FIVE PRIME THERAPEUTICS INC
Form 424B5
January 07, 2015
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Filed pursuant to Rule 424(b)(5)
Registration No. 333-200067

PROSPECTUS SUPPLEMENT

(To Prospectus dated December 8, 2014)

3,410,000 Shares

Five Prime Therapeutics, Inc.

Common Stock

We are offering up to 3,410,000 shares of common stock. Our common stock is listed on The NASDAQ Global Select Market under the symbol FPRX. On January 6, 2015, the closing price of our common stock on The NASDAQ Global Select Market was $23.00 per share.

You should read carefully this prospectus supplement, the accompanying prospectus, and the documents incorporated by reference in this prospectus supplement and the accompanying prospectus before you invest. Investing in our common stock involves risks. Please see Risk Factors beginning on page S-8 of this prospectus supplement for more information.

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

	Per Share	Total
Public Offering Price	$ 22.00	$ 75,020,000
Underwriting Discounts and Commissions[(1)]	$ 1.32	$ 4,501,200
Proceeds, before expenses, to us	$ 20.68	$ 70,518,800

(1) See Underwriting for additional disclosure regarding underwriting compensation.

We have granted the underwriters an option for 30 days from the date of this prospectus supplement to purchase up to an additional 511,500 shares of our common stock on the same terms as set forth above. See Underwriting for more information.

The underwriters expect to deliver the shares on or about January 12, 2015.

Joint Book-Running Managers

Citigroup **Leerink Partners** **Wells Fargo Securities**

Co-Managers

Guggenheim Securities **Oppenheimer & Co.**

The date of this prospectus supplement is January 6, 2015.

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Prospectus Supplement

Prospectus

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ABOUT THIS PROSPECTUS SUPPLEMENT

We provide information to you about this offering of shares of our common stock in two separate documents that are bound together: (i) this prospectus supplement, which describes the specific details regarding this offering; and (ii) the accompanying base prospectus, dated December 3, 2014, which provides general information, some of which may not apply to this offering. Generally, when we refer to this prospectus, we are referring to both documents combined. If information in this prospectus supplement is inconsistent with the accompanying base prospectus, you should rely on this prospectus supplement. However, if any statement in one of these documents is inconsistent with a statement in another document having a later date for example, a document incorporated by reference in this prospectus the statement in the document having the later date modifies or supersedes the earlier statement as our business, financial condition, results of operations and prospects may have changed since the earlier dates.

You should rely only on the information contained in, or incorporated by reference into, this prospectus and in any free writing prospectus that we may authorize for use in connection with this offering. We and the underwriters have not authorized any other person to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. We and the underwriters are not making an offer to sell or soliciting an offer to buy our securities in any jurisdiction in which an offer or solicitation is not authorized or in which the person making that offer or solicitation is not qualified to do so or to anyone to whom it is unlawful to make an offer or solicitation. You should assume that the information appearing in this prospectus, the documents incorporated by reference into this prospectus, and in any free writing prospectus that we may authorize for use in connection with this offering, is accurate only as of the date of those respective documents. Our business, financial condition, results of operations and prospects may have changed since those dates. You should read this prospectus, the documents incorporated by reference into this prospectus, and any free writing prospectus that we may authorize for use in connection with this offering, in their entirety before making an investment decision. You should also read and consider the information in the documents to which we have referred you in the sections of this prospectus entitled Where You Can Find More Information and Incorporation of Certain Information by Reference.

We are offering to sell, and seeking offers to buy, shares of common stock only in jurisdictions where offers and sales are permitted. The distribution of this prospectus and the offering of the 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 the 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.

Except as otherwise indicated herein or as the context otherwise requires, references in this prospectus to Five Prime, the company, we, us, ou and similar references refer to Five Prime Therapeutics, Inc. The Five Prime logo and RIPPS® are our registered trademarks. This prospectus also contains registered marks, trademarks and trade names of other companies. All other trademarks, registered marks and trade names appearing in this prospectus are the property of their respective holders.

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PROSPECTUS SUPPLEMENT SUMMARY

The following summary highlights selected information about us, this offering, and selected information appearing elsewhere in this prospectus supplement, in the accompanying prospectus and in the documents we incorporate by reference. Because this is only a summary, you should read the rest of this prospectus supplement, the accompanying prospectus, and our financial statements and related notes and the other information we incorporate by reference, and the information included in any free writing prospectus prepared by or on behalf of us or to which we have referred you, before you invest in our common stock. If you invest in our common stock, you are assuming a high degree of risk. Read this entire prospectus supplement carefully, especially the risks described under the section entitled Risk Factors and in our Annual Report on Form 10-K for the fiscal year ended December 31, 2013 and our Quarterly Report on Form 10-Q for the quarter ended September 30, 2014 incorporated herein by reference.

Our Company

We are a clinical-stage biotechnology company focused on discovering and developing novel protein therapeutics to improve the lives of patients with serious diseases. Our discovery platform, which we believe encompasses substantially all of the body s medically important targets for protein therapeutics, positions us to explore pathways in cancer and inflammation and their intersection in immuno-oncology, an area of oncology with significant therapeutic potential and a growing focus of our research and development activities.

We currently have three product candidates in clinical development covering multiple potential indications. Each of our product candidates has an innovative mechanism of action and addresses patient populations for which better therapies are still needed. In addition, we are pursuing companion diagnostics, where appropriate, for each of our lead programs to allow us to select patients most likely to benefit from treatment and therefore accelerate clinical development and improve patient care. Our most advanced product candidates are described below.

FPA008

FPA008 is an antibody that inhibits colony stimulating factor-1, or CSF1, receptor, or CSF1R. CSF1R is a cell surface protein that controls the survival and function of certain immune response cells called monocytes and macrophages. FPA008 blocks the activation and survival of these cell types. In many cancers, inhibition of CSF1R reduces the number of immunosuppressive tumor-associated macrophages, or TAMs, thereby facilitating an immune response against tumors. We believe the combination of FPA008 with T cell checkpoint inhibitors, such as PD-1 inhibitors, or immune agonists may have synergistic therapeutic effects in treating cancer. In pigmented villonodular synovitis, or PVNS, a rare CSF1-driven tumor for which there are no currently approved therapies, inhibition of CSF1R reduces infiltration into the joint of monocytes and macrophages, which form the bulk of the tumor mass, resulting in tumor shrinkage. Inhibition of CSF1R in inflamed joints in rheumatoid arthritis, or RA, patients should block the production of inflammatory cytokines by macrophages and inhibit osteoclasts, monocyte-lineage cells that can cause bone erosions and joint destruction.

FPA008 Study in Immuno-Oncology

In November 2014, we entered into a clinical trial collaboration agreement with Bristol-Myers Squibb Company, or BMS, under which we and BMS will collaborate under a development plan to evaluate the safety, tolerability and preliminary efficacy of combining Opdivo® (nivolumab), BMS s investigational PD-1 immune checkpoint inhibitor, with FPA008. We and BMS plan to initially study the FPA008-Opdivo combination

as a potential treatment for patients with non-small cell lung cancer, or NSCLC, melanoma, head and neck cancer, pancreatic cancer, colorectal cancer and malignant glioma in a Phase 1a/1b trial, which we expect to commence

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by mid-2015. We expect to explore tumor- and blood-based biomarkers to better understand which patients are more likely to respond to this novel combination. We are responsible for conducting the trial of the FPA008-Opdivo combination under the development plan with BMS.

We believe that FPA008 may have additive or synergistic therapeutic effects when combined with other T cell checkpoint inhibitors, in addition to PD-1 inhibitors such as Opdivo (nivolumab), or immune agonists. We plan to continue to evaluate the potential clinical development of FPA008 in combination with these other checkpoint inhibitors and immune agonists.

