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Filed Pursuant to Rule 424b(5)
Registration No. 333-232488

PROSPECTUS

Up to \$24,000,000



Common Stock

We have entered into a sales agreement, or Sales Agreement, with Cowen and Company, LLC, or Cowen, relating to shares of our common stock, par value \$0.01 per share, offered by this prospectus. In accordance with the terms of the Sales Agreement, we may offer and sell shares of our common stock having an aggregate offering price of up to \$50.0 million from time to time through or to Cowen, acting as sales agent or principal. This prospectus is offering of up to an aggregate of \$24.0 million in shares of our common stock. We will be required to file another prospectus or a prospectus supplement in the event we want to offer more than \$24.0 million in shares of our common stock in accordance with the Sales Agreement. Sales of the shares of common stock, if any, may be made on The Nasdaq Global Select Market at market prices and such other sales as agreed upon by us and Cowen, as the case may be.

As of June 28, 2019, the aggregate market value of our outstanding ordinary shares held by non-affiliates was approximately \$74.2 million, based on 33,664,070 shares of common stock outstanding, of which 18,690,917 shares of common stock were held by non-affiliates, and a per share price of \$3.97 based on the closing sale price of our common stock on May 9, 2019. We have not sold any securities pursuant to General Instruction I.B.6. of Form S-3 during the prior 12 calendar month period that ends on, and includes, the date of this prospectus.

Our common stock is listed on The Nasdaq Global Select Market under the symbol "APTIX." On June 28, 2019, the last reported sale price of our common stock, as reported on The Nasdaq Global Select Market, was \$3.34 per share.

Sales of our common stock, if any, under this prospectus will be made in sales deemed to be "at the market offerings" as defined in Rule 415 promulgated under the Securities Act of 1933, as amended, or the Securities Act. Cowen is not required to sell any specific number or dollar amount of securities, but will act as our sales agent using commercially reasonable efforts to sell on our behalf all of the shares of common stock requested to be sold by us, consistent with their normal trading and sales practices, on mutually agreed terms between Cowen and us. There is no arrangement for funds to be received in any escrow, trust or similar arrangement.

Cowen will be entitled to compensation at a fixed commission rate of 3.0% of the gross sales price per common stock sold under the Sales Agreement. See "Plan of Distribution" beginning on page S-22 for additional information regarding the compensation to be paid to Cowen. In connection with the sale of the common stock on our behalf, Cowen will be deemed to be an "underwriter" within the meaning of the Securities Act and the compensation of Cowen will be deemed to be underwriting commissions or discounts. We have also agreed to provide indemnification and contribution to Cowen with respect to certain liabilities, including liabilities under the Securities Act or the Securities Exchange Act of 1934, as amended, or the Exchange Act.

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

Investing in our common stock involves a high degree of risk. You should review carefully the risks and uncertainties referenced under the heading "Risk Factors" on page S-8 of this prospectus and in the 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.

Cowen

July 8, 2019

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We are responsible for the information contained and incorporated by reference in this prospectus and in any related free writing prospectus we prepare or authorize. We have not authorized anyone to give you any other information, and we take no responsibility for any other information that others may give you. If you are in a jurisdiction where offers to sell, or solicitations of offers to purchase, the securities offered by this documentation are unlawful, or if you are a person to whom it is unlawful to direct these types of activities, then the offer presented in this document does not extend to you. The information contained in this document speaks only as of the date of this document, unless the information specifically indicates that another date applies. Our business, financial condition, results of operations, and prospects may have changed since those dates.

ABOUT THIS PROSPECTUS

This prospectus relates to the offering of our common stock. Before buying any of the common stock that we are offering, we urge you to carefully read this prospectus, together with the information incorporated by reference as described under the headings "Where You Can Find More Information" and "Incorporation by Reference" in this prospectus, and any free writing prospectus or prospectus supplement that we have authorized for use in connection with this offering. These documents contain important information that you should consider when making your investment decision.

This prospectus describes the terms of this offering of common stock and also adds to and updates information contained in the documents incorporated by reference into this prospectus. If the information contained in this prospectus differs or varies from the information contained in any document incorporated by reference herein that was filed with the SEC before the date of this prospectus, you should rely on the information set forth in this prospectus. If any statement in one of these documents is inconsistent with a statement in another document having a later date (for example, a subsequently filed document deemed incorporated by reference in this prospectus), the statement in the document having the later date modifies or supersedes the earlier statement. Any statement so modified or superseded will not be deemed, except as so modified or superseded, to constitute a part of this prospectus.

You should rely only on the information contained or incorporated by reference in this prospectus. We have not, and the sales agent has not, authorized anyone to provide you with information that is in addition to or different from that contained or incorporated by reference in this prospectus or contained in any permitted free writing prospectuses we have authorized for use in connection with this offering. We and the sales agent take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may provide.

The information contained in this prospectus and the documents incorporated by reference herein is accurate only as of their respective dates, regardless of the time of delivery of any such document or the time of any sale of our common stock. Our business, financial condition, results of operations and prospects may have changed since those dates. It is important for you to read and consider all information contained or incorporated by reference in this prospectus in making your investment decision. You should read this prospectus, as well as the documents incorporated by reference herein, the additional information described under the section titled "Where You Can Find More Information" and "Incorporation of Certain Documents by Reference" in this prospectus and any free writing prospectus that we have authorized for use in connection with this offering, before investing in our common stock.

We further note that 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 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 affairs.

We use various trademarks and trade names in our business, including without limitation our corporate name and logo. All other trademarks or trade names referred to in this prospectus are the

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property of their respective owners. Solely for convenience, the trademarks and trade names in this prospectus may be referred to without the ® and ™ symbols, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto. This prospectus and the documents incorporated by reference herein also contain estimates, projections and other information concerning our industry, our business, and the markets for certain diseases, including data regarding the estimated size of those markets, and the incidence and prevalence of certain medical conditions. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances reflected in this information. Unless otherwise expressly stated, we obtained this industry, business, market and other data from reports, research surveys, studies and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data and similar sources.

We are offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where such offers and sales are permitted. The distribution of this prospectus and the offering of our common stock in certain jurisdictions may be restricted by law. Persons outside the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the offering of our common stock and the distribution of this prospectus outside the United States. This prospectus does not constitute, and may not be used in connection with, an offer to sell, or a solicitation of an offer to buy, any securities offered by this prospectus by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

As used in this prospectus, unless the context otherwise requires, references to the "company," "we," "us," and "our" refer to Aptinyx Inc.

PROSPECTUS SUMMARY

This summary highlights selected information about us and this offering and does not contain all of the information that you should consider before investing in our securities. Before investing in our common stock, you should carefully read the information contained and incorporated by reference in this prospectus, including the sections titled "Risk Factors" and the financial statements and accompanying notes.

Company Overview

We are a clinical-stage biopharmaceutical company focused on the discovery, development, and commercialization of novel, proprietary, synthetic small molecules for the treatment of brain and nervous system disorders. We focus our efforts on targeting and modulating N-methyl-D-aspartate receptors, or NMDARs, which are vital to normal and effective function of the brain and nervous system. We believe leveraging the therapeutic advantages of the differentiated modulatory mechanism of our compounds will drive a paradigm shift in the treatment of disorders of the brain and nervous system.

