

PROSPECTUS SUPPLEMENT
To Prospectus dated March 25, 2016

1,000,000 Shares of Common Stock



OPEXA THERAPEUTICS, INC.

This prospectus supplement relates to the issuance and sale of up to 1,000,000 shares of our common stock through our sales agent, IFS Securities, Inc. (doing business as Brinson Patrick, a division of IFS Securities, Inc.), which we refer to as “Brinson Patrick,” in an “at the market” offering program. These sales, if any, will be made pursuant to the terms of a Sales Agreement entered into between us and our sales agent.

Our common stock is traded on the NASDAQ Capital Market under the symbol “OPXA.” On March 24, 2016, the last reported sales price for our common stock was \$2.16 per share. Sales of shares of our common stock under this prospectus supplement, if any, may be made in sales deemed to be an “at the market” offering as defined in Rule 415 under the Securities Act of 1933. Consistent with instructions that may be delivered from time to time by us, the sales agent will make all sales using best efforts consistent with its normal trading and sales practices.

The commission we will pay to our sales agent for sales of common stock sold pursuant to the Sales Agreement will be 3% of the gross proceeds of the sales. The net proceeds that we receive from sales of our common stock will depend on the number of shares actually sold and the offering price for such shares. If all 1,000,000 shares of common stock were sold at the March 24, 2016 closing sales price, we would receive \$2,160,000 in gross proceeds, or \$2,095,200 in net proceeds after the sales agent fee of 3% and estimated offering expenses. The actual proceeds to us will vary.

In connection with the sale of common stock on our behalf, the sales agent may be deemed an “underwriter” within the meaning of the Securities Act of 1933, as amended, and the compensation of the sales agent may be deemed to be underwriting commissions or discounts. We have agreed to provide indemnification and contribution to the sales agent against certain liabilities, including liabilities under the Securities Act of 1933.

The aggregate market value of our outstanding common equity held by non-affiliates on February 23, 2016 was \$16,247,374 based on 6,982,909 shares of common stock outstanding, of which 6,658,760 are held by non-affiliates, and a closing sale price on the NASDAQ Capital Market on such date of \$2.44. During the 12 calendar months prior to and including the date hereof, we have sold an aggregate of \$723,776 of securities pursuant to General Instruction I.B.6. of Form S-3.

Investing in our securities involves a high degree of risk. See the section entitled “[Risk Factors](#)” beginning on page S-4 in this prospectus supplement and in the documents we incorporate by reference in this prospectus supplement and the accompanying prospectus. You should carefully consider these risk factors, as well as the information contained in this prospectus supplement and the accompanying prospectus, before you invest.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus supplement. Any representation to the contrary is a criminal offense.



The date of this Prospectus Supplement is March 25, 2016.

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You should rely only on the information incorporated by reference or provided in this prospectus supplement, the accompanying prospectus and the documents incorporated herein and therein by reference. We have not authorized anyone else to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. We are not making an offer to sell these securities in any state where the offer or sale is not permitted. You should assume that the information in this prospectus supplement and the accompanying prospectus, or incorporated by reference, is accurate only as of the dates of those documents. Our business, financial condition, results of operations and prospects may have changed since those dates.

ABOUT THIS PROSPECTUS SUPPLEMENT

We are providing this information to you about this offering of securities in two parts. The first part is this prospectus supplement, which provides the specific details regarding the shares of our common stock that we are selling in this offering and also adds to and updates information contained in or incorporated by reference into the accompanying prospectus. The second part is the base prospectus included in our registration statement on Form S-3 (SEC File No. 333-208314), which provides a general description of the securities we may offer from time to time under that registration statement. This prospectus supplement and the accompanying prospectus are part of a “shelf” registration statement that we filed with the U.S. Securities and Exchange Commission. Under the shelf registration process, we may offer from time to time securities up to an aggregate amount of \$100,000,000, of which this offering is a part. To date, we have not yet sold any securities under this shelf registration statement.

To the extent there is a conflict between information contained in this prospectus supplement, on the one hand, and information contained in the accompanying prospectus or any document incorporated by reference, on the other hand, the information in this prospectus supplement shall control.

The registration statement we filed with the SEC includes exhibits that provide more detail of the matters discussed in this prospectus supplement and the accompanying prospectus. You should read this prospectus supplement, the accompanying prospectus and the related exhibits filed with the SEC, together with the additional information described under the heading “Where You Can Find More Information” and “Incorporation of Certain Information by Reference,” before making your investment decision.

Unless the context otherwise requires, references in this prospectus supplement and the accompanying prospectus to “Opexa,” “the Company,” “we,” “us” and “our” refer to Opexa Therapeutics, Inc.

PROSPECTUS SUPPLEMENT SUMMARY

This summary contains basic information about us and this offering. Because it is a summary, it does not contain all of the information that you should consider before investing. Before you decide to invest in our common stock, you should read this entire prospectus supplement and the accompanying prospectus carefully, including the section entitled “Risk Factors,” our consolidated financial statements and the related notes, and other information and documents incorporated by reference in this prospectus supplement and the accompanying prospectus.

Our Company

Our Business

Opexa is a biopharmaceutical company developing personalized immunotherapies with the potential to treat major illnesses, including multiple sclerosis (MS) as well as other autoimmune diseases such as neuromyelitis optica (NMO). These therapies are based on our proprietary T-cell technology. Our mission is to lead the field of Precision Immunotherapy[®] by aligning the interests of patients, employees and shareholders. Information related to our product candidates, Tcelna[®] and OPX-212, is preliminary and investigative. Tcelna and OPX-212 have not been approved by the U.S. Food and Drug Administration (FDA) or other global regulatory agencies for marketing.

MS is an inflammatory autoimmune disease of the central nervous system (CNS), which is made up of the brain, spinal cord and optic nerves, with a clinically heterogeneous and unpredictable course that persists for decades. MS attacks the covering surrounding nerve cells, or myelin sheaths, leading to loss of myelin (demyelination) and nerve damage. In addition to demyelination, the neuropathology of MS is characterized by variable loss of oligodendroglial cells and axonal degeneration and manifests in neurological deficits. Symptoms may be mild, such as numbness in the limbs, or severe, such as paralysis or loss of vision. This inflammatory, demyelinating, autoimmune disease has varied clinical presentations, ranging from relapses and remissions (relapsing remitting MS, or RRMS) to slow accumulation of disability with or without relapses (secondary progressive MS, or SPMS). There are approximately 450,000 MS patients in North America and over 2,000,000 patients worldwide according to estimates from The National MS Society. The portion of the MS patient population that can be classified as SPMS is estimated by various industry sources to be between 30-45% of the total MS patient population.

We believe that our lead product candidate, Tcelna, has the potential to fundamentally address the root cause of MS by stopping the demyelination process and supporting the generation of new myelin sheaths where demyelination has occurred (remyelination). Tcelna is an autologous T-cell immunotherapy that is currently being developed for the treatment of SPMS and is specifically tailored to each patient’s immune response profile to myelin. Tcelna is designed to reduce the number and/or functional activity of specific subsets of myelin-reactive T-cells (MRTCs) known to attack myelin. This technology was originally licensed from Baylor College of Medicine in 2001.

Tcelna is manufactured using our proprietary method for the production of an autologous T-cell product, which comprises the collection of blood from the MS patient and the expansion of MRTCs from the blood. Upon completion of the manufacturing process, an annual course of therapy consisting of five doses is cryopreserved. At each dosing time point, a single dose of Tcelna is formulated and attenuated by irradiation before returning the final product to the clinical site for subcutaneous administration to the patient.

Tcelna has received Fast Track designation from the FDA in SPMS, and we believe it is positioned as a potential first-to-market personalized T-cell therapy for MS patients. The FDA’s Fast Track program is designed to facilitate the development and expedite the review of drug candidates intended to treat serious or life-threatening conditions and that demonstrate the potential to address unmet medical needs.

In addition to our ongoing clinical development of Tcelna, we are also in preclinical development of OPX-212 as an autologous T-cell immunotherapy for the treatment of NMO. NMO is an autoimmune disorder in which immune system cells and antibodies attack and destroy astrocytic/myelin cells in the optic nerves and the spinal cord leading to demyelination and loss of axons. There are currently no FDA-approved therapies for NMO, other than to treat an attack while it is happening, to reduce symptoms and to prevent relapses. OPX-212 is specifically tailored to each patient's immune response to a protein, aquaporin-4, which is the targeted antigen in NMO. In NMO, the immune system recognizes aquaporin-4 as foreign, thus triggering the attack. We believe a mechanism of action of OPX-212 may be to reduce the number and/or regulate aquaporin-4 reactive T-cells (ARTC), thereby reducing the frequency of clinical relapses and subsequent progression in disability.

Opexa was incorporated in Texas in March 1991. Our principal executive offices are located at 2635 Technology Forest Blvd., The Woodlands, Texas 77381, and our telephone number is (281) 775-0600. Our website address is www.opexatherapeutics.com. We do not incorporate the information on, or accessible through, our website into this prospectus supplement, and you should not consider any information on, or accessible through, our website as part of this prospectus supplement.

	The Offering
Common stock offered by Opexa	Up to 1,000,000 shares
Common stock outstanding after this offering	Up to 7,982,909 shares
Manner of offering	“At-the-market” offering that may be made from time to time through Brinson Patrick as our sales agent, subject to direction from us as to amount and timing. See “Plan of Distribution” on page S-7 of this prospectus supplement.
Use of proceeds	We currently intend to use the net proceeds from this offering for general corporate purposes (including working capital, research and development, business development and operational purposes) and to do the following: (i) continue funding the ongoing Abili-T clinical study of Teelna in patients with SPMS; and (ii) continue preclinical and manufacturing activities for OPX-212 in patients with NMO and, if such activities are successful, to file an IND application with the FDA to initiate a Phase 1/2 proof-of-concept study. See “Use of Proceeds” on page S-6 of this prospectus supplement.
Risk factors	See the “Risk Factors” section beginning on page S-4 of this prospectus supplement for factors to consider before deciding to purchase our securities.
NASDAQ listing	Our common stock is listed on the NASDAQ Capital Market under the symbol “OPXA.”