FPA008 Study in PVNS

We are preparing to initiate a Phase 1/2 clinical trial of FPA008 in patients with PVNS by mid-2015. In the Phase 1 component of this trial, we plan to select the optimal dose in PVNS patients for the Phase 2 portion. After identifying the optimal dose, the primary objectives of the Phase 2 portion of this trial are to assess tumor shrinkage, pain and joint function in patients with PVNS. In addition, we plan to measure the duration of response as a secondary objective. PVNS is an orphan indication, and we believe patients with this disease will benefit from CSF1R inhibition achieved with the administration of FPA008. We expect to have preliminary efficacy data from the Phase 1 portion of this trial in patients with PVNS by the end of 2015 or early 2016.

FPA008 Study in RA

We are conducting a randomized, double-blind, placebo-controlled, single- and multiple-ascending dose Phase 1 trial of FPA008 in three parts. During 2014, we completed parts 1 and 2 of this Phase 1 trial in healthy volunteers and began part 3, which consists of an open-label evaluation of FPA008 at multiple dose levels in RA patients whose disease is not responsive to methotrexate therapy. The primary endpoint of this Phase 1 trial in RA is safety, with secondary endpoints including pharmacokinetics, pharmacodynamics, or PD, and disease activity as measured by American College of Rheumatology scores and magnetic resonance imaging of affected joints.

In parts 1 and 2 of this Phase 1 trial, we administered FPA008 in either a single dose or two doses administered 14 days apart to 36 healthy volunteers. We also administered placebo to an additional 10 healthy volunteers during parts 1 and 2 of this trial. In November 2014, we presented results from the healthy volunteer cohorts in this Phase 1 trial in a poster presentation at the 2014 American College of Rheumatology and the Association of Rheumatology Health Professionals Annual Scientific Meeting. The preliminary results from the healthy volunteer portion of the trial show that FPA008 was well tolerated at doses up to 3 mg/kg. Additionally, at all dose levels tested, we observed PD effects of suppression of non-classical CD16+ monocytes and a decrease of bone turnover biomarkers (CTx, Trap5), all of which we believe indicate the potential for clinical benefit in RA patients. We observed no dose-limiting toxicities during parts 1 and 2 of this trial. The most common FPA008 treatment-related toxicities were pruritus, eyelid edema along with facial swelling, fatigue and headache. These events were mild (grade 1 or 2) and reversible. Some dose-dependent elevations of CK, LDH and AST enzymes were observed, but were not associated with clinical signs or symptoms, were reversible and were expected based on FPA008 s inhibition of Kupffer cells in the liver, which clear these enzymes from the blood.

We plan to present preliminary data from part 3 of this Phase 1 trial in RA patients by the end of 2015.

FPA144

FPA144 is an antibody that inhibits fibroblast growth factor receptor 2b, or FGFR2b, which we are developing to treat patients with gastric (stomach) cancer and potentially other solid tumors. FPA144 is designed to inhibit tumor growth by (i) preventing the binding of certain fibroblast growth factors, or FGFs, to FGFR2b

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and (ii) directly killing tumor cells in a process called antibody-dependent cell-mediated cytotoxicity, or ADCC. FGFs are a family of related extracellular proteins that normally regulate cell proliferation and survival in humans. They act by binding to and activating FGF receptors, or FGFRs, which are cell surface proteins that transmit growth signals to cells. In preclinical studies, FPA144 was highly effective in blocking the growth of gastric tumors that had abnormally high levels of FGFR2b. FGFR2b is selectively overexpressed in gastric cancer and occurs in an estimated 15% of gastric cancer patients (approximately 5% with fibroblast growth factor receptor 2, or *FGFR2,* gene amplification and an additional 10% with protein overexpression without gene amplification). We are initially developing FPA144 as a monotherapy for refractory gastric cancer, a significant unmet medical need that we think may warrant accelerated development and approval in the United States.

In December 2014, we began a Phase 1 clinical trial of FPA144. We are currently enrolling patients with solid tumors in the dose escalation portion of this trial to explore the safety of FPA144 and to identify a dose for expansion to test in patients with gastric cancer. After we identify the dose for expansion, we plan to enroll gastric cancer patients whose tumors have evidence of FGFR2b over-expression determined using our proprietary immuno-histochemistry, or IHC, assay. *FGFR2* gene amplification will be assessed by a fluorescent in situ hybridization, or FISH, assay. Endpoints of the trial include safety and overall response rate. We expect to complete the dose escalation portion of this trial and begin the expansion portion in gastric cancer patients by the end of 2015. We also plan to present preliminary safety data from this trial by the end of 2015.

If FPA144 demonstrates activity in gastric cancer patients in the Phase 1 trial, we plan to conduct a pivotal trial of FPA144 as a monotherapy in gastric cancer patients and, in a separate Phase 1b trial, test FPA144 in combination with standard of care chemotherapy in newly diagnosed gastric cancer patients.

FP-1039/GSK3052230

FP-1039 is a protein therapeutic that traps and neutralizes cancer-promoting FGFs involved in cancer cell proliferation and new blood vessel formation. These FGFs act by binding to and activating FGFRs. Unlike other therapies that indiscriminately block all FGFs, FP-1039 is designed to only block cancer-promoting FGFs that bind to FGF receptor 1, or FGFR1, and therefore may be associated with better tolerability than other known drug candidates targeting the FGF pathway less selectively. The FGFs trapped by FP-1039 are distinct from those blocked by FPA144.

We have completed a Phase 1 trial of FP-1039, and our partner, GlaxoSmithKline, or GSK, is conducting a three-arm Phase 1b trial:

- Arms A and B are enrolling patients with squamous NSCLC with abnormally high levels of the *FGFR1* gene in the first-line and second-line settings, respectively, and
- Arm C is enrolling patients with newly diagnosed malignant pleural mesothelioma, a tumor associated with abnormally high levels of fibroblast growth factor 2, or FGF2, ligand.

GSK is completing the planned dose escalation portion of Arms A and C, and we expect that the expansion portion of Arms A and C will begin by the end of the first quarter of 2015. We expect GSK to present data from this trial at a scientific meeting by the end of 2015. GSK is responsible for the development and commercialization of FP-1039 in the United States, the European Union and Canada. We have an option to co-promote FP-1039 in the United States.

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Our Pipeline

Our Platform

We have developed a library of more than 5,700 human extracellular proteins, which we believe represent substantially all of the body s medically important targets for protein therapeutics. We screen this comprehensive library with our proprietary high-throughput protein screening technologies to identify new targets for protein therapeutics.

The process of discovering targets for protein therapeutics has historically proven difficult and slow. There are more than 5,700 proteins in the body that represent potential protein therapeutic targets, but only about 30 are targeted by currently marketed protein drugs in cancer and inflammatory diseases. We spent seven years successfully developing a platform to improve and accelerate the protein therapeutic discovery process. We believe our platform improves and accelerates the discovery of new protein targets and protein therapeutics because it can:

- identify novel medically relevant protein targets and protein therapeutics that have little or no previously known biological function or are not in the public domain and cannot easily be discovered by other methods;
- determine the best protein target among many alternatives for a particular disease by screening and comparing nearly all possible medically important targets simultaneously; and
- identify new targets more quickly and efficiently than previously possible because it can produce and test thousands of proteins at a time, rather than one or just a few at a time.

In the past several years we have used this platform to identify dozens of targets validated in rodent models, including in collaboration with our partners, and to build a growing pipeline of drug candidates. We believe our platform is particularly well positioned to explore new pathways in cancer, inflammation and their intersection in immuno-oncology, a growing focus of our discovery and clinical activities. We have attracted numerous partnerships with leading biopharmaceutical companies, and such collaborations have generated approximately $307 million in funding for our business through December 31, 2014.

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Financial Condition

We had cash, cash equivalents and marketable securities of approximately $149 million as of December 31, 2014. We have no products approved for commercial sale and have not generated any revenue from product sales to date, and we continue to incur significant research and development and other expenses related to our ongoing operations. We have incurred losses in each period since our inception in 2002, with the exception of the fiscal year ended 2011 due to collaboration revenues from product candidates under collaboration agreements with third parties. For the nine months ended September 30, 2014 and for the year ended December 31, 2013, we reported a net loss of $25.6 million and $28.9 million, respectively. As of September 30, 2014, we had an accumulated deficit of $177.2 million.