We are advancing a pipeline of distinct product candidates derived from our NMDAR modulator discovery platform. We currently have three wholly owned, clinical-stage product candidates in development for various central nervous system, or CNS, disorders. Each of our development-stage assets has unique pharmacological properties, including with regard to binding, NMDAR subtype selectivity, potency, and activity in preclinical behavioral models. These unique properties inform the identification of the indication(s) for which each product candidate is developed.

Our product candidate, NYX-2925, is a novel, oral NMDAR modulator that has demonstrated effects on biomarkers of pain processing as well as alleviation of pain and other symptoms in clinical studies. NYX-2925 is currently in Phase 2 clinical development as a treatment for chronic pain. In June 2019, we reported positive results from a 23-patient, sequential design, Phase 2 neuroimaging biomarker study in which NYX-2925 was shown to have statistically significant effects on pain-processing biomarkers and patient-reported measures of pain and other fibromyalgia symptoms. Additionally, in January 2019, we completed a Phase 2 study in patients with painful diabetic peripheral neuropathy, or DPN. In the total study population (N=300), the primary endpoint was not met; however, a post-hoc sub-group analysis revealed robust analgesic activity in a large subset of patients—patients with advanced DPN (i.e. \geq 4 years since DPN diagnosis, N=127)—in which the preponderance of patients' pain is most likely to be centrally mediated and addressed by the central mechanism of NYX-2925. Together, the effects on neuroimaging biomarkers and the robust analgesic effects observed in these two studies strongly support the continued development of NYX-2925 for centralized chronic pain conditions. We expect to initiate one Phase 2 study in patients with advanced DPN and another Phase 2 study in patients with fibromyalgia in the second half of 2019.

Our product candidate, NYX-783, is a novel, oral small-molecule NMDAR modulator currently in Phase 2 clinical development for the treatment of post-traumatic stress disorder, or PTSD. NYX-783 has demonstrated robust activity in preclinical models of psychiatric disorders as well as models of fear conditioning and extinction learning. Based on these preclinical data and its mechanism of action, we believe NYX-783 has the potential to address the underlying learning and memory dysfunction that underpins PTSD. We are currently evaluating NYX-783 in a 144-subject Phase 2 clinical study to assess its safety and efficacy in patients with PTSD. We expect to report data from this study in 2020.

Our product candidate, NYX-458, is a novel, oral small molecule NMDA_R modulator in clinical development for the treatment of cognitive impairment associated with Parkinson's disease. NYX-458 has exhibited marked effects on cognitive performance across a number of preclinical models. Recently we reported the results from studies in non-human primates in which NYX-458 was shown to improve cognitive deficits akin to those seen in patients with Parkinson's disease. In the studies, NYX-458 demonstrated rapid, robust, and long-lasting effects on attention, working memory, and cognitive flexibility, did not have any negative effects on motor symptoms, and did not interfere with the anti-parkinsonian effects of levodopa, the standard of care. We also recently reported positive results from a Phase 1 study in healthy human volunteers in which NYX-458 was safe and well tolerated with no serious adverse events. NYX-458 demonstrated a linear and predictable pharmacokinetic profile and was found to readily achieve CNS concentrations in line with concentrations of preclinically efficacious dose levels. In the second half of 2019, we expect to initiate a Phase 2 study in patients with Parkinson's disease mild cognitive impairment.

Company Information

We were incorporated under the laws of the state of Delaware in June 2015. Our principal executive offices are located at 909 Davis Street, Suite 600, Evanston, Illinois 60201. Our telephone number is (847) 871-0377, and our website is located at www.aptinyx.com. We do not incorporate the information on or accessible through our website into this prospectus, and you should not consider any information on, or that can be accessed through, our website as part of this prospectus. You should not rely on any such information in making your decision to purchase our common stock. Our common stock trades on The Nasdaq Global Select Market under the symbol "APT_X".

On June 25, 2018, we closed our initial public offering, or IPO, in which we issued and sold 6,399,999 shares of common stock at a public offering price of \$16.00 per share, and issued an additional 959,999 shares of common stock at a price of \$16.00 per share pursuant to the exercise of the underwriters' over-allotment option. All of the shares of common stock issued and sold in our IPO were registered under the Securities Act pursuant to a registration statement on Form S-1 (Registration No. 333-225150), which was declared effective by the SEC on June 20, 2018. J.P. Morgan, Cowen, SVB Leerink, and BMO Capital Markets acted as joint book-running managers for the offering. The aggregate gross proceeds to us from our IPO, inclusive of the over-allotment exercise, were \$117.8 million.

Upon the closing of the IPO, all of the Company's outstanding shares of convertible preferred stock automatically converted into 20,306,497 shares of common stock at the applicable conversion ratio. On June 7, 2018, we effected a one-for-27.58621 reverse stock split of our issued and outstanding shares of common stock and a proportional adjustment to the existing conversion ratios for each series of our redeemable convertible preferred stock.

Implications of Being an Emerging Growth Company

As a company with less than \$1.07 billion in revenue during our most recently completed fiscal year, we qualify as an "emerging growth company" as defined in Section 2(a) of the Securities Act of 1933, as amended, or the Securities Act, as modified by the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. As an emerging growth company, we may take advantage of specified reduced disclosure and other requirements that are otherwise applicable, in general, to public companies that are not emerging growth companies. These provisions include:

- reduced disclosure about our executive compensation arrangements;

- exemption from the non-binding stockholder advisory votes on executive compensation or golden parachute arrangements;
- exemption from the auditor attestation requirement in the assessment of our internal control over financial reporting; and
- reduced disclosure of financial information in this prospectus, such as being permitted to include only two years of audited financial information and two years of selected financial information in addition to any required unaudited interim financial statements, with correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure.

We may take advantage of these exemptions for up to five years or such earlier time that we are no longer an emerging growth company. We would cease to be an emerging growth company if we have more than \$1.07 billion in annual revenues as of the end of a fiscal year, the date we qualify as a "large accelerated filer" with at least \$700 million of equity securities held by non-affiliates or if we issue more than \$1.0 billion of non-convertible debt over a three-year-period. We may choose to take advantage of some, but not all, of the available exemptions.

The JOBS Act permits an emerging growth company to take advantage of an extended transition period to comply with new or revised accounting standards applicable to public companies. We have elected to avail ourselves of the extended transition period for complying with new or revised financial accounting standards. As a result of the accounting standards election, we will not be subject to the same implementation timing for new or revised accounting standards as other public companies that are not emerging growth companies which may make comparison of our financials to those of other public companies more difficult. Additionally, because we have taken advantage of certain reduced reporting requirements, the information contained herein may be different from the information you receive from other public companies in which you hold stock.

