

ZOGENIX, INC.
Form 424B5
November 04, 2013
Table of Contents

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

**Filed Pursuant to Rule 424(b)(5)
Registration No. 333-185901**

SUBJECT TO COMPLETION, DATED NOVEMBER 4, 2013

PROSPECTUS SUPPLEMENT (TO PROSPECTUS DATED FEBRUARY 14, 2013)

\$60,000,000

Common Stock

We are offering \$60,000,000 of shares of our common stock. Our common stock is listed on the Nasdaq Global Market under the symbol ZGNX. On November 1, 2013, the last reported sale price of our common stock on the Nasdaq Global Market was \$2.92 per share.

Investing in our common stock involves risks. See Risk Factors beginning on page S-6.

| | Per Share | Total |
|----------------------------------|-----------|-------|
| Public offering price | \$ | \$ |
| Underwriting discount | \$ | \$ |
| Proceeds, before expenses, to us | \$ | \$ |

We have granted the underwriters an option for a period of 30 days to purchase up to an additional \$9,000,000 of shares of our common stock solely to cover over-allotments. Delivery of the securities offered hereby is expected to be made on or about November , 2013.

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 or the accompanying prospectus. Any representation to the contrary is a criminal offense.

Book-Running Managers

Stifel

Leerink Swann

Wells Fargo Securities

Co-Managers

Oppenheimer & Co.

William Blair

The date of this prospectus supplement is November , 2013.

Table of Contents

TABLE OF CONTENTS

| | Page |
|--|-------------|
| Prospectus Supplement | |
| <u>About this Prospectus Supplement</u> | S-ii |
| <u>Prospectus Supplement Summary</u> | S-1 |
| <u>Risk Factors</u> | S-6 |
| <u>Special Note Regarding Forward-looking Statements</u> | S-7 |
| <u>Use of Proceeds</u> | S-9 |
| <u>Dilution</u> | S-10 |
| <u>Underwriting</u> | S-11 |
| <u>Legal Matters</u> | S-19 |
| <u>Experts</u> | S-19 |
| <u>Where You Can Find More Information</u> | S-19 |
| <u>Information Incorporated by Reference</u> | S-19 |
| Prospectus | |
| <u>About this Prospectus</u> | i |
| <u>About Zogenix</u> | 1 |
| <u>Risk Factors</u> | 3 |
| <u>Special Note Regarding Forward-looking Statements</u> | 3 |
| <u>Use of Proceeds</u> | 5 |
| <u>Ratio of Earnings to Fixed Charges</u> | 5 |
| <u>Plan of Distribution</u> | 6 |
| <u>Description of Debt Securities</u> | 8 |
| <u>Description of Common Stock</u> | 15 |
| <u>Description of Preferred Stock</u> | 17 |
| <u>Description of Warrants</u> | 19 |
| <u>Description of Units</u> | 21 |
| <u>Global Securities</u> | 22 |
| <u>Certain Provisions of Delaware Law and of the Company's Certificate of Incorporation and Bylaws</u> | 25 |
| <u>Legal Matters</u> | 27 |
| <u>Experts</u> | 27 |
| <u>Limitation on Liability and Disclosure of Commission Position of Indemnification for Securities Act</u> | |
| <u>Liabilities</u> | 27 |
| <u>Where You Can Find More Information</u> | 28 |
| <u>Information Incorporated by Reference</u> | 28 |

Table of Contents

ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus dated February 14, 2013 are part of a registration statement that we filed with the Securities and Exchange Commission, or SEC, utilizing a shelf registration process. This prospectus supplement and the accompanying prospectus relate to the offer by us of shares of our common stock to certain investors. We provide information to you about this offering of shares of our common stock in two separate documents that are bound together: (1) this prospectus supplement, which describes the specific details regarding this offering; and (2) the accompanying prospectus, which provides general information, some of which may not apply to this offering. Generally, when we refer to this prospectus, we are referring to both documents combined. If information in this prospectus supplement is inconsistent with the accompanying prospectus, you should rely on this prospectus supplement. However, if any statement in one of these documents is inconsistent with a statement in another document having a later date for example, a document incorporated by reference in this prospectus supplement or the accompanying prospectus the statement in the document having the later date modifies or supersedes the earlier statement as our business, financial condition, results of operations and prospects may have changed since the earlier dates. You should read this prospectus supplement, the accompanying prospectus, the documents and information incorporated by reference in this prospectus supplement and the accompanying prospectus, and any free writing prospectus that we have authorized for use in connection with this offering when making your investment decision. You should also read and consider the information in the documents we have referred you to under the headings **Where You Can Find More Information** and **Information Incorporated by Reference**.

You should rely only on information contained in or incorporated by reference into this prospectus supplement and the accompanying prospectus. We have not, and the underwriters have not, authorized anyone to provide you with information that is different. We are offering to sell and seeking offers to buy shares of our common stock only in jurisdictions where offers and sales are permitted. The information contained in this prospectus supplement, the accompanying prospectus, the documents and information incorporated by reference in this prospectus supplement and the accompanying prospectus, and any free writing prospectus that we have authorized for use in connection with this offering are accurate only as of their respective dates, regardless of the time of delivery of this prospectus supplement or of any sale of our common stock.

In this prospectus supplement, unless the context otherwise indicates, the terms **Zogenix**, **the Company**, **we**, **our** and **and** or similar terms refer to Zogenix, Inc., including its consolidated subsidiary.

This prospectus supplement, the accompanying prospectus and the information incorporated by reference herein and therein include trademarks, service marks and trade names owned by us or other companies. All trademarks, service marks and trade names included or incorporated by reference into this prospectus supplement or the accompanying prospectus are the property of their respective owners.

Table of Contents**PROSPECTUS SUPPLEMENT SUMMARY**

The items in the following summary are described in more detail later in this prospectus supplement and in the accompanying prospectus. This summary provides an overview of selected information and does not contain all the information you should consider before investing in our common stock. Therefore, you should read the entire prospectus supplement, the accompanying prospectus and any free writing prospectus that we have authorized for use in connection with this offering carefully, including the Risk Factors section and other documents or information included or incorporated by reference in this prospectus supplement and the accompanying prospectus before making any investment decision.

Zogenix, Inc.**Overview**

We are a pharmaceutical company developing and commercializing products for the treatment of central nervous system disorders and pain. On October 25, 2013, we received marketing approval from the U.S. Food and Drug Administration, or FDA, for Zohydro ER (*hydrocodone* bitartrate) extended-release capsules, an opioid agonist, extended-release oral formulation of *hydrocodone* without *acetaminophen*, for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate. Zohydro ER is the first extended-release oral formulation of *hydrocodone* without *acetaminophen*. We currently expect to launch Zohydro ER in March 2014. In addition, we are currently commercializing Sumavel[®] DosePro[®] (*sumatriptan* injection) Needle-free Delivery System. Sumavel DosePro offers fast-acting, easy-to-use, needle-free subcutaneous administration of *sumatriptan* for the acute treatment of migraine and cluster headache in a pre-filled, single-use delivery system. Sumavel DosePro is the first drug product approved by the FDA that allows for the needle-free, subcutaneous delivery of medication. We commercialize Sumavel DosePro through our internal sales and marketing organization and in collaboration with Mallinckrodt LLC, our co-promotion partner.

We believe Zohydro ER has the potential to be an important therapeutic alternative to existing *hydrocodone* products, including the branded products Vicodin, Norco, Lorcet, Lortab and their generic equivalents. These products contain the analgesic combination ingredient *acetaminophen* which, if taken in high quantities over time, can lead to serious side effects such as liver toxicity. Zohydro ER does not contain *acetaminophen*. Zohydro ER utilizes the SODAS[®] Technology, Alkermes plc's proprietary multiparticulate drug delivery system that allows the development of customized extended-release profiles and serves to enhance the release profile of *hydrocodone* in Zohydro ER. We believe these release properties have the potential to provide longer lasting and more consistent pain relief with fewer daily doses than the commercially available formulations of *hydrocodone*. As a result of its unique single-entity extended-release profile, we believe Zohydro ER has the potential to generate sales from both patients who use immediate-release products on a chronic basis and patients already using extended-release products in the prescription opioid market. We in-licensed exclusive U.S. rights to Zohydro ER from Alkermes in 2007. In connection with the FDA's approval of Zohydro ER, we will implement the Risk Evaluation and Mitigation Strategy for extended-release and long-acting opioids required by the FDA for all the products in the class. In addition, we will participate in the design and implementation of post-marketing studies, as recently outlined by the FDA. NDA sponsors of extended-release and long-acting opioids are now required to conduct studies to assess the serious risks associated with long-term use. Zohydro ER capsules will be available in six dosage strengths ranging from 10 mg to 50 mg with dosing every 12 hours. Zohydro ER is classified as a Drug Enforcement Agency, or DEA, Schedule II drug under the Controlled Substances Act, making it subject to stricter prescribing and dispensing rules compared to the immediate-release *hydrocodone-acetaminophen* combination products, which are

S-1

Table of Contents

currently classified as Schedule III drugs. On October 24, 2013, the FDA announced its intention to submit a formal recommendation to the Department of Health and Human Services by early December 2013 to reclassify *hydrocodone* combination products from DEA Schedule III to Schedule II.

The Institute of Medicine Report from the Committee on Advancing Pain Research, Care, and Education reported in 2011 that an estimated 116 million people in the United States are burdened with chronic pain, at a national economic cost of \$560 to \$635 billion annually. Chronic pain can be treated with both immediate-release and extended-release opioids. We define our target market for Zohydro ER as prescription, non-injectable codeine-based and extended-release morphine-based pain products. This market generated U.S. sales of approximately \$14.0 billion for the year ended December 2012, based on average wholesale price, on approximately 216 million prescriptions. During the same period, existing *hydrocodone* products, the most commonly prescribed pharmaceutical products in the United States, generated \$3.5 billion in sales on approximately 131 million prescriptions. (Source[®] PHAST Prescription January 2012 - December 2012).

Sumavel DosePro serves as a treatment alternative to oral and nasal triptans, and may offer simple, convenient administration when compared to traditional, needle-based *sumatriptan* injection. According to its Prescribing Information, Sumavel DosePro can provide onset of migraine pain relief in as little as ten minutes for some patients. As a result, we believe that Sumavel DosePro has the potential to be prescribed by a broad physician audience, especially for difficult to treat migraine episodes. We launched the commercial sale of Sumavel DosePro in the United States in January 2010. In August 2012, Mallinckrodt began promoting Sumavel DosePro under our co-promotion agreement, pursuant to which we granted to Mallinckrodt a co-exclusive right (with us) to promote Sumavel DosePro to a mutually agreed prescriber audience in the United States. Mallinckrodt has committed to a minimum number of sales representatives for the initial term of the co-promotion agreement.

On June 27, 2013, we entered into a co-promotion agreement with Valeant Pharmaceuticals North America LLC, or Valeant, under which we were granted the exclusive right (with Valeant or any of its affiliates) to promote Migranal[®] (dihydroergotamine mesylate) Nasal Spray, or Migranal, to a prescriber audience of physicians and other health care practitioners in the United States. Our sales team began selling Migranal to prescribers in August 2013. We believe that Migranal is complementary to our Sumavel DosePro migraine franchise. The term of the co-promotion agreement will run through December 31, 2015, unless otherwise terminated, and can be extended by mutual agreement of the parties in additional 12-month increments. Valeant remains responsible for the manufacture, supply and distribution of Migranal for sale in the United States. In addition, Valeant will supply us with a specified amount of product samples every six months, and we will reimburse Valeant for the cost of additional samples and any promotional materials we order.

We are also developing Relday[®], a proprietary, long-acting injectable formulation of *risperidone* using Durect Corporation's SABER[®] controlled-release formulation technology through a development and license agreement with Durect. *Risperidone* is used to treat the symptoms of schizophrenia and bipolar disorder in adults and teenagers 13 years of age and older. If successfully developed and approved, we believe Relday may be the first subcutaneous antipsychotic product that allows for once-monthly dosing. The existing long-acting injectable *risperidone* product achieved global net sales of \$1.43 billion in 2012 with 69% of net sales outside of the United States, according to industry reports, and requires twice-monthly, 2 mL intramuscular injections with a 21 gauge or larger needle. We believe Durect's SABER controlled-release technology will allow Relday to be delivered subcutaneously on a once-monthly basis with a simplified dosing regimen, improved pharmacokinetic profile and significant reduction in injection volume versus currently marketed long-acting injectable antipsychotics. Based upon these characteristics, Relday may provide an important alternative to currently marketed long-acting injectable antipsychotics as well as a new long-acting treatment option for patients that currently use daily

S-2

Table of Contents

oral antipsychotic products. We announced positive single-dose pharmacokinetic results from a Phase 1 clinical trial of Relday in January 2013. This Phase 1 clinical trial was a single-center, open-label, safety and pharmacokinetic trial of 30 patients with chronic, stable schizophrenia or schizoaffective disorder. Adverse events in the Phase 1 trial in patients diagnosed with schizophrenia were generally mild to moderate and consistent with other *risperidone* products. Based on the favorable safety and pharmacokinetic profile demonstrated with the 25 mg and 50 mg once-monthly doses tested in the Phase 1 trial, we extended the study to include an additional cohort of 10 patients at a 100 mg dose of the same formulation. We announced positive top-line results from the extended Phase 1 clinical trial on May 2, 2013. The results for the extended Phase 1 clinical trial showed *risperidone* blood concentrations in the therapeutic range were achieved on the first day of dosing and maintained throughout the one-month period. In addition, dose proportionality has now been established across the full dose range that would be anticipated to be used in clinical practice (50 to 100 mg). The positive results from this study extension position us to begin a multi-dose clinical trial, which would provide the required steady-state pharmacokinetic and safety data prior to initiating Phase 3 development studies. We plan to commence this multi-dose clinical trial in the second half of 2014.

The development of Relday will first focus on its delivery by conventional needle and syringe in order to allow the administration of different volumes of the same formulation of Relday by a healthcare professional. We anticipate that the introduction of our DosePro needle-free technology for administration of Relday can occur later in development or as part of life cycle management after further work involving formulation development, technology enhancements, and applicable regulatory approvals.

Our DosePro technology is a novel, patent-protected, needle-free drug delivery system designed for self-administration of a pre-filled, single dose of liquid drug. We believe the FDA's approval of Sumavel DosePro represents an important validation of the technology. Results from our pre-clinical and clinical studies demonstrate that DosePro can be used successfully with small molecules and biological products, including protein therapeutics and monoclonal antibodies. We are building our internal product pipeline by investigating proven drugs that can be paired with DosePro to enhance their benefits and commercial attractiveness. We are also evaluating the market potential, formulation requirements and clinical development pathway of an additional central nervous system compound that could be paired with DosePro to enhance its commercial attractiveness. We are also seeking to capitalize on our DosePro technology by out-licensing it to potential partners enabling them to enhance, differentiate or extend the life cycle of their proprietary injectable products. We acquired the DosePro technology and related intellectual property from Aradigm Corporation in August 2006.

Recent Developments

On October 25, 2013, the FDA approved our new drug application, or NDA, for Zohydro ER. We currently expect to launch Zohydro ER in March 2014.