Implications of Being an Emerging Growth Company

We currently qualify as an emerging growth company as defined in the Jumpstart Our Business Startups Act of 2012, or JOBS Act. As an emerging growth company we have taken, and to the extent available may continue to take, advantage of specified reduced disclosure and other requirements that are otherwise applicable generally to other public companies that are not emerging growth companies, including not being required to comply with the auditor attestation requirements of Section 404(b) of the Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved. We cannot predict if investors will find our common stock less attractive because we rely 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 Corporate Information

We were incorporated under the laws of the State of Delaware in December 2001. Our principal executive office is located at Two Corporate Drive, South San Francisco, California 94080, and our telephone number is (415) 365-5600. Our website address is www.fiveprime.com. Our website and the information contained on, or that can be accessed through, the website will not be deemed to be incorporated by reference in, and are not considered part of, this prospectus. You should not rely on any such information in making your decision whether to purchase our common stock.

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THE OFFERING

Common stock to be offered by us	3,410,000 shares
Common stock to be outstanding immediately following this offering	24,938,566 shares
Option to purchase additional shares from us	We have granted the underwriters an option for 30 days from the date of this prospectus supplement to purchase up to an aggregate of 511,500 additional shares of our common stock.
Use of proceeds	We expect to use the net proceeds from this offering to advance clinical development of our FPA008 program in PVNS and immuno-oncology, to advance the clinical development of our FPA144 program, to fund additional research and pre-clinical development activities for our immuno-oncology program and for working capital and general corporate purposes. See Use of Proceeds on page S-11.
Risk factors	You should read the Risk Factors section of this prospectus beginning on page S-8 for a discussion of factors to consider carefully before deciding to invest in shares of our common stock.
NASDAQ Global Select Market symbol	FPRX

The number of shares of common stock outstanding immediately following this offering set forth above is based on 21,528,566 shares of common stock outstanding as of September 30, 2014. This number excludes:

- 2,769,130 shares of our common stock issuable upon the exercise of stock options outstanding as of September 30, 2014, under our 2002 Equity Incentive Plan, or 2002 Plan, our 2010 Equity Incentive Plan, or 2010 Plan, and our 2013 Omnibus Incentive Plan, or 2013 Plan, at a weighted-average exercise price of $7.67 per share;
- 3,393,083 shares of our common stock reserved as of September 30, 2014 for future issuance under our 2013 Plan, as well as any future increases in the number of shares of our common stock reserved for issuance under the 2013 Plan pursuant to evergreen provisions; and
- 367,656 shares of our common stock reserved as of September 30, 2014 for future issuance under our 2013 Employee Stock Purchase Plan, or the ESPP, as well as any future increases in the number of shares of our common stock reserved for issuance under the ESPP pursuant to evergreen provisions.

Unless otherwise indicated, all information in this prospectus assumes:

- no exercise of outstanding stock options since September 30, 2014; and

no exercise of the underwriters option to purchase additional shares.

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RISK FACTORS

You should consider carefully the risks described below, together with other information in this prospectus, and the information and documents incorporated by reference in this prospectus, and any free writing prospectus that we have authorized for use in connection with this offering before you make a decision to invest in our common stock. In particular, you should carefully consider and evaluate the risks and uncertainties described in Part I Item 1A. Risk Factors of our Quarterly Report on Form 10-Q for the quarter ended September 30, 2014, and any subsequent filings with the U.S. Securities and Exchange Commission, or the SEC, that we file after the date of this prospectus, each of which is incorporated by reference in this prospectus in their entirety, and all other information contained or incorporated by reference in this prospectus, as updated by our subsequent filings under the Securities Exchange Act of 1934, as amended, or the Exchange Act. 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 affect our business operations.

Risks Related to this Offering

We have broad discretion in the use of the net proceeds from this offering and may not use them effectively.

Our management will have broad discretion in the application of the net proceeds from this offering, and you will be relying on the judgment of our management regarding the application of these proceeds. You will not have the opportunity, as part of your investment decision, to assess whether we are using the proceeds appropriately. Our management might not apply our net proceeds in ways that ultimately increase the value of your investment. If we do not invest or apply the net proceeds from this offering in ways that enhance stockholder value, we may fail to achieve expected financial results, which could cause our stock price to decline.

If you purchase our common stock in this offering, you will experience immediate and substantial dilution in investment. You will experience further dilution if we issue additional equity securities in future fundraising transactions.

Since the price per share of our common stock being offered is substantially higher than the net tangible book value per share of our common stock, you will suffer immediate and substantial dilution in the net tangible book value of the common stock you purchase in this offering. Based on the public offering price of $22.00 per share and our net tangible book value as of September 30, 2014 of $4.41 per share, if you purchase shares of common stock in this offering, you will suffer immediate and substantial dilution of $15.39 per share with respect to the net tangible book value of the common stock. See the section entitled Dilution below for a more detailed discussion of the dilution you will incur if you purchase common stock in this offering.

In addition, we have a significant number of stock options outstanding. To the extent that outstanding stock options have been or may be exercised, investors purchasing our common stock in this offering may 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 these securities could result in further dilution to our stockholders or result in downward pressure on the price of our common stock.

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, including the documents incorporated by reference herein and therein, and any free writing prospectus that we have authorized for use in connection with this offering contain forward-looking statements, within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act that involve substantial risks and uncertainties. In some cases you can identify these statements by forward-looking words such as believe, may, will, estimate, continue, anticipate, intend, could, would, project, plan, expe expressions, or the negative or plural of these words or expressions. Discussions containing these forward-looking statements may be found, among other places, in Business, Risk Factors and Management s Discussion and Analysis of Financial Condition and Results of Operations incorporated by reference from our most recent Annual Report on Form 10-K and in our most recent Quarterly Report on Form 10-Q filed with the SEC, as well as any amendments thereto reflected in subsequent filings with the SEC. These statements involve risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from the information expressed or implied by these forward-looking statements. These forward-looking statements include, but are not limited to, statements concerning the following:

- our estimates regarding our expenses, revenues, anticipated capital requirements and our needs for additional financing;
- our expected use of proceeds from this offering;
- our or our partners ability to advance drug candidates into, and successfully complete, clinical trials alone or in combination with other drugs;
- the timing of the initiation, progress and results of preclinical studies and research and development programs;
- our expectations regarding the potential safety, efficacy or clinical utility of our product candidates;
- our ability to explore tumor- and blood-based biomarkers with respect to FP008;
- the implementation, timing and likelihood of success of our plans to develop companion diagnostics for our product candidates;
- our ability to maintain and establish collaborations;
- the implementation of our business model, strategic plans for our business, drug candidates and technology;
- the scope of protection we establish and maintain for intellectual property rights covering our drug candidates and technology;
- the size of patient populations targeted by products we or our partners develop and market adoption of our potential products by physicians and patients;
- the timing or likelihood of regulatory filings and approvals;

developments relating to our competitors and our industry; and

our expectations regarding licensing, acquisitions and strategic operations.

In addition, you should refer to the Risk Factors section in this prospectus supplement, or in any free writing prospectuses we may authorize for use in connection with a specific offering, for a discussion of other important factors, risks and uncertainties that may cause our actual results to differ materially from those expressed or implied by these forward-looking statements. Given these other important factors, risks and uncertainties, you should not place undue reliance on these forward-looking statements. Also, these forward-looking statements represent our estimates and assumptions only as of the date such forward-looking statements are made. You should carefully read this prospectus, together with the information incorporated herein by

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reference as described in the section titled Incorporation of Certain Information by Reference, completely and with the understanding that our actual future results may be materially different from what we expect. We can give no assurances that any of the events anticipated by the forward-looking statements will occur or, if any of them do, what impact they will have on our business, results of operations and financial condition.

You should rely only on information contained or incorporated by reference in this prospectus, the registration statement of which this prospectus is a part, including the exhibits that we have filed with the registration statement, or in any free writing prospectuses we may authorize for use in connection with a specific offering. You should understand that our actual future results may be materially different from what we expect. We qualify all of the forward-looking statements in the foregoing documents by these cautionary statements.

