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Registration Statement No. 333-221968

Prospectus



Leap Therapeutics, Inc.
3,734,914 Shares
Common Stock

This prospectus relates to the possible resale by the selling stockholders (the "Selling Stockholders") identified in this prospectus of up to 3,734,914 shares of our common stock, par value \$0.001 per share (the "Common Stock"), which includes (i) 1,867,457 shares of our Common Stock issued on November 14, 2017 and (ii) an aggregate of 1,867,457 shares of our Common Stock (the "Warrant Shares") issuable upon exercise of common stock purchase warrants issued on November 14, 2017 (the "Warrants") in a private placement transaction, which closed on November 14, 2017. We are registering these shares on behalf of the Selling Stockholders, to be offered and sold by them from time to time.

We are not selling any shares of Common Stock under this prospectus and will not receive any of the proceeds from the sale of shares of Common Stock by the Selling Stockholders. However, we may receive proceeds from the cash exercise of the Warrants, which, if exercised in cash at the current applicable exercise price with respect to all of the Warrants to purchase 1,867,457 shares of Common Stock, would result in gross proceeds to the Company of \$11.4 million.

The Selling Stockholders may offer the shares of our Common Stock and Warrant Shares from time to time and at such prices as each Selling Stockholder may determine through public or private transactions or through other means described in the section entitled "Plan of Distribution" or a supplement to this prospectus. Each Selling Stockholder may also sell the shares under Rule 144 under the Securities Act of 1933, as amended, if available, rather than under this prospectus.

We are registering the offer and sale of the shares of our Common Stock and Warrant Shares pursuant to certain registration rights granted to the Selling Stockholders. The registration of these shares does not necessarily mean that any of the shares will be offered or sold by the Selling Stockholders. The timing and amount of any sale is within the sole discretion of each Selling Stockholder.

The Selling Stockholders will pay all underwriting discounts and selling commissions, if any, in connection with the sale of the shares of Common Stock and Warrant Shares. We have agreed to pay certain expenses in connection with this registration statement and to indemnify the Selling Stockholders against certain liabilities. To our knowledge, as of the date of this prospectus, no underwriter or other person has been engaged to facilitate the sale of shares of Common Stock and Warrant Shares in this offering.

We are an emerging growth company as that term is used in the Jumpstart Our Business Startups Act of 2012 and, as such, have elected to comply with certain reduced public company reporting requirements for this prospectus and future filings.

Our Common Stock is listed on The NASDAQ Global Market under the symbol "LPTX." On December 7, 2017, the closing price of our Common Stock was \$6.76 per share.

Investing in our Common Stock involves a high degree of risk. You should carefully read the risks and uncertainties included herein under the heading "Risk Factors" on page 7 of this prospectus, and under similar headings in our Annual Report on Form 10-K for the fiscal year ended December 31, 2016 and our Quarterly Reports on Form 10-Q for the quarterly periods ended March 31, 2017, June 30, 2017 and September 30, 2017, which have been filed with the Securities and Exchange Commission and are incorporated by reference in this prospectus and in the other documents that are filed after the date hereof and incorporated by reference into this prospectus.

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

The date of this prospectus is December 15, 2017.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement on Form S-3 that we filed with the U.S. Securities and Exchange Commission (the "SEC"), using a "shelf" registration process. By using such registration statement, the selling stockholders identified herein (the "Selling Stockholders") may, from time to time, offer and sell (in one or more transactions as described under "Plan of Distribution") up to 3,734,914 shares of our common stock, par value \$0.001 per share (the "Common Stock"), including 1,867,457 shares of Common Stock issuable upon the exercise of the warrants (the "Warrant Shares") issued in our private placement offering which closed on November 14, 2017. We will not receive any of the proceeds from the sales of the Common Stock by the Selling Stockholders.

This prospectus provides you with a general description of us and our securities. We may add, update or change in a prospectus supplement any of the information contained in this prospectus or the documents incorporated by reference. For further information about our business and our securities, you should refer to the registration statement and the reports incorporated by reference in this prospectus, as described in "Additional Information" and "Incorporation of Certain Information by Reference". This prospectus contains summaries of certain provisions contained in some of the documents described herein, but reference is made to the actual documents for complete information. All of the summaries are qualified in their entirety by the actual documents. Copies of some of the documents referred to herein have been filed, will be filed or will be incorporated by reference as exhibits to the registration statement of which this prospectus is a part, and you may obtain copies of those documents as described below under the heading "Where You Can Find More Information."

You must not rely upon any information or representation not contained or incorporated by reference in this prospectus. You should rely only on the information contained in this prospectus and in any prospectus supplement (including in any documents incorporated by reference herein or therein). You should not assume that the information contained in this prospectus is accurate on any date subsequent to the date set forth on the front of the document or that any information we have incorporated by reference is correct on any date subsequent to the date of the document incorporated by reference, even though this prospectus is delivered or securities are sold on a later date. We and the Selling Stockholders have not authorized anyone to provide you with any different information. The Selling Stockholders are offering to sell our securities, and seeking offers to buy, only in jurisdictions where offers and sales are permitted.

Leap Therapeutics, Inc. and its subsidiaries are collectively referred to herein as "Leap", "the Company", "we", "us", and "our", unless otherwise specified or the context indicates otherwise.

PROSPECTUS SUMMARY

This summary highlights selected information appearing elsewhere or incorporated by reference into this prospectus and may not contain all of the information that you need to consider in making your investment decision. You should read this prospectus, any applicable prospectus supplement, and any related free writing prospectus that we have authorized for use in connection with this offering, and any documents incorporated by reference carefully, including the risks and uncertainties included herein under the heading "Risk Factors" beginning on page 7 in this prospectus and incorporated by reference from our most recent Annual Report on Form 10-K and our most recent Quarterly Report on Form 10-Q, before making an investment decision.

About Us

Corporate Information

Leap Therapeutics, Inc. was incorporated in the state of Delaware as Dekkun Corporation on January 3, 2011 and changed its name to HealthCare Pharmaceuticals, Inc. effective May 29, 2014, and then to Leap Therapeutics, Inc. effective November 16, 2015 (the "Company"). During 2015, HealthCare Pharmaceuticals Pty Ltd. ("HCP Australia") was formed and is a wholly owned subsidiary of the Company. During January 2017, the Company merged with Macrocare Ltd. (now "Leap Therapeutics Ltd.") and its wholly-owned subsidiary Macrocare, Inc. Our principal executive offices are located at 47 Thorndike Street, Suite B1-1, Cambridge, Massachusetts 02141, and our telephone number is (617) 714-0360. Our website address is www.leaptx.com. The information contained in, or that can be accessed through, our website is not part of this prospectus.

