

OPEXA THERAPEUTICS, INC.

FORM S-3

(Securities Registration Statement (simplified form))

Filed 10/10/13

Address	2635 TECHNOLOGY FOREST BLVD. THE WOODLANDS, TX 77381
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Fiscal Year	12/31

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

FORM S-3
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

OPEXA THERAPEUTICS, INC.

(Exact Name of Registrant as Specified in Its Charter)

Texas
(State or Other Jurisdiction of Incorporation or
Organization)

76-0333165
(I.R.S. Employer Identification Number)

2635 Technology Forest Blvd.
The Woodlands, Texas 77381
(281) 272-9331
(Address, Including Zip Code, and Telephone Number, Including Area Code, of Registrant's Principal Executive Offices)

Neil K. Warma
President and Chief Executive Officer
OPEXA THERAPEUTICS, INC.
2635 Technology Forest Blvd.
The Woodlands, Texas 77381
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(Name, Address, Including Zip Code, and Telephone Number, Including Area Code, of
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Approximate date of commencement of proposed sale to the public: From time to time after this registration statement becomes effective, as determined by market conditions and other factors.

If the only securities being registered on this form are being offered pursuant to dividend or interest reinvestment plans, please check the following box. ☐

If any of the securities being registered on this form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box. ☒

If this form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If this form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If this form is a registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box. ☐

If this form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box. ☐

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

Large accelerated filer ☐

Accelerated filer ☐

Non-accelerated filer ☐

Smaller reporting company ☒

(Do not check if a smaller reporting company)

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities To Be Registered	Amount to be Registered ⁽¹⁾	Proposed Maximum Offering Price Per Share	Proposed Maximum Aggregate Offering Price	Amount of Registration Fee
Common Stock, \$0.01 par value	1,714,697 ⁽²⁾	\$2.065	\$3,540,849 ⁽³⁾	\$456.06
Total	1,714,697	\$2.065	\$3,540,849	\$456.06

- (1) Pursuant to Rule 416(a) under the Securities Act of 1933, the registrant is also registering hereunder an indeterminate number of shares that may be issued and resold resulting from stock splits, stock dividends or similar transactions.
- (2) Represents shares of the registrant's common stock issued upon conversion of principal and accrued interest on 12% convertible secured promissory notes. The notes were originally issued in July 2012 in a private placement to certain accredited investors.
- (3) Estimated pursuant to Rule 457(c) solely for the purpose of calculating the registration fee, based upon the average of the high and low prices for the registrant's common stock as reported on The NASDAQ Capital Market on October 8, 2013, a date within five business days of the filing of this registration statement, of \$2.065 per share.

The Registrant hereby amends this registration statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this registration statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until the registration statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.

The information in this prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and is not soliciting an offer to buy these securities in any state where the offer or sale is not permitted.

Subject to Completion, Dated October 10, 2013

PROSPECTUS



OPEXA THERAPEUTICS, INC.

1,714,697 Shares of Common Stock

This prospectus relates to the resale of up to 1,714,697 shares of our common stock being offered by the selling shareholders named in this prospectus, all of which were issued upon conversion of our 12% convertible secured promissory notes originally issued in a July 2012 private placement to certain accredited investors.

We will not receive any of the proceeds from the sales by the selling shareholders.

Our common stock is traded on The NASDAQ Capital Market under the symbol "OPXA." On October 9, 2013, the last reported sale price of our common stock on The NASDAQ Capital Market was \$1.79 per share.

The shares of our common stock may be offered through public or private transactions at market prices prevailing at the time of sale, at a fixed price or fixed prices, at negotiated prices, at various prices determined at the time of sale or at prices related to prevailing market prices. In addition, shares of our common stock may be offered from time to time through ordinary brokerage transactions on The NASDAQ Capital Market. The timing and amount of any sale are within the sole discretion of the selling shareholders, subject to certain restrictions. See "Plan of Distribution."

Investing in our securities involves risks. See the section entitled "Risk Factors" beginning on page 9 in this prospectus and in the documents we incorporate by reference in this prospectus. You should carefully consider these risk factors, as well as the information contained in this 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. Any representation to the contrary is a criminal offense.

The date of this prospectus is _____, 2013.

TABLE OF CONTENTS

	<u>Page</u>
About this Prospectus	i
Prospectus Summary	1
Risk Factors	9
Forward-Looking Statements	9
Use of Proceeds	11
Selling Shareholders	11
Plan of Distribution	15
Legal Matters	17
Experts	17
Where You Can Find More Information	17

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 state 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 continuous offering process. Under this prospectus, the selling shareholders may, from time to time, sell shares of our common stock described in this prospectus in one or more offerings. This prospectus provides you with a general description of the securities offered by the selling shareholders. 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 to “Opexa,” “the Company,” “we,” “us” and “our” refer to Opexa Therapeutics, Inc.

PROSPECTUS 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 carefully, including the section entitled “Risk Factors,” and our consolidated financial statements and the related notes and other documents incorporated by reference in the prospectus.

Our Company

Our Business

Opexa is a biopharmaceutical company developing a personalized immunotherapy with the potential to treat major illnesses, including multiple sclerosis (MS). This therapy is 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 candidate, Tcelna®, is preliminary and investigative. Tcelna has not been approved by the U.S. Food and Drug Administration (FDA) or other global regulatory agencies for marketing.

MS is a chronic, often disabling disease that affects the central nervous system (CNS), which is made up of the brain, spinal cord and optic nerves. MS attacks the covering surrounding nerve cells, or myelin sheaths, leading to loss of myelin (demyelination) and nerve damage. Symptoms may be mild, such as numbness in the limbs, or severe, such as paralysis or loss of vision. The progress, severity and specific symptoms of MS are unpredictable and vary from one person to another. We believe that our product candidate, Tcelna, has the potential to fundamentally address the root cause of MS by stopping the demyelination process and in 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 Secondary Progressive MS (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.

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.

T-Cell Therapy and Tcelna®

Tcelna® is a novel T-cell immunotherapy in Phase IIb clinical development for the treatment of patients with SPMS. It is also positioned to enter Phase III clinical development for the treatment of patients with relapsing remitting MS (RRMS), subject to the availability of sufficient resources. Tcelna is a personalized therapy that is specifically tailored to each patient’s disease profile. Tcelna is manufactured using ImmPath™, our proprietary method for the production of a patient-specific T-cell immunotherapy which encompasses the collection of blood from the MS patient, isolation of peripheral blood mononuclear cells, generation of an autologous pool of MRTCs raised against selected peptides from myelin basic protein (MBP), myelin oligodendrocyte glycoprotein (MOG) and proteolipid protein (PLP), and the return of these expanded, irradiated T-cells back to the patient. These attenuated T-cells are reintroduced into the patient via subcutaneous injection to trigger a therapeutic immune system response.

Abili-T Trial: Phase IIb Clinical Study in Patients with SPMS

In September 2012, we announced the initiation of a Phase IIb clinical trial of Tcelna in patients with SPMS. The trial is entitled: A Phase II Double-Blind, Placebo Controlled Multi-Center Study to Evaluate the Efficacy and Safety of Tcelna in Subjects with Secondary Progressive Multiple Sclerosis and has been named the “Abili-T” trial. The Abili-T trial is a double-blind, 1:1 randomized, placebo-controlled study in SPMS patients who demonstrate evidence of disease progression with or without associated relapses. The trial is expected to enroll 180 patients who have Expanded Disability Status Scale (EDSS) scores between 3.0 and 6.0 at approximately 30 leading clinical sites in the U.S. and Canada. According to the study protocol, patients will receive two annual courses of Tcelna treatment consisting of five subcutaneous injections per year at weeks 0, 4, 8, 12 and 24.

