospectus supplement that occurred prior to the reverse split have been adjusted to give retrospective effect to the reverse split.

Our principal executive offices are located at 3579 Valley Centre Drive, Suite 100, San Diego, California 92130. The telephone number at our principal executive office is (858) 829-0829. Our website address is *www.ampliphio.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 prospectus supplement. You should not rely on our website or any such information in making your decision whether to purchase our shares of common stock in this offering.

The Offering

Common stock offered by us in this offering shares of our common stock.

Offering price \$ per share of common stock.

Common stock outstanding shares (assuming the sale of all shares covered by this prospectus supplement).
immediately after this offering

Use of proceeds We estimate that our net proceeds from this offering will be approximately \$ million after deducting estimated placement agent fees and other estimated offering expenses payable by us (assuming the sale of all shares covered by this prospectus supplement). We plan to use the net proceeds of this offering for general corporate purposes. See “Use of Proceeds.”

Risk factors Investing in our securities involves a high degree of risk. See “Risk Factors” beginning on page S-5 of this prospectus supplement.

Exchange listing Our common stock is listed on The NYSE American under the symbol “APHB.”

The number of shares of common stock to be outstanding immediately after this offering is based on 9,325,595 shares of our common stock outstanding as of September 30, 2017. Unless otherwise indicated, the number of shares of common stock presented in this prospectus supplement excludes as of September 30, 2017:

• 1,116,765 shares of common stock issuable upon the exercise of outstanding stock options, at a weighted-average exercise price of \$3.19 per share;

• 4,580 shares of common stock reserved for future grant under our 2016 Equity Incentive Plan, or the 2016 plan;

• 21,016 shares of common stock reserved for future issuance under our 2016 Employee Stock Purchase Plan, or the ESPP; and

8,712,220 shares of common stock issuable upon the exercise of outstanding warrants, at a weighted-average exercise price of \$2.91 per share.

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RISK FACTORS

Investing in our common stock involves a high degree of risk. Our business, prospects, financial condition or operating results could be materially adversely affected by the risks identified below, as well as other risks not currently known to us or that we currently consider immaterial. The trading price of our common stock could decline due to any of these risks, and you may lose all or part of your investment. In assessing the risks described below, you should also refer to the information contained in our Quarterly Report on Form 10-Q for the quarter ended September 30, 2017 and other documents which are incorporated by reference in this prospectus supplement and the accompanying prospectus in their entirety, and other documents that we file from time to time with the SEC.

Risks Related to This Offering

Management will have broad discretion as to the use of the proceeds from this offering, and we may not use the proceeds effectively.

Our management will have broad discretion in the application of the net proceeds from this offering, including for any of the purposes described in the section entitled “Use of Proceeds,” and you will not have the opportunity as part of your investment decision to assess whether the net proceeds are being used appropriately. Because of the number and variability of factors that will determine our use of the net proceeds from this offering, their ultimate use may vary substantially from their currently intended use. Our management may not apply the net proceeds from this offering in ways that ultimately increase the value of your investment. The failure by our management to apply these funds effectively could harm our business. Pending their use, we may invest the net proceeds from this offering in short-term, investment-grade, interest-bearing securities. These investments may not yield a favorable return to our stockholders. If we do not invest or apply the net proceeds from this offering in ways that enhance stockholder value, we may fail to achieve expected financial results, which could cause our stock price to decline.

You will experience immediate and substantial dilution in the net tangible book value per share of the common stock you purchase.

Since the price per share of our common stock being offered is substantially higher than the net tangible book value per share of our common stock, you will suffer immediate and substantial dilution in the net tangible book value of the common stock you purchase in this offering. As of September 30, 2017, our net tangible book value was approximately \$4.8 million, or \$0.52 per share. Based on the public offering price of \$ per share and our net tangible book value as of September 30, 2017, if you purchase shares of common stock in this offering, you will suffer immediate and substantial dilution of \$ per share with respect to the net tangible book value of the common stock

you purchase in this offering.