Our Company

We are a biopharmaceutical company acquiring and developing novel therapeutics at the leading edge of cancer biology. Our approach is designed to target compelling tumor-promoting and immuno-oncology pathways to generate durable clinical benefit and enhanced outcomes for patients. Our programs are monoclonal antibodies that target key cellular pathways that enable cancer to grow and spread and specific mechanisms that activate the body's immune system to identify and attack cancer. Our two clinical stage programs are:

- **DKN-01:** A monoclonal antibody targeting Dickkopf-related protein 1, or DKK1. DKK1 is a protein that regulates the Wnt signaling pathways, and has an important role in tumor cell signaling and in mediating an immuno-suppressive tumor microenvironment. DKN-01 has been engineered to bind to DKK1 and to generate an anti-tumor effect through altering the Wnt signaling pathways and the immune tumor microenvironment. We are testing DKN-01 in ongoing clinical trials in patients with esophagogastric cancer and biliary tract cancer. We have studied DKN-01 as a monotherapy in patients with non-small cell lung cancer. Based on the patient responses and clinical benefit in these trials, we are also studying or planning to study DKN-01 in patients with Wnt pathway alterations with gastric cancer, hepatocellular carcinoma, or endometrial cancer, and in combination with immune checkpoint inhibitors, such as Merck's KEYTRUDA® (pembrolizumab) or Roche's TECENTRIQ® (atezolizumab).
- **TRX518:** A monoclonal antibody targeting the glucocorticoid-induced tumor necrosis factor-related receptor, or GITR, a receptor found on the surface of a wide range of immune cells. TRX518 has been specifically engineered to enhance the immune system's anti-tumor response by activating GITR signaling, or GITR agonism, to activate tumor fighting white blood cells, or T effector cells, and decrease the activity of potentially tumor-protective white blood cells, or T regulatory cells, without causing the immune cells to be destroyed. We believe GITR is an ideal immune system agonist target through this two-pronged approach of stimulating an anti-tumor response and reducing immune suppression. We are conducting two clinical trials of TRX518 in patients with advanced solid tumors and have evidence of biomarker modulation and

clinical activity. Based on the results seen in these trials, we are studying the combination of TRX518 with a chemotherapy, gemcitabine, and in combination with immune checkpoint inhibitors in patients with advanced solid tumors.

We intend to apply our extensive experience identifying and developing transformational products to aggressively develop these antibodies and build a pipeline of programs that has the potential to change the practice of cancer medicine.

Our operations to date have been limited to organizing and staffing our Company, business planning, raising capital, undertaking preclinical studies and clinical trials of DKN-01 and TRX518, protecting our intellectual property and providing general and administrative support for these operations. To date, we have not generated any product revenue and have primarily financed our operations through the private placement of our equity securities, including the Private Placement described below, business development activities, convertible note financings, and the merger with Macrocare.

As of September 30, 2017, we had received an aggregate of \$88.3 million in net proceeds comprised of \$33.9 million from the issuance of private equity securities, \$34.7 million from the issuance of convertible notes and \$19.7 million from the merger with Macrocare.

We have never been profitable and have incurred net losses in each year since inception. As of September 30, 2017, we had an accumulated deficit of \$123.8 million. During the three months ended September 30, 2017, our second full quarter operating as a public company, we incurred a net loss of \$6.8 million and our cash and cash equivalents decreased by approximately \$3.0 million. The Company expects to continue to generate operating losses in the foreseeable future. We had cash and cash equivalents of \$14.2 million at September 30, 2017. We expect to incur significant expenses and increasing operating losses for the foreseeable future. We expect our research and development expenses to increase as we continue the clinical trials of, and seek regulatory approval for, DKN-01 and TRX-518. If we obtain regulatory approval for DKN-01 or TRX518, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution. Furthermore, we expect that our general and administrative costs will increase as we grow and operate as a public company. As a result, we will need to generate significant revenue if we are to achieve profitability, and we may never be able to do so.

Prior to the sale of our Common Stock and Warrants in the Private Placement as discussed below, we believed that our cash and cash equivalents and available-for-sale investments as of September 30, 2017 would be sufficient to fund our operating expenses and capital expenditure requirements into the second quarter of 2018. We closed the \$18.0 million Private Placement on November 14, 2017 and, when including net proceeds from the Private Placement along with our cash and cash equivalents and available-for-sale investments as of September 30, 2017, we believe we will have sufficient funds to cover our operating expenses and capital expenditure requirements into the first quarter of 2019.

Recent Events

Private Placement

On November 14, 2017, we entered into purchase agreements (collectively, the "Purchase Agreements") with certain institutional accredited investors (collectively, the "Purchasers"). Each of the Purchase Agreements was on terms and conditions substantially similar to each other Purchase Agreement and pursuant to such Purchase Agreements, we, in a private placement, agreed to issue and sell to the Purchasers an aggregate of 2,958,094 shares (the "Shares") of unregistered Common Stock, at a price per share of \$6.085 (the "Shares"), each share issued with a warrant (the "Warrants") to purchase one share of Common Stock (the "Warrant Shares") at an exercise price of \$6.085 (the "Exercise Price") with an exercise period expiring seven years after closing (the "Term"), for gross

proceeds of approximately \$18.0 million (the "Private Placement"). If all of the Warrants are exercised in cash at the Exercise Price during the Term, the Company will receive proceeds of approximately \$18.0 million and will issue an aggregate of 2,958,094 Warrant Shares.

HealthCare Ventures IX, L.P. and Eli Lilly and Company, each a more than 5% direct holder of our Common Stock, also purchased Common Stock and Warrants in the Private Placement. Each of HealthCare Ventures IX, L.P. and Eli Lilly and Company agreed to purchase the Common Stock and Warrants on the same terms and conditions as the other Purchasers. Three of our directors and executive officers are affiliated with HealthCare Ventures IX, L.P. and its affiliates. Additional information regarding Selling Stockholder ownership and affiliations is described below in "Selling Stockholders."

