

OTONOMY, INC.
Form S-3
September 10, 2018
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As filed with the Securities and Exchange Commission on September 10, 2018

Registration No. 333-

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM S-3

REGISTRATION STATEMENT

Under

The Securities Act of 1933

OTONOMY, INC.

(Exact name of Registrant as specified in its charter)

Delaware
(State or other jurisdiction of
incorporation or organization)

4796 Executive Drive

26-2590070
(I.R.S. Employer
Identification Number)

San Diego, California 92121

(619) 323-2200

(Address, including zip code, and telephone number, including area code, of Registrant's principal executive offices)

David A. Weber, Ph.D.

President and Chief Executive Officer

Otonomy, Inc.

4796 Executive Drive

San Diego, California 92121

(619) 323-2200

(Name, address, including zip code, and telephone number, including area code, of agent for service)

Copies to:

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650 Page Mill Road

Palo Alto, California 94304

(650) 493-9300

Approximate date of commencement of proposed sale to the public: From time to time, after the effective date of this Registration Statement.

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

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

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

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

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

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

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

| | |
|-------------------------|---------------------------|
| Large Accelerated filer | Accelerated filer |
| Non-accelerated filer | Smaller reporting company |
| Emerging growth company | |

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

CALCULATION OF REGISTRATION FEE

| Title of Each Class of | Amount | Proposed | Proposed | |
|--|---------------------------------|-------------------------------|-------------------------------------|---------------------------------------|
| | to be | Maximum | Maximum | Amount of |
| Securities to be Registered⁽¹⁾ | Registered⁽²⁾ | Offering Price | Offering Price⁽²⁾ | Registration Fee⁽⁴⁾ |
| | | Per Unit⁽²⁾ | | |
| Common Stock, \$0.001 par value per share | | | | |
| Preferred Stock, \$0.001 par value per share | | | | |
| Depositary Shares | | | | |
| Warrants | | | | |
| Debt Securities | | | | |
| Subscription Rights | | | | |
| Units ⁽³⁾ | | | | |
| Total Offering | | | \$150,000,000 | \$18,675.00 |

(1) The securities registered hereunder include such indeterminate (a) number of shares of common stock, (b) number of shares of preferred stock, (c) number of depositary shares, (d) debt securities, (e) warrants to purchase common

stock, preferred stock or debt securities of the registrant, (f) subscription rights to purchase common stock, preferred stock or debt securities of the registrant, and (g) units, consisting of some or all of these securities, as may be sold from time to time by the registrant. Any securities registered hereunder may be sold separately or as units with other securities registered hereunder. This registration statement covers offers, sales and other distributions of the securities listed in this table, from time to time, at prices to be determined, as well as securities distributable in connection with or upon conversion, exercise or exchange of other securities so offered, sold or distributed. This registration statement also covers shares of common stock, shares of preferred stock, depositary shares and warrants that may be offered or sold under delayed delivery contracts pursuant to which the counterparty may be required to purchase such securities, as well as such contracts themselves. Such contracts would be issued with the shares of common stock, shares of preferred stock, depositary shares or warrants. Pursuant to Rule 416(a) under the Securities Act of 1933, as amended (the Securities Act), this registration statement also covers any additional securities that may be offered or issued in connection with any stock split, stock dividend or similar transaction.

- (2) The amount to be registered and the proposed maximum aggregate offering price per unit are not specified as to each class of securities being registered pursuant to General Instruction II.D of Form S-3. The maximum aggregate offering price of all securities issued by the registrants pursuant to this Registration Statement shall not have a maximum aggregate offering price that exceeds \$150,000,000 in U.S. dollars (or the equivalent thereof in one or more foreign currencies, foreign currency units or composite currencies). The proposed maximum offering price per unit will be determined from time to time by the registrant in connection with, and at the time of, issuance by the registrant of the securities registered hereunder. The registrant has estimated the proposed maximum aggregate offering price solely for the purpose of calculating the registration fee pursuant to Rule 457(o) under the Securities Act. Separate consideration may not be received for shares of common stock or preferred stock that are issued upon conversion or exchange of shares of preferred stock or depositary shares registered hereunder or for shares of preferred stock distributed in accordance with, or upon termination of, a deposit arrangement for depositary shares.
- (3) Consisting of some or all of the securities listed above, in any combination, including common stock, preferred stock, debt securities, warrants and subscription rights.
- (4) Otonomy, Inc. previously paid \$34,860.00 in connection with the registration statement on Form S-3 (SEC File No. 333-206752) filed on September 3, 2015, and declared effective by the Commission on September 14, 2015, of which \$21,497.00 was not used and will be applied to the amount listed above. Accordingly, no filing fee is currently due in connection with the filing of this Registration Statement and \$2,822.00 remains available to offset future filing fees.

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

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

SUBJECT TO COMPLETION, DATED SEPTEMBER 10, 2018

PROSPECTUS

\$150,000,000

Otonomy, Inc.

By this prospectus, Otonomy may offer, from time to time:

Common stock

Preferred stock

Depositary shares

Warrants

Debt securities

Subscription Rights

Units

All of the securities listed above may be sold separately or as units with other securities.

We may offer and sell from time to time, in one or more series or issuances and on terms that we will determine at the time of the offering, any combination of the securities described in this prospectus, either individually or as units comprising one or more of the other classes of securities, up to an aggregate amount of \$150,000,000.

We will provide specific terms of any offering in a supplement to this prospectus. Any prospectus supplement may also add, update or change information contained in this prospectus. You should carefully read this prospectus and the applicable prospectus supplement as well as the documents incorporated or deemed to be incorporated by reference in this prospectus before you purchase any of the securities offered hereby.

These securities may be offered and sold in the same offering or in separate offerings; to or through underwriters, dealers and agents; or directly to purchasers. The names of any underwriters, dealers or agents involved in the sale of our securities, their compensation and any over-allotment options held by them will be described in the applicable prospectus supplement. See the section titled Plan of Distribution.

Our common stock is listed on The NASDAQ Global Select Market under the symbol OTIC . We will provide information in any applicable prospectus supplement regarding any listing of securities other than shares of our common stock on any securities exchange.

We are an emerging growth company as defined under the federal securities laws and, as such, have elected to comply with certain reduced public company reporting requirements.

INVESTING IN OUR SECURITIES INVOLVES SIGNIFICANT RISKS. YOU SHOULD REVIEW CAREFULLY THE RISK FACTORS ON PAGE 6 OF THIS PROSPECTUS AND IN THE APPLICABLE PROSPECTUS SUPPLEMENT BEFORE INVESTING IN OUR SECURITIES.

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

The date of this prospectus is _____, 2018

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement on Form S-3 that we filed with the United States Securities and Exchange Commission, or the SEC, using a shelf registration process. Under this shelf process, we may, from time to time, offer and sell any combination of the securities described in this prospectus in one or more offerings up to a total amount of \$150,000,000.

This prospectus provides you with a general description of the securities we may offer. Each time we sell securities, we will provide a prospectus supplement that will contain specific information about the terms of that offering. The prospectus supplement may also add to, update or change information contained in the prospectus and, accordingly, to the extent inconsistent, information in this prospectus is superseded by the information in the prospectus supplement.

The prospectus supplement to be attached to the front of this prospectus may describe, as applicable: the terms of the securities offered; the initial price to the public; the price paid for the securities; net proceeds; and the other specific terms related to the offering of the securities.

You should only rely on the information contained or incorporated by reference in this prospectus and any prospectus supplement or free writing prospectus relating to a particular offering. No person has been authorized to give any information or make any representations in connection with this offering other than those contained or incorporated by reference in this prospectus, any accompanying prospectus supplement and any related free writing prospectus in connection with the offering described herein and therein, and, if given or made, such information or representations must not be relied upon as having been authorized by us. Neither this prospectus nor any prospectus supplement nor any related free writing prospectus shall constitute an offer to sell or a solicitation of an offer to buy offered securities in any jurisdiction in which it is unlawful for such person to make such an offering or solicitation. This prospectus does not contain all of the information included in the registration statement. For a more complete understanding of the offering of the securities, you should refer to the registration statement, including its exhibits.

You should read the entire prospectus and any prospectus supplement and any related free writing prospectus, as well as the documents incorporated by reference into this prospectus or any prospectus supplement or any related free writing prospectus, before making an investment decision. Neither the delivery of this prospectus or any prospectus supplement or any free writing prospectus nor any sale made hereunder shall under any circumstances imply that the information contained or incorporated by reference herein or in any prospectus supplement or free writing prospectus is correct as of any date subsequent to the date hereof or of such prospectus supplement or free writing prospectus, as applicable. You should assume that the information appearing in this prospectus, any prospectus supplement or any document incorporated by reference is accurate only as of the date of the applicable documents, regardless of the time of delivery of this prospectus or any sale of securities. Our business, financial condition, results of operations and prospects may have changed since that date.

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Prospectus Summary

This summary description about us and our business highlights selected information contained elsewhere in this prospectus or incorporated in this prospectus by reference. This summary does not contain all of the information you should consider before buying securities in this offering. You should carefully read this entire prospectus and any applicable prospectus supplement, including each of the documents incorporated herein or therein by reference, before making an investment decision. Unless the context otherwise requires, the terms Otonomy, the Company, we, us and our in this prospectus refer to Otonomy, Inc., and its subsidiaries.

Otonomy, Inc.

Overview

We are a biopharmaceutical company dedicated to the development of innovative therapeutics for otology. We pioneered the application of drug delivery technology to the ear in order to develop products that achieve sustained drug exposure from a single local administration. This approach is covered by a broad patent estate and is being utilized to develop a pipeline of products addressing important unmet medical needs including Ménière's disease, hearing loss and tinnitus.

OTIVIDEX™ is a steroid in development for the treatment of Ménière's disease. Two Phase 3 trials in Ménière's disease patients were completed in the second half of 2017. The AVERTS-2 trial, conducted in Europe, achieved its primary endpoint (p value = 0.029) while the AVERTS-1 trial, conducted in the United States, did not (p value = 0.62). Based on a Type C meeting with the FDA, we believe that one additional successful pivotal trial is sufficient to support the U.S. registration of OTIVIDEX in Ménière's disease, and recently announced the initiation of such trial. We expect top-line results from this trial in the first half of 2020.

OTO-313 is a formulation of the potent and selective N-Methyl-D-Aspartate, or NMDA, receptor antagonist gacyclidine that is in development for the treatment of tinnitus. A Phase 1 clinical safety trial has been successfully completed using OTO-311, a poloxamer-based formulation of gacyclidine, with no safety concerns observed. We have shifted development to OTO-313, an alternative formulation of gacyclidine that has improved properties compared to OTO-311. We expect to initiate a Phase 1/2 clinical trial for OTO-313 in tinnitus patients in the first half of 2019.

We are advancing three distinct hearing loss programs that address different pathologies and broad patient populations. OTO-413 is a sustained exposure formulation of Brain-Derived Neurotrophic Factor, or BDNF, in development for the repair of cochlear synaptopathy and the treatment of speech-in-noise hearing difficulties. We have initiated nonclinical studies and manufacturing for OTO-413 to support an Investigational New Drug Application, with a Phase 1/2 clinical trial in hearing loss patients expected to begin in the first half of 2019. OTO-5XX is an otoprotectant in development for the prevention of cisplatin induced hearing loss. OTO-6XX induces hair cell regeneration in a nonclinical proof-of-concept model and is being developed for the treatment of severe hearing loss. We expect to select a candidate for clinical development for both the OTO-5XX and OTO-6XX programs by the end of 2018.

In addition, we developed, received FDA approval for and commercially launched OTIPRIO® (ciprofloxacin otic suspension) for use during tympanostomy tube placement, or TTP, surgery in pediatric patients. OTIPRIO was also approved by the FDA for the treatment of acute otitis externa, or AOE. In November 2017, we announced the discontinuation of promotional support for OTIPRIO in order to significantly reduce operating expenses related to the product. The Company recently announced the initiation of a partnership with privately held Mission Pharmacal, or

Mission, to support the promotion of OTIPRIO for the treatment of AOE in pediatric and primary care physician offices as well as urgent care clinics.

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Corporate Information

We were incorporated in the State of Delaware in May 2008. Our principal executive offices are located at 4796 Executive Drive, San Diego, California 92121, and our telephone number is (619) 323-2200. Our website is www.otonomy.com. Information contained on, or that can be accessed through, our website is not incorporated by reference into this prospectus, and you should not consider information on our website to be part of this prospectus.

Otonomy, the Otonomy logo, OTIPRIO, OTIVIDEX and other trademarks or service marks of Otonomy appearing in this report are the property of Otonomy. This prospectus and the documents incorporated by reference herein contain additional trade names, trademarks and service marks of other companies. We do not intend our use or display of other companies' trade names, trademarks or service marks to imply a relationship with, or endorsement or sponsorship of us by, these other companies. We have omitted the ® and ™ designations, as applicable, for the trademarks used in this prospectus.