Unless otherwise indicated, all offering information in this prospectus supplement is based on the number of shares of common stock outstanding as of March 10, 2016. Unless otherwise indicated, the number of shares that will be outstanding after this offering assumes or gives effect to no exercise of options or warrants outstanding on the date of this prospectus supplement or in the future.

RISK FACTORS

Investing in our securities involves a high degree of risk. You should review carefully the risks and uncertainties described below and those under the heading “Risk Factors” contained in our most recent annual report on Form 10-K and our quarterly reports on Form 10-Q, which have been filed with the SEC and are incorporated by reference into this prospectus supplement, as well as any updates thereto contained in subsequent filings with the SEC or any applicable supplement or free writing prospectus, before deciding whether to purchase any of the securities being registered pursuant to the registration statement of which this prospectus supplement is a part. Each of the risk factors could adversely affect our business, operating results and financial condition, as well as adversely affect the value of an investment in our securities, and the occurrence of any of these risks might cause you to lose all or a part of your investment. Moreover, the risks described are not the only risks that we face. Additional risks not presently known to us or that we currently believe are immaterial may also significantly impair our business operations.

Risks Related to This Offering

Sales of our common stock in this offering, or the perception that such sales may occur, could cause the market price of our common stock to fall.

We may issue and sell up to 1,000,000 shares of our common stock from time to time in connection with this offering. The issuance and sale from time to time of these new shares of common stock, or our ability to issue these new shares of common stock in this offering, could have the effect of depressing the market price of our common stock.

We presently do not intend to pay cash dividends on our common stock.

We currently anticipate that no cash dividends will be paid on the common stock in the foreseeable future. While our dividend policy will be based on the operating results and capital needs of the business, it is anticipated that all earnings, if any, will be retained to finance the future expansion of our business.

Our management has significant flexibility in using our current available cash and the net proceeds of this offering.

In addition to general corporate purposes (including working capital, research and development, business development and operational purposes), we currently intend to use our available cash and the net proceeds of this offering to do the following: (i) to continue funding the ongoing Abili-T clinical study of Tcelna in patients with SPMS, and (ii) to continue preclinical and manufacturing activities for OPX-212 in patients with NMO, and if such activities are successful, to file an IND application with the FDA to initiate a Phase 1/2 proof-of-concept study. We reached our enrollment target for the Abili-T trial in June 2014, and a total of 190 patients have been enrolled in this two-year study. We expect top-line data for Tcelna to be available early in the fourth quarter of 2016. While we believe we have sufficient resources to complete the trial and support our operations during the pendency of the trial, if our projections prove to be inaccurate or we encounter additional costs to complete the trial or to sustain our operations, we may need to raise additional capital or modify either the Abili-T clinical study, our development of OPX-212 in NMO, or other aspects of our current business plan.

Depending on future developments and circumstances, we may use some of our available cash or the net proceeds from this offering for other purposes which may have the potential to decrease any forecasted cash runway. Notwithstanding our current intention to use our available cash as noted above, our management will have significant flexibility in using our current available cash and the net proceeds of this offering. The actual amounts and timing of expenditures will vary significantly depending on a number of factors, including the amount and timing of cash used in our operations and our research and development efforts. Management’s failure to use these funds effectively would have an adverse effect on the value of our common stock and could make it more difficult and costly to raise funds in the future.

You may experience immediate dilution in the book value per share of the common stock you purchase.

Because the price per share of our common stock being offered may be substantially higher than the net tangible book value per share of our common stock, you may suffer substantial dilution in the net tangible book value of the common stock you purchase in this offering. If you purchase shares of common stock in this offering at the current market value, you may suffer immediate and substantial dilution in the net tangible book value of the common stock. See “Dilution” in this prospectus supplement for a more detailed discussion of the dilution which may incur in connection with this offering.

FORWARD-LOOKING STATEMENTS

When used in this prospectus supplement, the accompanying prospectus and the documents incorporated by referenced in this prospectus supplement, the words “expects,” “believes,” “hopes,” “anticipates,” “estimates,” “may,” “could,” “intends,” “exploring,” “evaluating,” “progressing,” “proceeding” and similar expressions are intended to identify forward-looking statements. These forward-looking statements include statements included in or incorporated by referenced into this prospectus supplement under the headings “Our Company” and “Risk Factors.” These forward-looking statements do not constitute guarantees of future performance. Investors are cautioned that statements which are not strictly historical statements, including, without limitation, statements regarding current or future financial payments, costs, returns, royalties, performance and position, plans and objectives for future operations, plans and objectives for product development, plans and objectives for present and future clinical trials and results of such trials, plans and objectives for regulatory approval, litigation, intellectual property, product development, manufacturing plans and performance, management’s initiatives and strategies, and the development of the Company’s product candidates, Tcelna and NMO-212, constitute forward-looking statements. Such forward-looking statements are subject to a number of risks and uncertainties that could cause actual results to differ materially from those anticipated. These risks and uncertainties include, but are not limited to, those risks discussed or incorporated into the “Risk Factors” section, as well as, without limitation, risks associated with:

- market conditions;
- our capital position;
- our ability to compete with larger, better financed pharmaceutical and biotechnology companies;
- new approaches to the treatment of our targeted diseases;
- our expectation of incurring continued losses;
- our uncertainty of developing a marketable product;
- our ability to raise additional capital to continue our development programs (including to undertake and complete any ongoing or further clinical studies for Tcelna or OPX-212);
- our ability to maintain compliance with NASDAQ listing standards;
- the success of our clinical trials (including the Phase IIb trial for Tcelna in SPMS which, depending upon results, may determine whether Merck Serono elects to exercise its option to acquire an exclusive, worldwide (excluding Japan) license of our Tcelna program for the treatment of MS;
- whether Merck Serono exercises its option and, if so, whether we receive any development or commercialization milestone payments or royalties from Merck Serono pursuant to the option;
- our dependence (if Merck Serono exercises its option) on the resources and abilities of Merck Serono for the further development of Tcelna;
- the efficacy of Tcelna for any particular indication, such as for relapsing remitting MS or secondary progressive MS, and the efficacy of OPX-212 for NMO;

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- our ability to develop and commercialize products;
- our ability to obtain required regulatory approvals;
- our compliance with all FDA regulations;
- our ability to obtain, maintain and protect intellectual property rights (including for Tcelna and OPX-212);
- the risk of litigation regarding our intellectual property rights or the rights of third parties;
- the success of third party development and commercialization efforts with respect to products covered by intellectual property rights that we may license or transfer;
- our limited manufacturing capabilities;
- our dependence on third-party manufacturers;
- our ability to hire and retain skilled personnel;
- our volatile stock price; and
- other risks detailed in our filings with the SEC.

These forward-looking statements speak only as of the date made. We assume no obligation or undertaking to update any forward-looking statements to reflect any changes in expectations with regard thereto or any change in events, conditions or circumstances on which any such statement is based. You should, however, review additional disclosures we make in our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, and Current Reports on Form 8-K filed with the SEC.

USE OF PROCEEDS

If all 1,000,000 shares of common stock were sold at the March 24, 2016 closing sales price, we would receive \$2,160,000 in gross proceeds, or \$2,095,200 in net proceeds after the sales agent fee of 3% and estimated offering expenses. However, there can be no assurance we will sell any or all of the shares offered hereby. Because there is no minimum offering amount required, we may sell less than all of the shares offered hereby, which may significantly reduce the amount of proceeds received by us.

In addition to general corporate purposes (including working capital, research and development, business development and operational purposes), we currently intend to use our available cash and the net proceeds of this offering to do the following: (i) to continue funding the ongoing Abili-T clinical study of Tcelna in patients with SPMS, and (ii) to continue preclinical and manufacturing activities for OPX-212 in patients with NMO, and if such activities are successful, to file an IND application with the FDA to initiate a Phase 1/2 proof-of-concept study. We reached our enrollment target for the Abili-T trial in June 2014, and a total of 190 patients have been enrolled in this two-year study. We expect top-line data for Tcelna to be available early in the fourth quarter of 2016. While we believe we have sufficient resources to complete the trial and support our operations during the pendency of the trial, if our projections prove to be inaccurate or we encounter additional costs to complete the trial or to sustain our operations, we may need to raise additional capital or modify either the Abili-T clinical study, our development of OPX-212 in NMO, or other aspects of our current business plan.

Our management will retain broad discretion as to the allocation of the net proceeds from this offering. Until we use the net proceeds of this offering, we intend to invest the funds in short-term, interest bearing investments.

DILUTION

Our net tangible book value as of December 31, 2015 was approximately \$9,615,262 or \$1.38 per share, based on 6,982,909 shares of our common stock outstanding on that date. Net tangible book value per share is determined by dividing our total tangible assets (total assets less intangible assets), less total liabilities, by the number of shares of our common stock outstanding.