Subject to stockholder approval of such provisions, the Warrants include full ratchet anti-dilution protection provisions. The Company expects to hold a special meeting of stockholders for the stockholders to approve the full ratchet anti-dilution protection provisions, on or about January 12, 2018. If the stockholders do not approve of the full ratchet anti-dilution protection provisions, such provisions shall be of no force and effect. In connection with such approval, the Company, on November 14, 2017, entered into a voting agreement with HealthCare Ventures VIII, L.P., HealthCare Ventures IX, L.P. and HealthCare Ventures Strategic Fund, L.P. (collectively, the "HealthCare Parties"), who hold more than 50% of the shares entitled to vote at such shareholder meeting, pursuant to which the HealthCare Parties agreed to vote all of their beneficially owned shares in favor of the any approval proposed at the special meeting of stockholders.

Raymond James & Associates, Inc. and Ladenburg Thalmann & Co. Inc. acted as the placement agents (the "Placement Agents") for the Private Placement pursuant to an agreement with us dated as of November 14, 2017 (the "Placement Agent Agreement"). Pursuant to the Placement Agent Agreement, we agreed to pay the Placement Agents a fee equal to 2.2% of the aggregate gross proceeds from the Private Placement plus the reimbursement of certain expenses. We plan to use the net proceeds from the Private Placement for general corporate purposes. The Private Placement raised gross proceeds to the Company of approximately \$18.0 million and net proceeds to the Company of approximately \$17.3 million, which is after deducting commissions to the Company's Placement Agents and estimated expenses of approximately \$0.7 million in the aggregate and excluding any potential proceeds to the Company upon the cash exercise of the Warrants.

Pursuant to the terms of the Purchase Agreements, we were obligated to prepare and file with the SEC a registration statement (the "Registration Statement") to register for resale the Shares and the Warrant Shares on or prior to the date 30 days following the closing of the Private Placement, and use our best commercially reasonable efforts, subject to receipt of necessary information from the Purchasers, to cause the SEC to declare the Registration Statement effective within 60 days following the closing of the Private Placement or, if the Registration Statement is selected for review by the SEC, within 90 days following the closing of the Private Placement. In order to comply with such obligation, we are filing the Registration Statement of which this prospectus forms a part. Two Purchasers have opted not to register their Shares or Warrant Shares and therefore, such Shares and Warrant Shares are not included in this offering.

Implications of Being an Emerging Growth Company

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012. We will remain an emerging growth company until the earlier of (i) the beginning of the first fiscal year following the fifth anniversary of our initial public offering, (ii) the beginning of the first fiscal year after our annual gross revenue is \$1.07 billion or more, (iii) the date on which we have, during the previous three-year period, issued more than \$1.0 billion in non-convertible debt securities

and (iv) as of the end of any fiscal year in which the market value of our Common Stock held by non-affiliates exceeded \$700 million as of the end of the second quarter of that fiscal year.

For as long as we remain an "emerging growth company," we may take advantage of certain exemptions from various reporting requirements that are applicable to public companies that are not "emerging growth companies" including, but not limited to, not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation and financial statements in our periodic reports and proxy statements, and exemptions from the requirements of holding a nonbinding advisory vote to approve executive compensation and shareholder approval of any golden parachute payments not previously approved. We plan to take advantage of these reporting exemptions until we are no longer an "emerging growth company."

THE OFFERING

Shares of
Common
Stock offered
for resale by
the Selling
Stockholders: 3,734,914 shares, including 1,867,457 Warrant Shares

Shares of
Common
Stock
Outstanding
at November
30, 2017: 12,354,014

Use of
Proceeds: We will not receive any of the proceeds from the sale of any of the shares that may be offered from time to time by the Selling Stockholders.

Risk Factors: Investing in our Common Stock involves risks. Please refer to the sections titled "Risk Factors" beginning on page 7 of this prospectus, as well as the risks and uncertainties discussed under the section titled "Risk Factors" in our most recent Annual Report on Form 10-K and any subsequent Quarterly Reports on Form 10-Q or Current Reports on Form 8-K; "Cautionary Note Regarding Forward-Looking Statements" on page 9 of this prospectus, and other information included or incorporated by reference in this prospectus supplement and the accompanying prospectus for a discussion of factors you should carefully consider before investing our securities.

NASDAQ
Global
Market
Symbol: LPTX

We are filing the Registration Statement of which this prospectus forms a part to permit the resale of shares of Common Stock that were issued, or will be issuable upon the exercise of Warrants that were issued in connection with the Private Placement, as required by certain registration rights granted to the purchasers pursuant to the Purchase Agreements in the Private Placement. Two Purchasers have opted not to register their Shares or Warrant Shares and therefore such Shares and Warrant Shares are not included in this offering.

Except as otherwise indicated, all information in this prospectus excludes the following:

- 2,958,094 shares Common Stock issuable upon the exercise of the Warrants issued on November 14, 2017 at an initial exercise price of \$6.085 per share;
- 156,016 shares of Common Stock issuable upon the exercise of stock options outstanding as of September 30, 2017, having a weighted average exercise price of \$41.43 per share, pursuant to awards granted under the Macrocare 2008 Stock Option Plan;
- 121,873 shares of Common Stock issuable upon the exercise of stock options outstanding as of September 30, 2017, having a weighted average exercise price of \$28.35 per share, pursuant to awards granted under the Macrocare 2013 Share Incentive Plan;
- 1,380,677 shares of Common Stock issuable upon the exercise of stock options outstanding as of September 30, 2017, having a weighted average exercise price of \$9.76 per share, pursuant to awards granted under our Amended and Restated 2012 Equity Incentive Plan;
- 204,055 shares of Common Stock issuable upon the exercise of stock options outstanding as of September 30, 2017, having a weighted average exercise price of \$9.78 per share, pursuant to awards granted under our 2016 Equity Incentive Plan; and
- 650,266 shares of our Common Stock reserved for future issuance under our 2016 Equity Incentive Plan as of September 30, 2017.

RISK FACTORS

An investment in our securities involves a high degree of risk. Before making an investment decision, you should carefully consider the risks described below and under "Risk Factors" in any applicable prospectus supplement and in our most recent Annual Report on Form 10-K, and in our updates to those Risk Factors in our Quarterly Reports on Form 10-Q or Current Reports on Form 8-K following the most recent Form 10-K, and in all other information appearing in this prospectus or incorporated by reference into this prospectus and any applicable prospectus supplement. The material risks and uncertainties that management believes affect us will be described in those documents. In addition to those risk factors, there may be additional risks and uncertainties of which management is not aware or focused on or that management deems immaterial. Our business, financial condition or results of operations could be materially adversely affected by any of these risks. The trading price of our securities could decline due to any of these risks, and you may lose all or part of your investment. This prospectus is qualified in its entirety by these risk factors.