Implications of Being an Emerging Growth Company

We qualify as an emerging growth company as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. An emerging growth company may take advantage of relief from certain reporting requirements and other burdens that are otherwise applicable generally to public companies. As an emerging growth company:

we have availed ourselves of the exemption from the requirement to obtain an attestation and report from our auditors on the assessment of our internal control over financial reporting pursuant to the Sarbanes-Oxley Act of 2002;

we will provide less extensive disclosure about our executive compensation arrangements; and

we will not require shareholder non-binding advisory votes on executive compensation or golden parachute arrangements.

We may use these provisions until the last day of our fiscal year following the fifth anniversary of our initial public offering, or December 31, 2019. However, if certain events occur prior to the end of such five-year period, including if we become a large accelerated filer, our annual gross revenues exceed \$1.07 billion or we issue more than \$1.0 billion of non-convertible debt in any three-year period, we will cease to be an emerging growth company prior to the end of such five-year period. We may choose to take advantage of some but not all of these reduced burdens. To the extent that we take advantage of these reduced burdens, the information that we provide stockholders may be different than you might obtain from other public companies in which you hold equity interests.

The Securities We May Offer

We may offer up to \$150,000,000 of common stock, preferred stock, depositary shares, warrants, debt securities, subscription rights and units in one or more offerings and in any combination.

Common Stock

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Holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders. Our amended and restated certificate of incorporation does not provide for cumulative voting rights. Subject to preferences that may apply to any shares of preferred stock outstanding at the time, the holders of our common stock are entitled to receive dividends out of funds legally available if our board of directors, in its discretion, determines to issue dividends and then only at the times and in the amounts that our board of

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directors may determine. If we become subject to a liquidation, dissolution or winding-up, the assets legally available for distribution to our stockholders would be distributable ratably among the holders of our common stock and any participating preferred stock outstanding at that time, subject to prior satisfaction of all outstanding debt and liabilities and the preferential rights of and the payment of liquidation preferences, if any, on any outstanding shares of preferred stock.

Preferred Stock and Depositary Shares

Our board of directors has the authority, subject to limitations prescribed by Delaware law, to issue preferred stock in one or more series, to establish from time to time the number of shares to be included in each series, and to fix the designation, powers, preferences and rights of the shares of each series and any of its qualifications, limitations or restrictions, in each case without further vote or action by our stockholders.

We may also issue fractional shares of preferred stock that will be represented by depositary shares and depositary receipts.

Each series of preferred stock, depositary shares or depositary receipts, if issued, will be more fully described in the particular prospectus supplement that will accompany this prospectus, including redemption provisions, rights in the event of our liquidation, dissolution or winding-up, voting rights and rights to convert into common stock. We have no present plans to issue any shares of preferred stock, depositary shares or depositary receipts nor are any shares of our preferred stock, depositary shares or depositary receipts presently outstanding.

Warrants

We may issue warrants for the purchase of common stock, preferred stock or debt securities. We may issue warrants independently or together with other securities.

Debt Securities

We may offer secured or unsecured obligations in the form of one or more series of senior or subordinated debt. The senior debt securities and the subordinated debt securities are together referred to in this prospectus as the debt securities. The subordinated debt securities generally will be entitled to payment only after payment of our senior debt. Senior debt generally includes all debt for money borrowed by us, except debt that is stated in the instrument governing the terms of that debt to be not senior to, or to have the same rank in right of payment as, or to be expressly junior to, the subordinated debt securities. We may issue debt securities that are convertible into shares of our common stock.

The senior and subordinated debt securities will be issued under separate indentures between us and a trustee. We have summarized the general features of the debt securities to be governed by the indentures. These indentures have been filed as exhibits to the registration statement of which this prospectus forms a part. We encourage you to read these indentures. Instructions on how you can get copies of these documents are provided in the section titled *Where You Can Find More Information*.

Subscription Rights

We may issue subscription rights to purchase our common stock, preferred stock or debt securities. These subscription rights may be offered independently or together with any other security offered hereby and may or may not be transferable by the stockholder receiving the subscription rights in such offering.

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Units

We may issue units comprising one or more of the other classes of securities issued by us as described in this prospectus in any combination. Each unit will be issued so that the holder of the unit is also the holder of each security included in the unit.

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RISK FACTORS

An investment in our securities involves a high degree of risk. The prospectus supplement applicable to each offering of our securities will contain a discussion of the risks applicable to an investment in our securities. Prior to making a decision about investing in our securities, you should carefully consider the specific factors discussed in the section titled "Risk Factors" in the applicable prospectus supplement, together with all of the other information contained or incorporated by reference in the prospectus supplement or appearing or incorporated by reference in this prospectus. You should also consider the risks, uncertainties and assumptions discussed under "Part I Item 1A Risk Factors" in our most recent Annual Report on Form 10-K and "Part II Item 1A Risk Factors" in our Quarterly Reports on Form 10-Q, all of which are incorporated herein by reference, and as may be amended, supplemented or superseded from time to time by other reports we file with the SEC in the future and any prospectus supplement related to a particular offering. The risks and uncertainties we have described are not the only ones we face. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also affect our operations.

FORWARD-LOOKING STATEMENTS

This prospectus, each prospectus supplement and the information incorporated by reference in this prospectus and each prospectus supplement contain certain statements that constitute "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act.

Our forward-looking statements include, but are not limited to, statements about:

our expectations regarding our OTIPRIO promotional partnership;

our expectations regarding our clinical development of OTIVIDEX, including availability of top-line results from the recently initiated additional Phase 3 trial in the first half of 2020;

our expectations regarding the clinical development of OTO-313, including but not limited to our plans to initiate a Phase 1/2 clinical trial in tinnitus patients in the first half of 2019;

our expectations regarding the clinical development of OTO-413, including but not limited to our plans to initiate a Phase 1/2 clinical trial in hearing loss patients in the first half of 2019;

the timing or likelihood of regulatory filings and approvals;

our expectations regarding the future development of other product candidates, including but not limited to our plans to select a candidate for clinical development for both the OTO-5XX and OTO-6XX programs by the end of 2018;

the potential for commercialization of our product candidates, if approved;

our expectations and statements regarding the pricing, market size, opportunity and growth potential for OTIVIDEX, OTO-313, OTO-413 and our other product candidates, if approved for commercial use;

our expectations and statements regarding the adoption and use of OTIPRIO and OTIVIDEX, OTO-313 and OTO-413, if approved;

our expectations regarding potential coverage and reimbursement relating to OTIPRIO, and OTIVIDEX, OTO-313 and OTO-413, if approved, or any other approved product candidates;

our plans regarding the use of contract manufacturers for the production of our product candidates for clinical trials and, if approved, commercial use;

our plans and ability to effectively establish and manage our own sales and marketing capabilities, or seek and establish collaborative partners, to commercialize our products;

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our ability to advance product candidates into, and successfully complete, clinical trials;

the implementation of our business model, strategic plans for our business, products and technology;

the initiation, timing, progress and results of future nonclinical studies and clinical trials;

the scope of protection we are able to establish and maintain for intellectual property rights covering our products and technology;

estimates of our expenses, future revenue, capital requirements and our needs for additional financing;

our financial performance;

accounting principles, policies and estimates;

developments and projections relating to our competitors and our industry; and

our expectations regarding the period during which we qualify as an emerging growth company under the JOBS Act.

These forward-looking statements are subject to a number of risks, uncertainties, and assumptions, including but not limited to: our limited operating history and our expectation that we will incur significant losses for the foreseeable future; our ability to obtain additional financing; our dependence on the commercial success of OTIPRIO and the regulatory success and advancement of additional product candidates, including but not limited to OTIVIDEX, OTO-313, and OTO-413; the uncertainties inherent in the clinical drug development process, including, without limitation, our ability to adequately demonstrate the safety and efficacy of our product candidates, the nonclinical and clinical results for our product candidates, which may not support further development, and challenges related to patient enrollment in clinical trials; our ability to obtain regulatory approval for our product candidates; side effects or adverse events associated with our product candidates; competition in the biopharmaceutical industry; our dependence on third parties to conduct nonclinical studies and clinical trials; the timing and outcome of hospital pharmacy and therapeutics reviews and other facility reviews; the impact of coverage and reimbursement decisions by third-party payors on the pricing and market acceptance of OTIPRIO; our dependence on third parties for the manufacture of OTIPRIO and product candidates; our dependence on a small number of suppliers for raw materials; our ability to protect our intellectual property related to OTIPRIO and our product candidates in the United States and throughout the world; expectations regarding potential market size, opportunity and growth; our ability to manage operating expenses; implementation of our business model and strategic plans for our business, products and technology; and other risks.

The words believe, may, will, potentially, estimate, continue, anticipate, intend, could, would, p expect and the negative and plural forms of these words and similar expressions are intended to identify forward-looking statements, but are not the exclusive means of identifying such statements. Those statements appear

in this prospectus, any accompanying prospectus supplement and the documents incorporated herein and therein by reference, particularly in the sections titled Prospectus Summary, Risk Factors, Management's Discussion and Analysis of Financial Condition and Results of Operations and Business, and include statements regarding the intent, belief or current expectations of the Company and management that are subject to known and unknown risks, uncertainties and assumptions.

This prospectus, any prospectus supplement and the information incorporated by reference in this prospectus and any prospectus supplement also contain statements that are based on the current expectations of our Company and management. You are cautioned that any such forward-looking statements are not guarantees of future performance and involve risks and uncertainties, and that actual results may differ materially from those projected in the forward-looking statements as a result of various factors.

In addition, statements that we believe and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this prospectus,

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and although we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted a thorough inquiry into, or review of, all potentially available relevant information.

Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified, you should not unduly rely upon forward-looking statements as predictions of future events. The events and circumstances reflected in the forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Except as required by applicable law, including the securities laws of the United States and the rules and regulations of the SEC, we do not plan to publicly update or revise any forward-looking statements contained herein after we distribute this prospectus, whether as a result of any new information, future events or otherwise.

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The following table sets forth our ratio of earnings to fixed charges for each of the periods indicated. You should read these ratios in connection with our annual report on Form 10-K for the period ended December 31, 2017 (including our financial statements and accompanying notes contained therein) incorporated by reference in this prospectus, and our quarterly report on Form 10-Q for the period ended June 30, 2018, incorporated by reference in this prospectus.

| | Six Months Ended June 30, 2018 | 2017 | Year Ended December 31, | |
|------------------------------------|---|-------------|------------------------------------|-------------|
| | | | 2016 | 2015 |
| Ratio of earnings to fixed charges | N/A | N/A | N/A | N/A |

The ratio of earnings to fixed charges represents the number of times that fixed charges are covered by earnings. Earnings consist of loss from continuing operations before income taxes and fixed charges. Fixed charges consist of estimated interest expense within rental expense.

We did not record positive earnings for the periods indicated in the table above. Accordingly, our earnings were insufficient to cover fixed charges for such periods and we are unable to disclose a ratio of earnings to fixed charges for such periods. For the six months ended June 30, 2018 and the years ended December 31, 2017, 2016, and 2015, the coverage deficiency necessary for the ratio of earnings to fixed charges to equal 1.00 (one-to-one coverage) was \$25.0 million, \$90.1 million, \$110.6 million, and \$61.7 million, respectively, for each of such periods.

As of the date of this prospectus, we have no shares of preferred stock outstanding, and consequently, our ratio of earnings to combined fixed charges and preferred share dividends and ratio of earnings to fixed charges would be identical.

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USE OF PROCEEDS

Unless otherwise indicated in a prospectus supplement, we will use the net proceeds from the sale of securities offered by this prospectus for general corporate purposes, which may include working capital, capital expenditures, other corporate expenses and acquisitions of complementary products, technologies or businesses. However, we do not have agreements or commitments for any specific acquisitions at this time. The timing and amount of our actual expenditures will be based on many factors, including cash flows from operations and the anticipated growth of our business, the progress of our development and commercialization efforts and the status and results of our clinical trials, as well as any collaborations that we may enter into with third parties and any unforeseen cash needs. As a result, unless otherwise indicated in the prospectus supplement, our management will have broad discretion to allocate the net proceeds of the offerings. Pending their ultimate use, we intend to invest the net proceeds in short-term, investment-grade, interest-bearing instruments.

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DESCRIPTION OF CAPITAL STOCK

General

The following description summarizes the most important terms of our capital stock as set forth in our amended and restated certificate of incorporation and amended and restated bylaws. This summary does not purport to be complete and is qualified in its entirety by the provisions of our amended and restated certificate of incorporation and amended and restated bylaws. For a complete description of our capital stock, you should refer to our amended and restated certificate of incorporation, amended and restated bylaws and third amended and restated investors rights agreement, that are filed as exhibits to the registration statement relating to our initial public offering, and to the applicable provisions of Delaware law. Our authorized capital stock consists of 200,000,000 shares of common stock, \$0.001 par value per share, and 10,000,000 shares of undesignated preferred stock, \$0.001 par value per share.