The primary efficacy endpoint of the trial is the percentage of brain volume change (whole brain atrophy) at 24 months. Study investigators will also measure several important secondary outcomes commonly associated with MS including sustained disease progression as measured by EDSS, changes in EDSS, time to sustained progression, annualized relapse rate (ARR), change in Multiple Sclerosis Functional Composite (MSFC) assessment of disability and change in Symbol Digit Modality Test. Data on certain exploratory endpoints such as quality of life metrics as measured by the Multiple Sclerosis Quality of Life Inventory (MSQLI), magnetic resonance imaging (MRI) measures and immune monitoring metrics are also being collected.

As part of the Abili-T trial, we are undertaking a comprehensive immune monitoring program for all patients enrolled in the study. The goals of this program are to further understand the biology behind the mechanism of action for Tcelna and to possibly identify novel biomarkers that are dominant in the pathophysiology of SPMS patients. The program encompasses an analysis of various pro-inflammatory and anti-inflammatory biomarkers. We believe that the blinded data, which will be analyzed during the course of the trial, may potentially signal responders and non-responders. Directional movement of certain biomarkers, when corroborated with final clinical trial data, may be indicative of responders and disease stabilization or progression.

As of August 8, 2013, the Abili-T clinical trial has randomized 68 patients. A scheduled Data Safety Monitoring Board meeting took place during the week of May 20, 2013, and a recommendation was made to continue the study. The Abili-T clinical study in North America of Tcelna is expected to complete enrollment of 180 patients by late 2013 or early 2014, with the resulting top-line data expected to be available in the first half of 2016.

During the first quarter of 2013, the pace of on-boarding clinical sites for the Abili-T clinical study was tempered pending the completion of our negotiations with Ares Trading SA (“Merck”), a wholly owned subsidiary of Merck Serono S.A., for the Option (see “— Option and License Agreement with Merck Serono”) as well as financial considerations. Upon receipt of the upfront payment of \$5 million for granting the Option, we were able to refocus on execution of the Abili-T clinical trial, including enrollment. The future costs of the study, which have been impacted by a slowed rate of enrollment prior to receipt of the upfront payment of \$5 million for granting the Option, as well as the ongoing expenses of our operations through the expected completion date of the study and release of top-line data, are estimated as of June 30, 2013 to be between \$30-\$32 million.

Our existing resources are not adequate to permit us to complete such study. In August and September 2013, we raised gross proceeds of \$19.35 million through an underwritten offering of 12.9 million shares of our common stock. The net proceeds from such offering were approximately \$17.5 million, after deducting underwriting discounts and commissions and estimated offering expenses. We will need to secure significant additional resources to complete the trial and support our operations during the pendency of the trial. We believe that with the proceeds from this public offering, we have sufficient liquidity to support our clinical trial activities into the second half of 2014. Given our need for substantial amounts of capital to continue the Abili-T clinical study in North America of Tcelna in SPMS, we intend to continue to explore potential opportunities and alternatives to obtain the significant additional resources, including one or more additional financings, that will be necessary to complete the Abili-T study and to support our operations during the pendency of such study. There can be no assurance that any such financings or potential opportunities and alternatives can be consummated on acceptable terms, if at all.

Option and License Agreement with Merck Serono

On February 4, 2013, we entered into an Option and License Agreement with Merck. Pursuant to the agreement, Merck has an option (the “Option”) to acquire an exclusive, worldwide (excluding Japan) license of our Tcelna program for the treatment of MS. The Option may be exercised by Merck prior to or upon completion of our ongoing Abili-T trial of Tcelna in patients with SPMS.

Under the terms of the agreement, we received an upfront payment of \$5 million for granting the Option. If the Option is exercised, Merck would pay us an upfront license fee of \$25 million unless Merck is unable to advance directly into a Phase III clinical trial of Tcelna for SPMS without a further Phase II clinical trial (as determined by Merck), in which event the upfront license fee would be \$15 million. After exercising the Option, Merck would be solely responsible for funding development, regulatory and commercialization activities for Tcelna in MS, although we would retain an option to co-fund certain development in exchange for increased royalty rates. We would also retain rights to Tcelna in Japan, certain rights with respect to the manufacture of Tcelna, and rights to use for other indications outside of MS.

Based upon the achievement of development milestones by Merck for Tcelna in SPMS, we would be eligible to receive one-time milestone payments totaling up to \$70 million as follows: (i) milestone payments aggregating \$35 million if Tcelna is submitted for regulatory approval and commercialized in the United States; (ii) milestone payments aggregating \$30 million if Tcelna is submitted for regulatory approval in Europe and commercialized in at least three major countries in Europe; and (iii) a milestone payment of \$5 million if Tcelna is commercialized in certain markets outside of the United States and Europe. If Merck elects to develop and commercialize Tcelna in RRMS, we would be eligible to receive milestone payments aggregating up to \$40 million based upon the achievement by Merck of various development, regulatory and first commercial sale milestones.

If Tcelna receives regulatory approval and is commercialized by Merck, we would be eligible to receive royalties pursuant to a tiered structure at rates ranging from 8% to 15% of annual net sales, with step-ups over such range occurring when annual net sales exceed \$500 million, \$1 billion and \$2 billion. Any royalties would be subject to offset or reduction in various situations, including if third party rights are required or if patent protection is not available in an applicable jurisdiction. We would also be responsible for royalty obligations to certain third parties, such as Baylor College of Medicine from which we originally licensed related technology. If we were to exercise an option to co-fund certain of Merck’s development, the royalty rates payable by Merck would be increased to rates ranging from 10% to 18%. In addition to royalty payments, we would be eligible to receive one-time commercial milestones totaling up to \$85 million, with \$55 million of such milestones achievable at annual net sales targets in excess of \$1 billion.

SPMS Overview and Tcelna Mechanism of Action

SPMS is characterized by a steady accrual of irreversible disability, despite, in some cases, relapses followed by remissions or clinical plateaus. Older age at onset of MS diagnosis is the strongest predictor of conversion to SPMS. Males have a shorter time to conversion to SPMS compared with females. Available immunomodulating and immunosuppressive therapies used for RRMS have not been effective in SPMS. In clinical trials, these therapies have demonstrated anti-inflammatory properties as measured by the reduction in number and volume of contrast-enhancing or acutely inflammatory CNS lesions most commonly seen in patients with RRMS. The typical SPMS patient, however, has little or no radiographic evidence of acute inflammation. It is commonly observed that contrast-enhancing CNS lesions are uncommon among these patients, despite a clearly deteriorating neurologic course.

The lack of effect of conventional MS therapeutics in SPMS suggests that the cerebral deterioration characterizing progressive disease may be driven by factors other than acute inflammation. For instance, the immunopathology of SPMS is more consistent with a transition to a chronic T-cell dependent inflammatory type, which may encompass the innate immune response and persistent activation of microglia cells.

Radiographic features that stand out among patients with SPMS include significantly more atrophy of gray matter compared with RRMS patients. Of note, long-term disability in MS in general appears more closely correlated to gray matter atrophy than to white matter inflammation. Such atrophy may be suggestive of progressive clinical disability. Both clinically and radiographically, SPMS represents a disease process with certain features distinct from those of RRMS, and one with extremely limited treatment options.

Tcelna immunotherapy in SPMS may reduce the drivers of this chronic disease by down-regulating anti-myelin immunity through priming regulatory responses that may act in the periphery as well as within the CNS. We believe that our clinical results show therapeutic subcutaneous dosing of 30-45 million cells of Tcelna stimulates host reactivity to the over-represented MRTCs and, as a consequence, a dominant negative regulatory T-cell response is induced leading to down-regulation of similar endogenous disease-causing MRTCs.