Additional Risks Relating to This Offering and Our Common Stock

The sale of a substantial amount of our Common Stock, including resale of the shares of Common Stock issuable upon the exercise of Warrants acquired in the Private Placement, in the public market after this offering could adversely affect the prevailing market price of our Common Stock and cause stockholders to experience dilution.

We have outstanding an aggregate of 12,354,014 shares of our Common Stock as of November 30, 2017. The Warrants are exercisable for an aggregate of 2,958,094 shares of Common Stock, subject to adjustment as provided in the Warrants, including 1,867,457 shares of Common Stock being offered pursuant to this prospectus. The Warrants are exercisable at any time. Pursuant to the registration rights granted in the Private Placement, we agreed to register the resale by the Selling Stockholders named herein of the shares of Common Stock issuable upon exercise of the Warrants. Two Purchasers have opted not to register their Shares or Warrant Shares and therefore, such Shares and Warrant Shares are not included in this offering. Upon such registration, these registered shares will become generally available for immediate resale.

Sales of substantial amounts of shares of our Common Stock in the public market, or the perception that such sales might occur, could adversely affect the market price of our Common Stock, and the market value of our other securities, and could result in dilution to shareholders who hold our Common Stock. Further, pursuant to the terms of the Purchase Agreements and the Warrants, we have agreed to solicit stockholder approval in connection with Nasdaq Rule 5635(d) pursuant to a proxy statement that we plan to file with the SEC for the inclusion of a full ratchet anti-dilution feature as a term of the Warrants. If stockholder approval of the inclusion of such anti-dilution feature is obtained, and if we issue Common Stock, options or Common Stock equivalents at a price less than the exercise price of the Warrants, subject to certain customary exceptions, the exercise price of the Warrants will be reduced to that lower price. Such a decrease in exercise price may cause holders to exercise the Warrants which could result in dilution to our existing stockholders at an accelerated rate.

In addition, we may issue additional shares of Common Stock or other equity or debt securities convertible into Common Stock in connection with a future financing, acquisition, employee arrangements or otherwise. Any such issuance could result in substantial dilution to our stockholders and could cause our stock price to decline.

A substantial number of shares of Common Stock are being offered by this prospectus, and we cannot predict if and when the purchasers may sell such shares in the public markets. In addition, certain holders of shares of our Common Stock have additional rights, subject to some conditions, to require us to file registration statements covering the sale of their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. We have also registered the

offer and sale of all shares of Common Stock that we may issue under our equity compensation plans. Furthermore, in the future, we may issue additional shares of Common Stock or other equity or debt securities convertible into Common Stock in connection with a financing, acquisition, litigation settlement, employee arrangements or otherwise. Any such issuance could result in substantial dilution to our existing stockholders and could cause our stock price to decline.

We may become obligated to pay liquidated damages if we fail to file, obtain effectiveness and maintain effectiveness of a registration statement under the Purchase Agreements we entered into with the Selling Stockholders.

We have granted to the Selling Stockholders resale registration rights pursuant to the terms of Purchase Agreements. In addition to the registration rights, the Selling Stockholders are entitled to receive liquidated damages upon the occurrence of a number of events relating to filing the Registration Statement, the Registration Statement becoming effective and maintaining an effective registration statement covering the securities being registered. The liquidated damages will be payable upon the occurrence of each of those events and each monthly anniversary thereof until cured. The amount of liquidated damages payable per 30-day period is equal to 1.0% of the purchase price paid by such Purchaser and may increase to 2.0% under certain circumstances, provided, however, the maximum aggregate liquidated damages payable to a Selling Stockholder is 10% of the aggregate purchase price paid by a Purchaser for the Shares and Warrants pursuant to the Purchase Agreement. We may also be responsible for the actual damages suffered by a Selling Stockholder in certain circumstances.

Our share price may be volatile, which could subject us to securities class action litigation and our stockholders could incur substantial losses.

The market price of shares of our Common Stock could be subject to wide fluctuations in response to many risk factors listed in this section, and others beyond our control, including:

- the results of clinical trials or development activities of our programs, or any future programs we may acquire;
- actual or anticipated fluctuations in our financial condition and operating results;
- failure to meet or exceed financial estimates and projections of the investment community or that we provide to the public;
- issuance of new or updated research or reports by securities analysts;
- fluctuations in the valuation of companies perceived by investors to be comparable to us;
- additions or departures of key management or other personnel;
- disputes or other developments related to proprietary rights, including patents, litigation matters, and our ability to obtain patent protection for our technologies;
- announcement or expectation of additional debt or equity financing efforts;
- sales of our Common Stock by us, our insiders or our other stockholders; and
- general economic and market conditions.

These and other market and industry factors may cause the market price and demand for our Common Stock to fluctuate substantially, regardless of our actual operating performance, which may limit or prevent investors from readily selling their shares of Common Stock and may otherwise negatively affect the liquidity of our Common Stock. In addition, the stock market in general, and NASDAQ and emerging growth companies in particular, have experienced extreme price and volume

fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. In the past, when the market price of a stock has been volatile, holders of that stock have instituted securities class action litigation against the company that issued the stock. If in the future any of our stockholders brought a lawsuit against us, we could incur significant legal expenses, settlement costs or damage awards that are not covered by, or exceed the limits of, our available directors' and officers' liability insurance, which could adversely impact our financial condition, results of operations or cash flows. Such a lawsuit could also divert the time and attention of our management.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and each prospectus supplement, including the documents that we incorporate by reference, contains or may contain forward-looking statements as that term is defined in the federal securities laws. The events described in forward-looking statements contained in this prospectus, including the documents that we incorporate by reference, may not occur. Generally, these statements relate to our business plans or strategies, projected or anticipated benefits or other consequences of our plans or strategies, financing plans, projected or anticipated benefits from acquisitions that we may make, or projections involving anticipated revenues, earnings or other aspects of our operating results or financial position, and the outcome of any contingencies. Any such forward-looking statements are based on current expectations, estimates and projections of management. We intend for these forward-looking statements to be covered by the safe-harbor provisions for forward-looking statements. Words such as "may," "expect," "believe," "anticipate," "project," "plan," "intend," "estimate," and "continue," and their opposites and similar expressions are intended to identify forward-looking statements. We caution you that these statements are not guarantees of future performance or events and are subject to a number of uncertainties, risks and other influences.