THE OFFERING

Common stock offered by us:	Shares of our common stock having an aggregate offering price of up to \$24.0 million.
Common stock to be outstanding immediately after this offering:	Up to 40,747,839 shares (as more fully described in the notes following this table), assuming sales of 7,185,628 shares of our common stock in this offering at an offering price of \$3.34 per share, which was the last reported sale price of our common stock on The Nasdaq Global Select Market on June 28, 2019. The actual number of shares issued will vary depending on how many shares of our common stock we choose to sell and the prices at which such sales occur.
Manner of offering:	"At the market offering" that may be made from time to time on The Nasdaq Global Select Market or other existing trading market for our common stock through or to Cowen and Company, LLC as sales agent or principal. See "Plan of Distribution" on page S-22 of this prospectus.
Use of proceeds:	Our management will retain broad discretion regarding the allocation and use of the net proceeds. We currently intend to use the net proceeds from this offering primarily to fund activities relating to the advancement of our product candidates, and for other general corporate purposes, including, but not limited to, research and development costs, potential strategic acquisitions of complementary businesses, services or technologies, expansion of our technology infrastructure and capabilities, working capital and capital expenditures. See "Use of Proceeds" on page S-17 of this prospectus.
Risk factors:	Investing in our common stock involves significant risks. See "Risk Factors" on page S-8 of this prospectus and under similar headings in the documents incorporated by reference into this prospectus for a discussion of the factors you should carefully consider before deciding to invest in our common stock.
The Nasdaq Global Select Market symbol:	"APTX"

All information in this prospectus related to the number of shares of our common stock to be outstanding immediately after this offering is based on 33,562,211 shares of our common stock outstanding as of March 31, 2019. The number of shares outstanding as of March 31, 2019 as used throughout this prospectus, unless otherwise indicated, excludes:

- 4,610,232 shares of common stock issuable upon the exercise of stock options outstanding as of March 31, 2019 at a weighted-average exercise price of \$9.74 per share;

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- 4,484,078 shares of common stock reserved for future issuance under our 2018 Stock Option and Incentive Plan; and
- 314,697 shares of common stock reserved for the future issuance under our 2018 Employee Stock Purchase Plan.

Unless otherwise stated, all information contained in this prospectus assumes no exercise of stock options after March 31, 2019 and reflects an assumed public offering price of \$3.34, which was the last reported sale price of our common stock on The Nasdaq Global Select Market on June 28, 2019.

RISK FACTORS

Investing in our common stock involves a high degree of risk. Before making an investment decision, you should carefully consider the risks described below and in our most recent Annual Report on Form 10-K and any subsequent Quarterly Reports on Form 10-Q or Current Reports on Form 8-K, as well as any amendments thereto reflected in subsequent filings with the SEC, each of which are incorporated by reference in this prospectus, and all of the other information in this prospectus, including our financial statements and related notes incorporated by reference herein. If any of these risks is realized, our business, financial condition, results of operations and prospects could be materially and adversely affected. In that event, the trading price of our common stock could decline and you could lose part or all of your investment. Additional risks and uncertainties that are not yet identified or that we currently believe to be immaterial may also materially harm our business, financial condition, results of operations and prospects and could result in a complete loss of your investment.

Risks Related to This Offering and Our Common Stock

An active trading market for our common stock may not be sustained, and you may not be able to resell your shares at or above the public offering price.

Prior to our IPO in June 2018, there had been no public market for our common stock. Although our common stock is listed on The Nasdaq Global Select Market, an active trading market for our shares may never be sustained. If an active market for our common stock is not sustained, it may be difficult for our stockholders to sell their shares without depressing the market price for the shares or sell their shares at or above the prices at which they acquired their shares or sell their shares at the time they would like to sell. Any inactive trading market for our common stock may also impair our ability to raise capital to continue to fund our operations by selling shares and may impair our ability to acquire other companies or technologies by using our shares as consideration.

Market volatility may affect our stock price and the value of your investment.

The market price for our common stock has been, and is likely to continue to be, volatile for the foreseeable future, in part because our common stock had not been previously traded publicly prior to our IPO. For example, in the year ended December 31, 2018, our common stock's sales price on The Nasdaq Global Select Market ranged from a low of \$16.15 to a high of \$31.85, and on January 16, 2019, following announcement of our Phase 2 painful DPN study results, the closing price of a share of our common stock was \$5.98. The market price of our common stock may fluctuate significantly in response to a number of factors, most of which we cannot control, including, among others:

- plans for, progress of, or results from preclinical studies and clinical studies of our product candidates;
- the failure of the FDA to approve our product candidates;
- announcements of new products, technologies, commercial relationships, acquisitions, or other events by us or our competitors;
- the success or failure of other therapies for disorders of the brain and nervous system;
- regulatory or legal developments in the United States and other countries;
- failure of our product candidates, if approved, to achieve commercial success;
- fluctuations in stock market prices and trading volumes of similar companies;
- general economic, industry, and market conditions and overall fluctuations in U.S. equity markets;

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- variations in our quarterly operating results or those of companies that are perceived to be similar to us;
- changes in our financial guidance or securities analysts' estimates of our financial performance;
- changes in accounting principles;
- our ability to raise additional capital and the terms on which we can raise it;
- sales of large blocks of our common stock, including sales by our executive officers, directors, and significant stockholders;
- additions or departures of key personnel;
- discussion of us or our stock price by the press and by online investor communities;
- market conditions in the pharmaceutical and biotechnology sectors; and
- other risks and uncertainties described in these risk factors.

In recent years, the stock market in general, and the market for pharmaceutical and biotechnology companies in particular, has experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to changes in the operating performance of the companies whose stock is experiencing those price and volume fluctuations. Broad market and industry factors may seriously affect the market price of our common stock, regardless of our actual operating performance. Following periods of such volatility in the market price of a company's securities, securities class action litigation has often been brought against that company. Because of the potential volatility of our stock price, we may become the target of securities litigation in the future. Securities litigation could result in substantial costs and divert management's attention and resources from our business.

We have broad discretion in the use of the net proceeds from this offering and may invest or spend the proceeds in ways with which you do not agree and in ways that may not yield a return on your investment.

Our management will have broad discretion in the application of the net proceeds from this offering, including for any of the purposes described in the section titled "Use of Proceeds," as well as our existing cash, and you will be relying on the judgment of our management regarding such application. You will not have the opportunity, as part of your investment decision, to assess whether the proceeds are being used effectively. Our management might not apply the net proceeds or our existing cash in ways that ultimately increase the value of your investment. If we do not invest or apply the net proceeds from this offering or our existing cash in ways that enhance stockholder value, we may fail to achieve expected results, which could cause our stock price to decline. Pending their use, we may invest the net proceeds from this offering in short-term U.S. Treasury securities with insignificant rates of return. These investments may not yield a favorable return to our stockholders.

If you purchase our common stock in this offering, you may incur substantial dilution in the net tangible book value of your shares.

Since the price per share of our common stock being offered will be determined based on market prices from time to time, it may be higher than the net tangible book value per share of our common stock at the time of sale. Investors participating in this offering may suffer substantial dilution in the net tangible book value of the common stock you purchase in this offering. In addition, we have a significant number of stock options outstanding. The exercise of any of these outstanding options may result in further dilution. As a result of the dilution to investors purchasing shares in this offering, investors may receive significantly less than the purchase price paid in this offering, if anything, in the event of our liquidation. Further, because we expect we will need to raise additional

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capital to fund our future activities, we may in the future sell substantial amounts of common stock or securities convertible into or exchangeable for common stock.

Future sales and issuances of our common stock or rights to purchase common stock, including pursuant to our equity incentive plans, could result in additional dilution of the percentage ownership of our stockholders and could cause our stock price to fall.