After giving effect to our assumed sale of all 1,000,000 shares of our common stock in this offering at an assumed public offering price of \$ 2.16 per share (based on the closing price of our common stock on March 24, 2016), our as adjusted net tangible book value as of December 31, 2015 would have been approximately \$ 11,710,462, or \$ 1.47 per share of common stock. This represents an immediate increase in net tangible book value of \$ 0.09 per share to existing shareholders and immediate dilution in net tangible book value of \$ 0.69 per share to new investors participating in this offering at the assumed offering price. The following table illustrates this dilution on a per share basis:

Public offering price per share (assumed at the March 24, 2016 closing price)		\$2.16
Net tangible book value per share as of December 31, 2015, before this offering	\$1.38	
Increase in pro forma net tangible book value per share attributable to existing shareholders	<u>\$0.09</u>	
Net tangible book value per share as of December 31, 2015, after giving effect to this offering		<u>\$1.47</u>
Dilution per share to new investors		<u>\$0.69</u>

Except as otherwise specifically indicated herein, all information in this prospectus supplement assumes or gives effect to no exercise of options or warrants outstanding on the date of this prospectus supplement or in the future.

PLAN OF DISTRIBUTION

Pursuant to General Instruction I.B.6. of Form S-3, we are permitted to utilize the registration statement of which this prospectus supplement and prospectus forms a part to sell a maximum amount of securities equal to one-third of the aggregate market value of the outstanding voting and non-voting common equity held by our non-affiliates in any 12-month period. We may, from time to time, offer the securities registered hereby up to an amount which, when considered with other sales made pursuant to General Instruction I.B.6. of Form S-3 within the then preceding 12-month period, would represent this maximum amount.

We have entered into a Sales Agreement, dated as of March 25, 2016, with IFS Securities, Inc. (doing business as Brinson Patrick, a division of IFS Securities, Inc.), which we refer to as “Brinson Patrick.” Under the terms of the Sales Agreement, we may sell shares of our common stock from time to time through Brinson Patrick as our sales agent. Based on the trading price of our common stock, we may not be able to sell all 1,000,000 shares offered hereby. Consistent with instructions that may be delivered from time to time by us, Brinson Patrick may sell the common stock by any method permitted by law deemed to be an “at the market” offering as defined in Rule 415 of the Securities Act. Brinson Patrick will sell any such shares on a best efforts basis into the existing trading market at the prevailing market price at the time of sale in ordinary brokerage transactions. Such sales will be open to all market participants and Brinson Patrick will make the shares available in the same way it makes available any other securities that it is requested to sell by any shareholder of any issuer.

Each time that we wish to issue and sell common stock under the Sales Agreement, we will provide Brinson Patrick with a placement notice describing the number/amount of shares to be issued, the time period during which sales are requested to be made, any limitation on the number/amount of shares of common stock that may be sold in any one day, and any minimum price below which sales may not be made.

Upon receipt of a placement notice from us, and subject to the terms and conditions of the Sales Agreement, Brinson Patrick has agreed to use best efforts, consistent with its normal trading and sales practices, to sell such

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shares up to the amount specified on such terms. The settlement between us and Brinson Patrick of our common stock will occur on the third trading day following the date on which the sale was made, or on such other date as we and Brinson Patrick may agree. We will maintain a trading account at the clearing agent designated by the sales manager to facilitate the transactions contemplated by the Sales Agreement. The obligation of Brinson Patrick under the Sales Agreement to sell our common stock pursuant to a placement notice is subject to a number of conditions.

We will pay Brinson Patrick a commission equal to 3% of the gross proceeds of the sales price of all common stock sold through it as sales agent under the Sales Agreement. If all 1,000,000 shares of common stock were sold at the March 24, 2016 closing sales price, we would receive \$ 2,160,000 in gross proceeds, or \$ 2,095,200 in net proceeds after the sales agent fee of 3% and estimated offering expenses. The actual proceeds to us will vary. Because there is no minimum offering amount required as a condition to the closing, the actual total (if any) may be substantially less than the amount set forth above. The Sales Agreement provides that we will reimburse certain costs and expenses of Brinson Patrick, up to a maximum of \$20,000.

In connection with the sale of our common stock contemplated in this prospectus supplement, Brinson Patrick may be deemed to be an “underwriter” within the meaning of the Securities Act of 1933, as amended, and the compensation paid to Brinson Patrick may be deemed to be underwriting commissions or discounts. We have agreed to indemnify Brinson Patrick against certain civil liabilities, including liabilities under the Securities Act of 1933.

Sales of our common stock as contemplated in this prospectus supplement will be settled through the facilities of The Depository Trust & Clearing Corporation or by such other means as we and Brinson Patrick may agree upon.

The offering of our common stock pursuant to the Sales Agreement will terminate (i) at such time as all 1,000,000 shares offered by this prospectus supplement have been sold or (ii) upon the termination of the Sales Agreement by us or Brinson Patrick. The Sales Agreement may be terminated at any time by either us or Brinson Patrick.

In connection with this offering, Brinson Patrick, has advised us that they will not engage in stabilizing transactions.

This is a brief summary of the material provisions of the Sales Agreement and does not purport to be a complete statement of its terms and conditions. The Sales Agreement has been included as an exhibit to our Current Report on Form 8-K dated March 25, 2016 which has been filed with the SEC and is incorporated by reference into the registration statement of which this prospectus supplement forms a part. See “Where You Can Find More Information” and “Incorporation of Certain Information by Reference.”

Other than the electronic formats of this prospectus supplement and the accompanying prospectus made available by the sales agent, the information contained on, or accessible through, either the sales agent’s website or any other website maintained by it is not part of the prospectus supplement, the accompanying prospectus or the registration statement of which this prospectus supplement and the accompanying prospectus form a part, has not been approved or endorsed by us and should not be relied upon by investors.

The transfer agent for our common stock is Continental Stock Transfer & Trust Company, New York, New York.

Our common stock is listed on the NASDAQ Capital Market under the symbol “OPXA.”

EXPERTS

The consolidated financial statements incorporated in this prospectus by reference from Opexa Therapeutics, Inc.'s Annual Report on Form 10-K for the year ended December 31, 2015, have been audited by MaloneBailey, LLP, an independent registered public accounting firm, as stated in their report, which is incorporated herein by reference, and have been so incorporated in reliance upon the report of such firm given upon their authority as experts in accounting and auditing.

LEGAL MATTERS

The validity of any securities offered by this prospectus supplement will be passed upon for us by Pillsbury Winthrop Shaw Pittman LLP, San Diego, California.

WHERE YOU CAN FIND MORE INFORMATION

We have filed a registration statement on Form S-3 with the SEC under the Securities Act of 1933. This prospectus supplement and the accompanying prospectus are part of the registration statement but the registration statement includes and incorporates by reference additional information and exhibits. We file annual, quarterly and current reports, proxy statements and other information with the SEC. You may read and copy the registration statement and any document we file with the SEC at the public reference room maintained by the SEC at 100 F Street, N.E., Washington, D.C. 20549. You may obtain information on the operation of the public reference room by calling the SEC at 1-800-SEC-0330. The SEC also maintains a web site that contains reports, proxy and information statements and other information regarding companies, such as ours, that file documents electronically with the SEC. The website address is www.sec.gov. The information on the SEC's website is not part of this prospectus supplement, and any references to this website or any other website are inactive textual references only.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC permits us to "incorporate by reference" the information contained in documents we file with the SEC, which means that we can disclose important information to you by referring you to those documents rather than by including them in this prospectus supplement and the accompanying prospectus. Information that is incorporated by reference is considered to be part of this prospectus supplement and the accompanying prospectus and you should read it with the same care that you read this prospectus supplement and the accompanying prospectus. Later information that we file with the SEC will automatically update and supersede the information that is either contained, or incorporated by reference, in this prospectus supplement and the accompanying prospectus, and will be considered to be a part of this prospectus supplement and the accompanying prospectus from the date those documents are filed. We have filed with the SEC, and incorporate by reference in this prospectus supplement and the accompanying prospectus:

- our Annual Report on Form 10-K for the year ended December 31, 2015;
- our Current Reports on Form 8-K filed with the SEC on March 2, 2016, March 15, 2016 (excluding Item 2.02 of such Current Report as well as Exhibit 99.1 to such Current Report) and March 25, 2016; and
- the description of our common stock contained in our Registration Statement on Form 8-A filed on August 30, 2006, as amended by our Form 8-12B/A filed on August 31, 2006.

We are not, however, incorporating any documents or information that we are deemed to furnish and not file in accordance with SEC rules (including with respect to the above-listed periodic reports). We also incorporate by reference all additional documents that we file with the SEC under the terms of Section 13(a), 13(c), 14 or 15(d) of the Exchange Act that are made between the date of this prospectus supplement and the termination of any offering of securities offered by this prospectus supplement or the accompanying prospectus.

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You may request a copy of any or all of the documents incorporated by reference but not delivered with this prospectus supplement, at no cost, by writing or telephoning us at the following address and number: Investor Relations, Opexa Therapeutics, Inc., 2635 Technology Forest Blvd., The Woodlands, Texas 77381, telephone (281) 775-0600. We will not, however, send exhibits to those documents, unless the exhibits are specifically incorporated by reference in those documents. We also maintain a website at www.opexatherapeutics.com. However, the information on our website is not part of this prospectus supplement and should not be relied upon with respect to this offering.

PROSPECTUS

\$100,000,000



OPEXA THERAPEUTICS

OPEXA THERAPEUTICS, INC.

**Debt Securities, Common Stock,
Preferred Stock, Depositary Shares,
Warrants and Rights**

We may, from time to time, offer and sell debt securities, preferred stock, either separately or represented by depositary shares, common stock, warrants or rights, either separately or together in any combination, in one or more offerings. The debt securities, preferred stock and warrants may be convertible into or exercisable or exchangeable for common or preferred stock or debt securities. The rights may be exercisable for common or preferred stock. The aggregate initial offering price of all securities sold under this prospectus will not exceed \$100,000,000.