Forward looking statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward looking statements. We believe that these factors include, but are not limited to, the following:

- our ability and plan to develop and commercialize DKN-01 and TRX518;
- the status, timing and results of preclinical studies and clinical trials;
- the potential benefits of DKN-01 and TRX518;
- the timing of our product candidate development programs;
- our ability to obtain and maintain regulatory approval of our product candidates;
- our estimates of expenses and future revenues and profitability;
- our estimates regarding our capital requirements and our needs for additional financing;
- our estimates of the size of the potential markets for DKN-01 and TRX518;
- our ability to attract collaborators with acceptable development, regulatory and commercial expertise;
- the benefits to be derived from any collaborations, license agreements, and other acquisition efforts, including those relating to the development and commercialization of DKN-01 and TRX518;
- sources of revenues and anticipated revenues, including contributions from any collaborations or license agreements for the development and commercialization of products;
- our ability to create an effective sales and marketing infrastructure if we elect to market and sell DKN-01 and TRX518 directly;
- the rate and degree of market acceptance of DKN-01 and TRX518;
- the timing and amount of reimbursement for DKN-01 and TRX518;
- the success of other competing therapies that may become available;
- the manufacturing capacity for DKN-01 and TRX518;
- our intellectual property position;

- our ability to maintain and protect our intellectual property rights;
- our results of operations, financial condition, liquidity, prospects, growth and strategies; and
- changes in the industry in which we operate and the trends that effect the industry.

You should also consider carefully the statements set forth in the section titled "Risk Factors" or elsewhere in this prospectus and the documents incorporated or deemed incorporated herein by reference, including but not limited to the risks described in under "Risk Factors" and elsewhere in our most recent Annual Report on Form 10-K and in our updates to those risk factors in our Quarterly Reports on Form 10-Q and Current Reports on Form 8-K and other factors described elsewhere in this prospectus. Any one or more of these uncertainties, risks and other influences could materially affect our results of operations and whether forward-looking statements made by us ultimately prove to be accurate. Our actual results, performance and achievements could differ materially from those expressed or implied in these forward-looking statements. Except as otherwise required by law, we undertake no obligation to publicly update or revise any forward-looking statements, whether from new information, future events or otherwise.

DKN-01 and TRX518 are investigational drugs undergoing clinical development and have not been approved by the U.S. Food and Drug Administration (the "FDA"), nor been submitted to the FDA for approval. DKN-01 and TRX518 have not been, and may never be, approved by any regulatory agency or marketed anywhere in the world. Statements contained in this prospectus should not be deemed to be promotional.

USE OF PROCEEDS

We will not receive any proceeds from the sale of our Common Stock by the Selling Stockholders. However, we may receive proceeds from the cash exercise of the Warrants, which, if exercised in cash at the current exercise price with respect to all 2,958,094 Warrant Shares, would result in gross proceeds to us of approximately \$18.0 million, and if exercised in cash at the current exercise price with respect to the 1,867,457 Warrant Shares registered in this offering, would result in gross proceeds to us of approximately \$11.4 million. The Warrants contain anti-dilution adjustments which, in the event that securities are issued by the Company in certain circumstances at a price lower than the current exercise price of the Warrants, would lower the exercise price of the Warrants and reduce the proceeds to be received by us. The use of proceeds from such Warrant exercises, if any, will not be subject to any restrictions. Under certain conditions set forth in the Warrants, the Warrants are exercisable on a cashless basis. If the Warrants are exercised on a cashless basis, we would not receive any cash payment from the Selling Stockholders upon any exercise of the Warrants. For information about the Selling Stockholders, see "Selling Stockholders."

The Selling Stockholders will pay any underwriting discounts and brokerage commissions and any similar expenses they incur in disposing of the Common Stock. We will bear all other reasonable costs, fees and expenses incurred in effecting the registration of the Common Stock covered by this prospectus, including all registration and filing fees, fees and expenses of compliance with securities or "blue sky" laws, listing application fees, printing expenses, transfer agent's and registrar's fees, costs of distributing prospectuses in preliminary and final form as well as any supplements thereto, and fees and disbursements of counsel for the Company and the independent registered public accounting firm and other persons retained by the Company.

SELLING STOCKHOLDERS

As described in the prospectus summary, in the Private Placement, the Purchasers acquired shares of our Common Stock and Warrants exercisable for shares of our Common Stock, subject to the limitations described below. In connection with the closing of the Private Placement, we entered into Purchase Agreements containing certain registration rights, pursuant to which we agreed to prepare and file one or more registration statements covering the resale of the shares of Common Stock issued in the Private Placement and issuable upon exercise of the Warrants (without regard to the limitation described below), and to maintain the effectiveness of such registration statement(s) until the earliest of (i) two years after the effective date of the registration statements(s), (ii) such time as all such shares of Common Stock and Warrant Shares have been sold in accordance with the registration statement(s) or in accordance with Rule 144 under the Securities Act, or (iii) such time as such shares of Common Stock and Warrant Shares may be sold by the Purchasers without volume limitations or other restrictions, pursuant to Rule 144 under the Securities Act. We are filing this Registration Statement to comply with our registration requirements under the Purchase Agreements. Two Purchasers have opted not to register their Shares or Warrant Shares and therefore such Shares and Warrant Shares are not included in this offering. For additional information regarding the issuance of Common Stock and the Warrants in the Private Placement, see "Prospectus Summary—Private Placement."

The following table sets forth for each Selling Stockholder, the name, the number and percentage of shares of Common Stock beneficially owned as of November 30, 2017, the maximum number of shares of Common Stock that may be offered pursuant to this prospectus and the number and percentage of shares of Common Stock that would be beneficially owned after the sale of the maximum number of shares of Common Stock pursuant to this prospectus. The information presented in the table is based on 12,354,014 shares of our Common Stock outstanding on November 30, 2017.

The Warrants held by the Selling Stockholders are immediately exercisable and therefore, for purposes of the table below, shares of Common Stock and percentage ownership of shares beneficially owned prior to the offering listed in the following table assumes the shares of Common Stock underlying the Warrants are deemed to be outstanding and to be beneficially owned by the Selling Stockholder holding the Warrants, but are not treated as outstanding for the purpose of computing the percentage ownership of any other Selling Stockholder.