On November 1, 2013, we entered into a development and option agreement with Altus Formulation Inc., or Altus, pursuant to which Altus will be responsible for the development of abuse deterrent formulations of *hydrocodone* using Altus' Intellitab drug delivery platform. We will reimburse Altus for its development efforts on the product and we are responsible for the conduct of clinical development of the product. Pursuant to the agreement, we have been granted an option to obtain an exclusive, royalty-bearing license, with the right to sublicense, to certain Altus intellectual property rights to make, have made, import, use, sell, have sold, offer for sale and import an abuse deterrent formulation of *hydrocodone* for the treatment or relief of pain in the United States. We may exercise our option at any time until the earlier of (1) the date upon which a NDA or similar application for regulatory approval is submitted by us for the Altus abuse resistant formulation of *hydrocodone*, or (2) November 1, 2016. However, we will need to obtain the consent of Alkermes or otherwise amend our license agreement with

S-3

Table of Contents

Alkermes for Zohydro ER in order to exercise the option and ultimately commercialize any Altus abuse deterrent formulation of *hydrocodone*. We will pay a non-refundable upfront fee to Altus of \$750,000. We are also obligated to pay Altus up to \$3.5 million in total future milestone payments upon the achievement of various development and regulatory milestones even if we do not exercise our option under the agreement. Altus will be eligible to receive additional regulatory and sales milestones and a royalty based on net sales of the licensed product if we exercise the option.

On November 1, 2013, we entered into an employment transition agreement with Cynthia Y. Robinson, Ph.D. who will be resigning as Chief Development Officer effective as of November 1, 2013. The employment transition agreement supersedes the existing employment agreement between us and Dr. Robinson and provides that, effective November 1, 2013, Dr. Robinson will continue to serve as our employee in the role of Advisor to our President through May 31, 2014.

Corporate Information

We were formed as a Delaware corporation on May 11, 2006 as SJ2 Therapeutics, Inc. We commenced our operations on August 25, 2006 and changed our name to Zogenix, Inc. on August 28, 2006. Our principal executive offices are located at 12400 High Bluff Drive, Suite 650, San Diego, CA 92130, and our telephone number is 1-866-ZOGENIX (1-866-964-3649). We formed a wholly-owned subsidiary, Zogenix Europe Limited, in June 2010, a company organized under the laws of England and Wales and which is located in the United Kingdom, and whose principal operations are to support the manufacture of the DosePro technology. Our website address is www.zogenix.com. The information on, or accessible through, our website is not part of, and is not incorporated into, this prospectus supplement or the accompanying prospectus and should not be considered part of this prospectus supplement or the accompanying prospectus.

Table of Contents

THE OFFERING

| | |
|---|--|
| Common stock offered by us | \$60,000,000 of shares of our common stock |
| Common stock to be outstanding after this offering | shares |
| Over-allotment option | We have granted the underwriters an option to purchase up to an additional \$9,000,000 of shares of our common stock to cover over-allotments, if any. This option is exercisable, in whole or in part, for a period of 30 days from the date of this prospectus supplement. |
| Use of proceeds | We intend to use the net proceeds from this offering to fund pre-commercialization and commercialization activities for Zohydro ER, additional development activities of Zohydro ER and Relday, and for working capital and other general corporate purposes. We may also use a portion of the net proceeds to in-license, acquire or invest in complementary businesses or products; however, we have no current commitments or obligations to do so. See <u>Use of Proceeds</u> on page S-9. |
| Risk factors | You should read the <u>Risk Factors</u> section of this prospectus supplement and in the documents incorporated by reference in this prospectus supplement for a discussion of factors to consider before deciding to invest in our common stock. |
| Nasdaq Global Market symbol | ZGNX |
| The number of shares of common stock to be outstanding after this offering is based on 107,767,008 shares outstanding as of September 30, 2013, and excludes: | |

16,292,471 shares of common stock issuable upon the exercise of warrants outstanding as of September 30, 2013, at a weighted average exercise price of \$2.72 per share;

13,118,943 shares of common stock issuable upon the exercise of options outstanding as of September 30, 2013, at a weighted average exercise price of \$2.44 per share;

1,286,000 shares of common stock issuable upon the exercise of restricted stock units outstanding as of September 30, 2013; and

738,876 additional shares of common stock reserved for future issuance under our amended and restated 2010 equity incentive award plan and our 2010 employee stock purchase plan as of September 30, 2013.

Except as otherwise indicated, all information in this prospectus supplement assumes no exercise by the underwriters of their option to purchase up to an additional \$9,000,000 of shares of our common stock to cover over-allotments.

Table of Contents

RISK FACTORS

You should consider carefully the risks described below and discussed under the section captioned Risk Factors contained in our annual report on Form 10-K for the year ended December 31, 2012 and in our subsequent quarterly reports on Form 10-Q, as updated by our subsequent filings under the Securities Exchange Act of 1934, as amended, or the Exchange Act, which are incorporated by reference in this prospectus supplement and the accompanying prospectus in their entirety, together with other information in this prospectus supplement, the accompanying prospectus and the information and documents incorporated by reference in this prospectus supplement and the accompanying prospectus, and any free writing prospectus that we have authorized for use in connection with this offering before you make a decision to invest in our common stock. If any of the following events actually occur, our business, operating results, prospects or financial condition could be materially and adversely affected. This could cause the trading price of our common stock to decline and you may lose all or part of your investment. The risks described below are not the only ones that we face. Additional risks not presently known to us or that we currently deem immaterial may also affect our business operations.

Risks Relating to this Offering

If you purchase shares of our common stock sold in this offering, you will experience immediate and substantial dilution in the net tangible book value of your shares. In addition, we may issue additional equity or convertible debt securities in the future, which may result in additional dilution to investors.

The offering price per share of common stock in this offering is considerably more than the net tangible book value per share of our outstanding common stock. As a result, investors purchasing shares of common stock in this offering will pay a price per share that substantially exceeds the value of our tangible assets after subtracting liabilities. Investors will incur immediate dilution of \$ per share, based on the public offering price of \$ per share and the net tangible book value as of September 30, 2013. For a more detailed discussion of the foregoing, see the section entitled Dilution below. To the extent outstanding stock options or warrants are exercised, there will be further dilution to new investors. In addition, to the extent we need to raise additional capital in the future and we issue additional equity or convertible debt securities, our then existing stockholders may experience dilution and the new securities may have rights senior to those of our common stock offered in this offering.

Our management team may invest or spend the proceeds of this offering in ways with which you may not agree or in ways which may not yield a significant return.

Our management will have broad discretion over the use of proceeds from this offering. We intend to use the net proceeds from this offering to fund pre-commercialization and commercialization activities for Zohydro ER, additional development activities of Zohydro ER and Relday, and for working capital and other general corporate purposes. We may also use a portion of the net proceeds to in-license, acquire or invest in complementary businesses or products; however, we have no current commitments or obligations to do so. Our management will have considerable discretion in the application of the net proceeds, and you will not have the opportunity, as part of your investment decision, to assess whether the proceeds are being used appropriately. The net proceeds may be used for corporate purposes that do not increase our operating results or enhance the value of our common stock.

Table of Contents**SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS**

This prospectus supplement and the accompanying prospectus, including the documents incorporated by reference herein and therein, and any free writing prospectus that we have authorized for use in connection with this offering contain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Exchange Act that involve substantial risks and uncertainties. In some cases, you can identify forward-looking statements by the following words: may, will, could, would, should, expect, intend, plan, anticipate, believe, estimate, predict, project, potential, continue, ongoing or the negative or other comparable terminology, although not all forward-looking statements contain these words. These statements relate to future events or our future financial performance or condition and involve known and unknown risks, uncertainties and other factors that could cause our actual results, levels of activity, performance or achievement to differ materially from those expressed or implied by these forward-looking statements. These forward-looking statements include, but are not limited to, statements about:

- our ability to maintain and increase market demand for, and sales of, Sumavel DosePro;
- the timing of the launch of Zohydro ER;
- our ability to successfully execute our sales and marketing strategy for the commercialization of Sumavel DosePro and Zohydro ER;
- the progress and timing of clinical trials for Relday and our other product candidates;
- the timing of submissions to, and decisions made by, the FDA and other regulatory agencies, including foreign regulatory agencies, and demonstrating the safety and efficacy of our product candidates to the satisfaction of the FDA and such other agencies;
- adverse side effects or inadequate therapeutic efficacy of Sumavel DosePro or Zohydro ER that could result in product recalls, market withdrawals or product liability claims;
- the safety and efficacy of our product candidates;
- the market potential for migraine treatments, and our ability to compete within that market;
- the FDA's proposal to change the schedule for *hydrocodone* combination products from Schedule III to Schedule II under the Controlled Substances Act;
- the ability to develop an abuse deterrent formulation of Zohydro ER;
- the goals of our development activities and estimates of the potential markets for our product candidates, and our ability to compete within those markets;
- estimates of the capacity of manufacturing and other facilities to support our products and product candidates;
- our ability to ensure adequate and continued supply of Sumavel DosePro to successfully meet anticipated market demand;
- our and our licensors ability to obtain, maintain and successfully enforce adequate patent and other intellectual property protection of our products and product candidates and the ability to operate our business without infringing the intellectual property rights of others;
- our ability to obtain and maintain adequate levels of coverage and reimbursement from third-party payors for Sumavel DosePro, Zohydro ER or any of our other product candidates that may be approved for sale, the extent of such coverage and reimbursement and the willingness of third-party payors to pay for our products versus less expensive therapies;
- the impact of healthcare reform legislation; and
- projected cash needs and our expected future revenues, operations and expenditures.

You should read this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein completely and with the understanding that our actual results may differ materially from

what we expect as expressed or implied by our forward-looking statements. In light of the significant risks and uncertainties to which our forward-looking statements are subject, you should not place undue reliance on or regard these statements as a representation or warranty by us or any other person that we

S-7

Table of Contents

will achieve our objectives and plans in any specified timeframe, or at all. We discuss many of these risks in greater detail in the documents incorporated by reference herein, including under the heading Risk Factors. These forward-looking statements represent our estimates and assumptions only as of the date of this prospectus supplement regardless of the time of delivery of this prospectus supplement or any sale of our common stock and, except as required by law, we undertake no obligation to update or revise publicly any forward-looking statements, whether as a result of new information, future events or otherwise after the date of this prospectus supplement. For all forward-looking statements, we claim the protection of the safe harbor for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995.

S-8

Table of Contents

USE OF PROCEEDS

We estimate that we will receive net proceeds of approximately \$ million from the sale of the shares of common stock offered by us in this offering, or approximately \$ million if the underwriters exercise in full their over-allotment option to purchase additional shares of common stock, based on the public offering price of \$ per share and after deducting the underwriting discounts and commissions and estimated offering costs payable by us.

We intend to use the net proceeds from this offering to fund pre-commercialization and commercialization activities for Zohydro ER, additional development activities of Zohydro ER and Relday, and for working capital and other general corporate purposes. Although it is difficult to predict future liquidity requirements, we believe, based on our current operating plan, that the net proceeds from this offering, together with our cash and cash equivalents as of September 30, 2013 and future product revenues, will be sufficient to fund our operations through the end of 2015, although we cannot assure you that this will occur. We may also use a portion of the net proceeds to in-license, acquire or invest in complementary businesses or products; however, we have no current commitments or obligations to do so.

The amounts and timing of our actual expenditures will depend on numerous factors, including the commercialization efforts for Zohydro ER, the commercial success of Sumavel DosePro and Zohydro ER and our research and development activities, as well as the amount of cash used in our operations. We therefore cannot estimate with certainty the amount of net proceeds to be used for the purposes described above. We may find it necessary or advisable to use the net proceeds for other purposes, and we will have broad discretion in the application of the net proceeds. Pending the uses described above, we plan to invest the net proceeds from this offering in short- and intermediate-term, interest-bearing obligations, investment-grade instruments, certificates of deposit or direct or guaranteed obligations of the U.S. government.

Table of Contents**DILUTION**

If you invest in our common stock in this offering, your interest will be diluted to the extent of the difference between the public offering price per share and the net tangible book value per share of our common stock after this offering. As of September 30, 2013, our historical net tangible book value was \$(13.9) million, or \$(0.13) per share, based on 107,767,008 shares of our common stock outstanding at September 30, 2013. Our historical net tangible book value per share represents the amount of our total tangible assets reduced by the amount of our total liabilities, divided by the total number of shares of our common stock outstanding as of September 30, 2013. After giving effect to our sale in this offering of shares of common stock at the public offering price of \$ per share, and after deducting underwriting discounts and commissions and estimated offering costs payable by us, our net tangible book value as of September 30, 2013 would have been \$ million, or \$ per share. This represents an immediate increase of net tangible book value of \$ per share to our existing stockholders and an immediate dilution of \$ per share to investors purchasing shares in this offering. The following table illustrates this per share dilution.

| | |
|---|----------|
| Public offering price per share | \$ |
| Historical net tangible book value per share at September 30, 2013 | \$(0.13) |
| Increase per share attributable to investors purchasing shares in this offering | |

Pro forma net tangible book value per share, as adjusted to give effect to this offering

| | |
|--|----|
| Dilution to investors in this offering | \$ |
|--|----|

If the underwriters exercise in full their over-allotment option to purchase up to an additional shares of our common stock at the public offering price of \$ per share, the pro forma net tangible book value after this offering would be \$ per share, representing an increase in net tangible book value of \$ per share to our existing stockholders and immediate dilution in net tangible book value of \$ per share to investors purchasing shares in this offering.

The above discussion and table are based on 107,767,008 shares outstanding as of September 30, 2013 and exclude:

- 16,292,471 shares of common stock issuable upon the exercise of warrants outstanding as of September 30, 2013, at a weighted average exercise price of \$2.72 per share;
- 13,118,943 shares of common stock issuable upon the exercise of options outstanding as of September 30, 2013, at a weighted average exercise price of \$2.44 per share;
- 1,286,000 shares of common stock issuable upon the exercise of restricted stock units outstanding as of September 30, 2013; and
- 738,876 additional shares of common stock reserved for future issuance under our amended and restated 2010 equity incentive award plan and our 2010 employee stock purchase plan as of September 30, 2013.

To the extent that outstanding exercisable options or warrants are exercised, you may experience further dilution. In addition, we may choose to raise additional capital due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. To the extent that we raise additional capital by issuing equity or convertible debt securities, your ownership will be further diluted.

Table of Contents**UNDERWRITING**

Subject to the terms and conditions set forth in an underwriting agreement, each of the underwriters named below has severally agreed to purchase from us the aggregate number of shares set forth opposite their respective names below:

| Underwriters | Number of Shares |
|--|-------------------------|
| Stifel, Nicolaus & Company, Incorporated | |
| Leerink Swann LLC | |
| Wells Fargo Securities, LLC | |
| Oppenheimer & Co. Inc. | |
| William Blair & Company, L.L.C. | |
| Total | |

The underwriting agreement provides that the obligations of the several underwriters are subject to various conditions, including approval of legal matters by counsel. The nature of the underwriters' obligations commits them to purchase and pay for all of the shares of common stock listed above if any are purchased.

Stifel, Nicolaus & Company, Incorporated and Leerink Swann LLC, as representatives of the several underwriters, expect to deliver the shares of common stock to purchasers on or about November 1, 2013.

Over-Allotment Option

We have granted a 30-day over-allotment option to the underwriters to purchase up to an additional _____ shares of common stock from us at the public offering price, less the underwriting discount payable by us, as set forth on the cover page of this prospectus supplement. If the underwriters exercise this option in whole or in part, then each of the underwriters will be separately committed, subject to the conditions described in the underwriting agreement, to purchase the additional shares of common stock in proportion to their respective commitments set forth in the table above.