Additional capital will be needed in the future to continue our planned operations. To the extent we raise additional capital by issuing equity securities, our stockholders may experience substantial dilution. We may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell common stock, convertible securities or other equity securities in more than one transaction, investors may be materially diluted by subsequent sales. These sales may also result in material dilution to our existing stockholders, and new investors could gain rights superior to our existing stockholders.

In addition, sales of a substantial number of shares of our outstanding common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares of common stock intend to sell shares, could reduce the market price of our common stock. Persons who were our stockholders prior to our IPO continue to hold a substantial number of shares of our common stock that many of them are now able to sell in the public market. Significant portions of these shares are held by a relatively small number of stockholders. Sales by our stockholders of a substantial number of shares, or the expectation that such sales may occur, could significantly reduce the market price of our common stock.

Our principal stockholders and management own a significant percentage of our stock and, if they choose to act together, will be able to control or exercise significant influence over matters subject to stockholder approval, which will limit your ability to influence corporate matters and could delay or prevent a change in corporate control.

Based on 33,562,211 shares outstanding as of March 31, 2019, our executive officers, directors, five percent stockholders and their affiliates beneficially owned approximately 60% of our voting stock. As a result, these stockholders, if they act together, will be able to influence our management and affairs and control the outcome of matters submitted to our stockholders for approval, including the election of directors and any sale, merger, consolidation, or sale of all or substantially all of our assets. In addition, this concentration of ownership might adversely affect the market price of our common stock by:

- delaying, deferring, or preventing a change of control of us;
- impeding a merger, consolidation, takeover, or other business combination involving us; or
- discouraging a potential acquirer from making a tender offer or otherwise attempting to obtain control of us.

Sales of a substantial number of shares of our common stock in the public market could cause our stock price to fall.

If our existing stockholders sell, or indicate an intention to sell, substantial amounts of our common stock in the public market, the market price of our common stock could decline. We have filed a registration statement on Form S-8 under the Securities Act to register 8,132,506 shares issued or reserved for issuance under our equity incentive plans. These shares are eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules and Rule 144 and Rule 701 under the Securities Act.

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In addition, as of March 31, 2019, the holders of approximately 18,114,132 shares of our common stock are entitled to rights with respect to the registration of their shares under the Securities Act. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares purchased by affiliates. Any sales of securities by these stockholders could have a material adverse effect on the market our common stock.

If securities or industry analysts do not publish or cease publishing research or reports or publish misleading, inaccurate, or unfavorable research about us, our business or our market, our stock price, and trading volume could decline.

The trading market for our common stock is influenced by the research and reports that securities or industry analysts publish about us, our business, our market, or our competitors. If one or more of the analysts who covers us downgrades our stock or publishes inaccurate or unfavorable research about our business, or provides more favorable relative recommendations about our competitors, our stock price would likely decline. If one or more of these analysts ceases coverage of us or fails to publish reports on us regularly, demand for our stock could decrease, which could cause our stock price or trading volume to decline.

We do not intend to pay dividends on our common stock and, consequently, your ability to achieve a return on your investment will depend on appreciation in the price of our common stock.

We have never declared or paid any cash dividend on our common stock and do not currently intend to do so in the foreseeable future. We currently anticipate that we will retain future earnings for the development, operation, and expansion of our business, and do not anticipate declaring or paying any cash dividends in the foreseeable future. Therefore, the success of an investment in shares of our common stock will depend upon any future appreciation in their value. There is no guarantee that shares of our common stock will appreciate in value or even maintain the price at which you purchased them.

We could be subject to securities class action litigation.

In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because biotechnology and pharmaceutical companies have experienced significant stock price volatility in recent years. If we face such litigation, it could result in substantial costs and a diversion of management's attention and resources, which could harm our business.

Changes in tax law could adversely affect our business and financial condition.

The rules dealing with U.S. federal, state, and local income taxation are constantly under review by persons involved in the legislative process and by the Internal Revenue Service and the U.S. Treasury Department. Changes to tax laws (which changes may have retroactive application) could adversely affect us or holders of our common stock. In recent years, many such changes have been made and changes are likely to continue to occur in the future. For example, the Tax Cuts and Jobs Act, or the TCJA, was enacted in 2017 and significantly reformed the Internal Revenue Code of 1986, as amended, or the Code. The TCJA, among other things, contains significant changes to corporate taxation, including reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, limitation of the tax deduction for net interest expense to 30% of adjusted earnings (except for certain small businesses), limitation of the deduction for net operating losses to 80% of current year taxable income and elimination of net operating loss carrybacks, in each case, for losses generated after December 31, 2017 (though any such net operating losses may be carried

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forward indefinitely), and the modification or repeal of many business deductions and credits (including reducing the business tax credit for certain clinical testing expenses incurred in the testing of certain drugs for rare diseases or conditions generally referred to as "orphan drugs"). Future changes in tax laws could have a material adverse effect on our business, cash flow, financial condition or results of operations. We urge investors to consult with their legal and tax advisers regarding the implications of the TCJA and other changes in tax laws on an investment in our common stock.

We are an "emerging growth company" and a "smaller reporting company", and the reduced disclosure requirements applicable to emerging growth companies and smaller reporting companies may make our common stock less attractive to investors.

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and may remain an emerging growth company until December 31, 2023, although if the market value of our common stock that is held by non-affiliates exceeds \$700 million as of the prior June 30th or if we have annual gross revenues of \$1.07 billion or more in any fiscal year, we would cease to be an emerging growth company as of December 31 of the applicable year. We also would cease to be an emerging growth company if we issue more than \$1 billion of non-convertible debt over a three-year period.

We are also a "smaller reporting company," as defined in Rule 12b-2 under the Exchange Act. We would cease to be a smaller reporting company if we have a public float in excess of \$250 million, or have annual revenues in excess of \$100 million and a public float in excess of \$700 million, determined on an annual basis.

As an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include:

- not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;
- reduced disclosure obligations regarding executive compensation; and
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved.

In addition to the above reduced disclosure requirements applicable to emerging growth companies, as a smaller reporting company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not smaller reporting companies. These exemptions include:

- being permitted to provide only two years of audited financial statements in our Annual Report on Form 10-K, with correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure; and
- not being required to furnish a stock performance graph in our annual report.

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We cannot predict whether investors will find our common stock less attractive as a result of our reliance on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

Our ability to use our net operating loss carryforwards and certain tax credit carryforwards may be subject to limitation.

As of December 31, 2018, we had federal and state net operating loss, or NOL, carryforwards of \$97.3 million and \$9.2 million, respectively. Of the \$97.3 million federal NOL carryforwards, \$48.9 million will begin to expire in 2035 and the remaining \$48.4 million has an indefinite carryforward period as a result of the TCJA. However, NOLs arising in tax years beginning after December 31, 2017, NOL carryforwards will be limited to 80% of taxable income. Under Section 382 of the Code, changes in our ownership may limit the amount of our NOL carryforwards and research and development tax credit carryforwards that could be utilized annually to offset our future taxable income, if any. This limitation would generally apply in the event of a cumulative change in ownership of our company of more than 50% within a three-year period. Any such limitation may significantly reduce our ability to utilize NOL carryforwards and research and development tax credit carryforwards before they expire. During 2018, we performed a detailed analysis of historical and current Section 382 ownership changes that may limit the utilization of NOL carryforwards. Except for approximately \$7.1 million of NOLs arising prior to May 2016, we expect the entire remaining federal NOL carryforward will not be subject to limitations under Section 382 of the Code. However, sales of our common stock by our existing stockholders, or additional sales of our common stock by us, could trigger additional limitations under Section 382 of the Code and have a material adverse effect on our results of operations in future years.