Under the terms of the Warrants, certain Selling Stockholders may not exercise the Warrants to the extent such exercise would cause such Selling Stockholder, together with its affiliates and attribution parties, to beneficially own a number of shares of Common Stock which would exceed 4.99% or 9.99% of our then outstanding Common Stock following such exercise, excluding for purposes of such determination shares of Common Stock issuable upon exercise of the Warrants which have not been exercised. The number of shares in the second column does not reflect this limitation.

Only those Selling Stockholders listed below may offer and sell the Common Stock pursuant to this prospectus and any accompanying prospectus supplement. The Selling Stockholders may offer all or less than all of the shares listed in the table below for sale pursuant to this prospectus and any accompanying prospectus supplement from time to time. Accordingly, no estimate can be given as to the shares of Common Stock that the Selling Stockholders will hold upon consummation of any such sales, but for purposes of the last two columns below, we have assumed that all of the shares of Common Stock that may be offered pursuant to this prospectus will be sold by the Selling Stockholders.

Beneficial ownership is determined in accordance with the rules of the SEC, except that the following table does not reflect any applicable beneficial ownership limitation described above, with the effect that beneficial ownership of the Selling Stockholders is calculated and presented (for purposes of disclosure in this prospectus only) on a fully as converted basis. Unless otherwise indicated, this table is based on information supplied to us by the Selling Stockholders and certain of our records and, unless

otherwise indicated, to our knowledge, the persons named in the table have sole voting and investment power with respect to all shares beneficially owned, subject to community property laws where applicable.

Name and Address of Selling Stockholder	Shares Beneficially Owned Prior to the Offering		Maximum Number of Shares of Currently Outstanding Common Stock Being Offered	Maximum Number of Shares of Common Stock Issuable Upon Exercise of Warrants Being Offered	Shares Beneficially Owned After the Offering	
	Number	Percent (%)			Number	Percent (%)
Valence Helix						
Investments, LLC(1) c/o Valence Life Sciences, 590 Madison Avenue, 21st Floor, New York, NY 10022	517,666	4.1	258,833	258,833	0	*
Kingsbrook Opportunities						
Master Fund LP(2) c/o Kingsbrook Partners LP 689 Fifth Avenue, 12th Floor New York, NY 10022	82,170	*	41,085	41,085	0	*
Lincoln Park Capital						
Fund, LLC(3) c/o Lincoln Park Capital, LLC 440 N. Wells Street Suite 410 Chicago, IL 60654	100,000	*	50,000	50,000	0	*
Tiburon Opportunity						
Fund LP(4) c/o Bortel Investment Management, LLC 13313 Point Richmond Beach Rd. NW Gig Harbor, WA 98332	164,338	1.3	82,169	82,169	0	*
DAFNA Lifescience L.P.(5)						
c/o DAFNA Capital MGM LLC 10990 Wilshire Blvd Suite 1400 Los Angeles, CA 90024	290,880	2.3	145,440	145,440	0	*
DAFNA Lifescience Select L.P.						
(6) c/o DAFNA Capital MGM LLC 10990 Wilshire Blvd Suite 1400 Los Angeles, CA 90024	202,136	1.6	101,068	101,068	0	*
Empery Asset Master, LTD(7)						
c/o Empery Asset Management, LP, 1 Rockefeller Plaza Suite 1205 New York, NY 10020	61,108	*	30,554	30,554	0	*
Empery Tax Efficient, LP(8)						
c/o Empery Asset Management, LP 1 Rockefeller Plaza Suite 1205, New York, NY 10020	29,176	*	14,588	14,588	0	*
Empery Tax Efficient II, LP(9)						
c/o Empery Asset Management, LP 1 Rockefeller Plaza Suite 1205 New York, NY 10020	74,054	*	37,027	37,027	0	*

Name and Address of Selling Stockholder	Shares Beneficially Owned Prior to the Offering		Maximum Number of Shares of Currently Outstanding Common Stock Being Offered	Maximum Number of Shares of Common Stock Issuable Upon Exercise of Warrants Being Offered	Shares Beneficially Owned After the Offering	
	Number	Percent (%)			Number	Percent (%)
Sabby Volatility Warrant Master Fund, Ltd.(10) c/o Sabby Management, 10 Mountainview Road, Suite 205 Upper Saddle River, NJ, 07458	400,000	3.2	200,000	200,000	0	*
CVI Investments, Inc.(11) c/o Heights Capital Management 101 California Street Suite 3250 San Francisco, CA 94111	170,000	1.4	85,000	85,000	0	*
Eli Lilly and Company Lilly Corporate Center Indianapolis, IN 46285	2,301,000	17.5	821,693	821,693	657,614	4.6

* Indicates beneficial ownership of less than 1%.

- (1) The managers of Valence Helix Investments LLC, are Eric Roberts, Rachel Leheny, Philip Sawyer, Graham Crooke and Evgeny Zaytsev with shared voting power of such shares and they may be deemed to have indirect beneficial ownership of such shares but they disclaim beneficial ownership of such shares except to the extent of any pecuniary interest therein. The address for Valence Helix Investments is 590 Madison Avenue, 21st Floor, New York, NY 10022.
- (2) Kingsbrook Partners LP ("Kingsbrook Partners") is the investment manager of Kingsbrook Opportunities Master Fund LP ("Kingsbrook Opportunities") and consequently has voting control and investment discretion over securities held by Kingsbrook Opportunities. Kingsbrook Opportunities GP LLC ("Opportunities GP") is the general partner of Kingsbrook Opportunities and may be considered the beneficial owner of any securities deemed to be beneficially owned by Kingsbrook Opportunities. KB GP LLC ("GP LLC") is the general partner of Kingsbrook Partners and may be considered the beneficial owner of any securities deemed to be beneficially owned by Kingsbrook Partners. Ari J. Storch, Adam J. Chill and Scott M. Wallace are the sole managing members of Opportunities GP and GP LLC and as a result may be considered beneficial owners of any securities deemed beneficially owned by Opportunities GP and GP LLC. Each of Kingsbrook Partners, Opportunities GP, GP LLC and Messrs. Storch, Chill and Wallace disclaim beneficial ownership of these securities.
- (3) Joshua Scheinfeld and Jonathan Cope, the principals of Lincoln Park are deemed to be beneficial owners of all the shares of common stock owned by Lincoln Park. Messrs. Scheinfeld and Cope have shared voting and disposition power over the shares being offered.
- (4) Mr. Peter Bortel has voting and investment power over these securities.
- (5) DAFNA Lifescience L.P. is managed by DAFNA Capital Mgmt. LLC. Nathan Fishel and Fariba Ghodsian have voting and dispositive control with respect to the securities being offered.
- (6) DAFNA Lifescience Select L.P. is managed by DAFNA Capital Mgmt. LLC. Nathan Fishel and Fariba Ghodsian have voting and dispositive control with respect to the securities being offered. The address for DAFNA Lifescience Select L.P. is 10990 Wilshire Boulevard, Suite 1400, Los Angeles, CA 90024.
- (7) Empery Asset Management LP, the authorized agent of Empery Asset Master Ltd ("EAM"), has discretionary authority to vote and dispose of the shares held by EAM and may be deemed to be the beneficial owner of these shares. Martin Hoe and Ryan Lane, in their capacity as investment managers of Empery Asset Management LP, may also be deemed to have investment discretion and voting power over the shares held by EAM. EAM, Mr. Hoe and Mr. Lane each disclaim any beneficial ownership of these shares.