Commissions and Discounts

The underwriters propose to offer the shares of common stock directly to the public at the public offering price set forth on the cover page of this prospectus supplement, and at this price less a concession not in excess of \$ _____ per share of common stock to other dealers. The underwriters may allow, and the other dealers may reallow, concessions not in excess of \$ _____ per share of common stock to these other dealers. After this offering, the offering price, concessions, and other selling terms may be changed by the underwriters. Our common stock is being offered subject to receipt and acceptance by the underwriters and to the other conditions, including the right to reject orders in whole or in part.

The following table summarizes the compensation to be paid to the underwriters by us and the proceeds, before expenses, payable to us:

Total

| | Per Share | With Over-Allotment | Without Over-Allotment |
|---|------------------|--------------------------------|-----------------------------------|
| Public offering price | \$ | \$ | \$ |
| Underwriting discount and commissions | | | |
| Proceeds, before expenses, to us | | | |
| We estimate expenses payable by us in connection with this offering, other than the underwriting discount and commissions referred to above, will be approximately \$. | | | |

S-11

Table of Contents

Indemnification of Underwriters

The underwriting agreement provides that we will indemnify the underwriters against liabilities specified in the underwriting agreement under the Securities Act, or will contribute to payments that the underwriters may be required to make relating to these liabilities.

No Sales of Similar Securities

We and each of our directors and executive officers have agreed, subject to certain exceptions described below, that, without the prior written consent of the representatives, we and they will not, during the period beginning on and including the date of this prospectus supplement through and including the date that is the 90th day after the date of this prospectus supplement, directly or indirectly:

issue (in the case of us), offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend or otherwise transfer or dispose of any shares of our common stock or other capital stock or any securities convertible into or exercisable or exchangeable for our common stock or other capital stock, other than (in the case of our directors and executive officers) shares of our capital stock or securities held by one or more of the following funds: Scale Venture Partners II, LP; Domain Associates, L.L.C.; Domain Partners VI, L.P.; DP VI Associates, L.P.; Domain Partners VII, L.P. and DP VII Associates, L.P. (the Excluded Shares);

in the case of us, file or cause the filing of any registration statement under the Securities Act with respect to any shares of our common stock or other capital stock or any securities convertible into or exercisable or exchangeable for our common stock or other capital stock other than registration statements filed to register shares of common stock to be sold to the underwriters pursuant to the underwriting agreement and other than registration statements on Form S-8 filed with the Securities and Exchange Commission, or SEC, after the closing date of this offering; or

enter into any swap or other agreement, arrangement, hedge or transaction that transfers to another, in whole or in part, directly or indirectly, any of the economic consequences of ownership of our common stock or other capital stock or any securities convertible into or exercisable or exchangeable for our common stock or other capital stock, other than (in the case of our directors and executive officers) with respect to the Excluded Shares,

whether any transaction described in first or third bullet point above is to be settled by delivery of our common stock, other capital stock, other securities, in cash or otherwise, or publicly announce an intention to do any of the foregoing. Moreover, if:

during the last 17 days of the lock-up period, we issue an earnings release or material news or a material event relating to us occurs; or

prior to the expiration of the lock-up period, we announce that we will release earnings results or become aware that material news or a material event relating to us will occur during the 16-day period beginning on the last day of the lock-up period,

the restrictions described in the immediately preceding sentence will continue to apply until the expiration of the 18-day period beginning on the date of issuance of the earnings release or the occurrence of the material news or material event, as the case may be, unless the representatives waive, in writing, that extension; provided, however, that such extension shall not apply if:

our securities are actively-traded securities (as defined in Regulation M of the Exchange Act); we meet the applicable requirements of paragraph (a)(1) of Rule 139 under the Securities Act in the manner contemplated by NASD Conduct Rule 2711(f)(4); and the provisions of NASD Conduct Rule 2711(f)(4) are not applicable to any research reports relating to us published or distributed by any of the underwriters during the 15 days before or after the last day of the lock-up period (before giving effect to such extension).

S-12

Table of Contents

Notwithstanding the provisions set forth in the immediately preceding paragraph, we may, without the prior written consent of the representatives:

- (1) issue shares of common stock to the underwriters pursuant to the underwriting agreement;
- (2) issue shares, and options to purchase shares, of common stock pursuant to equity incentive plans, employee stock option plans and employee stock purchase plans described in this prospectus supplement, as those plans are in effect on the date of this prospectus supplement;
- (3) issue shares of common stock (A) upon the exercise of stock options issued under equity incentive plans referred to in clause (2) above, as those plans are in effect on the date of this prospectus supplement, or (B) upon the exercise of warrants outstanding on the date of this prospectus supplement and described in this prospectus supplement, as those warrants are in effect on the date of this prospectus supplement; and
- (4) issue shares of common stock to one or more counterparties in connection with the consummation of a bona fide strategic partnership, joint venture, collaboration, merger, co-promotion or distribution arrangement, or the acquisition or in-licensing of any business products or technologies; provided that the aggregate number of shares of our common stock issued under this clause (4) shall not exceed 20% of the number of shares of common stock sold in this offering;

provided, however, that in the case of any issuance described in clause (4) above, it shall be a condition to the issuance that each recipient executes and delivers to the representatives, acting on behalf of the other underwriters, not later than one business day prior to the date of such issuance, a lock-up agreement satisfactory in form and substance to the representatives.

The restrictions of the lock-up agreements which our directors and executive officers are party to do not apply to the following:

- transfers of our securities by individuals as a bona fide gift, by will, intestate succession or pursuant to certain trusts, to certain family members pursuant to domestic relations or similar orders, or to us when we are entitled to repurchase securities from a terminated employee;
- transfers of our securities by entities to their equity owners or affiliated entities, provided such transfer is not for value;
- transfers to a nominee or custodian of a person or entity to whom a disposition or transfer would be permissible in the above circumstances; and
- the entry into or establishment of a trading plan meeting the requirements of Rule 10b5-1 of the Securities Exchange Act of 1934, as amended, or the Exchange Act, relating to any sale of shares of our common stock, if then permitted by us and applicable law, provided that the shares of our common stock subject to such plan may not be sold during the period the above restrictions apply (as the same may be extended) and the terms of such plan expressly includes such prohibition,

provided that (1) for all transfers described in the first three bullets above, the recipient enters into a lock-up agreement in a form satisfactory to the representatives no later than one business day before the transfer, (2) for transfers (a) by will, intestate succession or pursuant to certain trusts, any report required to be filed under specified sections of the Exchange Act will state the reason for the transfer and that the transfer was not for value, and (b) for all other transfers and for the entry into or establishment of any such trading plan, no report under specified sections of the Securities Act or Exchange Act is required to be filed during the period the above restrictions apply (as the same may be extended), and (3) no other filing with the SEC, the Financial Industry Regulatory Authority or any securities exchange or other public report, filing or announcement is made in connection with the transfer or the entry into or

establishment of such trading plan.

In addition, notwithstanding the lock-up restrictions described above, our executive officers and directors may at any time exercise any options or warrants to purchase shares of our common stock or other capital stock or any securities convertible into or exercisable or exchangeable for our common stock or other capital stock, including by cashless exercise.

S-13

Table of Contents

The representatives may, in their sole discretion and at any time or from time to time, without notice, release all or any portion of the shares or other securities subject to the lock-up agreements. Any determination to release any shares or other securities subject to the lock-up agreements would be based on a number of factors at the time of determination, which may include the market price of the common stock, the liquidity of the trading market for the common stock, general market conditions, the number of shares or other securities proposed to be sold or otherwise transferred and the timing, purpose and terms of the proposed sale or other transfer.

Nasdaq Global Market Listing

Our common stock is listed on the Nasdaq Global Market under the symbol ZGNX.

Short Sales, Stabilizing Transactions, and Penalty Bids

In order to facilitate this offering, persons participating in this offering may engage in transactions that stabilize, maintain, or otherwise affect the price of our common stock during and after this offering. Specifically, the underwriters may engage in the following activities in accordance with the rules of the Securities and Exchange Commission.

Short sales. Short sales involve the sales by the underwriters of a greater number of securities than they are required to purchase in the offering. Covered short sales are short sales made in an amount not greater than the underwriters over-allotment option to purchase additional securities from us in this offering. The underwriters may close out any covered short position by either exercising their over-allotment option to purchase securities or purchasing securities in the open market. In determining the source of securities to close out the covered short position, the underwriters will consider, among other things, the price of securities available for purchase in the open market as compared to the price at which they may purchase securities through the over-allotment option. Naked short sales are any short sales in excess of such over-allotment option. The underwriters must close out any naked short position by purchasing securities in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market after pricing that could adversely affect investors who purchase in this offering.

Stabilizing transactions. The underwriters may make bids for or purchases of the securities for the purpose of pegging, fixing, or maintaining the price of the securities, so long as stabilizing bids do not exceed a specified maximum.

Penalty bids. If the underwriters purchase securities in the open market in a stabilizing transaction or syndicate covering transaction, they may reclaim a selling concession from the underwriters and selling group members who sold those securities as part of this offering. Stabilization and syndicate covering transactions may cause the price of the securities to be higher than it would be in the absence of these transactions. The imposition of a penalty bid might also have an effect on the price of the securities if it discourages presales of the securities.

The transactions above may occur on the Nasdaq Global Market or otherwise. Neither we nor the underwriters make any representation or prediction as to the effect that the transactions described above may have on the price of the securities. If these transactions are commenced, they may be discontinued without notice at any time.

Miscellaneous

Some of the underwriters and/or their respective affiliates have in the past provided and all of the underwriters may in the future provide various financial advisory, investment banking, commercial banking and other financial services to us, for which they have received and in the future may receive compensation.

S-14

Table of Contents

Sales Outside the United States

No action has been or will be taken in any jurisdiction (except in the United States) that would permit a public offering of the shares of common stock, or the possession, circulation or distribution of this prospectus supplement or any other material relating to us or the shares of common stock in any jurisdiction where action for that purpose is required. Accordingly, the shares of common stock may not be offered or sold, directly or indirectly, and neither of this prospectus supplement nor any other offering material or advertisements in connection with the shares of common stock may be distributed or published, in or from any country or jurisdiction except in compliance with any applicable rules and regulations of any such country or jurisdiction.

Each of the underwriters may arrange to sell shares of common stock offered by this prospectus supplement in certain jurisdictions outside the United States, either directly or through affiliates, where they are permitted to do so.

European Economic Area

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a Relevant Member State) an offer to the public of any securities which are the subject of the offering contemplated by this prospectus supplement (the Shares) may not be made in that Relevant Member State except that an offer to the public in that Relevant Member State of any Shares may be made at any time under the following exemptions under the Prospectus Directive, if they have been implemented in that Relevant Member State:

- (a) to any legal entity which is a qualified investor as defined in the Prospectus Directive;
- (b) to fewer than 100 or, if the Relevant Member State has implemented the relevant provisions of the 2010 PD Amending Directive, 150 natural or legal persons (other than qualified investors as defined in the Prospectus Directive) subject to obtaining the prior consent of the representatives of the underwriters; or
- (c) in any other circumstances falling within Article 3(2) of the Prospectus Directive, provided that no such offer of Shares shall result in a requirement for the publication by us or any underwriter of a prospectus pursuant to Article 3 of the Prospectus Directive.

For the purposes of this provision, the expression an offer to the public in relation to any Shares in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and any Shares to be offered so as to enable an investor to decide to purchase any Shares, as the same may be varied in that Member State by any measure implementing the Prospectus Directive in that Member State; the expression Prospectus Directive means Directive 2003/71/EC (and amendments thereto, including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member State) and includes any relevant implementing measure in each Relevant Member State; and the expression 2010 PD Amending Directive means Directive 2010/73/EU.

United Kingdom

The securities may be offered in the United Kingdom only where each underwriter:

- (a) has only communicated or caused to be communicated and will only communicate or cause to be communicated an invitation or inducement to engage in investment activity (within the meaning of Section 21 of the Financial Services and Markets Act (the FSMA)) received by it in connection with the issue or sale of any securities in circumstances in which Section 21(1) of the FSMA does not apply to us; and
- (b) has complied and will comply with all applicable provisions of the FSMA with respect to anything done by it in relation to the securities in, from or otherwise involving the United Kingdom.

S-15

Table of Contents

This prospectus supplement and any other material in relation to the securities is only being distributed to, and is only directed at, persons in the United Kingdom that are qualified investors within the meaning of Article 2(1)(e) of the Prospective Directive (qualified investors) (i) that also have professional experience in matters relating to investments falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended, or the Order, (ii) who fall within Article 49(2)(a) to (d) of the Order or (iii) to whom it may otherwise lawfully be communicated (all such persons together being referred to as relevant persons). The securities are only available to, and any invitation, offer or agreement to purchase or otherwise acquire such securities will be engaged in only with, relevant persons. Any person in the United Kingdom that is not a relevant person should not act or rely on this prospectus supplement or any of its contents.

Notice to the Residents of Germany

This document has not been prepared in accordance with the requirements for a securities or sales prospectus under the German Securities Prospectus Act (Wertpapierprospektgesetz), the German Sales Prospectus Act (Verkaufprospektgesetz), or the German Investment Act (Investmentgesetz). Neither the German Federal Financial Services Supervisory Authority (Bundesanstalt für Finanzdienstleistungsaufsicht BaFin) nor any other German authority has been notified of the intention to distribute the securities in Germany. Consequently, the securities may not be distributed in Germany by way of public offering, public advertisement or in any similar manner AND THIS DOCUMENT AND ANY OTHER DOCUMENT RELATING TO THE OFFERING, AS WELL AS INFORMATION OR STATEMENTS CONTAINED HEREIN OR THEREIN, MAY NOT BE SUPPLIED TO THE PUBLIC IN GERMANY OR USED IN CONNECTION WITH ANY OFFER FOR SUBSCRIPTION OF THE SECURITIES TO THE PUBLIC IN GERMANY OR ANY OTHER MEANS OF PUBLIC MARKETING. The securities are being offered and sold in Germany only to qualified investors which are referred to in Section 3, paragraph 2 no. 1, in connection with Section 2, no. 6, of the German Securities Prospectus Act. This document is strictly for use of the person who has received it. It may not be forwarded to other persons or published in Germany.

Switzerland

This document does not constitute a prospectus within the meaning of Art. 652a of the Swiss Code of Obligations. The securities may not be sold directly or indirectly in or into Switzerland except in a manner which will not result in a public offering within the meaning of the Swiss Code of Obligations. Neither this document nor any other offering materials relating to the securities may be distributed, published or otherwise made available in Switzerland except in a manner which will not constitute a public offer of the securities in Switzerland.

Notice to Prospective Investors in France

We and the underwriters have not offered or sold and will not offer or sell, directly or indirectly, securities to the public in France, and have not distributed or caused to be distributed and will not distribute or cause to be distributed to the public in France, this prospectus supplement or any other offering material relating to the securities. Offers, sales and distributions that have been and will be made in France have been and will be made only to (a) providers of the investment service of portfolio management for the account of third parties, and (b) qualified investors (investisseurs qualifiés), other than individuals, all as defined in, and in accordance with, Articles L. 411-1, L. 411-2, and D. 411-1 of the French Code monétaire et financier.

Securities may be resold directly or indirectly only in compliance with Article L. 411-1, L. 411-2, L. 412-1 and L. 621-8 to L. 621-8-3 of the French Code monétaire et financier.

