

Use these links to rapidly review the document

[TABLE OF CONTENTS](#)

[Table of Contents](#)

Filed Pursuant to Rule 424(b)(5)
Registration No. 333-223419

PROSPECTUS SUPPLEMENT

(To Prospectus dated March 16, 2018)



LEAP THERAPEUTICS, INC.

**Shares of Common Stock
Having an Aggregate Offering Price of Up to
\$30,000,000**

We have entered into a distribution agreement with Raymond James & Associates, Inc., as our sales agent, relating to the shares of our common stock, par value \$0.001, offered by this prospectus supplement. In accordance with the terms of the distribution agreement, we may offer and sell shares of common stock having an aggregate offering price of up to \$30,000,000 from time to time through or to our sales agent.

Sales of common stock under this prospectus supplement, if any, will be made by means of ordinary brokers' transactions through the facilities of the Nasdaq Global Market, any other national securities exchange or facility thereof, a trading facility of a national securities association or an alternate trading system, to or through a market maker or directly on or through an electronic communication network or any similar market venue, at market prices, in block transactions or as otherwise agreed between us and the sales agent. Our common stock trades on the Nasdaq Global Market under the symbol "LPTX." On September 6, 2018, the last reported sale price of our common stock on the Nasdaq Global Market was \$7.47 per share.

The compensation of our sales agent for sales of our common stock pursuant to the distribution agreement shall be a commission rate equal to 3% of the gross sales price per share of common stock. The net proceeds from any sales under this prospectus supplement will be used as described under "Use of Proceeds" in this prospectus supplement.

Under the terms of the distribution agreement, we also may sell common stock to the sales agent as principal for its own account at a price agreed upon at the time of the sale. If we sell common stock to the sales agent as principal, we will enter into a separate terms agreement with the sales agent, and the sale will be made pursuant to the terms thereunder.

The sales agent is not required to sell any specific number or dollar amount of our common stock but will use its commercially reasonable efforts, consistent with its normal trading and sales practices, as our agent and subject to the terms of the distribution agreement, to sell the common stock offered, as instructed by us. The offering of common stock pursuant to the distribution agreement will terminate upon the earlier of (i) the sale of all common stock subject to the distribution agreement, and (ii) the termination of the distribution agreement by us or by the sales agent pursuant to the terms of the distribution agreement.

We are an "emerging growth company" under applicable federal securities laws and, as such, have elected to comply with certain reduced public company reporting requirements for this prospectus supplement and future filings. See "Prospectus Supplement Summary—Status as an Emerging Growth Company."

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

Investing in our common stock involves a high degree of risk. See "Risk Factors" beginning on page S-7 of this prospectus supplement, page 6 of the accompanying prospectus, and the documents incorporate by reference into this prospectus supplement.

RAYMOND JAMES

The date of this prospectus supplement is September 7, 2018.

TABLE OF CONTENTS**Prospectus Supplement**

About This Prospectus Supplement	S-1
Special Note Regarding Forward-Looking Statements	S-3
Prospectus Supplement Summary	S-4
The Offering	S-6
Risk Factors	S-7
Use Of Proceeds	S-9
Dilution	S-10
Dividend Policy	S-11
Material United States Federal Income and Estate Tax Consequences for Non-U.S. Holders of our Common Stock	S-12
Plan of Distribution	S-18
Legal Matters	S-20
Experts	S-20
Where You Can Find More Information	S-20
Incorporation of Certain Information by Reference	S-20

Prospectus

About This Prospectus	i
Special Note Regarding Forward-Looking Statements	i
Summary	1
Risk Factors	6
Ratio of Earnings to Fixed Charges	6
Description of Capital Stock	6
Description of Debt Securities	12
Description of Warrants	19
Legal Ownership of Securities	21
Plan of Distribution	25
Legal Matters	27
Experts	27
Where You Can Find More Information	27
Incorporation of Certain Information by Reference	27
Disclosure of Commission's Position on Indemnification for Securities Act Liability	28

Neither we nor the sales agent have done anything that would permit this offering or possession or distribution of this prospectus supplement in any jurisdiction where action for that purpose is required, other than in the United States. Persons who come into possession of this prospectus supplement and any free writing prospectus in jurisdictions outside the United States are required to inform themselves about and to observe any restrictions as to this offering and the distribution of this prospectus supplement and any free writing prospectus applicable to that jurisdiction.

ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus are part of a registration statement that we filed with the U.S. Securities and Exchange Commission, or SEC, utilizing a "shelf" registration process. This document is in two parts. The first part is this prospectus supplement, which describes the terms of the offering of the securities offered hereby and also adds to and updates the information contained in the accompanying prospectus and the documents incorporated by reference into this prospectus supplement and the accompanying prospectus. The second part is the accompanying prospectus, which provides more general information, some of which may not apply to this offering and some of which may have been supplemented or superseded by information in this prospectus supplement or documents incorporated or deemed to be incorporated by reference into this prospectus supplement that we filed with the SEC subsequent to the date of the prospectus. To the extent that there is any conflict between the information contained in this prospectus supplement, on the one hand, and the information contained in the accompanying prospectus or any document incorporated by reference herein or therein, on the other hand, you should rely on the information in this prospectus supplement.

You should rely only on the information contained in this prospectus supplement, the accompanying prospectus or incorporated herein or therein by reference and in any free writing prospectus that we have authorized for use in connection with this offering. We have not, and the sales agent has not, authorized anyone to provide you with information that is different. If anyone provides you with different or inconsistent information you should not rely on it. We and the sales agent are offering to sell, and seeking offers to buy, the securities offered hereby only in jurisdictions where offers and sales are permitted. The information contained, or incorporated by reference, in this prospectus supplement and contained, or incorporated by reference, in the accompanying prospectus is accurate only as of the respective dates thereof, regardless of the time of delivery of those respective documents, or of any sale of our shares of common stock. It is important for you to read and consider all information contained in this prospectus supplement and the accompanying prospectus, including the documents we have referred you to in the sections titled "Where You Can Find More Information" and "Incorporation of Certain Information by Reference" below.

We own or have rights to trademarks or trade names that we use in conjunction with the operation of our business. KEYTRUDA® is a registered trademark of Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc. Opdivo® is a registered trademark of Bristol Myers Squibb Company. TECENTRIQ® is a registered trademark of Genentech, a member of the Roche Group. BAVENCIO® is a registered trademark of Pfizer, Inc. Each trademark, trade name or service mark of any other company appearing in this prospectus supplement, the accompanying prospectus or any document incorporated herein or therein belongs to its holder. Use or display by us of other parties' trademarks, trade names or service marks is not intended to and does not imply a relationship with, or endorsement or sponsorship by us of, the trademark, trade name or service mark owner.

The industry and market data contained or incorporated by reference into this prospectus supplement are based on independent industry publications, reports by market research firms or other published independent sources. Although we believe these sources are reliable, we have not independently verified the information and cannot guarantee its accuracy and completeness, as industry and market data are subject to change and cannot always be verified with complete certainty due to limits on the availability and reliability of raw data, the voluntary nature of the data gathering process and other limitations and uncertainties inherent in any statistical survey of market shares. Although we are not aware of any misstatements regarding the market and

industry data presented or incorporated by reference into this prospectus supplement, these estimates involve risks and uncertainties and are subject to change based on various factors including those discussed in the section titled "Risk Factors." Accordingly, investors should not place undue reliance on this information.

The representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference in this prospectus supplement or the accompanying prospectus were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our business.

Information contained on, or that can be accessed through, our website does not constitute part of this prospectus supplement, the accompanying prospectus or any related free writing prospectus.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus and the information incorporated by reference herein or therein contain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act, that involve a number of risks and uncertainties and that are intended to be covered by the "safe harbor" created by those sections. Although our forward-looking statements reflect the good faith judgment of our management, these statements can only be based on facts and factors currently known by us. Consequently, these forward-looking statements are inherently subject to known and unknown risks, uncertainties and other factors that may cause actual results and outcomes to differ materially from results and outcomes discussed in the forward-looking statements.

Forward-looking statements can generally be identified by the use of forward-looking terms such as "believe," "hope," "expect," "may," "will," "should," "could," "would," "seek," "intend," "plan," "estimate," "anticipate" and "continue," or other comparable terms (including their use in the negative), or by discussions of future matters. All statements other than statements of historical facts included in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein or therein are forward-looking statements. These statements include but are not limited to statements under the captions "Prospectus Supplement Summary—Company Overview," "Risk Factors" and "Use of Proceeds" and in other sections included in the accompanying prospectus or incorporated by reference from our Annual Report on Form 10-K and Quarterly Reports on Form 10-Q, as applicable, as well as our other filings with the Securities and Exchange Commission, or the SEC. You should be aware that the occurrence of any of the events discussed under the heading "Risk Factors" in this prospectus supplement, the accompanying prospectus and any documents incorporated by reference herein or therein could substantially harm our business, operating results and financial condition and that if any of these events occurs, it could adversely affect the value of an investment in our securities.

The cautionary statements made in this prospectus supplement are intended to be applicable to all related forward-looking statements wherever they may appear in this prospectus supplement, in the accompanying prospectus or any documents incorporated by reference herein or therein. We urge you not to place undue reliance on these forward-looking statements, which speak only as of the date they are made. Except as required by law, we assume no obligation to update our forward-looking statements, even if new information becomes available in the future.

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights certain information about us, this offering and selected information contained elsewhere in or incorporated by reference into this prospectus supplement or the accompanying prospectus. This summary is not complete and does not contain all of the information that you should consider before deciding whether to invest in our securities. For a more complete understanding of our company and this offering, we encourage you to read and consider carefully the more detailed information in this prospectus supplement and the accompanying prospectus, including the information under the heading "Risk Factors" in this prospectus supplement beginning on page S-7, in the accompanying prospectus beginning on page 6, and in our most recent Annual Report on Form 10-K, Quarterly Reports on Form 10-Q and the information incorporated by reference in this prospectus supplement and the accompanying prospectus. References to the "Company," "Leap," "we," "us," and "our" mean Leap Therapeutics, Inc. and its consolidated subsidiaries unless the context otherwise indicates. In this regard, references to the "Company," "we," "us," and "our" in the context of rights or obligations under any contract or agreement mean Leap Therapeutics, Inc. only and not its consolidated subsidiaries.

THE COMPANY

Overview

Leap Therapeutics, Inc. is a biopharmaceutical company focused on developing novel therapies designed to treat patients with cancer by inhibiting fundamental tumor-promoting pathways and by harnessing the immune system to attack cancer cells. Our strategy is to identify, acquire, and develop molecules that will rapidly translate into high impact therapeutics that generate durable clinical benefit and enhanced patient outcomes.

Our two clinical stage programs are:

- **DKN-01:** A monoclonal antibody that inhibits Dickkopf-related protein 1, or DKK1. DKK1 is a protein that regulates the Wnt signaling pathways and enables tumor cells to proliferate and spread, as well as suppresses the immune system from attacking the tumor. When DKN-01 binds to DKK1, an anti-tumor effect can be generated. DKN-01-based therapies have generated responses and clinical benefit in several patient populations. We are currently studying DKN-01 in multiple ongoing clinical trials in patients with esophagogastric cancer, biliary tract cancer, or gynecologic cancers, and we are initiating a trial in hepatocellular carcinoma in 2018. We are focused on two parallel development strategies involving targeted patient populations with Wnt pathway alterations and as a combination with other cancer immunotherapy agents.
- **TRX518:** A monoclonal antibody targeting the glucocorticoid-induced tumor necrosis factor-related receptor, or GITR. GITR is a receptor found on the surface of a wide range of immune cells. GITR stimulation activates tumor fighting white blood cells and decreases the activity of potentially tumor-protective immunosuppressive cells. TRX518 has been specifically engineered to enhance the immune system's anti-tumor response by activating GITR signaling without causing the immune cells to be destroyed. We are conducting two clinical trials of TRX518 in patients with advanced solid tumors and have recently begun enrolling combination therapy arms utilizing TRX518 with gemcitabine chemotherapy or with cancer immunotherapies known as PD-1 antagonists.

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.

We commenced business operations in 2011. 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 revenue, have incurred significant losses from operations and have primarily financed our operations through the private placement of our equity securities, business development activities, convertible note financings, and our merger with MacroCure Ltd. ("MacroCure"), which was completed in January 2017. We expect to continue to incur operating losses for the foreseeable future as we develop our product candidates.

Status as an Emerging Growth Company

We are an "emerging growth company", or EGC, as defined in the Jumpstart Our Business Startups Act of 2012 (the "JOBS Act"). The JOBS Act, permits an "emerging growth company" such as us to take advantage of an extended transition period to comply with new or revised accounting standards applicable to public companies until those standards would otherwise apply to private companies. We have elected to use the extended transition period for complying with new or revised accounting standards under Section 102(b)(1) of the JOBS Act. This election allows us to delay the adoption of new or revised accounting standards that have different effective dates for public and private companies until those standards apply to private companies. As a result of this election, our financial statements may not be comparable to companies that comply with public company effective dates.

We may take advantage of these reporting exemptions until we are no longer an emerging growth company, which in certain circumstances could be for up to five years. We will remain an "emerging growth company" until the earliest of (a) the last day of the first fiscal year in which our annual gross revenues exceed \$1.07 billion, (b) the date that we become a "large accelerated filer" as defined in Rule 12b-2 under the Exchange Act, which would occur if the market value of our shares that are held by non-affiliates exceeds \$700 million as of the last business day of our most recently completed second fiscal quarter, (c) the date on which we have issued more than \$1.0 billion in nonconvertible debt during the preceding three-year period, and (d) the last day of our 2022 fiscal year containing the fifth anniversary of the date on which shares of our common stock became publicly traded in the United States. As of June 30, 2018, the last day of our second fiscal quarter, we remain an EGC.

Corporate Information

Our principal executive office is located at 47 Thorndike Street, Suite B1-1, Cambridge, MA 02141. Our telephone number is 617-714-0360, and our website address is www.leaptx.com (the information contained therein or linked thereto shall not be considered incorporated by reference in this prospectus supplement).