Except as required by law, we undertake no obligation to update or revise any forward-looking statements to reflect new information or future events or developments. You should not assume that our silence over time means that actual events are bearing out as expressed or implied in such forward-looking statements. Before deciding to invest, you should carefully consider the risk factors discussed and incorporated by reference in this prospectus, any free writing prospectus and, if required, any post-effective amendment to the registration statement of which this prospectus is a part.

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USE OF PROCEEDS

We expect to receive approximately $70.0 million in net proceeds from the sale of 3,410,000 shares of common stock offered by us in this offering (approximately $80.6 million if the underwriters exercise their option to purchase additional shares in full), after deducting underwriting discounts and commissions, structuring fees and estimated offering expenses payable by us.

We expect to use the net proceeds from this offering to advance clinical development of our FPA008 program in PVNS and immuno-oncology, to advance the clinical development of our FPA144 program, to fund additional research and pre-clinical development activities for our internal immuno-oncology program and for working capital and general corporate purposes.

The expected use of the net proceeds from this offering represents our intentions based upon our current plans and business conditions, which could change in the future as our plans and business conditions evolve. The amounts and timing of our actual expenditures depend on numerous factors, including the progress of our preclinical development efforts, the ongoing status of and results from our clinical trials and other studies and any unforeseen cash needs. As a result, our management will have broad discretion in applying the net proceeds from this offering. Although we may use a portion of the net proceeds from this offering for the licensing or acquisition of, or the development of, additional product candidates, technologies, compounds, other assets or complementary businesses, we have no current understandings, agreements or commitments to do so. Pending their ultimate use, we intend to invest the net proceeds from this offering in interest-bearing, investment-grade securities.

DIVIDEND POLICY

We have never declared or paid any cash dividends on our capital stock and do not anticipate paying any cash dividends in the foreseeable future. Payment of cash dividends, if any, in the future will be at the discretion of our board of directors and will depend on then-existing conditions, including our financial condition, operating results, contractual restrictions, capital requirements, business prospects and other factors our board of directors may deem relevant.

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DILUTION

If you invest in our common stock in this offering, your ownership interest will be immediately diluted to the extent of the difference between the public offering price per share of our common stock and the as adjusted net tangible book value per share of our common stock immediately after this offering. Net tangible book value per share of our common stock is determined at any date by subtracting our total liabilities from the amount of our total tangible assets (total assets less intangible assets) and dividing the difference by the number of shares of our common stock deemed to be outstanding at that date.

Our historical net tangible book value as of September 30, 2014, was approximately $94.9 million, or $4.41 per share, based on 21,528,566 shares of common stock outstanding as of September 30, 2014.

After giving effect to the sale of 3,410,000 shares of our common stock offered by us at the public offering price of $22.00 per share, after deducting underwriting discounts and commissions, structuring fees and estimated offering expenses payable by us, our net tangible book value as of September 30, 2014, would have been approximately $164.9 million, or $6.61 per share of common stock. This represents an immediate increase in net tangible book value of $2.20 per share to existing stockholders and an immediate dilution in net tangible book value of $15.39 per share to new investors purchasing shares of common stock in this offering at the public offering price. The following table illustrates this dilution on a per share basis:

Public offering price per share		$ 22.00
Historical net tangible book value per share as of September 30, 2014	$ 4.41	
Increase in net tangible book value per share attributable to new investors	2.20	
As adjusted net tangible book value per share after this offering		6.61
Dilution per share to new investors purchasing common stock in this offering		$ 15.39

If the underwriters exercise in full their option to purchase up to 511,500 additional shares of common stock at the public offering price of $22.00 per share, the as adjusted net tangible book value after this offering would be $6.89 per share, representing an increase in net tangible book value of $2.48 per share to existing stockholders and immediate dilution in net tangible book value would be $15.11 per share to investors purchasing our common stock in this offering at the public offering price.

The above discussion and table are based on 21,528,566 shares of our common stock outstanding as of September 30, 2014, and excludes:

- 2,769,130 shares of our common stock issuable upon the exercise of stock options outstanding as of September 30, 2014, under our 2002 Plan, our 2010 Plan and our 2013 Plan, at a weighted-average exercise price of $7.67 per share;

- 3,393,083 shares of our common stock reserved as of September 30, 2014 for future issuance under our 2013 Plan, as well as any future increases in the number of shares of our common stock reserved for issuance under the 2013 Plan pursuant to evergreen provisions; and

367,656 shares of our common stock reserved as of September 30, 2014 for future issuance under our ESPP, as well as any future increases in the number of shares of our common stock reserved for issuance under the ESPP pursuant to evergreen provisions.

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MATERIAL U.S. FEDERAL INCOME AND ESTATE TAX CONSEQUENCES TO NON-U.S. HOLDERS

The following summary describes the material U.S. federal income and estate tax consequences of the acquisition, ownership and disposition of our common stock acquired in this offering by Non-U.S. Holders (as defined below). This discussion does not address all aspects of U.S. federal income and estate taxes and does not deal with foreign, state and local consequences that may be relevant to Non-U.S. Holders in light of their particular circumstances, nor does it address U.S. federal tax consequences other than income and estate taxes. Special rules different from those described below may apply to certain Non-U.S. Holders that are subject to special treatment under the Code, such as financial institutions, insurance companies, tax-exempt organizations, broker-dealers and traders in securities, U.S. expatriates, controlled foreign corporations, passive foreign investment companies, corporations that accumulate earnings to avoid U.S. federal income tax, persons that hold our common stock as part of a straddle, hedge, conversion transaction, synthetic security or integrated investment or other risk reduction strategy, partnership and other pass-through entities, and investors in such pass-through entities. Such Non-U.S. Holders are urged to consult their own tax advisors to determine the U.S. federal, state, local and other tax consequences that may be relevant to them. Furthermore, the discussion below is based upon the provisions of the Code, and Treasury regulations, rulings and judicial decisions thereunder as of the date hereof, and such authorities may be repealed, revoked or modified, perhaps retroactively, so as to result in U.S. federal income and estate tax consequences different from those discussed below. We have not requested a ruling from the U.S. Internal Revenue Service, or IRS, with respect to the statements made and the conclusions reached in the following summary, and there can be no assurance that the IRS will agree with such statements and conclusions. This discussion assumes that the Non-U.S. Holder holds our common stock as a capital asset within the meaning of Section 1221 of the Code (generally, property held for investment).

The following discussion is for general information only and is not tax advice. Persons considering the purchase of our common stock pursuant to this offering should consult their own tax advisors concerning the U.S. federal income and estate tax consequences of acquiring, owning and disposing of our common stock in light of their particular situations as well as any consequences arising under the laws of any other taxing jurisdiction, including any state, local or foreign tax consequences.

For the purposes of this discussion, a Non-U.S. Holder is, for U.S. federal income tax purposes, a beneficial owner of common stock that is neither a U.S. Holder, a partnership (or other entity treated as a partnership for U.S. federal income tax purposes regardless of its place of organization or formation), nor an entity that is treated as a disregarded entity for U.S. federal income tax purposes (regardless of its place of organization or formation). A U.S. Holder means a beneficial owner of our common stock that is for U.S. federal income tax purposes (a) an individual who is a citizen or resident of the United States, (b) a corporation or other entity treated as a corporation created or organized in or under the laws of the United States, any state thereof or the District of Columbia, (c) an estate the income of which is subject to U.S. federal income taxation regardless of its source or (d) a trust if it (1) is subject to the primary supervision of a court within the United States and one or more U.S. persons have the authority to control all substantial decisions of the trust or (2) has a valid election in effect under applicable U.S. Treasury regulations to be treated as a U.S. person.