We will specify in an accompanying prospectus supplement more specific information about any such offering. This prospectus may not be used to sell any of these securities unless accompanied by the applicable prospectus supplement.

We may offer and sell the securities described in this prospectus and any prospectus supplement directly to investors or through underwriters, dealers or agents. We will set forth the names of any underwriters, dealers or agents and their compensation in the accompanying prospectus supplement.

Our common stock is listed on The NASDAQ Capital Market under the symbol "OPXA." On March 17, 2016, the last reported sale price of our common stock on The NASDAQ Capital Market was \$2.08 per share. The aggregate market value of our outstanding common equity held by non-affiliates on February 23, 2016 was \$16,247,374 based on 6,982,909 shares of common stock outstanding, of which 6,658,750 are held by non-affiliates, and a closing sale price on such date of \$2.44. During the 12 calendar months prior to and including the date hereof, we have sold securities with aggregate market value of \$723,776 pursuant to General Instruction I.B.6. of Form S-3.

Investing in our securities involves risks. See the section entitled "[Risk Factors](#)" in the accompanying prospectus supplement and in the documents we incorporate by reference in this prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.

The date of this prospectus is March 25, 2016

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You should rely only on the information incorporated by reference or provided in this prospectus, any prospectus supplement and the registration statement. We have not authorized anyone else to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. We are 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 in this prospectus and any prospectus supplement, or incorporated by reference, is accurate only as of the dates of those documents. Our business, financial condition, results of operations and prospects may have changed since those dates.

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, or SEC, using a “shelf” registration, or continuous offering, process. Under this shelf registration process, we may, from time to time, offer and sell separately or together in any combination the securities described in this prospectus in one or more offerings up to a maximum aggregate offering price of \$100,000,000.

This prospectus provides you with a general description of the securities we may offer. Each time we sell securities, we will provide a prospectus supplement that will contain specific information about the terms of that offering and the offered securities. Any prospectus supplement may also add, update or change information contained in this prospectus. Any statement that we make in this prospectus will be modified or superseded by any inconsistent statement made by us in a prospectus supplement. The registration statement we filed with the SEC includes exhibits that provide more detail of the matters discussed in this prospectus. You should read this prospectus and the related exhibits filed with the SEC and any prospectus supplement, together with additional information described under the heading “Where You Can Find More Information,” before making your investment decision.

Unless the context otherwise requires, references in this prospectus and the accompanying prospectus supplement to “Opexa,” the “Company,” “we,” “us” and “our” refer to Opexa Therapeutics, Inc.

Tcelna[®], ImmPath[®] and Precision Immunotherapy[®] are registered trademarks of Opexa Therapeutics, Inc. This prospectus and the documents incorporated by reference into this prospectus may also contain trademarks and trade names that are the property of their respective owners. We do not intend our use or display of other companies’ trade names, trademarks or service marks to imply relationships with, or endorsements or sponsorship of us by, these other companies.

RISK FACTORS

Investing in our securities involves risk. The prospectus supplement relating to a particular offering will contain a discussion of risks applicable to an investment in the securities offered. Prior to making a decision about investing in our securities, you should carefully consider the specific factors discussed under the heading “Risk Factors” in the applicable prospectus supplement together with all of the other information contained in the prospectus supplement or appearing or incorporated by reference in this prospectus, including the risk factors incorporated by reference to our most recent Annual Report on Form 10-K and any subsequent Quarterly Reports on Form 10-Q or Current Reports on Form 8-K. The occurrence of any of these risks might cause you to lose all or part of your investment in the offered securities.

OPEXA THERAPEUTICS, INC.

Opexa is a biopharmaceutical company developing a personalized immunotherapy with the potential to treat major illnesses, including multiple sclerosis (MS) as well as other autoimmune diseases such as neuromyelitis optica (NMO). These therapies are based on our proprietary T-cell technology. Our mission is to lead the field of Precision Immunotherapy[®] by aligning the interests of patients, employees and shareholders. Information related to our product candidates, Tcelna[®] and OPX-212, is preliminary and investigative. Tcelna and OPX-212 have not been approved by the U.S. Food and Drug Administration (FDA) or other global regulatory agencies for marketing.

MS is an inflammatory autoimmune disease of the central nervous system (CNS), which is made up of the brain, spinal cord and optic nerves, with a clinically heterogeneous and unpredictable course that persists for decades. MS attacks the covering surrounding nerve cells, or myelin sheaths, leading to loss of myelin (demyelination) and nerve damage. In addition to demyelination, the neuropathology of MS is characterized by variable loss of oligodendroglial cells and axonal degeneration and manifests in neurological deficits. Symptoms

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may be mild, such as numbness in the limbs, or severe, such as paralysis or loss of vision. This inflammatory, demyelinating, autoimmune disease has varied clinical presentations, ranging from relapses and remissions (relapsing remitting MS, or RRMS) to slow accumulation of disability with or without relapses (secondary progressive MS, or SPMS). There are approximately 450,000 MS patients in North America and over 2,000,000 patients worldwide according to estimates from The National MS Society. The portion of the MS patient population that can be classified as SPMS is estimated by various industry sources to be between 30-45% of the total MS patient population.

We believe that our lead product candidate, Tcelna, has the potential to fundamentally address the root cause of MS by stopping the demyelination process and supporting the generation of new myelin sheaths where demyelination has occurred (remyelination). Tcelna is an autologous T-cell immunotherapy that is currently being developed for the treatment of SPMS and is specifically tailored to each patient's immune response profile to myelin. Tcelna is designed to reduce the number and/or functional activity of specific subsets of myelin-reactive T-cells (MRTCs) known to attack myelin. This technology was originally licensed from Baylor College of Medicine in 2001.

Tcelna is manufactured using our proprietary method for the production of an autologous T-cell product, which comprises the collection of blood from the MS patient and the expansion of MRTCs from the blood. Upon completion of the manufacturing process, an annual course of therapy consisting of five doses is cryopreserved. At each dosing time point, a single dose of Tcelna is formulated and attenuated by irradiation before returning the final product to the clinical site for subcutaneous administration to the patient.

Tcelna has received Fast Track designation from the FDA in SPMS, and we believe it is positioned as a potential first-to-market personalized T-cell therapy for MS patients. The FDA's Fast Track program is designed to facilitate the development and expedite the review of drug candidates intended to treat serious or life-threatening conditions and that demonstrate the potential to address unmet medical needs.

In addition to our ongoing clinical development of Tcelna, we are also in preclinical development of OPX-212 as an autologous T-cell immunotherapy for the treatment of NMO. NMO is an autoimmune disorder in which immune system cells and antibodies attack and destroy astrocytic/myelin cells in the optic nerves and the spinal cord leading to demyelination and loss of axons. There are currently no FDA-approved therapies for NMO, other than to treat an attack while it is happening, to reduce symptoms and to prevent relapses. OPX-212 is specifically tailored to each patient's immune response to a protein, aquaporin-4, which is the targeted antigen in NMO. In NMO, the immune system recognizes aquaporin-4 as foreign, thus triggering the attack. We believe a mechanism of action of OPX-212 may be to reduce the number and/or regulate aquaporin-4 reactive T-cells (ARTC), thereby reducing the frequency of clinical relapses and subsequent progression in disability.

Opexa was incorporated in Texas in March 1991. Our principal executive offices are located at 2635 Technology Forest Blvd., The Woodlands, Texas 77381, and our telephone number is (281) 775-0600. Our website address is www.opexatherapeutics.com. We do not incorporate the information on, or accessible through, our website into this prospectus, and you should not consider any information on, or accessible through, our website as part of this prospectus.

FORWARD-LOOKING STATEMENTS

When used in this prospectus, the words "expects," "believes," "anticipates," "estimates," "may," "could," "intends," and similar expressions are intended to identify forward-looking statements. These statements are subject to known and unknown risks and uncertainties that could cause actual results to differ materially from those projected or otherwise implied by the forward-looking statements. These forward-looking statements speak only as of the date of this prospectus. Given these risks and uncertainties, you should not place undue reliance on these forward-looking statements. We will discuss many of these risks and uncertainties in greater detail in any prospectus supplement under the heading "Risk Factors." Additional cautionary statements or discussions of

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risks and uncertainties that could affect our results or the achievement of the expectations described in forward-looking statements may also be contained in the documents we incorporate by reference into this prospectus.

These forward-looking statements speak only as of the date of this prospectus. We expressly disclaim any obligation or undertaking to release publicly any updates or revisions to any forward-looking statements contained herein to reflect any change in our expectations with regard thereto or any change in events, conditions or circumstances on which any such statement is based. You should, however, review additional disclosures we make in our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, and Current Reports on Form 8-K filed with the SEC.

USE OF PROCEEDS

Unless we state otherwise in the applicable prospectus supplement, we intend to use the net proceeds from the sale of the securities offered by this prospectus for general corporate purposes. General corporate purposes may include additions to working capital, financing of capital expenditures, repayment or redemption of existing indebtedness, and future acquisitions and strategic investment opportunities. Unless we state otherwise in the applicable prospectus supplement, pending the application of net proceeds, we expect to invest the net proceeds in short- and intermediate-term, interest-bearing obligations, investment-grade instruments, certificates of deposit or direct or guaranteed obligations of the U.S. government.

DESCRIPTION OF DEBT SECURITIES

The following is a summary of the general terms of the debt securities. We will file a prospectus supplement that may contain additional terms when we issue debt securities. The terms presented here, together with the terms in a related prospectus supplement, together with any pricing supplement or term sheet, will be a description of the material terms of the debt securities.