THE OFFERING

Shares we are offering	Shares of common stock, par value \$0.001 per share, having an aggregate offering price of up to \$30,000,000.
Manner of offering	"At-the-market" offerings that may be made from time to time through our sales agent, Raymond James & Associates, Inc., or Raymond James. See "Plan of Distribution" on page S-18.
Use of Proceeds	We currently intend to use the net proceeds from this offering, after deducting the sales agent's commissions and our offering expenses, for general corporate purposes, which may include, without limitation, funding new clinical trials of DKN-01 and TRX518 and the continuation of ongoing studies, and for working capital. See "Use of Proceeds" on page S-9 for additional information.
Risk Factors	Investing in our common stock involves a high degree of risk. You should carefully consider all the information included or incorporated by reference in this prospectus supplement prior to investing in our common stock. In particular, we urge you to carefully read the "Risk Factors" section of this prospectus supplement beginning on page S-7 and in the documents incorporated by reference in this prospectus supplement and the accompanying prospectus.
Nasdaq Global Market Symbol	"LPTX"

RISK FACTORS

Before you make a decision to invest in our securities, you should consider carefully the risks described below, together with other information in this prospectus supplement, the accompanying prospectus and the information incorporated by reference herein and therein, including those risks identified under "Item 1A. Risk Factors" in our Annual Report on Form 10-K for the year ended December 31, 2017 and our Quarterly Reports on Form 10-Q for the periods ended March 31, 2018 and June 30, 2018, which are incorporated by reference in this prospectus supplement and which may be amended, supplemented or superseded by other reports that we subsequently file with the SEC. If any of the following events actually occur, our business, operating results, prospects or financial condition could be materially and adversely affected. This could cause the trading price of our common stock to decline and you may lose all or part of your investment. The risks described below are not the only ones that we face. Additional risks not presently known to us or that we currently deem immaterial may also significantly impair our business operations and could result in a complete loss of your investment. Please also read carefully the section entitled "Special Note Regarding Forward-Looking Statements."

Risks Related to this Offering

Our management will have broad discretion as to the use of the proceeds from this offering, and we may not use the proceeds effectively.

Our management will have broad discretion as to the application of the net proceeds from this offering. Our management may, among other possible uses of proceeds, use proceeds to fund clinical trials of products we are developing, to finance our research and develop our programs, to acquire one or more businesses or new business assets and for general working capital. We may use the proceeds for purposes that are not contemplated at the time of this offering. All of these potential uses of proceeds involve risks and may not improve the performance or prospects of our business or the business or prospects of our subsidiaries, and may not increase the market value of our shares of common stock.

You may experience immediate and substantial dilution in the book value per share of the shares of common stock you purchase in this offering.

The offering price per share in this offering may exceed the pro forma net tangible book value per share of our common stock outstanding prior to this offering. Assuming that an aggregate of 4,016,064 shares of our common stock are sold at a price of \$7.47 per share, the last reported sale price of our common stock on the Nasdaq Global Market, for aggregate gross proceeds of up to approximately \$30 million, and after deducting commissions and estimated aggregate offering expenses payable by us, you will experience immediate dilution of \$5.28 per share, representing the difference between our pro forma as adjusted net tangible book value per share as of June 30, 2018 after giving effect to this offering and the assumed offering price. The exercise of outstanding stock options will result in further dilution of your investment. See the section below entitled "Dilution" for a more detailed illustration of the dilution you may incur if you participate in this offering.

Our stockholders may experience future dilution as a result of future equity offerings as well as the exercise of our outstanding options and warrants and the vesting of our outstanding restricted stock units.

In order to raise additional capital, we may in the future offer additional shares of our common stock or other securities convertible into or exchangeable for shares of our common stock at prices that may not be the same as the prices per share in this offering. We may sell shares of our common stock or other securities in any other offering at a price per share that is less than the prices per share paid by investors in this offering, and investors purchasing shares of our common stock or other securities in the future could have rights superior to existing stockholders. The price per share at which we sell additional shares of our common stock, or securities convertible or exchangeable into shares of our common stock, in future transactions may be higher or lower than the prices per share paid by investors in this offering. In addition, the exercise of our outstanding options and warrants and the vesting of our outstanding restricted stock units may adversely affect our stock price due to sales of a large number of shares or the perception that such sales could occur. These factors also could make it more difficult to raise funds through future offerings of our securities, and could adversely impact the terms under which we could obtain additional equity capital. Exercise of outstanding options and warrants, vesting of outstanding restricted stock units or any future issuance of additional shares of common stock or other equity securities, including but not limited to options, warrants, restricted stock units or other derivative securities convertible into shares of our common stock, may result in significant dilution to our stockholders and may decrease our stock price.

The shares of our common stock offered under this prospectus supplement and the accompanying base prospectus may be sold in "at-the-market" offerings, and investors who buy shares at different times will likely pay different prices.

Investors who purchase shares under this prospectus supplement and the accompanying base prospectus at different times will likely pay different prices, and so may experience different outcomes in their investment results. We will have discretion, subject to market demand, to vary the timing, prices, and numbers of shares sold, and to determine the minimum sales price for shares sold. Investors may experience declines in the value of their shares as a result of share sales made in connection with "at-the-market" offerings at prices lower than the prices they paid.

The actual number of shares we will issue under the distribution agreement, at any one time or in total, is uncertain.

Subject to certain limitations in the distribution agreement and compliance with applicable law, we and our sales agent may mutually agree to sell shares of our common stock under a transaction acceptance at any time throughout the term of the distribution agreement. The number of shares that are sold by Raymond James after agreement on the terms of the transaction acceptance will fluctuate based on the market price of the shares of our common stock during the sales period and limits we set with our sales agent. Because the price per share of each share sold will fluctuate based on the market price of our shares of common stock during the sales period, it is not possible to predict the number of shares that will ultimately be issued.

USE OF PROCEEDS

We may issue and sell shares of our common stock having aggregate sale proceeds of up to \$30,000,000 from time to time. There can be no assurance that we will be able to sell any shares under or fully utilize the distribution agreement with Raymond James as a source of financing. Because there is no minimum offering amount required as a condition to close this offering, the actual total public offering amount, commissions and proceeds to us, if any, are not determinable at this time.

We currently intend to use the net proceeds, after deducting the sales agent's commissions and our offering expenses, for general corporate purposes, which may include, without limitation, funding new clinical trials of DKN-01 and TRX518 and the continuation of ongoing studies, and for working capital. As of the date of this prospectus supplement, we cannot specify with certainty all of the particular uses for the net proceeds that we will have from the sale of the shares of common stock. Accordingly, our management will have broad discretion in the application of the net proceeds. We may use the proceeds for purposes that are not contemplated at the time of this offering.

DILUTION

If you purchase shares of our common stock in this offering, your interest will be diluted immediately to the extent of the difference between the public offering price per share and the net tangible book value per share of our common stock immediately after this offering. We calculate net tangible book value per share by dividing our net tangible assets (tangible assets less total liabilities) by the number of shares of our common stock outstanding.

Our historical net tangible book value at June 30, 2018 was approximately \$12.0 million, or \$0.82 per share. After giving effect to the sale of shares of common stock in this offering in an aggregate amount of approximately \$30 million at an assumed offering price of \$7.47 per share, the last reported sale price of our common stock on the Nasdaq Global Market on September 6, 2018, and after deducting estimated offering expenses, our adjusted net tangible book value as of June 30, 2018 would have been approximately \$40.9 million, or \$2.19 per share. This represents an immediate increase in the net tangible book value of \$1.37 per share of our common stock to our existing shareholders and an immediate dilution in net tangible book value of \$5.28 per share to new investors purchasing shares of common stock in this offering. The following table illustrates this per share dilution:

Assumed offering price per share	\$ 7.47
Net tangible book value per share as of June 30, 2018	\$ 0.82
Increase in net tangible book value per share attributable to this offering	<u>\$ 1.37</u>
Net tangible book value per share as of June 30, 2018, as adjusted after giving effect to this offering	<u>\$ 2.19</u>
Dilution per share to new investors purchasing shares in this offering	<u>\$ 5.28</u>

The above discussion and table is based on 14,700,681 shares of common stock outstanding as of June 30, 2018, and excludes:

- 2,650,445 shares of common stock issuable upon exercise of outstanding stock options as of June 30, 2018 under our Amended and Restated 2012 Equity Incentive Plan, our 2016 Equity Incentive Plan and the assumed Macrocore 2013 Plan and 2008 Plan, with a weighted average exercise price of \$11.70 per share;
- 359,613 shares of common stock available for future issuance as of June 30, 2018 under our Amended and Restated 2012 Equity Incentive Plan and our 2016 Equity Incentive Plan; and
- 2,812,610 shares of common stock issuable upon exercise of outstanding warrants as of June 30, 2018, with a weighted average exercise price of \$5.967 per share.

To the extent that outstanding options or warrants are exercised, or other shares are issued, investors purchasing shares in this offering could experience further dilution. In addition, we may choose to raise additional capital due to market conditions or strategic considerations, even if we believe we have sufficient funds for our current or future operating plans. To the extent that additional capital is raised through the sale of equity or convertible debt securities, the issuance of those securities could result in further dilution to our shareholders.

DIVIDEND POLICY

We have never paid cash dividends on our common stock and we do not anticipate paying cash dividends in the foreseeable future, but intend to retain our capital resources for reinvestment in our business. Any future determination to pay cash dividends on our common stock will be at the discretion of our Board of Directors and will be dependent upon our financial condition, results of operations, capital requirements and other factors as the Board of Directors deems relevant.

**MATERIAL UNITED STATES FEDERAL INCOME AND ESTATE TAX CONSEQUENCES
FOR NON-U.S. HOLDERS OF OUR COMMON STOCK**

The following is a discussion of the material U.S. federal income and estate tax consequences of the acquisition, ownership, and disposition of our common stock to a non-U.S. holder that purchases shares of our common stock for cash in this offering. For purposes of this discussion, a "non-U.S. holder" means a beneficial owner (other than a partnership or other pass-through entity) of our common stock that is not, for U.S. federal income tax purposes:

- an individual who is a citizen or resident of the United States;
- a corporation or any other organization taxable as a corporation for U.S. federal income tax purposes, created or organized in the United States or under the laws of the United States or of any state thereof or the District of Columbia;
- an estate, the income of which is subject to U.S. federal income tax regardless of its source; or
- a trust if (i) the trust is subject to the primary supervision of a U.S. court and all substantial decisions of the trust are controlled by one or more U.S. persons or (ii) the trust has a valid election in effect under applicable U.S. Treasury regulations to be treated as a U.S. person.

This discussion does not address the tax treatment of partnerships (or other entities that are treated as partnerships, grantor trusts, or other pass-through entities for U.S. federal income tax purposes) or persons that hold their common stock through partnerships, grantor trusts, or other pass-through entities. The tax treatment of a partner in a partnership or holder of an interest in another pass-through entity that will hold our common stock generally will depend upon the status of the partner or interest holder and the activities of the partner or interest holder and the partnership or other pass-through entity, as applicable. Such a partner or interest holder should consult his, her, or its own tax advisor regarding the tax consequences of the acquisition, ownership and disposition of our common stock through a partnership or other pass-through entity, as applicable.

This discussion is based upon the provisions of the Internal Revenue Code of 1986, as amended, or the Code, the U.S. Treasury regulations promulgated thereunder, judicial decisions, and published rulings, administrative procedures, and other guidance of the Internal Revenue Service, or the IRS, all as in effect as of the date hereof. These authorities are subject to change and to differing interpretations, possibly with retroactive effect, which could result in U.S. federal income or estate tax consequences different from those summarized below. No ruling has been or is expected to be sought from the IRS with respect to the matters summarized below, and there can be no assurance that the IRS will not take a contrary position regarding the U.S. federal income or estate tax consequences of the acquisition, ownership, or disposition of our common stock, or that any such contrary position would not be sustained by a court.

This discussion is not a complete analysis of all of the potential U.S. federal income and estate tax consequences relating to the acquisition, ownership, and disposition of our common stock by non-U.S. holders, nor does it address any U.S. federal gift or generation-skipping transfer tax consequences, any tax consequences arising under any state, local, or non-U.S. tax laws, the impact of any applicable tax treaty, any consequences under the Medicare contribution tax on net investment income, the alternative minimum tax, or any consequences under other U.S. federal tax laws. In addition, this discussion does not address tax consequences resulting

from a non-U.S. holder's particular circumstances or to non-U.S. holders that may be subject to special tax rules, including, without limitation:

- non-U.S. governments, agencies or instrumentalities thereof, or entities they control;
- "controlled foreign corporations" and their shareholders;
- "passive foreign investment companies" and their shareholders;
- partnerships, grantor trusts or other entities that are treated as pass-through entities for U.S. federal income tax purposes, and their owners;
- corporations that accumulate earnings to avoid U.S. federal income tax;
- former citizens or former long-term residents of the United States;
- banks, insurance companies or other financial institutions;
- tax-exempt pension funds or other tax-exempt organizations;
- persons who acquired our common stock pursuant to the exercise of employee stock options or otherwise as compensation;
- tax-qualified retirement plans;
- traders, brokers, or dealers in securities, commodities, or currencies;
- persons who hold our common stock as a position in a hedging transaction, wash sale, "straddle," "conversion transaction" or other risk reduction transaction or synthetic security;
- persons who do not hold our common stock as a capital asset within the meaning of Section 1221 of the Code (generally, for investment purposes);
- persons subject to special tax accounting rules as a result of any item of gross income with respect to common stock being taken into account in a financial statement;
- persons who own or have owned, or are deemed to own or to have owned, more than 5% of our common stock (except to the extent specifically set forth below); or
- persons deemed to sell our common stock under the constructive sale provisions of the Code.

Prospective investors should consult their own tax advisors regarding the particular U.S. federal income, estate, gift, and generation-skipping transfer tax consequences to them of acquiring, owning, and disposing of our common stock, as well as any tax consequences arising under any state, local, or foreign tax laws and any other U.S. federal tax laws. Prospective investors should also consult their tax advisors regarding the potential impact of any applicable income or estate tax treaty between the United States and such prospective investor's country of residence and of the rules described below under the heading "Foreign Account Tax Compliance Act."

Distributions on Common Stock

As described in the section entitled "Dividend Policy," we currently intend to retain any earnings for use in the operation of our business and do not anticipate paying any dividends on our common stock in the foreseeable future. The disclosure in this section addresses the consequences should our board of directors, in the future, determine to make a distribution of cash or property with respect to our common stock (other than certain distributions of stock which may be made free of tax), or to effect a redemption that is treated for tax purposes as a distribution. Any such distribution will generally constitute a dividend for U.S. federal tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. To the extent such a distribution exceeds both our current and our accumulated earnings and profits, such excess will be allocated ratably among the shares of common stock with respect to which the distribution is made. Any such excess allocated to a share of common stock will constitute a return of capital to the extent of the non-U.S. holder's adjusted tax basis in that share of common stock, reducing that adjusted tax basis, but not below zero. After the non-U.S. holder's adjusted tax basis in a share of common stock has been reduced to zero, any remaining excess allocated to that share of common stock will be treated as capital gain from the sale of that share of common stock, subject to the tax treatment described below under "Gain on Disposition of Common Stock." Any such distributions will also be subject to the discussion below regarding backup withholding and foreign accounts. A non-U.S. holder's adjusted tax basis in a share of common stock is generally the purchase price of the share, reduced by the amount of any distributions constituting a return of capital with respect to that share.