Common Stock

Outstanding Shares

As of June 30, 2018, there were 30,630,125 shares of common stock outstanding. Our board of directors is authorized, without stockholder approval, to issue additional shares of our capital stock.

As of June 30, 2018, there were 5,146,089 shares of common stock subject to outstanding options.

Dividend Rights and Policy

Subject to preferences that may be applicable to any then outstanding convertible preferred stock, holders of our common stock are entitled to receive dividends, if any, as may be declared from time to time by our board of directors out of legally available funds.

We have never declared or paid cash dividends on any of our capital stock. We currently intend to retain all available funds and any future earnings, if any, for the operation and expansion of our business and, therefore, we do not anticipate declaring or paying cash dividends in the foreseeable future. In addition, we may become subject to covenants under future debt arrangements that place restrictions on our ability to pay dividends. The payment of dividends, if any, will be at the discretion of our board of directors and will depend on our results of operations, capital requirements, financial condition, prospects, contractual arrangements, any limitations on payment of dividends present in our future debt agreements, and other factors that our board of directors may deem relevant.

Voting Rights

Pursuant to our amended and restated certificate of incorporation, each holder of our common stock is entitled to one vote for each share on all matters submitted to a vote of stockholders; provided, however, that, except as otherwise required by law, holders of our common stock, as such, shall not be entitled to vote on any amendment to our amended and restated certificate of incorporation that relates solely to the terms of one or more outstanding series of preferred stock if the holders of such affected series are entitled, either separately or together with the holders of one or more other such series, to vote thereon pursuant to our amended and restated certificate of incorporation. Pursuant to our amended and restated certificate of incorporation and amended and restated bylaws, corporate actions can generally be taken by a majority of our board and/or stockholders holding a majority of our outstanding shares, except as otherwise indicated in the section entitled *Anti-Takeover Effects of Delaware Law and Our Certificate of Incorporation and Bylaws*, where certain amendments to our amended and restated certificate of incorporation and

amended and restated bylaws require the vote of at least two-thirds of our then outstanding voting securities. Additionally, our stockholders do not have cumulative voting rights in the election of directors. Accordingly, holders of a plurality of the votes cast at a meeting of stockholders will be able to elect all of the directors then standing for election.

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Right to Receive Liquidation Distributions

In the event of our liquidation, dissolution or winding up, holders of our common stock are entitled to share ratably in the net assets legally available for distribution to stockholders after the payment of all of our debts and other liabilities and the satisfaction of any liquidation preference granted to the holders of any then outstanding shares of preferred stock.

Rights and Preferences

Holders of our common stock have no preemptive, conversion, subscription or other rights, and there are no redemption or sinking fund provisions applicable to our common stock. The rights, preferences and privileges of the holders of our common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of our preferred stock that we may designate in the future.

Fully Paid and Nonassessable

All of our outstanding shares of common stock are, and the shares of common stock to be issued pursuant to this offering, when paid for, will be fully paid and nonassessable.

Preferred Stock

Our board of directors has the authority, without further action by our stockholders, to issue up to 10,000,000 shares of preferred stock in one or more series and to fix the rights, preferences, privileges and restrictions thereof. These rights, preferences and privileges could include dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences, sinking fund terms and the number of shares constituting any series or the designation of such series, any or all of which may be greater than the rights of common stock. The issuance of preferred stock by us could adversely affect the voting power of holders of common stock and the likelihood that such holders will receive dividend payments and payments upon liquidation. In addition, the issuance of preferred stock could have the effect of delaying, deferring or preventing a change of control of our company or other corporate action. No shares of preferred stock are outstanding, and we have no present plan to issue any shares of preferred stock.

Stock Options

As of June 30, 2018, there were approximately 5,146,089 shares of our common stock issuable upon exercise of outstanding stock options, at a weighted-average exercise price of \$5.79 per share.

Employee Stock Purchase Plan

As of June 30, 2018, 1,698,108 shares of our common stock were available for sale under our 2014 Employee Stock Purchase Plan.

Exclusive Jurisdiction

Unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware is the sole and exclusive forum for: (1) any derivative action or proceeding brought on behalf of us; (2) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or other employees to us or our stockholders; (3) any action asserting a claim against us arising pursuant to any provision of the Delaware General Corporation Law or our amended and restated certificate of incorporation or amended and restated bylaws; (4) any

action asserting a claim against us governed by the internal affairs doctrine. The enforceability of similar choice of forum provisions in other companies' certificates of incorporation has been challenged in legal proceedings, and it is possible that, in connection with any action, a court could find the choice of forum provisions contained in our amended and restated certificate of incorporation to be inapplicable or unenforceable in such action.

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Registration Rights

The holders of an aggregate of up to 4,192,638 shares of our common stock, including shares of common stock issuable upon the exercise of outstanding options and warrants, or their permitted transferees, are entitled to rights with respect to the registration of such shares under the Securities Act. We refer to these shares as registrable securities. These rights are provided under the terms of our third amended and restated investors' rights agreement between us and the holders of registrable securities, and include demand registration rights, piggyback registration rights and Form S-3 registration rights.

These registration rights will terminate as to a given holder of registrable securities upon the earliest of (1) August 18, 2019 or (2) when such holder and such holder's affiliates can sell all of such holder's registrable securities during a three-month period without registration in compliance with Rule 144 of the Securities Act.

Generally, we are required to pay the registration expenses (other than underwriters' and brokers' discounts and commissions) in connection with the registrations described below, including the reasonable fees and disbursements of one counsel for the selling holder or holders of registrable securities. In an underwritten offering, the underwriters have the right to limit the number of shares registered by the holders of registrable securities for marketing reasons, subject to certain limitations.

Demand Registration Rights

Upon the written request of at least a majority of the then outstanding registrable securities that we file a registration statement under the Securities Act (provided that the anticipated aggregate offering price of such shares is greater than \$5.0 million), we will be obligated to notify all holders of registrable securities of such request and to use our reasonable best efforts to register the sale of all registrable securities that holders may request to be registered. We are only obligated to file up to two registration statements which are declared or ordered effective in connection with the exercise of these demand registration rights. These demand registration rights are subject to specified conditions and limitations, including the right of the underwriters to limit the number of shares included in any such registration under certain circumstances.

Piggyback Registration Rights

If we propose to register any of our securities under the Securities Act in connection with the public offering of such securities, the holders of registrable securities will be entitled to certain piggyback registration rights allowing such holders to include their shares in such registration, subject to certain limitations. As a result, whenever we propose to file a registration statement under the Securities Act, other than with respect to a registration related to either to the sale of securities to our employees pursuant to a stock plan, stock purchase or similar plan or a registration related to a corporate reorganization or transaction under Rule 145 of the Securities Act of registrable securities are entitled to notice of the registration and have the right to include their shares in the registration. These registration rights are subject to specified conditions and limitations, including the right of the underwriters to limit the number of shares included in any such registration statement under certain circumstances.

Form S-3 Registration Rights

Upon the written request from the holders of at least 10% of the outstanding shares of registrable securities, holders of registrable securities have the right to demand that we file a registration statement on Form S-3 so long as the aggregate amount of shares to be offered and sold under such registration statement on Form S-3 is at least \$1.0 million (net of any underwriters' discounts or commissions). We are not required to effect a registration on Form

S-3 if we have already effected two registrations on Form S-3 for the holders pursuant to Form S-3 registration rights within the twelve-month period preceding the date of the request. Additionally, we are not required to effect such registration in any jurisdiction in which we would be required to qualify to do business or execute a general consent of process in effecting such registration.

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

The provisions of Delaware law, our amended and restated certificate of incorporation and our amended and restated bylaws may have the effect of delaying, deferring or discouraging another person from acquiring control of our company. These provisions, which are summarized below, may have the effect of discouraging takeover bids. They are also designed, in part, to encourage persons seeking to acquire control of us to negotiate first with our board of directors. We believe that the benefits of increased protection of our potential ability to negotiate with an unfriendly or unsolicited acquirer outweigh the disadvantages of discouraging a proposal to acquire us because negotiation of these proposals could result in an improvement of their terms.

Delaware Law

We are subject to the provisions of Section 203 of the Delaware General Corporation Law regulating corporate takeovers. In general, Section 203 prohibits a publicly-held Delaware corporation from engaging, under certain circumstances, in a business combination with an interested stockholder for a period of three years following the date the person became an interested stockholder unless:

prior to the date of the transaction, the board of directors approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;

upon completion of the transaction that resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding, but not for determining the outstanding voting stock owned by the interested stockholder, (1) voting stock owned by persons who are directors and also officers, and (2) voting stock owned by employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; or

at or subsequent to the date of the transaction, the business combination is approved by the board of directors and authorized at an annual or special meeting of stockholders, and not by written consent, by the affirmative vote of at least 66 2/3% of the outstanding voting stock which is not owned by the interested stockholder.

Generally, a business combination includes a merger, asset or stock sale, or other transaction resulting in a financial benefit to the interested stockholder. 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 outstanding voting stock. These provisions may have the effect of delaying, deferring or preventing a change in our control.

Amended and Restated Certificate of Incorporation and Amended and Restated Bylaw Provisions

Our amended and restated certificate of incorporation and our amended and restated bylaws include a number of provisions that could deter hostile takeovers or delay or prevent changes in control of our management team, including the following:

Board of directors vacancies. Our amended and restated certificate of incorporation and amended and restated bylaws authorize only our board of directors to fill vacant directorships, including newly created seats. In addition, the number of directors constituting our board of directors is permitted to be set only by a resolution adopted by our board of directors. These provisions prevent a stockholder from increasing the size of our board of directors and then gaining control of our board of directors by filling the resulting vacancies with its own nominees. This makes it more difficult to change the composition of our board of directors but promotes continuity of management.

Classified board. Our amended and restated certificate of incorporation and amended and restated bylaws provide that our board is classified into three classes of directors. A third party may be

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discouraged from making a tender offer or otherwise attempting to obtain control of us as it is more difficult and time consuming for stockholders to replace a majority of the directors on a classified board of directors.

Stockholder action; special meeting of stockholders. Our amended and restated certificate of incorporation provides that our stockholders may not take action by written consent, but may only take action at annual or special meetings of our stockholders. As a result, a holder controlling a majority of our capital stock is not be able to amend our amended and restated bylaws or remove directors without holding a meeting of our stockholders called in accordance with our amended and restated bylaws. Our amended and restated certificate of incorporation and amended and restated bylaws further provide that special meetings of our stockholders may be called only by a majority of our board of directors, the Chairman of our Board of Directors, our Chief Executive Officer or our President (in the absence of a Chief Executive Officer), thus prohibiting a stockholder from calling a special meeting. These provisions might delay the ability of our stockholders to force consideration of a proposal or for stockholders controlling a majority of our capital stock to take any action, including the removal of directors.

Advance notice requirements for stockholder proposals and director nominations. Our amended and restated bylaws provide advance notice procedures for stockholders seeking to bring business before our annual meeting of stockholders or to nominate candidates for election as directors at our annual meeting of stockholders. Our amended and restated bylaws also specify certain requirements regarding the form and content of a stockholder's notice. These provisions might preclude our stockholders from bringing matters before our annual meeting of stockholders or from making nominations for directors at our annual meeting of stockholders if the proper procedures are not followed. We expect that these provisions may also discourage or deter a potential acquirer from conducting a solicitation of proxies to elect the acquirer's own slate of directors or otherwise attempting to obtain control of our company.

No cumulative voting. The Delaware General Corporation Law provides that stockholders are not entitled to the right to cumulate votes in the election of directors unless a corporation's certificate of incorporation provides otherwise. Our amended and restated certificate of incorporation does not provide for cumulative voting.

Directors removed only for cause. Our amended and restated certificate of incorporation provides that stockholders may remove directors only for cause.

Amendment of charter provisions. Any amendment of the above provisions in our amended and restated certificate of incorporation would require approval by a majority of our board of directors and the holders of at least two-thirds of our then outstanding voting securities.

Issuance of undesignated preferred stock. Our board of directors will have the authority, without further action by the stockholders, to issue up to 10,000,000 shares of undesignated preferred stock with rights and preferences, including voting rights, designated from time to time by our board of directors. The existence of authorized but unissued shares of preferred stock would enable our board of directors to render more difficult or to discourage an attempt to obtain control of us by means of a merger, tender offer, proxy contest

or other means.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is EQ Shareowner Services. The transfer agent and registrar's address is EQ Shareowner Services, 110 Centre Pointe Curve, Suite 101, Mendota Heights, MN 55120-4101. Our shares of common stock are issued in uncertificated form only, subject to limited circumstances.

Market Listing

Our common stock is listed on The NASDAQ Global Select Market under the symbol OTIC.

