

ZOGENIX, INC.
Form 424B5
October 02, 2017
Table of Contents

Filed Pursuant to Rule 424(b)(5)
Registration No. 333-220759

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.

SUBJECT TO COMPLETION, DATED OCTOBER 2, 2017

PRELIMINARY PROSPECTUS SUPPLEMENT

(To Prospectus dated October 2, 2017)

4,300,000 Shares

Common Stock

We are offering 4,300,000 shares of our common stock. Our common stock is listed on the Nasdaq Global Market under the symbol ZGNX. On September 29, 2017, the last reported sale price of our common stock on the Nasdaq Global Market was \$35.05 per share.

Investing in our common stock involves risks. See Risk Factors beginning on page S-6 of this prospectus supplement and the documents incorporated by reference into this prospectus supplement.

	Per Share	Total
Public offering price	\$	\$
Underwriting discounts and commissions(1)	\$	\$
Proceeds, before expenses, to us	\$	\$

(1) We have agreed to reimburse the underwriters for certain expenses. See Underwriting. We have granted the underwriters an option for a period of 30 days to purchase up to an additional 645,000 shares of our common stock on the same terms as set forth above. If the underwriters exercise their option in full, the total underwriting discounts and commissions payable by us will be \$ and the total proceeds to us, before expenses, will be \$. See Underwriting for more information.

The underwriters expect to deliver shares of common stock to purchasers on October , 2017.

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.

Joint Book-Running Managers

Leerink Partners **Stifel**
Co-Lead Managers

Mizuho Securities **JMP Securities**
Co-Manager

LifeSci Capital

Prospectus Supplement dated October , 2017

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>Cautionary Note Regarding Forward-looking Statements</u>	S-8
<u>Use of Proceeds</u>	S-9
<u>Dilution</u>	S-10
<u>Underwriting</u>	S-12
<u>Legal Matters</u>	S-18
<u>Experts</u>	S-18
<u>Where You Can Find More Information: Information Incorporated by Reference</u>	S-18
Prospectus	
<u>About this Prospectus</u>	1
<u>Zogenix</u>	1
<u>Risk Factors</u>	2
<u>Forward-Looking Statements</u>	3
<u>Ratio of Earnings to Fixed Charges</u>	3
<u>Use of Proceeds</u>	4
<u>Dividend Policy</u>	4
<u>Description of Capital Stock</u>	5
<u>Description of Debt Securities</u>	9
<u>Description of Depositary Shares</u>	17
<u>Description of Warrants</u>	20
<u>Description of Units</u>	22
<u>Description of Rights</u>	23
<u>Global Securities</u>	24
<u>Selling Securityholders</u>	27
<u>Plan of Distribution</u>	27
<u>Legal Matters</u>	27
<u>Experts</u>	27
<u>Where You Can Find More Information</u>	27
<u>Information Incorporated by Reference</u>	29

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.

S-i

Table of Contents

ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus dated October 10, 2017 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 to under the headings **Where You Can Find More Information**; **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 subsidiaries.

We use our registered trademarks, **Zogenix** and **DosePr**® in this prospectus. 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. Solely for convenience, trademarks and tradenames referred to in this prospectus appear without the ® and ™ symbols, but those references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights or that the applicable owner will not assert its rights, to these trademarks and tradenames.

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.

We are a pharmaceutical company committed to developing and commercializing central nervous system, or CNS, therapies that address specific clinical needs for people living with orphan and other CNS disorders who need innovative treatment alternatives to help them improve their daily functioning. Our current primary area of focus is orphan or rare childhood-onset epilepsy disorders.

We currently own and control worldwide development and commercialization rights to ZX008, our lead product candidate. ZX008 is low-dose fenfluramine for the treatment of seizures associated with Dravet syndrome. Dravet syndrome is a rare and catastrophic form of pediatric epilepsy with life threatening consequences for patients and for which current treatment options are very limited. ZX008 has received orphan drug designation in the United States and European Union, or the EU, for the treatment of Dravet syndrome. In January 2016, we received notification of Fast Track designation from the U.S. Food and Drug Administration, or the FDA, for ZX008 for the treatment of Dravet syndrome. We initiated our Phase 3 clinical trials in North America (Study 1501) in January 2016 and in Europe and Australia in June 2016 (Study 1502). Study 1501 and Study 1502 are each identical randomized, double-blind placebo-controlled studies of ZX008 as adjunctive therapy for patients with uncontrolled seizures who have Dravet syndrome. In January 2017, we announced our plan to report top-line results from Study 1501 and Study 1502 via a prospective merged study analysis approach whereby top-line results from the first 119 subjects randomized into either Study 1501 or 1502 would be reported initially as Study 1. In April 2017, we completed enrollment of Study 1 and, in September 2017, we announced positive top-line results for Study 1. In September 2016, we initiated the pharmacokinetic and safety profile portion of Study 1504, a double blind, randomized, two arm pivotal Phase 3 clinical trial of ZX008 in Dravet syndrome patients who are taking stiripentol, valproate and clobazam as part of their baseline standard care. In February 2017, we initiated the safety and efficacy portion of Study 1504, a two-arm study that compares ZX008 versus placebo across the titration and 12-week maintenance periods at multiple sites, which currently includes sites in France, the Netherlands, United States, Canada, Germany, the United Kingdom and Spain. Study 1504 will enroll 40 patients per treatment group. We expect to report top-line results from Study 1504 in the first half of 2018. We believe we are on track to submit applications for regulatory approvals for ZX008 in the United States and Europe in the second half of 2018.

Beginning in first quarter of 2016, we funded an open-label dose-finding twenty-patient investigator initiated study in patients with Lennox-Gastaut Syndrome, or LGS, another rare and catastrophic form of pediatric epilepsy with life threatening consequences for patients and for which current treatment options are very limited. In December 2016, we presented initial data from an interim analysis of the first 13 patients to have completed at least 12 weeks of this Phase 2 open-label, dose-finding clinical trial at the American Epilepsy Society Meeting. These data demonstrated that ZX008 provided clinically meaningful improvement in major motor seizure frequency in patients with severe refractory LGS, with seven out of 13 patients (54%) achieving at least a 50% reduction in the number of major motor seizures, at doses below the 0.8 mg/kg/day maximum. In addition, ZX008 was generally well tolerated, as expected based on our epilepsy program to date. We believe these data indicate that ZX008 has the potential to be a safe and

effective adjunctive treatment for LGS. Based on the

S-1

Table of Contents

strength of the LGS data generated, in the first quarter of 2017, we submitted an investigational new drug, or IND, application to the FDA to initiate a Phase 3 program of ZX008 in LGS, which became effective in April 2017. We intend to initiate a Phase 3 program of ZX008 in LGS in the fourth quarter of 2017. In February 2017, ZX008 received orphan drug designation for the treatment of LGS in the EU. In June 2017, ZX008 received orphan drug designation for the treatment of LGS in the United States from the FDA.

Recent Developments*ZX008 Phase 3 Top-line Clinical Trial Results*

On September 29, 2017, we announced positive top-line results from Study 1. The trial met its primary objective of demonstrating that ZX008, at a dose of 0.8 mg/kg/day, is superior to placebo as adjunctive therapy in the treatment of Dravet syndrome in children and young adults based on change in the frequency of convulsive seizures between the 6-week baseline observation period and the 14-week treatment period ($p < 0.001$). ZX008 0.8 mg/kg/day also demonstrated statistically significant improvements versus placebo in all key secondary measures, including the proportion of patients with clinically meaningful reductions in seizure frequency and longest seizure-free interval. The same analyses comparing a 0.2 mg/kg/day ZX008 dose versus placebo also demonstrated statistically significant improvement compared with placebo.

The study enrolled 119 patients across sites in the United States, Canada, Europe, and Australia. The median age of patients was 8 years (range, 2-18 years). Following a six-week baseline observation period, patients were randomized to one of three treatment groups: ZX008 0.8 mg/kg/day (30 mg maximum daily dose; $n=40$), ZX008 0.2 mg/kg/day ($n=39$) and placebo ($n=40$) in which ZX008 or placebo was added to current regimens of antiepileptic drugs. Patients were titrated to their target dose over two weeks and then remained at that fixed dose for 12 weeks. The mean baseline convulsive seizure frequency across the study groups was approximately 40 seizures per month.

The primary efficacy measure was a comparison of the change in mean monthly convulsive seizure frequency between ZX008 0.8 mg/kg/day and placebo during the 14-week treatment period compared with the 6-week baseline observation period. Patients taking ZX008 0.8 mg/kg/day achieved a 63.9% reduction in mean monthly convulsive seizures compared to placebo ($p < 0.001$). The median percent reduction in monthly convulsive seizure frequency was 72.4% among ZX008 0.8 mg/kg/day patients compared to 17.4% in placebo patients.

A key secondary endpoint was the same analysis for a comparison of ZX008 0.2 mg/kg/day and placebo. Patients taking ZX008 0.2 mg/kg/day achieved a reduction in mean monthly convulsive seizures of 33.7% compared to placebo ($p=0.019$). Collectively, these top-line data suggest a dose-response relationship for ZX008 in the adjunctive treatment of convulsive seizures in Dravet syndrome.