Any dividend paid to a non-U.S. holder of our common stock generally will be subject to U.S. federal withholding tax at a rate of 30% of the gross amount of the dividend, or such lower rate as may be specified by an applicable income tax treaty between the United States and such non-U.S. holder's country of residence. If a non-U.S. holder is eligible for benefits under an income tax treaty and wishes to claim a reduced rate of withholding, the non-U.S. holder generally will be required to provide us or our paying agent with a properly completed IRS Form W-8BEN, Form W-8BEN-E, or other applicable form, certifying under penalties of perjury the non-U.S. holder's qualification for the reduced rate. This certification must be provided to us or our paying agent prior to the payment of the dividend and may be required to be updated periodically. Special certification requirements apply to non-U.S. holders that hold common stock through certain foreign intermediaries. Non-U.S. holders that do not timely provide the required certifications, but that qualify for a reduced treaty rate, may obtain a refund of any excess amounts withheld by timely filing an appropriate claim for refund with the IRS. If we are not able to determine whether or not a distribution will exceed current and accumulated earnings and profits at the time the distribution is made, we may withhold tax on the entire amount of any distribution at the same rate as we would withhold on a dividend. However, a non-U.S. holder may obtain a refund of amounts that we withhold to the extent attributable to the portion of the distribution in excess of our current and accumulated earnings and profits.

If a non-U.S. holder holds our common stock in connection with the conduct of a trade or business in the U.S., and dividends paid on the common stock are effectively connected with the non-U.S. holder's U.S. trade or business (and, if required by an applicable income tax treaty between the United States and such non-U.S. holder's country of residence, are attributable to a permanent establishment or fixed base maintained by the non-U.S. holder in the U.S., as defined under the applicable treaty), the non-U.S. holder will be exempt from U.S. federal withholding tax on the dividends. To claim the exemption, the non-U.S. holder must furnish a properly executed IRS Form W-8ECI (or other applicable form) prior to the payment of the dividends. Any dividends paid on our common stock that are effectively connected with a non-U.S. holder's

U.S. trade or business (and satisfy any other applicable treaty requirements) generally will be subject to U.S. federal income tax on a net income basis at the regular graduated U.S. federal income tax rates generally applicable to U.S. persons (as defined in the Code). A non-U.S. holder that is treated as a corporation for U.S. federal income tax purposes also may be subject to an additional branch profits tax equal to 30% (or such lower rate as is specified by an applicable income tax treaty between the United States and such non-U.S. holder's country of residence) of a portion of its earnings and profits for the taxable year that are effectively connected with a U.S. trade or business, as adjusted for certain items.

Gain on Disposition of Common Stock

Subject to the discussion below regarding backup withholding and foreign accounts, a non-U.S. holder generally will not be subject to U.S. federal income tax on any gain realized upon the sale, exchange, or other taxable disposition of our common stock unless:

- the gain is effectively connected with the non-U.S. holder's conduct of a U.S. trade or business (and, if required by an applicable income tax treaty between the United States and such non-U.S. holder's country of residence, the gain is attributable to a permanent establishment or fixed base maintained by the non-U.S. holder in the U.S.), in which case the non-U.S. holder will generally be required to pay tax on the gain derived from the sale, exchange, or other taxable disposition (net of certain deductions or credits) under regular graduated U.S. federal income tax rates generally applicable to U.S. persons, and in the case of a non-U.S. holder that is treated as a corporation for U.S. federal income tax purposes, such non-U.S. holder may be subject to a branch profits tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and such non-U.S. holder's country of residence;
- the non-U.S. holder is an individual who is present in the U.S. for a period or periods aggregating 183 days or more during the taxable year in which the sale, exchange, or other taxable disposition occurs and certain other conditions are met, in which case the non-U.S. holder will be subject to U.S. federal income tax at a flat 30% rate (or such lower rate as is specified by an applicable income tax treaty between the United States and such non-U.S. holder's country of residence) on the net gain derived from the sale, exchange, or other taxable disposition, which gain may be offset by U.S. source capital losses (even though the non-U.S. holder is not considered a resident of the U.S.) provided that the non-U.S. holder has timely filed U.S. federal income tax returns reporting those losses; or
- our common stock is a "United States real property interest" by reason of our status as a "United States real property holding corporation," or USRPHC, for U.S. federal income tax purposes during the five-year period preceding such sale, exchange or other taxable disposition (or the non-U.S. holder's holding period, if shorter).

Generally, a corporation is a USRPHC only if the fair market value of its U.S. real property interests equals or exceeds 50% of the sum of the fair market value of its worldwide real property interests plus its other assets used or held for use in a trade or business. We believe we are not now and we do not anticipate becoming a USRPHC. However, there can be no assurance that we are not now a USRPHC or will not become one in the future. Even if we are or become a USRPHC, for so long as our common stock is "regularly traded," as defined by applicable U.S. Treasury regulations, on an established securities market, sales of our common stock generally will not be subject to tax for non-U.S. holders that have not held more than 5% of our common stock, actually or constructively, during the five-year period preceding such non-U.S. holder's

sale, exchange or other taxable disposition of our common stock (or the non-U.S. holder's holding period, if shorter). If we are determined to be a USRPHC and the foregoing exception does not apply, then the non-U.S. holder generally will be taxed on its net gain derived from the disposition at the graduated U.S. federal income tax rates applicable to U.S. persons. No assurance can be provided that our common stock will be regularly traded on an established securities market for purposes of the rule described above.

Information Reporting and Backup Withholding

Generally, we or certain financial middlemen must report annually to the IRS and to each non-U.S. holder the gross amount of dividends and other distributions on our common stock paid to the non-U.S. holder and the amount of tax withheld, if any, with respect to those distributions. Pursuant to applicable income tax treaties or other agreements, the IRS may make these reports available to tax authorities in the non-U.S. holder's country of residence or incorporation.

A non-U.S. holder may be subject to backup withholding with respect to dividends paid on shares of our common stock, unless, generally, the non-U.S. holder certifies under penalties of perjury (usually on IRS Form W-8BEN or W-8BEN-E) that the non-U.S. holder is not a U.S. person or otherwise establishes an exemption. The backup withholding rate is currently 24%. Dividends that are paid to non-U.S. holders subject to the withholding of U.S. federal income tax, as described above under the heading "Distributions on Common Stock," generally will be exempt from U.S. backup withholding.

Additional rules relating to information reporting requirements and backup withholding with respect to payments of the proceeds from the disposition of shares of our common stock are as follows:

- If the proceeds are paid to or through the U.S. office of a broker, the proceeds generally will be subject to backup withholding and information reporting, unless the non-U.S. holder certifies under penalties of perjury (usually on IRS Form W-8BEN or W-8BEN-E) that the non-U.S. holder is not a U.S. person and satisfies certain other requirements or otherwise establishes an exemption.
- If the proceeds are paid to or through a non-U.S. office of a broker that is not a U.S. person and is not a foreign person with certain specified U.S. connections, which we refer to below as a "U.S.-related person," information reporting and backup withholding generally will not apply.
- If the proceeds are paid to or through a non-U.S. office of a broker that is a U.S. person or a U.S.-related person, the proceeds generally will be subject to information reporting (but not to backup withholding), unless the non-U.S. holder certifies under penalties of perjury (usually on IRS Form W-8BEN or W-8BEN-E) that the non-U.S. holder is not a U.S. person. A "U.S.-related person" includes (i) an entity classified as a "controlled foreign corporation" for U.S. federal income tax purposes, (ii) a foreign person, 50% or more of whose gross income from certain periods is effectively connected with a U.S. trade or business, or (iii) a foreign partnership if at any time during its tax year (a) one or more of its partners are U.S. persons who, in the aggregate, hold more than 50% of the income or capital interests of the partnership or (b) the foreign partnership is engaged in a U.S. trade or business.

Backup withholding is not an additional tax. Any amounts withheld from a non-U.S. holder under the backup withholding rules may be allowed as a refund or a credit against the non-U.S. holder's U.S. federal income tax liability, if any, provided that the non-U.S. holder timely furnishes the required information to the IRS. Non-U.S. holders should consult their own tax advisors regarding the application of the information reporting and backup withholding rules to them.

Foreign Account Tax Compliance Act

Sections 1471 to 1474 of the Code (commonly referred to as the Foreign Account Tax Compliance Act, or FATCA) generally impose withholding tax on certain types of payments made to "foreign financial institutions" (as defined in the Code) and other non-U.S. entities unless those institutions and entities meet additional certification, information reporting and other requirements. FATCA generally imposes a 30% withholding tax on dividends on, or gross proceeds from the sale or other disposition of, our common stock paid to a foreign financial institution unless the foreign financial institution enters into an agreement with the U.S. Treasury to, among other things, (i) undertake to identify accounts held by certain U.S. persons (including certain equity and debt holders of such institution) or by U.S.-owned foreign entities, (ii) annually report certain information about such accounts, and (iii) withhold 30% on payments to account holders whose actions prevent it from complying with these reporting and other requirements. In addition, subject to certain exceptions, FATCA imposes a 30% withholding tax on the same types of payments to a "non-financial foreign entity" (as defined in the Code) unless the entity certifies that it does not have any substantial U.S. owners (which generally include any U.S. persons who directly or indirectly own more than 10% of the entity) or furnishes identifying information regarding each such substantial U.S. owner or agrees to report that information to the IRS. These withholding taxes will be imposed on dividends paid on our common stock and, after December 31, 2018, on gross proceeds from sales or other dispositions of our common stock. Withholding under FATCA generally will not be reduced or limited by bilateral income tax treaties. However, intergovernmental agreements between the U.S. and other countries with respect to the implementation of FATCA and non-U.S. laws, regulations and other authorities enacted or issued with respect to those intergovernmental agreements may modify the FATCA requirements described above. Non-U.S. holders should consult their own tax advisors regarding the possible implications of FATCA on their investment in our common stock and the entities through which they hold our common stock, including, without limitation, the process and deadlines for meeting the applicable requirements to prevent the imposition of the 30% withholding tax under FATCA.

Federal Estate Tax

Common stock owned or treated as owned at the time of death by an individual who is not a citizen or resident of the United States (as specifically defined for U.S. federal estate tax purposes) is considered a U.S. situs asset and will be included in the individual's gross estate for U.S. federal estate tax purposes and, therefore, may be subject to U.S. federal estate tax, unless an applicable estate tax or other treaty between the United States and such individual's country of residence provides otherwise.

The preceding discussion of U.S. federal tax considerations is for information only. It is not tax advice. Each prospective investor should consult its own tax advisor regarding the particular U.S. federal, state and local and non-U.S. tax consequences of purchasing, holding and disposing of our common stock, including the consequences of any proposed change in applicable laws.

PLAN OF DISTRIBUTION

We have entered into a distribution agreement under which we may issue and sell our common stock having an aggregate sales price of up to \$30,000,000 from time to time through or to Raymond James as our sales agent. Sales of our common stock, if any, may be made by means of ordinary brokers' transactions on the Nasdaq Global Market or otherwise at market prices, in block transactions or as otherwise agreed with Raymond James.

Raymond James, as sales agent, is not required to sell any specific number or dollar amount of common stock but will use commercially reasonable efforts, consistent with its normal trading and sales practices, to solicit offers to purchase the common stock upon entering into a transaction notice with us that will specify the number of common stock to be sold and such other matters as may be agreed upon by us and Raymond James. Subject to the terms and conditions of the distribution agreement, Raymond James will use commercially reasonable efforts, consistent with its normal trading and sales practices, to sell on our behalf all of the designated common stock pursuant to the terms agreed to with us, which terms will include the number of common stock to be offered and any minimum price below which sales may not be made. The obligation of Raymond James under the distribution agreement to sell shares pursuant to any transaction notice is subject to a number of conditions, which Raymond James reserves the right to waive in its sole discretion.

Raymond James, in its capacity as sales agent, may arrange for or make sales at the market in the existing trading market for our common stock, including sales made to or through a market maker or through an electronic communications network, or in any other manner that may be deemed to be an "at-the-market" offering as defined in Rule 415 promulgated under the Securities Act. If agreed to in a separate terms agreement, we may also sell common stock to Raymond James as principal, at a purchase price agreed upon by Raymond James and us.

We will pay Raymond James a commission equal to 3% of the gross sales price of any such shares sold through it as sales agent, or purchased by it as principal, as set forth in the distribution agreement. The remaining sales proceeds, after deducting any transaction fees imposed by any governmental or self-regulatory organization in connection with the sales, will equal our net proceeds for the sale of the common stock. Raymond James shall be responsible for costs and expenses associated with the sale and marketing of the common stock, as provided in the distribution agreement. We also have agreed to reimburse Raymond James for all fees and expenses of counsel for Raymond James, up to \$30,000, as provided in the distribution agreement.

Settlement for sales of common stock will occur on the second business day following the date on which any sales are made in return for payment of the net proceeds to us. There is no arrangement for funds to be received in an escrow, trust or similar arrangement. We will report at least quarterly the number of common stock sold through Raymond James, as agent, in at-the-market offerings, the gross and net proceeds to us and the compensation paid by us to Raymond James in connection with such sales.

While any sale transactions are pending, we will not (i) offer, pledge, publicly announce the intention to sell, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase or otherwise transfer or dispose of, directly or indirectly, any of our common stock or any securities convertible into or exercisable, redeemable or exchangeable for such shares or (ii) enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of such shares, whether any such transaction described in clause (i) or (ii) above is to be settled by

delivery of common stock or such other securities, in cash or otherwise, without the prior written consent of Raymond James, other than the shares to be sold pursuant to the distribution agreement and shares issued upon the exercise or conversion of any of our securities, convertible securities, options or rights outstanding at the beginning of such period or any grants of options or awards or securities issued pursuant to existing stock-based compensation plans.

LEGAL MATTERS

Morgan, Lewis & Bockius LLP, Boston, Massachusetts, will pass upon the validity of the shares of common stock offered hereby. Mintz, Levin, Cohn, Ferris, Glovsky, and Popeo, P.C., New York, New York, is acting as counsel for the sales agent in connection with this offering.

EXPERTS

The consolidated balance sheets of Leap Therapeutics, Inc. and subsidiaries as of December 31, 2017 and 2016, and the related consolidated statements of operations, comprehensive loss, redeemable convertible and convertible preferred stock and stockholders' equity (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.

WHERE YOU CAN FIND MORE INFORMATION

This prospectus supplement constitutes a part of a registration statement on Form S-3 filed under the Securities Act. As permitted by the SEC's rules, this prospectus supplement, which forms a part of the registration statement, does not contain all the information that is included in the registration statement. You will find additional information about us in the registration statement. Any statements made in this prospectus supplement concerning legal documents are not necessarily complete and you should read the documents that are filed as exhibits to the registration statement or otherwise filed with the SEC for a more complete understanding of the document or matter.