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DESCRIPTION OF THE DEPOSITARY SHARES

General

At our option, we may elect to offer fractional shares of preferred stock, rather than full shares of preferred stock. If we do elect to offer fractional shares of preferred stock, we will issue receipts for depositary shares and each of these depositary shares will represent a fraction of a share of a particular series of preferred stock, as specified in the applicable prospectus supplement. Each owner of a depositary share will be entitled, in proportion to the applicable fractional interest in shares of preferred stock underlying that depositary share, to all rights and preferences of the preferred stock underlying that depositary share. These rights may include dividend, voting, redemption and liquidation rights.

The shares of preferred stock underlying the depositary shares will be deposited with a bank or trust company selected by us to act as depositary, under a deposit agreement by and among us, the depositary and the holders of the depositary receipts. The depositary will be the transfer agent, registrar and dividend disbursing agent for the depositary shares.

The depositary shares will be evidenced by depositary receipts issued pursuant to the depositary agreement. 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 terms of the depositary shares contained in this prospectus is not complete, and is subject to modification in any prospectus supplement for any issuance of depositary shares. You should refer to the forms of the deposit agreement, our amended and restated certificate of incorporation and the certificate of designation that are, or will be, filed with the SEC for the applicable series of preferred stock. The prospectus supplement relating to a particular issue of depositary shares will include, if applicable, a discussion of material U.S. federal income tax considerations.

Dividends

The depositary will distribute cash dividends or other cash distributions, if any, received in respect of the series of preferred stock underlying the depositary shares to the record holders of depositary receipts in proportion to the number of depositary shares owned by those holders on the relevant record date. The relevant record date for depositary shares will be the same date as the record date for the preferred stock.

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 that are entitled to receive the distribution, unless the depositary determines that it is not feasible to make the distribution. If this occurs, the depositary, with our approval, may adopt another method for the distribution, including selling the property and distributing the net proceeds to the holders.

Liquidation Preference

If a series of preferred stock underlying the depositary shares has a liquidation preference, in the event of our voluntary or involuntary liquidation, dissolution or winding up, holders of depositary shares will be entitled to receive 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 a series of preferred stock underlying the depositary shares is subject to redemption, the 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,

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the depositary will redeem, as of the same redemption date, the number of depositary shares representing the preferred stock so redeemed. The depositary will mail the notice of redemption to the record holders of the depositary receipts promptly upon receiving the notice from us and not fewer than 20 or more than 60 days, unless otherwise provided in the applicable prospectus supplement, prior to the date fixed for redemption of the preferred stock.

Voting

Upon receipt of notice of any meeting at which the holders of preferred stock are entitled to vote, the depositary will mail the information contained in the notice of meeting to the record holders of the depositary receipts underlying the preferred stock. Each record holder of those depositary receipts on the record date will be entitled to instruct the depositary as to the exercise of the voting rights pertaining to the amount of preferred stock underlying that holder's depositary shares. The record date for the depositary will be the same date as the record date for the preferred stock. The depositary will, to the extent practicable, vote the preferred stock underlying the depositary shares in accordance with these instructions. We will agree to take all action that may be deemed necessary by the depositary in order to enable the depositary to vote the preferred stock in accordance with these instructions. The depositary will not vote the preferred stock to the extent that it does not receive specific instructions from the holders of depositary receipts.

Withdrawal of Preferred Stock

Owners of depositary shares will be entitled to receive upon surrender of depositary receipts at the principal office of the depositary and payment of any unpaid amount due to the depositary, the number of whole shares of preferred stock underlying their depositary shares.

Partial shares of preferred stock will not be issued. Holders of preferred stock will not be entitled to deposit the shares under the deposit agreement or to receive depositary receipts evidencing depositary shares for the preferred stock.

Amendment and Termination of the Deposit Agreement

The form of depositary receipt evidencing the depositary shares and any provision of the deposit agreement may be amended by agreement between the depositary and us. However, any amendment which materially and adversely alters the rights of the holders of depositary shares, other than fee changes, will not be effective unless the amendment has been approved by at least a majority of the outstanding depositary shares. The deposit agreement may be terminated by the depositary or us only if:

all outstanding depositary shares have been redeemed; or

there has been a final distribution of the preferred stock in connection with our dissolution and such distribution has been made to all the holders of depositary shares.

Charges of Depositary

We will pay all transfer and other taxes and governmental charges arising solely from the existence of the depositary arrangement. We will also pay charges of the depositary in connection with:

the initial deposit of the preferred stock;

the initial issuance of the depositary shares;

any redemption of the preferred stock; and

all withdrawals of preferred stock by owners of depositary shares.

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Holders of depositary receipts will pay transfer, income and other taxes and governmental charges and other specified charges as provided in the deposit agreement for their accounts. If these charges have not been paid, the depositary may:

refuse to transfer depositary shares;

withhold dividends and distributions; and

sell the depositary shares evidenced by the depositary receipt.

Miscellaneous

The depositary will forward to the holders of depositary receipts all reports and communications we deliver to the depositary that 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 reports and communications we deliver to the depositary as the holder of preferred stock.

Neither the depositary nor we will be liable if either the depositary or we are prevented or delayed by law or any circumstance beyond the control of either the depositary or us in performing our respective obligations under the deposit agreement. Our obligations and the depositary's obligations will be limited to the performance in good faith of our or the depositary's respective duties under the deposit agreement. Neither the depositary nor we will be obligated to prosecute or defend any legal proceeding in respect of any depositary shares or preferred stock unless satisfactory indemnity is furnished. The depositary and we may rely on:

written advice of counsel or accountants;

information provided by holders of depositary receipts or other persons believed in good faith to be competent to give such information; and

documents believed to be genuine and to have been signed or presented by the proper party or parties.

Resignation and Removal of Depositary

The depositary may resign at any time by delivering a notice to us. We may remove the depositary at any time. Any such resignation or removal will take effect upon the appointment of a successor depositary and its acceptance of such appointment. The successor depositary must be appointed within 60 days after delivery of the notice for resignation or removal. The successor depositary must be a bank and trust company having its principal office in the United States of America and having a combined capital and surplus of at least \$50,000,000.

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DESCRIPTION OF THE WARRANTS

General

We may issue warrants for the purchase of our debt securities, preferred stock or common stock, or any combination thereof. Warrants may be issued independently or together with our debt securities, preferred stock or common stock and 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 a bank or trust company, as warrant agent. The warrant agent will act solely as our agent in connection with the warrants. The warrant agent will not have any obligation or relationship of agency or trust for or with any holders or beneficial owners of warrants. This summary of certain provisions of the warrants is not complete. For the terms of a particular series of warrants, you should refer to the prospectus supplement for that series of warrants and the warrant agreement for that particular series.

Debt Warrants

The prospectus supplement relating to a particular issue of warrants to purchase debt securities will describe the terms of the debt warrants, including the following:

the title of the debt warrants;

the offering price for the debt warrants, if any;

the aggregate number of the debt warrants;

the designation and terms of the debt securities, including any conversion rights, purchasable upon exercise of the debt warrants;

if applicable, the date from and after which the debt warrants and any debt securities issued with them will be separately transferable;

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

if applicable, the minimum or maximum amount of the debt warrants that may be exercised at any one time;

whether the debt warrants represented by the debt warrant certificates or debt securities that may be issued upon exercise of the debt warrants will be issued in registered or bearer form;

information with respect to book-entry procedures, if any; the currency or currency units in which the offering price, if any, and the exercise price are payable;

if applicable, a discussion of material U.S. federal income tax considerations;

the antidilution provisions of the debt warrants, if any;

the redemption or call provisions, if any, applicable to the debt warrants;

any provisions with respect to the holder's right to require us to repurchase the warrants upon a change in control or similar event; and

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

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

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Equity Warrants

The prospectus supplement relating to a particular series of warrants to purchase our common stock or preferred stock will describe the terms of the warrants, including the following:

the title of the warrants;

the offering price for the warrants, if any;

the aggregate number of warrants;

the designation and terms of the common stock or preferred stock that may be purchased upon exercise of the warrants;

if applicable, the designation and terms of the securities with which the warrants are issued and the number of warrants issued with each security;

if applicable, the date from and after which the warrants and any securities issued with the warrants will be separately transferable;

the number of shares of common stock or preferred stock that may be purchased upon exercise of a warrant and the exercise price for the warrants;

the dates on which the right to exercise the warrants shall commence and expire;

if applicable, the minimum or maximum amount of the warrants that may be exercised at any one time;

the currency or currency units in which the offering price, if any, and the exercise price are payable;

if applicable, a discussion of material U.S. federal income tax considerations;

the antidilution provisions of the warrants, if any;

the redemption or call provisions, if any, applicable to the warrants;

any provisions with respect to the holder's right to require us to repurchase the warrants upon a change in control or similar event; and

any additional terms of the warrants, including 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 us.

The descriptions of the warrants in this prospectus and in any prospectus supplement are summaries of the material provisions of the applicable warrants. These descriptions do not restate those warrants in their entirety and may not contain all the information that you may find useful. We urge you to read the applicable warrants because they, and not the summaries, define your rights as holders of the warrants. For more information, please review the forms of the relevant warrants, which will be filed with the SEC promptly after the offering of warrants and will be available as described in the section titled "Where You Can Find More Information."

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DESCRIPTION OF THE DEBT SECURITIES

The debt securities may be either secured or unsecured and will either be our senior debt securities or our subordinated debt securities. The debt securities will be issued under one or more separate indentures between us and a trustee to be specified in an accompanying prospectus supplement. Senior debt securities will be issued under a senior indenture and subordinated debt securities will be issued under a subordinated indenture. Together, the senior indenture and the subordinated indenture are called indentures in this description. This prospectus, together with the applicable prospectus supplement, will describe the terms of a particular series of debt securities.

The following is a summary of selected provisions and definitions of the indentures and debt securities to which any prospectus supplement may relate. The summary of selected provisions of the indentures and the debt securities appearing below is not complete and is subject to, and qualified entirely by reference to, all of the provisions of the applicable indenture and certificates evidencing the applicable debt securities. For additional information, you should look at the applicable indenture and the certificate evidencing the applicable debt security that is filed as an exhibit to the registration statement that includes the prospectus. In this description of the debt securities, the words we, us, or our refer only to Otonomy, Inc. and not to any of our subsidiaries, unless we expressly state or the context otherwise requires.

The following description sets forth selected general terms and provisions of the applicable indenture and debt securities to which any prospectus supplement may relate. Other specific terms of the applicable indenture and debt securities will be described in the applicable prospectus supplement. If any particular terms of the indenture or debt securities described in a prospectus supplement differ from any of the terms described below, then the terms described below will be deemed to have been superseded by that prospectus supplement.

General

Debt securities may be issued in separate series without limitation as to aggregate principal amount. We may specify a maximum aggregate principal amount for the debt securities of any series.

We are not limited as to the amount of debt securities we may issue under the indentures. Unless otherwise provided in a prospectus supplement, a series of debt securities may be reopened to issue additional debt securities of such series.

The prospectus supplement relating to a particular series of debt securities will set forth:

whether the debt securities are senior or subordinated;

the offering price;

the title;

any limit on the aggregate principal amount;

the person who shall be entitled to receive interest, if other than the record holder on the record date;

the date or dates the principal will be payable;

the interest rate or rates, which may be fixed or variable, if any, the date from which interest will accrue, the interest payment dates and the regular record dates, or the method for calculating the dates and rates;

the place where payments may be made;

any redemption provisions at our option and any applicable redemption prices associated with these provisions;

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any obligation by us to redeem or repurchase any debt securities pursuant to any sinking fund or similar provision or any redemption or repurchase at the option of the holder and any applicable redemption or repurchase terms and conditions and prices associated with these provisions;

if issued other than in denominations of U.S. \$1,000 or any multiple of U.S. \$1,000, the denominations in which the debt securities shall be issuable;

if applicable, the method for determining how the principal, premium, if any, or interest will be calculated by reference to an index or formula;

if other than U.S. currency, the currency or currency units in which principal, premium, if any, or interest will be payable and whether we or a holder may elect payment to be made in a different currency;

if the principal, premium or interest on debt securities is payable at our option or the holder thereof in one or more currencies or currency units other than those in which debt securities are payable, the currency or currency units in which the principal, premium or interest on the debt securities as to which such election is made shall be payable on the terms and conditions associated with these provisions;

the percentage of the principal amount at which the debt securities may be issued, and if other than the entire amount, the portion of the principal amount that will be payable upon acceleration of maturity;

if the principal amount payable at stated maturity will not be determinable as of any date prior to stated maturity, the amount or method for determining the amount which will be deemed to be the principal amount;

if applicable, whether the debt securities shall be subject to the defeasance provisions described below under Satisfaction and Discharge; Defeasance or such other defeasance provisions specified in the applicable prospectus supplement for the debt securities;

any conversion or exchange provisions;

whether the debt securities will be issuable in the form of a global security, the depositary for any such global security, the form of legends for any global security and the terms for exchanging any such global security into a definitive registered debt security;

the deletion, addition or change in any event of default, and any change in the right of the trustee or the requisite percentage of holders to declare the principal amount due and payable;

any change or modification to the subordination provisions applicable to the subordinated debt securities if different from those described below under Subordinated Debt Securities;

any deletion, addition or change in the covenants set forth in Article 10 of the indentures;

any paying agents, authenticating agents, security registrars or other agents for the debt securities, if other than the trustee;

any provisions relating to any security provided for the debt securities, including any provisions regarding the circumstances under which collateral may be released or substituted;

any provisions relating to guaranties for the securities and any circumstances under which there may be additional obligors;

any provisions granting special rights to holders when a specified event occurs;

any provision with respect to any special interest premium or other premium;

any special tax provisions that apply to the debt securities;

with respect to the debt securities that do not bear interest, the dates for certain required reports to the applicable trustee;

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any and all additional, eliminated or changed terms that will apply to the debt securities; and

any other terms of such debt securities.

