ZOGENIX, INC.
Form 424B5
November 04, 2013
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The information in this preliminary prospectus supplement is not complete and may be changed. A registration statement relating to these securities has been declared effective by the Securities and Exchange Commission. This preliminary prospectus supplement and the accompanying prospectus are not an offer to sell these securities, and we are not soliciting offers to buy these securities in any 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.

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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 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.

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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

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

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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 our 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

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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.

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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 Use of Proceeds on page S-9.
Risk factors	You should read the Risk Factors 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.

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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.

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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, ex intend, plan, anticipate, believe, estimate, predict, project, potential, continue, ongoing or the neg 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 formation 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

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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.

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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.

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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.

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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 , 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 $.

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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).

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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.

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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.

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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.

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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 (Verkaufsprospektgesetz), or the German Investment Act (Investmentgesetz). Neither the German Federal Financial Services Supervisory Authority (Bundesanstalt fur 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.