We will need to raise additional capital in the future to continue operations, which may not be available on acceptable terms, or at all. Failure to obtain this necessary capital when needed may force us to delay, limit or terminate our product development efforts or other operations.

We have had recurring losses from operations, negative operating cash flow and an accumulated deficit. We do not generate any cash from operations and must raise additional funds in order to continue operating our business. Even if this offering is successful, we expect to continue to fund our operations primarily through equity and debt financings in the future. If additional capital is not available to us when needed or on acceptable terms, we may not be able to continue to operate our business pursuant to our business plan or we may have to discontinue our operations entirely. As of December 31, 2017, we had cash and cash equivalents of \$5.1 million. We estimate that we will receive net proceeds of approximately \$ million from the sale of the securities offered by us in this offering, if all of the shares being offered by this prospectus supplement are sold. However, there is no minimum offering amount required as a condition to closing this offering, and therefore the actual total offering proceeds to us, before expenses, may be substantially less. In addition, we cannot provide assurances that our plans will not change or that changed circumstances will not result in the depletion of our capital resources more rapidly than we currently anticipate.

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Developing drugs and conducting clinical trials is expensive. Our future funding requirements will depend on many factors, including:

- the costs and timing of our research and development activities;

- the progress and cost of our clinical trials and other research and development activities;

- the cost and timing of securing manufacturing capabilities for our clinical product candidates and commercial products, if any;

- the terms and timing of any collaborative, licensing, acquisition or other arrangements that we may establish;

- whether and when we receive future Australian tax rebates, if any;

- the costs and timing of seeking regulatory approvals;

- the costs of filing, prosecuting, defending and enforcing any patent applications, claims, patents and other intellectual property rights; and

- the costs of lawsuits involving us or our product candidates.

We may seek funds through arrangements with collaborators or others that may require us to relinquish rights to the products candidates that we might otherwise seek to develop or commercialize independently. We cannot be certain that we will be able to enter into any such arrangements on reasonable terms, if at all.

We may seek to raise capital through a variety of sources, including:

- the public equity market;

- private equity financings;

- collaborative arrangements;

licensing arrangements; and/or

public or private debt.

Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize our product candidates. Our ability to raise additional funds will depend, in part, the success of our preclinical studies and clinical trials and other product development activities, regulatory events, our ability to identify and enter into in-licensing or other strategic arrangements, and other events or conditions that may affect our value or prospects, as well as factors related to financial, economic and market conditions, many of which are beyond our control. We cannot be certain that sufficient funds will be available to us when required or on acceptable terms, if at all. Raising additional capital through the sale of securities could cause significant dilution to our stockholders. If we are unable to secure additional funds on a timely basis or on acceptable terms, we may be required to defer, reduce or eliminate significant planned expenditures, restructure, curtail or eliminate some or all of our development programs or other operations, dispose of technology or assets, pursue an acquisition of our company by a third party at a price that may result in a loss on investment for our stockholders, enter into arrangements that may require us to relinquish rights to certain of our product candidates, technologies or potential markets, file for bankruptcy or cease operations altogether. Any of these events could have a material adverse effect on our business, financial condition and results of operations. Moreover, if we are unable to obtain additional funds on a timely basis, there will be substantial doubt about our ability to continue as a going concern and increased risk of insolvency and loss of investment by our stockholders.

There may be future sales of our securities or other dilution of our equity, which may adversely affect the market price of our common stock.