Unfavorable global economic conditions could adversely affect our business, financial condition, or results of operations.

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. A global financial crisis can cause extreme volatility and disruptions in the capital and credit markets. A severe or prolonged economic downturn, such as the global financial crisis years ago, could result in a variety of risks to our business, including, weakened demand for our product candidates and our ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy could also strain our suppliers, possibly resulting in supply disruption, or cause our customers to delay making payments for our services. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business.

Our bylaws contain exclusive forum provisions, which may limit a stockholder's ability to bring a claim in a judicial forum it finds favorable and may discourage lawsuits with respect to such claims.

Our amended and restated bylaws provide that, unless we consent in writing to an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for state law claims for (1) any derivative action or proceeding brought on our behalf; (2) any action asserting a claim of or based on a breach of a fiduciary duty owed by any of our current or former directors, officers or other employees to us or our stockholders; (3) any action asserting a claim against us or any of our current or former directors, officers, employees or stockholders 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 (4) any action asserting a claim governed by the internal affairs doctrine (the "Delaware Forum Provision"). The Delaware Forum Provision will

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not apply to any causes of action arising under the Securities Act or the Exchange Act. Our amended and restated bylaws further provide that, unless we consent in writing to an alternative forum, the United States District Court for the Northern District of Illinois will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act (the "Federal Forum Provision"). We have chosen the United States District Court for the Northern District of Illinois as the exclusive forum for such Securities Act causes of action because our principal executive offices are located in Evanston, Illinois. In addition, our amended and restated bylaws provide that any person or entity purchasing or otherwise acquiring any interest in shares of our common stock is deemed to have notice of and consented to the foregoing Delaware Forum Provision and the Federal Forum Provision.

On December 19, 2018, in *Sciabacucchi v. Salzberg*, C.A. No. 2017-0931-JTL (Del. Ch.), the Court of Chancery of the State of Delaware issued a decision declaring that federal forum selection provisions that purport to require claims under the Securities Act be brought in federal court are ineffective and invalid under Delaware law. On January 17, 2019, the decision was appealed to the Delaware Supreme Court. While the Delaware Supreme Court dismissed the appeal on jurisdictional grounds, we expect that the appeal will be re-filed once the Court of Chancery issues a final judgment. Unless and until the Court of Chancery's decision in *Sciabacucchi* is reversed by the Delaware Supreme Court or otherwise abrogated, we do not intend to enforce our Federal Forum Provision designating the Northern District of Illinois as the exclusive forum for Securities Act claims. In the event that the Delaware Supreme Court affirms the Court of Chancery's *Sciabacucchi* decision or otherwise makes a determination that provisions such as the Federal Forum Provision are invalid, our board of directors intends to amend promptly our bylaws to remove the Federal Forum Provision. Such amendment could cause us to incur additional costs, which could have an adverse effect on our business, financial condition or results of operations.

We recognize that the Delaware Forum Provision and the Federal Forum Provision may impose additional litigation costs on stockholders who assert the provision is not enforceable and may impose more general additional litigation costs in pursuing any such claims, particularly if the stockholders do not reside in or near the State of Delaware or the State of Illinois. Additionally, these forum selection clauses in our amended and restated bylaws may limit our stockholders' ability to bring a claim in a judicial forum that they find favorable for disputes with us or our directors, officers or employees, which may discourage such lawsuits against us and our directors, officers and employees even though an action, if successful, might benefit our stockholders. The Federal Forum Provision may also impose additional litigation costs on stockholders who assert the provision is not enforceable. The Court of Chancery of the State of Delaware and the United States District Court for the Northern District of Illinois may also reach different judgments or results than would other courts, including courts where a stockholder considering an action may be located or would otherwise choose to bring the action, and such judgments may be more or less favorable to us than our stockholders.

CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and the information and documents incorporated by reference herein, contain forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act. Any statements about our expectations, beliefs, plans, objectives, assumptions or future events or performance are not historical facts and may be forward-looking. These statements are often, but are not always, made through the use of words or phrases such as "may," "will," "could," "should," "expects," "intends," "plans," "anticipates," "believes," "estimates," "predicts," "projects," "potential," "continue," and similar expressions, or the negative of these terms, or similar expressions. Accordingly, these statements involve estimates, assumptions, risks and uncertainties which could cause actual results to differ materially from those expressed in them. Any forward-looking statements are qualified in their entirety by reference to the factors discussed throughout this prospectus and the documents incorporated by reference herein, and in particular those factors referenced in the section "Risk Factors."

This prospectus, any related free writing prospectus and the information and documents incorporated by reference herein contain forward-looking statements that are based on our management's belief and assumptions and on information currently available to our management. These statements relate to future events or our future financial performance, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from any future results, levels of activity, performance or achievements expressed or implied by these forward-looking statements. Forward-looking statements include, but are not limited to, statements about:

- the timing, progress, and results of preclinical studies and clinical trials for NYX-2925, NYX-783, NYX-458, and any future product candidates we may develop, including statements regarding the timing of initiation and completion of studies or trials and related preparatory work, the period during which the results of the studies will become available, and our research and development programs;
- the existence or absence of side effects or other properties relating to our product candidates which could delay or prevent their regulatory approval, limit their commercial potential, or result in significant negative consequences following any potential marketing approval;
- the potential for our identified research priorities to advance our technologies;
- the potential timelines for our clinical studies or our ability to demonstrate safety and efficacy of our product candidates to the satisfaction of applicable regulatory authorities;
- our ability to obtain and maintain regulatory approval of our product candidates, NYX-2925, NYX-783, NYX-458, and any other future product candidates, and any statements regarding the label of an approved product candidate, including any restrictions, limitations and/or warnings therein;
- our intellectual property position, including the scope of protection we are able to establish and maintain for intellectual property rights covering NYX-2925, NYX-783, NYX-458, and any additional product candidates we may develop, and any statements as to whether we do or do not infringe, misappropriate, or otherwise violate any third-party intellectual property rights;
- our ability and the potential to successfully manufacture our product candidates for clinical studies and for commercial use, if approved;
- our ability to commercialize our products in light of the intellectual property rights of others;
- our ability to obtain funding for our operations, including funding necessary to complete further development and commercialization of our product candidates;

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- our plans to research, develop, and commercialize our product candidates;
- our ability to attract collaborators with development, regulatory, and commercialization expertise;
- the size and growth potential of the markets for our product candidates and our ability to serve those markets;
- the rate and degree of market acceptance and clinical utility of NYX-2925, NYX-783, NYX-458, and any future product candidates we may develop, if approved;
- the pricing and reimbursement of NYX-2925, NYX-783, NYX-458, and any future product candidates we may develop, if approved;
- regulatory developments in the United States and foreign countries;
- our ability to contract with third-party suppliers and manufacturers and their ability to perform adequately;
- the success of competing therapies that are or may become available;
- our ability to retain the continued service of our key professionals and to identify, hire, and retain additional qualified professionals;
- the accuracy of our estimates regarding expenses, future revenue, capital requirements, and needs for additional financing;
- our financial performance;
- our expectation related to the use of our cash reserves;
- the impact of laws and regulations, including, without limitation, recently enacted tax reform legislation;
- the use of proceeds from our IPO; and
- our expectations regarding the time during which we will be an "emerging growth company" under the JOBS Act.