Distributions

Subject to the discussion below, distributions, if any, made on our common stock to a Non-U.S. Holder of our common stock to the extent made out of our current or accumulated earnings and profits (as determined under U.S. federal income tax principles) generally will constitute dividends for U.S. tax purposes and will be subject to withholding tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty. To obtain a reduced rate of withholding under a treaty, a Non-U.S. Holder generally will be required to provide us with a properly executed IRS Form W-8BEN, or other appropriate form, certifying the Non-U.S. Holder s entitlement to benefits under that treaty. In the case of a Non-U.S. Holder that is an entity, Treasury regulations and the relevant tax treaty provide rules to determine whether, for purposes of determining the applicability of a tax treaty, dividends will be treated as paid to the entity or to those holding an interest in that

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entity. If a Non-U.S. Holder holds stock through a financial institution or other agent acting on the holder s behalf, the holder will be required to provide appropriate documentation to such agent. The holder s agent will then be required to provide certification to us or our paying agent, either directly or through other intermediaries. If a Non-U.S. Holder is eligible for a reduced rate of U.S. federal withholding tax under an income tax treaty, the Non-U.S. Holder should contact its tax advisor regarding the possibility of obtaining a refund or credit of any excess amounts withheld by timely filing an appropriate claim for a refund with the IRS.

We generally are not required to withhold tax on dividends paid to a Non-U.S. Holder that are effectively connected with the Non-U.S. Holder s conduct of a trade or business within the United States (and, if required by an applicable income tax treaty, are attributable to a permanent establishment that such holder maintains in the United States) if a properly executed IRS Form W-8ECI, stating that the dividends are so connected, is furnished to us (or, if stock is held through a financial institution or other agent, to such agent). In general, such effectively connected dividends will be subject to U.S. federal income tax, on a net income basis at the regular graduated rates, unless a specific treaty exemption applies. A corporate Non-U.S. Holder receiving effectively connected dividends may also be subject to an additional branch profits tax, which is imposed, under certain circumstances, at a rate of 30% (or such lower rate as may be specified by an applicable treaty) on the corporate Non-U.S. Holder s effectively connected earnings and profits, subject to certain adjustments.

To the extent distributions on our common stock, if any, exceed our current and accumulated earnings and profits, they will constitute a non-taxable return of capital and will first reduce the Non-U.S. Holder s adjusted basis in our common stock, but not below zero, and then will be treated as gain and taxed in the same manner as gain realized from a sale or other disposition of common stock as described in the next section.

Gain on Disposition of Our Common Stock

Subject to the discussion below, a Non-U.S. Holder generally will not be subject to U.S. federal income tax with respect to gain realized on a sale or other disposition of our common stock unless (a) the gain is effectively connected with a trade or business of such holder in the United States (and, if required by an applicable income tax treaty, is attributable to a permanent establishment that such holder maintains in the United States), (b) the Non-U.S. Holder is a nonresident alien individual and is present in the United States for 183 or more days in the taxable year of the disposition and certain other conditions are met, or (c) we are or have been a United States real property holding corporation within the meaning of Code Section 897(c)(2) at any time within the shorter of the five-year period preceding such disposition or such holder s holding period. In general, we would be a United States real property holding corporation if interests in U.S. real estate comprised (by fair market value) at least half of our business assets. We believe that we are not, and do not anticipate becoming, a United States real property holding corporation. Even if we are treated as a United States real property holding corporation, gain realized by a Non-U.S. Holder on a disposition of our common stock will not be subject to U.S. federal income tax so long as (1) the Non-U.S. Holder owned, directly, indirectly and constructively, no more than 5% of our common stock at all times within the shorter of (i) the five-year period preceding the disposition or (ii) the holder s holding period and (2) our common stock is regularly traded on an established securities market. There can be no assurance that our common stock will qualify as regularly traded on an established securities market.

If you are a Non-U.S. Holder described in (a) above, you will be required to pay tax on the net gain derived from the sale at regular graduated U.S. federal income tax rates, unless a specific treaty exemption applies, and corporate Non-U.S. Holders described in (a) above may be subject to the additional branch profits tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty. If you are an individual Non-U.S. Holder described in (b) above, you will be required to pay a flat 30% tax on the gain derived from the sale, which gain may be offset by U.S. source capital losses (even though you are not considered a resident of the United States).

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Information Reporting Requirements and Backup Withholding

Generally, we must report information to the IRS with respect to any dividends we pay on our common stock including the amount of any such dividends, the name and address of the recipient, and the amount, if any, of tax withheld. A similar report is sent to the holder to whom any such dividends are paid. Pursuant to tax treaties or certain other agreements, the IRS may make its reports available to tax authorities in the recipient s country of residence.

Dividends paid by us (or our paying agents) to a Non-U.S. Holder may also be subject to U.S. backup withholding. U.S. backup withholding generally will not apply to a Non-U.S. Holder who provides a properly executed IRS Form W-8BEN or otherwise establishes an exemption. The current backup withholding rate is 28%.

Under current U.S. federal income tax law, U.S. information reporting and backup withholding requirements generally will apply to the proceeds of a disposition of our common stock effected by or through a U.S. office of any broker, U.S. or foreign, except that information reporting and such requirements may be avoided if the holder provides a properly executed IRS Form W-8BEN or otherwise meets documentary evidence requirements for establishing Non-U.S. Holder status or otherwise establishes an exemption. Generally, U.S. information reporting and backup withholding requirements will not apply to a payment of disposition proceeds to a Non-U.S. Holder where the transaction is effected outside the United States through a non-U.S. office of a non-U.S. broker. Information reporting and backup withholding requirements may, however, apply to a payment of disposition proceeds if the broker has actual knowledge, or reason to know, that the holder is, in fact, a U.S. person. For information reporting purposes, certain brokers with substantial U.S. ownership or operations will generally be treated in a manner similar to U.S. brokers.

Backup withholding is not an additional tax. A holder subject to backup withholding should contact the holder s tax advisor regarding the possibility of obtaining a refund or a tax credit and any associated requirements to provide information to the IRS or other relevant tax authority.

Legislation Affecting Taxation of Our Common Stock Held by or Through Foreign Entities

The Foreign Account Tax Compliance Act, or FATCA, which was enacted in 2010, imposes a 30% withholding tax on certain types of payments made to foreign financial institutions and certain other non-U.S. entities unless certain due diligence, reporting, withholding, and certification requirements are satisfied.

The Treasury Department and the IRS have issued final regulations under FATCA. As a general matter, FATCA imposes a 30% withholding tax on dividends on, and gross proceeds from the sale or other disposition of, our common stock if paid to a foreign entity unless either (i) the foreign entity is a foreign financial institution that undertakes certain due diligence, reporting, withholding, and certification obligations, or in the case of a foreign financial institution that is a resident in a jurisdiction that has entered into an intergovernmental agreement to implement FATCA, the entity complies with the diligence and reporting requirements of such agreement, (ii) the foreign entity is not a foreign financial institution and identifies certain of its U.S. investors, or (iii) the foreign entity otherwise is exempted under FATCA. An intergovernmental agreement between the United States and an applicable non-U.S. government may modify these rules.

Pursuant to the delayed effective dates provided for in the final regulations and subsequent guidance, the required withholding with respect to dividends on our common stock began on July 1, 2014 and the required withholding with respect to gross proceeds from a sale or other

disposition of our common stock will begin on January 1, 2017.

If withholding is required under FATCA on a payment related to our common stock, investors that otherwise would not be subject to withholding (or that otherwise would be entitled to a reduced rate of

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withholding) generally will be required to seek a refund or credit from the IRS to obtain the benefit of such exemption or reduction (provided that such benefit is available). Prospective investors should consult their tax advisors regarding the effect of FATCA in their particular circumstances.

Federal Estate Tax

An individual Non-U.S. Holder who is treated as the owner of, or has made certain lifetime transfers of, an interest in our common stock will be required to include the value thereof in his or her gross estate for U.S. federal estate tax purposes, and may be subject to U.S. federal estate tax unless an applicable estate tax treaty provides otherwise, even though such individual was not a citizen or resident of the United States at the time of his or her death.

THE PRECEDING DISCUSSION OF U.S. FEDERAL INCOME AND ESTATE TAX CONSIDERATIONS IS FOR GENERAL INFORMATION ONLY. IT IS NOT TAX ADVICE. EACH PROSPECTIVE INVESTOR SHOULD CONSULT ITS OWN TAX ADVISOR REGARDING THE TAX CONSEQUENCES OF PURCHASING, HOLDING AND DISPOSING OF OUR COMMON STOCK, INCLUDING THE CONSEQUENCES OF ANY PROPOSED CHANGE IN APPLICABLE LAW.