Table of Contents

Additional key secondary objectives of the study were to compare 0.8 mg/kg/day and 0.2 mg/kg/day ZX008 (independently) with placebo in terms of (1) the proportion of patients who achieved ^{350%} reductions in monthly convulsive seizures and (2) the median of the longest convulsive seizure-free interval. These results are shown in the following table. The proportion of patients who achieved ^{375%} seizure reductions, a secondary efficacy measure, is also presented.

	ZX008 0.8 mg/kg/day (N=40)	ZX008 0.2 mg/kg/day (N=39)	Placebo (N=40)
Patients with ^{350%} reduction in monthly convulsive seizures	70.0% (p<0.001)	41.0% (p=0.001)	7.5%
Patients with ^{375%} reduction in monthly convulsive seizures	45.0% (p=0.001)	20.5% (p=0.033)	2.5%
Longest seizure-free interval (median)	20.5 days (p<0.001)	14 days (p=0.011)	9 days

In addition, the proportion of patients who experienced zero seizures or one seizure throughout the full treatment period was 7.5% and 17.5%, respectively, in the 0.8 mg/kg/day group, 7.7% and 5.1%, respectively, in the 0.2 mg/kg/day group, and 0% in the placebo group. ZX008 was generally well-tolerated in this study with the adverse events consistent with the known safety profile of fenfluramine. The incidence of treatment emergent adverse events was higher in the treatment groups as compared to the placebo group, with 95% (n=38) of patients in the 0.8mg/kg/day group and 94.9% (n=37) of patients in the 0.2 mg/kg/day group experiencing at least one treatment emergent adverse event compared to 65.0% (n=26) of patients in the placebo group. The incidence of serious adverse events was similar in all three groups with 12.5% (n=5) of patients in the 0.8mg/kg/day group and 10.3% (n=4) of patients in the 0.2 mg/kg/day group experiencing at least one treatment emergent serious adverse event compared to 10.0% (n=4) of patients in the placebo group. Five patients in the 0.8 mg/kg/day group had an adverse event leading to study discontinuation compared to none in the other treatment groups. Prospective cardiac safety monitoring throughout the study demonstrated no clinical or echocardiographic evidence of cardiac valvulopathy or pulmonary hypertension.

Termination of Contract Manufacturing Agreement with Endo

Following our previously announced decision with Endo Ventures Limited, or Endo, to discontinue the manufacturing and supply of Sumavel DosePro, on September 19, 2017, we and Endo entered into a Termination Agreement, or the Termination Agreement, which terminates the License Agreement dated May 16, 2014, by and between us and Endo, or the License Agreement, and the Manufacturing and Supply Agreement dated May 16, 2014, by and between the Company and Endo, or the Supply Agreement, as well as certain quality agreements related thereto. Upon the termination of the Supply Agreement, the associated interest-free working capital advance provided by Endo to support our Sumavel DosePro operations of \$7.0 million became due and payable in accordance with its terms. The

entire outstanding principal balance of \$7.0 million was immediately repaid in full and the corresponding promissory note extinguished. We expect to record a non-cash charge upon extinguishment of debt of approximately \$3.4 million due to the write-off of unamortized discount related to imputed interest in the third quarter of 2017. We previously sold our Sumavel DosePro Needle-free Delivery system to Endo, but retained the exclusive right and contractual obligation to manufacture and supply Sumavel DosePro to Endo under the License Agreement and Supply Agreement. In connection with the Termination Agreement, we have also terminated our relationships with other third-party suppliers and manufacturers related to the Sumavel DosePro product.

Table of Contents

At-the-Market Sales

Subsequent to June 30, 2017, we sold 1,550,880 shares of our common stock under our \$25.0 million Controlled Equity OfferingSM Sales Agreement with Cantor Fitzgerald & Co. for aggregate net proceeds of \$19.5 million, after deducting commissions and other stock issuance costs.

Certain Financial Data

We estimate that our cash and cash equivalents were approximately \$64.7 million as of September 30, 2017. This amount is unaudited and preliminary and is subject to completion of financial closing procedures. As a result, this amount may differ from the amount that will be reflected in our financial statements as of and for the quarter ended September 30, 2017. Our financial statements for the quarter ended September 30, 2017 will not be available until after this offering is completed, and consequently will not be available to you prior to investing in this offering.

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 5858 Horton Street, Suite 455, Emeryville, California 94608, 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 were to support the manufacture of the DosePro technology. Zogenix International Limited is a wholly-owned subsidiary of Zogenix Europe Limited which was acquired in October 2014. 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	4,300,000 shares
Common stock to be outstanding after this offering	29,139,141 shares (or 29,784,141 shares if the underwriters exercise in full their option to purchase additional shares)
Option to purchase additional shares	We have granted the underwriters an option to purchase up to an additional 645,000 shares of our common stock. 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 clinical research and development of ZX008, including the completion of our ongoing clinical trials and regulatory submissions for Dravet syndrome and to fund Phase 3 clinical development for Lennox-Gastaut syndrome, commercial infrastructure for ZX008 for Dravet syndrome and working capital and general corporate purposes. See Use of Proceeds.
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 24,839,141 shares outstanding as of June 30, 2017, and excludes as of that date:	

1,974,842 shares of common stock issuable upon the exercise of outstanding warrants with a weighted average exercise price of \$20.92 per share, of which warrants exercisable for 1,901,918 shares of common stock expired unexercised on July 27, 2017;

4,089,707 shares of common stock issuable upon the exercise of outstanding stock options with a weighted average exercise price of \$14.47 per share;

271,603 shares of common stock issuable upon the vesting of outstanding restricted stock units;

Edgar Filing: ZOGENIX, INC. - Form 424B5

849,053 shares of common stock reserved for future issuance under our 2010 amended and restated equity incentive award plan, our 2010 employee stock purchase plan and our 2013 employment inducement equity incentive award plan; and

1,550,880 shares of common stock sold under our Controlled Equity OfferingSM Sales Agreement with Cantor Fitzgerald & Co. subsequent to June 30, 2017.

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 645,000 shares of our common stock.

S-5

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, 2016 and in our quarterly report on Form 10-Q for the period ended June 30, 2017, 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

Top-line data may not accurately reflect the complete results of a particular study or trial.

We may publicly disclose top-line or interim data from time to time, which is based on a preliminary analysis of then-available efficacy and safety data such as the top-line results we reported from Study 1, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the top-line results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Top-line data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, top-line data should be viewed with caution until the final data are available.

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimations, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular drug candidate or drug and our company in general. In addition, the information we may publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure, and any information we determine not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise regarding a particular drug, drug candidate or our business. If the top-line data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our product candidates may be harmed, which could harm our business, operating results, prospects or financial condition.

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. Based upon an assumed public offering price of \$35.05 per share, which is the last reported sale price of our common stock on the Nasdaq Global Market on September 29, 2017, new investors will incur immediate

S-6

Table of Contents

dilution of \$31.20 per share based on the net tangible book deficit as of June 30, 2017. 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 clinical research and development of ZX008, including the completion of our ongoing clinical trials and regulatory submissions for Dravet syndrome and to fund Phase 3 clinical development for Lennox-Gastaut syndrome, commercial infrastructure for ZX008 for Dravet syndrome and working capital and general corporate purposes. 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

CAUTIONARY 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. All statements other than statements of historical facts contained in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein are forward-looking statements, including statements regarding our future results of operations and financial position, business strategy, prospective products, product approvals, research and development costs, timing and likelihood of success, plans and objectives of management for future operations and future results of anticipated products. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. This prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein also contain estimates and other statistical data made by independent parties and by us relating to market size and growth and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.

In some cases, you can identify forward-looking statements by terms such as may, will, should, expect, plan, anticipate, could, intend, target, project, contemplates, believes, estimates, predicts, potential or negative of these terms or other similar expressions. The forward-looking statements in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein are only predictions. We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our business, financial condition and results of operations. These forward-looking statements speak only as of the date of this this prospectus supplement and are subject to a number of risks, uncertainties and assumptions, which we discuss in greater detail in the documents incorporated by reference herein, including under the heading Risk Factors. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Moreover, we operate in an evolving environment. New risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all risk factors and uncertainties. Given these risks and uncertainties, you should not place undue reliance on these forward-looking statements. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained in this prospectus supplement, the accompanying prospectus or the documents incorporated by reference herein, whether as a result of any new information, future events, changed circumstances or otherwise. 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

Based upon an assumed public offering price of \$35.05 per share, which is the last reported sale price of our common stock on the Nasdaq Global Market on September 29, 2017, we estimate that we will receive net proceeds of approximately \$141.4 million from the sale of the shares of common stock offered by us in this offering, or approximately \$162.6 million if the underwriters exercise in full their option to purchase 645,000 additional shares of common stock, after deducting the underwriting discounts and commissions and estimated offering costs payable by us. A one million increase (decrease) in the amount of shares offered by us, as set forth on the cover page of this prospectus supplement, would increase (decrease) the net proceeds to us by approximately \$32.9 million, assuming the assumed offering price of \$35.05 per share remains the same 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 clinical research and development of ZX008, including the completion of our ongoing clinical trials and regulatory submissions for Dravet syndrome and to fund Phase 3 clinical development for Lennox-Gastaut syndrome, commercial infrastructure for ZX008 for Dravet syndrome and working capital and 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 on hand, will be sufficient to fund our operations into the second half of 2019, although we cannot assure you that this will occur.