Neither this prospectus supplement prepared in connection with the securities nor any other offering material relating to the securities has been submitted to the clearance procedures of the Autorité des marchés financiers or notified to the Autorité des marchés financiers by the competent authority of another member state of the European Economic Area.

S-16

Table of Contents

Notice to Prospective Investors in Ireland

This prospectus supplement and any other material in relation to the securities described herein is only being distributed in Ireland:

- (a) in circumstances which do not require the publication of a prospectus pursuant to Article 3(2) of Directive 2003/71/EC as amended by Directive 2010/73/EC;
- (b) in compliance with the provisions of the Irish Companies Acts 1963-2009; and
- (c) in compliance with the provisions of the European Communities (Markets in Financial Instruments) Regulations 2007 (S.I. No. 60 of 2007) (as amended), and in accordance with any codes or rules of conduct and any conditions or requirements, or any other enactment, imposed or approved by the Central Bank of Ireland with respect to anything done by them in relation to the securities.

Notice to Prospective Investors in Italy

The offering of the securities has not been registered pursuant to Italian securities legislation and, accordingly, no securities may be offered, sold or delivered, nor may copies of the prospectus supplement or of any other document relating to the securities be distributed in the Republic of Italy, except:

- (i) to qualified investors (investitori qualificati), as defined pursuant to Article 100 of Legislative Decree No. 58 of 24 February 1998, as amended (the Financial Services Act) and Article 34-ter, first paragraph, letter b) of CONSOB Regulation No. 11971 of 14 May 1999, as amended from time to time (Regulation No. 11971); or
 - (ii) in other circumstances which are exempted from the rules on public offerings pursuant to Article 100 of the Financial Services Act and Article 34-ter of Regulation No. 11971.
- Any offer, sale or delivery of the securities or distribution of copies of the prospectus supplement or any other document relating to the securities in the Republic of Italy under (i) or (ii) above must be:

- (a) made by an investment firm, bank or financial intermediary permitted to conduct such activities in the Republic of Italy in accordance with the Financial Services Act, CONSOB Regulation No. 16190 of 29 October 2007 (as amended from time to time) and Legislative Decree No. 385 of 1 September 1993, as amended (the Banking Act); and
- (b) in compliance with Article 129 of the Banking Act, as amended, and the implementing guidelines of the Bank of Italy, as amended from time to time, pursuant to which the Bank of Italy may request information on the issue or the offer of securities in the Republic of Italy; and
- (c) in compliance with any other applicable laws and regulations or requirement imposed by CONSOB or other Italian authority.

Please note that in accordance with Article 100-bis of the Financial Services Act, where no exemption from the rules on public offerings applies under (i) and (ii) above, the subsequent distribution of the securities on the secondary market in Italy must be made in compliance with the public offer and the prospectus requirement rules provided under the Financial Services Act and Regulation No. 11971. Failure to comply with such rules may result in the sale of such securities being declared null and void and in the liability of the intermediary transferring the securities for any damages suffered by the investors.

S-17

Table of Contents

Notice to Prospective Investors in the Netherlands

The securities will not be offered or sold, directly or indirectly, in the Netherlands, other than:

- (a) with a minimum denomination of 50,000 or the equivalent in another currency per investor;
- (b) for a minimum consideration of 50,000 or the equivalent in another currency per investor;
- (c) to fewer than 100 individuals or legal entities other than Qualified Investors (see below); or

(d) solely to Qualified Investors,
all within the meaning of Article 4 of the Financial Supervision Act Exemption Regulation (Vrijstellingsregeling Wet op het financieel toezicht) and Article 1:12 and Article 5:3 of the Financial Supervision Act (Wet op het financieel toezicht, FSA).

Table of Contents

LEGAL MATTERS

The validity of the issuance of the securities offered hereby will be passed upon by our counsel, Latham & Watkins LLP, San Diego, California. The underwriters are being represented in connection with this offering by Goodwin Procter LLP, New York, New York.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements and schedule included in our annual report on Form 10-K for the year ended December 31, 2012, as set forth in their report (which contains an explanatory paragraph describing conditions that raise substantial doubt about our ability to continue as a going concern as described in Note 1 to our consolidated financial statements), which is incorporated by reference in this prospectus supplement. Our consolidated financial statements and schedule are incorporated by reference in reliance on Ernst & Young LLP's report, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement on Form S-3 under the Securities Act, of which this prospectus supplement forms a part. The rules and regulations of the SEC allow us to omit from this prospectus supplement and the accompanying prospectus certain information included in the registration statement. For further information about us and the securities we are offering under this prospectus supplement, you should refer to the registration statement and the exhibits and schedules filed with the registration statement. With respect to the statements contained in this prospectus supplement and the accompanying prospectus regarding the contents of any agreement or any other document, in each instance, the statement is qualified in all respects by the complete text of the agreement or document, a copy of which has been filed as an exhibit to the registration statement.

We file reports, proxy statements and other information with the SEC under the Exchange Act. You may read and copy this information from the Public Reference Room of the SEC, 100 F Street, N.E., Room 1580, Washington, D.C. 20549, at prescribed rates. 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 an Internet website that contains reports, proxy statements and other information about issuers, like us, that file electronically with the SEC. The address of that website is www.sec.gov.

INFORMATION INCORPORATED BY REFERENCE

The SEC allows us to incorporate by reference the information we file with them which means that we can disclose important information to you by referring you to those documents instead of having to repeat the information in this prospectus supplement and the accompanying prospectus. The information incorporated by reference is considered to be part of this prospectus supplement and the accompanying prospectus, and later information that we file with the SEC will automatically update and supersede this information. We incorporate by reference the documents listed below and any future information filed (rather than furnished) with the SEC under Sections 13(a), 13(c), 14, or 15(d) of the Exchange Act between the date of this prospectus supplement and the termination of this offering, provided, however, that we are not incorporating any information furnished under Item 2.02 or Item 7.01 of any current report on Form 8-K:

our quarterly reports on Form 10-Q for the quarters ended March 31, 2013, June 30, 2013 and September 30, 2013, which were filed on May 9, 2013, August 8, 2013 and November 4, 2013, respectively; our definitive proxy statement on Schedule 14A (other than information furnished rather than filed), which was filed on April 26, 2013;

S-19

Table of Contents

our annual report on Form 10-K for the year ended December 31, 2012, which was filed on March 15, 2013; our current reports on Form 8-K filed on January 3, 2013, February 7, 2013, February 27, 2013, March 1, 2013, March 21, 2013, March 27, 2013, May 2, 2013, June 4, 2013, June 19, 2013, June 24, 2013, June 27, 2013 and August 29, 2013, October 2, 2013 and October 28, 2013; and the description of our common stock contained in our registration statement on Form 8-A, which was filed on November 12, 2010, including any amendments or reports filed for the purpose of updating the description.

These documents may also be accessed on our website at *www.zogenix.com*. Except as otherwise specifically incorporated by reference in this prospectus supplement, information contained in, or accessible through, our website is not a part of this prospectus supplement or the accompanying prospectus.

We will furnish without charge to you, upon written or oral request, a copy of any or all of the documents incorporated by reference, including exhibits to these documents by writing or telephoning us at the following address:

Zogenix, Inc.

12400 High Bluff Drive, Suite 650

San Diego, California 92130

Attention: Corporate Secretary

(858) 259-1165

S-20

Table of Contents

PROSPECTUS

\$75,000,000

Debt Securities

Preferred Stock

Common Stock

Debt Warrants

Equity Warrants

Units

We may from time to time offer to sell any combination of debt securities, preferred stock, common stock, debt warrants and equity warrants described in this prospectus, either individually or in units, in one or more offerings. The aggregate initial offering price of all securities sold under this prospectus will not exceed \$75,000,000.

This prospectus provides a general description of the securities we may offer. Each time we sell securities, we will provide specific terms of the securities offered in a supplement to this prospectus. The prospectus supplement may also add, update or change information contained in this prospectus. You should read this prospectus and the applicable prospectus supplement carefully before you invest in any securities. This prospectus may not be used to consummate a sale of securities unless accompanied by the applicable prospectus supplement.

We will sell these securities directly to our stockholders or to purchasers or through agents on our behalf or through underwriters or dealers as designated from time to time. If any agents or underwriters are involved in the sale of any of these securities, the applicable prospectus supplement will provide the names of the agents or underwriters and any applicable fees, commissions or discounts.

Our common stock is traded on the Nasdaq Global Market under the symbol ZGNX. On January 4, 2013, the closing price of our common stock was \$1.49

Investing in our securities involves risks. See Risk Factors on page 3.

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

The date of this prospectus is February 14, 2013

Table of Contents**TABLE OF CONTENTS**

| | Page |
|--|-------------|
| <u>ABOUT THIS PROSPECTUS</u> | i |
| <u>ABOUT ZOGENIX</u> | 1 |
| <u>RISK FACTORS</u> | 3 |
| <u>SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS</u> | 3 |
| <u>USE OF PROCEEDS</u> | 5 |
| <u>RATIO OF EARNINGS TO FIXED CHARGES</u> | 5 |
| <u>PLAN OF DISTRIBUTION</u> | 6 |
| <u>DESCRIPTION OF DEBT SECURITIES</u> | 8 |
| <u>DESCRIPTION OF COMMON STOCK</u> | 15 |
| <u>DESCRIPTION OF PREFERRED STOCK</u> | 17 |
| <u>DESCRIPTION OF WARRANTS</u> | 19 |
| <u>DESCRIPTION OF UNITS</u> | 21 |
| <u>GLOBAL SECURITIES</u> | 22 |
| <u>CERTAIN PROVISIONS OF DELAWARE LAW AND OF THE COMPANY S CERTIFICATE OF INCORPORATION AND BYLAWS</u> | 25 |
| <u>LEGAL MATTERS</u> | 27 |
| <u>EXPERTS</u> | 27 |
| <u>LIMITATION ON LIABILITY AND DISCLOSURE OF COMMISSION POSITION ON INDEMNIFICATION FOR SECURITIES</u> | 27 |
| <u>ACT LIABILITIES</u> | 27 |
| <u>WHERE YOU CAN FIND MORE INFORMATION</u> | 28 |
| <u>INFORMATION INCORPORATED BY REFERENCE</u> | 28 |

ABOUT THIS PROSPECTUS

This prospectus is a part of a registration statement that we filed with the Securities and Exchange Commission, or the Commission, utilizing a shelf registration process. Under this shelf registration process, we may offer to sell any combination of the securities described in this prospectus, either individually or in units, in one or more offerings up to a total dollar amount of \$75,000,000. This prospectus provides you with a general description of the securities we may offer. Each time we sell securities under this shelf registration, we will provide a prospectus supplement that will contain specific information about the terms of that offering. The prospectus supplement may also add, update or change information contained in this prospectus. To the extent that any statement that we make in a prospectus supplement is inconsistent with statements made in this prospectus, the statements made in this prospectus will be deemed modified or superseded by those made in the prospectus supplement. You should read both this prospectus and any prospectus supplement, including all documents incorporated herein or therein by reference, together with additional information described under Where You Can Find More Information and Information Incorporated by Reference. We may only use this prospectus to sell the securities if it is accompanied by a prospectus supplement.

We have not authorized any dealer, salesman or other person to give any information or to make any representation other than those contained or incorporated by reference in this prospectus and the accompanying prospectus supplement. You must not rely upon any information or representation not contained or incorporated by reference in this prospectus or the accompanying prospectus supplement. This prospectus and the accompanying prospectus supplement do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the registered securities to which they relate, nor do this prospectus and the accompanying prospectus supplement constitute an offer to sell or the solicitation of an offer to buy securities in any jurisdiction to any person to whom it is unlawful to make such offer or solicitation in such jurisdiction. You should not assume that the information contained in this prospectus and the accompanying prospectus supplement is accurate on any date subsequent to the date set forth on the front of the document or that any information we have incorporated by reference is correct on any date subsequent to the date of the document incorporated by reference, even though this prospectus and any accompanying prospectus supplement is delivered or securities are sold on a later date.

Table of Contents**ABOUT ZOGENIX**

We are a pharmaceutical company commercializing and developing products for the treatment of central nervous system disorders and pain. Our first commercial product, Sumavel[®] DosePro[®] (sumatriptan injection) Needle-free Delivery System, was launched in January 2010. Sumavel DosePro offers fast-acting, easy-to-use, needle-free subcutaneous administration of sumatriptan for the acute treatment of migraine and cluster headache in a pre-filled, single-use delivery system. Sumavel DosePro is the first drug product approved by the U.S. Food and Drug Administration, or FDA, that allows for the needle-free, subcutaneous delivery of medication. In June 2012, we entered into a co-promotion agreement with Mallinckrodt LLC pursuant to which we granted to Mallinckrodt a co-exclusive right to promote Sumavel DosePro to a mutually agreed prescriber audience in the United States, beginning no later than August 2012. Our lead product candidate, Zohydro ER (hydrocodone bitartrate, formerly ZX002) is a 12-hour extended-release formulation of hydrocodone without acetaminophen for the treatment of moderate to severe chronic pain requiring around-the-clock opioid therapy. We completed Phase 3 development of Zohydro ER in 2011, and we submitted the New Drug Application, or NDA, for Zohydro ER to the FDA in May 2012. In July 2012, the FDA accepted our NDA as being sufficiently complete for a full review and assigned a Prescription Drug User Fee Act, or PDUFA, target action date of March 1, 2013. In December 2012, an advisory committee convened by the FDA voted 2-11 (with 1 abstention) against the approval of Zohydro ER. The advisory committee provides the FDA with independent expert advice and recommendations; however, the final decision regarding approval is made by the FDA. Sumavel DosePro and Zohydro ER each has the potential to address significant unmet medical needs and become important and widely-used additions to the treatment options available to patients and physicians in the United States multi-billion dollar migraine and chronic pain markets, respectively.

We are also developing Relday, a proprietary, long-acting injectable formulation of risperidone using Durect Corporation's SABER controlled-release formulation technology through a July 2011 development and license agreement with Durect. Risperidone is used to treat the symptoms of schizophrenia and bipolar disorder in adults and teenagers 13 years of age and older. If successfully developed and approved, we believe Relday may be the first subcutaneous antipsychotic product that allows for once-monthly dosing. The existing long-acting injectable risperidone product achieved global net sales of \$1.58 billion in 2011 with 72% of net sales outside of the United States, according to industry reports, and requires twice monthly, 2 mL intramuscular injections with a 21 gauge or larger needle. We believe Durect's SABER controlled-release technology will allow Relday to be delivered subcutaneously on a once-monthly basis with a simplified dosing regimen, improved pharmacokinetic profile and significant reduction in injection volume versus currently marketed long-acting injectable antipsychotics. Based upon these characteristics, Relday may provide an important alternative to currently marketed long-acting injectable antipsychotics as well as a new long-acting treatment option for patients that currently use daily oral antipsychotic products. In May 2012, we filed an investigational new drug, or IND, application with the FDA. In July 2012, we initiated our first IND clinical trial for Relday. This Phase 1 clinical trial was a single-center, open-label, safety and pharmacokinetic trial of 30 patients with chronic, stable schizophrenia or schizoaffective disorder. We announced positive single-dose pharmacokinetic results from the Phase 1 clinical trial on January 3, 2013. Adverse events in the Phase 1 trial in patients diagnosed with schizophrenia were generally mild to moderate and consistent with other risperidone products. Based on the favorable safety and pharmacokinetic profile demonstrated with the 25 mg and 50 mg once-monthly doses tested in the Phase 1 trial, we extended the study to include an additional cohort of 10 patients at a 100 mg dose of the same formulation. The addition of this 100 mg dose to the study will enable evaluation of dose proportionality across the full dose range that would be anticipated to be used in clinical practice. Positive results from this study extension would better position us to begin a multi-dose clinical trial, which would provide the required steady-state pharmacokinetic and safety data prior to initiating Phase 3 development studies. We expect to complete the extension of the Phase 1 clinical trial during the second quarter of 2013. The development of Relday will first focus on its delivery by conventional needle and syringe in order to allow the administration of different volumes of the same formulation of Relday by a healthcare professional. We anticipate that the introduction of our DosePro needle-free technology for administration of Relday can occur later in development or as part of life cycle management after further work involving formulation development, technology enhancements, and applicable regulatory approvals.