We believe that Tcelna has the potential to induce an up-regulation of regulatory cells, such as Foxp3+ Treg cells and IL-10 secreting Tr1 cells, which may effect a reduction in inflammation and provide neuroprotection should they gain entry to the CNS. Data from our TERMS study showed statistically significant changes from baseline ($p=0.02$) in Foxp3+ Treg cells for the subset of Tcelna patients who had ARR >1. The placebo arm for this subset was not statistically different from its baseline levels. Three SPMS patients from prior clinical studies, whose blood samples were analyzed to measure Tr1 cells prior to treatment and post treatment, showed an increase in the levels of Tr1 cells from non-detectable levels to the range of healthy donor samples. These three patients who had relapses in the preceding 12-24 month period remained relapse free during the 52-week assessment period and also showed a 57% to 67% reduction in MRTCs.

Current Treatment Options for SPMS

Only one product, mitoxantrone, is currently approved for the indication of SPMS. However, as of 2005, this drug carries a black box warning, due to significant risks of decreased systolic function, heart failure, and leukemia. The American Academy of Neurology has issued a report indicating that these risks are even higher than suggested in the original report leading to the black box warning. Hence, a safe and effective treatment for SPMS remains a significant unmet medical need.

Tcelna Clinical Overview in SPMS

In multiple previously conducted clinical trials for the treatment of patients with MS (which have been weighted significantly toward patients with RRMS), Tcelna has demonstrated one of the safest side effect profiles for any marketed or development-stage MS therapy, as well as encouraging efficacy signals. A total of 144 MS patients have received Tcelna in previously conducted Opexa trials for RRMS and SPMS. The therapy has been well-tolerated in all subjects and has demonstrated an excellent overall safety profile. The most common side effect is mild to moderate irritation at the site of injection, which is typically resolved in 24 hours. Tcelna has been administered to a total of 36 subjects with SPMS across three previous clinical studies.

In a pooled assessment of data from 36 SPMS patients treated in Phase I open label studies at the Baylor College of Medicine completed in 1998 and in Opexa sponsored studies completed in 2006 and 2007, approximately 80% of the 35 SPMS patients who completed two years of treatment showed disease stabilization as measured by EDSS following two years of treatment with Tcelna, with the other 20% showing signs of progression. This compares to historical control data which showed a progression rate of 40% in SPMS patients (as reported in ESIMS Study published in *Hommes Lancet* 2004). The 10 SPMS patients in Opexa sponsored studies showed a substantial reduction in ARR at two years from 0.5 to an ARR less than 0.1. Only 1 out of the 10 patients experienced one episode of relapse during the two years of assessment. This same cohort showed no worsening of physical or psychological condition (key quality of life indicators as measured by the MS Impact Scale) after two years of treatment with Tcelna. Additionally, there were no reported serious adverse events (SAEs) in any of the patients. Based on preliminary data suggesting stabilized or improved disability among SPMS subjects receiving Tcelna, we believe that further development of this product candidate in SPMS is warranted.

Summary of Phase I Dose Escalation Study in MS

A Phase 1 dose escalation study completed in 2006 was conducted in patients with both RRMS and SPMS who were intolerant or unresponsive to current approved therapies for MS. The open-label, dose escalation study evaluated safety and clinical benefit by administering a primary series of four treatments at one of three dose levels administered at baseline and weeks four, eight, and twelve. Results of the efficacy analyses provide some evidence of the effectiveness of Tcelna in the treatment of MS. The follow-on TERMS Phase IIb clinical study provided further encouraging signs of efficacy in ARR and Multiple Sclerosis Impact Scale (MSIS-29). Data from the Phase I study evaluating the EDSS showed improvements in some subjects in comparison to baseline for weeks 20 and 28.

Subjects showed statistically significant improvement in overall reduction of MRTC counts over baseline at all visits through week 52 for subjects receiving 30-45 million cells per dose, as assessed by total MRTC count percentage changes. These data indicate that Tcelna treatment causes a depletion or immunomodulation of these cells, most obvious at time points closer to the injections.

Overall, results of the safety analyses indicate that treatment with Tcelna is well-tolerated. Reported adverse events were mostly mild or moderate in intensity. Mild injection site reactions were observed but all resolved rapidly without treatment. In conclusion, data from this study suggest that Tcelna is safe for the treatment of MS.

Summary of Phase I/IIA Clinical Trial Data in MS

The second clinical study performed by Opexa was an open-label extension study completed in 2007 to treat patients who were previously treated with T-cell immunotherapy but who saw a rebound in MRTC activity. The purpose of this extension study was to continue evaluating the efficacy, safety and tolerability of Tcelna in patients with RRMS and SPMS with repeated administration of Tcelna. Results of the study provide evidence of the effectiveness of Tcelna in the treatment of MS with repeated dosing. Improvements from baseline at both week 28 and week 52 of the extension study were observed for the frequency of MS exacerbations, or ARR. Evaluation of MSIS-29 component scores suggests a trend for Tcelna therapy in the improvement of physical and psychological parameters assessed by the MSIS-29. The EDSS score analysis revealed an upward trend for the percentage of subjects that reported improvement and sustained improvement over baseline as a result of Tcelna treatment.

Subjects showed statistically significant improvement over baseline in the MRTC counts for each time point through month nine of the extension study. These results indicate that Tcelna treatment results in a statistically significant impact on these cells.

Overall, results of the safety analyses indicate that repeated treatment with Tcelna is well-tolerated. Reported adverse events (AEs) were mostly mild or moderate in intensity. Mild injection site reactions were observed but all resolved rapidly without treatment. Furthermore, results from this study suggest that repeated dosing of Tcelna has a substantive effect in reduction of ARR in subjects with MS and was well-tolerated.

Summary of TERMS Phase IIb Clinical Trial Data in RRMS

Tovaxin for Early Relapsing Multiple Sclerosis (TERMS) was a Phase IIb clinical study of Tcelna in RRMS patients completed in 2008. Although the study did not show statistical significance in its primary endpoint (the cumulative number of gadolinium-enhanced brain lesions using MRI scans summed at various points in the study), the study showed compelling evidence of efficacy in various clinical and other MRI endpoints.

The TERMS study was a multi-center, randomized, double blind, placebo-controlled trial in 150 patients with RRMS or high risk Clinically Isolated Syndrome. Patients received a total of five subcutaneous injections at weeks 0, 4, 8, 12 and 24. Key results from the TERMS trial included:

- In the modified intent to treat patient population consisting of all patients who received at least one dose of study product and had at least one MRI scan at week 28 or later (n=142), the ARR for Tcelna-treated patients was 0.214 as compared to 0.339 for placebo-treated patients, which represented a 37% decrease in ARR for Tcelna as compared to placebo in the general population;
- In a prospective group of patients with more active disease (ARR>1, n=50), Tcelna demonstrated a 55% reduction in ARR as compared to placebo, an 88% reduction in whole brain atrophy and a statistically significant improvement in disability (EDSS) compared to placebo (p<0.045) during the 24-week period following the administration of the full course of treatment; and

- In a retrospective analysis in patients naïve to previous disease modifying treatment, the results showed that patients, when treated with Tcelna, had a 56% to 73% reduction in ARR versus placebo for the various subsets and p values ranged from 0.009 to 0.06.

We remain committed to further advancing Tcelna in RRMS at a later date assuming the availability of sufficient resources. For Opexa, however, SPMS is an area which we believe represents a higher unmet medical need. Depending upon the outcome of further feasibility analyses, the T-cell platform may have applications in development treatments for other autoimmune disorders such as rheumatoid arthritis, Type 1 diabetes, and orphan indications such as myasthenia gravis. The primary focus of Opexa remains the development of Tcelna in SPMS.

Other Opportunities

Our proprietary T-cell technology has enabled us to develop intellectual property and a comprehensive sample database that may enable discovery of novel biomarkers associated with MS.

We have developed (and, in part, licensed from the University of Chicago) a proprietary adult stem cell technology to produce monocyte-derived stem cells (MDSC) from blood. These MDSC can be derived from a patient's monocytes, expanded ex vivo, and then administered to the same patient. Our initial focus for this technology is the further development of this monocyte-derived stem cell technology as a platform for the in vitro generation of highly specialized cells for potential application in autologous cell therapy for patients with diabetes mellitus. The diabetes program is in an early (pre-clinical) development stage.