Unless otherwise specified in the prospectus supplement, the debt securities will be registered debt securities. Debt securities may be sold at a substantial discount below their stated principal amount, bearing no interest or interest at a rate which at time of issuance is below market rates. The U.S. federal income tax considerations applicable to debt securities sold at a discount will be described in the applicable prospectus supplement.

Exchange and Transfer

Debt securities may be transferred or exchanged at the office of the security registrar or at the office of any transfer agent designated by us.

We will not impose a service charge for any transfer or exchange, but we may require holders to pay any tax or other governmental charges associated with any transfer or exchange.

In the event of any partial redemption of debt securities of any series, we will not be required to:

issue, register the transfer of, or exchange, any debt security of that series during a period beginning at the opening of business 15 days before the day of mailing of a notice of redemption and ending at the close of business on the day of the mailing; or

register the transfer of or exchange any debt security of that series selected for redemption, in whole or in part, except the unredeemed portion of the debt security being redeemed in part.

We will appoint the trustee as the initial security registrar. Any transfer agent, in addition to the security registrar initially designated by us, will be named in the prospectus supplement. We may designate additional transfer agents or change transfer agents or change the office of the transfer agent. However, we will be required to maintain a transfer agent in each place of payment for the debt securities of each series.

Global Securities

The debt securities of any series may be represented, in whole or in part, by one or more global securities. Each global security will:

be registered in the name of a depositary, or its nominee, that we will identify in a prospectus supplement;

be deposited with the depositary or nominee or custodian; and

bear any required legends.

No global security may be exchanged in whole or in part for debt securities registered in the name of any person other than the depositary or any nominee unless:

the depositary has notified us that it is unwilling or unable to continue as depositary or has ceased to be qualified to act as depositary;

an event of default is continuing with respect to the debt securities of the applicable series; or

any other circumstance described in a prospectus supplement has occurred permitting or requiring the issuance of any such security.

As long as the depositary, or its nominee, is the registered owner of a global security, the depositary or nominee will be considered the sole owner and holder of the debt securities represented by the global security for

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all purposes under the indentures. Except in the above limited circumstances, owners of beneficial interests in a global security will not be:

entitled to have the debt securities registered in their names;

entitled to physical delivery of certificated debt securities; or

considered to be holders of those debt securities under the indenture.

Payments on a global security will be made to the depositary or its nominee as the holder of the global security. Some jurisdictions have laws that require that certain purchasers of securities take physical delivery of such securities in definitive form. These laws may impair the ability to transfer beneficial interests in a global security.

Institutions that have accounts with the depositary or its nominee are referred to as participants. Ownership of beneficial interests in a global security will be limited to participants and to persons that may hold beneficial interests through participants. The depositary will credit, on its book-entry registration and transfer system, the respective principal amounts of debt securities represented by the global security to the accounts of its participants.

Ownership of beneficial interests in a global security will be shown on and effected through records maintained by the depositary, with respect to participants' interests, or any participant, with respect to interests of persons held by participants on their behalf.

Payments, transfers and exchanges relating to beneficial interests in a global security will be subject to policies and procedures of the depositary. The depositary policies and procedures may change from time to time. Neither any trustee nor we will have any responsibility or liability for the depositary's or any participant's records with respect to beneficial interests in a global security.

Payment and Paying Agents

Unless otherwise indicated in a prospectus supplement, the provisions described in this paragraph will apply to the debt securities. Payment of interest on a debt security on any interest payment date will be made to the person in whose name the debt security is registered at the close of business on the regular record date. Payment on debt securities of a particular series will be payable at the office of a paying agent or paying agents designated by us. However, at our option, we may pay interest by mailing a check to the record holder. The trustee will be designated as our initial paying agent.

We may also name any other paying agents in a prospectus supplement. We may designate additional paying agents, change paying agents or change the office of any paying agent. However, we will be required to maintain a paying agent in each place of payment for the debt securities of a particular series.

All moneys paid by us to a paying agent for payment on any debt security that remain unclaimed for a period ending the earlier of:

10 business days prior to the date the money would be turned over to the applicable state; or

at the end of two years after such payment was due,
will be repaid to us thereafter. The holder may look only to us for such payment.

No Protection in the Event of a Change of Control

Unless otherwise indicated in a prospectus supplement with respect to a particular series of debt securities, 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.

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Covenants

Unless otherwise indicated in a prospectus supplement with respect to a particular series of debt securities, the debt securities will not contain any financial or restrictive covenants.

Consolidation, Merger and Sale of Assets

Unless we indicate otherwise in a prospectus supplement with respect to a particular series of debt securities, we may not consolidate with or merge into any other person (other than one of our subsidiaries), in a transaction in which we are not the surviving corporation, or convey, transfer or lease our properties and assets substantially as an entirety to, any person (other than to one or more subsidiaries of Otonomy, Inc.), unless:

the successor entity, if any, is a U.S. corporation, limited liability company, partnership, trust or other business entity;

the successor entity assumes our obligations on the debt securities and under the indentures;

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

certain other conditions specified in the applicable indenture are met.

Events of Default

Unless we indicate otherwise in a prospectus supplement, the following will be events of default for any series of debt securities under the indentures:

- (1) we fail to pay principal of or any premium or the redemption price on any debt security of that series when due;
- (2) we fail to pay any interest on any debt security of that series for 30 days after it becomes due;
- (3) we fail to deposit any sinking fund payment when due;
- (4) we default or breach any covenant or warranty in the applicable indenture and such failure continues for 90 days after we are given the notice required in the indentures; and
- (5) certain events involving our bankruptcy, insolvency or reorganization.

Additional or different events of default applicable to a series of debt securities may be described in a prospectus supplement. An event of default of one series of debt securities is not necessarily an event of default for any other series of debt securities.

The trustee may withhold notice to the holders of any default, except defaults in the payment of principal, premium, if any, interest, any sinking fund installment on, or with respect to any conversion right of, the debt securities of such series. However, the trustee must consider it to be in the interest of the holders of the debt securities of such series to withhold this notice.

Unless we indicate otherwise in a prospectus supplement, if an event of default, other than an event of default described in clause (5) above, shall occur and be continuing with respect to any series of debt securities, either the trustee or the holders of at least 25% in aggregate principal amount of the outstanding securities of that series may declare the principal amount and premium, if any, of the debt securities of that series, or if any debt securities of that series are original issue discount securities, such other amount as may be specified in the applicable prospectus supplement, in each case together with accrued and unpaid interest thereon, if any, to be due and payable immediately.

Unless we indicate otherwise in a prospectus supplement, if an event of default described in clause (5) above shall occur, the principal amount and premium, if any, of all the debt securities of that series, or if any

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debt securities of that series are original issue discount securities, such other amount as may be specified in the applicable prospectus supplement, in each case together with accrued and unpaid interest thereon, if any, will automatically become immediately due and payable. Any payment by us on the subordinated debt securities following any such acceleration will be subject to the subordination provisions described below under Subordinated Debt Securities.

Notwithstanding the foregoing, each indenture will provide that we may, at our option, elect that the sole remedy for an event of default relating to our failure to comply with our obligations described under the section entitled Reports below or our failure to comply with the requirements of Section 314(a)(1) of the Trust Indenture Act will for the first 360 days after the occurrence of such an event of default consist exclusively of the right to receive additional interest on the relevant series of debt securities at an annual rate equal to (1) 0.25% of the principal amount of such series of debt securities for the first 180 days after the occurrence of such event of default and (2) 0.50% of the principal amount of such series of debt securities from the 181st day to, and including, the 360th day after the occurrence of such event of default, which we call additional interest. If we so elect, the additional interest will accrue on all outstanding debt securities from and including the date on which such event of default first occurs until such violation is cured or waived and shall be payable on each relevant interest payment date to holders of record on the regular record date immediately preceding the interest payment date. On the 361st day after such event of default (if such violation is not cured or waived prior to such 361st day), the debt securities will be subject to acceleration as provided above. In the event we do not elect to pay additional interest upon any such event of default in accordance with this paragraph, the debt securities will be subject to acceleration as provided above.

In order to elect to pay the additional interest as the sole remedy during the first 360 days after the occurrence of any event of default relating to the failure to comply with the reporting obligations in accordance with the preceding paragraph, we must notify all holders of debt securities and the trustee and paying agent of such election prior to the close of business on the first business day following the date on which such event of default occurs. Upon our failure to timely give such notice or pay the additional interest, the debt securities will be immediately subject to acceleration as provided above.

After acceleration, the holders of a majority in aggregate principal amount of the outstanding securities of that series may, under certain circumstances, rescind and annul such acceleration if all events of default, other than the non-payment of accelerated principal, or other specified amounts or interest, have been cured or waived.

Other than the duty to act with the required care during an event of default, the trustee will not be obligated to exercise any of its rights or powers at the request of the holders unless the holders shall have offered to the trustee reasonable indemnity. Generally, the holders of a majority in aggregate 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.

A holder of debt securities of any series will not have any right to institute any proceeding under the indentures, or for the appointment of a receiver or a trustee, or for any other remedy under the indentures, unless:

- (1) the holder has previously given to the trustee written notice of a continuing event of default with respect to the debt securities of that series;

- (2)

the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series have made a written request and have offered reasonable indemnity to the trustee to institute the proceeding; and

- (3) the trustee has failed to institute the proceeding and has not received direction inconsistent with the original request from the holders of a majority in aggregate principal amount of the outstanding debt securities of that series within 60 days after the original request.

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Holders may, however, sue to enforce the payment of principal, premium or interest on any debt security on or after the due date or to enforce the right, if any, to convert any debt security (if the debt security is convertible) without following the procedures listed in (1) through (3) above.

We will furnish the trustee an annual statement from our officers as to whether or not we are in default in the performance of the conditions and covenants under the applicable indenture and, if so, specifying all known defaults.

Modification and Waiver

Unless we indicate otherwise in a prospectus supplement, the applicable trustee and we may make modifications and amendments to an indenture with the consent of the holders of a majority in aggregate principal amount of the outstanding securities of each series affected by the modification or amendment.

We may also make modifications and amendments to the indentures for the benefit of holders without their consent, for certain purposes including, but not limited to:

to evidence the succession of another person to Otonomy, or successive successions, and the assumption by any such successor of the covenants of Otonomy in the indentures in compliance with Article 8 of the indentures;

adding covenants for the benefit of holders or surrendering any right or power conferred upon Otonomy;

adding events of default for the benefit of holders;

making certain changes to facilitate the issuance of the debt securities in bearer form, registrable or not registrable as to the principal, with or without interest coupons, or to permit or facilitate the issuance of debt securities in uncertificated form;

to add to, change or eliminate any of the provisions of the indentures or series of securities, provided that any such addition, change or elimination (1) shall neither (a) apply to any security of any series created prior to the execution of such supplemental indenture and entitled to the benefit of such provision nor (b) modify the rights of the holder of any such security with respect to such provision or (2) shall become effective only when there is no such security outstanding;

securing the debt securities, including provisions regarding the circumstances under which collateral may be released and substituted;

providing for guaranties of, or adding additional obligors on, the debt securities;

to establish the form or term of debt securities as permitted by Sections 2.1 and 3.1 of the indentures;

providing for a successor trustee or additional trustees;

conforming the indentures to the description of the securities set forth in this prospectus or the accompanying prospectus supplement;

curing any ambiguity, defect or inconsistency or to make any other provisions with respect to matters or questions arising under the indentures;

supplementing any of the provisions of the indentures to such extent as shall be necessary to permit or facilitate the defeasance and discharge of the debt securities, provided that such action shall not adversely affect the interest of the holders in any material respect;

make such other provisions in regard to matters or questions arising under the indentures or under any supplemental indentures as our board of directors may deem necessary or desirable, and which does not in each case adversely affect the interests of the holders of the debt securities of a series; and

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comply with requirements of the SEC in order to effect or maintain the qualifications of the indentures under the Trust Indenture Act of 1939, as amended (the Trust Indenture Act).