Table of Contents

Our DosePro technology is a novel, patent-protected, needle-free drug delivery system designed for self-administration of a pre-filled, single dose of liquid drug. We believe the FDA's approval of Sumavel DosePro represents an important validation of the technology. Results from our pre-clinical and clinical studies demonstrate that DosePro can be used successfully with small molecules and biological products, including protein therapeutics and monoclonal antibodies. We are building our internal product pipeline by investigating proven drugs that can be paired with DosePro to enhance their benefits and commercial attractiveness. We are evaluating the market potential, formulation requirements and clinical development pathway of an additional central nervous system compound that could be paired with DosePro to enhance its commercial attractiveness. We are also seeking to capitalize on our DosePro technology by out-licensing it to potential partners enabling them to enhance, differentiate or extend the life cycle of their proprietary injectable products. In March 2012, we entered into a Co-Marketing and Option Agreement with Battelle Memorial Institute, or Battelle, pursuant to which we granted to Battelle the exclusive right to co-market our DosePro drug delivery technology to a specified list of Battelle's pharmaceutical clients. We acquired the DosePro technology and related intellectual property from Aradigm Corporation in August 2006.

We were formed as a Delaware corporation on May 11, 2006 as SJ2 Therapeutics, Inc. We commenced our operations on August 25, 2006 and changed our name to Zogenix, Inc. on August 28, 2006. Our principal executive offices are located at 12400 High Bluff Drive, Suite 650, San Diego, CA 92130, and our telephone number is 1-866-ZOGENIX (1-866-964-3649). We formed a wholly-owned subsidiary, Zogenix Europe Limited, in June 2010, a company organized under the laws of England and Wales and which is located in the United Kingdom, and whose principal operations are to support the manufacture of the DosePro technology. Our website address is www.zogenix.com. The information on, or accessible through, our website is not part of this prospectus. Unless the context requires otherwise, references in this prospectus to Zogenix, we, us and our refer to Zogenix, Inc., including, as of June 7, 2010, its consolidated subsidiary.

DosePro®, Intraject®, Relday®, Sumavel®, Zogenix® and Zohydro ER are our trademarks. All other trademarks, trade names and service marks appearing in this prospectus or the documents incorporated by reference herein are the property of their respective owners. Use or display by us of other parties' trademarks, trade dress or products is not intended to and does not imply a relationship with, or endorsements or sponsorship of, us by the trademark or trade dress owner.

Table of Contents

RISK FACTORS

You should carefully consider the specific risks set forth under **Risk Factors** in the applicable prospectus supplement, under **Risk Factors** under Item 1A of Part I of our most recent annual report on Form 10-K, and under **Risk Factors** under Item 1A of Part II of our subsequent quarterly reports on Form 10-Q, as updated by our subsequent filings under the Securities Exchange Act of 1934, as amended, or the Exchange Act, each of which is incorporated by reference in this prospectus, before making an investment decision. For more information, see **Information Incorporated by Reference**.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and the documents incorporated by reference herein contain **forward-looking statements** within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Exchange Act that involve substantial risks and uncertainties. In some cases, you can identify forward-looking statements by the following words: **may, will, could, would, should, expect, intend, plan, anticipate, estimate, predict, project, potential, continue, ongoing** or the negative of these terms or other comparable terminology, although not all forward-looking statements contain these words. These statements relate to future events or our future financial performance or condition and involve known and unknown risks, uncertainties and other factors that could cause our actual results, levels of activity, performance or achievement to differ materially from those expressed or implied by these forward-looking statements. These forward-looking statements include, but are not limited to, statements about:

our ability to maintain and increase market demand for, and sales of, Sumavel DosePro;

our ability to successfully execute our sales and marketing strategy for the commercialization of Sumavel DosePro;

the progress and timing of clinical trials for our product candidates; , including the initiation of a multi-dose clinical trial and Phase 3 development studies for Relday, the timing of completion of the extension of the Phase 1 trial for Relday and the introduction of DosePro technology with Relday and the timing thereof;

the potential for the FDA to approve the NDA for Zohydro ER despite the advisory committee's recommendation against approval,;

the timing of submissions to, and decisions made by, the FDA and other regulatory agencies, including foreign regulatory agencies, and demonstrating the safety and efficacy of Zohydro ER or any other product candidates to the satisfaction of the FDA and such other agencies;

adverse side effects or inadequate therapeutic efficacy of Sumavel DosePro that could result in product recalls, market withdrawals or product liability claims;

the safety and efficacy of Zohydro ER and our other product candidate;

the market potential for migraine treatments, and our ability to compete within that market;

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the goals of our development activities and estimates of the potential markets for our product candidates, and our ability to compete within those markets;

estimates of the capacity of manufacturing and other facilities to support our product and product candidates;

our ability to ensure adequate and continued supply of Sumavel DosePro to successfully meet anticipated market demand;

our and our licensors ability to obtain, maintain and successfully enforce adequate patent and other intellectual property protection of our products and product candidates and the ability to operate our business without infringing the intellectual property rights of others;

Table of Contents

our ability to obtain and maintain adequate levels of coverage and reimbursement from third-party payors for Sumavel DosePro or any of our other product candidates that may be approved for sale, the extent of such coverage and reimbursement and the willingness of third-party payors to pay for our products versus less expensive therapies;

the impact of healthcare reform legislation; and

projected cash needs and our expected future revenues, operations and expenditures.

You should read this prospectus and the documents incorporated by reference herein completely and with the understanding that our actual results may differ materially from what we expect as expressed or implied by our forward-looking statements. In light of the significant risks and uncertainties to which our forward-looking statements are subject, you should not place undue reliance on or regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified timeframe, or at all. These forward-looking statements represent our estimates and assumptions only as of the date of this prospectus regardless of the time of delivery of this prospectus or any sale of our securities and, except as required by law, we undertake no obligation to update or revise publicly any forward-looking statements, whether as a result of new information, future events or otherwise after the date of this prospectus. For all forward-looking statements, we claim the protection of the safe harbor for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995.

Table of Contents**USE OF PROCEEDS**

Unless otherwise indicated in the applicable prospectus supplement, we intend to use the net proceeds from the sale of securities under this prospectus to fund the ongoing commercialization of Sumavel DosePro, clinical development of our product candidates, and, if approved by the FDA, the commercialization of Zohydro ER, and for working capital and other general corporate purposes. We will set forth in the particular prospectus supplement our intended use for the net proceeds we receive from the sale of our securities under such prospectus supplement. Pending the uses described above, we plan to invest the net proceeds from this offering in short- and intermediate-term, interest-bearing obligations, investment-grade instruments, certificates of deposit or direct or guaranteed obligations of the U.S. government.

RATIO OF EARNINGS TO FIXED CHARGES

The following summary is qualified by the more detailed information appearing in the computation table found in Exhibit 12.1 to the registration statement of which this prospectus is part and the historical financial statements, including the notes to those financial statements, incorporated by reference in this prospectus. Our ratio of earnings to fixed charges for each of the years ended December 31, 2007 to 2011 and for the nine months ended September 30, 2012 was as follows:

| | Year Ended December 31, | | | | | Nine Months Ended September 30, |
|---|-------------------------|-------------|-------------|-------------|-------------|---------------------------------------|
| | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 |
| | (in thousands) | | | | | |
| Ratio of earnings to fixed charges(1) | | | | | | |
| Deficiency of earnings available to cover fixed charges | \$ (27,680) | \$ (45,570) | \$ (45,889) | \$ (73,554) | \$ (83,912) | \$ (46,738) |

- (1) For purposes of computing this ratio of earnings to fixed charges, fixed charges consist of interest expense and estimated interest component of rent and earnings consist of loss before income taxes plus fixed charges. In each of the periods presented, earnings were insufficient to cover fixed charges. The ratio of earnings to fixed charges was less than one-to-one for each of the periods presented. We have not included a ratio of earnings to combined fixed charges and preferred stock dividends because we do not have any preferred stock outstanding as of the date of this prospectus.

Table of Contents

PLAN OF DISTRIBUTION

We may sell the securities from time to time pursuant to underwritten public offerings, negotiated transactions, block trades or a combination of these methods. We may sell the securities separately or together:

through one or more underwriters or dealers in a public offering and sale by them;

through agents; and/or

directly to one or more purchasers.

We may distribute the securities from time to time in one or more transactions:

at a fixed price or prices, which may be changed;

at market prices prevailing at the time of sale;

at prices related to such prevailing market prices; or

at negotiated prices.

We may solicit directly offers to purchase the securities being offered by this prospectus. We may also designate agents to solicit offers to purchase the securities from time to time. We may sell the securities being offered by this prospectus by any method permitted by law, including sales deemed to be an at the market offering as defined in Rule 415(a)(4) of the Securities Act of 1933, as amended, or the Securities Act, including without limitation sales made directly on the Nasdaq Global Market, on any other existing trading market for our securities or to or through a market maker. We will name in a prospectus supplement any agent involved in the offer or sale of our securities.

If we utilize a dealer in the sale of the securities being offered by this prospectus, we will sell the securities to the dealer, as principal. The dealer may then resell the securities to the public at varying prices to be determined by the dealer at the time of resale.

If we utilize an underwriter in the sale of the securities being offered by this prospectus, we will execute an underwriting agreement with the underwriter at the time of sale and we will provide the name of any underwriter in the prospectus supplement that the underwriter will use to make resales of the securities to the public. In connection with the sale of the securities, we or the purchasers of securities for whom the underwriter may act as agent may compensate the underwriter in the form of underwriting discounts or commissions. The underwriter may sell the securities to or through dealers, and the underwriter may compensate those dealers in the form of discounts, concessions or commissions.

We will provide in the applicable prospectus supplement any compensation we will pay to underwriters, dealers or agents in connection with the offering of the securities, and any discounts, concessions or commissions allowed by underwriters to participating dealers. In compliance with guidelines of the Financial Industry Regulatory Authority, or FINRA, the maximum consideration or discount to be received by any FINRA member or independent broker dealer may not exceed 8% of the aggregate amount of the securities offered pursuant to this prospectus and any applicable prospectus supplement. Underwriters, dealers and agents participating in the distribution of the securities may be deemed to be underwriters within the meaning of the Securities Act, and any discounts and commissions received by them and any profit realized by them on resale of the securities may be deemed to be underwriting discounts and commissions. We may enter into agreements to indemnify underwriters, dealers and agents against civil liabilities, including liabilities under the Securities Act, or to contribute to payments they may be required to make in respect thereof. In the event that an offering made pursuant to this prospectus is subject to FINRA Rule 5121, the prospectus supplement will comply with the prominent disclosure provisions of that rule.

Table of Contents

The 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 involves the sale by persons participating in the offering of more securities than we 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. 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.

We may authorize underwriters, dealers or agents to solicit offers by certain purchasers to purchase the securities from us at the public offering price set forth in the prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on a specified date in the future. The contracts will be subject only to those conditions set forth in the prospectus supplement, and the prospectus supplement will set forth any commissions we pay for solicitation of these contracts.

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 any derivative transaction, 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 identified in the applicable prospectus supplement or a post-effective amendment to the registration statement of which this prospectus is a part. 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. 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.

The underwriters, dealers and agents may engage in transactions with us, or perform services for us, in the ordinary course of business.

Table of Contents

DESCRIPTION OF DEBT SECURITIES

The following description, together with the additional information we include in any applicable prospectus supplement, summarizes certain general terms and provisions of the debt securities that we may offer under this prospectus. When we offer to sell a particular series of debt securities, we will describe the specific terms of the series in a supplement to this prospectus. We will also indicate in the supplement to what extent the general terms and provisions described in this prospectus apply to a particular series of debt securities.

We may issue debt securities either separately, or together with, or upon the conversion or exercise of or in exchange for, other securities described in this prospectus. Debt securities may be our senior, senior subordinated or subordinated obligations and, unless otherwise specified in a supplement to this prospectus, the debt securities will be our direct, unsecured obligations and may be issued in one or more series.

The debt securities will be issued under an indenture between us and Wilmington Trust, National Association, as trustee. We have summarized select portions of the indenture below. The summary is not complete. The form of the indenture has been filed as an exhibit to the registration statement and you should read the indenture for provisions that may be important to you. In the summary below, we have included references to the section numbers of the indenture so that you can easily locate these provisions. Capitalized terms used in the summary and not defined herein have the meanings specified in the indenture.

As used in this section only, Zogenix, we, our or us refer to Zogenix, Inc. excluding our subsidiary, unless expressly stated or the context otherwise requires.

General

The terms of each series of debt securities will be established by or pursuant to a resolution of our board of directors and set forth or determined in the manner provided in a resolution of our board of directors, in an officer's certificate or by a supplemental indenture. (Section 2.2) The particular terms of each series of debt securities will be described in a prospectus supplement relating to such series (including any pricing supplement or term sheet).

We can issue an unlimited amount of debt securities under the indenture that may be in one or more series with the same or various maturities, at par, at a premium, or at a discount. (Section 2.1) We will set forth in a prospectus supplement (including any pricing supplement or term sheet) relating to any series of debt securities being offered, the aggregate principal amount and the following terms of the debt securities, if applicable:

the title and ranking of the debt securities (including the terms of any subordination provisions);

the price or prices (expressed as a percentage of the principal amount) at which we will sell the debt securities;

any limit on the aggregate principal amount of the debt securities;

the date or dates on which the principal of the debt securities of the series is payable;

the rate or rates (which may be fixed or variable) per annum or the method used to determine the rate or rates (including any commodity, commodity index, stock exchange index or financial index) at which the debt securities will bear interest, the date or dates from which interest will accrue, the date or dates on which interest will commence and be payable and any regular record date for the interest payable on any interest payment date;

the place or places where principal of, and interest, if any, on the debt securities will be payable (and the method of such payment), where the securities of such series may be surrendered for registration of transfer or exchange, and where notices and demands to us in respect of the debt securities may be delivered;

Table of Contents

the period or periods within which, the price or prices at which and the terms and conditions upon which we may redeem the debt securities;

any obligation we have to redeem or purchase the debt securities pursuant to any sinking fund or analogous provisions or at the option of a holder of debt securities and the period or periods within which, the price or prices at which and in the terms and conditions upon which debt securities of the series shall be redeemed or purchased, in whole or in part, pursuant to such obligation;

the dates on which and the price or prices at which we will repurchase debt securities at the option of the holders of debt securities and other detailed terms and provisions of these repurchase obligations;

the denominations in which the debt securities will be issued, if other than denominations of \$1,000 and any integral multiple thereof;

whether the debt securities will be issued in the form of certificated debt securities or global debt securities;

the portion of principal amount of the debt securities payable upon declaration of acceleration of the maturity date, if other than the principal amount;

the currency of denomination of the debt securities, which may be United States Dollars or any foreign currency, and if such currency of denomination is a composite currency, the agency or organization, if any, responsible for overseeing such composite currency;

the designation of the currency, currencies or currency units in which payment of principal of, premium and interest on the debt securities will be made;

if payments of principal of, premium or interest on the debt securities will be made in one or more currencies or currency units other than that or those in which the debt securities are denominated, the manner in which the exchange rate with respect to these payments will be determined;

the manner in which the amounts of payment of principal of, premium, if any, or interest on the debt securities will be determined, if these amounts may be determined by reference to an index based on a currency or currencies other than that in which the debt securities are denominated or designated to be payable or by reference to a commodity, commodity index, stock exchange index or financial index;

any provisions relating to any security provided for the debt securities;

any addition to, deletion of or change in the Events of Default described in this prospectus or in the indenture with respect to the debt securities and any change in the acceleration provisions described in this prospectus or in the indenture with respect to the debt securities;

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any addition to, deletion of or change in the covenants described in this prospectus or in the indenture with respect to the debt securities;

any depositaries, interest rate calculation agents, exchange rate calculation agents or other agents with respect to the debt securities;

the provisions, if any, relating to conversion or exchange of any securities of such series, including if applicable, the conversion or exchange price and period, provisions as to whether conversion or exchange will be mandatory, the events requiring an adjustment of the conversion or exchange price and provisions affecting conversion or exchange; and

any other terms of the debt securities, which may supplement, modify or delete any provision of the indenture as it applies to that series, including any terms that may be required under applicable law or regulations or advisable in connection with the marketing of the securities. (Section 2.2)

We may issue debt securities that provide for an amount less than their stated principal amount to be due and payable upon declaration of acceleration of their maturity pursuant to the terms of the indenture. We will provide you with information on the federal income tax considerations and other special considerations applicable to any of these debt securities in the applicable prospectus supplement.