We are subject to the informational requirements of the Exchange Act, and in accordance therewith file quarterly, annual, and current reports and proxy statements and other information with the SEC. You may read and copy any materials we file with the SEC at the SEC's Public Reference Room at 100 F Street N.E., Washington, D.C. 20549. 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 that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC. The address of the site is <http://www.sec.gov>.

We make available free of charge on or through our Internet website www.leaptx.com, our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act as soon as reasonably practicable after we electronically file the material with, or furnish it to, the SEC. Information on our Internet website is not incorporated by reference in this prospectus supplement or the accompanying prospectus, and you should not consider it a part of this prospectus supplement or the accompanying prospectus.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

This prospectus supplement is part of the registration statement but the registration statement includes and incorporates by reference additional information and exhibits. The SEC permits us to "incorporate by reference" the information contained in documents we file with the SEC, which means that we can disclose important information to you by referring you to those documents rather than by including them in this prospectus supplement. Information that

is incorporated by reference is considered to be part of this prospectus supplement and you should read it with the same care that you read this prospectus supplement and the accompanying prospectus. Information that we file later with the SEC will automatically update and supersede the information that is either contained, or incorporated by reference, in this prospectus supplement, and will be considered to be a part of this prospectus supplement from the date those documents are filed.

We incorporate by reference the documents listed below, all filings filed by us pursuant to the Exchange Act after the date of the registration statement of which this prospectus supplement forms a part, and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act prior to the time that all securities covered by this prospectus supplement have been sold; provided, however, that we are not incorporating any documents or information deemed to have been furnished and not filed in accordance with SEC rules:

- our Annual Report on Form 10-K for the fiscal year ended December 31, 2017, filed with the SEC on February 23, 2018;
- our Quarterly Reports on Form 10-Q for the quarter ended March 31, 2018, filed with the SEC on May 11, 2018; and for the quarter ended June 30, 2018, filed with the SEC on August 8, 2018; 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.

In addition, all documents subsequently filed by us pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act before the date our offering is terminated or completed are deemed to be incorporated by reference into, and to be a part of, this prospectus supplement.

Any statement contained in this prospectus supplement or in a document incorporated or deemed to be incorporated by reference into this prospectus supplement will be deemed to be modified or superseded for purposes of this prospectus supplement to the extent that a statement contained in this prospectus supplement or any other subsequently filed document that is deemed to be incorporated by reference into this prospectus supplement modifies or supersedes the statement. Any statement so modified or superseded will not be deemed, except as so modified or superseded, to constitute a part of this prospectus supplement.

We will provide to each person, including any beneficial holder, to whom a prospectus supplement is delivered, at no cost, upon written or oral request, a copy of any or all of the information that has been incorporated by reference in the prospectus supplement but not delivered with the prospectus supplement. You should direct any requests for copies to us at Attention: Secretary, 47 Thorndike Street, Suite B1-1, Cambridge, Massachusetts 02141 or you may call us at (617) 714-0360. Exhibits to the filings will not be sent, however, unless those exhibits have specifically been incorporated by reference into this prospectus supplement and accompanying prospectus.

You should rely only on information contained in, or incorporated by reference into, this prospectus supplement and the accompanying prospectus. We have not, and the sales agent has not, authorized anyone to provide you with information different from that contained in this prospectus supplement or the accompanying prospectus, or incorporated by reference in this prospectus supplement or the accompanying prospectus and in any free writing prospectus that

we have authorized for use in connection with this offering. We and the sales agent are not making offers to sell the securities in any jurisdiction in which such an offer or solicitation is not authorized or in which the person making such offer or solicitation is not qualified to do so or to anyone to whom it is unlawful to make such offer or solicitation.

\$100,000,000



**Common Stock
Preferred Stock
Debt Securities
Warrants**

This prospectus relates to common stock, preferred stock, debt securities and warrants that we may sell from time to time in one or more offerings up to a total public offering price of \$100,000,000 on terms to be determined at the time of sale. We will provide specific terms of these securities in supplements to this prospectus. You should read this prospectus and any supplement carefully before you invest. This prospectus may not be used to offer and sell securities unless accompanied by a prospectus supplement for those securities.

Our common stock trades on the NASDAQ Global Market under the symbol "LPTX." On February 28, 2018, the closing price of our common stock was \$6.61 per share.

These securities may be sold directly by us, through dealers or agents designated from time to time, to or through underwriters or through a combination of these methods. See "Plan of Distribution" in this prospectus. We may also describe the plan of distribution for any particular offering of these securities in any applicable prospectus supplement. If any agents, underwriters or dealers are involved in the sale of any securities in respect of which this prospectus is being delivered, we will disclose their names and the nature of our arrangements with them in a prospectus supplement. The net proceeds we expect to receive from any such sale will also be included in a prospectus supplement.

Investing in our securities involves a high degree of risk. You should review carefully the risks and uncertainties described under the heading "Risk Factors" contained in the applicable prospectus supplement and any related free writing prospectus, and under similar headings in the other documents that are 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 DETERMINED IF THIS PROSPECTUS IS TRUTHFUL OR COMPLETE. ANY REPRESENTATION TO THE CONTRARY IS A CRIMINAL OFFENSE.

The date of this prospectus is March 16, 2018

TABLE OF CONTENTS

ABOUT THIS PROSPECTUS	i
SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS	i
SUMMARY	1
RISK FACTORS	6
RATIO OF EARNINGS TO FIXED CHARGES	6
DESCRIPTION OF CAPITAL STOCK	6
DESCRIPTION OF DEBT SECURITIES	12
DESCRIPTION OF WARRANTS	19
LEGAL OWNERSHIP OF SECURITIES	21
PLAN OF DISTRIBUTION	25
LEGAL MATTERS	27
EXPERTS	27
WHERE YOU CAN FIND MORE INFORMATION	27
INCORPORATION OF CERTAIN INFORMATION BY REFERENCE	27
DISCLOSURE OF COMMISSION'S POSITION ON INDEMNIFICATION FOR SECURITIES ACT LIABILITY	28

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, each prospectus supplement and the information incorporated by reference in this prospectus and each prospectus supplement contain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, which we refer to as the Securities Act, and Section 21E of the Exchange Act of 1934, as amended, which we refer to as the Exchange Act, that involve a number of risks and uncertainties. Although our forward-looking statements reflect the good faith judgment of our management, these statements can only be based on facts and factors currently known by us. Consequently, these forward-looking statements are inherently subject to risks and uncertainties, and actual results and outcomes may differ materially from results and outcomes discussed in the forward-looking statements.

Forward-looking statements can be identified by the use of forward-looking words such as "believes," "expects," "hopes," "may," "will," "plan," "intends," "estimates," "could," "should," "would," "continue," "seeks," "pro forma," or "anticipates," or other similar words (including their use in the negative), or by discussions of future matters. These statements include but are not limited to statements under the captions "Business," "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" and in other sections included in any applicable prospectus supplement or incorporated by reference from our Annual Report on Form 10-K and Quarterly Reports on Form 10-Q, as applicable, as well as our other filings with the Securities and Exchange Commission, or the SEC. You should be aware that the occurrence of any of the events discussed under the heading "Risk Factors" in any applicable prospectus supplement and any documents incorporated by reference herein or therein could substantially harm our business, operating results and financial condition and that if any of these events occurs, it could adversely affect the value of an investment in our securities.

The cautionary statements made in this prospectus are intended to be applicable to all related forward-looking statements wherever they may appear in this prospectus or in any prospectus supplement or any documents incorporated by reference herein or therein. We urge you not to place undue reliance on these forward-looking statements, which speak only as of the date they are made. Except as required by law, we assume no obligation to update our forward-looking statements, even if new information becomes available in the future.

ABOUT THIS PROSPECTUS

This prospectus is a part of a registration statement on Form S-3 that we filed with the SEC, utilizing a "shelf" registration process. Under this shelf registration process, we may, from time to time, sell any combination of the securities described in this prospectus in one or more offerings up to a total aggregate offering price of \$100,000,000. This prospectus provides you with a general description of the securities we may offer.

Each time we sell securities under this prospectus, we will provide prospective investors with a prospectus supplement that will contain specific information about the terms of that offering. We may also authorize one or more free writing prospectuses to be provided to you that may contain material information relating to these offerings. The prospectus supplement and any related free writing prospectus that we may authorize to be provided to you may also add, update or change information contained in this prospectus or in any documents that we have incorporated by reference into this prospectus. You should read this prospectus, any applicable prospectus supplement and any related free writing prospectus, together with the information incorporated herein by reference as described under the heading "Incorporation of Certain Information By Reference," before investing in any of the securities offered.

This prospectus may not be used to consummate a sale of securities unless it is accompanied by a prospectus supplement.

Neither we, nor any agent, underwriter or dealer has authorized any person to give any information or to make any representation other than those contained or incorporated by reference in this prospectus, any applicable prospectus supplement or any related free writing prospectus prepared by or on behalf of us or to which we have referred you. This prospectus, any applicable supplement to this prospectus or any related free writing prospectus do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the registered securities to which they relate, nor does this prospectus, any applicable supplement to this prospectus or any related free writing prospectus constitute an offer to sell or the solicitation of an offer to buy securities in any jurisdiction to any person to whom it is unlawful to make such offer or solicitation in such jurisdiction.

You should not assume that the information contained in this prospectus, any applicable prospectus supplement or any related free writing 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, any applicable prospectus supplement or any related free writing prospectus is delivered, or securities are sold, on a later date.

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."

SUMMARY

This summary highlights selected information from this prospectus and does not contain all of the information that you need to consider in making your investment decision. You should carefully read the entire prospectus, the applicable prospectus supplement and any related free writing prospectus, including the risks of investing in our securities discussed under the heading "Risk Factors" contained in the applicable prospectus supplement and any related free writing prospectus, and under similar headings in the other documents that are incorporated by reference into this prospectus. You should also carefully read the information incorporated by reference into this prospectus, including our consolidated financial statements, and the exhibits to the registration statement of which this prospectus is a part.

Unless the context indicates otherwise, as used in this prospectus, the terms "Leap," "the Company," "we," "us" and "our" refer to Leap Therapeutics, Inc., a Delaware corporation, and, where appropriate, our consolidated subsidiaries.

Company Overview

Leap Therapeutics, Inc. is a biopharmaceutical company developing novel therapies designed to treat patients with cancer by inhibiting fundamental tumor-promoting pathways and by harnessing the immune system to attack cancer cells. Our strategy is to identify, acquire, and develop molecules that will rapidly translate into high impact therapeutics that generate durable clinical benefit and enhanced patient outcomes.

Our two clinical stage programs are:

- **DKN-01:** A monoclonal antibody that inhibits Dickkopf-related protein 1, or DKK1. DKK1 is a protein that regulates the Wnt signaling pathways and enables tumor cells to proliferate and spread, as well as suppresses the immune system from attacking the tumor. When DKN-01 binds to DKK1, an anti-tumor effect can be generated. DKN-01-based therapies have generated responses and clinical benefit in several patient populations. We are currently studying DKN-01 in multiple ongoing clinical trials in patients with esophagogastric cancer, biliary tract cancer, or gynecologic cancers, and we are initiating a trial in hepatocellular carcinoma in 2018. We are focused on two parallel development strategies involving targeted patient populations with Wnt pathway alterations and as a combination with other cancer immunotherapy agents.
- **TRX518:** A monoclonal antibody targeting the glucocorticoid-induced tumor necrosis factor-related receptor, or GITR. GITR is a receptor found on the surface of a wide range of immune cells. GITR stimulation activates tumor fighting white blood cells and decreases the activity of potentially tumor-protective immunosuppressive cells. TRX518 has been specifically engineered to enhance the immune system's anti-tumor response by activating GITR signaling without causing the immune cells to be destroyed. We are conducting two clinical trials of TRX518 in patients with advanced solid tumors and have recently begun enrolling combination therapy arms utilizing TRX518 with gemcitabine chemotherapy or with cancer immunotherapies known as PD-1 antagonists.

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.

We commenced business operations in 2011. 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, business development activities, convertible note financings, and our merger with MacroCure Ltd.

("Macrocure") completed in January 2017. Through December 31, 2017, we had not generated revenue, and have incurred significant losses from operations. We expect to continue to incur operating losses for the foreseeable future as we develop our product candidates.

Corporate Information

We were incorporated in the state of Delaware as Dekkun Corporation on January 3, 2011 and changed our name to HealthCare Pharmaceuticals, Inc. effective May 29, 2014, and then to Leap Therapeutics, Inc. effective November 16, 2015. During 2015, HealthCare Pharmaceuticals Pty Ltd. ("HCP Australia") was formed and is our wholly owned subsidiary.

On December 10, 2015, we entered into a merger agreement with GTR Inc. ("GTR"), an entity under common control, whereby a wholly owned subsidiary was merged with GTR and the surviving name of the wholly owned subsidiary was GTR Inc.

On August 29, 2016, we entered into a definitive merger agreement with Macrocare Ltd ("Macrocare"), a publicly held, clinical-stage biotechnology company based in Petach Tikva, Israel, and M-Co Merger Sub Ltd. ("Merger Sub"), a wholly owned subsidiary of the Company which provided for the merger of Macrocare with and into Merger Sub, with Macrocare continuing after the merger as a wholly owned subsidiary of the Company. On February 1, 2017, Macrocare's name was changed to Leap Therapeutics Ltd.

The mailing address of Leap's principal executive office is 47 Thorndike Street, Suite B1-1, Cambridge, MA 02141. Leap's telephone number is 617-714-0360. Leap's website address is www.leaptx.com (the information contained therein or linked thereto shall not be considered incorporated by reference in this Registration Statement on Form S-3).

Status as an Emerging Growth Company

We are an "emerging growth company", or EGC, as defined in the Jumpstart Our Business Startups Act of 2012 (the "JOBS Act"). The JOBS Act, permits an "emerging growth company" such as us to take advantage of an extended transition period to comply with new or revised accounting standards applicable to public companies until those standards would otherwise apply to private companies. We have elected to use the extended transition period for complying with new or revised accounting standards under Section 102(b)(1) of the JOBS Act. This election allows us to delay the adoption of new or revised accounting standards that have different effective dates for public and private companies until those standards apply to private companies. As a result of this election, our financial statements may not be comparable to companies that comply with public company effective dates.

We may take advantage of these reporting exemptions until we are no longer an emerging growth company, which in certain circumstances could be for up to five years. We will remain an "emerging growth company" until the earliest of (a) the last day of the first fiscal year in which our annual gross revenues exceed \$1.07 billion, (b) the date that we become a "large accelerated filer" as defined in Rule 12b-2 under the Exchange Act, which would occur if the market value of our shares that are held by non-affiliates exceeds \$700 million as of the last business day of our most recently completed second fiscal quarter, (c) the date on which we have issued more than \$1.0 billion in nonconvertible debt during the preceding three-year period and (d) the last day of our 2022 fiscal year containing the fifth anniversary of the date on which shares of our common stock became publicly traded in the U.S. As of December 31, 2017, we remain an EGC.