These forward-looking statements are neither promises nor guarantees of future performance due to a variety of risks and uncertainties, many of which are beyond our control, which could cause actual results to differ materially from those indicated by these forward-looking statements, including, without limitation the risk factors and cautionary statements described in other documents that we file from time to time with the SEC, specifically under "Item 1A: Risk Factors" and elsewhere in our most recent Annual Report on Form 10-K and any subsequent Quarterly Reports on Form 10-Q or Current Reports on Form 8-K, and the section of the prospectus titled "Risk Factors."

The forward-looking statements in this prospectus, any related free writing prospectus and the documents incorporated by reference represent our views as of their respective dates. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we assume no obligation to update or revise any forward-looking statements except to the extent required by applicable law. You should, therefore, not rely on these forward-looking statements as representing our views as of any date subsequent to the dates on which they were made.

This prospectus, any related free writing prospectus and the documents incorporated by reference also contain estimates, projections and other information concerning our industry, our business, and the markets for certain diseases, including data regarding the estimated size of those markets, and the incidence and prevalence of certain medical conditions. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances reflected in this information. Unless otherwise expressly stated, we obtained this industry, business, market and other data from reports, research surveys, studies and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data and similar sources.

USE OF PROCEEDS

We may issue and sell shares of our common stock having aggregate sales proceeds of up to \$24.0 million from time to time. The amount of proceeds from this offering will depend upon the number of shares of our common stock sold and the market price at which they are sold. There can be no assurance that we will be able to sell any shares under or fully utilize the sales agreement with Cowen and Company, LLC as a source of financing. Therefore, the actual total public offering amount, commissions and proceeds to us, if any, are not determinable at this time.

We intend to use any net proceeds from this offering primarily to fund activities relating to the advancement of our product candidates, and for other general corporate purposes. General corporate purposes may include research and development costs, including the conduct of one or more clinical trials and process development and manufacturing of our product candidates, potential strategic acquisitions of complementary businesses, services or technologies, expansion of our technology infrastructure and capabilities, working capital and capital expenditures. We may temporarily invest the net proceeds in a variety of capital preservation instruments, including investment grade, interest bearing instruments and U.S. government securities, until they are used for their stated purpose. We have not determined the amount of net proceeds to be used specifically for such purposes. As a result, management will retain broad discretion over the allocation of net proceeds.

DIVIDEND POLICY

We have never declared or paid cash dividends on our capital stock. We intend to retain all of our future earnings, if any, to finance the growth and development of our business. We do not intend to pay cash dividends to our stockholders in the foreseeable future.

CERTAIN MATERIAL U.S. FEDERAL INCOME TAX CONSIDERATIONS TO NON-U.S. HOLDERS

The following discussion is a summary of the material U.S. federal income tax considerations applicable to non-U.S. holders (as defined below) with respect to their ownership and disposition of shares of our common stock issued pursuant to this offering. For purposes of this discussion, a non-U.S. holder means a beneficial owner of our common stock that is for U.S. federal income tax purposes:

- a non-resident alien individual;
- a foreign corporation or any other foreign organization taxable as a corporation for U.S. federal income tax purposes; or
- a foreign estate or trust, the income of which is not subject to U.S. federal income tax on a net income basis.

This discussion does not address the tax treatment of partnerships or other entities that are pass-through entities for U.S. federal income tax purposes or persons that hold their common stock through partnerships or other pass-through entities. A partner in a partnership or other pass-through entity that will hold our common stock should consult his, her or its tax advisor regarding the tax consequences of acquiring, holding and disposing of our common stock through a partnership or other pass-through entity, as applicable.

This discussion is based on current provisions of the U.S. Internal Revenue Code of 1986, as amended, which we refer to as the Code, existing and proposed U.S. Treasury Regulations promulgated thereunder, current administrative rulings and judicial decisions, all as in effect as of the date of this prospectus and, all of which are subject to change or to differing interpretation, possibly with retroactive effect. Any such change or differing interpretation could alter the tax consequences to non-U.S. holders described in this prospectus. There can be no assurance that the Internal Revenue Service, which we refer to as the IRS, will not challenge one or more of the tax consequences described herein. We assume in this discussion that a non-U.S. holder holds shares of our common stock as a capital asset within the meaning of Section 1221 of the Code, generally property held for investment.

This discussion does not address all aspects of U.S. federal income taxation that may be relevant to a particular non-U.S. holder in light of that non-U.S. holder's individual circumstances, nor does it address U.S. state, local or non-U.S. taxes, the alternative minimum tax, or the Medicare tax on net investment income, the rules regarding qualified small business stock within the meaning of Section 1202 of the Code, or any other aspects of any U.S. federal tax other than the income tax. This discussion also does not consider any specific facts or circumstances that may apply to a non-U.S. holder and does not address the special tax rules applicable to particular non-U.S. holders, such as:

- insurance companies;
- tax-exempt or governmental organizations;
- financial institutions;
- brokers or dealers in securities;
- regulated investment companies;
- pension plans;
- "controlled foreign corporations," "passive foreign investment companies," and corporations that accumulate earnings to avoid U.S. federal income tax;

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- "qualified foreign pension funds," or entities wholly owned by a "qualified foreign pension fund";
- partnerships or other entities or arrangements treated as partnerships for U.S. federal income tax purposes (and partners and investors therein);
- persons deemed to sell our common stock under the constructive sale provisions of the Code;
- persons that hold our common stock as part of a straddle, hedge, conversion transaction, synthetic security or other integrated investment;
- persons who hold or receive our common stock pursuant to the exercise of any employee stock option or otherwise as compensation; and
- certain U.S. expatriates.

Accordingly, all prospective non-U.S. holders of our common stock should consult their tax advisors with respect to the U.S. federal, state, local, and non-U.S. tax consequences of the purchase, ownership and disposition of our common stock.

Distributions on our common stock

Distributions, if any, on our common stock will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. If a distribution exceeds our current and accumulated earnings and profits, the excess will be treated as a tax-free return of the non-U.S. holder's investment, up to such holder's tax basis in the common stock. Any remaining excess will be treated as capital gain, subject to the tax treatment described below in "Gain on sale or other taxable disposition of our common stock." Any such distributions will also be subject to the discussions below under the sections titled "Backup withholding and information reporting" and "Withholding and information reporting requirements—FATCA."

Subject to the discussion in the following two paragraphs in this section, dividends paid to a non-U.S. holder generally will be subject to withholding of U.S. federal income 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 holder's country of residence.