Table of Contents

If we denominate the purchase price of any of the debt securities in a foreign currency or currencies or a foreign currency unit or units, or if the principal of and any premium and interest on any series of debt securities is payable in a foreign currency or currencies or a foreign currency unit or units, we will provide you with information on the restrictions, elections, general tax considerations, specific terms and other information with respect to that issue of debt securities and such foreign currency or currencies or foreign currency unit or units in the applicable prospectus supplement.

Transfer and Exchange

Each debt security will be represented by either one or more global securities registered in the name of The Depository Trust Company, or the Depository, or a nominee of the Depository (we will refer to any debt security represented by a global debt security as a book-entry debt security), or a certificate issued in definitive registered form (we will refer to any debt security represented by a certificated security as a certificated debt security) as set forth in the applicable prospectus supplement. Except as set forth under the heading Global Debt Securities and Book-Entry System below, book-entry debt securities will not be issuable in certificated form.

Certificated Debt Securities. You may transfer or exchange certificated debt securities at any office we maintain for this purpose in accordance with the terms of the indenture. (Section 2.4) No service charge will be made for any transfer or exchange of certificated debt securities, but we may require payment of a sum sufficient to cover any tax or other governmental charge payable in connection with a transfer or exchange. (Section 2.7)

You may effect the transfer of certificated debt securities and the right to receive the principal of, premium and interest on certificated debt securities only by surrendering the certificate representing those certificated debt securities and either reissuance by us or the trustee of the certificate to the new holder or the issuance by us or the trustee of a new certificate to the new holder.

Global Debt Securities and Book-Entry System. Each global debt security representing book-entry debt securities will be deposited with, or on behalf of, the Depository, and registered in the name of the Depository or a nominee of the Depository. Please see Global Securities.

Covenants

We will set forth in the applicable prospectus supplement any restrictive covenants applicable to any issue of debt securities. (Article IV)

No Protection In the Event of a Change of Control

Unless we state otherwise in the applicable prospectus supplement, the debt securities will not contain any provisions which may afford holders of the debt securities protection in the event we have a change in control or in the event of a highly leveraged transaction (whether or not such transaction results in a change in control) which could adversely affect holders of debt securities.

Consolidation, Merger and Sale of Assets

We may not consolidate with or merge with or into, or convey, transfer or lease all or substantially all of our properties and assets to any person (a successor person) unless:

we are the surviving corporation or the successor person (if other than us) is a corporation organized and validly existing under the laws of any U.S. domestic jurisdiction and expressly assumes our obligations on the debt securities and under the indenture; and

immediately after giving effect to the transaction, no Default or Event of Default, shall have occurred and be continuing.

Table of Contents

Notwithstanding the above, any of our subsidiaries may consolidate with, merge into or transfer all or part of its properties to us. (Section 5.1)

Events of Default

Event of Default means with respect to any series of debt securities, any of the following:

default in the payment of any interest upon any debt security of that series when it becomes due and payable, and continuance of such default for a period of 30 days (unless the entire amount of the payment is deposited by us with the trustee or with a paying agent prior to the expiration of the 30-day period);

default in the payment of principal of any debt security of that series at its maturity;

default in the performance or breach of any other covenant or warranty by us in the indenture (other than a covenant or warranty that has been included in the indenture solely for the benefit of a series of debt securities other than that series), which default continues uncured for a period of 60 days after we receive written notice from the trustee or Zogenix and the trustee receive written notice from the holders of not less than 25% in principal amount of the outstanding debt securities of that series as provided in the indenture;

certain voluntary or involuntary events of bankruptcy, insolvency or reorganization of Zogenix; and

any other Event of Default provided with respect to debt securities of that series that is described in the applicable prospectus supplement. (Section 6.1)

No Event of Default with respect to a particular series of debt securities (except as to certain events of bankruptcy, insolvency or reorganization) necessarily constitutes an Event of Default with respect to any other series of debt securities. (Section 6.1) The occurrence of certain Events of Default or an acceleration under the indenture may constitute an event of default under certain indebtedness of ours or our subsidiaries outstanding from time to time.

If an Event of Default with respect to debt securities of any series at the time outstanding occurs and is continuing, then the trustee or the holders of not less than 25% in principal amount of the outstanding debt securities of that series may, by a notice in writing to us (and to the trustee if given by the holders), declare to be due and payable immediately the principal of (or, if the debt securities of that series are discount securities, that portion of the principal amount as may be specified in the terms of that series) and accrued and unpaid interest, if any, on all debt securities of that series. In the case of an Event of Default resulting from certain events of bankruptcy, insolvency or reorganization, the principal (or such specified amount) of and accrued and unpaid interest, if any, on all outstanding debt securities will become and be immediately due and payable without any declaration or other act on the part of the trustee or any holder of outstanding debt securities. At any time after a declaration of acceleration with respect to debt securities of any series has been made, but before a judgment or decree for payment of the money due has been obtained by the trustee, the holders of a majority in principal amount of the outstanding debt securities of that series may rescind and annul the acceleration if all Events of Default, other than the non-payment of accelerated principal and interest, if any, with respect to debt securities of that series, have been cured or waived as provided in the indenture. (Section 6.2) We refer you to the prospectus supplement relating to any series of debt securities that are discount securities for the particular provisions relating to acceleration of a portion of the principal amount of such discount securities upon the occurrence of an Event of Default.

The indenture provides that the trustee will be under no obligation to exercise any of its rights or powers under the indenture unless the trustee receives indemnity satisfactory to it against any cost, liability or expense which might be incurred by it in exercising such right of power. (Section 7.1(e)) Subject to certain rights of the

Table of Contents

trustee, the holders of a majority in principal amount of the outstanding debt securities of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the trustee or exercising any trust or power conferred on the trustee with respect to the debt securities of that series. (Section 6.12)

No holder of any debt security of any series will have any right to institute any proceeding, judicial or otherwise, with respect to the indenture or for the appointment of a receiver or trustee, or for any remedy under the indenture, unless:

that holder has previously given to the trustee written notice of a continuing Event of Default with respect to debt securities of that series; and

the holders of not less than 25% in principal amount of the outstanding debt securities of that series have made written request, and offered reasonable indemnity or security, to the trustee to institute the proceeding as trustee, and the trustee has not received from the holders of not less than a majority in principal amount of the outstanding debt securities of that series a direction inconsistent with that request and has failed to institute the proceeding within 60 days. (Section 6.7)

Notwithstanding any other provision in the indenture, the holder of any debt security will have an absolute and unconditional right to receive payment of the principal of, premium and any interest on that debt security on or after the due dates expressed in that debt security and to institute suit for the enforcement of payment. (Section 6.8)

The indenture requires us, within 120 days after the end of our fiscal year, to furnish to the trustee a statement as to compliance with the indenture. (Section 4.3) If a Default or Event of Default occurs and is continuing with respect to the debt securities of any series and if it is known to a responsible officer of the trustee, the trustee shall mail to each Securityholder of the debt securities of that series notice of a Default or Event of Default within 90 days after it occurs. The indenture provides that the trustee may withhold notice to the holders of debt securities of any series of any Default or Event of Default (except in payment on any debt securities of that series) with respect to debt securities of that series if the trustee determines in good faith that withholding notice is in the interest of the holders of those debt securities. (Section 7.5)

Modification and Waiver

We and the trustee may modify and amend the indenture or the debt securities of any series without the consent of any holder of any debt security:

to cure any ambiguity, defect or inconsistency;

to comply with covenants in the indenture described above under the heading Consolidation, Merger and Sale of Assets ;

to provide for uncertificated securities in addition to or in place of certificated securities;

to make any change that does not adversely affect the rights of any holder of debt securities;

to provide for the issuance of and establish the form and terms and conditions of debt securities of any series as permitted by the indenture;

to effect the appointment of a successor trustee with respect to the debt securities of any series and to add to or change any of the provisions of the indenture to provide for or facilitate administration by more than one trustee; or

to comply with requirements of the Commission in order to effect or maintain the qualification of the indenture under the Trust Indenture Act. (Section 9.1)

Table of Contents

We may also modify and amend the indenture with the consent of the holders of at least a majority in principal amount of the outstanding debt securities of each series affected by the modifications or amendments. We may not make any modification or amendment without the consent of the holders of each affected debt security then outstanding if that amendment will:

reduce the amount of debt securities whose holders must consent to an amendment, supplement or waiver;

reduce the rate of or extend the time for payment of interest (including default interest) on any debt security;

reduce the principal of or premium on or change the fixed maturity of any debt security or reduce the amount of, or postpone the date fixed for, the payment of any sinking fund or analogous obligation with respect to any series of debt securities;

reduce the principal amount of discount securities payable upon acceleration of maturity;

waive a default in the payment of the principal of, premium or interest on any debt security (except a rescission of acceleration of the debt securities of any series by the holders of at least a majority in aggregate principal amount of the then outstanding debt securities of that series and a waiver of the payment default that resulted from such acceleration);

make the principal of or premium or interest on any debt security payable in currency other than that stated in the debt security;

make any change to certain provisions of the indenture relating to, among other things, the right of holders of debt securities to receive payment of the principal of, premium and interest on those debt securities and to institute suit for the enforcement of any such payment and to waivers or amendments; or

waive a redemption payment with respect to any debt security. (Section 9.3)

Except for certain specified provisions, the holders of at least a majority in principal amount of the outstanding debt securities of any series may on behalf of the holders of all debt securities of that series waive our compliance with provisions of the indenture. (Section 9.2) The holders of a majority in principal amount of the outstanding debt securities of any series may on behalf of the holders of all the debt securities of such series waive any past default under the indenture with respect to that series and its consequences, except a default in the payment of the principal of, premium or any interest on any debt security of that series; provided, however, that the holders of a majority in principal amount of the outstanding debt securities of any series may rescind an acceleration and its consequences, including any related payment default that resulted from the acceleration. (Section 6.13)

Defeasance of Debt Securities and Certain Covenants in Certain Circumstances

Legal Defeasance. The indenture provides that, unless otherwise provided by the terms of the applicable series of debt securities, we may be discharged from any and all obligations in respect of the debt securities of any series (subject to certain exceptions). We will be so discharged upon the deposit with the trustee, in trust, of money and/or U.S. government obligations or, in the case of debt securities denominated in a single currency other than U.S. Dollars, government obligations of the government that issued or caused to be issued such currency, that, through the payment of interest and principal in accordance with their terms, will provide money in an amount sufficient in the opinion of a nationally recognized firm of independent public accountants or investment bank to pay and discharge each installment of principal, premium and interest on and any mandatory sinking fund payments in respect of the debt securities of that series on the stated maturity of those payments in accordance with the terms of the indenture and those debt securities.

This discharge may occur only if, among other things, we have delivered to the trustee an opinion of counsel stating that we have received from, or there has been published by, the United States Internal Revenue Service a

Table of Contents

ruling or, since the date of execution of the indenture, there has been a change in the applicable United States federal income tax law, in either case to the effect that, and based thereon such opinion shall confirm that, the holders of the debt securities of that series will not recognize income, gain or loss for United States federal income tax purposes as a result of the deposit, defeasance and discharge and will be subject to United States federal income tax on the same amounts and in the same manner and at the same times as would have been the case if the deposit, defeasance and discharge had not occurred. (Section 8.3)

Defeasance of Certain Covenants. The indenture provides that, unless otherwise provided by the terms of the applicable series of debt securities, upon compliance with certain conditions:

we may omit to comply with the covenant described under the heading *Consolidation, Merger and Sale of Assets* and certain other covenants set forth in the indenture, as well as any additional covenants which may be set forth in the applicable prospectus supplement; and

any omission to comply with those covenants will not constitute a Default or an Event of Default with respect to the debt securities of that series (*covenant defeasance*).

The conditions include:

depositing with the trustee money and/or U.S. government obligations or, in the case of debt securities denominated in a single currency other than U.S. Dollars, government obligations of the government that issued or caused to be issued such currency, that, through the payment of interest and principal in accordance with their terms, will provide money in an amount sufficient in the opinion of a nationally recognized firm of independent public accountants or investment bank to pay and discharge each installment of principal of, premium and interest on and any mandatory sinking fund payments in respect of the debt securities of that series on the stated maturity of those payments in accordance with the terms of the indenture and those debt securities; and

delivering to the trustee an opinion of counsel to the effect that the holders of the debt securities of that series will not recognize income, gain or loss for United States federal income tax purposes as a result of the deposit and related covenant defeasance and will be subject to United States federal income tax on the same amounts and in the same manner and at the same times as would have been the case if the deposit and related covenant defeasance had not occurred. (Section 8.4)

Covenant Defeasance and Events of Default. In the event we exercise our option to effect covenant defeasance with respect to any series of debt securities and the debt securities of that series are declared due and payable because of the occurrence of any Event of Default, the amount of money and/or U.S. government obligations or foreign government obligations on deposit with the trustee will be sufficient to pay amounts due on the debt securities of that series at the time of their stated maturity but may not be sufficient to pay amounts due on the debt securities of that series at the time of the acceleration resulting from the Event of Default. However, we shall remain liable for those payments. (Section 8.4).

Governing Law

The indenture and the debt securities, including any claim or controversy arising out of or relating to the indenture or the securities, will be governed by the laws of the State of New York (without regard to the conflicts of laws provisions thereof other than Section 5-1401 of the General Obligations Law). (Section 10.10)

Table of Contents

DESCRIPTION OF COMMON STOCK

The following summary of the terms of our common stock does not purport to be complete and is subject to and qualified in its entirety by reference to our Amended and Restated Certificate of Incorporation, as amended, or certificate of incorporation, and Amended and Restated Bylaws, or bylaws, copies of which are on file with the Commission as exhibits to registration statements previously filed by us. See Where You Can Find More Information.