Subject to the terms and conditions of the securities purchase agreements we expect to enter into with certain institutional investors in this offering which will restrict our ability to sell common stock or common stock equivalents for a period of 60 days, we are generally not restricted from issuing additional common stock, including any securities that are convertible into or exchangeable for, or that represent the right to receive, common stock. The market price of our common stock could decline as a result of sales of common stock or securities that are convertible into or exchangeable for, or that represent the right to receive, common stock after this offering or the perception that such sales could occur.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement and the accompanying prospectus, including the documents that we incorporate by reference herein and therein, contain statements that are not strictly historical in nature and are forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. These forward-looking statements are subject to the “safe harbor” created by Section 27A of the Securities Act and Section 21E of the Exchange Act and may include, but are not limited to, statements about:

This prospectus supplement and the accompanying prospectus, including the documents that we incorporate by reference herein and therein, contain forward-looking statements. The forward-looking statements are contained principally in the sections entitled “Prospectus Summary,” “Risk Factors,” “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and “Business” in this prospectus supplement, the accompanying prospectus or the documents incorporated herein by reference. 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 estimates regarding anticipated operating losses, capital requirements and needs for additional funds;
- our ability to raise additional capital when needed and to continue as a going concern;
- 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 and other research and development plans and expectations;
- 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 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 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;

our expectations with respect to our new targeted phage therapies strategy, including the ability to demonstrate on the timeframe we anticipate, or at all, proof-of-concept sufficient to support regulatory approval;

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 outcome of any litigation in which we or any of our officers or directors may be involved;

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;

our expectations regarding the period during which we qualify as an emerging growth company under the JOBS 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 expected use of the net proceeds from this offering; 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,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “should,” “will,” “would” or the negative of those terms, and similar expressions convey uncertainty of future events or outcomes. 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 prospectus and are subject to risks and uncertainties. We discuss many of these risks in greater detail in the documents incorporated by reference herein, usually under the heading “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 carefully read this prospectus supplement, the accompanying prospectus and the documents that we incorporate by reference 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 prospectus supplement and the accompanying prospectus 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 any forward-looking statements, whether as a result of new information, future events or otherwise.

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USE OF PROCEEDS

We estimate that the net proceeds from the sale of shares of our common stock offered under this prospectus supplement, after deducting estimated placement agent fees and estimated offering expenses payable by us, will be \$ million if we sell the maximum amount of common stock offered hereby. However, this is a best efforts offering with no minimum, and we may not sell all or any of these shares; as a result, we may receive significantly less in net proceeds, and the net proceeds received may not be sufficient to continue to operate our business.

We intend to use the net proceeds from this offering for general corporate purposes, including manufacturing expenses, clinical trial expenses, research and development expenses and general and administrative expenses. We may also use a portion of the net proceeds from this offering to in-license, invest in or acquire businesses or technologies that we believe are complementary to our own, although we have no current plans, commitments or agreements with respect to any acquisitions. As of the date of this prospectus supplement, we cannot specify with certainty all of the particular uses of the proceeds from this offering. Accordingly, we will retain broad discretion over the use of such proceeds. Pending the use of the net proceeds from this offering, we intend to invest the net proceeds in investment-grade, interest-bearing instruments.

Investors are cautioned that the proceeds from this offering are expected to be sufficient to enable us to continue operations for only a short period of time. We expect that we will have to raise additional capital through the sale of additional equity or convertible debt securities. It may be difficult for us to raise additional funds when needed and on favorable terms, or at all.

PLAN OF DISTRIBUTION

Pursuant to an engagement agreement, we have engaged H.C. Wainwright & Co., LLC as our exclusive placement agent, to solicit offers to purchase the common stock offered by this prospectus supplement. The placement agent is not purchasing any common stock for its own account in this offering, and is not required to arrange the purchase or sale of any additional specific number or dollar amount of the securities.

The placement agent has agreed to use its reasonable best efforts to arrange for the sale of all of the securities in this offering. There is no requirement that any minimum number of shares of common stock or dollar amount of common stock be sold in this offering and there can be no assurance that we will sell all or any of the common stock being offered. Certain large investors will have the option to execute a securities purchase agreement with us.

We currently anticipate that the closing of this offering will occur on or about January , 2018, subject to customary closing conditions. On the closing date, the following will occur:

- we will receive funds in the amount of the aggregate purchase price;
- the placement agent will receive the placement agent fees in accordance with the terms of the engagement agreement; and
- we will deliver the shares of common stock to the investors.