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UNDERWRITING

Citigroup Global Markets Inc., Leerink Partners LLC and Wells Fargo Securities, LLC are acting as joint book-running managers of this offering and as representatives of the underwriters named below. Subject to the terms and conditions stated in the underwriting agreement dated the date of this prospectus supplement, each underwriter named below has severally agreed to purchase, and we have agreed to sell to that underwriter, the number of shares set forth opposite the underwriter s name in the following table.

Underwriters	Number of Shares
Citigroup Global Markets Inc.	1,381,050
Leerink Partners LLC	1,176,450
Wells Fargo Securities, LLC	511,500
Guggenheim Securities, LLC	170,500
Oppenheimer & Co. Inc.	170,500
Total	3,410,000

The underwriting agreement provides that the obligations of the underwriters to purchase the shares included in this offering are subject to approval of legal matters by counsel and to other conditions. The underwriters are obligated to purchase all the shares (other than those covered by the option to purchase additional shares described below) if they purchase any of the shares.

Shares sold by the underwriters to the public will initially be offered at the public offering price set forth on the cover of this prospectus supplement. Any shares sold by the underwriters to securities dealers may be sold at a discount from the public offering price not to exceed $0.792 per share. If all the shares are not sold at the initial offering price, the underwriters may change the offering price and the other selling terms. The representatives have advised us that the underwriters do not intend to make sales to discretionary accounts.

We have granted to the underwriters an option, exercisable for 30 days from the date of this prospectus supplement, to purchase up to 511,500 additional shares at the public offering price less the underwriting discount. To the extent the option is exercised, each underwriter must purchase a number of additional shares approximately proportionate to that underwriter s initial purchase commitment. Any shares issued or sold under the option will be issued and sold on the same terms and conditions as the other shares that are the subject of this offering.

We, our officers, directors and certain of our existing holders of our securities have agreed that, subject to specified limited exceptions, for a period of 90 days from the date of this prospectus supplement, we and they will not, without the prior written consent of the Citigroup Global Markets Inc. and Leerink Partners LLC, dispose of or hedge any shares or any securities convertible into or exchangeable for shares of our common stock. Citigroup Global Markets Inc. and Leerink Partners LLC, in their sole discretion, may release any of the securities subject to these lock-up agreements at any time.

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

The following table shows the underwriting discounts and commissions that we are to pay to the underwriters in connection with this offering. These amounts are shown assuming both no exercise and full exercise of the underwriters option to purchase additional shares.

	Paid by Five Prime Therapeutics, Inc.	
	No Exercise	Full Exercise
Per share	$ 1.32	$ 1.32
Total	$ 4,501,200	$ 5,176,380

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In addition, we have agreed to pay Wells Fargo Securities, LLC, one of the underwriters in this offering, structuring fees of $225,060, equal to 0.30% of the gross proceeds of this offering. We estimate that our portion of the total expenses of this offering will be $500,000. We have also agreed to reimburse the underwriters for certain FINRA-related and other expenses incurred by them in connection with this offering in an amount up to $20,000.

In connection with the offering, the underwriters may purchase and sell shares in the open market. Purchases and sales in the open market may include short sales, purchases to cover short positions, which may include purchases pursuant to the option to purchase additional shares, and stabilizing purchases.

Short sales involve secondary market sales by the underwriters of a greater number of shares than they are required to purchase in the offering.

Covered short sales are sales of shares in an amount up to the number of shares represented by the underwriters option to purchase additional shares.

Naked short sales are sales of shares in an amount in excess of the number of shares represented by the underwriters option to purchase additional shares.

Covering transactions involve purchases of shares either pursuant to the underwriters option to purchase additional shares or in the open market in order to cover short positions.

To close a naked short position, the underwriters must purchase shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the shares in the open market after pricing that could adversely affect investors who purchase in the offering.

To close a covered short position, the underwriters must purchase shares in the open market or must exercise the option to purchase additional shares. In determining the source of shares to close the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the option to purchase additional shares.

Stabilizing transactions involve bids to purchase shares so long as the stabilizing bids do not exceed a specified maximum.

Purchases to cover short positions and stabilizing purchases, as well as other purchases by the underwriters for their own accounts, may have the effect of preventing or retarding a decline in the market price of the shares. They may also cause the price of the shares to be higher than the price that would otherwise exist in the open market in the absence of these transactions. The underwriters may conduct these transactions on The NASDAQ Global Select Market, in the over-the-counter market or otherwise. If the underwriters commence any of these transactions, they may discontinue them at any time.

Relationships

The underwriters are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, principal investment, hedging, financing and brokerage activities. The underwriters and their respective affiliates may, from time to time, engage in transactions with and perform services for us in the ordinary course of their business for which they may receive customary fees and reimbursement of expenses. In the ordinary course of their various business activities, the underwriters and their respective affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (which may include bank loans and credit default swaps) for their own account and for the accounts of their customers and may at any time hold long and short positions in such securities and instruments. Such investments and securities activities may involve securities and instruments of ours or our affiliates. The

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underwriters and their affiliates may also make investment recommendations and publish or express independent research views in respect of such securities or financial instruments and may hold, or recommend to clients that they acquire, long and short positions in such securities and instruments.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act, or to contribute to payments the underwriters may be required to make because of any of those liabilities.

Notice to Prospective Investors in the European Economic Area

In relation to each member state of the European Economic Area that has implemented the Prospectus Directive (each, a relevant member state), with effect from and including the date on which the Prospectus Directive is implemented in that relevant member state (the relevant implementation date), an offer of shares described in this prospectus may not be made to the public in that relevant member state other than:

to any legal entity which is a qualified investor as defined in the Prospectus Directive;

to fewer than 100 or, if the relevant member state has implemented the relevant provision of the 2010 PD Amending Directive, 150 natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the relevant Dealer or Dealers nominated by us for any such offer; or

in any other circumstances falling within Article 3(2) of the Prospectus Directive, provided that no such offer of shares shall require us or any underwriter to publish a prospectus pursuant to Article 3 of the Prospectus Directive.

For purposes of this provision, the expression an offer of securities to the public in any relevant member state means the communication in any form and by any means of sufficient information on the terms of the offer and the shares to be offered so as to enable an investor to decide to purchase or subscribe for the shares, as the expression may be varied in that member state by any measure implementing the Prospectus Directive in that member state, and the expression Prospectus Directive means Directive 2003/71/EC (and amendments thereto, including the 2010 PD Amending Directive, to the extent implemented in the relevant member state) and includes any relevant implementing measure in the relevant member state. The expression 2010 PD Amending Directive means Directive 2010/73/EU.

The sellers of the shares have not authorized and do not authorize the making of any offer of shares through any financial intermediary on their behalf, other than offers made by the underwriters with a view to the final placement of the shares as contemplated in this prospectus. Accordingly, no purchaser of the shares, other than the underwriters, is authorized to make any further offer of the shares on behalf of the sellers or the underwriters.

Notice to Prospective Investors in the United Kingdom

This prospectus is only being distributed to, and is only directed at, persons in the United Kingdom that are qualified investors within the meaning of Article 2(1)(e) of the Prospectus Directive that are also (1) investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, or the Order, or (2) high net worth entities, and other persons to whom it may

lawfully be communicated, falling within Article 49(2)(a) to (d) of the Order (each such person being referred to as a relevant person). This prospectus and its contents are confidential and should not be distributed, published or reproduced (in whole or in part) or disclosed by recipients to any other persons in the United Kingdom. Any person in the United Kingdom that is not a relevant person should not act or rely on this document or any of its contents.

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Notice to Prospective Investors in France

Neither this prospectus nor any other offering material relating to the shares described in this prospectus has been submitted to the clearance procedures of the *Autorité des Marchés Financiers* or of the competent authority of another member state of the European Economic Area and notified to the *Autorité des Marchés Financiers.* The shares have not been offered or sold and will not be offered or sold, directly or indirectly, to the public in France. Neither this prospectus nor any other offering material relating to the shares has been or will be:

- released, issued, distributed or caused to be released, issued or distributed to the public in France; or
- used in connection with any offer for subscription or sale of the shares to the public in France.