Dividends that are treated as effectively connected with a trade or business conducted by a non-U.S. holder within the United States and, if an applicable income tax treaty so provides, that are attributable to a permanent establishment or a fixed base maintained by the non-U.S. holder within the United States, are generally exempt from the 30% withholding tax if the non-U.S. holder satisfies applicable certification and disclosure requirements. However, such U.S. effectively connected income, net of specified deductions and credits, is taxed at the same graduated U.S. federal income tax rates applicable to U.S. persons (as defined in the Code). Any U.S. effectively connected income received by a non-U.S. holder that is a corporation may also, under certain circumstances, be subject to an additional "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 holder's country of residence.

A non-U.S. holder of our common stock who claims the benefit of an applicable income tax treaty between the United States and such holder's country of residence generally will be required to provide a properly executed IRS Form W-8BEN or W-8BEN-E (or successor form) to the applicable withholding agent and satisfy applicable certification and other requirements. Non-U.S. holders are urged to consult their tax advisors regarding their entitlement to benefits under a relevant income tax treaty. A non-U.S. holder that is eligible for a reduced rate of U.S. withholding tax under an income tax treaty may obtain a refund or credit of any excess amounts withheld by timely filing a U.S. tax return with the IRS.

Gain on sale or other taxable disposition of our common stock

Subject to the discussions below under "Backup withholding and information reporting" and "Withholding and information reporting requirements—FATCA," a non-U.S. holder generally will not be subject to any U.S. federal income tax on any gain realized upon such holder's sale or other taxable disposition of shares 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 an applicable income tax treaty so provides, is attributable to a permanent establishment or a fixed-base maintained by such non-U.S. holder in the United States, in which case the non-U.S. holder generally will be taxed on a net income basis at the graduated U.S. federal income tax rates applicable to U.S. persons (as defined in the Code) and, if the non-U.S. holder is a foreign corporation, the branch profits tax described above in "Distributions on our common stock" also may apply;
- the non-U.S. holder is a nonresident alien individual who is present in the United States for 183 days or more in the taxable year of the disposition and certain other conditions are met, in which case the non-U.S. holder will be subject to a 30% tax (or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder's country of residence) on the net gain derived from the disposition, which may be offset by certain U.S. source capital losses of the non-U.S. holder, if any (even though the individual is not considered a resident of the United States), provided that the non-U.S. holder has timely filed U.S. federal income tax returns with respect to such losses; or
- we are, or have been, at any time during the five-year period preceding such sale or other taxable disposition (or the non-U.S. holder's holding period, if shorter) a "U.S. real property holding corporation," unless our common stock is regularly traded on an established securities market and the non-U.S. holder holds no more than 5% of our outstanding common stock, directly or indirectly, actually or constructively, during the shorter of the 5-year period ending on the date of the disposition or the period that the non-U.S. holder held our common stock. Generally, a corporation is a U.S. real property holding corporation 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. Although there can be no assurance, we do not believe that we are, or have been, a U.S. real property holding corporation, or that we are likely to become one in the future. No assurance can be provided that our common stock will be regularly traded on an established securities market for purposes of the rules described above.

Backup withholding and information reporting

We must report annually to the IRS and to each non-U.S. holder the gross amount of the distributions on our common stock paid to such holder and the tax withheld, if any, with respect to such distributions. Non-U.S. holders may have to comply with specific certification procedures to establish that the holder is not a U.S. person (as defined in the Code) in order to avoid backup withholding at the applicable rate with respect to dividends on our common stock. Dividends paid to non-U.S. holders subject to withholding of U.S. federal income tax, as described above in "Distributions on our common stock," generally will be exempt from U.S. backup withholding.

Information reporting and backup withholding will generally apply to the proceeds of a disposition of our common stock by a non-U.S. holder effected by or through the U.S. office of any broker, U.S. or foreign, unless the holder certifies its status as a non-U.S. holder and satisfies certain other requirements, or otherwise establishes an exemption. Generally, information reporting and backup withholding will not apply to a payment of disposition proceeds to a non-U.S. holder

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where the transaction is effected outside the United States. through a non-U.S. office of a broker. However, for information reporting purposes, dispositions effected through a non-U.S. office of a broker with substantial U.S. ownership or operations generally will be treated in a manner similar to dispositions effected through a U.S. office of a broker. Non-U.S. holders should consult their tax advisors regarding the application of the information reporting and backup withholding rules to them. Copies of information returns may be made available to the tax authorities of the country in which the non-U.S. holder resides or is incorporated under the provisions of a specific treaty or agreement. Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules from a payment to a non-U.S. holder can be refunded or credited against the non-U.S. holder's U.S. federal income tax liability, if any, provided that an appropriate claim is filed with the IRS in a timely manner.

Withholding and information reporting requirements—FATCA

The Foreign Account Tax Compliance Act, or FATCA, generally imposes a U.S. federal withholding tax at a rate of 30% on payments of dividends on our common stock paid to a foreign entity unless (i) if the foreign entity is a "foreign financial institution," such foreign entity undertakes certain due diligence, reporting, withholding, and certification obligations, (ii) if the foreign entity is not a "foreign financial institution," such foreign entity identifies certain of its U.S. investors, if any, or (iii) the foreign entity is otherwise exempt under FATCA. Such withholding may also apply to gross proceeds from the sale or other disposition of our common stock, although under recently proposed U.S. Treasury Regulations, no withholding would apply to such gross proceeds. The preamble to the proposed regulations specifies that taxpayers (including withholding agents) are permitted to rely on the proposed regulations pending finalization. Under certain circumstances, a non-U.S. holder may be eligible for refunds or credits of this withholding tax. An intergovernmental agreement between the United States and an applicable foreign country may modify the requirements described in this paragraph. Non-U.S. holders should consult their tax advisors regarding the possible implications of this legislation 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.

PLAN OF DISTRIBUTION

We have entered into a sales agreement with Cowen and Company, LLC, or Cowen, under which we may offer and sell from time to time up to an aggregate of \$50.0 million of our common stock through Cowen as our sales agent. This prospectus is offering up to an aggregate of \$24.0 million in shares of our common stock. We will be required to file another prospectus or a prospectus supplement in the event we want to offer more than \$24.0 million in shares of our common stock in accordance with the sales agreement. Sales of our common stock, if any, will be made at market prices by any method that is deemed to be an "at the market offering" as defined in Rule 415 under the Securities Act.

Cowen will offer our common stock subject to the terms and conditions of the sales agreement on a daily basis or as otherwise agreed upon by us and Cowen. We will designate the maximum amount of common stock to be sold through Cowen on a daily basis or otherwise determine such maximum amount together with Cowen. Subject to the terms and conditions of the sales agreement, Cowen will use its commercially reasonable efforts to sell on our behalf all of the shares of common stock requested to be sold by us. We may instruct Cowen not to sell common stock if the sales cannot be effected at or above the price designated by us in any such instruction. Cowen or we may suspend the offering of our common stock being made through Cowen under the sales agreement upon proper notice to the other party. Cowen and we each have the right, by giving written notice as specified in the sales agreement, to terminate the sales agreement in each party's sole discretion at any time.

The aggregate compensation payable to Cowen as sales agent is equal to 3.0% of the gross sales price of the shares sold through it pursuant to the sales agreement. We have also agreed to reimburse Cowen up to \$62,500 of Cowen's actual outside legal expenses incurred by Cowen in connection with this offering, and for certain other expenses. We estimate that the total expenses of the offering payable by us, excluding commissions payable to Cowen under the sales agreement, will be approximately \$480,000.