The amounts and timing of our actual expenditures will depend on numerous factors, including interactions with and feedback from regulatory authorities, the timing of initiation and progress of our clinical trials and results of such trials, other development efforts for our product candidates, including ZX008, and other factors, 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 June 30, 2017, our net tangible book deficit was \$(29.3 million), or \$(1.18) per share, based on 24,839,141 shares of our common stock outstanding as of June 30, 2017. Our net tangible book deficit 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 June 30, 2017. After giving effect to our sale in this offering of 4,300,000 shares of common stock at the assumed public offering price of \$35.05 per share, which is the last reported sale price of our common stock on the Nasdaq Global Market on September 29, 2017, after deducting underwriting discounts and commissions and estimated offering costs payable by us, our net tangible book value as of June 30, 2017 would have been \$112.1 million, or \$3.85 per share. This represents an immediate increase of net tangible book value of \$5.03 per share to our existing stockholders and an immediate dilution of \$31.20 per share to new investors purchasing our common stock in this offering. The following table illustrates this per share dilution.

Assumed public offering price per share	\$ 35.05
Net tangible book deficit per share at June 30, 2017	\$ (1.18)
Increase per share attributable to investors purchasing shares in this offering	\$ 5.03
Pro forma net tangible book value per share, as adjusted to give effect to this offering	\$ 3.85
Dilution to investors purchasing our common stock in this offering	\$ 31.20

A \$1.00 increase (decrease) in the assumed public offering price of \$35.05 per share would increase (decrease) the dilution per share to new investors by approximately \$0.86 per share, assuming that the amount of shares offered by us, as set forth on the cover page of this prospectus supplement, remains the same.

We may also increase or decrease the amount of shares we are offering from the assumed amount of shares set forth on the cover page of this prospectus supplement. An increase of one million in the amount of shares offered by us from the assumed amount of shares set forth on the cover page of this prospectus supplement would increase our pro forma net tangible book value after this offering by approximately \$32.9 million, or approximately \$0.96 per share, and the dilution per share to new investors would be approximately \$30.24 per share, assuming that the assumed public offering price remains the same. Similarly, a decrease of one million in the amount of shares offered by us from the assumed amount of shares set forth on the cover page of this prospectus supplement would decrease our pro forma net tangible book value after this offering by approximately \$32.9 million, or approximately \$1.04 per share, and the dilution per share to new investors would be approximately \$32.24 per share, assuming that the assumed public offering price remains the same.

If the underwriters exercise in full their option to purchase up to an additional 645,000 shares of our common stock at the assumed public offering price of \$35.05 per share, which is the last reported sale price of our common stock on the Nasdaq Global Market on September 29, 2017, the pro forma net tangible book value after this offering would be \$4.48 per share, representing an increase in net tangible book value of \$5.66 per share to our existing stockholders and immediate dilution in net tangible book value of \$30.57 per share to new investors purchasing shares in this offering.

The above discussion and table are based on 24,839,141 shares outstanding as of June 30, 2017, and excludes as of that date:

1,974,842 shares of common stock issuable upon the exercise of outstanding warrants with a weighted average exercise price of \$20.92 per share, of which warrants exercisable for 1,901,918 shares of common stock expired unexercised on July 27, 2017;

S-10

Table of Contents

4,089,707 shares of common stock issuable upon the exercise of outstanding stock options with a weighted average exercise price of \$14.47 per share;

271,603 shares of common stock issuable upon the vesting of outstanding restricted stock units;

849,053 shares of common stock reserved for future issuance under our 2010 amended and restated equity incentive award plan, our 2010 employee stock purchase plan and our 2013 employment inducement equity incentive award plan; and

1,550,880 shares of common stock sold under our Controlled Equity OfferingSM Sales Agreement with Cantor Fitzgerald & Co. subsequent to June 30, 2017.

To the extent that outstanding 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**

Leerink Partners LLC and Stifel, Nicolaus & Company, Incorporated are acting as representatives of each of the underwriters named below. Subject to the terms and conditions set forth in an underwriting agreement among us and the underwriters, we have agreed to sell to the underwriters, and each of the underwriters has agreed, severally and not jointly, to purchase from us, the number of shares of common stock set forth opposite its name below.

Underwriter	Number of Shares
Leerink Partners LLC	
Stifel, Nicolaus & Company, Incorporated	
Mizuho Securities USA LLC	
JMP Securities LLC	
LifeSci Capital LLC	
Total	4,300,000

Subject to the terms and conditions set forth in the underwriting agreement, the underwriters have agreed, severally and not jointly, to purchase all of the shares sold under the underwriting agreement if any of these shares are purchased. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the non-defaulting underwriters may be increased or the underwriting agreement may be terminated.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act, or to contribute to payments the underwriters may be required to make in respect of those liabilities.

The underwriters are offering the shares, subject to prior sale, when, as and if issued to and accepted by them, subject to approval of legal matters by their counsel, including the validity of the shares, and other conditions contained in the underwriting agreement, such as the receipt by the underwriters of officers' certificates and legal opinions. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Commissions and Discounts

The representatives have advised us that the underwriters propose initially to offer the shares to the public at the public offering price set forth on the cover of this prospectus and to dealers at that price less a concession not in excess of \$ per share. After the initial offering, the public offering price, concession or any other term of the offering may be changed.

The following table shows the public offering price, underwriting discount and proceeds before expenses to us. The information assumes either no exercise or full exercise by the underwriters of their option to purchase additional shares of our common stock.

Total

	Per Share	Without Option	With Option
Public offering price	\$	\$	\$
Underwriting discount	\$	\$	\$
Proceeds, before expenses, to us	\$	\$	\$

We estimate expenses payable by us in connection with this offering, other than the underwriting discounts and commissions referred to above, will be approximately \$320,000.

S-12

Table of Contents

Option to Purchase Additional Shares

We have granted an option to the underwriters, exercisable for 30 days after the date of this prospectus, to purchase up to 645,000 additional shares at the public offering price, less the underwriting discount. If the underwriters exercise this option, each will be obligated, subject to conditions contained in the underwriting agreement, to purchase a number of additional shares proportionate to that underwriter's initial amount reflected in the above table.

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 for us, and the 60th day after the date of this prospectus supplement for our directors and executive officers, 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;

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,

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.

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;

Table of Contents

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 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, 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.

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.

The Nasdaq Global Market Listing

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

Price Stabilization, Short Positions and Penalty Bids

Until the distribution of the shares is completed, SEC rules may limit underwriters and selling group members from bidding for and purchasing our common stock. However, the representatives may engage in transactions that stabilize the price of the common stock, such as bids or purchases to peg, fix or maintain that price.

S-14

Table of Contents

In connection with the offering, the underwriters may purchase and sell our common stock in the open market. These transactions may include short sales, purchases on the open market to cover positions created by short sales and stabilizing transactions. Short sales involve the sale by the underwriters of a greater number of shares than they are required to purchase in the offering. Covered short sales are sales made in an amount not greater than the underwriters option described above. The underwriters may close out any covered short position by either exercising their option or purchasing shares in the open market. In determining the source of shares to close out the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the option granted to them. Naked short sales are sales in excess of such option. The underwriters must close out any naked short position by purchasing shares 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 our common stock in the open market after pricing that could adversely affect investors who purchase in the offering. Stabilizing transactions consist of various bids for or purchases of shares of common stock made by the underwriters in the open market prior to the closing of the offering.

The underwriters may also impose a penalty bid. This occurs when a particular underwriter repays to the underwriters a portion of the underwriting discount received by it because the representatives have repurchased shares sold by or for the account of such underwriter in stabilizing or short covering transactions.

Similar to other purchase transactions, the underwriters purchases to cover the syndicate short sales may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock may be higher than the price that might otherwise exist in the open market. The underwriters may conduct these transactions on The Nasdaq Global Market, in the over-the-counter market or otherwise.

Neither we nor any of the underwriters make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of our common stock. In addition, neither we nor any of the underwriters make any representation that the representatives will engage in these transactions or that these transactions, once commenced, will not be discontinued without notice.

Electronic Distribution

In connection with the offering, certain of the underwriters or securities dealers may distribute prospectuses by electronic means, such as e-mail.

Other Relationships

Some of the underwriters and their affiliates may in the future engage in investment banking and other commercial dealings in the ordinary course of business with us or our affiliates. They may in the future receive customary fees and commissions for these transactions.

In addition, in the ordinary course of their business activities, the underwriters and their affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers.