We may issue, from time to time, debt securities, in one or more series. These debt securities that we may issue include senior debt securities, senior subordinated debt securities, subordinated debt securities, convertible debt securities and exchangeable debt securities. The debt securities we offer will be issued under an indenture between us and the trustee named in the indenture. The following is a summary of the material provisions of the form of indenture filed as an exhibit to the registration statement of which this prospectus is a part. For each series of debt securities, the applicable prospectus supplement for the series may change and supplement the summary below.

General Terms of the Indenture

The indenture does not limit the amount of debt securities that we may issue. It provides that we may issue debt securities for any series of debt securities up to the principal amount that we may authorize. Except for the limitations on consolidation, merger and sale of all or substantially all of our assets contained in the indenture, the terms of the indenture do not contain any covenants or other provisions designed to give holders of any debt securities protection against changes in our operations, financial condition or transactions involving us. For each series of debt securities, any restrictive covenants for those debt securities will be described in the applicable prospectus supplement for those debt securities.

We may issue the debt securities issued under the indenture as “discount securities,” which means they may be sold at a discount below their stated principal amount. These debt securities, as well as other debt securities that are not issued at a discount, may, for United States federal income tax purposes, be treated as if they were issued with “original issue discount,” or OID, because of interest payment and other characteristics. Special United States federal income tax considerations applicable to debt securities issued with original issue discount will be described in more detail in any applicable prospectus supplement.

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You should refer to the prospectus supplement relating to a particular series of debt securities for a description of the following terms of the debt securities offered by that prospectus supplement and by this prospectus:

- the title and authorized denominations of those debt securities;
- any limit on the aggregate principal amount of that series of debt securities;
- the date or dates on which principal and premium, if any, of the debt securities of that series is payable;
- interest rates, and the dates from which interest, if any, on the debt securities of that series will accrue, and the dates when interest is payable and the maturity;
- the right, if any, to extend the interest payment periods and the duration of the extensions;
- if the amount of payments of principal or interest is to be determined by reference to an index or formula, or based on a coin or currency other than that in which the debt securities are stated to be payable, the manner in which these amounts are determined and the calculation agent, if any, with respect thereto;
- the place or places where and the manner in which principal of, premium, if any, and interest, if any, on the debt securities of that series will be payable and the place or places where those debt securities may be presented for transfer and, if applicable, conversion or exchange;
- the period or periods within which, the price or prices at which, and other terms and conditions upon which those debt securities may be redeemed, in whole or in part, at our option or the option of a holder of those securities, if we or a holder is to have that option;
- our obligation or right, if any, to redeem, repay or purchase those debt securities pursuant to any sinking fund or analogous provision or at the option of a holder of those securities, and the terms and conditions upon which the debt securities will be redeemed, repaid or purchased, in whole or in part, pursuant to that obligation;
- the terms, if any, on which the debt securities of that series will be subordinate in right and priority of payment to our other debt;
- the denominations in which those debt securities will be issuable;
- if other than the entire principal amount of the debt securities when issued, the portion of the principal amount payable upon acceleration of maturity as a result of a default on our obligations;
- whether any securities of that series are to be issued in whole or in part in the form of one or more global securities and the depository for those global securities;
- if the principal of or any premium or interest on the debt securities of that series is to be payable, or is to be payable at our election or the election of a holder of those securities, in securities or other property, the type and amount of those securities or other property, or the manner of determining that amount, and the period or periods within which, and the terms and conditions upon which, any such election may be made;
- the events of default and covenants relating to the debt securities that are in addition to, modify or delete those described in this prospectus;

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- conversion or exchange provisions, if any, including conversion or exchange prices or rates and adjustments thereto;
- whether and upon what terms the debt securities may be defeased, if different from the provisions set forth in the indenture;
- the nature and terms of any security for any secured debt securities;
- the terms applicable to any debt securities issued at a discount from their stated principal amount; and
- any other specific terms of any debt securities.

The applicable prospectus supplement will present material United States federal income tax considerations for holders of any debt securities and the securities exchange or quotation system on which any debt securities are to be listed or quoted.

Conversion or Exchange Rights

Debt securities may be convertible into or exchangeable for shares of our equity securities or other securities. The terms and conditions of conversion or exchange will be stated in the applicable prospectus supplement. The terms will include, among others, the following:

- the conversion or exchange price;
- the conversion or exchange period;
- provisions regarding our ability or the ability of any holder to convert or exchange the debt securities;
- events requiring adjustment to the conversion or exchange price; and
- provisions affecting conversion or exchange in the event of our redemption of the debt securities.

Consolidation, Merger or Sale

The indenture provides that we cannot consolidate with or merge with or into, or transfer or lease all or substantially all of our assets to, any person, unless we are the surviving corporation or the successor person is a corporation organized under the laws of the United States, any state of the United States or the District of Columbia and expressly assumes our obligations under the debt securities and the indenture. In addition, we cannot complete such a transaction unless immediately after completing the transaction, no event of default under the indenture, and no event that, after notice or lapse of time or both, would become an event of default under the indenture, has occurred and is continuing. When the successor person has assumed our obligations under the debt securities and the indenture, we will be discharged from all our obligations under the debt securities and the indenture except in limited circumstances.

This covenant would not apply to any recapitalization transaction, a change of control affecting us or a highly leveraged transaction, unless the transaction or change of control were structured to include a merger or consolidation or transfer or lease of all or substantially all of our assets.

Events of Default

The indenture provides that the following will be “events of default” with respect to any series of debt securities:

- failure to pay interest for 30 days after the date payment is due and payable;
- failure to pay principal or premium, if any, on any debt security when due, either at maturity, upon any redemption, by declaration or otherwise and, in the case of technical or administrative difficulties, only if such default persists for a period of more than three business days;
- failure to make sinking fund payments when due and continuance of such default for a period of 30 days;
- failure to perform other covenants for 60 days after notice that performance was required;
- events in bankruptcy, insolvency or reorganization relating to us; or
- any other event of default provided in the applicable officer’s certificate, resolution of our board of directors or the supplemental indenture under which we issue a series of debt securities.

An event of default for a particular series of debt securities does not necessarily constitute an event of default for any other series of debt securities issued under the indenture. For each series of debt securities, any modifications to the above events of default will be described in the applicable prospectus supplement for those debt securities.

The indenture provides that if an event of default specified in the first, second, third, fourth or sixth bullets above occurs and is continuing, either the trustee or the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series may declare the principal amount of all those debt securities (or, in the case of discount securities or indexed securities, that portion of the principal amount as may be specified in the terms of that series) to be due and payable immediately. If an event of default specified in the fifth bullet above occurs and is continuing, then the principal amount of all those debt securities (or, in the case of discount securities or indexed securities, that portion of the principal amount as may be specified in the terms of that series) will be due and payable immediately, without any declaration or other act on the part of the trustee or any holder. In certain cases, holders of a majority in principal amount of the outstanding debt securities of any series may, on behalf of holders of all those debt securities, rescind and annul a declaration of acceleration.

The indenture imposes limitations on suits brought by holders of debt securities against us. Except for actions for payment of overdue principal or interest, no holder of debt securities of any series may institute any action against us under the indenture unless:

- the holder has previously given to the trustee written notice of default and continuance of such default;
- the holders of at least 25% in principal amount of the outstanding debt securities of the affected series have requested that the trustee institute the action;
- the requesting holders have offered the trustee indemnity for the reasonable expenses and liabilities that may be incurred by bringing the action;
- the trustee has not instituted the action within 60 days of the request and offer of indemnity; and
- the trustee has not received inconsistent direction by the holders of a majority in principal amount of the outstanding debt securities of the affected series.

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We will be required to file annually with the trustee a certificate, signed by one of our officers, stating whether or not the officer knows of any default by us in the performance, observance or fulfillment of any condition or covenant of the indenture.

Discharge, Defeasance and Covenant Defeasance

We can discharge or decrease our obligations under the indenture as stated below.

We may discharge obligations to holders of any series of debt securities that have not already been delivered to the trustee for cancellation and that have either become due and payable or are by their terms to become due and payable, or are scheduled for redemption, within one year. We may effect a discharge by irrevocably depositing with the trustee cash or government obligations, as trust funds, in an amount certified to be enough to pay when due, whether at maturity, upon redemption or otherwise, the principal of, and any premium and interest on, the debt securities and any mandatory sinking fund payments.

Unless otherwise provided in the applicable prospectus supplement, we may also discharge any and all of our obligations to holders of any series of debt securities at any time, which we refer to as defeasance. We may also be released from the obligations imposed by any covenants of any outstanding series of debt securities and provisions of the indenture, and we may omit to comply with those covenants without creating an event of default under the trust declaration, which we refer to as covenant defeasance. We may effect defeasance and covenant defeasance only if, among other things:

- we irrevocably deposit with the trustee cash or government obligations denominated in the currency of the debt securities, as trust funds, in an amount certified to be enough to pay at maturity, or upon redemption, the principal (including any mandatory sinking fund payments) of, and any premium and interest on, all outstanding debt securities of the series; and
- we deliver to the trustee an opinion of counsel from a nationally recognized law firm to the effect that the holders of the series of debt securities will not recognize income, gain or loss for U.S. federal income tax purposes as a result of the defeasance or covenant defeasance and that defeasance or covenant defeasance will not otherwise alter the holders' U.S. federal income tax treatment of principal, and any premium and interest payments on, the series of debt securities.

In the case of a defeasance by us, the opinion we deliver must be based on a ruling of the Internal Revenue Service issued, or a change in U.S. federal income tax law occurring, after the date of the indenture, since such a result would not occur under the U.S. federal income tax laws in effect on that date.

Although we may discharge or decrease our obligations under the indenture as described in the two preceding paragraphs, we may not avoid, among other things, our duty to register the transfer or exchange of any series of debt securities, to replace any temporary, mutilated, destroyed, lost or stolen series of debt securities or to maintain an office or agency in respect of any series of debt securities.