However, neither the trustee nor we may make any modification or amendment without the consent of the holder of each outstanding security of that series affected by the modification or amendment if such modification or amendment would:

change the stated maturity of the principal of, or any installment of principal or interest on, any debt security;

reduce the principal, premium, if any, or interest on any debt security or any premium payable upon redemption or repurchase, whether at our option or the option of any holder, or reduce the amount of any sinking fund payments;

reduce the principal of an original issue discount security or any other debt security payable on acceleration of maturity;

change the place of payment or the currency in which any debt security is payable;

impair the right to enforce any payment after the stated maturity (or in the case of redemption, on or after the redemption date);

if subordinated debt securities, modify the subordination provisions in a materially adverse manner to the holders;

adversely affect the right to convert any debt security if the debt security is a convertible debt security; or

change the provisions in the indentures that relate to modifying or amending the indentures.

Satisfaction and Discharge; Defeasance

We may be discharged from our obligations on the debt securities, subject to limited exceptions, of any series that have matured or will mature or be redeemed within one year if we deposit enough money with the trustee to pay all the principal, interest and any premium due to the stated maturity date or redemption date of the debt securities.

Each indenture contains a provision that permits us to elect either or both of the following:

we may elect to be discharged from all of our obligations, subject to limited exceptions, with respect to any series of debt securities then outstanding. If we make this election, the holders of the debt securities of the series will not be entitled to the benefits of the indenture, except for the rights of holders to receive payments

on debt securities or the registration of transfer and exchange of debt securities and replacement of lost, stolen or mutilated debt securities.

we may elect to be released from our obligations under some or all of any financial or restrictive covenants applicable to the series of debt securities to which the election relates and from the consequences of an event of default resulting from a breach of those covenants.

To make either of the above elections, we must irrevocably deposit in trust with the trustee enough money to pay in full the principal, interest and premium on the debt securities. This amount may be made in cash and/or U.S. government obligations or, in the case of debt securities denominated in a currency other than U.S. dollars, cash in the currency in which such series of securities is denominated and/or foreign government obligations. As a condition to either of the above elections, for debt securities denominated in U.S. dollars we must deliver to the trustee an opinion of counsel that the holders of the debt securities will not recognize income, gain or loss for U.S. federal income tax purposes as a result of the action.

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With respect to debt securities of any series that are denominated in a currency other than United States dollars, foreign government obligations means:

direct obligations of the government that issued or caused to be issued the currency in which such securities are denominated and for the payment of which obligations its full faith and credit is pledged, or, with respect to debt securities of any series which are denominated in Euros, direct obligations of certain members of the European Union for the payment of which obligations the full faith and credit of such members is pledged, which in each case are not callable or redeemable at the option of the issuer thereof; or

obligations of a person controlled or supervised by or acting as an agency or instrumentality of a government described in the bullet above the timely payment of which is unconditionally guaranteed as a full faith and credit obligation by such government, which are not callable or redeemable at the option of the issuer thereof.

Notices

Notices to holders will be given by mail to the addresses of the holders in the security register.

Governing Law

The indentures and the debt securities will be governed by, and construed under, the laws of the State of New York.

No Personal Liability of Directors, Officers, Employees and Stockholders

No incorporator, stockholder, employee, agent, officer, director or subsidiary of ours will have any liability for any obligations of ours, or because of the creation of any indebtedness under the debt securities, the indentures or supplemental indentures. The indentures provide that all such liability is expressly waived and released as a condition of, and as a consideration for, the execution of such indentures and the issuance of the debt securities.

Regarding the Trustee

The indentures limit the right of the trustee, should it become our creditor, to obtain payment of claims or secure its claims.

The trustee will be permitted to engage in certain other transactions with us. However, if the trustee acquires any conflicting interest, and there is a default under the debt securities of any series for which it is trustee, the trustee must eliminate the conflict or resign.

Subordinated Debt Securities

The following provisions will be applicable with respect to each series of subordinated debt securities, unless otherwise stated in the prospectus supplement relating to that series of subordinated debt securities.

The indebtedness evidenced by the subordinated debt securities of any series is subordinated, to the extent provided in the subordinated indenture and the applicable prospectus supplement, to the prior payment in full, in cash or other payment satisfactory to the holders of senior debt, of all senior debt, including any senior debt securities.

Upon any distribution of our assets upon any dissolution, winding up, liquidation or reorganization, whether voluntary or involuntary, marshalling of assets, assignment for the benefit of creditors, or in bankruptcy,

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insolvency, receivership or other similar proceedings, payments on the subordinated debt securities will be subordinated in right of payment to the prior payment in full in cash or other payment satisfactory to holders of senior debt of all senior debt.

In the event of any acceleration of the subordinated debt securities of any series because of an event of default with respect to the subordinated debt securities of that series, holders of any senior debt would be entitled to payment in full in cash or other payment satisfactory to holders of senior debt of all senior debt before the holders of subordinated debt securities are entitled to receive any payment or distribution.

In addition, the subordinated debt securities will be structurally subordinated to all indebtedness and other liabilities of our subsidiaries, including trade payables and lease obligations. This occurs because our right to receive any assets of our subsidiaries upon their liquidation or reorganization, and your right to participate in those assets, will be effectively subordinated to the claims of that subsidiary's creditors, including trade creditors, except to the extent that we are recognized as a creditor of such subsidiary. If we are recognized as a creditor of that subsidiary, our claims would still be subordinate to any security interest in the assets of the subsidiary and any indebtedness of the subsidiary senior to us.

We are required to promptly notify holders of senior debt or their representatives under the subordinated indenture if payment of the subordinated debt securities is accelerated because of an event of default.

Under the subordinated indenture, we may not make payment on the subordinated debt securities if:

a default in our obligations to pay principal, premium, if any, interest or other amounts on our senior debt occurs and the default continues beyond any applicable grace period, which we refer to as a payment default; or

any other default occurs and is continuing with respect to designated senior debt that permits holders of designated senior debt to accelerate its maturity, which we refer to as a non-payment default, and the trustee receives a payment blockage notice from us or some other person permitted to give the notice under the subordinated indenture.

We will resume payments on the subordinated debt securities:

in case of a payment default, when the default is cured or waived or ceases to exist, and

in case of a non-payment default, the earlier of when the default is cured or waived or ceases to exist or 179 days after the receipt of the payment blockage notice.

No new payment blockage period may commence on the basis of a non-payment default unless 365 days have elapsed from the effectiveness of the immediately prior payment blockage notice. No non-payment default that existed or was continuing on the date of delivery of any payment blockage notice to the trustee shall be the basis for a subsequent payment blockage notice.

As a result of these subordination provisions, in the event of our bankruptcy, dissolution or reorganization, holders of senior debt may receive more, ratably, and holders of the subordinated debt securities may receive less, ratably, than our other creditors. The subordination provisions will not prevent the occurrence of any event of default under the subordinated indenture.

The subordination provisions will not apply to payments from money or government obligations held in trust by the trustee for the payment of principal, interest and premium, if any, on subordinated debt securities pursuant to the provisions described under the section entitled Satisfaction and Discharge; Defeasance, if the subordination provisions were not violated at the time the money or government obligations were deposited into trust.

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If the trustee or any holder receives any payment that should not have been made to them in contravention of subordination provisions before all senior debt is paid in full in cash or other payment satisfactory to holders of senior debt, then such payment will be held in trust for the holders of senior debt.

Senior debt securities will constitute senior debt under the subordinated indenture.

Additional or different subordination provisions may be described in a prospectus supplement relating to a particular series of debt securities.

Definitions

Designated senior debt means our obligations under any particular senior debt in which the instrument creating or evidencing the same or the assumption or guarantee thereof, or related agreements or documents to which we are a party, expressly provides that such indebtedness shall be designated senior debt for purposes of the subordinated indenture. The instrument, agreement or other document evidencing any designated senior debt may place limitations and conditions on the right of such senior debt to exercise the rights of designated senior debt.

Indebtedness means the following, whether absolute or contingent, secured or unsecured, due or to become due, outstanding on the date of the applicable indenture for such series of securities or thereafter created, incurred or assumed:

our indebtedness evidenced by a credit or loan agreement, note, bond, debenture or other written obligation;

all of our obligations for money borrowed;

all of our obligations evidenced by a note or similar instrument given in connection with the acquisition of any businesses, properties or assets of any kind,

our obligations:

as lessee under leases required to be capitalized on the balance sheet of the lessee under generally accepted accounting principles, or

as lessee under leases for facilities, capital equipment or related assets, whether or not capitalized, entered into or leased for financing purposes;

all of our obligations under interest rate and currency swaps, caps, floors, collars, hedge agreements, forward contracts or similar agreements or arrangements;

all of our obligations with respect to letters of credit, bankers' acceptances and similar facilities, including reimbursement obligations with respect to the foregoing;

all of our obligations issued or assumed as the deferred purchase price of property or services, but excluding trade accounts payable and accrued liabilities arising in the ordinary course of business;

all obligations of the type referred to in the above clauses of another person, the payment of which, in either case, we have assumed or guaranteed, for which we are responsible or liable, directly or indirectly, jointly or severally, as obligor, guarantor or otherwise, or which are secured by a lien on our property; and

renewals, extensions, modifications, replacements, restatements and refundings of, or any indebtedness or obligation issued in exchange for, any such indebtedness or obligation described in the above clauses of this definition.

Senior debt means the principal of, premium, if any, and interest, including all interest accruing subsequent to the commencement of any bankruptcy or similar proceeding, whether or not a claim for post-

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petition interest is allowable as a claim in any such proceeding, and rent payable on or in connection with, and all fees and other amounts payable in connection with, our indebtedness. However, senior debt shall not include:

any debt or obligation if its terms or the terms of the instrument under which or pursuant to which it is issued expressly provide that it shall not be senior in right of payment to the subordinated debt securities or expressly provide that such indebtedness is on the same basis or junior to the subordinated debt securities; or

debt to any of our subsidiaries, a majority of the voting stock of which is owned, directly or indirectly, by us.

Subsidiary means a corporation more than 50% of the outstanding voting stock of which is owned, directly or indirectly, by us or by one or more of our other subsidiaries or by a combination of us and our other subsidiaries. For purposes of this definition, voting stock means stock or other similar interests which ordinarily has or have voting power for the election of directors, or persons performing similar functions, whether at all times or only so long as no senior class of stock or other interests has or have such voting power by reason of any contingency.

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DESCRIPTION OF SUBSCRIPTION RIGHTS

We may issue subscription rights to purchase our common stock, preferred stock or debt securities. These subscription rights may be offered independently or together with any other security offered hereby and may or may not be transferable by the stockholder receiving the subscription rights in such offering. In connection with any offering of subscription rights, we may enter into a standby arrangement with one or more underwriters or other purchasers pursuant to which the underwriters or other purchasers may be required to purchase any securities remaining unsubscribed for after such offering.

The prospectus supplement relating to any subscription rights we offer, if any, will, to the extent applicable, include specific terms relating to the offering, including some or all of the following:

the price, if any, for the subscription rights;

the exercise price payable for our common stock, preferred stock or debt securities upon the exercise of the subscription rights;

the number of subscription rights to be issued to each stockholder;

the number and terms of our common stock, preferred stock or debt securities which may be purchased per each subscription right;

the extent to which the subscription rights are transferable;

any other terms of the subscription rights, including the terms, procedures and limitations relating to the exchange and exercise of the subscription rights;

the date on which the right to exercise the subscription rights shall commence, and the date on which the subscription rights shall expire;

the extent to which the subscription rights may include an over-subscription privilege with respect to unsubscribed securities or an over-allotment privilege to the extent the securities are fully subscribed; and

if applicable, the material terms of any standby underwriting or purchase arrangement which may be entered into by Otonomy in connection with the offering of subscription rights.

The description in the applicable prospectus supplement of any subscription rights we offer will not necessarily be complete and will be qualified in its entirety by reference to the applicable subscription rights certificate, which will be filed with the SEC if we offer subscription rights. We urge you to read the applicable subscription rights certificate

and any applicable prospectus supplement in their entirety.

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DESCRIPTION OF UNITS

We may issue units comprising one or more of the other classes of securities described in this prospectus in any combination. Each unit will be issued so that the holder of the unit is also the holder of each security included in the unit. Thus, the holder of a unit will have the rights and obligations of a holder of each included security. The units may be issued under unit agreements to be entered into between us and a unit agent, as detailed in the prospectus supplement relating to the units being offered. The prospectus supplement will describe:

the designation and terms of the units and of the securities comprising the units, including whether and under what circumstances the securities comprising the units may be held or transferred separately;

a description of the terms of any unit agreement governing the units;

a description of the provisions for the payment, settlement, transfer or exchange of the units;

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

whether the units if issued as a separate security will be issued in fully registered or global form.