Such investments and securities activities may involve securities and/or instruments of ours or our affiliates. The underwriters and their affiliates may also make investment recommendations and/or publish or express independent research views in respect of such securities or financial instruments and may hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

Table of Contents

Notice to Prospective Investors in the European Economic Area

In relation to each Member State of the European Economic Area (each, a Relevant Member State), no offer of shares may be made to the public in that Relevant Member State other than:

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 provision of the 2010 PD Amending Directive, 150, natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the representatives; or

C. in any other circumstances falling within Article 3(2) of the Prospectus Directive, provided that no such offer of shares shall require the Company or the representatives to publish a prospectus pursuant to Article 3 of the Prospectus Directive or supplement a prospectus pursuant to Article 16 of the Prospectus Directive.

Each person in a Relevant Member State who initially acquires any shares or to whom any offer is made will be deemed to have represented, acknowledged and agreed that it is a qualified investor within the meaning of the law in that Relevant Member State implementing Article 2(1)(e) of the Prospectus Directive. In the case of any shares being offered to a financial intermediary as that term is used in Article 3(2) of the Prospectus Directive, each such financial intermediary will be deemed to have represented, acknowledged and agreed that the shares acquired by it in the offer have not been acquired on a non-discretionary basis on behalf of, nor have they been acquired with a view to their offer or resale to, persons in circumstances which may give rise to an offer of any shares to the public other than their offer or resale in a Relevant Member State to qualified investors as so defined or in circumstances in which the prior consent of the representatives has been obtained to each such proposed offer or resale.

The company, the representatives and their affiliates will rely upon the truth and accuracy of the foregoing representations, acknowledgements and agreements.

This prospectus has been prepared on the basis that any offer of shares in any Relevant Member State will be made pursuant to an exemption under the Prospectus Directive from the requirement to publish a prospectus for offers of shares. Accordingly, any person making or intending to make an offer in that Relevant Member State of shares which are the subject of the offering contemplated in this prospectus may only do so in circumstances in which no obligation arises for the company or any of the underwriters to publish a prospectus pursuant to Article 3 of the Prospectus Directive in relation to such offer. Neither the company nor the underwriters have authorized, nor do they authorize, the making of any offer of shares in circumstances in which an obligation arises for the company or the underwriters to publish a prospectus for such offer.

For the purpose of the above provisions, 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 the shares to be offered so as to enable an investor to decide to purchase or subscribe the shares, as the same may be varied in the Relevant Member State by any measure implementing the Prospectus Directive in the Relevant Member State and the expression Prospectus Directive means Directive 2003/71/EC (including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member States) and includes any relevant implementing measure in the Relevant Member State and the expression 2010 PD Amending Directive means Directive 2010/73/E.

Notice to Prospective Investors in Canada

The shares may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 Prospectus Exemptions or subsection 73.3(1) of the Securities Act (Ontario), and are permitted clients, as defined in National Instrument 31-103 Registration

S-16

Table of Contents

Requirements, Exemptions and Ongoing Registrant Obligations. Any resale of the shares must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser's province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 of National Instrument 33-105 Underwriting Conflicts (NI 33-105), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

S-17

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 included in our Annual Report on Form 10-K for the year ended December 31, 2016, and the effectiveness of our internal control over financial reporting as of December 31, 2016, as set forth in their reports, which are incorporated by reference in this prospectus supplement and elsewhere in the registration statement. Our consolidated financial statements are incorporated by reference in reliance on Ernst & Young LLP's reports, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION; INFORMATION INCORPORATED BY REFERENCE

Available 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. Information filed with the SEC by us can be inspected and copied at the Public Reference Room maintained by the SEC at 100 F Street, N.E., Washington, D.C. 20549. You may also obtain copies of this information by mail from the Public Reference facilities of the SEC at prescribed rates. Further information on the operation of the SEC's Public Reference Room in Washington, D.C. can be obtained by calling the SEC at 1-800-SEC-0330. The SEC also maintains a website that contains reports, proxy and information statements and other information about issuers, such as us, who file electronically with the SEC. The address of that website is <http://www.sec.gov>.

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.

Incorporation by Reference

The SEC's rules allow us to incorporate by reference information into this prospectus supplement, which means that we can disclose important information to you by referring you to another document filed separately with the SEC. The information incorporated by reference is deemed to be part of this prospectus supplement and the accompanying prospectus, and subsequent information that we file with the SEC will automatically update and supersede that information. Any statement contained in a previously filed document incorporated by reference will be deemed to be modified or superseded for purposes of this prospectus supplement and accompanying prospectus to the extent that a

statement contained in this prospectus supplement or the accompanying prospectus modifies or replaces that statement.

S-18

Table of Contents

We incorporate by reference our documents listed below and any future filings made by us with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, which we refer to as the Exchange Act in this prospectus supplement, between the date of this prospectus supplement and the termination of the offering of the securities described in this prospectus supplement. We are not, however, incorporating by reference any documents or portions thereof, whether specifically listed below or filed in the future, that are not deemed filed with the SEC, including our Compensation Committee report and performance graph or any information furnished pursuant to Items 2.02 or 7.01 of Form 8-K or related exhibits furnished pursuant to Item 9.01 of Form 8-K.

This prospectus supplement and the accompanying prospectus incorporate by reference the documents set forth below that have previously been filed with the SEC:

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

our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2017 and June 30, 2017, filed with the SEC on May 4, 2017 and August 8, 2017, respectively;

our Current Reports on Form 8-K filed with the SEC on January 5, 2017, January 30, 2017, March 1, 2017, April 28, 2017, May 23, 2017, June 22, 2017, August 3, 2017, September 22, 2017 and September 29, 2017;

our Definitive Proxy Statement on Schedule 14A (other than information furnished rather than filed), filed with the SEC on April 12, 2017; and

the description of our Common Stock contained in our registration statement on Form 8-A, filed with the SEC on November 12, 2010 and any amendment or report filed with the SEC for the purpose of updating the description.

All reports and other documents we subsequently file pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act prior to the termination of this offering, including, but excluding any information furnished to, rather than filed with, the SEC, will also be incorporated by reference into this prospectus supplement and the accompanying prospectus and deemed to be part of this prospectus supplement and the accompanying prospectus from the date of the filing of such reports and documents.

You may request a free copy of any of the documents incorporated by reference in this prospectus supplement and the accompanying prospectus (other than exhibits, unless they are specifically incorporated by reference in the documents) by writing or telephoning us at the following address:

Zogenix, Inc.

Attn: Corporate Secretary

5858 Horton Street, Suite 455

Edgar Filing: ZOGENIX, INC. - Form 424B5

Emeryville, California 94608

(510) 550-8300

S-19

Table of Contents

PROSPECTUS

Common Stock

Preferred Stock

Debt Securities

Depository Shares

Warrants

Units

Rights

We may offer and sell the securities identified above, and any selling securityholders may offer and sell shares of common stock identified above, in each case from time to time in one or more offerings. This prospectus provides you with a general description of the securities. We will not receive any proceeds from the sale of our common stock by any selling securityholders.

Each time we or any of the selling securityholders offer and sell securities, we or such selling securityholders will provide a supplement to this prospectus that contains specific information about the offering and, if applicable, the selling securityholders, as well as the amounts, prices and terms of the securities. The supplement may also add, update or change information contained in this prospectus with respect to that offering. You should carefully read this prospectus and the applicable prospectus supplement, together with the documents we incorporate by reference, before you invest in any of our securities.

We may offer and sell the securities described in this prospectus and any prospectus supplement to or through one or more underwriters, dealers and agents, or directly to purchasers, or through a combination of these methods. In addition, any selling securityholders may offer and sell shares of our common stock from time to time, together or separately. If any underwriters, dealers or agents are involved in the sale of any of the securities, their names and any applicable purchase price, fee, commission or discount arrangement between or among them will be set forth, or will be calculable from the information set forth, in the applicable prospectus supplement. See the sections of this prospectus entitled *About this Prospectus* and *Plan of Distribution* for more information. No securities may be sold without delivery of this prospectus and the applicable prospectus supplement describing the method and terms of the offering of such securities.

Our common stock is listed on the Nasdaq Global Market under the symbol ZGNX. On September 29, 2017, the last reported sale price of our common stock was \$35.05 per share.

INVESTING IN OUR SECURITIES INVOLVES RISKS. SEE THE RISK FACTORS ON PAGE 2 OF THIS PROSPECTUS AND ANY SIMILAR SECTION CONTAINED IN THE APPLICABLE PROSPECTUS SUPPLEMENT CONCERNING FACTORS YOU SHOULD CONSIDER BEFORE INVESTING IN OUR SECURITIES.

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

The date of this prospectus is October 2, 2017

Table of Contents

TABLE OF CONTENTS

	Page
<u>About this Prospectus</u>	1
<u>Zogenix</u>	1
<u>Risk Factors</u>	2
<u>Forward-Looking Statements</u>	3
<u>Ratio of Earnings to Fixed Charges</u>	3
<u>Use of Proceeds</u>	4
<u>Dividend Policy</u>	4
<u>Description of Capital Stock</u>	5
<u>Description of Debt Securities</u>	9
<u>Description of Depositary Shares</u>	17
<u>Description of Warrants</u>	20
<u>Description of Units</u>	22
<u>Description of Rights</u>	23
<u>Global Securities</u>	24
<u>Selling Securityholders</u>	27
<u>Plan of Distribution</u>	27
<u>Legal Matters</u>	27
<u>Experts</u>	27
<u>Where You Can Find More Information</u>	27
<u>Information Incorporated by Reference</u>	29

Table of Contents

ABOUT THIS PROSPECTUS

Whenever we refer to Zogenix, we, our or us in this prospectus, we mean Zogenix, Inc. and its consolidated subsidiaries, unless the context otherwise requires. When we refer to you or yours, we mean the holders of the applicable series of securities.