General

Our authorized capital stock consists of 200,000,000 shares of common stock, \$0.001 par value per share, and 10,000,000 shares of preferred stock, \$0.001 par value per share. As of September 30, 2012, we had 100,666,197 shares of common stock outstanding. As of September 30, 2012, we had an aggregate of 9,476,489 shares of common stock reserved for issuance upon the exercise of options and restricted stock units outstanding under our 2010 Equity Incentive Award Plan; 1,732,693 additional shares of common stock reserved for issuance under our 2010 Equity Incentive Award Plan and our 2010 Employee Stock Purchase Plan; and 16,284,506 shares of common stock reserved for issuance upon exercise of warrants outstanding.

The following summary of the rights of our common stock is not complete and is qualified in its entirety by reference to our certificate of incorporation and bylaws, copies of which are filed as exhibits to the registration statement of which this prospectus is a part.

Voting Rights

The holders of our common stock are entitled to one vote for each share held of record on all matters submitted to a vote of the stockholders, including the election of directors, and do not have cumulative voting rights. Accordingly, the holders of a majority of the outstanding shares of common stock entitled to vote in any election of directors can elect all of the directors standing for election, if they so choose, other than any directors that holders of any preferred stock we may issue may be entitled to elect.

Dividends

Subject to limitations under Delaware law and preferences that may be applicable to any then outstanding preferred stock, holders of common stock are entitled to receive ratably those dividends, if any, as may be declared by our board of directors out of legally available funds.

Liquidation

In the event of our liquidation, dissolution or winding up, the holders of common stock will be entitled to share ratably in the net assets legally available for distribution to stockholders after the payment of or provision for all of our debts and other liabilities, subject to the prior rights of any preferred stock then outstanding.

Rights and Preferences

Holders of common stock have no preemptive or conversion rights or other subscription rights and there are no redemption or sinking funds provisions applicable to the common stock.

Fully Paid and Nonassessable

All outstanding shares of common stock are, and the common stock to be outstanding upon completion of this offering will be, duly authorized, validly issued, fully paid and nonassessable.

Table of Contents

Registration Rights

Investors Rights Agreement

As of the date of this prospectus, the holders of approximately 12,669,839 shares of common stock and the holders of warrants to purchase 508,271 shares of common stock are entitled to rights with respect to the registration of these shares under the Securities Act. These shares are referred to as registrable securities. Under the terms of the agreement between us and the holders of the registrable securities, if we propose to register any of our securities under the Securities Act, these holders are entitled to notice of such registration and are entitled to include their shares of registrable securities in our registration. Certain of these holders are also entitled to demand registration, pursuant to which they may require us to use our best efforts to register their registrable securities under the Securities Act at our expense, up to a maximum of three such registrations. Holders of registrable securities may also require us to file an unlimited number of additional registration statements on Form S-3 at our expense so long as the holders propose to sell registrable securities of at least \$5.0 million and we have not already filed two such registration statements on Form S-3 in the previous 12 months.

All of these registration rights are subject to certain conditions and limitations, among them the right of the underwriters of an offering to limit the number of shares included in such registration and our right not to effect a requested registration 60 days prior to or 180 days after an offering of our securities, including this offering. These registration rights will continue in effect following this offering and will terminate upon the earlier of November 22, 2015, or for any particular holder with registration rights, at such time when all securities held by that stockholder entitled to registration rights may be immediately sold pursuant to Rule 144 under the Securities Act during any 90-day period. These registration rights have been waived with respect to this offering.

Certificate of Incorporation and Bylaw Provisions

See Certain Provisions of Delaware Law and of the Company's Certificate of Incorporation and Bylaws Anti-Takeover Effects of Provisions of Our Certificate of Incorporation, Our Bylaws and Delaware Law for a description of provisions of our certificate of incorporation and bylaws which may have the effect of delaying changes in our control or management.

Transfer Agent and Registrar

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

Table of Contents

DESCRIPTION OF PREFERRED STOCK

We currently have authorized 10,000,000 shares of preferred stock, \$0.001 par value per share. As of the date of this prospectus, we did not have any shares of preferred stock outstanding.

General

Prior to issuance of shares of each series of our undesignated preferred stock, our board of directors is required by the Delaware General Corporate Law, or DGCL, and our certificate of incorporation to adopt resolutions and file a Certificate of Designations with the Secretary of State of the State of Delaware, fixing for each such series the designations, powers, preferences, rights, qualifications, limitations and restrictions of the shares of such series. Our board of directors could authorize the issuance of shares of preferred stock with terms and conditions which could have the effect of discouraging a takeover or other transaction which holders of some, or a majority, of such shares might believe to be in their best interests or in which holders of some, or a majority, of such shares might receive a premium for their shares over the then-market price of such shares.

Subject to limitations prescribed by the DGCL, our certificate of incorporation and our bylaws, our board of directors is authorized to fix the number of shares constituting each series of preferred stock and the designations, powers, preferences, rights, qualifications, limitations and restrictions of the shares of such series, including such provisions as may be desired concerning voting, redemption, dividends, dissolution or the distribution of assets, conversion or exchange, and such other subjects or matters as may be fixed by resolution of the board of directors. Each series of preferred stock that we offer under this prospectus will, when issued, be fully paid and nonassessable and will not have, or be subject to, any preemptive or similar rights.

The applicable prospectus supplement(s) will describe the following terms of the series of preferred stock in respect of which this prospectus is being delivered:

the title and stated value of the preferred stock;

the number of shares of the preferred stock offered, the liquidation preference per share and the purchase price of the preferred stock;

the dividend rate(s), period(s) and/or payment date(s) or the method(s) of calculation for dividends;

whether dividends shall be cumulative or non-cumulative and, if cumulative, the date from which dividends on the preferred stock shall accumulate;

the procedures for any auction and remarketing, if any, for the preferred stock;

the provisions for a sinking fund, if any, for the preferred stock;

the provisions for redemption, if applicable, of the preferred stock;

any listing of the preferred stock on any securities exchange or market;

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the terms and conditions, if applicable, upon which the preferred stock will be convertible into common stock or another series of our preferred stock, including the conversion price (or its manner of calculation) and conversion period;

the terms and conditions, if applicable, upon which preferred stock will be exchangeable into our debt securities, including the exchange price, or its manner of calculation, and exchange period;

voting rights, if any, of the preferred stock;

a discussion of any material and/or special U.S. federal income tax considerations applicable to the preferred stock;

whether interests in the preferred stock will be represented by depositary shares;

Table of Contents

the relative ranking and preferences of the preferred stock as to dividend rights and rights upon liquidation, dissolution or winding up of our affairs;

any limitations on issuance of any series of preferred stock ranking senior to or on a parity with the preferred stock as to dividend rights and rights upon liquidation, dissolution or winding up of our affairs; and

any other specific terms, preferences, rights, limitations or restrictions on the preferred stock.

Unless otherwise specified in the prospectus supplement, with respect to dividend rights and rights upon our liquidation, dissolution or winding up, the preferred stock will rank:

senior to all classes or series of our common stock, and to all equity securities issued by us the terms of which specifically provide that such equity securities rank junior to the preferred stock with respect to dividend rights or rights upon the liquidation, dissolution or winding up of us;

on a parity with all equity securities issued by us that do not rank senior or junior to the preferred stock with respect to dividend rights or rights upon the liquidation, dissolution or winding up of us; and

junior to all equity securities issued by us the terms of which do not specifically provide that such equity securities rank on a parity with or junior to the preferred stock with respect to dividend rights or rights upon the liquidation, dissolution or winding up of us (including any entity with which we may be merged or consolidated or to which all or substantially all of our assets may be transferred or which transfers all or substantially all of our assets).

As used for these purposes, the term "equity securities" does not include convertible debt securities.

Transfer Agent and Registrar

The transfer agent and registrar for any series of preferred stock will be set forth in the applicable prospectus supplement.

Table of Contents

DESCRIPTION OF WARRANTS

We may issue debt warrants to purchase debt securities, as well as equity warrants to purchase common stock or preferred stock. The warrants may be issued independently or together with any securities and may be attached to or separate from the securities. The warrants are to be issued under warrant agreements to be entered into between us and a bank or trust company, as warrant agent, all as shall be set forth in the prospectus supplement relating to warrants being offered pursuant to such prospectus supplement. The following description of warrants will apply to the warrants offered by this prospectus unless we provide otherwise in the applicable prospectus supplement. The applicable prospectus supplement for a particular series of warrants may specify different or additional terms.

Debt Warrants

The applicable prospectus supplement will describe the terms of debt warrants offered, the warrant agreement relating to the debt warrants and the debt warrant certificates representing the debt warrants, including the following:

the title of the debt warrants;

the aggregate number of the debt warrants;

the price or prices at which the debt warrants will be issued;

the designation, aggregate principal amount and terms of the debt securities purchasable upon exercise of the debt warrants, and the procedures and conditions relating to the exercise of the debt warrants;

the designation and terms of any related debt securities with which the debt warrants are issued, and the number of debt warrants issued with each debt security;

the date, if any, on and after which the debt warrants and the related debt securities will be separately transferable;

the principal amount of debt securities purchasable upon exercise of each debt warrant;

the date on which the right to exercise the debt warrants will commence, and the date on which this right will expire;

the maximum or minimum number of debt warrants which may be exercised at any time;

a discussion of any material Federal income tax considerations; and

any other terms of the debt warrants and terms, procedures and limitations relating to the exercise of debt warrants.

Debt warrants may be exercised at the corporate trust office of the warrant agent or any other office indicated in the prospectus supplement. Prior to the exercise of their debt warrants, holders of debt warrants will not have any of the rights of holders of the debt securities purchasable upon exercise and will not be entitled to payment of principal or any premium, if any, or interest on the debt securities purchasable upon exercise.

Equity Warrants

The applicable prospectus supplement will describe the following terms of equity warrants offered:

the title of the equity warrants;

the securities (i.e., common stock or preferred stock) for which the equity warrants are exercisable;

the price or prices at which the equity warrants will be issued;

Table of Contents

if applicable, the designation and terms of the common stock or preferred stock with which the equity warrants are issued, and the number of equity warrants issued with each share of common stock or preferred stock;

if applicable, the date on and after which the equity warrants and the related common stock or preferred stock will be separately transferable;

if applicable, a discussion of any material Federal income tax considerations; and

any other terms of the equity warrants, including terms, procedures and limitations relating to the exchange and exercise of equity warrants.

Prior to exercise of the equity warrants, holders of equity warrants will not be entitled, by virtue of being such holders, to vote, consent, receive dividends, receive notice as stockholders with respect to any meeting of stockholders for the election of our directors or any other matter, or to exercise any rights whatsoever as our stockholders.

The exercise price payable and the number of shares of common stock or preferred stock purchasable upon the exercise of each equity warrant will be subject to adjustment in certain events, including the issuance of a stock dividend to holders of common stock or preferred stock or a stock split, reverse stock split, combination, subdivision or reclassification of common stock or preferred stock. In lieu of adjusting the number of shares of common stock or preferred stock purchasable upon exercise of each equity warrant, we may elect to adjust the number of equity warrants. No adjustments in the number of shares purchasable upon exercise of the equity warrants will be required until cumulative adjustments require an adjustment of at least 1% thereof. We may, at our option, reduce the exercise price at any time. No fractional shares will be issued upon exercise of equity warrants, but we will pay the cash value of any fractional shares otherwise issuable. Notwithstanding the foregoing, in case of any consolidation, merger, or sale or conveyance of our property in its entirety or substantially in its entirety, the holder of each outstanding equity warrant shall have the right to the kind and amount of shares of stock and other securities and property, including cash, receivable by a holder of the number of shares of common stock or preferred stock into which the equity warrant was exercisable immediately prior to such transaction.

Exercise of Warrants

Each warrant will entitle the holder to purchase for cash such principal amount of securities or shares of stock at such exercise price as shall in each case be set forth in, or be determinable as set forth in, the prospectus supplement relating to the warrants offered thereby. Warrants may be exercised at any time up to the close of business on the expiration date set forth in the prospectus supplement relating to the warrants offered thereby. After the close of business on the expiration date, unexercised warrants will become void.

The warrants may be exercised as set forth in the prospectus supplement relating to the warrants offered. Upon receipt of payment and the warrant certificate properly completed and duly executed at the corporate trust office of the warrant agent or any other office indicated in the prospectus supplement, we will, as soon as practicable, forward the securities purchasable upon such exercise. If less than all of the warrants represented by such warrant certificate are exercised, a new warrant certificate will be issued for the remaining warrants.

Table of Contents

DESCRIPTION OF UNITS

The following description, together with the additional information we include in any applicable prospectus supplement, summarizes the general features of the units that we may offer under this prospectus. We may issue units consisting of two or more other constituent securities. These units may be issuable as, and for a specified period of time may be transferable only as a single security, rather than as the separate constituent securities comprising such units. While the features we have summarized below will generally apply to any units we may offer under this prospectus, we will describe the particular terms of any units that we may offer in more detail in the applicable prospectus supplement. The specific terms of any units may differ from the description provided below as a result of negotiations with third parties in connection with the issuance of those units, as well as for other reasons. Because the terms of any units we offer under a prospectus supplement may differ from the terms we describe below, you should rely solely on information in the applicable prospectus supplement if that summary is different from the summary in this prospectus.

We urge you to read the applicable prospectus supplement related to the specific units being offered, as well as the complete instruments that contain the terms of the securities that comprise those units. Certain of those instruments, or forms of those instruments, have been or will be filed as exhibits to the registration statement of which this prospectus is a part, and supplements to those instruments or forms may be incorporated by reference into the registration statement of which this prospectus is a part from reports we file with the Commission.

If we offer any units, certain terms of that series of units will be described in the applicable prospectus supplement, including, without limitation, the following, as applicable:

the title of the series of units;

identification and description of the separate constituent securities comprising the units;

the price or prices at which the units will be issued;

the date, if any, on and after which the constituent securities comprising the units will be separately transferable;

a discussion of certain United States federal income tax considerations applicable to the units; and

any other terms of the units and their constituent securities.

Enforceability of Rights by Holders of Units

Any unit agent will act solely as our agent under the applicable unit agreement and will not assume any obligation or relationship of agency or trust with any holder of any unit. A single bank or trust company may act as unit agent for more than one series of units. A unit agent will have no duty or responsibility in case of any default by us under the applicable unit agreement or unit, including any duty or responsibility to initiate any proceedings at law or otherwise, or to make any demand upon us. Any holder of a unit may, without the consent of any related unit agent or the holder of any other unit, enforce by appropriate legal action its rights as holder under any security included in the unit.

Table of Contents

GLOBAL SECURITIES

Book-Entry, Delivery and Form

Unless we indicate differently in a prospectus supplement, the securities initially will be issued in book-entry form and represented by one or more global notes or global securities, or, collectively, global securities. The global securities will be deposited with, or on behalf of, The Depository Trust Company, New York, New York, as depository, or DTC, and registered in the name of Cede & Co., the nominee of DTC. Unless and until it is exchanged for individual certificates evidencing securities under the limited circumstances described below, a global security may not be transferred except as a whole by the depository to its nominee or by the nominee to the depository, or by the depository or its nominee to a successor depository or to a nominee of the successor depository.

DTC has advised us that it is:

- a limited-purpose trust company organized under the New York Banking Law;
- a banking organization within the meaning of the New York Banking Law;
- a member of the Federal Reserve System;
- a clearing corporation within the meaning of the New York Uniform Commercial Code; and
- a clearing agency registered pursuant to the provisions of Section 17A of the Exchange Act.