Modification of the Indenture

The indenture provides that we and the trustee may enter into supplemental indentures without the consent of the holders of debt securities to, among other things:

- evidence the assumption by a successor entity of our obligations;
- add to our covenants for the benefit of the holders of debt securities, or to surrender any rights or power conferred upon us;
- add any additional events of default;

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- add to, change or eliminate any of the provisions of the indenture in a manner that will become effective only when there is no outstanding debt security which is entitled to the benefit of the provision as to which the modification would apply;
- add guarantees with respect to or secure any debt securities;
- establish the forms or terms of debt securities of any series;
- evidence and provide for the acceptance of appointment by a successor trustee and add to or change any of the provisions of the indenture as is necessary for the administration of the trusts by more than one trustee;
- cure any ambiguity or correct any inconsistency or defect in the indenture;
- modify, eliminate or add to the provisions of the indenture as shall be necessary to effect the qualification of the indenture under the Trust Indenture Act of 1939 or under any similar federal statute later enacted, and to add to the indenture such other provisions as may be expressly required by the Trust Indenture Act; and
- make any other provisions with respect to matters or questions arising under the indenture that will not be inconsistent with any provision of the indenture as long as the new provisions do not adversely affect the interests of the holders of any outstanding debt securities of any series created prior to the modification.

The indenture also provides that we and the trustee may, with the consent of the holders of not less than a majority in aggregate principal amount of debt securities of each series of debt securities affected by such supplemental indenture then outstanding, add any provisions to, or change in any manner, eliminate or modify in any way the provisions of, the indenture or any supplemental indenture or modify in any manner the rights of the holders of the debt securities. We and the trustee may not, however, without the consent of the holder of each outstanding debt security affected thereby:

- extend the final maturity of any debt security;
- reduce the principal amount or premium, if any;
- reduce the rate or extend the time of payment of interest;
- reduce the amount of the principal of any debt security issued with an original issue discount that is payable upon acceleration;
- change the currency in which the principal, and any premium or interest, is payable;
- impair the right to institute suit for the enforcement of any payment on any debt security when due;
- if applicable, adversely affect the right of a holder to convert or exchange a debt security; or
- reduce the percentage of holders of debt securities of any series whose consent is required for any modification of the indenture or for waivers of compliance with or defaults under the indenture with respect to debt securities of that series.

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The indenture provides that the holders of not less than a majority in aggregate principal amount of the then outstanding debt securities of any series, by notice to the relevant trustee, may on behalf of the holders of the debt securities of that series waive any default and its consequences under the indenture except:

- a default in the payment of, any premium and any interest on, or principal of, any such debt security held by a nonconsenting holder; or
- a default in respect of a covenant or provision of the indenture that cannot be modified or amended without the consent of the holder of each outstanding debt security of each series affected.

Registered Global Securities and Book Entry System

The debt securities of a series may be issued in whole or in part in book-entry form and will be represented by one or more fully registered global securities. We will deposit any registered global securities with a depository or with a nominee for a depository identified in the applicable prospectus supplement and registered in the name of such depository or nominee. In such case, we will issue one or more registered global securities denominated in an amount equal to the aggregate principal amount of all of the debt securities of the series to be issued and represented by such registered global security or securities. This means that we will not issue certificates to each holder.

Unless and until it is exchanged in whole or in part for debt securities in definitive registered form, a registered global security may not be transferred except as a whole:

- by the depository for the registered global security to its nominee;
- by a nominee of the depository to the depository or another nominee of the depository; or
- by the depository or its nominee to a successor of the depository or a nominee of the successor.

The prospectus supplement relating to a series of debt securities will describe the specific terms of the depository arrangement involving any portion of the series represented by a registered global security. We anticipate that the following provisions will apply to all depository arrangements for debt securities:

- ownership of beneficial interests in a registered global security will be limited to persons that have accounts with the depository for such registered global security, these persons being referred to as “participants,” or persons that may hold interests through participants;
- upon the issuance of a registered global security, the depository for the registered global security will credit, on its book-entry registration and transfer system, the participants’ accounts with the respective principal amounts of the debt securities represented by the registered global security beneficially owned by the participants;
- any dealers, underwriters, or agents participating in the distribution of the debt securities will designate the accounts to be credited; and
- ownership of beneficial interest in the registered global security will be shown on, and the transfer of the ownership interest will be effected only through, records maintained by the depository for the registered global security for interests of participants, and on the records of participants for interests of persons holding through participants.

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The laws of some states may require that specified purchasers of securities take physical delivery of the securities in definitive form. These laws may limit the ability of those persons to own, transfer or pledge beneficial interests in registered global securities.

So long as the depositary for a registered global security, or its nominee, is the registered owner of the registered global security, the depositary or such nominee, as the case may be, will be considered the sole owner or holder of the debt securities represented by the registered global security for all purposes under the indenture. Except as stated below, owners of beneficial interests in a registered global security:

- will not be entitled to have the debt securities represented by a registered global security registered in their names;
- will not receive or be entitled to receive physical delivery of the debt securities in the definitive form; and
- will not be considered the owners or holders of the debt securities under the relevant indenture.

Accordingly, each person owning a beneficial interest in a registered global security must rely on the procedures of the depositary for the registered global security and, if the person is not a participant, on the procedures of a participant through which the person owns its interest, to exercise any rights of a holder under the indenture.

We understand that under existing industry practices, if we request any action of holders or if an owner of a beneficial interest in a registered global security desires to give or take any action that a holder is entitled to give or take under the indenture, the depositary for the registered global security would authorize the participants holding the relevant beneficial interests to give or take the action, and the participants would authorize beneficial owners owning through the participants to give or take the action or would otherwise act upon the instructions of beneficial owners holding through them.

We will make payments of principal and premium, if any, and interest, if any, on debt securities represented by a registered global security registered in the name of a depositary or its nominee to the depositary or its nominee, as the case may be, as the registered owners of the registered global security. Neither we nor the trustee, or any other agent of ours or the trustee will be responsible or liable for any aspect of the records relating to, or payments made on account of, beneficial ownership interests in the registered global security or for maintaining, supervising or reviewing any records relating to the beneficial ownership interests.

We expect that the depositary for any debt securities represented by a registered global security, upon receipt of any payments of principal and premium, if any, and interest, if any, in respect of the registered global security, will immediately credit participants' accounts with payments in amounts proportionate to their respective beneficial interests in the registered global security as shown on the records of the depositary. We also expect that standing customer instructions and customary practices will govern payments by participants to owners of beneficial interests in the registered global security held through the participants, as is now the case with the securities held for the accounts of customers in bearer form or registered in "street name." We also expect that any of these payments will be the responsibility of the participants.

If the depositary for any debt securities represented by a registered global security is at any time unwilling or unable to continue as depositary or stops being a clearing agency registered under the Exchange Act, we will appoint an eligible successor depositary. If we fail to appoint an eligible successor depositary within 90 days, we will issue the debt securities in definitive form in exchange for the registered global security. In addition, we may at any time and in our sole discretion decide not to have any of the debt securities of a series represented by one or more registered global securities. In that event, we will issue debt securities of the series in a definitive form in exchange for all of the registered global securities representing the debt securities. The trustee will register any

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debt securities issued in definitive form in exchange for a registered global security in the name or names as the depository, based upon instructions from its participants, shall instruct the trustee.

Concerning the Trustee

The indenture provides that there may be more than one trustee under the indenture, each for one or more series of debt securities. If there are different trustees for different series of debt securities, each trustee will be a trustee of a trust under the indenture separate and apart from the trust administered by any other trustee under that indenture. Except as otherwise indicated in this prospectus or any prospectus supplement, any action permitted to be taken by a trustee may be taken by such trustee only on the one or more series of debt securities for which it is the trustee under the indenture. Any trustee under the indenture may resign or be removed from one or more series of debt securities. All payments of principal of, and any premium and interest on, and all registration, transfer, exchange, authentication and delivery of, the debt securities of a series will be effected by the trustee for that series at an office designated by the trustee in New York, New York.

The indenture provides that, except during the continuance of an event of default, the trustee will perform only such duties as are specifically set forth in the indenture. During the existence of an event of default, the trustee will exercise those rights and powers vested in it under the indenture and use the same degree of care and skill in its exercise as a prudent person would exercise under the circumstances in the conduct of such person's own affairs.

If the trustee becomes a creditor of ours, the indenture places limitations on the right of the trustee to obtain payment of claims or to realize on property received in respect of any such claim as security or otherwise. The trustee may engage in other transactions. If it acquires any conflicting interest relating to any duties concerning the debt securities, however, it must eliminate the conflict or resign as trustee.

No Individual Liability of Incorporators, Shareholders, Officers or Directors

The indenture provides that no past, present or future director, officer, shareholder or employee of ours, any of our affiliates, or any successor corporation, in their capacity as such, shall have any individual liability for any of our obligations, covenants or agreements under the debt securities or the indenture.

Governing Law

The indenture and the debt securities will be governed by, and construed in accordance with, the laws of the State of New York.