The Securities We May Offer

We may offer shares of our common stock and preferred stock, various series of debt securities and warrants to purchase any of such securities, up to a total aggregate offering price of \$100,000,000 from time to time in one or more offerings under this prospectus, together with any applicable prospectus supplement and any related free writing prospectus, at prices and on terms to be determined by market conditions at the time of the relevant offering. This prospectus provides you with a general description of the securities we may offer.

Each time we offer a type or series of securities under this prospectus, we will provide a prospectus supplement that will describe the specific amounts, prices and other important terms of the securities, including, to the extent applicable:

- designation or classification;
- aggregate principal amount or aggregate offering price;
- maturity, if applicable;
- original issue discount, if any;
- rates and times of payment of interest or dividends, if any;
- redemption, conversion, exchange or sinking fund terms, if any;
- conversion or exchange prices or rates, if any, and, if applicable, any provisions for changes to or adjustments in the conversion or exchange prices or rates and in the securities or other property receivable upon conversion or exchange;
- ranking, if applicable;
- restrictive covenants, if any;
- voting or other rights, if any; and
- important United States federal income tax considerations.

The prospectus supplement and any related free writing prospectus that we may authorize to be provided to you may also add, update or change information contained in this prospectus or in documents we have incorporated by reference. However, no prospectus supplement or free writing prospectus will offer a security that is not registered and described in this prospectus at the time of the effectiveness of the registration statement of which this prospectus is a part.

This prospectus may not be used to consummate a sale of securities unless it is accompanied by a prospectus supplement.

We may sell the securities directly to investors or through underwriters, dealers or agents. We, and our underwriters or agents, reserve the right to accept or reject all or part of any proposed purchase of securities. If we do offer securities through underwriters or agents, we will include in the applicable prospectus supplement:

- the names of those underwriters or agents;
- applicable fees, discounts and commissions to be paid to them;
- details regarding option to purchase additional securities, if any; and
- the estimated net proceeds to us.

Common stock. We may issue shares of our common stock from time to time. Each holder of our common stock is entitled to one vote for each share on all matters submitted to a vote of the

stockholders, including the election of directors. Our stockholders do not have cumulative voting rights in the election of directors. An election of directors by our stockholders shall be determined by a plurality of votes cast by the stockholders entitled to vote on the election. Subject to preferences that may be applicable to any then outstanding 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. In the event of our liquidation, dissolution or winding up, holders of our common stock will be 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. Holders of common stock have no preemptive, conversion or subscription rights and there are no redemption or sinking fund provisions applicable to the common stock. The rights, preferences and privileges of the holders of common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of preferred stock that we may designate in the future. When we issue shares of common stock under this prospectus, the shares will be fully paid and non-assessable. In this prospectus, we have summarized certain general features of our common stock under "Description of Capital Stock—Common Stock." We urge you, however, to read the applicable prospectus supplement (and any related free writing prospectus that we may authorize to be provided to you) related to any common stock being offered.

Preferred stock. We may issue shares of our preferred stock from time to time, in one or more series. Under our amended and restated certificate of incorporation, our board of directors has the authority, without further action by the stockholders, to issue up to 10,000,000 shares of preferred stock in one or more series, to establish from time to time the number of shares to be included in each such series, to fix the rights, preferences and privileges of the shares of each wholly unissued series and any qualifications, limitations or restrictions thereon and to increase or decrease the number of shares of any such series, but not below the number of shares of such series then outstanding. Since our amended and restated certificate of incorporation became effective, we have not designated or issued any series of preferred stock, and therefore we are not offering previously designated series of preferred stock under this prospectus. If we sell any new series of preferred stock under this prospectus and any applicable prospectus supplement, our board of directors will determine the designations, voting powers, preferences and rights of the preferred stock being offered, as well as the qualifications, limitations or restrictions thereof, including dividend rights, conversion rights, preemptive rights, terms of redemption or repurchase, liquidation preferences, sinking fund terms and the number of shares constituting any series or the designation of any series. Convertible preferred stock may be convertible into our common stock or exchangeable for our other securities. Conversion may be mandatory or at the holder's option and would be at prescribed conversion rates. We will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of the certificate of designation that describes the terms of the series of preferred stock that we are offering before the issuance of the related series of preferred stock. In this prospectus, we have summarized certain general features of the preferred stock under "Description of Capital Stock—Preferred Stock." We urge you, however, to read the applicable prospectus supplement (and any related free writing prospectus that we may authorize to be provided to you) related to the series of preferred stock being offered, as well as the complete certificate of designation that contains the terms of the applicable series of preferred stock.

Debt securities. We may issue debt securities from time to time, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt. The senior debt securities will rank equally with any other unsecured and unsubordinated debt. The subordinated debt securities will be subordinate and junior in right of payment, to the extent and in the manner described in the instrument governing the debt, to all of our senior indebtedness. Convertible debt securities will be convertible into our common stock or preferred stock. Conversion may be mandatory or at the holder's option and would be at prescribed conversion rates.

The debt securities will be issued under one or more documents called indentures, which are contracts between us and a national banking association or other eligible party, as trustee. In this prospectus, we have summarized certain general features of the debt securities. We urge you, however, to read the applicable prospectus supplement (and any free writing prospectus that we may authorize to be provided to you) related to the series of debt securities being offered, as well as the complete indentures that contain the terms of the debt securities. A form of indenture has been filed as an exhibit to the registration statement of which this prospectus is a part, and supplemental indentures and forms of debt securities containing the terms of the debt securities being offered will be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from reports that we file with the SEC.

Warrants. We may issue warrants for the purchase of common stock, preferred stock and/or debt securities in one or more series. We may issue warrants independently or together with common stock, preferred stock and/or debt securities, and the warrants may be attached to or separate from these securities. In this prospectus, we have summarized certain general features of the warrants. We urge you, however, to read the applicable prospectus supplement (and any free writing prospectus that we may authorize to be provided to you) related to the particular series of warrants being offered, as well as the complete warrant agreements and warrant certificates that contain the terms of the warrants. Forms of the warrant agreements and forms of warrant certificates containing the terms of the warrants to be offered will be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from reports that we file with the SEC.

We will evidence each series of warrants by warrant certificates that we will issue. Warrants may be issued under an applicable warrant agreement that we enter into with a warrant agent. We will indicate the name and address of the warrant agent, if applicable, in the prospectus supplement relating to the particular series of warrants being offered.

RISK FACTORS

Investing in our securities involves a high degree of risk. You should carefully review the risks and uncertainties described under the heading "Risk Factors" contained in any applicable prospectus supplement and any related free writing prospectus, and under similar headings in our Annual Report on Form 10-K for the year ended December 31, 2017, as updated by our annual, quarterly and other reports and documents that are incorporated by reference into this prospectus, before deciding whether to purchase any of the securities being registered pursuant to the registration statement of which this prospectus is a part. Each of the risk factors could adversely affect our business, operating results and financial condition, as well as adversely affect the value of an investment in our securities, and the occurrence of any of these risks might cause you to lose all or part of your investment.

The prospectus supplement applicable to each type or series of securities we offer may contain a discussion of risks applicable to the particular types of securities that we are offering under that prospectus supplement. Prior to making a decision about investing in our securities, you should carefully consider the specific factors discussed under the caption "Risk Factors" in the applicable prospectus supplement, together with all of the other information contained in the prospectus supplement or appearing or incorporated by reference in this prospectus. These risks could materially affect our business, results of operations or financial condition and cause the value of our securities to decline. You could lose all or part of your investment. Additional risks not presently known to us or that we currently believe are immaterial may also significantly impair our business operations. Please also read carefully the section above titled "Special Note Regarding Forward-Looking Statements."

RATIO OF EARNINGS TO FIXED CHARGES

Any time debt securities are offered pursuant to this prospectus, we will provide a table setting forth our ratio of earnings to fixed charges on a historical basis in the applicable prospectus supplement, if required.

USE OF PROCEEDS

We will retain broad discretion over the use of the net proceeds from the sale of the securities offered hereby. Except as described in any prospectus supplement or any related free writing prospectus that we may authorize to be provided to you, we currently intend to use the estimated net proceeds from the sale of the securities offered hereby for general corporate purposes, which may include capital expenditures, working capital and general and administrative expenses. We may also use a portion of the net proceeds to acquire or invest in businesses that are complementary to our own, although we have no current plans, commitments or agreements with respect to any acquisitions as of the date of this prospectus. We have not yet determined the amount of net proceeds to be used specifically for any of the foregoing purposes. We will set forth in the applicable prospectus supplement or free writing prospectus our intended use for the net proceeds received from the sale of any securities sold pursuant to the prospectus supplement or free writing prospectus.

DESCRIPTION OF CAPITAL STOCK

The description below of our capital stock and provisions of our amended and restated certificate of incorporation and amended and restated bylaws are summaries and are qualified by reference to the amended and restated certificate of incorporation, the amended and restated bylaws, and the applicable provisions of Delaware law.

General

Our amended and restated certificate of incorporation authorizes us to issue up to 100,000,000 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, the rights and preferences of which may be established from time to time by Leap's board of directors.

As of February 28, 2018, there were 12,354,014 shares of common stock outstanding, no shares of preferred stock outstanding, and warrants for the purchase of up to 3,012,610 shares of our common stock outstanding.

Common Stock

Voting rights. Each holder of our common stock is entitled to one vote for each share on all matters submitted to a vote of the stockholders, including the election of directors. Our stockholders do not have cumulative voting rights in the election of directors. An election of directors by our stockholders shall be determined by a plurality of votes cast by the stockholders entitled to vote on the election.

Dividends. Subject to preferences that may be applicable to any then outstanding 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.

Liquidation. In the event of our liquidation, dissolution or winding up, holders of our common stock will be entitled to share ratably in proportion to the number of shares held by them 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 common stock have no preemptive, conversion or subscription rights and there are no redemption or sinking fund provisions applicable to the common stock. The rights, preferences and privileges of the holders of common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of preferred stock that we may designate 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 in this offering, if any, will be, fully paid and nonassessable.

Preferred Stock

Under our amended and restated certificate of incorporation, our board of directors has the authority, without further action by the stockholders (unless such stockholder action is required by applicable law or the rules of any stock exchange or market on which our securities are then traded), to designate and issue up to 10,000,000 shares of preferred stock in one or more series, to establish from time to time the number of shares to be included in each such series, to fix the rights, preferences and privileges of the shares of each wholly unissued series and any qualifications, limitations or restrictions thereon and to increase or decrease the number of shares of any such series, but not below the number of shares of such series then outstanding.

We will fix the designations, voting powers, preferences and rights of the preferred stock of each series, as well as the qualifications, limitations or restrictions thereof, in a certificate of designation relating to that series. We will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of any certificate of designation that describes the terms of the series of preferred stock we are offering before the issuance of that series of preferred stock. This description will include:

- the title and stated value;
- the number of shares we are offering;

- the liquidation preference per share;
- the purchase price;
- the dividend rate, period and payment date and method of calculation for dividends;
- whether dividends will be cumulative or non-cumulative and, if cumulative, the date from which dividends will accumulate;
- the procedures for any auction and remarketing, if any;
- the provisions for a sinking fund, if any;
- the provisions for redemption or repurchase, if applicable, and any restrictions on our ability to exercise those redemption and repurchase rights;
- any listing of the preferred stock on any securities exchange or market;
- whether the preferred stock will be convertible into our common stock, and, if applicable, the conversion price, or how it will be calculated, and the conversion period;
- whether the preferred stock will be exchangeable into debt securities, and, if applicable, the exchange price, or how it will be calculated, and the exchange period;
- voting rights, if any, of the preferred stock;
- preemptive rights, if any;
- restrictions on transfer, sale or other assignment, if any;
- whether interests in the preferred stock will be represented by depositary shares;
- a discussion of any material U.S. federal income tax considerations applicable to the preferred stock;
- the relative ranking and preferences of the preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs;
- any limitations on the issuance of any class or series of preferred stock ranking senior to or on a parity with the series of preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs; and
- any other specific terms, preferences, rights or limitations of, or restrictions on, the preferred stock.

Delaware law provides that the holders of preferred stock will have the right to vote separately as a class (or, in some cases, as a series) on an amendment to our certificate of incorporation if the amendment would change the par value or, unless the certificate of incorporation provided otherwise, the number of authorized shares of the class or change the powers, preferences or special rights of the class or series so as to adversely affect the class or series, as the case may be. This right is in addition to any voting rights that may be provided for in the applicable certificate of designation.

Our board of directors may authorize the issuance of preferred stock with voting or conversion rights that could adversely affect the voting power or other rights of the holders of the common stock. The issuance of preferred stock, while providing flexibility in connection with possible acquisitions and other corporate purposes, could, among other things, have the effect of delaying, deferring or preventing a change in our control that may otherwise benefit holders of our common stock and may adversely affect the market price of the common stock and the voting and other rights of the holders of common stock.

Warrants

As of February 28, 2018, we had 3,012,610 outstanding warrants to purchase shares of our capital stock.

On November 14, 2017, the Company entered into purchase agreements (the "Purchase Agreements") with certain purchasers (the "Purchasers"). Each of the Purchase Agreement was on terms and conditions substantially similar to each other Purchase Agreement and pursuant to such Purchase Agreements, the Company, in a private placement, agreed to issue and sell to the Purchasers an aggregate of 2,958,094 shares of unregistered common stock, at a price per share of \$6.085, each share issued with a warrant to purchase one share of common stock at an exercise price of \$6.085. HealthCare Ventures IX, L.P. and Eli Lilly and Company, each a more than 5% direct holder of the Company's common stock, 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. Our stockholders approved the inclusion of a full ratchet anti-dilution feature as a term of the warrants. As a result, 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 or amend the terms of any outstanding security of the Company, 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.

Registration Rights

We agreed to provide certain registration rights to certain holders of our common stock pursuant to the terms of the Registration Rights Agreement filed as Exhibit 4.1 to this registration statement.

Anti-Takeover Effects of Provisions of Our Amended and Restated Certificate of Incorporation and Bylaws

Our amended and restated certificate of incorporation and amended and restated bylaws contain certain provisions that are intended to enhance the likelihood of continuity and stability in the composition of the board of directors and which may have the effect of delaying, deferring or preventing a future takeover or change in control of the Company unless such takeover or change in control is approved by the board of directors. These provisions include:

No Cumulative Voting. Under Delaware law, the right to vote cumulatively does not exist unless the certificate of incorporation specifically authorizes cumulative voting. Our amended and restated certificate of incorporation does not grant shareholders the right to vote cumulatively.