Risks Associated with our Business

We are a development stage company and have generated minimal revenues to date. Since our inception, we have incurred substantial losses. Our business and our ability to execute our business strategy are subject to a number of risks of which you should be aware before making an investment decision. These risks are discussed more fully in the "Risk Factors" section of this prospectus, and among these important risks are the following:

- We will be required to raise significant additional capital, and our ability to obtain funding is uncertain. If sufficient capital is not available, we may not be able to continue our operations as proposed (including any Phase IIb clinical trial initiated or ongoing for Tcelna), which may require us to modify our business plan, curtail various aspects of our operations, cease operations or seek relief under applicable bankruptcy laws.
- We have a history of operating losses and do not expect to be profitable in the foreseeable future.
- Our business is at an early stage of development. We are largely dependent on the success of our product candidate, Tcelna, and we cannot be certain that Tcelna will receive regulatory approval or be successfully commercialized.
- The issuance of securities upon the exercise of outstanding warrants and options will result in significant dilution for our shareholders.
- We have provided Merck with the Option, which provides Merck with the opportunity, if exercised, to control the development and commercialization of Tcelna in MS.
- We will need regulatory approvals for any product candidate, including Tcelna, prior to introduction to the market, which will require successful testing in clinical trials. Clinical trials are subject to extensive regulatory requirements, and are very expensive, time-consuming and difficult to design and implement. Any product candidate, such as Tcelna, may fail to achieve necessary safety and efficacy endpoints during clinical trials in which case we will be unable to generate revenue from the commercialization and sale of our products.

- We will rely on third parties to conduct our clinical trials and perform data collection and analysis, which may result in costs and delays that may hamper our ability to successfully develop and commercialize any product candidate, including Tcelna.
- We are dependent upon our management team and a small number of employees.

Corporate Information

We were incorporated in Texas in March 1991. Our principal executive offices are located at 2653 Technology Forest Blvd., The Woodlands, Texas 77381, and our telephone number is (281) 775-0600. Our website address is www.opexatherapeutics.com. The information contained on, or that can be accessed through, our website is not part of this prospectus.

The Offering

Common stock offered by selling shareholders	1,714,697 shares
Common stock outstanding now and after this offering	22,729,487 shares
Use of proceeds	We will not receive any proceeds from the sales by the selling shareholders.
NASDAQ Capital Market Symbol	OPXA
Risk factors	See “Risk Factors” beginning on page 9 of this prospectus for a discussion of the factors you should consider before deciding to invest in our common stock.

RISK FACTORS

Investing in our common stock involves a high degree of risk. You should consider the important factors set forth below and in the documents incorporated by reference in this prospectus, including the discussion under the section entitled “Risk Factors” in our Quarterly Report on Form 10-Q for the quarter ended June 30, 2013, which is incorporated herein by reference, together with all of the other information contained in this prospectus, before deciding to invest in our common stock. Additional risks and uncertainties not presently known to us, or that we may view as immaterial, may also impair our business. If any of these risks or uncertainties actually occur, they could materially and adversely affect our business, financial condition, results of operations, cash flows or prospects, which could in turn materially and adversely affect the price of our common stock and you could lose all or part of your investment.

The number of shares being registered for sale is significant in relation to our trading volume.

All of the shares registered for sale on behalf of the selling shareholders are “restricted securities” as that term is defined in Rule 144 under the Securities Act. We have filed this registration statement to register these restricted shares for sale into the public market by the selling shareholders. These restricted shares, if sold in the market all at once or at about the same time, could depress the market price during the period the registration statement remains effective and also could affect our ability to raise equity capital. Any outstanding shares not sold by the selling shareholders pursuant to this prospectus will remain as “restricted securities” in the hands of the holders, except for those held by non-affiliates for a period of six months, calculated pursuant to Rule 144.

FORWARD-LOOKING STATEMENTS

This prospectus contains forward-looking statements which are made pursuant to the safe harbor provisions of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. Statements contained in this prospectus, other than statements of historical fact, constitute “forward-looking statements.” The words “expects,” “believes,” “anticipates,” “estimates,” “enables,” “may,” “could,” “intends,” and similar expressions are intended to identify forward-looking statements. In particular, these forward-looking statements may be found, among other places, under the headings “The Company” and “Risk Factors.” 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, returns, royalties, performance and position, management’s strategy, 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, and management’s initiatives and strategies, and the financing and development of the Company’s product candidate, Tcelna (imilecleucel-T), 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, risks discussed in “Risk Factors,” 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), including in this regard our ability to satisfy various conditions required to access the financing potentially available under the purchase agreements with Lincoln Park Capital Fund, LLC (“Lincoln Park”) (such as the minimum closing price for our common stock and the requirement for an ongoing trading market for our stock); our ability to raise additional capital through the sale of shares of our common stock under the purchase agreements with Lincoln Park or under our at-the-market (ATM) facility; our ability to maintain compliance with NASDAQ listing standards; the success of our clinical trials (including the Phase IIb trial for Tcelna in secondary progressive MS which, depending upon results, may determine whether Ares Trading SA (“Merck”) elects to exercise its option for an exclusive license to Tcelna for the treatment of MS (the “Option”)); whether Merck exercises its Option and, if so, whether we receive any development or commercialization milestone payments or royalties from Merck pursuant to the Option; our dependence (if Merck exercises its Option) on the resources and abilities of Merck for the further development of Tcelna; the efficacy of Tcelna for any particular indication, such as for relapsing remitting MS or secondary progressive MS; our ability to develop and commercialize products; our ability to obtain required regulatory approvals; our compliance with all Food and Drug Administration regulations; our ability to obtain, maintain and protect intellectual property rights (including for Tcelna);

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 Reports on Form 10 K, Quarterly Reports on Form 10-Q, and Current Reports on Form 8-K filed with the SEC.

USE OF PROCEEDS

We will not receive any proceeds from the sale of the common stock by the selling shareholders.

SELLING SHAREHOLDERS

This prospectus relates to the resale by the selling shareholders named below from time to time of up to an aggregate of 1,714,697 shares of our common stock issued to the selling shareholders pursuant to a transaction exempt from registration under the Securities Act. All of the common stock offered by this prospectus is being offered by the selling shareholders for their own accounts.

Private Placement

On July 25, 2012, we completed a private placement in which we issued to certain accredited investors, some of whom are the selling shareholders, an aggregate principal amount \$4,085,000 of our 12% convertible secured promissory notes, pursuant to a note purchase agreement of even date. The notes were secured by substantially all of our tangible and intangible assets, and a portion of the proceeds from the note offering was held in a controlled deposit account as part of the security interest granted to the noteholders. The notes were originally convertible into shares of Series A convertible preferred stock at a conversion price of \$100, which was ultimately convertible into common stock at a conversion price of \$3.1225 (as adjusted). Accrued interest on the notes was payable in cash or registered shares of common stock, at our election. We granted the noteholders registration rights related to the shares of common stock ultimately underlying the notes. The notes were issued in reliance on exemptions provided by Section 4(2) of the Securities Act for the offer and sale of securities not involving a public offering and Regulation D promulgated thereunder.

On September 23, 2013, we entered into an amendment with certain of the noteholders with respect to certain terms relating to conversion of the notes. Pursuant to such amendment, all outstanding notes and the related registration rights agreement were amended such that, in addition to the existing conversion arrangements, the notes became convertible at our election directly into shares of common stock (rather than any intermediate conversion to shares of Series A convertible preferred stock), at a conversion price of not less than \$1.50 nor more than \$2.25, based on the most recent closing market price of our common stock on The NASDAQ Stock Market at the time of our election to convert the notes plus any accrued but unpaid interest through the conversion date into shares of common stock. Pursuant to the amendment, upon conversion of the notes into common stock, we covenanted to promptly file a Form S-3 registration statement, of which this prospectus is a part, to register for resale the shares of common stock and to use commercially reasonable efforts to cause such registration statement to be declared effective under the Securities Act. Notes in the aggregate principal amount of \$3,185,000 were outstanding at the time of the amendment. The amendment was approved by requisite holders of more than 75% of the outstanding notes, thereby amending all outstanding notes and the registration rights agreement.