DTC holds securities that its participants deposit with DTC. DTC also facilitates the settlement among its participants of securities transactions, such as transfers and pledges, in deposited securities through electronic computerized book-entry changes in participants' accounts, thereby eliminating the need for physical movement of securities certificates. Direct participants in DTC include securities brokers and dealers, including underwriters, banks, trust companies, clearing corporations and other organizations. DTC is a wholly-owned subsidiary of The Depository Trust & Clearing Corporation, or DTCC. DTCC is the holding company for DTC, National Securities Clearing Corporation and Fixed Income Clearing Corporation, all of which are registered clearing agencies. DTCC is owned by the users of its regulated subsidiaries. Access to the DTC system is also available to others, which we sometimes refer to as indirect participants, that clear through or maintain a custodial relationship with a direct participant, either directly or indirectly. The rules applicable to DTC and its participants are on file with the Commission.

Purchases of securities under the DTC system must be made by or through direct participants, which will receive a credit for the securities on DTC's records. The ownership interest of the actual purchaser of a security, which we sometimes refer to as a beneficial owner, is in turn recorded on the direct and indirect participants' records. Beneficial owners of securities will not receive written confirmation from DTC of their purchases. However, beneficial owners are expected to receive written confirmations providing details of their transactions, as well as periodic statements of their holdings, from the direct or indirect participants through which they purchased securities. Transfers of ownership interests in global securities are to be accomplished by entries made on the books of participants acting on behalf of beneficial owners. Beneficial owners will not receive certificates representing their ownership interests in the global securities, except under the limited circumstances described below.

To facilitate subsequent transfers, all global securities deposited by direct participants with DTC will be registered in the name of DTC's partnership nominee, Cede & Co., or such other name as may be requested by an authorized representative of DTC. The deposit of securities with DTC and their registration in the name of Cede & Co. or such other nominee will not change the beneficial ownership of the securities. DTC has no knowledge of the actual beneficial owners of the securities. DTC's records reflect only the identity of the direct participants to whose accounts the securities are credited, which may or may not be the beneficial owners. The participants are responsible for keeping account of their holdings on behalf of their customers.

Table of Contents

So long as the securities are in book-entry form, you will receive payments and may transfer securities only through the facilities of the depository and its direct and indirect participants. We will maintain an office or agency in the location specified in the prospectus supplement for the applicable securities, where notices and demands in respect of the securities and the indenture may be delivered to us and where certificated securities may be surrendered for payment, registration of transfer or exchange.

Conveyance of notices and other communications by DTC to direct participants, by direct participants to indirect participants and by direct participants and indirect participants to beneficial owners will be governed by arrangements among them, subject to any legal requirements in effect from time to time.

Redemption notices will be sent to DTC. If less than all of the securities of a particular series are being redeemed, DTC's practice is to determine by lot the amount of the interest of each direct participant in the securities of such series to be redeemed.

Neither DTC nor Cede & Co. (or such other DTC nominee) will consent or vote with respect to the securities. Under its usual procedures, DTC will mail an omnibus proxy to us as soon as possible after the record date. The omnibus proxy assigns the consenting or voting rights of Cede & Co. to those direct participants to whose accounts the securities of such series are credited on the record date, identified in a listing attached to the omnibus proxy.

So long as securities are in book-entry form, we will make payments on those securities to the depository or its nominee, as the registered owner of such securities, by wire transfer of immediately available funds. If securities are issued in definitive certificated form under the limited circumstances described below, we will have the option of making payments by check mailed to the addresses of the persons entitled to payment or by wire transfer to bank accounts in the United States designated in writing to the applicable trustee or other designated party at least 15 days before the applicable payment date by the persons entitled to payment.

Redemption proceeds, distributions and dividend payments on the securities will be made to Cede & Co., or such other nominee as may be requested by an authorized representative of DTC. DTC's practice is to credit direct participants' accounts upon DTC's receipt of funds and corresponding detail information from us on the payment date in accordance with their respective holdings shown on DTC records. Payments by participants to beneficial owners will be governed by standing instructions and customary practices, as is the case with securities held for the account of customers in bearer form or registered in street name. Those payments will be the responsibility of participants and not of DTC or us, subject to any statutory or regulatory requirements in effect from time to time. Payment of redemption proceeds, distributions and dividend payments to Cede & Co., or such other nominee as may be requested by an authorized representative of DTC, is our responsibility, disbursement of payments to direct participants is the responsibility of DTC, and disbursement of payments to the beneficial owners is the responsibility of direct and indirect participants.

Except under the limited circumstances described below, purchasers of securities will not be entitled to have securities registered in their names and will not receive physical delivery of securities. Accordingly, each beneficial owner must rely on the procedures of DTC and its participants to exercise any rights under the securities and the indenture.

The laws of some jurisdictions may require that some purchasers of securities take physical delivery of securities in definitive form. Those laws may impair the ability to transfer or pledge beneficial interests in securities.

DTC may discontinue providing its services as securities depository with respect to the securities at any time by giving reasonable notice to us. Under such circumstances, in the event that a successor depository is not obtained, securities certificates are required to be printed and delivered.

Table of Contents

As noted above, beneficial owners of a particular series of securities generally will not receive certificates representing their ownership interests in those securities. However, if:

DTC notifies us that it is unwilling or unable to continue as a depository for the global security or securities representing such series of securities or if DTC ceases to be a clearing agency registered under the Exchange Act at a time when it is required to be registered and a successor depository is not appointed within 90 days of the notification to us or of our becoming aware of DTC's ceasing to be so registered, as the case may be;

we determine, in our sole discretion, not to have such securities represented by one or more global securities; or

an Event of Default has occurred and is continuing with respect to such series of securities, we will prepare and deliver certificates for such securities in exchange for beneficial interests in the global securities. Any beneficial interest in a global security that is exchangeable under the circumstances described in the preceding sentence will be exchangeable for securities in definitive certificated form registered in the names that the depository directs. It is expected that these directions will be based upon directions received by the depository from its participants with respect to ownership of beneficial interests in the global securities.

We have obtained the information in this section and elsewhere in this prospectus concerning DTC and DTC's book-entry system from sources that are believed to be reliable, but we take no responsibility for the accuracy of this information.

Table of Contents

**CERTAIN PROVISIONS OF DELAWARE LAW AND OF THE
COMPANY S CERTIFICATE OF INCORPORATION AND BYLAWS**

**Anti-Takeover Effects of Provisions of Our Amended and Restated Certificate of Incorporation,
as Amended, Our Amended and Restated Bylaws and Delaware Law**

Some provisions of Delaware law, our amended and restated certificate of incorporation, as amended, and our amended and restated bylaws contain provisions that could make the following transactions more difficult: an acquisition of us by means of a tender offer; an acquisition of us by means of a proxy contest or otherwise; or the removal of our incumbent officers and directors. It is possible that these provisions could make it more difficult to accomplish or could deter transactions that stockholders may otherwise consider to be in their best interest or in our best interests, including transactions which provide for payment of a premium over the market price for our shares.

These provisions, summarized below, are intended to discourage coercive takeover practices and inadequate takeover bids. These provisions are also designed to encourage persons seeking to acquire control of us to first negotiate with our board of directors. We believe that the benefits of the increased protection of our potential ability to negotiate with the proponent of an unfriendly or unsolicited proposal to acquire or restructure us outweigh the disadvantages of discouraging these proposals because negotiation of these proposals could result in an improvement of their terms.

Undesignated Preferred Stock

The ability of our board of directors, without action by the stockholders, to issue up to 10,000,000 shares of undesignated preferred stock with voting or other rights or preferences as designated by our board of directors could impede the success of any attempt to change control of us. These and other provisions may have the effect of deferring hostile takeovers or delaying changes in control or management of our company.

Stockholder Meetings

Our amended and restated bylaws provide that a special meeting of stockholders may be called only by our chairman of the board, chief executive officer or president, or by a resolution adopted by a majority of our board of directors.

Requirements for Advance Notification of Stockholder Nominations and Proposals

Our amended and restated bylaws establish advance notice procedures with respect to stockholder proposals to be brought before a stockholder meeting and the nomination of candidates for election as directors, other than nominations made by or at the direction of the board of directors or a committee of the board of directors.

Elimination of Stockholder Action by Written Consent

Our amended and restated certificate of incorporation, as amended, and amended and restated bylaws eliminate the right of stockholders to act by written consent without a meeting.

Staggered Board

Our board of directors is divided into three classes. The directors in each class will serve for a three-year term, one class being elected each year by our stockholders. This system of electing and removing directors may tend to discourage a third-party from making a tender offer or otherwise attempting to obtain control of us, because it generally makes it more difficult for stockholders to replace a majority of the directors.

Table of Contents

Removal of Directors

Our amended and restated certificate of incorporation, as amended, provides that no member of our board of directors may be removed from office by our stockholders except for cause and, in addition to any other vote required by law, upon the approval of not less than 66 2/3% of the total voting power of all of our outstanding voting stock then entitled to vote in the election of directors.

Stockholders Not Entitled to Cumulative Voting

Our amended and restated certificate of incorporation, as amended, does not permit stockholders to cumulate their votes in the election of directors. Accordingly, the holders of a majority of the outstanding shares of our common stock entitled to vote in any election of directors can elect all of the directors standing for election, if they choose, other than any directors that holders of our preferred stock may be entitled to elect.

Delaware Anti-Takeover Statute

We are subject to Section 203 of the DGCL, which prohibits persons deemed to be interested stockholders from engaging in a business combination with a publicly held Delaware corporation for three years following the date these persons become interested stockholders unless the business combination is, or the transaction in which the person became an interested stockholder was, approved in a prescribed manner or another prescribed exception applies. Generally, an interested stockholder is a person who, together with affiliates and associates, owns, or within three years prior to the determination of interested stockholder status did own, 15% or more of a corporation's voting stock. Generally, a business combination includes a merger, asset or stock sale, or other transaction resulting in a financial benefit to the interested stockholder. The existence of this provision may have an anti-takeover effect with respect to transactions not approved in advance by the board of directors.

Amendment of Charter Provisions

The amendment of any of the above provisions, except for the provision making it possible for our board of directors to issue preferred stock, would require approval by holders of at least 66 2/3% of the total voting power of all of our outstanding voting stock.

The provisions of Delaware law, our amended and restated certificate of incorporation, as amended, and our amended and restated bylaws could have the effect of discouraging others from attempting hostile takeovers and, as a consequence, they may also inhibit temporary fluctuations in the market price of our common stock that often result from actual or rumored hostile takeover attempts. These provisions may also have the effect of preventing changes in the composition of our board and management. It is possible that these provisions could make it more difficult to accomplish transactions that stockholders may otherwise deem to be in their best interests.

Table of Contents

LEGAL MATTERS

Latham & Watkins LLP, San Diego, California, will issue an opinion about certain legal matters with respect to the securities.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements and schedule included in our Annual Report on Form 10-K for the year ended December 31, 2011 (which contains an explanatory paragraph describing conditions that raise substantial doubt about our ability to continue as a going concern as described in Note 1 to our consolidated financial statements), as set forth in their report, which is incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements and schedule are incorporated by reference in reliance on Ernst & Young LLP's report, given on their authority as experts in accounting and auditing.

LIMITATION ON LIABILITY AND DISCLOSURE OF COMMISSION POSITION ON INDEMNIFICATION FOR SECURITIES ACT LIABILITIES

Our certificate of incorporation and bylaws provide that we will indemnify our directors and officers, and may indemnify our employees and other agents, to the fullest extent permitted by the DGCL. Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons pursuant to the foregoing provisions, or otherwise, we have been advised that, in the opinion of the Commission, such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

Table of Contents

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the Commission a registration statement on Form S-3 under the Securities Act, of which this prospectus forms a part. The rules and regulations of the Commission allow us to omit from this prospectus certain information included in the registration statement. For further information about us and our securities, you should refer to the registration statement and the exhibits and schedules filed with the registration statement. With respect to the statements contained in this prospectus regarding the contents of any agreement or any other document, in each instance, the statement is qualified in all respects by the complete text of the agreement or document, a copy of which has been filed as an exhibit to the registration statement.

We file reports, proxy statements and other information with the Commission under the Exchange Act. You may read and copy this information from the Public Reference Room of the Commission, 100 F Street, N.E., Room 1580, Washington, D.C. 20549, at prescribed rates. You may obtain information on the operation of the Public Reference Room by calling the Commission at 1-800-SEC-0330. The Commission also maintains an Internet website that contains reports, proxy statements and other information about issuers, like us, that file electronically with the Commission. The address of that website is www.sec.gov.

INFORMATION INCORPORATED BY REFERENCE

The Commission allows us to incorporate by reference the information we file with it which means that we can disclose important information to you by referring you to those documents instead of having to repeat the information in this prospectus. The information incorporated by reference is considered to be part of this prospectus, and later information that we file with the Commission will automatically update and supersede this information. We incorporate by reference the documents listed below and any future information filed (rather than furnished) with the Commission under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act between the date of this prospectus and the termination of the offering and also between the date of the initial registration statement and prior to effectiveness of the registration statement, provided, however, that we are not incorporating any information furnished under Item 2.02 or Item 7.01 of any current report on Form 8-K:

our annual report on Form 10-K for the year ended December 31, 2011, which was filed on March 12, 2012;

our quarterly report on Form 10-Q for the quarter ended March 31, 2012, which was filed on May 15, 2012, the quarter ended June 30, 2012, which was filed on August 9, 2012, and the quarter ended September 30, 2012, which was filed on November 8, 2012;

our definitive proxy statement on Schedule 14A (other than information furnished rather than filed), which was filed on April 30, 2012;

our current reports on Form 8-K, which were filed on March 30, 2012, April 17, 2012, May 2, 2012, May 30, 2012, June 6, 2012, June 7, 2012, July 12, 2012, July 16, 2012, July 24, 2012, August 1, 2012, November 2, 2012, November 26, 2012, December 10, 2012 and January 3, 2013;

our current report on Form 8-K/A, which was filed on July 25, 2012; and

the description of our common stock contained in our registration statement on Form 8-A, which was filed on November 12, 2010, including any amendments or reports filed for the purpose of updating the description.

These documents may also be accessed on our website at www.zogenix.com. Except as otherwise specifically incorporated by reference in this prospectus, information contained in, or accessible through, our website is not a part of this prospectus.

Table of Contents

We will furnish without charge to you, upon written or oral request, a copy of any or all of the documents incorporated by reference, including exhibits to these documents by writing or telephoning us at the following address:

Zogenix, Inc.

12400 High Bluff Drive, Suite 650

San Diego, CA 92130

Attention: Corporate Secretary

(858) 259-1165

Table of Contents

\$60,000,000

Common Stock

PROSPECTUS SUPPLEMENT

November , 2013

Book-Running Managers

Stifel

Leerink Swann

Wells Fargo Securities

Co-Managers

Oppenheimer & Co.

William Blair

Neither we nor any of the underwriters have authorized anyone to provide information different from that contained in this prospectus supplement. When you make a decision about whether to invest in our common stock, you should not rely upon any information other than the information in this prospectus supplement. Neither the delivery of this prospectus supplement nor the sale of shares of our common stock means that information contained in this prospectus supplement is correct after the date of this prospectus supplement. This prospectus supplement is not an offer to sell or solicitation of an offer to buy shares of our common stock in any circumstances under which the offer or solicitation is unlawful.