Blank Check Preferred Stock. We believe that the availability of the preferred stock under the amended and restated certificate of incorporation provides the board of directors with flexibility in addressing corporate issues that may arise. Having these authorized shares available for issuance allows the Company to issue shares of preferred stock without the expense and delay of a special shareholders' meeting. The authorized shares of preferred stock will be available for issuance without further action by the Company's shareholders, with the exception of any actions required by applicable law or the rules of any stock exchange on which Leap's securities may be listed. The board of directors has the power, subject to applicable law, to issue classes or series of preferred stock that could, depending on the terms of the class or series, impede the completion of a merger, tender offer or other takeover attempt.

Advance Notice Procedure.

Our amended and restated bylaws provide an advance notice procedure for shareholders to nominate director candidates for election or to bring business before an annual meeting of shareholders, including proposed nominations of persons for election to the board of directors.

Our amended and restated bylaws provide that as to the notice of shareholder proposals of business to be brought at the annual meeting of shareholders, notice must be delivered to Leap's secretary (i) not less than 90 days nor more than 120 days prior to the first anniversary of the preceding year's annual meeting or (ii) if the date of the annual meeting is advanced by more than 30 days or delayed by more than 60 days from the first anniversary of the preceding year's annual meeting, not more than 120 days nor less than 90 days prior to the date of such annual meeting or, if less than 90 days' notice is given of such annual meeting, the 10th day following the day on which public announcement of the date of such meeting is first made by us. In addition, any proposed business other than the nomination of persons for election to the Company's board of directors must constitute a proper matter for shareholder action.

In the case of nominations for election at an annual meeting, notice must be delivered to Leap's secretary (i) not less than 90 days nor more than 120 days prior to the first anniversary of the preceding year's annual meeting or (ii) if the date of the annual meeting is advanced by more than 30 days or delayed by more than 60 days from the first anniversary of the preceding year's annual meeting, not more than 120 days nor less than 90 days prior to the date of such annual meeting or, if less than 90 days' notice is given of such annual meeting, the 10th day following the day on which public announcement of the date of such meeting is first made by Leap. In the case of nominations for election at a special meeting of shareholders called for the election of directors, a shareholder may nominate candidates by delivering notice to Leap's secretary by not later than the close of business on the seventh day following the date on which notice of such meeting is first given to the shareholders. In addition, each such shareholder's notice must include certain information regarding the shareholder and the director nominee as set forth in our amended and restated bylaws.

Staggered Board. Our amended and restated certificate of incorporation provides that our board of directors is divided into three classes of directors, with the classes as nearly equal in number as possible. At each annual meeting of the stockholders, a class of directors will be elected for a three-year term to succeed the directors of the same class whose terms are then expiring. As a result, approximately one-third of our directors will be elected each year. The initial term of office of the directors of Class I expires at the annual meeting of Leap's stockholders in 2018; the initial term of office of the directors of Class II shall expires at the annual meeting of Leap's stockholders to be held in 2019; and the initial term of office of the directors of Class III shall expires at the annual meeting of Leap's stockholders to be held in 2020.

- Our Class I directors are James Cavanaugh and John Littlechild;
- Our Class II directors are William Li and Thomas Dietz; and
- Our Class III directors are Nissim Mashiach, Joseph Loscalzo and Christopher Mirabelli.

Our amended and restated certificate of incorporation and amended and restated bylaws provide that the number of our directors shall be fixed from time to time by a resolution of the majority of our board of directors. Any additional directorships resulting from an increase in the number of directors will be distributed among the three classes so that, as nearly as possible, each class shall consist of one third of the board of directors.

The division of our board of directors into three classes with staggered three-year terms may delay or prevent stockholder efforts to effect a change of our management or a change in control.

Action by Written Consent; Special Meetings of Stockholders. Our amended and restated certificate of incorporation provides that stockholder action can be taken only at an annual or special meeting of stockholders and cannot be taken by written consent in lieu of a meeting. Our amended and restated certificate of incorporation and amended and restated bylaws also provides that, except as otherwise required by law, special meetings of the stockholders can be called only by or at the direction of the board of directors pursuant to a resolution adopted by a majority of the total number of directors, by the chairperson of the Board, chief executive officer or president (in the absence of a chief executive officer). Except as provided above, stockholders are not permitted to call a special meeting or to require the board of directors to call a special meeting.

Removal of Directors. Our amended and restated certificate of incorporation provides that that our directors may be removed only for cause by the affirmative vote of at least two-thirds of the voting power of our outstanding shares of capital stock, voting together as a single class and entitled to vote in the election of directors. This requirement of a supermajority vote to remove directors could enable a minority of our stockholders to prevent a change in the composition of our board.

Exclusive Forum. Our amended and restated certificate of incorporation provides that, subject to limited exceptions, the state or federal courts located in the State of Delaware will be the sole and exclusive forum for (i) any derivative action or proceeding brought on our behalf, (ii) 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, (iii) any action asserting a claim against us arising pursuant to any provision of the Delaware General Corporation Law, our amended and restated certificate of incorporation or our amended and restated bylaws, or (iv) any other action asserting a claim against us that is governed by the internal affairs doctrine. Any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock shall be deemed to have notice of and to have consented to the provisions of our amended and restated certificate of incorporation described above. Although we believe these provisions benefit us by providing increased consistency in the application of Delaware law for the specified types of actions and proceedings, the provisions may have the effect of discouraging lawsuits against our directors and officers. 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 one or more actions or proceedings described above, a court could find the choice of forum provisions contained in our amended and restated certificate of incorporation to be inapplicable or unenforceable.

Section 203 Of Delaware Law

We are subject to Section 203 of Delaware Law, or Section 203. In general, Section 203 prohibits a publicly-held Delaware corporation from engaging in a "business combination" with an "interested stockholder" for a three-year period following the time that this stockholder becomes an interested stockholder, unless the business combination is approved in a prescribed manner. A "business combination" includes, among other things, 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 did own within three years prior to the determination of interested stockholder status, 15% or more of the corporation's voting stock. Under Section 203, a business combination between a corporation and an interested stockholder is prohibited unless it satisfies one of the following conditions: before the stockholder became interested, the board of directors approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder; upon consummation of the transaction which 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, shares owned by persons who are directors and also officers, and employee stock plans, in some instances; or at or after the time the stockholder

became interested, the business combination was approved by the board of directors of the corporation and authorized at an annual or special meeting of the stockholders by the affirmative vote of at least two-thirds of the outstanding voting stock which is not owned by the interested stockholder. A Delaware corporation may "opt out" of these provisions with an express provision in its original certificate of incorporation or an express provision in its certificate of incorporation or bylaws resulting from a stockholders' amendment approved by at least a majority of the outstanding voting shares. We have not opted out of these provisions. As a result, mergers or other takeover or change in control attempts of us may be discouraged or prevented.

Transfer Agent And Registrar

The transfer agent and registrar for our common stock is Continental Stock Transfer & Trust Company. Its address is 1 State Street, 30th Floor, New York, NY 10004-1561. The transfer agent for any series of preferred stock, debt securities or warrants that we may offer under this prospectus will be named and described in the prospectus supplement for that series.

NASDAQ Global Market Listing

Our common stock is listed on The NASDAQ Global Market under the symbol "LPTX."

DESCRIPTION OF DEBT SECURITIES

We may issue debt securities from time to time, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt. While the terms we have summarized below will apply generally to any debt securities that we may offer under this prospectus, we will describe the particular terms of any debt securities that we may offer in more detail in the applicable prospectus supplement. The terms of any debt securities offered under a prospectus supplement may differ from the terms described below. Unless the context requires otherwise, whenever we refer to the indenture, we also are referring to any supplemental indentures that specify the terms of a particular series of debt securities.

We will issue the debt securities under the indenture that we will enter into with the trustee named in the indenture. The indenture will be qualified under the Trust Indenture Act of 1939, as amended, or the Trust Indenture Act. We will file the form of indenture as an exhibit to the registration statement of which this prospectus is a part, and supplemental indentures and forms of debt securities containing the terms of the debt securities being offered will be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from reports that we file with the SEC.

The following summary of material provisions of the debt securities and the indenture is subject to, and qualified in its entirety by reference to, all of the provisions of the indenture applicable to a particular series of debt securities. We urge you to read the applicable prospectus supplements and any related free writing prospectuses related to the debt securities that we may offer under this prospectus, as well as the complete indenture that contains the terms of the debt securities.

General

The indenture will not limit the amount of debt securities that we may issue. It provides that we may issue debt securities up to the principal amount that we may authorize and may be in any currency or currency unit that we may designate. Except for the limitations on consolidation, merger and sale of all or substantially all of our assets contained in the indenture, the terms of the indenture do not contain any covenants or other provisions designed to give holders of any debt securities protection against changes in our operations, financial condition or transactions involving us.

We may issue the debt securities issued under the indenture as "discount securities," which means they may be sold at a discount below their stated principal amount. These debt securities, as well as other debt securities that are not issued at a discount, may be issued with "original issue discount," or OID, for U.S. federal income tax purposes because of interest payment and other characteristics or terms of the debt securities. Material U.S. federal income tax considerations applicable to debt securities issued with OID will be described in more detail in any applicable prospectus supplement.

We will describe in the applicable prospectus supplement the terms of the series of debt securities being offered, including:

- the title of the series of debt securities;
- any limit upon the aggregate principal amount that may be issued;
- the maturity date or dates;
- the form of the debt securities of the series;
- whether or not the debt securities will be secured or unsecured, and the terms of any secured debt;
- whether the debt securities rank as senior debt, senior subordinated debt, subordinated debt or any combination thereof, and the terms of any subordination;
- if the price (expressed as a percentage of the aggregate principal amount thereof) at which such debt securities will be issued is a price other than the principal amount thereof, the portion of the principal amount thereof payable upon declaration of acceleration of the maturity thereof, or if applicable, the portion of the principal amount of such debt securities that is convertible into another security or the method by which any such portion shall be determined;
- the interest rate or rates, which may be fixed or variable, or the method for determining the rate and the date interest will begin to accrue, the dates interest will be payable and the regular record dates for interest payment dates or the method for determining such dates;
- our right, if any, to defer payment of interest and the maximum length of any such deferral period;
- if applicable, the date or dates after which, or the period or periods during which, and the price or prices at which, we may, at our option, redeem the series of debt securities pursuant to any optional or provisional redemption provisions and the terms of those redemption provisions;
- the date or dates, if any, on which, and the price or prices at which we are obligated, pursuant to any mandatory sinking fund or analogous fund provisions or otherwise, to redeem, or at the holder's option to purchase, the series of debt securities and the currency or currency unit in which the debt securities are payable;
- the denominations in which we will issue the series of debt securities, if other than denominations of \$1,000 and any integral multiple thereof;
- any and all terms, if applicable, relating to any auction or remarketing of the debt securities of that series and any security for our obligations with respect to such debt securities and any other terms which may be advisable in connection with the marketing of debt securities of that series;
- whether the debt securities of the series shall be issued in whole or in part in the form of a global security or securities; the terms and conditions, if any, upon which such global security or securities may be exchanged in whole or in part for other individual securities; and the depositary for such global security or securities;

- if applicable, the provisions relating to conversion or exchange of any debt securities of the series and the terms and conditions upon which such debt securities will be so convertible or exchangeable, including the conversion or exchange price, as applicable, or how it will be calculated and may be adjusted, any mandatory or optional (at our option or the holders' option) conversion or exchange features, the applicable conversion or exchange period and the manner of settlement for any conversion or exchange;
- additions to or changes in the covenants applicable to the particular debt securities being issued, including, among others, the consolidation, merger or sale covenant;
- additions to or changes in the events of default with respect to the securities and any change in the right of the trustee or the holders to declare the principal, premium, if any, and interest, if any, with respect to such securities to be due and payable;
- additions to or changes in or deletions of the provisions relating to covenant defeasance and legal defeasance;
- additions to or changes in the provisions relating to satisfaction and discharge of the indenture;
- additions to or changes in the provisions relating to the modification of the indenture both with and without the consent of holders of debt securities issued under the indenture;
- the currency of payment of debt securities if other than U.S. dollars and the manner of determining the equivalent amount in U.S. dollars;
- whether interest will be payable in cash or additional debt securities at our or the holders' option and the terms and conditions upon which the election may be made;
- the terms and conditions, if any, upon which we will pay amounts in addition to the stated interest, premium, if any, and principal amounts of the debt securities of the series to any holder that is not a "United States person" for federal tax purposes;
- any restrictions on transfer, sale or assignment of the debt securities of the series; and
- any other specific terms, preferences, rights or limitations of, or restrictions on, the debt securities, any other additions or changes in the provisions of the indenture, and any terms that may be required by us or advisable under applicable laws or regulations.

Conversion Or Exchange Rights

We will set forth in the applicable prospectus supplement the terms on which a series of debt securities may be convertible into or exchangeable for our common stock or our other securities. We will include provisions as to settlement upon conversion or exchange and whether conversion or exchange is mandatory, at the option of the holder or at our option. We may include provisions pursuant to which the number of shares of our common stock or our other securities that the holders of the series of debt securities receive would be subject to adjustment.

Consolidation, Merger Or Sale

Unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, the indenture will not contain any covenant that restricts our ability to merge or consolidate, or sell, convey, transfer or otherwise dispose of our assets as an entirety or substantially as an entirety. However, any successor to or acquirer of such assets (other than a subsidiary of ours) must assume all of our obligations under the indenture or the debt securities, as appropriate.

Events Of Default Under The Indenture

Unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, the following are events of default under the indenture with respect to any series of debt securities that we may issue:

- if we fail to pay any installment of interest on any series of debt securities, as and when the same shall become due and payable, and such default continues for a period of 90 days; provided, however, that a valid extension of an interest payment period by us in accordance with the terms of any indenture supplemental thereto shall not constitute a default in the payment of interest for this purpose;
- if we fail to pay the principal of, or premium, if any, on any series of debt securities as and when the same shall become due and payable whether at maturity, upon redemption, by declaration or otherwise, or in any payment required by any sinking or analogous fund established with respect to such series; provided, however, that a valid extension of the maturity of such debt securities in accordance with the terms of any indenture supplemental thereto shall not constitute a default in the payment of principal or premium, if any;
- if we fail to observe or perform any other covenant or agreement contained in the debt securities or the indenture, other than a covenant specifically relating to another series of debt securities, and our failure continues for 90 days after we receive written notice of such failure, requiring the same to be remedied and stating that such is a notice of default thereunder, from the trustee or holders of at least 25% in aggregate principal amount of the outstanding debt securities of the applicable series; and
- if specified events of bankruptcy, insolvency or reorganization occur.

If an event of default with respect to debt securities of any series occurs and is continuing, other than an event of default specified in the last bullet point above, the trustee or the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series, by notice to us in writing, and to the trustee if notice is given by such holders, may declare the unpaid principal of, premium, if any, and accrued interest, if any, of such series of debt securities due and payable immediately. If an event of default specified in the last bullet point above occurs with respect to us, the principal amount of and accrued interest, if any, of each issue of debt securities then outstanding shall be due and payable without any notice or other action on the part of the trustee or any holder.