DESCRIPTION OF PREFERRED STOCK

As of March 10, 2016, our authorized preferred stock, no par value, was 10,000,000 shares, none of which were issued and outstanding. We may issue preferred stock, in series, with such designations, powers, preferences and other rights and qualifications, limitations or restrictions as our board of directors may authorize, without further action by our shareholders, including:

- the distinctive designation of each series and the number of shares that will constitute the series;
- the voting rights, if any, of shares of the series and the terms and conditions of the voting rights;
- the dividend rate on the shares of the series, the dates on which dividends are payable, any restriction, limitation or condition upon the payment of dividends, whether dividends will be cumulative, and the dates from and after which dividends shall accumulate;

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- the prices at which, and the terms and conditions on which, the shares of the series may be redeemed, if the shares are redeemable;
- the terms and conditions of a sinking or purchase fund for the purchase or redemption of shares of the series, if such a fund is provided;
- any preferential amount payable upon shares of the series in the event of the liquidation, dissolution or winding up of, or upon the distribution of any of our assets; and
- the prices or rates of conversion or exchange at which, and the terms and conditions on which, the shares of the series may be converted or exchanged into other securities, if the shares are convertible or exchangeable.

The particular terms of any series of preferred stock, and the transfer agent and registrar for that series, will be described in a prospectus supplement. Any material United States federal income tax consequences and other special considerations with respect to any preferred stock offered under this prospectus will also be described in the applicable prospectus supplement.

DESCRIPTION OF DEPOSITARY SHARES

The following description of the depositary shares does not purport to be complete and is subject to and qualified in its entirety by the relevant deposit agreement and the depositary receipts with respect to the depositary shares relating to any particular series of preferred stock. You should read these documents as they, and not this description, will define your rights as a holder of depositary shares. Forms of these documents will be filed with the SEC in connection with the offering of depositary shares.

General

If we elect to offer fractional interests in shares of preferred stock, we will provide for the issuance by a depositary to the public of receipts for depositary shares. Each depositary share will represent fractional interests of preferred stock. We will deposit the shares of preferred stock underlying the depositary shares under a deposit agreement between us and a bank or trust company selected by us. The bank or trust company must have its principal office in the United States and a combined capital and surplus of at least \$50 million. The depositary receipts will evidence the depositary shares issued under the deposit agreement.

The deposit agreement will contain terms applicable to the holders of depositary shares in addition to the terms stated in the depositary receipts. Each owner of depositary shares will be entitled to all the rights and preferences of the preferred stock underlying the depositary shares in proportion to the applicable fractional interest in the underlying shares of preferred stock. The depositary will issue the depositary receipts to individuals purchasing the fractional interests in shares of the related preferred stock according to the terms of the offering described in a prospectus supplement.

Dividends and Other Distributions

The depositary will distribute all cash dividends or other cash distributions received for the preferred stock to the entitled record holders of depositary shares in proportion to the number of depositary shares that the holder owns on the relevant record date. The depositary will distribute only an amount that can be distributed without attributing to any holder of depositary shares a fraction of one cent. The depositary will add the undistributed balance to and treat it as part of the next sum received by the depositary for distribution to holders of depositary shares.

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If there is a non-cash distribution, the depositary will distribute property received by it to the entitled record holders of depositary shares, in proportion, insofar as possible, to the number of depositary shares owned by the holders, unless the depositary determines, after consultation with us, that it is not feasible to make such distribution. If this occurs, the depositary may, with our approval, sell such property and distribute the net proceeds from the sale to the holders. The deposit agreement also will contain provisions relating to how any subscription or similar rights that we may offer to holders of the preferred stock will be available to the holders of the depositary shares.

Conversion, Exchange, Redemption and Liquidation

If any series of preferred stock underlying the depositary shares may be converted or exchanged, each record holder of depositary receipts will have the right or obligation to convert or exchange the depositary shares represented by the depositary receipts.

The terms on which the depositary shares relating to the preferred stock of any series may be redeemed, and any amounts distributable upon our liquidation, dissolution or winding up, will be described in the relevant prospectus supplement.

Voting

When the depositary receives notice of a meeting at which the holders of the preferred stock are entitled to vote, the depositary will mail the particulars of the meeting to the record holders of the depositary shares. Each record holder of depositary shares on the record date may instruct the depositary on how to vote the shares of preferred stock underlying the holder's depositary shares. The depositary will try, if practical, to vote the number of shares of preferred stock underlying the depositary shares according to the instructions. We will agree to take all reasonable action requested by the depositary to enable it to vote as instructed.

Amendments

We and the depositary may agree to amend the deposit agreement and the depositary receipt evidencing the depositary shares. Any amendment that (a) imposes or increases certain fees, taxes or other charges payable by the holders of the depositary shares as described in the deposit agreement or that (b) otherwise prejudices any substantial existing right of holders of depositary shares, will not take effect until 30 days after the depositary has mailed notice of the amendment to the record holders of depositary shares. Any holder of depositary shares that continues to hold its shares at the end of the 30-day period will be deemed to have agreed to the amendment.

Termination

We may direct the depositary to terminate the deposit agreement by mailing a notice of termination to holders of depositary shares at least 30 days prior to termination. In addition, a deposit agreement will automatically terminate if the depositary has redeemed all related outstanding depositary shares, or we have liquidated, terminated or wound up our business and the depositary has distributed the preferred stock of the relevant series to the holders of the related depositary shares.

Payment of Fees and Expenses

We will pay all fees, charges and expenses of the depositary, including the initial deposit of the preferred stock and any redemption of the preferred stock. Holders of depositary shares will pay transfer and other taxes and governmental charges and any other charges as are stated in the deposit agreement for their accounts.

Resignation and Removal of Depositary

At any time, the depositary may resign by delivering notice to us, and we may remove the depositary. Resignations or removals will take effect upon the appointment of a successor depositary and its acceptance of the appointment. The successor depositary must be appointed within 60 days after delivery of the notice of resignation or removal and must be a bank or trust company having its principal office in the United States and having a combined capital and surplus of at least \$50 million.

Reports

The depositary will forward to the holders of depositary shares all reports and communications from us that are delivered to the depositary and that we are required by law, the rules of an applicable securities exchange or our restated certificate of formation, as amended, to furnish to the holders of the preferred stock. Neither we nor the depositary will be liable if the depositary is prevented or delayed by law or any circumstances beyond its control in performing its obligations under the deposit agreement. The deposit agreement limits our obligations and the depositary's obligations to performance in good faith of the duties stated in the deposit agreement. Neither we nor the depositary will be obligated to prosecute or defend any legal proceeding connected with any depositary shares or preferred stock unless the holders of depositary shares requesting us to do so furnish us with satisfactory indemnity. In performing our obligations, we and the depositary may rely upon the written advice of our counsel or accountants, on any information that competent people provide to us and on documents that we believe are genuine.

DESCRIPTION OF COMMON STOCK

This section describes the general terms and provisions of the shares of our common stock, \$0.01 par value. This description is only a summary and is qualified in its entirety by reference to the description of our common stock incorporated by reference in this prospectus. Our restated certificate of formation, as amended, and our amended and restated bylaws, as amended, have been filed as exhibits to our periodic reports filed with the SEC, which are incorporated by reference in this prospectus. You should read our restated certificate of formation, as amended, and our amended and restated bylaws, as amended, for additional information before you buy any of our common stock or other securities. See "Where You Can Find More Information."

We have 150,000,000 shares of authorized common stock. As of March 10, 2016, there were 6,982,909 shares of common stock issued and outstanding. Each holder of common stock is entitled to one vote for each share of common stock held on all matters submitted to a vote of shareholders. We have not provided for cumulative voting for the election of directors in our restated certificate of formation, as amended. This means that the holders of a majority of the shares voted can elect all of the directors then standing for election. Subject to preferences that may apply to shares of preferred stock outstanding at the time, the holders of outstanding shares of our common stock are entitled to receive dividends out of assets legally available at the times and in the amounts that our board of directors may determine from time to time. Upon our liquidation, dissolution or winding-up, the holders of common stock are entitled to share ratably in all assets remaining after payment of all liabilities and the liquidation preferences of any outstanding preferred stock. Holders of common stock have no preemptive or conversion rights or other subscription rights. There are no redemption or sinking fund provisions applicable to the common stock. All outstanding shares of common stock are fully paid and nonassessable.

Anti-Takeover Effects of Our Restated Certificate of Formation and Bylaws

Certain provisions of our restated certificate of formation, as amended, and our amended and restated bylaws, as amended, could have the effect of delaying, deferring or discouraging another party from acquiring control of us. These provisions, which are summarized below, are expected to discourage certain types of coercive takeover practices and inadequate takeover bids. These provisions are also designed, in part, to

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encourage persons seeking to acquire control of us to first negotiate with our board of directors. Our restated certificate of formation, as amended, and our amended and restated bylaws, as amended, include provisions that:

- authorize our board of directors to issue, without further action by the shareholders, up to 10,000,000 shares of undesignated preferred stock; and
- authorize us to indemnify officers and directors against losses that they may incur in investigations and legal proceedings resulting from their services to us, which may include services in connection with takeover defense measures.

Transfer Agent

The transfer agent and registrar for our common stock is Continental Stock Transfer and Trust Company.

DESCRIPTION OF WARRANTS

We may issue warrants for the purchase of debt securities, preferred stock, common stock, depositary shares, or any combination thereof. We may issue warrants independently or together with any other securities offered by any prospectus supplement and may be attached to or separate from the other offered securities. Each series of warrants may be issued under a separate warrant agreement to be entered into by us with a warrant agent. The applicable warrant agent will act solely as our agent in connection with the warrants and will not assume any obligation or relationship of agency or trust for or with any holders or beneficial owners of warrants. Further terms of the warrants and the applicable warrant agreements will be set forth in the applicable prospectus supplement.