The descriptions of the units in this prospectus and in any prospectus supplement are summaries of the material provisions of the applicable unit agreements. These descriptions do not restate those unit agreements in their entirety and may not contain all the information that you may find useful. We urge you to read the applicable unit agreements because they, and not the summaries, define your rights as holders of the units. For more information, please review the forms of the relevant unit agreements, which will be filed with the SEC promptly after the offering of units and will be available as described in the section titled **Where You Can Find More Information**.

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PLAN OF DISTRIBUTION

We may sell the securities offered through this prospectus (1) to or through underwriters or dealers, (2) directly to purchasers, including our affiliates, (3) through agents, or (4) through a combination of any of these methods. The securities may be distributed at a fixed price or prices, which may be changed, market prices prevailing at the time of sale, prices related to the prevailing market prices, or negotiated prices. The prospectus supplement will include the following information:

the terms of the offering;

the names of any underwriters or agents;

the name or names of any managing underwriter or underwriters;

the purchase price of the securities;

the net proceeds from the sale of the securities;

any delayed delivery arrangements;

any underwriting discounts, commissions or agency fees, and other items constituting underwriters' or agents' compensation;

any initial price to the public;

any discounts or concessions allowed or reallocated or paid to dealers; and

any commissions paid to agents.

We may engage in at-the-market offerings into an existing trading market in accordance with Rule 415(a)(4) in the manner described below under "At-the-Market Offerings."

We may issue to the holders of our common stock, on a pro rata basis for no consideration, subscription rights to purchase shares of our common stock or preferred stock. These subscription rights may or may not be transferable by stockholders. The applicable prospectus supplement will describe the specific terms of any offering of our common or preferred stock through the issuance of subscription rights, including the terms of the subscription rights offering, the terms, procedures and limitations relating to the exchange and exercise of the subscription rights and, if applicable, the material terms of any standby underwriting or purchase arrangement entered into by us in connection with the offering.

of common or preferred stock through the issuance of subscription rights.

Sale through Underwriters or Dealers

If underwriters are used in the sale, the underwriters will acquire the securities for their own account, including through underwriting, purchase, security lending or repurchase agreements with us. The underwriters may resell the securities from time to time in one or more transactions, including negotiated transactions. Underwriters may sell the securities in order to facilitate transactions in any of our other securities (described in this prospectus or otherwise), including other public or private transactions and short sales. Underwriters may offer securities to the public either through underwriting syndicates represented by one or more managing underwriters or directly by one or more firms acting as underwriters. Unless otherwise indicated in the prospectus supplement, the obligations of the underwriters to purchase the securities will be subject to certain conditions, and the underwriters will be obligated to purchase all the offered securities if they purchase any of them (other than any securities purchased upon exercise of any option to purchase additional securities). In connection with any offering of common stock pursuant to this prospectus, underwriters may have an option to purchase additional shares of common stock from us. We will provide information regarding any such option to purchase additional shares of common stock from us in the applicable prospectus supplement. The underwriters may change from time to time any initial price to the public and any discounts or concessions allowed or

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reallowed or paid to dealers. The prospectus supplement will include the names of the principal underwriters the respective amount of securities underwritten, the nature of the obligation of the underwriters to take the securities and the nature of any material relationship between an underwriter and us.

Some or all of the securities that we offer through this prospectus may be new issues of securities with no established trading market. Any underwriters to whom we sell securities for public offering and sale may make a market in those securities, but they will not be obligated to do so and they may discontinue any market making at any time without notice. Accordingly, we cannot assure you of the liquidity of, or continued trading markets for, any securities offered pursuant to this prospectus.

If dealers are used in the sale of securities offered through this prospectus, we will sell the securities to them as principals. They may then resell those securities to the public at varying prices determined by the dealers at the time of resale. The prospectus supplement will include the names of the dealers and the terms of the transaction.

Direct Sales and Sales through Agents

We may sell the securities offered through this prospectus directly. In this case, no underwriters or agents would be involved. Such securities may also be sold through agents designated from time to time. The prospectus supplement will name any agent involved in the offer or sale of the offered securities and will describe any commissions payable to the agent by us. Unless otherwise indicated in the prospectus supplement, any agent will agree to use its reasonable best efforts to solicit purchases for the period of its appointment.

We may sell the securities directly to institutional investors or others who may be deemed to be underwriters within the meaning of the Securities Act with respect to any sale of those securities. The terms of any such sales will be described in the prospectus supplement.

Delayed Delivery Contracts

If the prospectus supplement indicates, we may authorize agents, underwriters or dealers to solicit offers from certain types of institutions to purchase securities at the public offering price under delayed delivery contracts. These contracts would provide for payment and delivery on a specified date in the future. The contracts would be subject only to those conditions described in the prospectus supplement. The applicable prospectus supplement will describe the commission payable for solicitation of those contracts.

At-the-Market Offerings

To the extent that we make sales through one or more underwriters or agents in at-the-market offerings, we will do so pursuant to the terms of a sales agency financing agreement or other at-the-market offering arrangement between us, on one hand, and the underwriters or agents, on the other. If we engage in at-the-market sales pursuant to any such agreement, we will issue and sell our securities through one or more underwriters or agents, which may act on an agency basis or a principal basis. During the term of any such agreement, we may sell securities on a daily basis in exchange transactions or otherwise as we agree with the underwriters or agents. Any such agreement will provide that any securities sold will be sold at prices related to the then prevailing market prices for our securities. Therefore, exact figures regarding proceeds that will be raised or commissions to be paid cannot be determined as of the date of this prospectus. Pursuant to the terms of the agreement, we may agree to sell, and the relevant underwriters or agents may agree to solicit offers to purchase, blocks of our common stock or other securities. The terms of any such agreement will be set forth in more detail in the applicable prospectus or prospectus supplement.

Market Making, Stabilization and Other Transactions

Unless the applicable prospectus supplement states otherwise, each series of offered securities will be a new issue and will have no established trading market. We may elect to list any series of offered securities on an

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exchange. Any underwriters that we use in the sale of offered securities may make a market in such securities, but may discontinue such market making at any time without notice. Therefore, we cannot assure you that the securities will have a liquid trading market.

Any underwriter may also over-allot or engage in stabilizing transactions, syndicate covering transactions and penalty bids in accordance with Rule 104 of Regulation M under the Exchange Act. Over-allotment or short sales involve sales by persons participating in the offering of more securities than were sold to them. In these circumstances, these persons would cover such over-allotments or short positions by making purchases in the open market or by exercising their over-allotment option, if any. Stabilizing transactions involve bids to purchase the underlying security in the open market for the purpose of pegging, fixing or maintaining the price of the securities. Syndicate covering transactions involve purchases of the securities in the open market after the distribution has been completed in order to cover syndicate short positions.

Penalty bids permit the underwriters to reclaim a selling concession from a syndicate member when the securities originally sold by the syndicate member are purchased in a syndicate covering transaction to cover syndicate short positions. These transactions may cause the price of the securities to be higher than it would be in the absence of the transactions. The underwriters may, if they commence these transactions, discontinue them at any time.

Derivative Transactions and Hedging

We, the underwriters or other agents may engage in derivative transactions involving the securities. These derivatives may consist of short sale transactions and other hedging activities. The underwriters or agents may acquire a long or short position in the securities, hold or resell securities acquired and purchase options or futures on the securities and other derivative instruments with returns linked to or related to changes in the price of the securities. In order to facilitate these derivative transactions, we may enter into security lending or repurchase agreements with the underwriters or agents. The underwriters or agents may effect the derivative transactions through sales of the securities to the public, including short sales, or by lending the securities in order to facilitate short sale transactions by others. The underwriters or agents may also use the securities purchased or borrowed from us or others (or, in the case of derivatives, securities received from us in settlement of those derivatives) to directly or indirectly settle sales of the securities or close out any related open borrowings of the securities.

Electronic Auctions

We may also make sales through the Internet or through other electronic means. Since we may from time to time elect to offer securities directly to the public, with or without the involvement of agents, underwriters or dealers, utilizing the Internet or other forms of electronic bidding or ordering systems for the pricing and allocation of such securities, you should pay particular attention to the description of that system we will provide in a prospectus supplement.

Such electronic system may allow bidders to directly participate, through electronic access to an auction site, by submitting conditional offers to buy that are subject to acceptance by us, and which may directly affect the price or other terms and conditions at which such securities are sold. These bidding or ordering systems may present to each bidder, on a so-called real-time basis, relevant information to assist in making a bid, such as the clearing spread at which the offering would be sold, based on the bids submitted, and whether a bidder's individual bids would be accepted, prorated or rejected. For example, in the case of a debt security, the clearing spread could be indicated as a number of basis points above an index treasury note. Of course, many pricing methods can and may also be used.

Upon completion of such an electronic auction process, securities will be allocated based on prices bid, terms of bid or other factors. The final offering price at which securities would be sold and the allocation of securities among bidders

would be based in whole or in part on the results of the Internet or other electronic bidding process or auction.

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General Information

Agents, underwriters, and dealers may be entitled, under agreements entered into with us, to indemnification by us against certain liabilities, including liabilities under the Securities Act. Our agents, underwriters, and dealers, or their affiliates, may engage in transactions with, or perform services for us in the ordinary course of business.

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LEGAL MATTERS

The validity of the securities offered by this prospectus will be passed upon by Wilson Sonsini Goodrich & Rosati, P.C., Palo Alto, California. Certain members of, and investment partnerships comprised of members of, and persons associated with, Wilson Sonsini Goodrich & Rosati, Professional Corporation, own an aggregate of 15,627 shares of our common stock. Additional legal matters may be passed on for us, 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 financial statements included in our Annual Report on Form 10-K for the fiscal year ended December 31, 2017, as set forth in their report, which is incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP's report, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and other reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC's website at <http://www.sec.gov>. You may also read and copy any document we file at the SEC's Public Reference Room at 100 F Street, NE, Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the Public Reference Room. Our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, and Current Reports on Form 8-K, including any amendments to those reports, and other information that we file with or furnish to the SEC pursuant to Section 13(a) or 15(d) of the Exchange Act can also be accessed free of charge through the Internet. These filings will be available as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC.

We have filed with the SEC a registration statement under the Securities Act of 1933 relating to the offering of these securities. The registration statement, including the attached exhibits, contains additional relevant information about us and the securities. This prospectus does not contain all of the information set forth in the registration statement. You can obtain a copy of the registration statement, at prescribed rates, from the SEC at the address listed above. The registration statement and the documents referred to below under "Information Incorporated by Reference" are also available on our Internet website, www.otonomy.com. We have not incorporated by reference into this prospectus the information on our website, and you should not consider it to be a part of this prospectus.

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INFORMATION INCORPORATED BY REFERENCE

The SEC allows us to incorporate by reference into this prospectus certain information we file with it, which means that we can disclose important information by referring you to those documents. The information incorporated by reference is considered to be a part of this prospectus, and information that we file later with the SEC will automatically update and supersede information contained in this prospectus and any accompanying prospectus supplement. We incorporate by reference the documents listed below that we have previously filed with the SEC (excluding any portions of any Form 8-K that are not deemed filed pursuant to the General Instructions of Form 8-K):

our Annual Report on Form 10-K for the fiscal year ended December 31, 2017, filed with the SEC on March 8, 2018;

the information specifically incorporated by reference into the Annual Report from our definitive proxy statement on Schedule 14A, filed with the SEC on April 27, 2018;

our Quarterly Reports on Form 10-Q for the fiscal quarters ended March 31, 2018 (filed with the SEC on May 9, 2018) and June 30, 2018 (filed with the SEC on August 8, 2018);

our Current Report on Form 8-K filed with the SEC on June 21, 2018; and

the description of our common stock contained in our Registration Statement on Form 8-A as filed with the SEC on August 5, 2014 pursuant to Section 12(b) of the Exchange Act.

We also incorporate by reference into this prospectus additional documents that we may file with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act prior to the completion or termination of the offering, including all such documents we may file with the SEC after the date of the initial registration statement and prior to the effectiveness of the registration statement, but excluding any information deemed furnished and not filed with the SEC. Any statements contained in a previously filed document incorporated by reference into this prospectus is deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained in this prospectus, or in a subsequently filed document also incorporated by reference herein, modifies or supersedes that statement.

This prospectus may contain information that updates, modifies or is contrary to information in one or more of the documents incorporated by reference in this prospectus. You should rely only on the information incorporated by reference or provided in this prospectus. We have not authorized anyone else to provide you with different information. You should not assume that the information in this prospectus is accurate as of any date other than the date of this prospectus or the date of the documents incorporated by reference in this prospectus.

We will provide to each person, including any beneficial owner, to whom this prospectus is delivered, upon written or oral request, at no cost to the requester, a copy of any and all of the information that is incorporated by reference in this prospectus.

Requests for such documents should be directed to:

Otonomy, Inc.