On September 24, 2013, we converted the outstanding principal and accrued interest of an aggregate of \$3,275,053 into an aggregate of 1,714,697 shares of common stock at a conversion price of \$1.91, which was the most recent closing market price of our common stock on The NASDAQ Stock Market when we effected the conversion. As a result of our conversion of all outstanding notes into shares of common stock, the security interest granted to the noteholders in all of our assets was released, including the restricted cash that was held in a controlled deposit account. The issuance of the shares of common stock upon conversion of the notes was made in reliance on exemptions provided by Section 4 (2) of the Securities Act for the offer and sale of securities not involving a public offering and Regulation D promulgated thereunder.

Selling Shareholders

The table below, which was prepared based on information filed publicly or supplied to us by the selling shareholders, sets forth information regarding the beneficial ownership of outstanding shares of our common stock by the selling shareholders and the shares that they may sell or otherwise dispose of from time to time under this prospectus. Each of the selling shareholders, or their respective transferees, donees or their successors, may resell, from time to time, all, some or none of the shares of our common stock covered by this prospectus, as provided in this prospectus under the section entitled "Plan of Distribution" and in any applicable prospectus supplement. However, we do not know when or in what amount the selling shareholders may offer their shares for sale under this prospectus, if any.

The number of shares disclosed in the table below as “beneficially owned” are those beneficially owned as determined under the rules of the SEC. Such information is not necessarily indicative of ownership for any other purpose. Under the rules of the SEC, a person is deemed to be a “beneficial owner” of a security if that person has or shares “voting power,” which includes the power to vote or to direct the voting of such security, or “investment power,” which includes the power to dispose of or to direct the disposition of such security. In computing the number of shares beneficially owned by a selling shareholder and the percentage of ownership of that selling shareholder, shares of common stock held by that selling shareholder are included. Those shares, however, are not deemed outstanding for the purpose of computing the percentage ownership of any other selling shareholder. Each selling shareholder’s percentage of ownership in the following table is based upon 22,729,487 shares of common stock outstanding as of October 8, 2013.

Unless otherwise indicated and subject to community property laws where applicable, the selling shareholders named in the following table have, to our knowledge, sole voting and investment power with respect to the shares beneficially owned by them. In addition, none of the selling shareholders has any family relationships with our officers, directors or controlling shareholders. Furthermore, unless otherwise indicated below, no selling shareholder is a registered broker-dealer or an affiliate of a registered broker-dealer.

Information concerning any of the selling shareholders may change from time to time, and any changed information will be presented in a prospectus supplement as necessary. Please carefully read the footnotes located below the table in conjunction with the information presented in the table.

Name of Selling Shareholder	Beneficial Ownership Before the Offering	Shares of Common Stock Included in Prospectus ⁽¹⁾	Beneficial Ownership After the Offering	Percentage of Common Stock Owned After Offering
Albert and Margaret Alkek Foundation ⁽²⁾	662,582	161,510	501,072	2.19%
Alkek & Williams Ventures Ltd. ⁽³⁾	717,438	269,182	448,256	1.96%
DLD Family Investments, LLC ⁽⁴⁾	728,383	269,182	459,201	2.00%
Charles E. Sheedy ⁽⁵⁾	539,723	134,591	405,132	1.77%
George McDaniel ⁽⁶⁾	251,067	107,673	143,394	*
Robert and Susan deRose Family Trust ⁽⁷⁾	96,245	53,837	42,408	*
David L. Anderson ⁽⁸⁾	73,089	40,378	32,711	*
The Arnold Corporation ⁽⁹⁾	187,165	107,673	79,492	*
Paul Anthony Jacobs and Nancy E. Jacobs Joint Trust ⁽¹⁰⁾	172,451	53,837	118,614	*
J.R. Seward Revocable Trust ⁽¹¹⁾	101,447	53,837	47,610	*
Mossman Partners LP ⁽¹²⁾	50,725	26,919	23,806	*
Arrow Realty, LLC ⁽¹³⁾	202,894	107,673	95,221	*
William F. Miller III ⁽¹⁴⁾	48,727	26,919	21,808	*
Neil K. Warma ⁽¹⁵⁾	229,445	8,076	221,369	*
David E. Jorden ⁽¹⁶⁾	434,452	61,912	372,540	1.63%
Brio Capital Master Fund Ltd. ⁽¹⁷⁾	280,763	161,510	119,253	*
The James P. Miscoll Bypass Trust ⁽¹⁸⁾	28,074	16,151	11,923	*
Iroquois Master Fund Ltd. ⁽¹⁹⁾	154,770	53,837	100,933	*

* Less than 1%.

- (1) The shares of common stock included in this prospectus and shown in the table for each selling shareholder were issued upon our conversion of the 12% convertible secured promissory notes. Any other securities listed in the table or the footnotes to the table are not included in this prospectus.

- (2) Consisting of: (i) 543,343 shares of common stock; (ii) 105,469 shares of common stock underlying Series I warrants; and (iii) 13,770 shares of common stock underlying Series K warrants. This information is based on the Schedule 13D/A filed with the SEC on August 23, 2012, by Albert and Margaret Alkek Foundation (the “Foundation”), Alkek & Williams Ventures, Ltd. (“Ventures”), Chaswil, Ltd. (“Chaswil”), Scott Seaman, DLD Family Investments, LLC (“DLD Family”), and the other reporting persons named therein (the “Foundation 13D”) and other information available to us. The Foundation acts through an investment committee of its board of directors, which includes Charles Williams, Daniel Arnold, Joe Bailey, Mr. Seaman and Randa Duncan Williams. Mr. Seaman is also the executive director of the Foundation and chairman of the investment committee. The investment committee has sole voting and investment power over all of the shares of common stock beneficially owned by the Foundation. However, pursuant to the Foundation 13D, neither the executive director nor any member of the investment committee may act individually to vote or sell shares of common stock held by the Foundation; therefore, the Foundation has concluded that no individual committee member is deemed to beneficially own, within the meaning of Rule 13d-3 of the Exchange Act, any shares of common stock held by the Foundation solely by virtue of the fact that he or she is a member of the investment committee. Additionally, pursuant to the Foundation 13D, the Foundation has concluded that because Mr. Seaman, in his capacity as executive director or chairman of the investment committee, cannot act in such capacity to vote or sell shares of common stock held by the Foundation without the approval of the investment committee, he is not deemed to beneficially own, within the meaning of Rule 13d-3 of the Exchange Act, any shares of common stock held by the Foundation by virtue of his position as executive director or chairman of the investment committee. Pursuant to the Foundation 13D, the Foundation, Ventures, Chaswil, Mr. Seaman and certain other reporting persons named therein may be deemed to constitute a group for purposes of Section 13(d) or Section 13(g) of the Exchange Act. However, the Foundation, Ventures, Chaswil and Mr. Seaman expressly disclaim that (i) for purposes of Section 13(d) or Section 13(g) of the Exchange Act, they are a member of a group with respect to securities of Opexa held by certain other reporting persons named therein and (ii) they have agreed to act together with certain other reporting persons named therein other than as described in the Foundation 13D. Each reporting person disclaims beneficial ownership with respect to all other shares of common stock other than those securities whereby the reporting person possesses sole voting power and sole dispositive power. Mr. Seaman has served as a director of Opexa since 2006 and as chair of the Audit Committee of Opexa’s Board of Directors since August 2012.
- (3) Consisting of: (i) 518,707 shares of common stock; (ii) 175,781 shares of common stock underlying Series I warrants; and (iii) 22,950 shares of common stock underlying Series K warrants. This information is based on the Foundation 13D and other information available to us. Chaswil is the investment manager of Ventures and holds voting power and investment power with respect to Opexa securities held by Ventures pursuant to a written agreement. Mr. Seaman is a principal of Chaswil and has shared voting power and shared investment power over all of the shares of common stock beneficially owned by Ventures. Until conversion of the notes in September 2013, Ventures served as the collateral agent under a security agreement and a patent and trademark security agreement, and as the secured party under a deposit account control agreement, each of which was entered into with Opexa in connection with the original issuance of the notes in July 2012. Mr. Seaman has served as a director of Opexa since 2006, and has served as chair of Audit Committee of Opexa’s Board of Directors since August 2012.
- (4) Consisting of: (i) 509,652 shares of common stock; (ii) 20,000 shares of common stock underlying Series H warrants; (iii) 175,781 shares of common stock underlying Series I warrants; and (iv) 22,950 shares of common stock underlying Series K warrants. This information is based on the Foundation 13D and other information available to us. Randa Duncan Williams, Richard H. Bachmann and W. Randall Fowler are each a manager of DLD Family and may be deemed to exercise voting and investment power with respect to such shares.
- (5) Consisting of: (i) 388,858 shares of common stock; (ii) 14,000 shares of common stock underlying Series H warrants; (iii) 87,890 shares of common stock underlying Series I warrants; (iv) 37,500 shares of common stock underlying Series J warrants; and (v) 11,475 shares of common stock underlying Series K warrants. This information is based on information reported on the Schedule 13G/A filed with the SEC on February 14, 2013 by Charles E. Sheedy and other information available to us.
- (6) Consisting of: (i) 134,075 shares of common stock; (ii) 70,312 shares of common stock underlying Series I warrants; (iii) 37,500 shares of common stock underlying Series J warrants; and (iv) 9,180 shares of common stock underlying Series K warrants.