This prospectus is part of a registration statement that we filed with the U.S. Securities and Exchange Commission (the SEC) as a well-known seasoned issuer as defined in Rule 405 under the Securities Act of 1933, as amended (the Securities Act) using a shelf registration process. By using a shelf registration statement, we may sell any combination of the securities described in this prospectus from time to time and in one or more offerings. In addition, selling securityholders to be named in a supplement to this prospectus may sell shares of our common stock from time to time in one or more offerings. This prospectus provides you with a general description of the securities we may offer. Each time that we or the selling securityholders offer and sell securities, we or the selling securityholders will provide a prospectus supplement to this prospectus that contains specific information about the securities being offered and sold and the specific terms of that offering. The prospectus supplement may also add, update or change information contained in this prospectus with respect to that offering. If there is any inconsistency between the information in this prospectus and the applicable prospectus supplement, you should rely on the prospectus supplement. Before purchasing any securities, you should carefully read both this prospectus and the applicable prospectus supplement, together with the additional information described under the heading **Where You Can Find More Information**.

You should rely only on the information contained in this prospectus, in an accompanying prospectus supplement or incorporated by reference herein or therein. Neither we, nor any selling securityholders, have authorized any other person to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. This prospectus and any accompanying prospectus supplement do not constitute an offer to sell or a solicitation of an offer to buy any securities other than the registered securities to which they relate, and this prospectus and any accompanying prospectus supplement do not constitute an offer to sell or the solicitation of an offer to buy securities in any jurisdiction where, or to any person to whom, it is unlawful to make such an offer or solicitation. You should assume that the information appearing in this prospectus and the applicable prospectus supplement to this prospectus is accurate as of the date on its respective cover, and that any information incorporated by reference is accurate only as of the date of the document incorporated by reference, unless we indicate otherwise. Our business, financial condition, results of operations and prospects may have changed since those dates.

ZOGENIX

We are a pharmaceutical company committed to developing and commercializing central nervous system, or CNS, therapies that address specific clinical needs for people living with orphan and other CNS disorders who need innovative treatment alternatives to help them improve their daily functioning. Our current primary area of focus is orphan or rare childhood-onset epilepsy disorders.

We currently own and control worldwide development and commercialization rights to ZX008, our lead product candidate. ZX008 is low-dose fenfluramine for the treatment of seizures associated with Dravet syndrome. Dravet syndrome is a rare and catastrophic form of pediatric epilepsy with life threatening consequences for patients and for which current treatment options are very limited. ZX008 has received orphan drug designation in the United States and European Union, or the EU, for the treatment of Dravet syndrome. In January 2016, we received notification of Fast Track designation from the U.S. Food and Drug Administration, or the FDA, for ZX008 for the treatment of Dravet syndrome. We initiated our Phase 3 clinical trials in North America (Study 1501) in January 2016 and in Europe and Australia in June 2016 (Study 1502). Study 1501 and Study 1502 are each identical randomized, double-blind placebo-controlled studies of ZX008 as adjunctive therapy for patients with uncontrolled seizures who

have Dravet syndrome. In January 2017, we announced our

Table of Contents

plan to report top-line results from Study 1501 and Study 1502 via a prospective merged study analysis approach whereby top-line results from the first 119 subjects randomized into either Study 1501 or 1502 would be reported initially as Study 1. In April 2017, we completed enrollment of Study 1 and, in September 2017, we announced positive top-line results for Study 1. In September 2016, we initiated the pharmacokinetic and safety profile portion of Study 1504, a double blind, randomized, two arm pivotal Phase 3 clinical trial of ZX008 in Dravet syndrome patients who are taking stiripentol, valproate and clobazam as part of their baseline standard care. In February 2017, we initiated the safety and efficacy portion of Study 1504, a two-arm study that compares ZX008 versus placebo across the titration and 12-week maintenance periods at multiple sites, which currently includes sites in France, the Netherlands, United States, Canada, Germany, the United Kingdom and Spain. Study 1504 will enroll 40 patients per treatment group. We expect to report top-line results from Study 1504 in the first half of 2018. We believe we are on track to submit applications for regulatory approvals for ZX008 in the United States and Europe in the second half of 2018.

Beginning in first quarter of 2016, we funded an open-label dose-finding twenty-patient investigator initiated study in patients with Lennox-Gastaut Syndrome, or LGS, another rare and catastrophic form of pediatric epilepsy with life threatening consequences for patients and for which current treatment options are very limited. In December 2016, we presented initial data from an interim analysis of the first 13 patients to have completed at least 12 weeks of this Phase 2 open-label, dose-finding clinical trial at the American Epilepsy Society Meeting. These data demonstrated that ZX008 provided clinically meaningful improvement in major motor seizure frequency in patients with severe refractory LGS, with seven out of 13 patients (54%) achieving at least a 50% reduction in the number of major motor seizures, at doses below the 0.8 mg/kg/day maximum. In addition, ZX008 was generally well tolerated, as expected based on our epilepsy program to date. We believe these data indicate that ZX008 has the potential to be a safe and effective adjunctive treatment for LGS. Based on the strength of the LGS data generated, in the first quarter of 2017, we submitted an investigational new drug, or IND, application to the FDA to initiate a Phase 3 program of ZX008 in LGS, which became effective in April 2017. We intend to initiate a Phase 3 program of ZX008 in LGS in the fourth quarter of 2017. In February 2017, ZX008 received orphan drug designation for the treatment of LGS in the EU. In June 2017, ZX008 received orphan drug designation for the treatment of LGS in the United States from the FDA.

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 5858 Horton Street, Suite 455, Emeryville, California 94608, 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 were to support the manufacture of the DosePro technology. Zogenix International Limited is a wholly-owned subsidiary of Zogenix Europe Limited which was acquired in October 2014. 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.

RISK FACTORS

Investment in any securities offered pursuant to this prospectus and the applicable prospectus supplement involves risks. You should carefully consider the risk factors incorporated by reference to our most recent Annual Report on Form 10-K and our subsequent Quarterly Reports on Form 10-Q or Current Reports on Form 8-K we file after the date of this prospectus, and all other information contained in or incorporated by reference into this prospectus, as updated by our subsequent filings under the Securities Exchange Act of 1934, as amended (the Exchange Act), and the risk factors and other information contained in the applicable prospectus supplement before acquiring any of such securities. The occurrence of any of these risks might cause you to lose all or part of your investment in the offered

securities. Please also refer to the section below entitled Forward-Looking Statements.

Table of Contents**FORWARD-LOOKING STATEMENTS**

This prospectus, including the documents incorporated by reference herein, contains forward-looking statements. All statements other than statements of historical facts contained in this prospectus and the documents incorporated by reference herein are forward-looking statements, including statements regarding our future results of operations and financial position, business strategy, prospective products, product approvals, research and development costs, timing and likelihood of success, plans and objectives of management for future operations and future results of anticipated products. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. This prospectus and the documents incorporated by reference herein also contain estimates and other statistical data made by independent parties and by us relating to market size and growth and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.

In some cases, you can identify forward-looking statements by terms such as may, will, should, expect, plan, anticipate, could, intend, target, project, contemplates, believes, estimates, predicts, potential or negative of these terms or other similar expressions. The forward-looking statements in this prospectus and the documents incorporated by reference herein are only predictions. We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our business, financial condition and results of operations. These forward-looking statements speak only as of the date of this prospectus and are subject to a number of risks, uncertainties and assumptions, which we discuss in greater detail in the documents incorporated by reference herein, including under the heading Risk Factors. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Moreover, we operate in an evolving environment. New risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all risk factors and uncertainties. Given these risks and uncertainties, you should not place undue reliance on these forward-looking statements. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained in this prospectus or the documents incorporated by reference herein, whether as a result of any new information, future events, changed circumstances or otherwise. 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.

RATIO OF EARNINGS TO FIXED CHARGES

Our ratios of earnings to fixed charges are as follows for the periods indicated:

	Six months ended		Year ended December 31,			
	June 30,	2016	2015	2014	2013	2012
	2017					
Ratio of earnings to fixed charges and preferred stock dividends ⁽¹⁾						20.2:1

(1)

Our earnings were inadequate to cover combined fixed charges and preferred stock dividends for the years ended December 31, 2012, 2013, 2015 and 2016 by \$33.9 million, \$72.6 million, \$57.6 million and \$69.6 million, respectively. Our earnings from continuing operations were inadequate to cover combined fixed charges and preferred stock dividends for the six months ended June 30, 2017 by \$43.6 million.