The remaining sales proceeds, after deducting any expenses payable by us and any transaction fees imposed by any governmental, regulatory, or self-regulatory organization in connection with the sales, will equal our net proceeds for the sale of such common stock.

Cowen will provide written confirmation to us following the close of trading on The Nasdaq Global Select Market on each day in which common stock is sold through it as sales agent under the sales agreement. Each confirmation will include the number of shares of common stock sold through it as sales agent on that day, the volume weighted average price of the shares sold, the percentage of the daily trading volume and the net proceeds to us.

We will report at least quarterly the number of shares of common stock sold through Cowen under the sales agreement, the net proceeds to us and the compensation paid by us to Cowen in connection with the sales of common stock.

Settlement for sales of common stock will occur, unless the parties agree otherwise, on the second business day that is also a trading day following the date on which any sales were 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.

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In connection with the sales of our common stock on our behalf, Cowen will be deemed to be an "underwriter" within the meaning of the Securities Act, and the compensation paid to Cowen will be deemed to be underwriting commissions or discounts. We have agreed in the sales agreement to provide indemnification and contribution to Cowen against certain liabilities, including liabilities under the Securities Act. As sales agent, Cowen will not engage in any transactions that stabilizes our common stock.

Our common stock is listed on The Nasdaq Global Select Market and trades under the symbol "APTX." The transfer agent of our common stock is Computershare Trust Company, N.A.

Cowen and/or its affiliates have provided, and may in the future provide, various investment banking and other financial services for us for which services they have received and, may in the future receive, customary fees.

LEGAL MATTERS

Certain legal matters in connection with this offering and the validity of the securities offered by this prospectus will be passed upon for us by Goodwin Procter LLP, Boston, MA. Cowen and Company, LLC is being represented in connection with this offering by Duane Morris LLP, New York, NY.

EXPERTS

The financial statements incorporated in this prospectus by reference from the Company's Annual Report on Form 10-K have been audited by Deloitte & Touche LLP, an independent registered public accounting firm, as stated in their report, which is incorporated herein by reference. Such financial statements have been so incorporated in reliance upon the report of such firm given upon their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

This prospectus is part of a registration statement on Form S-3 that we have filed with the SEC. This prospectus, filed as part of the registration statement, does not contain all the information set forth in the registration statement and its exhibits and schedules, portions of which have been omitted as permitted by the rules and regulations of the SEC. For further information about us, we refer you to the registration statement and to its exhibits and schedules. Certain information in the registration statement has been omitted from this prospectus in accordance with the rules of the SEC.

We are subject to the reporting and information requirements of the Exchange Act and, in accordance therewith, file annual, quarterly and special reports, proxy statements and other information with the SEC. These documents also may be accessed through the SEC's electronic data gathering, analysis and retrieval system, or EDGAR, via electronic means, including the SEC's home page on the Internet (www.sec.gov). Written requests for such copies should be directed to Investor Relations Department, Aptinyx Inc., 909 Davis Street, Suite 600, Evanston, IL 60201, and our website is located at www.aptinyx.com.

We have the authority to designate and issue more than one class or series of stock having various preferences, conversion and other rights, voting powers, restrictions, limitations as to dividends, qualifications, and terms and conditions of redemption. See "Description of Capital Stock" in the accompanying base prospectus. We will furnish a full statement of the relative rights and preferences of each class or series of our stock which has been so designated and any restrictions on the ownership or transfer of our stock to any shareholder upon request and without charge. Information contained on our website is not incorporated by reference into this prospectus and, therefore, is not part of this prospectus or any accompanying prospectus supplement.

INCORPORATION BY REFERENCE

The SEC allows us to incorporate by reference the information and reports we file with it, which means that we can disclose important information to you by referring you to these documents. The information incorporated by reference is an important part of this prospectus, and information that we file later with the SEC will automatically update and supersede the information already incorporated by reference. We are incorporating by reference the documents listed below, which we have already

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filed with the SEC, and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act, including all filings made after the date of this prospectus, except as to any portion of any future report or document that is not deemed filed under such provisions, until we sell all of the securities:

- our [Annual Report on Form 10-K for the year ended December 31, 2018, filed with the SEC on March 21, 2019](#);
- the information specifically incorporated by reference into our [Annual Report on Form 10-K for the year ended December 31, 2018](#) from our definitive proxy statement on Schedule 14A (other than information furnished rather than filed), which was filed with the SEC on [April 1, 2019](#), as amended on [May 1, 2019](#);
- our [Quarterly Report on Form 10-Q for the quarter ended March 31, 2019, filed with the SEC on May 14, 2019](#);
- our Current Reports on Form 8-K filed with the SEC on [January 16, 2019](#), [January 23, 2019](#), [March 11, 2019](#), [March 29, 2019](#), [May 7, 2019](#), [May 17, 2019](#), and [June 10, 2019](#) (in each case, except for information contained therein which is furnished rather than filed); and
- the description of our common stock contained in our registration statement on [Form 8-A filed with the SEC on June 18, 2018](#), including any amendments or reports filed for the purposes of updating this description.

We incorporate by reference any future filings made with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act between the date of this prospectus and the termination of the offering.

Notwithstanding the foregoing, unless specifically stated to the contrary, information that we furnish (and that is not deemed "filed" with the SEC) under Items 2.02 and 7.01 of any Current Report on Form 8-K, including the related exhibits under Item 9.01, is not incorporated by reference into this prospectus or the registration statement of which this prospectus is a part.

Any statement contained in a document that is incorporated by reference will be modified or superseded for all purposes to the extent that a statement contained in this prospectus, or in any other document that is subsequently filed with the SEC and incorporated by reference into this prospectus, modifies or is contrary to that previous statement. Any statement so modified or superseded will not be deemed a part of this prospectus, except as so modified or superseded. Since information that we later file with the SEC will update and supersede previously incorporated information, you should look at all of the SEC filings that we incorporate by reference to determine if any of the statements in this prospectus or in any documents previously incorporated by reference have been modified or superseded.

Upon request, we will provide, without charge, to each person, including any beneficial owner, to whom a copy of this prospectus is delivered, a copy of the documents incorporated by reference into this prospectus but not delivered therewith. You may request a copy of these filings, and any exhibits we have specifically incorporated by reference as an exhibit in this prospectus, at no cost by writing or telephoning us at the following address: Investor Relations Department, Aptinyx Inc., 909 Davis Street, Suite 600, Evanston, IL 60201, and our website is located at www.aptinyx.com.

You may also access these documents, free of charge on the SEC's website at www.sec.gov or on our website at www.aptinyx.com. Information contained on our website is not incorporated by reference into this prospectus and you should not consider any information on, or that can be accessed from, our website as part of this prospectus.

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This prospectus is part of a registration statement we filed with the SEC. We have incorporated exhibits into this registration statement. You should read the exhibits carefully for provisions that may be important to you.

You should rely only on the information incorporated by reference or provided in this prospectus. We have not authorized anyone to provide you with different information. We are not making an offer of these securities in any state where the offer is not permitted. You should not assume that the information in this prospectus or in the documents incorporated by reference is accurate as of any date other than the date on the front of this prospectus or those documents.

Up to \$24,000,000



Common Stock

PROSPECTUS

Cowen

July 8, 2019