The applicable prospectus supplement relating to any particular issue of warrants will describe the terms of the warrants, including, as applicable, the following:

- the title of the warrants;
- the aggregate number of the warrants;
- the price or prices at which the warrants will be issued;
- the designation, terms and number of shares of debt securities, preferred stock or common stock purchasable upon exercise of the warrants;
- the designation and terms of the offered securities, if any, with which the warrants are issued and the number of the warrants issued with each offered security;
- the date, if any, on and after which the warrants and the related debt securities, preferred stock or common stock will be separately transferable;
- the price at which each share of debt securities, preferred stock or common stock purchasable upon exercise of the warrants may be purchased;
- the date on which the right to exercise the warrants shall commence and the date on which that right shall expire;
- the minimum or maximum amount of the warrants which may be exercised at any one time;
- information with respect to book-entry procedures, if any;

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- a discussion of certain federal income tax considerations; and
- any other terms of the warrants, including terms, procedures and limitations relating to the exchange and exercise of the warrants.

We and the applicable warrant agent may amend or supplement the warrant agreement for a series of warrants without the consent of the holders of the warrants issued thereunder to effect changes that are not inconsistent with the provisions of the warrants and that do not materially and adversely affect the interests of the holders of the warrants.

DESCRIPTION OF RIGHTS

We may issue rights to purchase common stock or preferred stock. This prospectus and any accompanying prospectus supplement will contain the material terms and conditions for each right. The accompanying prospectus supplement may add, update or change the terms and conditions of the rights as described in this prospectus.

We will describe in the applicable prospectus supplement the terms and conditions of the issue of rights being offered, the rights agreement relating to the rights and the rights certificates representing the rights, including, as applicable:

- the title of the rights;
- the date of determining the shareholders entitled to the rights distribution;
- the title, aggregate number of shares of common stock or preferred stock purchasable upon exercise of the rights;
- the exercise price;
- the aggregate number of rights issued;
- the date, if any, on and after which the rights will be separately transferable;
- the date on which the right to exercise the rights will commence and the date on which the right will expire; and
- any other terms of the rights, including terms, procedures and limitations relating to the distribution, exchange and exercise of the rights.

Each right will entitle the holder of rights to purchase for cash the principal amount of shares of common stock or preferred stock at the exercise price provided in the applicable prospectus supplement. Rights may be exercised at any time up to the close of business on the expiration date for the rights provided in the applicable prospectus supplement. After the close of business on the expiration date, all unexercised rights will be void.

Holders may exercise rights as described in the applicable prospectus supplement. Upon receipt of payment and the rights certificate properly completed and duly executed at the corporate trust office of the rights agent or any other office indicated in the prospectus supplement, we will, as soon as practicable, forward the shares of common stock or preferred stock purchasable upon exercise of the rights. If less than all of the rights issued in any rights offering are exercised, we may offer any unsubscribed securities directly to persons other than shareholders, to or through agents, underwriters or dealers or through a combination of such methods, including pursuant to standby underwriting arrangements, as described in the applicable prospectus supplement.

PLAN OF DISTRIBUTION

We may sell the securities offered by this prospectus to one or more underwriters or dealers for public offering and sale by them or to investors directly or through agents. The accompanying prospectus supplement will set forth the terms of the offering and the method of distribution and will identify any firms acting as underwriters, dealers or agents in connection with the offering, including:

- the name or names of any underwriters, dealers or agents;
- the purchase price of the securities and the proceeds to us from the sale;
- any underwriting discounts and other items constituting compensation to underwriters, dealers or agents;
- any public offering price;
- any discounts or concessions allowed or reallowed or paid to dealers; and
- any securities exchange or market on which the securities offered in the prospectus supplement may be listed.

Only those underwriters identified in such prospectus supplement are deemed to be underwriters in connection with the securities offered in the prospectus supplement.

The distribution of the securities may be effected from time to time in one or more transactions at a fixed price or prices, which may be changed, or at prices determined as the applicable prospectus supplement specifies. The securities may be sold through an at-the-market offering, a rights offering, forward contracts or similar arrangements. In addition, we may enter into derivative transactions with third parties, or sell securities not covered by this prospectus to third parties in privately negotiated transactions. If the applicable prospectus supplement so indicates, in connection with those derivatives, the third parties may sell securities covered by this prospectus and the applicable prospectus supplement, including in short sale transactions. If so, the third party may use securities pledged by us or borrowed from us or others to settle those sales or to close out any related open borrowings of stock, and may use securities received from us in settlement of those derivatives to close out any related open borrowings of stock. The third party in such sale transactions will be an underwriter and, if not identified in this prospectus, will be named in the applicable prospectus supplement (or a post-effective amendment). In addition, we may otherwise loan or pledge securities to a financial institution or other third party that in turn may sell the securities short using this prospectus and an applicable prospectus supplement. Such financial institution or other third party may transfer its economic short position to investors in our securities or in connection with a concurrent offering of other securities.

In connection with the sale of the securities, underwriters, dealers or agents may be deemed to have received compensation from us in the form of underwriting discounts or commissions and also may receive commissions from securities purchasers for whom they may act as agent. Underwriters may sell the securities to or through dealers, and the dealers may receive compensation in the form of discounts, concessions or commissions from the underwriters or commissions from the purchasers for whom they may act as agent.

We will provide in the applicable prospectus supplement information regarding any underwriting discounts or other compensation that we pay to underwriters or agents in connection with the securities offering, and any discounts, concessions or commissions that underwriters allow to dealers. Underwriters, dealers and agents participating in the securities distribution may be deemed to be underwriters, and any discounts, commissions or concessions they receive and any profit they realize on the resale of the securities may be deemed to be underwriting discounts and commissions under the Securities Act of 1933. Underwriters and their controlling

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persons, dealers and agents may be entitled, under agreements entered into with us, to indemnification against and contribution toward specific civil liabilities, including liabilities under the Securities Act. Some of the underwriters, dealers or agents who participate in the securities distribution may engage in other transactions with, and perform other services for, us or our subsidiaries in the ordinary course of business.

Our common stock is currently listed on The NASDAQ Capital Market, but any other securities may or may not be listed on a national securities exchange. To facilitate the offering of securities, certain persons participating in the offering may engage in transactions that stabilize, maintain or otherwise affect the price of the securities. This may include over-allotments or short sales of the securities, which involve the sale by persons participating in the offering of more securities than were sold to them. In these circumstances, these persons would cover such over-allotments or short positions by making purchases in the open market or by exercising their over-allotment option, if any. In addition, these persons may stabilize or maintain the price of the securities by bidding for or purchasing securities in the open market or by imposing penalty bids, whereby selling concessions allowed to dealers participating in the offering may be reclaimed if securities sold by them are repurchased in connection with stabilization transactions. The effect of these transactions may be to stabilize or maintain the market price of the securities at a level above that which might otherwise prevail in the open market. These transactions may be discontinued at any time.

LEGAL MATTERS

The validity of any securities offered by this prospectus will be passed upon for us by Pillsbury Winthrop Shaw Pittman LLP, San Diego, California.

EXPERTS

The consolidated financial statements incorporated in this prospectus by reference from Opexa Therapeutics, Inc.'s Annual Report on Form 10-K for the year ended December 31, 2015, have been audited by MaloneBailey, LLP, an independent registered public accounting firm, as stated in their report, which is incorporated herein by reference, and have been so incorporated in reliance upon the report of such firm given upon their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We have filed a registration statement on Form S-3 with the SEC under the Securities Act of 1933. This prospectus is part of the registration statement but the registration statement includes and incorporates by reference additional information and exhibits. We file annual, quarterly and current reports, proxy statements and other information with the SEC. You may read and copy the registration statement and any other document we file with the SEC at the public reference room maintained by the SEC at 100 F Street, N.E., Washington, D.C. 20549. You may obtain information on the operation of the public reference room by calling the SEC at 1-800-SEC-0330. The SEC also maintains a web site that contains reports, proxy and information statements and other information regarding companies, such as ours, that file documents electronically with the SEC. The address of that site on the world wide web is <http://www.sec.gov>. The information on the SEC's web site is not part of this prospectus, and any references to this web site or any other web site are inactive textual references only.

The SEC permits us to "incorporate by reference" the information contained in documents we file with the SEC, which means that we can disclose important information to you by referring you to those documents rather than by including them in this prospectus. Information that is incorporated by reference is considered to be part of this prospectus and you should read it with the same care that you read this prospectus. Later information that we file with the SEC will automatically update and supersede the information that is either contained, or incorporated by reference, in this prospectus, and will be considered to be a part of this prospectus from the date those documents are filed. We have filed with the SEC, and incorporate by reference in this prospectus:

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- our Annual Report on Form 10-K for the year ended December 31, 2015;
- our Current Reports on Form 8-K filed with the SEC on March 2, 2016 and March 15, 2016 (excluding Item 2.02 of such Current Report as well as Exhibit 99.1 to such Current Report); and
- the description of our common stock contained in our Registration Statement on Form 8-A filed on August 30, 2006, as amended by our Form 8-12B/A filed on August 31, 2006.

We are not, however, incorporating any documents or information that we are deemed to furnish and not file in accordance with SEC rules (including with respect to the above-listed periodic reports). We also incorporate by reference all additional documents that we file with the SEC under the terms of Section 13(a), 13(c), 14 or 15(d) of the Exchange Act that are made after the initial filing date of the registration statement of which this prospectus is a part and the effectiveness of the registration statement, as well as between the date of this prospectus and the termination of any offering of securities offered by this prospectus.

You may request a copy of any or all of the documents incorporated by reference but not delivered with this prospectus, at no cost, by writing or telephoning us at the following address and number: Investor Relations, Opexa Therapeutics, Inc., 2635 Technology Forest Blvd., The Woodlands, Texas 77381, telephone (281) 272-9331. We will not, however, send exhibits to those documents, unless the exhibits are specifically incorporated by reference in those documents.

1,000,000 of Shares Common Stock



PROSPECTUS SUPPLEMENT



March 25, 2016