4796 Executive Drive

San Diego, California 92121

Attention: Secretary

You may also access the documents incorporated by reference in this prospectus through our website at www.otonomy.com. Except for the specific incorporated documents listed above, no information available on or through our website shall be deemed to be incorporated in this prospectus or the registration statement of which it forms a part.

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\$150,000,000

Common Stock

Preferred Stock

Depository Shares

Warrants

Debt Securities

Subscription Rights

Units

PROSPECTUS

, 2018

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The following table sets forth the estimated costs and expenses, other than underwriting discounts and commissions, payable by the registrant in connection with the sale of the securities being registered:

| | |
|---|-----------|
| Securities and Exchange Commission registration fee | \$ 18,675 |
| FINRA filing fee | 23,000 |
| Accounting fees and expenses | * |
| Legal fees and expenses | * |
| Printing and engraving | * |
| Transfer agent fees and expenses | * |
| Miscellaneous | * |
| Total | \$ 41,175 |

* These fees and expenses depend on the securities offered and the number of issuances, and accordingly cannot be estimated as of the date of this prospectus.

Item 15. Indemnification of Directors and Officers

The registrant is a Delaware corporation. Section 145(a) of the Delaware General Corporation Law, or the DGCL, provides that a Delaware corporation may indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative, other than an action by or in the right of the corporation, by reason of the fact that such person is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, against expenses (including attorney fees), judgments, fines and amounts paid in settlement actually and reasonably incurred by the person in connection with such action, suit or proceeding if the person acted in good faith and in a manner the person reasonably believed to be in or not opposed to the best interests of the corporation, and, with respect to any criminal action or proceeding, had no reasonable cause to believe his or her conduct was unlawful.

Section 145(b) of the DGCL provides that a Delaware corporation may indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action or suit by or in the right of the corporation to procure a judgment in its favor by reason of the fact that such person acted in any of the capacities set forth above, against expenses (including attorney fees) actually and reasonably incurred by such person in connection with the defense or settlement of such action or suit if the person acted in good faith and in a manner the person reasonably believed to be in or not opposed to the best interests of the corporation, except that no indemnification shall be made in respect of any claim, issue or matter as to which such person shall have been adjudged to be liable to the corporation, unless and only to the extent that the Court of Chancery or the court in which such action or suit was brought shall determine that, despite the adjudication of liability but in view of all the circumstances of the case, such person is fairly and reasonably entitled to indemnification for such expenses which the court shall deem proper.

Further subsections of DGCL Section 145 provide that:

- (1) to the extent a present or former director or officer of a corporation has been successful on the merits or otherwise in the defense of any action, suit or proceeding referred to in subsections (a) and (b) of Section 145 or in the defense of any claim, issue or matter therein, such person shall be indemnified against expenses, including attorneys' fees, actually and reasonably incurred by such person in connection therewith;

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- (2) the indemnification and advancement of expenses provided for pursuant to Section 145 shall not be deemed exclusive of any other rights to which those seeking indemnification or advancement of expenses may be entitled under any bylaw, agreement, vote of stockholders or disinterested directors or otherwise; and
- (3) the corporation shall have the power to purchase and maintain insurance on behalf of any person who is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, against any liability asserted against such person and incurred by such person in any such capacity, or arising out of such person's status as such, whether or not the corporation would have the power to indemnify such person against such liability under Section 145.

As used in this Item 15, the term "proceeding" means any threatened, pending, or completed action, suit, or proceeding, whether or not by or in the right of the registrant, and whether civil, criminal, administrative, investigative or otherwise.

Section 145 of the DGCL makes provision for the indemnification of officers and directors in terms sufficiently broad to indemnify officers and directors of the registrant under certain circumstances from liabilities (including reimbursement for expenses incurred) arising under the Securities Act of 1933, as amended, or the Securities Act. The registrant's amended and restated certificate of incorporation provides, in effect, that, to the fullest extent and under the circumstances permitted by Section 145 of the DGCL, the registrant will indemnify any and all of its executive officers and directors. The registrant may, in its discretion, similarly indemnify its employees and agents. The registrant's amended and restated certificate of incorporation also relieves its directors from monetary damages to registrant or its stockholders for breach of such director's fiduciary duty as a director to the fullest extent permitted by the DGCL. Under Section 102(b)(7) of the DGCL, a corporation may relieve its directors from personal liability to such corporation or its stockholders for monetary damages for any breach of their fiduciary duty as directors except (1) for a breach of the duty of loyalty, (2) for failure to act in good faith, (3) for intentional misconduct or knowing violation of law, (4) for willful or negligent violations of certain provisions in the DGCL imposing certain requirements with respect to stock repurchases, redemptions and dividends, or (5) for any transactions from which the director derived an improper personal benefit.

The registrant has entered into indemnification agreements with its directors and executive officers that provide, in general, that the registrant will indemnify them to the fullest extent permitted by law in connection with their service to the registrant or on the registrant's behalf. The registrant intends to enter into indemnification agreements with any new directors and executive officers in the future.

The registrant has purchased and intends to maintain insurance on behalf of each and any person who is or was a director or officer of the Company against any loss arising from any claim asserted against him or her and incurred by him or her in any such capacity, subject to certain exclusions.

See also the undertakings set out in response to Item 17 herein.

Item 16. Exhibits

A list of exhibits filed herewith is contained in the exhibit index that immediately precedes such exhibits and is incorporated herein by reference.

Item 17. Undertakings

(a) The undersigned registrant hereby undertakes:

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

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

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- (ii) To reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the SEC pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20% change in the maximum aggregate offering price set forth in the Calculation of Registration Fee table in the effective registration statement; and
 - (iii) To include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement; *provided, however*, that paragraphs (a)(1)(i), (a)(1)(ii) and (a)(1)(iii) of this section do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the SEC by the registrant pursuant to Section 13 or Section 15(d) of the Securities Exchange Act of 1934 that are incorporated by reference in the registration statement, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of the registration statement.
- (2) That, for the purpose of determining any liability under the Securities Act of 1933, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.
 - (3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.
 - (4) That, for the purpose of determining liability under the Securities Act of 1933 to any purchaser:
 - (i) If the registrant is relying on Rule 430B,
 - (A) Each prospectus filed by the registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the registration statement as of the date the filed prospectus was deemed part of and included in the registration statement; and
 - (B) Each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5) or (b)(7) as part of a registration statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(1)(i), (vii) or (x) for the purpose of providing the information required by Section 10(a) of the Securities Act of 1933 shall be deemed to be part of and included in the registration statement as of the earlier of the date such form of prospectus is first used after effectiveness or the date of the first contract of sale of securities in the offering described in the prospectus. As provided in Rule 430B, for liability purposes of the issuer and any person that is at

that date an underwriter, such date shall be deemed to be a new effective date of the registration statement relating to the securities in the registration statement to which that prospectus relates, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof. *Provided, however,* that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such effective date, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to the effective date; or

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

- (5) That, for the purpose of determining liability of the registrant under the Securities Act of 1933 to any purchaser in the initial distribution of the securities, the undersigned registrant undertakes that in a primary offering of securities of the undersigned registrant pursuant to this registration statement, regardless of the underwriting method used to sell the securities to the purchaser, if the securities are offered or sold to such purchaser by means of any of the following communications, the undersigned registrant will be a seller to the purchaser and will be considered to offer and sell such securities to such purchaser:
 - (i) Any preliminary prospectus or prospectus of the undersigned registrant relating to the offering required to be filed pursuant to Rule 424;
 - (ii) Any free writing prospectus relating to the offering prepared by or on behalf of the undersigned registrant or used or referred to by the undersigned registrant;
 - (iii) The portion of any other free writing prospectus relating to the offering containing material information about the undersigned registrant or its securities provided by or on behalf of the undersigned registrant; and
 - (iv) Any other communication that is an offer in the offering made by the undersigned registrant to the purchaser.

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

- (c) Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against

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

(d) The undersigned registrant hereby undertakes that:

- (1) For purposes of determining any liability under the Securities Act of 1933, the information omitted from the form of prospectus filed as part of this registration statement in reliance upon Rule 430A and contained in a form of prospectus filed by the registrant pursuant to Rule 424(b)(1) or (4) or 497(h)

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under the Securities Act shall be deemed to be part of this registration statement as of the time it was declared effective.

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

- (e) The undersigned registrant hereby undertakes to file an application for the purpose of determining the eligibility of the trustee to act under subsection (a) of Section 310 of the Trust Indenture Act in accordance with the rules and regulations prescribed by the SEC under Section 305(b)(2) of the Trust Indenture Act.

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| Exhibit Number | Exhibit Title |
|---------------------------|--|
| 1.1* | Form of Underwriting Agreement. |
| 3.1** | <u>Amended and Restated Certificate of Incorporation of the Registrant (Exhibit 3.2).</u> |
| 3.2** | <u>Amended and Restated Bylaws of the Registrant. (Exhibit 3.4).</u> |
| 4.1** | <u>Third Amended and Restated Investors Rights Agreement among the Registrant and certain of its stockholders, dated April 23, 2014 (Exhibit 4.1).</u> |
| 4.2** | <u>Specimen Common Stock Certificate of the Registrant (Exhibit 4.2).</u> |
| 4.3 | <u>Form of senior indenture, to be entered into between the Registrant and the trustee designated therein.</u> |
| 4.4* | Form of senior note with respect to each particular series of senior notes issued hereunder. |
| 4.5 | <u>Form of subordinated indenture to be entered into between the Registrant and the trustee designated therein.</u> |
| 4.6* | Form of subordinated note with respect to each particular series of subordinated notes issued hereunder. |
| 4.7* | Form of warrant with respect to each warrant issued hereunder. |
| 4.8* | Certificate of designation, preferences and rights with respect to any preferred stock issued hereunder. |
| 4.9* | Form of Depositary Agreement with respect to the depositary shares. |
| 4.10* | Form of Subscription Agreement. |
| 4.11* | Form of Unit with respect to any contractual units. |
| 5.1 | <u>Opinion of Wilson Sonsini Goodrich & Rosati, P.C.</u> |
| 12.1 | <u>Statement re Computation of Ratio of Earnings to Fixed Charges</u> |
| 23.1 | <u>Consent of Independent Registered Public Accounting Firm.</u> |
| 23.2 | <u>Consent of Wilson Sonsini Goodrich & Rosati, P.C. (included in Exhibit 5.1).</u> |
| 24.1 | <u>Power of Attorney (included on the signature page to this registration statement on Form S-3).</u> |
| 25.1* | Form T-1 Statement of Eligibility under the Trust Indenture Act of 1939, as amended, of designated trustee under the senior indenture. |
| 25.2* | Form T-1 Statement of Eligibility under the Trust Indenture Act of 1939, as amended, of designated trustee under the subordinated indenture. |

* If applicable, to be filed by amendment or as an exhibit to a report pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, and incorporated herein by reference.

** Incorporated by reference to the exhibits to the registrant's Registration Statement on Form S-1, dated August 1, 2014 (No. 333-197365). The number given in parentheses indicates the corresponding exhibit number in such Form S-1.

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Pursuant to the requirements of the Securities Act of 1933, the registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this registration statement on Form S-3 to be signed on its behalf by the undersigned, thereunto duly authorized, in the city of San Diego, State of California, on the 10th day of September, 2018.

By: /s/ David A. Weber
David A. Weber, Ph.D.
President and Chief Executive Officer

Power of Attorney

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below hereby constitutes and appoints David A. Weber and Paul E. Cayer and each of them acting individually, as his or her true and lawful attorneys-in-fact and agents, with full power of each to act alone, with full powers of substitution and resubstitution, for him or her and in his or her name, place and stead, in any and all capacities (including his or her capacity as a director and/or officer of Otonomy, Inc.), to sign any and all amendments to this registration statement on Form S-3 (including post-effective amendments) with all exhibits thereto and all documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, with full power of each to act alone, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully for all intents and purposes as they, he or she might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, or his, her or their substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933 this registration statement has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

| Signature | Title | Date |
|---|---|--------------------|
| /s/ David A. Weber David A. Weber, Ph.D. | President, Chief Executive Officer and Director (Principal Executive Officer) | September 10, 2018 |
| /s/ Paul E. Cayer Paul E. Cayer | Chief Financial and Business Officer (Principal Financial and Accounting Officer) | September 10, 2018 |
| /s/ Jay Lichter Jay Lichter, Ph.D. | Chairman of the Board | September 10, 2018 |
| /s/ James B. Breitmeyer | Director | September 10, 2018 |

James B. Breitmeyer, M.D., Ph.D.

/s/ Vickie Capps Director September 10, 2018

Vickie Capps

/s/ Iain McGill Director September 10, 2018

Iain McGill

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| Signature | Title | Date |
|--|--------------|--------------------|
| /s/ Heather Preston Heather Preston, M.D. | Director | September 10, 2018 |
| /s/ Theodore R. Schroeder Theodore R. Schroeder | Director | September 10, 2018 |

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