- (8) Empery Asset Management LP, the authorized agent of Empery Tax Efficient, LP ("ETE"), has discretionary authority to vote and dispose of the shares held by ETE and may be deemed to be the beneficial owner of these shares. Martin Hoe and Ryan Lane, in their capacity as investment managers of Empery Asset Management LP, may also be deemed to have investment discretion and voting power over the shares held by ETE. ETE, Mr. Hoe and Mr. Lane each disclaim any beneficial ownership of these shares.
- (9) Empery Asset Management LP, the authorized agent of Empery Tax Efficient II, LP ("ETE II"), has discretionary authority to vote and dispose of the shares held by ETE II and may be deemed to be the beneficial owner of these shares. Martin Hoe and Ryan Lane, in their capacity as investment managers of Empery Asset Management LP, may also be deemed to have investment discretion and voting power over the shares held by ETE II. ETE II, Mr. Hoe and Mr. Lane each disclaim any beneficial ownership of these shares.
- (10) Sabby Management, LLC serves as the investment manager of Sabby Volatility Warrant Master Fund Ltd. Hal Mintz is the manager of Sabby Management, LLC and has voting and investment control of the securities held by Sabby VWMF. Each of Sabby Management, LLC and Hal Mintz disclaims beneficial ownership over the securities beneficially owned by Sabby VWMF except to the extent of their respective pecuniary interest therein.
- (11) Heights Capital Management, Inc., the authorized agent of CVI Investments, Inc. ("CVI"), has discretionary authority to vote and dispose of the securities held by CVI and may be deemed to be the beneficial owner of these securities. Martin Kobinger, in his capacity as Investment Manager of Heights Capital Management, Inc., may also be deemed to have investment discretion and voting power over the securities held by CVI. Mr. Kobinger disclaims any such beneficial ownership of the securities. CVI Investments, Inc. is affiliated with one or more FINRA members, none of whom is currently expected to participate in the sale pursuant to the prospectus contained in this registration statement of the securities purchased by CVI in the offering.

No offer or sale pursuant to this prospectus may occur unless the Registration Statement that includes this prospectus has been declared effective by the SEC and remains effective at the time a Selling Stockholder offers or sells shares of Common Stock. We are required, under certain circumstances, to update, supplement or amend this prospectus to reflect material developments in our business, financial position and results of operations and may do so by an amendment to this prospectus, a prospectus supplement or a future filing with the SEC incorporated by reference in this prospectus.

Relationships with the Selling Stockholders

Prior to the Closing of the Private Placement, Eli Lilly and Company was a more than 5% direct holder of our outstanding Common Stock. The purchase by Eli Lilly and Company of shares of our Common Stock and Warrant to purchase shares of our Common Stock in the Private Placement was approved by our board of directors in accordance with our amended and restated by-laws and related party transaction policy.

PLAN OF DISTRIBUTION

Each Selling Stockholder of the securities named herein may, from time to time, sell any or all of their securities covered hereby on any stock exchange, market or trading facility on which the securities are traded, in private transactions or otherwise. These sales may be at fixed or negotiated prices or at market prices prevailing at the time of sale. A Selling Stockholder may use any one or more of the following methods when selling securities:

- ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;
- block trades in which the broker-dealer will attempt to sell the securities as agent but may position and resell a portion of the block as principal to facilitate the transaction;
- purchases by a broker-dealer as principal and resale by the broker-dealer for its account;
- an exchange distribution in accordance with the rules of the applicable exchange;
- privately negotiated transactions;
- settlement of short sales;
- in transactions through broker-dealers that agree with the Selling Stockholders to sell a specified number of such securities at a stipulated price per security;
- through the writing or settlement of options or other hedging transactions, whether through an options exchange or otherwise;
- a combination of any such methods of sale; or
- any other method permitted pursuant to applicable law.

The Selling Stockholders may also sell securities under Rule 144 or any other exemption from registration under the Securities Act, if available, rather than under this prospectus.

Broker-dealers engaged by the Selling Stockholders may arrange for other brokers-dealers to participate in sales. Broker-dealers may receive commissions or discounts from the Selling Stockholders (or, if any broker-dealer acts as agent for the purchaser of securities, from the purchaser) in amounts to be negotiated, but, except as set forth in a supplement to this Prospectus, in the case of an agency transaction not in excess of a customary brokerage commission in compliance with FINRA Rule 2440; and in the case of a principal transaction a markup or markdown in compliance with FINRA IM-2440.

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

The Selling Stockholders may pledge or grant a security interest in some of all of the shares of Common Stock owned by them and, if any of them defaults in the performance of its secured obligations, the pledgees or secured parties may offer and sell the shares of Common Stock from time to time pursuant to this prospectus or any supplement or amendment to this prospectus under Rule 424(b)(3) or other applicable provision of the Securities Act, amending, if necessary, the list of Selling Stockholders to include the pledgee, transferee or other successors in interest as Selling

Stockholders under this prospectus. The Selling Stockholders also may transfer and donate the shares of Common Stock in other circumstances in which case the transferees, donees or other successors in interest will be the selling beneficial owners for purposes of this prospectus.

The Selling Stockholders and any broker-dealers or agents that are involved in selling the securities may be deemed to be "underwriters" within the meaning of the Securities Act in connection with such sales. In such event, any commissions received by such broker-dealers or agents and any profit on the resale of the securities purchased by them may be deemed to be underwriting commissions or discounts under the Securities Act. We are not aware that any Selling Stockholder has any written or oral agreement or understanding, directly or indirectly, with any person to distribute the securities.