We have agreed to pay the placement agent a placement agent fee an amount equal to 6.0 % of the aggregate gross proceeds in this offering and management fee of 1.0% of the gross proceeds of this offering. We have also agreed to reimburse H.C. Wainwright & Co., LLC for its expenses in connection with this offering on a non-accountable basis in an amount equal to \$25,000 and reimbursement for the placement agent's legal fees and expenses in the amount of up to \$100,000.

The following table shows the per share and total fees we will pay in connection with the sale of the common stock, assuming the purchase of all of the common stock we are offering.

Per share placement agent fees \$

Total \$

We estimate the total expenses of this offering which will be payable by us, excluding the placement agent fees, will be approximately \$125,000.

We have agreed to indemnify the placement agent and certain other persons against certain liabilities relating to or arising out of the placement agent's activities under the engagement agreement. We have also agreed to contribute to payments that the placement agent may be required to make in respect of such liabilities.

H.C. Wainwright & Co., LLC may be deemed to be an underwriter within the meaning of Section 2(a)(11) of the Securities Act of 1933, as amended, and any commissions received by it and any profit realized on the resale of the common stock sold by it while acting as principal might be deemed to be underwriting discounts or commissions under the Securities Act of 1933, as amended. As an underwriter, H.C. Wainwright & Co., LLC would be required to comply with the requirements of the Securities Act of 1933, as amended, and the Securities Exchange Act of 1934, as amended, including, without limitation, Rule 415(a)(4) under the Securities Act of 1933, as amended, and Rule 10b-5 and Regulation M under the Securities Exchange Act of 1934, as amended. These rules and regulations may limit the timing of purchases and sales of shares of common stock by H.C. Wainwright & Co., LLC acting as principal. Under these rules and regulations, H.C. Wainwright & Co., LLC:

• may not engage in any stabilization activity in connection with our securities; and

• may not bid for or purchase any of our securities or attempt to induce any person to purchase any of our securities, other than as permitted under the Securities Exchange Act of 1934, as amended, until it has completed its participation in the distribution.

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LEGAL MATTERS

The validity of the securities offered by this prospectus supplement and the accompanying prospectus will be passed upon for us by Cooley LLP, San Diego, California. The placement agent is being represented by Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., New York, New York.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2016, as set forth in their report (which contains an explanatory paragraph describing conditions that raise substantial doubt about our ability to continue as a going concern as described in Note 2 to the consolidated financial statements), which is incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP's report, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

This prospectus supplement and the accompanying prospectus are part of the registration statement on Form S-3 we filed with the SEC under the Securities Act and do not contain all the information set forth in the registration statement. Whenever a reference is made in this prospectus supplement or the accompanying prospectus to any of our contracts, agreements or other documents, the reference may not be complete and you should refer to the exhibits that are a part of the registration statement or the exhibits to the reports or other documents incorporated by reference in this prospectus supplement and the accompanying prospectus for a copy of such contract, agreement or other document. Because we are subject to the information and reporting requirements of the Exchange Act, we file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the internet at the SEC's website at <http://www.sec.gov>. You may also read and copy any document we file at the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the operation of the Public Reference Room.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to "incorporate by reference" information from other documents that we file with it, which means that we can disclose important information to you by referring you to those documents. The information incorporated

by reference is considered to be part of this prospectus. Information in this prospectus supersedes information incorporated by reference that we filed with the SEC prior to the date of this prospectus.