Table of Contents

For purposes of calculating the ratio of earnings to combined fixed charges and preferred stock dividends, earnings represent net income (loss) from continuing operations before provision for income taxes plus fixed charges. Fixed charges consist of interest expense (including amortization of debt issuance costs and debt discount) and estimated interest component of rent. For the periods indicated above, we had no outstanding shares of preferred stock with required dividend payments. Therefore, the ratios of earnings to combined fixed charges and preferred stock dividends are identical to the ratios presented in the table above.

USE OF PROCEEDS

We intend to use the net proceeds from the sale of the securities as set forth in the applicable prospectus supplement. We will not receive any of the proceeds from the sale of common stock being offered by any of the selling securityholders.

DIVIDEND POLICY

We have never declared or paid any cash dividends on our capital stock and do not anticipate paying any cash dividends in the foreseeable future. We expect to retain available cash to finance ongoing operations and the potential growth of our business. Any future determination to pay dividends on our common stock will be at the discretion of our board of directors and will depend upon, among other factors, our results of operations, financial condition, capital requirements, business prospects and other factors our board of directors may deem relevant, and subject to the restrictions contained in any future financing instruments. In addition, our ability to pay dividends is currently restricted by the terms of a loan and security agreement we entered into with Oxford Finance LLC and Silicon Valley Bank in December 2014.

Table of Contents

DESCRIPTION OF CAPITAL STOCK

The following description of our capital stock is not complete and may not contain all the information you should consider before investing in our capital stock. This description is summarized from, and qualified in its entirety by reference to, our amended and restated certificate of incorporation, which has been publicly filed with the SEC. See [Where You Can Find More Information](#) and [Incorporation by Reference](#).

Our authorized capital stock as of June 30, 2017 consists of:

50,000,000 shares of common stock, \$0.001 par value; and

10,000,000 shares of preferred stock, \$0.001 par value.

Common Stock

As of June 30, 2017, there were 24,839,141 shares of our common stock outstanding.

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.

The rights, preferences and privileges of holders of common stock are subject to and may be adversely affected by the rights of the holders of shares of any series of preferred stock that we may designate and issue in the future.

Fully Paid and Nonassessable

All outstanding shares of common stock are duly authorized, validly issued, fully paid and nonassessable.

Transfer Agent and Registrar

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

Table of Contents

Preferred Stock

We currently have no outstanding shares of preferred stock. Prior to issuance of shares of each series of our undesignated preferred stock, our board of directors is required by the Delaware General Corporation Law, or DGCL, and our amended and restated 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 amended and restated certificate of incorporation and our amended and restated 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.

We will describe in a prospectus supplement relating to the class or series of preferred stock being offered the following terms:

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 offering price of the preferred stock;

the dividend rate(s), period(s) or payment date(s) or method(s) of calculation applicable to the preferred stock;

whether dividends are cumulative or non-cumulative and, if cumulative, the date from which dividends on the preferred stock will 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 provision for redemption, if applicable, of the preferred stock;

any listing of the preferred stock on any securities exchange;

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

voting rights, if any, of the preferred stock;

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

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

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

any limitations on issuance of any class or series of preferred stock ranking senior to or on a parity with the class or series of 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 of the preferred stock.

Table of Contents

Unless we specify otherwise in the applicable prospectus supplement, the preferred stock will rank, relating to dividends and upon our liquidation, dissolution or winding up:

senior to all classes or series of our common stock and to all of our equity securities ranking junior to the preferred stock;

on a parity with all of our equity securities the terms of which specifically provide that the equity securities rank on a parity with the preferred stock; and

junior to all of our equity securities the terms of which specifically provide that the equity securities rank senior to the preferred stock.

The term equity securities does not include convertible debt securities.

Warrants

As of June 30, 2017, there were outstanding warrants to purchase 1,974,842 shares of our common stock, of which warrants exercisable for 1,901,918 shares of common stock expired unexercised on July 27, 2017. The warrants contain customary anti-dilution and net issuance provisions and are not callable by us. 1,974,842 shares of common stock issuable upon the exercise of outstanding warrants with a weighted average exercise price of \$20.92 per share, of which warrants exercisable for 1,901,918 shares of common stock expired unexercised on July 27, 2017.

Anti-Takeover Effects of Delaware Law and Our Certificate of Incorporation and Bylaws

Some provisions of Delaware law, our amended and restated certificate of incorporation 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.

Table of Contents

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 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.

Removal of Directors

Our amended and restated certificate of incorporation 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 two-thirds 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 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 two-thirds of the total voting power of all of our

outstanding voting stock.

The provisions of Delaware law, our amended and restated certificate of incorporation 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

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. To the extent the information contained in the prospectus supplement differs from this summary description, you should rely on the information in the prospectus supplement.

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 a trustee named in the prospectus supplement. 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.

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 on a particular series of debt securities 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 debt 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 the terms and conditions upon which the debt securities of a particular 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 U.S. 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, and premium and interest on the debt securities will be made;

if payments of principal of, or 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, and premium, if any, and 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 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;

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 debt 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;

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; and

whether any of our direct or indirect subsidiaries will guarantee the debt securities of that series, including the terms of subordination, if any, of such guarantees. (Section 2.2)

Table of Contents

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.

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 premium, if any, 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 (DTC 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 the section entitled Global Securities for more information.

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 that 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) that could adversely affect holders of debt securities.

Table of Contents

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 Zogenix) 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;

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

certain other conditions are met.

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 or any debt security (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; or

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.

We will provide the trustee written notice of any Default or Event of Default within 30 days of becoming aware of the occurrence of such Default or Event of Default, which notice will describe in reasonable detail the status of such Default or Event of Default and what action we are taking or propose to take in respect thereof. (Section 6.1)

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

Table of Contents

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 may refuse to perform any duty or exercise any of its rights or powers under the indenture, unless the trustee receives indemnity satisfactory to it against any cost, liability or expense that might be incurred by it in performing such duty or exercising such right or power. (Section 7.1(e)) Subject to certain rights of the 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 indemnity or security satisfactory to the trustee, 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, and 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 securities of any series and if it is known to a responsible officer of the trustee, the trustee shall mail to each holder of the securities of that series notice of a Default or Event of Default within 90 days after it occurs or, if later, after a responsible officer of the trustee has knowledge of such Default or Event of Default. 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, amend or supplement 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;

Table of Contents

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 add guarantees with respect to debt securities of any series or secure debt securities of any series;

to surrender any of our rights or powers under the indenture;

to add covenants or Events of Default for the benefit of the holders of debt securities of any series;

to comply with the applicable procedures of the applicable depositary;

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 SEC in order to effect or maintain the qualification of the indenture under the Trust Indenture Act. (Section 9.1)

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 or Event of Default in the payment of the principal of, or 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, and 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

Table of Contents

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 or U.S. government obligations 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.

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 U.S. Internal Revenue Service a ruling or, since the date of execution of the indenture, there has been a change in the applicable U.S. 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 U.S. federal income tax purposes as a result of the deposit, defeasance and discharge and will be subject to U.S. 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 that 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 we have received from, or there has been published by, the U.S. Internal Revenue Service a ruling or, since the date of execution of the indenture, there has been a change in the applicable U.S. 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

Table of Contents

series will not recognize income, gain or loss for U.S. federal income tax purposes as a result of the deposit and related covenant defeasance and will be subject to U.S. 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)

No Personal Liability of Directors, Officers, Employees or Stockholders

None of our past, present or future directors, officers, employees or stockholders, as such, will have any liability for any of our obligations under the debt securities or the indenture or for any claim based on, or in respect or by reason of, such obligations or their creation. By accepting a debt security, each holder waives and releases all such liability. This waiver and release is part of the consideration for the issue of the debt securities. However, this waiver and release may not be effective to waive liabilities under U.S. federal securities laws, and it is the view of the SEC that such a waiver is against public policy.

Governing Law

The indenture and the debt securities, including any claim or controversy arising out of or relating to the indenture or the debt securities, will be governed by the laws of the State of New York. (Section 10.10)

Table of Contents

DESCRIPTION OF DEPOSITARY SHARES

We may, at our option, elect to offer depositary shares rather than full shares of preferred stock. Each depositary share will represent ownership of and entitlement to all rights and preferences of a fraction of a share of preferred stock of a specified series (including dividend, voting, redemption and liquidation rights). The applicable fraction will be specified in a prospectus supplement. The shares of preferred stock represented by the depositary shares will be deposited with a depositary named in the applicable prospectus supplement, under a deposit agreement among us, the depositary and the holders of the certificates evidencing depositary shares, or depositary receipts. Depositary receipts will be delivered to those persons purchasing depositary shares in the offering. The depositary will be the transfer agent, registrar and dividend disbursing agent for the depositary shares. Holders of depositary receipts agree to be bound by the deposit agreement, which requires holders to take certain actions such as filing proof of residence and paying certain charges.

The summary of the terms of the depositary shares contained in this prospectus does not purport to be complete and is subject to, and qualified in its entirety by, the provisions of the deposit agreement and our certificate of incorporation and the certificate of designation that are, or will be, filed with the SEC for the applicable series of preferred stock.