We are required to pay certain fees and expenses incurred by us incident to the registration of the securities. We have agreed to indemnify the Selling Stockholders against certain losses, claims, damages and liabilities, including liabilities under the Securities Act.

We agreed to keep this prospectus effective until the earlier of (i) two years after the effective date of the registration statement(s) covering the resale of the shares of Common Stock issued in the Private Placement and issuable upon exercise of the Warrants, (ii) such time as all such shares of Common Stock and the Warrant Shares have been sold in accordance with the registration statement(s) or in accordance with Rule 144 under the Securities Act, or (iii) such time as such shares of Common Stock and the Warrant Shares may be sold by the Selling Stockholders without volume limitations or other restrictions pursuant to Rule 144 under the Securities Act. The resale securities will be sold only through registered or licensed brokers or dealers if required under applicable state securities laws.

Under applicable rules and regulations under the Exchange Act, any person engaged in the distribution of the shares of Common Stock may not simultaneously engage in market making activities with respect to the Common Stock for the applicable restricted period, as defined in Regulation M, prior to the commencement of the distribution. In addition, the Selling Stockholders will be subject to applicable provisions of the Exchange Act and the rules and regulations thereunder, including Regulation M, which may limit the timing of purchases and sales of the Common Stock by the Selling Stockholders or any other person. We will make copies of this prospectus available to the Selling Stockholders. Registration of the securities named herein does not mean any of such securities will be offered and sold.

LEGAL MATTERS

The validity of the securities being offered hereby will be passed upon by Morgan, Lewis & Bockius LLP. Julio E. Vega, a partner at Morgan, Lewis & Bockius, purchased 32,868 shares of Common Stock and Warrants to purchase 32,868 shares of Common Stock in the Private Placement, but is not included as a Selling Stockholder in this prospectus and such shares are not being registered in this offering.

EXPERTS

The consolidated balance sheets of Leap Therapeutics, Inc. and Subsidiaries as of December 31, 2016 and 2015, and the related consolidated statements of operations and comprehensive loss, redeemable preferred stock and stockholders' deficiency, and cash flows for each of the years then ended, have been audited by EisnerAmper LLP, independent registered public accounting firm, as stated in their report, which is incorporated herein by reference. Such financial statements have been incorporated herein by reference in reliance on the report of such firm given upon their authority as experts in accounting and auditing.

DISCLOSURE OF COMMISSION POSITION ON INDEMNIFICATION FOR SECURITIES ACT LIABILITIES

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to our directors, officers and controlling persons pursuant to the foregoing provisions, or otherwise, we have been advised that in the opinion of the SEC such indemnification is against public policy as expressed in the Securities Act 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, we will, unless in the opinion of our counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by us is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

ADDITIONAL INFORMATION

This prospectus is part of a Registration Statement on Form S-3 that we have filed with the SEC relating to the shares of our securities being offered hereby. This prospectus does not contain all of the information in the Registration Statement and its exhibits. The Registration Statement, its exhibits and the documents incorporated by reference in this prospectus and their exhibits, all contain information that is material to the offering of the Securities hereby. Whenever a reference is made in this prospectus to any of our contracts or other documents, the reference may not be complete. You should refer to the exhibits that are a part of the Registration Statement in order to review a copy of the contract or documents. The Registration Statement and the exhibits are available at the SEC's Public Reference Room or through its Website.

We file annual, quarterly and current reports, proxy statements and other information with the SEC. You can read and copy any materials we file with the SEC at its Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549 and at its regional offices, a list of which is available on the Internet at <http://www.sec.gov/contact/addresses.htm>. You may obtain information on the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. The SEC maintains an Internet site at <http://www.sec.gov> that contains reports, proxy and information statements, and other information regarding issuers, such as us, that file electronically with the SEC. Additionally, you may access our

filings with the SEC through our website at <http://www.leaptx.com>. The information on our website is not part of this prospectus.

We will provide you without charge, upon your oral or written request, with a copy of any or all reports, proxy statements and other documents we file with the SEC, as well as any or all of the documents incorporated by reference in this prospectus or the Registration Statement (other than exhibits to such documents unless such exhibits are specifically incorporated by reference into such documents). Requests for such copies should be directed to:

Investor Relations
Leap Therapeutics, Inc.
47 Thorndike Street, Suite B1-1
Cambridge, Massachusetts 02141
Telephone number: (617) 714-0360

You should rely only on the information in this prospectus and the additional information described above and under the heading "Incorporation of Certain Information by Reference" below. We have not, and the Selling Stockholders have not, authorized any other person to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely upon it. The Selling Stockholders are not making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information in this prospectus was accurate on the date of the front cover of this prospectus only, and that any information we have incorporated by reference was accurate on the date of the document incorporated by reference only. Our business, financial condition, results of operations and prospects may have changed since such date.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to "incorporate by reference" information that we file with it into this prospectus, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is an important part of this prospectus. 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 documents filed earlier with the SEC or 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:

- our Annual Report on Form 10-K for the fiscal year ended December 31, 2016, filed with the SEC on March 31, 2017;
- our Quarterly Reports on Form 10-Q for the fiscal quarter ended March 31, 2017, filed with the SEC on May 12, 2017, for the fiscal quarter ended June 30, 2017, filed with the SEC on August 11, 2017, and for the fiscal quarter ended September 30, 2017, filed with the SEC on November 13, 2017;
- our Current Report on Form 8-K filed with the SEC on January 26, 2017, including the exhibits attached thereto and filed therewith;
- our Current Report on Form 8-K filed with the SEC on June 21, 2017;
- our Current Report on Form 8-K filed with the SEC on November 17, 2017, including the exhibits attached thereto and filed therewith; and

- the description of our common stock contained in our Registration Statement on Form 8-A, filed on January 20, 2017, including any amendments thereto or reports filed for the purposes of updating this description.

All reports and other documents that we file with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of the Registration Statement but before the termination of the offering of the Securities hereunder will also be considered to be incorporated by reference into this prospectus from the date of the filing of these reports and documents, and will supersede the information herein; provided, however, that all reports or portions thereof that we "furnish" to the SEC will not be considered incorporated by reference into this prospectus. We undertake to provide without charge to each person (including any beneficial owner) who receives a copy of this prospectus, upon written or oral request, a copy of all of the preceding documents that are incorporated by reference (other than exhibits, unless the exhibits are specifically incorporated by reference into these documents). You may request a copy of these materials in the manner set forth under the heading "Additional Information," above.

3,734,914 Shares

Common Stock



PROSPECTUS

December 15, 2017