Such offers, sales and distributions will be made in France only:

- to qualified investors (*investisseurs qualifiés*) or to a restricted circle of investors (*cercle restreint d investisseurs*), in each case investing for their own account, all as defined in, and in accordance with articles L.411-2, D.411-1, D.411-2, D.734-1, D.744-1, D.754-1 and D.764-1 of the French *Code monétaire et financier*;
- to investment services providers authorized to engage in portfolio management on behalf of third parties; or
- in a transaction that, in accordance with article L.411-2-II-1°-or-2°-or 3° of the French *Code monétaire et financier* and article 211-2 of the General Regulations (*Règlement Général*) of the *Autorité des Marchés Financiers*, does not constitute a public offer (*appel public à l épargne*).

The shares may be resold directly or indirectly, only in compliance with articles L.411-1, L.411-2, L.412-1 and L.621-8 through L.621-8-3 of the French *Code monétaire et financier*.

Notice to Prospective Investors in Hong Kong

The shares may not be offered or sold in Hong Kong by means of any document other than (1) in circumstances which do not constitute an offer to the public within the meaning of the Companies Ordinance (Cap. 32, Laws of Hong Kong), (2) to professional investors within the meaning of the Securities and Futures Ordinance (Cap. 571, Laws of Hong Kong) and any rules made thereunder, or (3) in other circumstances which do not result in the document being a prospectus within the meaning of the Companies Ordinance (Cap. 32, Laws of Hong Kong) and no advertisement, invitation or document relating to the shares may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public in Hong Kong (except if permitted to do so under the laws of Hong Kong) other than with respect to shares which are or are intended to be disposed of only to persons outside Hong Kong or only to professional investors within the meaning of the Securities and Futures Ordinance (Cap. 571, Laws of Hong Kong) and any rules made thereunder.

Notice to Prospective Investors in Japan

The shares offered in this prospectus have not been and will not be registered under the Financial Instruments and Exchange Law of Japan. The shares have not been offered or sold and will not be offered or sold, directly or indirectly, in Japan or to or for the account of any resident of Japan (including any corporation or other entity organized under the laws of Japan), except (1) pursuant to an exemption from the registration requirements of the Financial Instruments and Exchange Law and (2) in compliance with any other applicable requirements of Japanese law.

Notice to Prospective Investors in Singapore

This prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the shares may not be circulated or distributed, nor may the shares be

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offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (1) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore, or the SFA, (2) to a relevant person pursuant to Section 275(1), or any person pursuant to Section 275(1A), and in accordance with the conditions specified in Section 275 of the SFA, or (3) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA, in each case subject to compliance with conditions set forth in the SFA.

Where the shares are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or

a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor, shares, debentures and units of shares and debentures of that corporation or the beneficiaries rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the shares pursuant to an offer made under Section 275 of the SFA except:

to an institutional investor (for corporations, under Section 274 of the SFA) or to a relevant person defined in Section 275(2) of the SFA, or to any person pursuant to an offer that is made on terms that such shares, debentures and units of shares and debentures of that corporation or such rights and interest in that trust are acquired at a consideration of not less than S$200,000 (or its equivalent in a foreign currency) for each transaction, whether such amount is to be paid for in cash or by exchange of securities or other assets, and further for corporations, in accordance with the conditions specified in Section 275 of the SFA;

where no consideration is or will be given for the transfer; or

where the transfer is by operation of law.

Notice to Prospective Investors in Australia

No prospectus or other disclosure document (as defined in the Corporations Act 2001 (Cth) of Australia, or the Corporations Act) in relation to the common stock has been or will be lodged with the Australian Securities & Investments Commission, or ASIC. This document has not been lodged with ASIC and is only directed to certain categories of exempt persons. Accordingly, if you receive this document in Australia:

you confirm and warrant that you are either:

a sophisticated investor under section 708(8)(a) or (b) of the Corporations Act;

a sophisticated investor under section 708(8)(c) or (d) of the Corporations Act and that you have provided an accountant s certificate to us which complies with the requirements of section 708(8)(c)(i) or (ii) of the Corporations Act and related regulations before the offer has been made;

a person associated with the company under section 708(12) of the Corporations Act; or

a professional investor within the meaning of section 708(11)(a) or (b) of the Corporations Act, and to the extent that you are unable to confirm or warrant that you are an exempt sophisticated investor, associated person or professional investor under the Corporations Act any offer made to you under this document is void and incapable of acceptance; and

you warrant and agree that you will not offer any of the common stock for resale in Australia within 12 months of that common stock being issued unless any such resale offer is exempt from the requirement to issue a disclosure document under section 708 of the Corporations Act.

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LEGAL MATTERS

The validity of the shares of our common stock to be issued in this offering will be passed upon for us by our counsel, Hogan Lovells US LLP, Menlo Park, California. Certain legal matters relating to this offering will be passed upon for the underwriters by Cooley LLP, San Francisco, California.

EXPERTS

Ernst & Young LLP, an independent registered public accounting firm, has audited our financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2013, as set forth in their report, which is incorporated by reference in this prospectus supplement. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP s report, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We are currently subject to the reporting requirements of the Exchange Act, and in accordance therewith file periodic reports, proxy statements and other information with the SEC. You may read and copy (at prescribed rates) any such 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 operation of the public reference room. Our SEC filings are also available to you on the SEC s website at www.sec.gov and in the Investors section of our website at www.fiveprime.com. Our website and the information contained on that site, or connected to that site, are not incorporated into and are not a part of this prospectus supplement.

This prospectus supplement and accompanying prospectus are part of a registration statement on Form S-3 we filed with the SEC and do not contain all of the information in the registration statement. The full registration statement may be obtained from the SEC or us, as provided below. Whenever a reference is made in this prospectus supplement or the accompanying prospectus to any of our contracts, agreements or other documents, the reference may not be complete and you should refer to the exhibits that are a part of the registration statement or the exhibits to the reports or other documents incorporated by reference in this prospectus supplement and the accompanying prospectus for a copy of such contract, agreement or other document. You may inspect a copy of the registration statement at the SEC s Public Reference Room in Washington, D.C. or through the SEC s website, as provided above.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC s rules allow us to incorporate by reference information into this prospectus supplement, which means that we can disclose important information to you by referring you to another document filed separately with the SEC. The information incorporated by reference is deemed to be part of this prospectus supplement, and subsequent information that we file with the SEC will automatically update and supersede that information. Any statement in a document we incorporate by reference into this prospectus supplement or the accompanying prospectus will be considered to be modified or superseded to the extent a statement contained in this prospectus supplement or any other subsequently filed document that is incorporated by reference into this prospectus supplement modifies or supersedes that statement. The modified or superseded statement will not be considered to be a part of this prospectus supplement or accompanying prospectus, as applicable, except as modified or superseded.

We incorporate by reference our documents listed below and any future filings made by us with the SEC under Section 13(a), 13(c), 14 or 15(d) of the Exchange Act, including those made after the date of this

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prospectus supplement and until we file a post-effective amendment that indicates the termination of the offering of the securities made by this prospectus supplement. We are not, however, incorporating by reference any documents or portions thereof, whether specifically listed below or filed in the future, that are not deemed filed with the SEC, including any information furnished pursuant to Item 2.02 or 7.01 of Form 8-K or related exhibits furnished pursuant to Item 9.01 of Form 8-K.