Dividends

The depositary will distribute all cash dividends or other cash distributions received in respect of the series of preferred stock represented by the depositary shares to the record holders of depositary receipts in proportion to the number of depositary shares owned by such holders on the relevant record date, which will be the same date as the record date fixed by us for the applicable series of preferred stock. The depositary, however, will distribute only such amount as can be distributed without attributing to any depositary share a fraction of one cent, and any balance not so distributed will be added to and treated as part of the next sum received by the depositary for distribution to record holders of depositary receipts then outstanding.

In the event of a distribution other than in cash, the depositary will distribute property received by it to the record holders of depositary receipts entitled thereto, in proportion, as nearly as may be practicable, to the number of depositary shares owned by such holders on the relevant record date, unless the depositary determines (after consultation with us) that it is not feasible to make such distribution, in which case the depositary may (with our approval) adopt any other method for such distribution as it deems equitable and appropriate, including the sale of such property (at such place or places and upon such terms as it may deem equitable and appropriate) and distribution of the net proceeds from such sale to such holders.

Liquidation Preference

In the event of the liquidation, dissolution or winding up of the affairs of Zogenix, whether voluntary or involuntary, the holders of each depositary share will be entitled to the fraction of the liquidation preference accorded each share of the applicable series of preferred stock as set forth in the applicable prospectus supplement.

Redemption

If the series of preferred stock represented by the applicable series of depositary shares is redeemable, such depositary shares will be redeemed from the proceeds received by the depositary resulting from the redemption, in whole or in part, of the preferred stock held by the depositary. Whenever we redeem any preferred stock held by the depositary, the depositary will redeem as of the same redemption date the number of depositary shares representing the shares of preferred stock so redeemed. The depositary will mail the notice of redemption promptly upon receipt of such notice

from us and not less than 30 nor more than 60 days prior to the date fixed for redemption of the preferred stock and the depositary shares to the record holders of the depositary receipts.

Table of Contents

Voting

Promptly upon receipt of notice of any meeting at which the holders of the series of preferred stock represented by the applicable series of depositary shares are entitled to vote, the depositary will mail the information contained in such notice of meeting to the record holders of the depositary receipts as of the record date for such meeting. Each such record holder of depositary receipts will be entitled to instruct the depositary as to the exercise of the voting rights pertaining to the number of shares of preferred stock represented by such record holder's depositary shares. The depositary will endeavor, insofar as practicable, to vote such preferred stock represented by such depositary shares in accordance with such instructions, and we will agree to take all action which may be deemed necessary by the depositary in order to enable the depositary to do so. The depositary will abstain from voting any of the preferred stock to the extent that it does not receive specific instructions from the holders of depositary receipts.

Withdrawal of Preferred Stock

Upon surrender of depositary receipts at the principal office of the depositary and payment of any unpaid amount due the depositary, and subject to the terms of the deposit agreement, the owner of the depositary shares evidenced thereby is entitled to delivery of the number of whole shares of preferred stock and all money and other property, if any, represented by such depositary shares. Partial shares of preferred stock will not be issued. If the depositary receipts delivered by the holder evidence a number of depositary shares in excess of the number of depositary shares representing the number of whole shares of preferred stock to be withdrawn, the depositary will deliver to such holder at the same time a new depositary receipt evidencing such excess number of depositary shares. Holders of preferred stock thus withdrawn will not thereafter be entitled to deposit such shares under the deposit agreement or to receive depositary receipts evidencing depositary shares therefor.

Amendment and Termination of Deposit Agreement

The form of depositary receipt evidencing the depositary shares and any provision of the deposit agreement may at any time and from time to time be amended by agreement between us and the depositary. However, any amendment which materially and adversely alters the rights of the holders (other than any change in fees) of depositary shares will not be effective unless such amendment has been approved by at least a majority of the depositary shares then outstanding. No such amendment may impair the right, subject to the terms of the deposit agreement, of any owner of any depositary shares to surrender the depositary receipt evidencing such depositary shares with instructions to the depositary to deliver to the holder of the preferred stock and all money and other property, if any, represented thereby, except in order to comply with mandatory provisions of applicable law.

The deposit agreement will be permitted to be terminated by us upon not less than 30 days prior written notice to the applicable depositary if a majority of each series of preferred stock affected by such termination consents to such termination, whereupon such depositary will be required to deliver or make available to each holder of depositary receipts, upon surrender of the depositary receipts held by such holder, such number of whole or fractional shares of preferred stock as are represented by the depositary shares evidenced by such depositary receipts together with any other property held by such depositary with respect to such depositary receipts. In addition, the deposit agreement will automatically terminate if (a) all outstanding depositary shares thereunder shall have been redeemed, (b) there shall have been a final distribution in respect of the related preferred stock in connection with any liquidation, dissolution or winding-up of Zogenix and such distribution shall have been distributed to the holders of depositary receipts evidencing the depositary shares representing such preferred stock, or (c) each share of the related preferred stock shall have been converted into stock of Zogenix not so represented by depositary shares.

Charges of Depositary

We will pay all transfer and other taxes and governmental charges arising solely from the existence of the depositary arrangements. We will pay charges of the depositary in connection with the initial deposit of the

Table of Contents

preferred stock and initial issuance of the depositary shares, and redemption of the preferred stock and all withdrawals of preferred stock by owners of depositary shares. Holders of depositary receipts will pay transfer, income and other taxes and governmental charges and certain other charges as are provided in the deposit agreement to be for their accounts. In certain circumstances, the depositary may refuse to transfer depositary shares, may withhold dividends and distributions and sell the depositary shares evidenced by such depositary receipt if such charges are not paid. The applicable prospectus supplement will include information with respect to fees and charges, if any, in connection with the deposit or substitution of the underlying securities, the receipt and distribution of dividends, the sale or exercise of rights, the withdrawal of the underlying security, and the transferring, splitting or grouping of receipts. The applicable prospectus supplement will also include information with respect to the right to collect the fees and charges, if any, against dividends received and deposited securities.

Miscellaneous

The depositary will forward to the holders of depositary receipts all notices, reports and proxy soliciting material from us which are delivered to the depositary and which we are required to furnish to the holders of the preferred stock. In addition, the depositary will make available for inspection by holders of depositary receipts at the principal office of the depositary, and at such other places as it may from time to time deem advisable, any notices, reports and proxy soliciting material received from us which are received by the depositary as the holder of preferred stock. The applicable prospectus supplement will include information about the rights, if any, of holders of receipts to inspect the transfer books of the depositary and the list of holders of receipts.

Neither the depositary nor Zogenix assumes any obligation or will be subject to any liability under the deposit agreement to holders of depositary receipts other than for its negligence or willful misconduct. Neither the depositary nor Zogenix will be liable if it is prevented or delayed by law or any circumstance beyond its control in performing its obligations under the deposit agreement. The obligations of Zogenix and the depositary under the deposit agreement will be limited to performance in good faith of their duties thereunder, and they will not be obligated to prosecute or defend any legal proceeding in respect of any depositary shares or preferred stock unless satisfactory indemnity is furnished. Zogenix and the depositary may rely on written advice of counsel or accountants, on information provided by holders of the depositary receipts or other persons believed in good faith to be competent to give such information, and on documents believed to be genuine and to have been signed or presented by the proper party or parties.

In the event the depositary shall receive conflicting claims, requests or instructions from any holders of depositary receipts, on the one hand, and us, on the other hand, the depositary shall be entitled to act on such claims, requests or instructions received from us.

Resignation and Removal of Depositary

The depositary may resign at any time by delivering to us notice of its election to do so, and we may at any time remove the depositary, any such resignation or removal to take effect upon the appointment of a successor depositary and its acceptance of such appointment. Such successor depositary must be appointed within 60 days after delivery of the notice for resignation or removal and must be a bank or trust company having its principal office in the United States and having a combined capital and surplus of at least \$150,000,000.

Table of Contents

DESCRIPTION OF WARRANTS

We may issue warrants for the purchase of shares of our common stock or preferred stock or of debt securities. We may issue warrants independently or together with other securities, and the warrants may be attached to or separate from any offered securities. Each series of warrants will be issued under a separate warrant agreement to be entered into between us and the investors or a warrant agent. The following summary of material provisions of the warrants and warrant agreements is subject to, and qualified in its entirety by reference to, all the provisions of the warrant agreement and warrant certificate applicable to a particular series of warrants. The terms of any warrants offered under a prospectus supplement may differ from the terms described below. We urge you to read the applicable prospectus supplement, as well as the complete warrant agreements and warrant certificates that contain the terms of the warrants.

The particular terms of any issue of warrants will be described in the prospectus supplement relating to the issue. Those terms may include:

the number of shares of common stock or preferred stock purchasable upon the exercise of warrants to purchase such shares and the price at which such number of shares may be purchased upon such exercise;

the designation, stated value and terms (including, without limitation, liquidation, dividend, conversion and voting rights) of the series of preferred stock purchasable upon exercise of warrants to purchase preferred stock;

the principal amount of debt securities that may be purchased upon exercise of a debt warrant and the exercise price for the warrants, which may be payable in cash, securities or other property;

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

the terms of any rights to redeem or call the warrants;

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

U.S. federal income tax consequences applicable to the warrants; and

any additional terms of the warrants, including terms, procedures and limitations relating to the exchange, exercise and settlement of the warrants.