- (7) Consisting of: (i) 56,500 shares of common stock; (ii) 35,155 shares of common stock underlying Series I warrants; and (iii) 4,590 shares of common stock underlying Series K warrants. Robert deRose and Susan deRose, co-trustees of the Trust, may be deemed to exercise voting and investment power with respect to such shares.
- (8) Consisting of: (i) 43,280 shares of common stock; (ii) 26,367 shares of common stock underlying Series I warrants; and (iii) 3,442 shares of common stock underlying Series K warrants.
- (9) Consisting of: (i) 107,673 shares of common stock; (ii) 70,312 shares of common stock underlying Series I warrants; and (iii) 9,180 shares of common stock underlying Series K warrants. Isaac Arnold, Jr., Isaac Arnold, III, Robert T. Arnold and Antoinette Arnold Maywald are the owners of The Arnold Corporation and may be deemed to exercise voting and investment power with respect to such shares.
- (10) Consisting of: (i) 82,706 shares of common stock held by the Paul Anthony Jacobs and Nancy E. Jacobs Joint Trust (the “Jacobs Joint Trust”); (ii) 35,155 shares of common stock underlying Series I warrants held by the Jacobs Joint Trust; (iii) 4,590 shares of common stock underlying Series K warrants held by the Jacobs Joint Trust; (iv) 25,000 shares of common stock held by the Nancy E. Jacobs Separate Trust (the “Nancy Jacobs Trust”); and (v) 25,000 shares of common stock held by the Paul Anthony Jacobs Separate Trust (the “Paul Jacobs Trust”). Paul Anthony Jacobs and Nancy E. Jacobs, co-trustees of the Jacobs Joint Trust, may be deemed to exercise voting and investment power with respect to the shares held by the Jacobs Joint Trust, as well as the shares held by the Nancy Jacobs Trust and the Paul Jacobs Trust.
- (11) Consisting of: (i) 61,702 shares of common stock; (ii) 35,155 shares of common stock underlying Series I warrants; and (iii) 4,590 shares of common stock underlying Series K warrants. James R. Seward, trustee of the Trust, may be deemed to exercise voting and investment power with respect to such shares.
- (12) Consisting of: (i) 30,852 shares of common stock; (ii) 17,578 shares of common stock underlying Series I warrants; and (iii) 2,295 shares of common stock underlying Series K warrants. Gary Mossman, managing partner, may be deemed to exercise voting and investment power with respect to such shares.
- (13) Consisting of: (i) 123,402 shares of common stock; (ii) 70,312 shares of common stock underlying Series I warrants; and (iii) 9,180 shares of common stock underlying Series K warrants. S. Reed Morian and William L. Hixon, owners of Arrow Realty, LLC, may be deemed to exercise voting and investment power with respect to such shares.
- (14) Consisting of: (i) 28,854 shares of common stock; (ii) 17,578 shares of common stock underlying Series I warrants; and (iii) 2,295 shares of common stock underlying Series K warrants.
- (15) Consisting of: (i) 17,315 shares of common stock; (ii) 5,273 shares of common stock underlying Series I warrants; (iii) 688 shares of common stock underlying Series K warrants; and (iv) 206,169 shares of common stock underlying currently exercisable stock options. Mr. Warma has served as President and Chief Executive Officer of Opexa since June 2008 and as a director since September 2008. He served as Acting Chief Financial Officer from March 2009 to August 2012.
- (16) Consisting of: (i) 293,456 shares of common stock; (ii) 40,429 shares of common stock underlying Series I warrants; (iii) 37,500 shares of common stock underlying Series J warrants; (iv) 5,278 shares of common stock underlying Series K warrants; and (v) 57,789 shares of common stock underlying currently exercisable stock options. Mr. Jorden has served as a director since August 2008. He previously served as Chair of the Audit Committee of Opexa’s Board of Directors until August 2012, and served as Acting Chief Financial Officer of Opexa from August 2012 and to March 2013.
- (17) Consisting of: (i) 161,524 shares of common stock; (ii) 105,469 shares of common stock underlying Series I warrants; and (iii) 13,770 shares of common stock underlying Series K warrants. Shaye Hirsch, director, may be deemed to exercise voting and investment power with respect to such shares.
- (18) Consisting of: (i) 16,151 shares of common stock; (ii) 10,546 shares of common stock underlying Series I warrants; and (iii) 1,377 shares of common stock underlying Series K warrants. Douglas P. Miscoll and Ingeburg W. Miscoll, co-trustees of the Trust, may be deemed to exercise voting and investment power with respect to such shares.
- (19) Consisting of: (i) 53,837 shares of common stock; (ii) 37,188 shares of common stock underlying Series A warrants; (iii) 24,000 shares of common stock underlying Series H warrants; (iv) 35,155 shares of common stock underlying Series I warrants; and (v) 4,590 shares of common stock underlying Series K warrants. Iroquois Capital Management L.L.C. (“Iroquois Capital”) is the investment manager of Iroquois Master Fund, Ltd. (“IMF”). Consequently, Iroquois Capital has voting control and investment discretion over securities held by IMF. As managing members of Iroquois Capital, Joshua Silverman and Richard Abbe make voting and investment decisions on behalf of Iroquois Capital in its capacity as investment manager to IMF. As a result of the foregoing, Mr. Silverman and Mr. Abbe may be deemed to have beneficial ownership (as determined under Section 13(d) of the Securities Exchange Act of 1934, as amended) of the securities held by IMF.

PLAN OF DISTRIBUTION

The selling shareholders, which as used herein includes donees, pledgees, transferees or other successors-in-interest selling shares of common stock or interests in shares of common stock received after the date of this prospectus from a selling shareholder as a gift, pledge, partnership distribution or other transfer, may, from time to time, sell, transfer or otherwise dispose of any or all of their shares of common stock or interests in shares of common stock on any stock exchange, market or trading facility on which the shares are traded or in private transactions. These dispositions may be at fixed prices, at prevailing market prices at the time of sale, at prices related to the prevailing market price, at varying prices determined at the time of sale, or at negotiated prices.