The holders of a majority in principal amount of the outstanding debt securities of an affected series may waive any default or event of default with respect to the series and its consequences, except defaults or events of default regarding payment of principal, premium, if any, or interest, unless we have cured the default or event of default in accordance with the indenture. Any waiver shall cure the default or event of default.

Subject to the terms of the indenture, if an event of default under an indenture shall occur and be continuing, the trustee will be under no obligation to exercise any of its rights or powers under such indenture at the request or direction of any of the holders of the applicable series of debt securities, unless such holders have offered the trustee reasonable indemnity. The holders of a majority in principal amount of the outstanding debt securities of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the trustee, or exercising any trust or power conferred on the trustee, with respect to the debt securities of that series, provided that:

- the direction so given by the holder is not in conflict with any law or the applicable indenture; and

- subject to its duties under the Trust Indenture Act, the trustee need not take any action that might involve it in personal liability or might be unduly prejudicial to the holders not involved in the proceeding.

A holder of the debt securities of any series will have the right to institute a proceeding under the indenture or to appoint a receiver or trustee, or to seek other remedies only if:

- the holder has given written notice to the trustee of a continuing event of default with respect to that series;
- the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series have made written request;
- such holders have offered to the trustee indemnity satisfactory to it against the costs, expenses and liabilities to be incurred by the trustee in compliance with the request; and
- the trustee does not institute the proceeding, and does not receive from the holders of a majority in aggregate principal amount of the outstanding debt securities of that series other conflicting directions within 90 days after the notice, request and offer.

These limitations do not apply to a suit instituted by a holder of debt securities if we default in the payment of the principal, premium, if any, or interest on, the debt securities.

We will periodically file statements with the trustee regarding our compliance with specified covenants in the indenture.

Modification Of Indenture; Waiver

Unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, we and the trustee may change an indenture without the consent of any holders with respect to specific matters:

- to cure any ambiguity, defect or inconsistency in the indenture or in the debt securities of any series;
- to comply with the provisions described above under "Description of Debt Securities—Consolidation, Merger or Sale;"
- to provide for uncertificated debt securities in addition to or in place of certificated debt securities;
- to add to our covenants, restrictions, conditions or provisions such new covenants, restrictions, conditions or provisions for the benefit of the holders of all or any series of debt securities, to make the occurrence, or the occurrence and the continuance, of a default in any such additional covenants, restrictions, conditions or provisions an event of default or to surrender any right or power conferred upon us in the indenture;
- to add to, delete from or revise the conditions, limitations, and restrictions on the authorized amount, terms, or purposes of issue, authentication and delivery of debt securities, as set forth in the indenture;
- to make any change that does not adversely affect the interests of any holder of debt securities of any series in any material respect;
- to provide for the issuance of and establish the form and terms and conditions of the debt securities of any series as provided above under "Description of Debt Securities—General" to establish the form of any certifications required to be furnished pursuant to the terms of the

indenture or any series of debt securities, or to add to the rights of the holders of any series of debt securities;

- to evidence and provide for the acceptance of appointment under any indenture by a successor trustee; or
- to comply with any requirements of the SEC in connection with the qualification of any indenture under the Trust Indenture Act.

In addition, under the indenture, the rights of holders of a series of debt securities may be changed by us and the trustee with the written consent of the holders of at least a majority in aggregate principal amount of the outstanding debt securities of each series that is affected. However, unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, we and the trustee may make the following changes only with the consent of each holder of any outstanding debt securities affected:

- extending the fixed maturity of any debt securities of any series;
- reducing the principal amount, reducing the rate of or extending the time of payment of interest, or reducing any premium payable upon the redemption of any series of any debt securities; or
- reducing the percentage of debt securities, the holders of which are required to consent to any amendment, supplement, modification or waiver.

Discharge

The indenture will provide that we can elect to be discharged from our obligations with respect to one or more series of debt securities, except for specified obligations, including obligations to:

- provide for payment;
- register the transfer or exchange of debt securities of the series;
- replace stolen, lost or mutilated debt securities of the series;
- pay principal of and premium and interest on any debt securities of the series;
- maintain paying agencies;
- hold monies for payment in trust;
- recover excess money held by the trustee;
- compensate and indemnify the trustee; and
- appoint any successor trustee.

In order to exercise our rights to be discharged, we must deposit with the trustee money or government obligations sufficient to pay all the principal of, any premium, if any, and interest on, the debt securities of the series on the dates payments are due.

Form, Exchange And Transfer

We will issue the debt securities of each series only in fully registered form without coupons and, unless we provide otherwise in the applicable prospectus supplement, in denominations of \$1,000 and any integral multiple thereof. The indenture will provide that we may issue debt securities of a series in temporary or permanent global form and as book-entry securities that will be deposited with, or on behalf of, The Depository Trust Company, or DTC, or another depository named by us and identified in the applicable prospectus supplement with respect to that series. To the extent the debt securities of

a series are issued in global form and as book-entry, a description of terms relating to any book-entry securities will be set forth in the applicable prospectus supplement.

At the option of the holder, subject to the terms of the indenture and the limitations applicable to global securities described in the applicable prospectus supplement, the holder of the debt securities of any series can exchange the debt securities for other debt securities of the same series, in any authorized denomination and of like tenor and aggregate principal amount.

Subject to the terms of the indenture and the limitations applicable to global securities set forth in the applicable prospectus supplement, holders of the debt securities may present the debt securities for exchange or for registration of transfer, duly endorsed or with the form of transfer endorsed thereon duly executed if so required by us or the security registrar, at the office of the security registrar or at the office of any transfer agent designated by us for this purpose. Unless otherwise provided in the debt securities that the holder presents for transfer or exchange, we will impose no service charge for any registration of transfer or exchange, but we may require payment of any taxes or other governmental charges.

We will name in the applicable prospectus supplement the security registrar, and any transfer agent in addition to the security registrar, that we initially designate for any debt securities. We may at any time designate additional transfer agents or rescind the designation of any transfer agent or approve a change in the office through which any transfer agent acts, except that we will be required to maintain a transfer agent in each place of payment for the debt securities of each series.

If we elect to redeem the debt securities of any series, we will not be required to:

- issue, register the transfer of, or exchange any debt securities of that series during a period beginning at the opening of business 15 days before the day of mailing of a notice of redemption of any debt securities that may be selected for redemption and ending at the close of business on the day of the mailing; or
- register the transfer of or exchange any debt securities so selected for redemption, in whole or in part, except the unredeemed portion of any debt securities we are redeeming in part.

Information Concerning The Trustee

The trustee, other than during the occurrence and continuance of an event of default under an indenture, undertakes to perform only those duties as are specifically set forth in the applicable indenture. Upon an event of default under an indenture, the trustee must use the same degree of care as a prudent person would exercise or use in the conduct of his or her own affairs. Subject to this provision, the trustee is under no obligation to exercise any of the powers given it by the indenture at the request of any holder of debt securities unless it is offered reasonable security and indemnity against the costs, expenses and liabilities that it might incur.

Payment And Paying Agents

Unless we otherwise indicate in the applicable prospectus supplement, we will make payment of the interest on any debt securities on any interest payment date to the person in whose name the debt securities, or one or more predecessor securities, are registered at the close of business on the regular record date for the interest.

We will pay principal of and any premium and interest on the debt securities of a particular series at the office of the paying agents designated by us, except that unless we otherwise indicate in the applicable prospectus supplement, we will make interest payments by check that we will mail to the holder or by wire transfer to certain holders. Unless we otherwise indicate in the applicable prospectus supplement, we will designate the corporate trust office of the trustee as our sole paying agent for

payments with respect to debt securities of each series. We will name in the applicable prospectus supplement any other paying agents that we initially designate for the debt securities of a particular series. We will maintain a paying agent in each place of payment for the debt securities of a particular series.

All money we pay to a paying agent or the trustee for the payment of the principal of or any premium or interest on any debt securities that remains unclaimed at the end of two years after such principal, premium or interest has become due and payable will be repaid to us, and the holder of the debt security thereafter may look only to us for payment thereof.

Governing Law

The indenture and the debt securities, and any claim, controversy or dispute arising under or related to the indenture or the debt securities, will be governed by and construed in accordance with the laws of the State of New York, except to the extent that the Trust Indenture Act of 1939 is applicable.

DESCRIPTION OF WARRANTS

The following description, together with the additional information we may include in any applicable prospectus supplements and free writing prospectuses, summarizes the material terms and provisions of the warrants that we may offer under this prospectus, which may consist of warrants to purchase common stock, preferred stock or debt securities and may be issued in one or more series. Warrants may be issued independently or together with common stock, preferred stock or debt securities offered by any prospectus supplement, and may be attached to or separate from those securities. While the terms we have summarized below will apply generally to any warrants that we may offer under this prospectus, we will describe the particular terms of any series of warrants that we may offer in more detail in the applicable prospectus supplement and any applicable free writing prospectus. The terms of any warrants offered under a prospectus supplement may differ from the terms described below. However, no prospectus supplement will fundamentally change the terms that are set forth in this prospectus or offer a security that is not registered and described in this prospectus at the time of its effectiveness.

We will file as exhibits to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of warrant agreement, if any, including a form of warrant certificate, that describes the terms of the particular series of warrants we are offering. The following summaries of material provisions of the warrants and the warrant agreements are subject to, and qualified in their entirety by reference to, all the provisions of the warrant agreement and warrant certificate applicable to the particular series of warrants that we may offer under this prospectus. We urge you to read the applicable prospectus supplements related to the particular series of warrants that we may offer under this prospectus, as well as any related free writing prospectuses, and the complete warrant agreements and warrant certificates that contain the terms of the warrants.

General

We will describe in the applicable prospectus supplement the terms relating to a series of warrants being offered, including:

- the title of such securities;
- the offering price or prices and aggregate number of warrants offered;
- the currency or currencies for which the warrants may be purchased;

- if applicable, the designation and terms of the securities with which the warrants are issued and the number of warrants issued with each such security or each principal amount of such security;
- if applicable, the date on and after which the warrants and the related securities will be separately transferable;
- if applicable, the minimum or maximum amount of such warrants which may be exercised at any one time;
- in the case of warrants to purchase debt securities, the principal amount of debt securities purchasable upon exercise of one warrant and the price at which, and currency in which, this principal amount of debt securities may be purchased upon such exercise;
- in the case of warrants to purchase common stock or preferred stock, the number of shares of common stock or preferred stock, as the case may be, purchasable upon the exercise of one warrant and the price at which, and the currency in which, these shares may be purchased upon such exercise;
- the effect of any merger, consolidation, sale or other disposition of our business on the warrant agreements and the warrants;
- the terms of any rights to redeem or call the warrants;
- the terms of any rights to force the exercise of the warrants;
- any provisions for changes to or adjustments in the exercise price or number of securities issuable upon exercise of the warrants;
- the dates on which the right to exercise the warrants will commence and expire;
- the manner in which the warrant agreements and warrants may be modified;
- a discussion of any material or special United States federal income tax consequences of holding or exercising the warrants;
- the terms of the securities issuable upon exercise of the warrants; and
- any other specific terms, preferences, rights or limitations of or restrictions on the warrants.

Before exercising their warrants, holders of warrants will not have any of the rights of holders of the securities purchasable upon such exercise, including:

- in the case of warrants to purchase debt securities, the right to receive payments of principal of, or premium, if any, or interest on, the debt securities purchasable upon exercise or to enforce covenants in the applicable indenture; or
- in the case of warrants to purchase common stock or preferred stock, the right to receive dividends, if any, or, payments upon our liquidation, dissolution or winding up or to exercise voting rights, if any.

Exercise Of Warrants

Each warrant will entitle the holder to purchase the securities that we specify in the applicable prospectus supplement at the exercise price that we describe in the applicable prospectus supplement. Unless we otherwise specify in the applicable prospectus supplement, holders of the warrants may exercise the warrants at any time up to the specified time on the expiration date that we set forth in the applicable prospectus supplement. After the close of business on the expiration date, unexercised warrants will become void.

Unless we otherwise specify in the applicable prospectus supplement, holders of the warrants may exercise the warrants by delivering the warrant certificate representing the warrants to be exercised together with specified information, and paying the required amount to the warrant agent in immediately available funds, as provided in the applicable prospectus supplement. We will set forth on the reverse side of the warrant certificate and in the applicable prospectus supplement the information that the holder of the warrant will be required to deliver to the warrant agent in connection with the exercise of the warrant.

Upon receipt of the required payment and the warrant certificate properly completed and duly executed at the corporate trust office of the warrant agent or any other office indicated in the applicable prospectus supplement, we will issue and deliver the securities purchasable upon such exercise. If fewer than all of the warrants represented by the warrant certificate are exercised, then we will issue a new warrant certificate for the remaining amount of warrants. If we so indicate in the applicable prospectus supplement, holders of the warrants may surrender securities as all or part of the exercise price for warrants.

Governing Law

Unless we provide otherwise in the applicable prospectus supplement, the warrants and warrant agreements, and any claim, controversy or dispute arising under or related to the warrants or warrant agreements, will be governed by and construed in accordance with the laws of the State of New York.

Enforceability Of Rights By Holders Of Warrants

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

LEGAL OWNERSHIP OF SECURITIES

We can issue securities in registered form or in the form of one or more global securities. We describe global securities in greater detail below. We refer to those persons who have securities registered in their own names on the books that we or any applicable trustee or depository maintain for this purpose as the "holders" of those securities. These persons are the legal holders of the securities. We refer to those persons who, indirectly through others, own beneficial interests in securities that are not registered in their own names, as "indirect holders" of those securities. As we discuss below, indirect holders are not legal holders, and investors in securities issued in book-entry form or in street name will be indirect holders.

Book-Entry Holders

We may issue securities in book-entry form only, as we will specify in the applicable prospectus supplement. This means securities may be represented by one or more global securities registered in the name of a financial institution that holds them as depository on behalf of other financial institutions that participate in the depository's book-entry system. These participating institutions, which are referred to as participants, in turn, hold beneficial interests in the securities on behalf of themselves or their customers.

Only the person in whose name a security is registered is recognized as the holder of that security. Global securities will be registered in the name of the depositary or its participants. Consequently, for global securities, we will recognize only the depositary as the holder of the securities, and we will make all payments on the securities to the depositary. The depositary passes along the payments it receives to its participants, which in turn pass the payments along to their customers who are the beneficial owners. The depositary and its participants do so under agreements they have made with one another or with their customers; they are not obligated to do so under the terms of the securities.

As a result, investors in a global security will not own securities directly. Instead, they will own beneficial interests in a global security, through a bank, broker or other financial institution that participates in the depositary's book-entry system or holds an interest through a participant. As long as the securities are issued in global form, investors will be indirect holders, and not legal holders, of the securities.