Holders of equity warrants will not be entitled to:

vote, consent or receive dividends;

receive notice as stockholders with respect to any meeting of stockholders for the election of our directors or any other matter; or

exercise any rights as stockholders of Zogenix.

Each warrant will entitle its holder to purchase the principal amount of debt securities or the number of shares of preferred stock or common stock at the exercise price set forth in, or calculable as set forth in, the applicable prospectus supplement. Unless we otherwise specify in the applicable prospectus supplement, holders of the warrants may exercise the warrants at any time up to the specified time on the expiration date that we set forth in the applicable prospectus supplement. After the close of business on the expiration date, unexercised warrants will become void.

Table of Contents

A holder of warrant certificates may exchange them for new warrant certificates of different denominations, present them for registration of transfer and exercise them at the corporate trust office of the warrant agent or any other office indicated in the applicable prospectus supplement. Until any warrants to purchase debt securities are exercised, the holder of the warrants will not have any rights of holders of the debt securities that can be purchased upon exercise, including any rights to receive payments of principal, premium or interest on the underlying debt securities or to enforce covenants in the applicable indenture. Until any warrants to purchase common stock or preferred stock are exercised, the holders of the warrants will not have any rights of holders of the underlying common stock or preferred stock, including any rights to receive dividends or payments upon any liquidation, dissolution or winding up on the common stock or preferred stock, if any.

Table of Contents

DESCRIPTION OF UNITS

We may issue units consisting of any combination of the other types of securities offered under this prospectus in one or more series. We may evidence each series of units by unit certificates that we will issue under a separate agreement. We may enter into unit agreements with a unit agent. Each unit agent will be a bank or trust company that we select. We will indicate the name and address of the unit agent in the applicable prospectus supplement relating to a particular series of units.

The following description, together with the additional information included in any applicable prospectus supplement, summarizes the general features of the units that we may offer under this prospectus. You should read any prospectus supplement that we may authorize to be provided to you related to the series of units being offered, as well as the complete unit agreements that contain the terms of the units. Specific unit agreements will contain additional important terms and provisions and we will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from another report that we file with the SEC, the form of each unit agreement relating to units offered under this prospectus.

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 U.S. federal income tax considerations applicable to the units; and

any other terms of the units and their constituent securities.

Table of Contents

DESCRIPTION OF RIGHTS

General

We may issue rights to purchase our common stock, preferred stock, warrants or units. Each series of rights will be issued under a separate rights agreement to be entered into between us and a bank or trust company, as rights agent. The rights agent will act solely as our agent in connection with the certificates relating to the rights of the series of certificates and will not assume any obligation or relationship of agency or trust for or with any holders of rights certificates or beneficial owners of rights. The statements made in this section relating to the rights are summaries only. These summaries are not complete. When we issue rights, we will provide the specific terms of the rights and the applicable rights agreement in a prospectus supplement. To the extent the information contained in the prospectus supplement differs from this summary description, you should rely on the information in the prospectus supplement. For more detail, we refer you to the applicable rights agreement itself, which we will file as an exhibit to, or incorporate by reference in, the registration statement of which this prospectus is a part.

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

the date of determining the stockholders entitled to the rights distribution;

the title and aggregate number of shares of common stock, preferred stock, warrants or units purchasable upon exercise of the rights;

the exercise price;

the aggregate number of rights issued;

the date, if any, on and after which the rights will be separately transferable;

the date on which the right to exercise the rights will commence and the date on which the right will expire;

a discussion of certain U.S. federal income tax considerations applicable to an investment in the rights; and

any other terms of the rights, including terms, procedures and limitations relating to the distribution, exchange and exercise of the rights.

Exercise of Rights

Each right will entitle the holder of rights to purchase for cash the principal amount of shares of common stock, preferred stock, warrants or units at the exercise price provided in the applicable prospectus supplement. Rights may

be exercised at any time up to the close of business on the expiration date for the rights provided in the applicable prospectus supplement. After the close of business on the expiration date, all unexercised rights will be void.

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

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 (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 (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 SEC.

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, unless a shorter period is satisfactory to the applicable trustee or other designated party.

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

SELLING SECURITYHOLDERS

Information about selling securityholders, where applicable, will be set forth in a prospectus supplement, in a post-effective amendment or in filings we make with the SEC under the Exchange Act that are incorporated by reference.

PLAN OF DISTRIBUTION

We or any of the selling securityholders may sell the offered securities from time to time:

through underwriters or dealers;

through agents;

directly to one or more purchasers; or

through a combination of any of these methods of sale.

We will identify the specific plan of distribution, including any underwriters, dealers, agents or direct purchasers and their compensation in the applicable prospectus supplement.

LEGAL MATTERS

Latham & Watkins LLP, San Diego, California, will pass upon certain legal matters relating to the issuance and sale of the securities offered hereby on behalf of Zogenix. Additional legal matters may be passed upon for us, the selling securityholders or any underwriters, dealers or agents, by counsel that we will name in the applicable prospectus supplement.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2016, and the effectiveness of our internal control over financial reporting as of December 31, 2016, as set forth in their reports, which are incorporated by reference in this prospectus supplement and elsewhere in the registration statement. Our consolidated financial statements are incorporated by reference in reliance on Ernst & Young LLP's reports, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We file reports, proxy statements and other information with the SEC. Information filed with the SEC by us can be inspected and copied at the Public Reference Room maintained by the SEC at 100 F Street, N.E., Washington, D.C. 20549. You may also obtain copies of this information by mail from the Public Reference Room of the SEC at prescribed rates. Further information on the operation of the SEC's Public Reference Room in Washington, D.C. can be obtained by calling the SEC at 1-800-SEC-0330. The SEC also maintains a website that contains reports, proxy and

information statements and other information about issuers, such as us, who file electronically with the SEC. You may also access filed documents at the SEC's website at www.sec.gov or by accessing the Investor Relations section of our website at www.zogenix.com. The information found on or accessed through our website is not, and should not be deemed to be, a part of this prospectus.

Table of Contents

This prospectus and any prospectus supplement are part of a registration statement that we filed with the SEC and do not contain all of the information in the registration statement. The full registration statement may be obtained from the SEC or us, as provided above. Forms of the indenture and other documents establishing the terms of the offered securities are or may be filed as exhibits to the registration statement. Statements in this prospectus or any prospectus supplement about these documents are summaries and each statement is qualified in all respects by reference to the document to which it refers. You should refer to the actual documents for a more complete description of the relevant matters.

Table of Contents

INFORMATION INCORPORATED BY REFERENCE

The SEC's rules allow us to incorporate by reference information into this prospectus, which means that we can disclose important information to you by referring you to another document filed separately with the SEC. The information incorporated by reference is deemed to be part of this prospectus, and subsequent information that we file with the SEC will automatically update and supersede that information. Any statement contained in a previously filed document incorporated by reference will be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained in this prospectus modifies or replaces that statement.

We incorporate by reference our documents listed below and any future filings made by us with the SEC 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 of the securities described in this prospectus. We are not, however, incorporating by reference any documents or portions thereof, whether specifically listed below or filed in the future, that are not deemed filed with the SEC, including our Compensation Committee report and performance graph or any information furnished pursuant to Items 2.02 or 7.01 of Form 8-K or related exhibits furnished pursuant to Item 9.01 of Form 8-K.

This prospectus and any accompanying prospectus supplement incorporate by reference the documents set forth below that have previously been filed with the SEC:

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

our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2017 and June 30, 2017, filed with the SEC on May 4, 2017 and August 8, 2017, respectively;

our Current Reports on Form 8-K filed with the SEC on January 5, 2017, January 30, 2017, March 1, 2017, April 28, 2017, May 23, 2017, June 22, 2017, August 3, 2017, September 22, 2017 and September 29, 2017;

our Definitive Proxy Statement on Schedule 14A (other than information furnished rather than filed), filed with the SEC on April 12, 2017; and

the description of our Common Stock contained in our registration statement on Form 8-A, filed with the SEC on November 12, 2010 and any amendment or report filed with the SEC for the purpose of updating the description.

All reports and other documents we subsequently file pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act prior to the termination of this offering, but excluding any information furnished to, rather than filed with, the SEC, will also be incorporated by reference into this prospectus and deemed to be part of this prospectus from the date of the filing of such reports and documents.

You may request a free copy of any of the documents incorporated by reference in this prospectus by writing or telephoning us at the following address:

Edgar Filing: ZOGENIX, INC. - Form 424B5

Zogenix, Inc.

Attn: Corporate Secretary

5858 Horton Street, Suite 455

Emeryville, California 94608

(510) 550-8300

Exhibits to the filings will not be sent, however, unless those exhibits have specifically been incorporated by reference in this prospectus and any accompanying prospectus supplement.

Table of Contents

4,300,000 Shares

Common Stock

Leerink Partners

Stifel

Mizuho Securities

JMP Securities

LifeSci Capital

October , 2017