The selling shareholders may use any one or more of the following methods when disposing of shares or interests therein:

- ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;
- block trades in which the broker-dealer will attempt to sell the shares as agent, but may position and resell a portion of the block as principal to facilitate the transaction;
- purchases by a broker-dealer as principal and resale by the broker-dealer for its account;
- an exchange distribution in accordance with the rules of the applicable exchange;
- privately negotiated transactions;
- short sales effected after the date the registration statement of which this prospectus is a part is declared effective by the SEC;
- through the writing or settlement of options or other hedging transactions, whether through an options exchange or otherwise;
- broker-dealers may agree with the selling shareholders to sell a specified number of such shares at a stipulated price per share;
- a combination of any such methods of sale; and
- any other method permitted by law.

The selling shareholders may, from time to time, pledge or grant a security interest in some or all of the shares of common stock owned by them and, if they default in the performance of their secured obligations, the pledgees or secured parties may offer and sell the shares of common stock, from time to time, under this prospectus, or under an amendment to this prospectus under Rule 424(b)(3) or other applicable provision of the Securities Act amending the list of selling shareholders to include the pledgee, transferee or other successors in interest as selling shareholders under this prospectus. The selling shareholders also may transfer the shares of common stock in other circumstances, in which case the transferees, pledgees or other successors in interest will be the selling beneficial owners for purposes of this prospectus.

In connection with the sale of our common stock or interests therein, the selling shareholders may enter into hedging transactions with broker-dealers or other financial institutions, which may in turn engage in short sales of the common stock in the course of hedging the positions they assume. The selling shareholders may also sell shares of our common stock short and deliver these securities to close out their short positions, or loan or pledge the common stock to broker-dealers that in turn may sell these securities. The selling shareholders may also enter into option or other transactions with broker-dealers or other financial institutions or the creation of one or more derivative securities which require the delivery to such broker-dealer or other financial institution of shares offered by this prospectus, which shares such broker-dealer or other financial institution may resell pursuant to this prospectus (as supplemented or amended to reflect such transaction).

The aggregate proceeds to the selling shareholders from the sale of the common stock offered by them will be the purchase price of the common stock less discounts or commissions, if any. Each of the selling shareholders reserves the right to accept and, together with their agents from time to time, to reject, in whole or in part, any proposed purchase of common stock to be made directly or through agents. We will not receive any of the proceeds from this offering.

The selling shareholders also may resell all or a portion of the shares in open market transactions in reliance upon Rule 144 under the Securities Act of 1933, provided that they meet the criteria and conform to the requirements of that rule.

The selling shareholders and any underwriters, broker-dealers or agents that participate in the sale of the common stock or interests therein may be “underwriters” within the meaning of Section 2(11) of the Securities Act. Any discounts, commissions, concessions or profit they earn on any resale of the shares may be underwriting discounts and commissions under the Securities Act. Selling shareholders will be subject to the prospectus delivery requirements of the Securities Act, unless an exemption therefrom is available.

To the extent required, the shares of our common stock to be sold, the names of the selling shareholders, the respective purchase prices and public offering prices, the names of any agents, dealer or underwriter, any applicable commissions or discounts with respect to a particular offer will be set forth in an accompanying prospectus supplement or, if appropriate, a post-effective amendment to the registration statement that includes this prospectus.

In order to comply with the securities laws of some states, if applicable, the common stock may be sold in these jurisdictions only through registered or licensed brokers or dealers. In addition, in some states the common stock may not be sold unless it has been registered or qualified for sale or an exemption from registration or qualification requirements is available and is complied with.

There can be no assurance that any selling shareholder will sell any or all of the shares of common stock registered pursuant to the shelf registration statement, of which this prospectus forms a part.

We have advised the selling shareholders that the anti-manipulation rules of Regulation M under the Exchange Act may apply to sales of shares in the market and to the activities of the selling shareholders and their affiliates. In addition, to the extent applicable we will make copies of this prospectus (as it may be supplemented or amended from time to time) available to the selling shareholders for the purpose of satisfying the prospectus delivery requirements of the Securities Act. The selling shareholders may indemnify any broker-dealer that participates in transactions involving the sale of the shares against certain liabilities, including liabilities arising under the Securities Act.

We have agreed to indemnify the selling shareholders against liabilities, including liabilities under the Securities Act and state securities laws, relating to the registration of the shares offered by this prospectus.

We will pay all expenses of the registration of the shares of common stock pursuant to the registration rights agreement, estimated to be approximately \$45,000 in total, including, without limitation, Securities and Exchange Commission filing fees and expenses of compliance with state securities or “blue sky” laws and the selling shareholders’ expenses; provided, however, that a selling shareholder will pay all underwriting discounts and selling commissions, if any.

We have agreed with the selling shareholders to keep the registration statement of which this prospectus constitutes a part effective until the earlier of (1) such time as all of the shares covered by this prospectus have been disposed of pursuant to and in accordance with the registration statement or (2) the date on which the shares may be sold pursuant to Rule 144 of the Securities Act without regard to any volume limitation requirements under Rule 144 of the Securities Act.

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 financial statements of Opexa as of December 31, 2012, and for the years ended December 31, 2012 and 2011, incorporated in this prospectus by reference to our Annual Report on Form 10-K for the year ended December 31, 2012, have been audited by MaloneBailey, LLP, an independent registered public accounting firm, and are incorporated in reliance upon their report dated March 28, 2013, given upon such firm's authority as experts in auditing and accounting.

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 website address is www.sec.gov. The information on the SEC's website is not part of this prospectus, and any references to this website or any other website 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:

- our Annual Report on Form 10-K for the year ended December 31, 2012;
- our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2013 and June 30, 2013;
- our Current Reports on Form 8-K filed January 15, 2013, January 23, 2013, January 30, 2013, February 5, 2013, February 7, 2013, February 11, 2013, February 27, 2013, April 1, 2013, August 8, 2013, August 13, 2013, September 4, 2013, September 11, 2013, September 25, 2013 and September 27, 2013 (other than the portions of these reports furnished but not filed pursuant to SEC rules and the exhibits filed on such form that relate to such portions); 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 also incorporate by reference all additional documents that we file with the SEC under the terms of Sections 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. We are not, however, incorporating, in each case, any documents or information that we are deemed to furnish and not file in accordance with SEC rules.

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. We also maintain a website at www.opexatherapeutics.com. However, the information on our website is not part of this prospectus.

1,714,697 Shares of Common Stock



OPEXA THERAPEUTICS, INC.

PROSPECTUS

, 2013

PART II
Information Not Required In Prospectus

Item 14. Other Expenses of Issuance and Distribution.

The following is a statement of estimated expenses in connection with the issuance and distribution of the securities being registered, other than underwriting discounts and commission.

	Amount to be Paid*
SEC Registration Fee	\$ 456
Printing Expenses*	2,000
Legal Fees and Expenses*	30,000
Accounting Fees and Expenses*	10,000
Miscellaneous*	2,000
	<u>\$ 44,456</u>

* All amounts shown, except the SEC registration fee, are estimated and may vary based upon, among other things, the number of issuances and amount of securities offered. We will pay all of these expenses.

Item 15. Indemnification of Directors and Officers.

Section 8.101 of the Texas Corporations Law (the “TCA”) authorizes the Registrant to indemnify certain persons, including any person who was, is or is threatened to be made a named defendant or respondent in a threatened, pending or completed action or other proceeding, because the person is or was a director or officer, against judgments and reasonable expenses actually incurred by the person in connection with the threatened, pending or completed action or other proceeding. The Registrant is required by Section 8.051 of the TCA to indemnify a director or officer against reasonable expenses actually incurred by him or her in connection with a threatened, pending, or completed action or other proceeding in which he or she is a named defendant or respondent because he or she is or was a director or officer if he or she has been wholly successful, on the merits or otherwise, in the defense of the action or proceeding.

