

PROSPECTUS SUPPLEMENT

(To Prospectus dated March 16, 2018 and the Prospectus Supplement dated September 7, 2018)



LEAP THERAPEUTICS, INC.

**Shares of Common Stock
Having an Aggregate Offering Price of Up to
\$13,596,653**

This Prospectus Supplement amends and supplements the information in our prospectus, dated March 16, 2018 (File No. 333-223419), or the Prospectus, and the shelf registration statement on Form S-3 of which the Prospectus is a part, or the Registration Statement, and our Prospectus Supplement, dated September 7, 2018, or the September 2018 Prospectus Supplement, filed under the Registration Statement for the offer and sale of shares of common stock having an aggregate offering price of up to \$30,000,000 under the Distribution Agreement (as defined below). This Prospectus Supplement should be read in conjunction with the Prospectus and the September 2018 Prospectus Supplement, and is qualified by reference thereto, except to the extent that the information herein amends or supersedes the information contained in the Prospectus or the September 2018 Prospectus Supplement. This Prospectus Supplement is not complete without, and may only be delivered or utilized in connection with, the Prospectus and the September 2018 Prospectus Supplement, and any future amendments or supplements thereto.

On April 1, 2019, the date we filed our Annual Report on Form 10-K for the fiscal year ended December 31, 2018, our Prospectus became subject to the offering limits in General Instruction I.B.6 of Form S-3. At that time and as of the date of this Prospectus Supplement, the aggregate market value of our common stock held by non-affiliates pursuant to General Instruction I.B.6 of Form S-3 is \$40,789,960, which was calculated based on 17,544,069 shares of our common stock outstanding held by non-affiliates and a price of \$2.325 per share, the closing price of our common stock on March 18, 2019, which is the highest closing sale price of our common stock on Nasdaq Global Market within the prior 60 days. As of the date of this Prospectus Supplement, we have not sold any securities pursuant to General Instruction I.B.6 of Form S-3 during the 12 calendar months prior to, and including, the date of this Prospectus Supplement. Pursuant to General Instruction I.B.6 of Form S-3, in no event will we sell securities in public primary offerings on Form S-3 with a value exceeding more than one-third of our public float (as defined by General Instruction I.B.6) in any 12 calendar month period so long as our public float remains below \$75.0 million.

We filed the September 2018 Prospectus Supplement on September 7, 2018 to register the offer and sale of shares of common stock having an aggregate offering price of up to \$30,000,000 pursuant to the terms of a distribution agreement, or the Distribution Agreement, with Raymond James & Associates, Inc. Through the date hereof, we have not sold any shares of our common stock through Raymond James & Associates, Inc. under the Distribution Agreement. We are filing this Prospectus Supplement to amend the September 2018 Prospectus Supplement to update the maximum amount of shares that we are eligible to sell under General Instruction I.B.6. As a result of these limitations and the current public float of our common stock, and in accordance with the terms of the Distribution Agreement, we may offer and sell additional shares of our common stock having an aggregate offering price of up to \$13,596,653 from time to time through Raymond James & Associates, Inc. If our public float increases such that we may sell additional amounts under the Distribution Agreement and the Registration Statement and Prospectus of which this Prospectus Supplement and the September 2018 Prospectus Supplement are a part, we will file another prospectus supplement prior to making sales of such additional amounts.

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 March 29, 2019, the last reported sale price of our common stock on the Nasdaq Global Market was \$1.87 per share.

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 6 of the accompanying Prospectus and page S-7 of the accompanying September 2018 Prospectus Supplement, and the documents incorporate by reference into this Prospectus Supplement.

RAYMOND JAMES

The date of this prospectus supplement is April 1, 2019.