We incorporate by reference into this prospectus and the registration statement of which this prospectus is a part the information or documents listed below (other than current reports or portions thereof furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits filed on such form that are related to such items and other portions of documents that are furnished, but not filed, pursuant to applicable rules promulgated by the SEC) that we have filed with the SEC (Commission File No. 001-37544):

our annual report on Form 10-K for the year ended December 31, 2016, filed with the SEC on March 27, 2017;

our quarterly reports on Form 10-Q for the quarters ended March 31, 2017, June 30, 2017 and September 30, 2017, filed with the SEC on May 15, 2017, August 14, 2017 and November 14, 2017, respectively;

our current reports on Form 8-K and any amendments thereto on Form 8-K/A, filed with the SEC on February 2, 2017, April 4, 2017, April 19, 2017, April 24, 2017, May 1, 2017, May 8, 2017, May 10, 2017, June 5, 2017, June 30, 2017, September 11, 2017, September 20, 2017, December 14, 2017 and January 3, 2018;

the information specifically incorporated by reference into our annual report on Form 10-K for the year ended December 31, 2016 from our Definitive Proxy Statement on Schedule 14A, filed with the SEC on July 24, 2017; and

the description of our common stock contained in our registration statement on Form 8-A, filed with the SEC on August 18, 2015, including all amendments and reports filed for the purpose of updating such description.

In addition, all documents subsequently filed by us pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act, prior to the termination of the offering (excluding any information furnished rather than filed) shall be deemed to be incorporated by reference into this prospectus.

We will provide to each person, including any beneficial owners, to whom a prospectus is delivered, a copy of any or all of the reports or documents that have been incorporated by reference in the prospectus contained in the registration statement but not delivered with the prospectus. We will provide these reports or documents upon written or oral request at no cost to the requester. You should direct any written requests for documents to AmpliPhi Biosciences Corporation, Attn: Chief Financial Officer, 3579 Valley Centre Drive, Suite 100, San Diego, California 92130. You may also telephone us at (858) 829-0829.

In accordance with Rule 412 of the Securities Act, any statement contained in a document incorporated by reference herein shall be deemed modified or superseded to the extent that a statement contained herein or in any other subsequently filed document which also is or is deemed to be incorporated by reference herein modifies or supersedes such statement.

PROSPECTUS

\$75,000,000

Common Stock

Common Stock Warrants

From time to time, we may sell up to an aggregate of \$75,000,000 of our common stock or warrants to purchase common stock, individually or in units, in amounts, at prices and on terms described in one or more supplements to this prospectus. We may also authorize one or more free writing prospectuses to be provided to you in connection with these offerings.

Our common stock is traded on the NYSE MKT under the trading symbol “APHB.” On April 27, 2016, the last reported sale price of our common stock on the NYSE MKT was \$3.20. The applicable prospectus supplement will contain information, where applicable, as to other listings, if any, on the NYSE MKT or other securities exchanges of the securities covered by the prospectus supplement.

Our principal executive offices are located at 3579 Valley Centre Drive, San Diego, California 92130, and our telephone number at that address is (858) 829-0829.

You should read this prospectus and any prospectus supplement carefully before you invest.

INVESTING IN OUR SECURITIES INVOLVES A HIGH DEGREE OF RISK. YOU SHOULD REVIEW CAREFULLY THE RISKS AND UNCERTAINTIES REFERENCED UNDER THE HEADING “RISK FACTORS” ON PAGE 4 OF THIS PROSPECTUS AS WELL AS THOSE CONTAINED IN THE APPLICABLE PROSPECTUS SUPPLEMENT AND ANY RELATED FREE WRITING PROSPECTUS, AND UNDER SIMILAR HEADINGS IN THE OTHER DOCUMENTS THAT ARE INCORPORATED BY REFERENCE INTO THIS PROSPECTUS.

This prospectus may not be used to offer or sell any securities unless accompanied by a prospectus supplement.

As of the date of this prospectus, the aggregate market value of our outstanding common stock held by non-affiliates, or public float, was approximately \$29.5 million, based on 6,066,466 shares of outstanding common stock held by non-affiliates as of the date of this prospectus, at a price of \$4.86 per share, which was the last reported sale price of our common stock on the NYSE MKT on March 22, 2016