The Registrant’s restated certificate of formation provides that none of its directors shall be personally liable to the Registrant or its shareholders for monetary damages for an act or omission in such director’s capacity as a director; provided, however, that the liability of such director is not limited to the extent that such director is found liable for (i) a breach of the director’s duty of loyalty to the Registrant or its shareholders, (ii) an act or omission not in good faith that constitutes a breach of duty of the director to the Registrant or an act or omission that involves intentional misconduct or a knowing violation of the law, (iii) a transaction from which the director received an improper benefit, whether or not the benefit resulted from an action taken within the scope of the director’s office, or (iv) an act or omission for which the liability of the director is expressly provided by an applicable statute.

The Registrant’s restated certificate of formation and amended and restated bylaws provide that the Registrant shall indemnify its officers, directors, agents and any other persons to the fullest extent permitted by applicable law. The Registrant’s directors and officers are covered by insurance indemnifying them against certain liabilities which might be incurred by them in their capacities as such. Pursuant to terms of their employment contracts, certain of the Registrant’s officers are entitled to indemnification in their capacity as such and to the fullest extent permitted by applicable law.

At the present time, there is no pending litigation or proceeding involving a director, officer, employee or other agent of the Registrant in which indemnification would be required or permitted. The Registrant is not aware of any threatened litigation or proceeding which may result in a claim for such indemnification.

Item 16. Exhibits .

The list of exhibits in the Exhibit Index to this registration statement is incorporated herein by reference.

Item 17. Undertakings .

The undersigned registrant hereby undertakes:

(1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:

(i) To include any prospectus required by section 10(a)(3) of the Securities Act of 1933;

(ii) To reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Securities and Exchange Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20 percent change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective registration statement; and

(iii) To include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement.

Provided, however, that paragraphs (i), (ii) and (iii) do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the Securities and Exchange Commission by the registrant pursuant to Section 13 or Section 15(d) of the Securities Exchange Act of 1934 that are incorporated by reference in the registration statement, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of the registration statement.

(2) That, for the purpose of determining any liability under the Securities Act of 1933, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

(3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.

(4) That, for the purpose of determining liability under the Securities Act of 1933 to any purchaser:

(A) Each prospectus filed by the registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the registration statement as of the date the filed prospectus was deemed part of and included in the registration statement; and

(B) Each prospectus filed pursuant to Rule 424(b) as part of a registration statement relating to an offering, other than registration statements relying on Rule 430B or other than prospectuses filed in reliance on Rule 430A, shall be deemed to be part of and included in the registration statement as of the date it is first used after effectiveness. Provided, however, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such first use, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such date of first use.

(5) That, for the purposes of determining any liability under the Securities Act of 1933, each filing of the registrant's annual report pursuant to Section 13(a) or Section 15(d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefit plan's annual report pursuant to Section 15(d) of the Securities Exchange Act of 1934) that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.

(6) Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the registrant pursuant to any charter provision, by law or otherwise, the registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act of 1933 and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the Registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized in the City of The Woodlands, State of Texas, on October 10, 2013.

OPEXA THERAPEUTICS, INC.

By: /s/ Neil K. Warma

Neil K. Warma

President and Chief Executive Officer

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below hereby constitutes and appoints Neil K. Warma and Karthik Radhakrishnan, and each of them, his or her true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution, for him or her and in his or her name, place and stead, in any and all capacities, to sign any and all amendments, including post-effective amendments, to this Registration Statement, and to file the same, with exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done, as fully for all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that each of said attorneys in fact and agents or their substitute or substitutes may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, this Registration Statement has been signed by the following persons in the capacities and on the dates indicated.

<u>Name</u>	<u>Title</u>	<u>Date</u>
/s/ Neil K. Warma Neil K. Warma	President, Chief Executive Officer and Director (Principal Executive Officer)	October 10, 2013
/s/ Karthik Radhakrishnan Karthik Radhakrishnan	Chief Financial Officer (Principal Financial and Accounting Officer)	October 10, 2013
/s/ David E. Jordan David E. Jordan	Director	October 10, 2013
/s/ Gail J. Maderis Gail J. Maderis	Director	October 10, 2013
/s/ Michael S. Richman Michael S. Richman	Director	October 10, 2013
/s/ Scott B. Seaman Scott B. Seaman	Director	October 10, 2013

EXHIBIT INDEX

<u>Exhibit No.</u>	<u>Description</u>
3.1	Restated Certificate of Formation of Opexa Therapeutics, Inc. (incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K filed on July 26, 2012).
3.2	Amended and Restated Bylaws, as amended (incorporated by reference to Exhibit 3.3 to the Company's Annual Report on Form 10-K filed on March 8, 2011).
4.1	Specimen Common Stock Certificate (incorporated by reference to Exhibit 4.7 to the Company's Registration Statement on Form S-3 filed on November 13, 2009, File No. 333-163108).
4.4	Form of Registration Rights Agreement, dated July 25, 2012, by and among Opexa Therapeutics, Inc. and the investors signatory thereto (incorporated by reference to Exhibit 10.5 to the Company's Current Report on Form 8-K filed July 26, 2012).
4.5	Form of 12% Convertible Secured Promissory Note issued to investors (incorporated by reference to Exhibit 10.2 to the Company's Current Report on Form 8-K filed July 26, 2012).
4.6	Form of Omnibus Amendment to All Outstanding 12% Convertible Secured Promissory Notes of Opexa Therapeutics, Inc. and Associated Registration Rights Agreement, made effective as of September 23, 2013, by and among Opexa Therapeutics, Inc. and certain holders of its 12% Convertible Secured Promissory Notes (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed September 25, 2013).
5.1	Opinion of Pillsbury Winthrop Shaw Pittman LLP.
23.1	Consent of Pillsbury Winthrop Shaw Pittman LLP (included in Exhibit 5.1).
23.2	Consent of MaloneBailey, LLP.
24.1	Power of Attorney (included on the signature page hereof).

PILLSBURY WINTHROP SHAW PITTMAN LLP
12255 El Camino Real, Suite 300
San Diego, CA 92130

October 10, 2013

Opexa Therapeutics, Inc.
2635 Technology Forest Blvd.
The Woodlands, Texas 77381

Re: Registration Statement on Form S-3

Ladies and Gentlemen:

We are acting as counsel for Opexa Therapeutics, Inc., a Texas corporation (the “Company”), in connection with the Registration Statement on Form S-3 relating to the registration under the Securities Act of 1933 (the “Act”) of 1,714,697 shares of common stock, \$0.01 par value (the “Common Stock”), of the Company, all of which are to be offered and sold by certain stockholders of the Company (the “Selling Stockholders”). Such Registration Statement, as amended, is herein referred to as the “Registration Statement.”

We have reviewed and are familiar with such corporate proceedings and other matters as we have deemed necessary for the opinions expressed in this letter. Based upon the foregoing, we are of the opinion that the shares of Common Stock to be offered and sold by the Selling Stockholders have been duly authorized and validly issued and are fully paid and nonassessable. The opinions set forth in this letter are limited to the Texas Corporation Law of the State of Texas, as in effect on the date hereof.

We hereby consent to the filing of this opinion letter as Exhibit 5.1 to the Registration Statement and to the use of our name under the caption “Legal Matters” in the Registration Statement and in the Prospectus included therein. In giving this consent, we do not thereby admit that we are within the category of persons whose consent is required under Section 7 of the Act or the rules and regulations of the Securities and Exchange Commission promulgated thereunder.

Very truly yours,

/s/ Pillsbury Winthrop Shaw Pittman LLP

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in this Registration Statement on Form S-3 of our report dated March 28, 2013 with respect to the audited financial statements of Opexa Therapeutics, Inc. for the year ended December 31, 2012.

We also consent to the reference to us under the heading “Experts” in such Registration Statement.

/s/ MaloneBailey, LLP
www.malone-bailey.com
Houston, Texas

October 10, 2013