Street Name Holders

A global security may be terminated in certain situations as described under "—Special Situations When A Global Security Will Be Terminated," or issue securities that are not issued in global form. In these cases, investors may choose to hold their securities in their own names or in "street name." Securities held by an investor in street name would be registered in the name of a bank, broker or other financial institution that the investor chooses, and the investor would hold only a beneficial interest in those securities through an account he or she maintains at that institution.

For securities held in street name, we or any applicable trustee or depositary will recognize only the intermediary banks, brokers and other financial institutions in whose names the securities are registered as the holders of those securities, and we or any such trustee or depositary will make all payments on those securities to them. These institutions pass along the payments they receive to their customers who are the beneficial owners, but only because they agree to do so in their customer agreements or because they are legally required to do so. Investors who hold securities in street name will be indirect holders, not holders, of those securities.

Legal Holders

Our obligations, as well as the obligations of any applicable trustee or third party employed by us or a trustee, run only to the legal holders of the securities. We do not have obligations to investors who hold beneficial interests in global securities, in street name or by any other indirect means. This will be the case whether an investor chooses to be an indirect holder of a security or has no choice because we are issuing the securities only in global form.

For example, once we make a payment or give a notice to the legal holder, we have no further responsibility for the payment or notice even if that legal holder is required, under agreements with its participants or customers or by law, to pass it along to the indirect holders but does not do so. Similarly, we may want to obtain the approval of the holders to amend an indenture, to relieve us of the consequences of a default or of our obligation to comply with a particular provision of an indenture, or for other purposes. In such an event, we would seek approval only from the legal holders, and not the indirect holders, of the securities. Whether and how the legal holders contact the indirect holders is up to the legal holders.

Special Considerations For Indirect Holders

If you hold securities through a bank, broker or other financial institution, either in book-entry form because the securities are represented by one or more global securities or in street name, you should check with your own institution to find out:

- how it handles securities payments and notices;
- whether it imposes fees or charges;
- how it would handle a request for the holders' consent, if ever required;
- whether and how you can instruct it to send you securities registered in your own name so you can be a holder, if that is permitted in the future;
- how it would exercise rights under the securities if there were a default or other event triggering the need for holders to act to protect their interests; and
- if the securities are in book-entry form, how the depositary's rules and procedures will affect these matters.

Global Securities

A global security is a security that represents one or any other number of individual securities held by a depositary. Generally, all securities represented by the same global securities will have the same terms.

Each security issued in book-entry form will be represented by a global security that we issue to, deposit with and register in the name of a financial institution or its nominee that we select. The financial institution that we select for this purpose is called the depositary. Unless we specify otherwise in the applicable prospectus supplement, The Depository Trust Company, New York, New York, known as DTC, will be the depositary for all securities issued in book-entry form.

A global security may not be transferred to or registered in the name of anyone other than the depositary, its nominee or a successor depositary, unless special termination situations arise. We describe those situations below under "—Special Situations When A Global Security Will Be Terminated." As a result of these arrangements, the depositary, or its nominee, will be the sole registered owner and legal holder of all securities represented by a global security, and investors will be permitted to own only beneficial interests in a global security. Beneficial interests must be held by means of an account with a broker, bank or other financial institution that in turn has an account with the depositary or with another institution that does. Thus, an investor whose security is represented by a global security will not be a legal holder of the security, but only an indirect holder of a beneficial interest in the global security.

If the prospectus supplement for a particular security indicates that the security will be issued as a global security, then the security will be represented by a global security at all times unless and until the global security is terminated. If termination occurs, we may issue the securities through another book-entry clearing system or decide that the securities may no longer be held through any book-entry clearing system.

Special Considerations For Global Securities

As an indirect holder, an investor's rights relating to a global security will be governed by the account rules of the investor's financial institution and of the depositary, as well as general laws relating to securities transfers. We do not recognize an indirect holder as a holder of securities and instead deal only with the depositary that holds the global security.

If securities are issued only as global securities, an investor should be aware of the following:

- an investor cannot cause the securities to be registered in his or her name, and cannot obtain non-global certificates for his or her interest in the securities, except in the special situations we describe below;
- an investor will be an indirect holder and must look to his or her own bank or broker for payments on the securities and protection of his or her legal rights relating to the securities, as we describe above;
- an investor may not be able to sell interests in the securities to some insurance companies and to other institutions that are required by law to own their securities in non-book-entry form;
- an investor may not be able to pledge his or her interest in the global security in circumstances where certificates representing the securities must be delivered to the lender or other beneficiary of the pledge in order for the pledge to be effective;
- the depositary's policies, which may change from time to time, will govern payments, transfers, exchanges and other matters relating to an investor's interest in the global security;
- we and any applicable trustee have no responsibility for any aspect of the depositary's actions or for its records of ownership interests in the global security, nor will we or any applicable trustee supervise the depositary in any way;
- the depositary may, and we understand that DTC will, require that those who purchase and sell interests in the global security within its book-entry system use immediately available funds, and your broker or bank may require you to do so as well; and
- financial institutions that participate in the depositary's book-entry system, and through which an investor holds its interest in the global security, may also have their own policies affecting payments, notices and other matters relating to the securities.

There may be more than one financial intermediary in the chain of ownership for an investor. We do not monitor and are not responsible for the actions of any of those intermediaries.

Special Situations When A Global Security Will Be Terminated

In a few special situations described below, a global security will terminate and interests in it will be exchanged for physical certificates representing those interests. After that exchange, the choice of whether to hold securities directly or in street name will be up to the investor. Investors must consult their own banks or brokers to find out how to have their interests in securities transferred to their own names, so that they will be direct holders. We have described the rights of holders and street name investors above.

Unless we provide otherwise in the applicable prospectus supplement, a global security will terminate when the following special situations occur:

- if the depositary notifies us that it is unwilling, unable or no longer qualified to continue as depositary for that global security and we do not appoint another institution to act as depositary within 90 days;
- if we notify any applicable trustee that we wish to terminate that global security; or
- if an event of default has occurred with regard to securities represented by that global security and has not been cured or waived.

The applicable prospectus supplement may also list additional situations for terminating a global security that would apply only to the particular series of securities covered by the applicable prospectus

supplement. When a global security terminates, the depository, and neither we nor any applicable trustee, is responsible for deciding the names of the institutions that will be the initial direct holders.

PLAN OF DISTRIBUTION

We may sell the securities covered hereby from time to time pursuant to underwritten public offerings, direct sales to the public, negotiated transactions, block trades or a combination of these methods. A distribution of the securities offered by this prospectus may also be effected through the issuance of derivative securities, including without limitation, warrants and subscriptions. We may sell the securities to or through underwriters or dealers, through agents, or directly to one or more purchasers. We may distribute securities from time to time in one or more transactions:

- at a fixed price or prices, which may be changed;
- at market prices prevailing at the time of sale;
- at prices related to such prevailing market prices;
- at varying prices determined at the time of sale; or
- at negotiated prices.

We may also sell equity securities covered by this registration statement in an "at the market offering" as defined in Rule 415 under the Securities Act. Such offering may be made into an existing trading market for such securities in transactions at other than a fixed price, either:

- on or through the facilities of The Nasdaq Global Market or any other securities exchange or quotation or trading service on which such securities may be listed, quoted or traded at the time of sale; and/or
- to or through a market maker otherwise than on The Nasdaq Global Market or such other securities exchanges or quotation or trading services.

Such at-the-market offerings, if any, may be conducted by financial institutions acting as principal or agent.

A prospectus supplement or supplements (and any related free writing prospectus that we may authorize to be provided to you) will describe the terms of the offering of the securities, including, to the extent applicable:

- the name or names of any underwriters, dealers or agents participating in the offering, if any;
- the purchase price of the securities sold by us to any underwriter or dealer and the net proceeds we expect to receive from the offering;
- any option, under which underwriters may purchase additional securities from us;
- any agency fees or underwriting discounts or commissions and other items constituting agents' or underwriters' compensation;
- any public offering price;
- any discounts or concessions allowed or reallocated or paid to dealers; and
- any securities exchange or market on which the securities may be listed.

Only underwriters named in the prospectus supplement are underwriters of the securities offered by the prospectus supplement.

If underwriters are used in the sale, they will acquire the securities for their own account and may resell the securities from time to time in one or more transactions at a fixed public offering price or at

varying prices determined at the time of sale. The obligations of the underwriters to purchase the securities will be subject to the conditions set forth in the applicable underwriting agreement. We may offer the securities to the public through underwriting syndicates represented by managing underwriters or by underwriters without a syndicate. Subject to certain conditions, the underwriters will be obligated to purchase all of the securities offered by the prospectus supplement, other than securities covered by any option to purchase additional securities. Any public offering price and any discounts, commissions or concessions allowed or reallocated or paid to dealers may change from time to time. We may use underwriters with whom we have a material relationship. We will describe in the prospectus supplement, naming the underwriter, the nature of any such relationship.

We may sell securities directly or through agents we designate from time to time. We will name any agent involved in the offering and sale of securities, and we will describe any commissions and other compensation we will pay the agent in the prospectus supplement. Unless the prospectus supplement states otherwise, our agent will act on a best-efforts basis for the period of its appointment.

We may authorize agents or underwriters to solicit offers by certain types of institutional investors to purchase securities from us at the public offering price set forth in the prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on a specified date in the future. We will describe the conditions to these contracts and the commissions we must pay for solicitation of these contracts in the prospectus supplement.

We may provide agents and underwriters with indemnification against civil liabilities related to this offering, including liabilities under the Securities Act, or contribution with respect to payments that the agents or underwriters may make with respect to these liabilities. Agents and underwriters may engage in transactions with, or perform services for, us in the ordinary course of business.

All securities we may offer, other than common stock, will be new issues of securities with no established trading market. Any agents or underwriters may make a market in these securities, but will not be obligated to do so and may discontinue any market making at any time without notice. We cannot guarantee the liquidity of the trading markets for any securities. There is currently no market for any of the offered securities, other than our common stock which is listed on the The Nasdaq Global Market. We have no current plans for listing of the debt securities, preferred stock, warrants or subscription rights on any securities exchange or quotation system; any such listing with respect to any particular debt securities, preferred stock, warrants or subscription rights will be described in the applicable prospectus supplement or other offering materials, as the case may be.

Any underwriter may engage in over-allotment, stabilizing transactions, short covering transactions and penalty bids in accordance with Regulation M under the Exchange Act. Over-allotment involves sales in excess of the offering size, which create a short position. Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum. Short covering transactions involve purchases of the securities in the open market after the distribution is completed to cover short positions. Penalty bids permit the underwriters to reclaim a selling concession from a dealer when the securities originally sold by the dealer are purchased in a stabilizing or covering transaction to cover short positions. Those activities may cause the price of the securities to be higher than it would otherwise be. If commenced, the underwriters may discontinue any of the activities at any time. These transactions may be effected on any exchange or over-the-counter market or otherwise.

Any agents and underwriters who are qualified market makers on The Nasdaq Global Market may engage in passive market making transactions in the securities on The Nasdaq Global Market in accordance with Rule 103 of Regulation M, during the business day prior to the pricing of the offering, before the commencement of offers or sales of the securities. Passive market makers must comply with applicable volume and price limitations and must be identified as passive market makers. In general, a passive market maker must display its bid at a price not in excess of the highest independent bid for

such security; if all independent bids are lowered below the passive market maker's bid, however, the passive market maker's bid must then be lowered when certain purchase limits are exceeded. Passive market making may stabilize the market price of the securities at a level above that which might otherwise prevail in the open market and, if commenced, may be discontinued at any time.

In compliance with guidelines of the Financial Industry Regulatory Authority, Inc., or FINRA, the maximum compensation to be received by any FINRA member or independent broker dealer may not exceed 8% of the aggregate amount of the securities offered pursuant to this prospectus and any applicable prospectus supplement.

LEGAL MATTERS

Unless otherwise indicated in the applicable prospectus supplement, certain legal matters in connection with the offering and the validity of the securities offered by this prospectus, and any supplement thereto, will be passed upon for us by Morgan, Lewis & Bockius LLP. Additional legal matters may be passed upon for us or any underwriters, dealers or agents, by counsel that we will name in the applicable prospectus supplement.

EXPERTS

The consolidated balance sheets of Leap Therapeutics, Inc. and Subsidiaries as of December 31, 2017 and 2016, and the related consolidated statements of operations, comprehensive loss, redeemable convertible and convertible preferred stock and stockholders' equity (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.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and special reports, proxy statements and other information with the Securities and Exchange Commission (the "SEC"). You can inspect and copy these reports, proxy statements and other information at the SEC's Public Reference Room at 100 F Street, N.E., Washington, D. C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the Public Reference Room. The SEC also maintains a web site that contains reports, proxy and information statements and other information regarding issuers, such as Leap Therapeutics, Inc. at www.sec.gov.

We maintain a website at www.leaptx.com. Information contained in or accessible through our website does not constitute a part of this prospectus.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

This prospectus "incorporates by reference" certain information that we have filed with the SEC under the Exchange Act. This means we are disclosing important information to you by referring you to those documents. We incorporate by reference the documents listed below and any future filings made by us with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act until the offering is terminated:

- our Annual Report on Form 10-K for the fiscal year ended December 31, 2017 filed with the SEC on February 23, 2018;
- our Current Report on Form 8-K filed with the SEC on January 17, 2018; 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.

You should rely only on the information incorporated by reference or provided in this prospectus. We have authorized no one 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 on the front of this document. All documents that we file subsequently pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act and prior to the termination or completion of the offering (including all such documents that we may file with the SEC after the date of the initial registration statement and prior to the effectiveness of the registration statement) will be deemed to be incorporated in this prospectus by reference and will be a part of this prospectus from the date of the filing of the document. Any statement contained in a document incorporated or deemed to be incorporated by reference in this prospectus will be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained in this prospectus or in any other subsequently filed document which also is or is deemed to be incorporated by reference in this prospectus modifies or supersedes that statement. Any statement that is modified or superseded will not constitute a part of this prospectus, except as modified or superseded.

We will provide, upon written or oral request, without charge to you, including any beneficial owner to whom this prospectus is delivered, a copy of any or all of the documents incorporated herein by reference other than the exhibits to those documents, unless the exhibits are specifically incorporated by reference into the information that this prospectus incorporates. You should direct a request for copies to us at Attention: Secretary, 47 Thorndike Street, Suite B1-1, Cambridge, Massachusetts 02141 or you may call us at (617) 714-0360.

DISCLOSURE OF COMMISSION'S POSITION ON INDEMNIFICATION FOR SECURITIES ACT LIABILITY

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers or persons controlling the Company pursuant to the foregoing provisions, we have been informed 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.



LEAP THERAPEUTICS, INC.

**Shares of Common Stock
Having an Aggregate Offering Price of Up to
\$30,000,000**

PROSPECTUS SUPPLEMENT

RAYMOND JAMES

September 7, 2018