This prospectus supplement incorporates by reference the documents set forth below that have previously been filed with the SEC:

- our Annual Report on Form 10-K for the year ended December 31, 2013, which was filed with the SEC on March 26, 2014;
- the information specifically incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2013 from our definitive proxy statement on Schedule 14A filed with the SEC on April 4, 2014;
- our Quarterly Reports on Form 10-Q for the fiscal quarters ended: (i) March 31, 2014, as filed with the SEC on May 12, 2014, and as amended by Form 10-Q/A as filed with the SEC on August 26, 2014; (ii) June 30, 2014, as filed with the SEC on August 7, 2014; and (iii) September 30, 2014, as filed with the SEC on November 12, 2014;
- our Current Reports on Form 8-K, which were filed with the SEC on January 23, 2014, March 19, 2014, May 20, 2014, October 2, 2014, October 23, 2014, November 14, 2014 (two reports), November 18, 2014, November 24, 2014, December 4, 2014 and January 7, 2015; and
- the description of our common stock contained in our registration statement on Form 8-A, which was filed on September 16, 2013, including any amendments or reports filed for the purpose of updating the description

All filings filed by us pursuant to the Exchange Act after the date of the initial filing of the registration statement of which this prospectus is a part and prior to effectiveness of the registration statement shall be deemed to be incorporated by reference into this prospectus.

You may obtain copies of any of these filings by contacting us at the address and telephone number indicated below or by contacting the SEC as described above in the section titled Where You Can Find More Information. Documents incorporated by reference are available from us without charge, excluding all exhibits unless an exhibit has been specifically incorporated by reference into this prospectus supplement, by requesting them in writing or by telephone at:

Five Prime Therapeutics, Inc.

Attention: Aron Knickerbocker, Chief Business Officer

Two Corporate Drive

South San Francisco, California 94080

(415) 365-5750

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PROSPECTUS

$100,000,000

Common Stock

From time to time, we may offer and sell shares of our common stock with total gross proceeds of up to $100,000,000. Each time we offer shares of our common stock, we will provide a supplement to this prospectus that contains specific information about the offering. The supplement may also add, update or change information contained in this prospectus with respect to that offering. We may also authorize one or more free writing prospectuses to be provided to you in connection with an offering. You should carefully read this prospectus, the information incorporated by reference in this prospectus, any prospectus supplement and any related free writing prospectus before you invest.

We may sell shares of common stock directly to investors, to or through one or more underwriters, dealers and agents, or through a combination of these methods. If any underwriters, dealers or agents are involved in the sale of our common stock, their names and any applicable purchase price, fee, commission or discount arrangement between or among them, and any applicable over-allotment options, will be set forth, or will be calculable from the information set forth, in the applicable prospectus supplement. See the sections of this prospectus titled About this Prospectus and Plan of Distribution for more information. **This prospectus may not be used to offer or sell any common stock unless accompanied by a prospectus supplement.**

Our common stock is listed on The NASDAQ Global Select Market under the symbol FPRX. As of December 1, 2014, the closing price of our common stock was $20.28.

Investing in our common stock involves risks. Please see Risk Factors on page 3 and as updated in our future filings made with the Securities and Exchange Commission, which are incorporated by reference in this prospectus.

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

The date of this prospectus is December 8, 2014.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement on Form S-3 that we filed with the U.S. Securities and Exchange Commission, or the SEC, using a shelf registration process. Under this shelf registration process, we may offer and sell shares of our common stock in one or more offerings for total gross proceeds of up to $100,000,000.

Each time that we offer shares of our common stock under this registration statement, we will provide a supplement to this prospectus that contains specific information about the terms of that offering. If there is any inconsistency between the information in this prospectus and the applicable prospectus supplement, you should rely on the prospectus supplement. Before purchasing our common stock, you should carefully read this prospectus, any applicable prospectus supplement and any related free writing prospectus, together with the additional information described under the headings Where You Can Find More Information and Incorporation of Certain Information by Reference.

This prospectus may not be used to offer or sell any common stock unless it is accompanied by a prospectus supplement.

You should rely only on the information incorporated by reference or provided in this prospectus. We have not authorized any other person to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. We will not make an offer to sell common stock in any jurisdiction where the offer or sale is not permitted.

The information appearing in this prospectus, any applicable prospectus supplement or any related free writing prospectus is accurate only as of the date on the front of such document and any information we have incorporated by reference is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of this prospectus, any applicable prospectus supplement or any related free writing prospectus, or any sale of our common stock. Our business, financial condition, results of operations and prospects may have changed since those dates.

This prospectus contains and incorporates by reference, and any prospectus supplement or free writing prospectus may contain and incorporate by reference, market data and industry statistics and forecasts that are based on independent industry publications and other publicly available information. While we believe that each of these studies and publications is reliable, we have not independently verified market and industry data from third-party sources. Although we are not aware of any misstatements regarding the market and industry data presented in this prospectus and the documents incorporated herein by reference, these estimates involve risks and uncertainties and are subject to change based on various factors, including those 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. Accordingly, investors should not place undue reliance on this information.

Except as otherwise indicated herein or as the context otherwise requires, references in this prospectus to Five Prime, the company, we, us, our and similar references refer to Five Prime Therapeutics, Inc. The Five Prime logo and RIPPS® are our registered trademarks. This prospectus also contains registered marks, trademarks and trade names of other companies. All other trademarks, registered marks and trade names appearing in this prospectus are the property of their respective holders.

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PROSPECTUS SUMMARY

This summary contains a general summary of the information contained in this prospectus. It may not include all the information that is important to you. You should read the entire prospectus, the prospectus supplement delivered with the prospectus, if any, and the documents incorporated by reference before making an investment decision.

The Company

We are a clinical-stage biotechnology company focused on discovering and developing novel protein therapeutics. Protein therapeutics are antibodies or drugs developed from extracellular proteins or protein fragments that block disease processes, including for cancer and inflammatory diseases. We have developed a library of more than 5,700 human extracellular proteins, which we believe represent substantially all of the body s medically important targets for protein therapeutics. We screen this comprehensive library with our proprietary high-throughput protein screening technologies to identify new targets for protein therapeutics. This platform has allowed us to develop a pipeline of novel product candidates for cancer and inflammatory diseases and to generate $274.7 million under our collaboration arrangements through September 30, 2014.

Each of our product candidates has an innovative mechanism of action and addresses patient populations for which better therapies are needed. In addition, we are pursuing companion diagnostics for each of our lead programs to allow us to select patients most likely to benefit from treatment and therefore accelerate clinical development and improve patient care. Our most advanced product candidates are as follows:

FP-1039/GSK3052230*, or *FP-1039, is a protein therapeutic that traps and neutralizes cancer-promoting fibroblast growth factors, or FGFs, involved in cancer cell proliferation and new blood vessel formation. FGFs are a family of related extracellular proteins that normally regulate cell proliferation and survival in humans. They act by binding to and activating FGF receptors, or FGFRs, which are cell surface proteins that transmit growth signals to cells. Certain FGFs promote growth of multiple solid tumors by binding and activating FGFRs. Unlike other therapies that indiscriminately block all FGFs, FP-1039 is designed to only block cancer-promoting FGFs and therefore may be associated with better tolerability than other known drug candidates targeting the FGF pathway. We have completed a Phase 1 clinical trial, and our partner, GlaxoSmithKline, or GSK, is conducting a three-arm Phase 1b clinical trial in squamous non-small cell lung cancer (NSCLC) patients with abnormally high levels of *FGFR1* and malignant pleural mesothelioma (MPM) patients. We expect clinical results from the dose escalation phase from one or two arms of this trial by the end of 2014. GSK is responsible for the development and commercialization of FP-1039 in the United States, the European Union and Canada. We have an option to co-promote FP-1039 in the United States.

FPA008 is an antibody that inhibits colony stimulating factor-1 receptor, or CSF1R, and is being developed to treat patients with inflammatory diseases, including rheumatoid arthritis, or RA. CSF1R is a cell surface protein that controls the survival and function of certain immune response cells called monocytes and macrophages. Monocytes and macrophages are commonly involved in the aberrant immune response and inflammatory processes seen in some chronic inflammatory conditions, such as RA. By inhibiting CSF1R activation, FPA008 prevents the production of multiple inflammatory factors, such as tumor necrosis factor, interleukin-6 and interleukin-1, that are individually targeted by approved therapeutics such as *Humira*® (adalimumab), *Actemra*® (tocilizumab) and *Kineret*® (anakinra), respectively. As a result, we believe FPA008 has the potential to have better efficacy than each of these approved drugs. In addition, unlike

currently marketed RA drugs, FPA008 directly inhibits bone-destroying cells called osteoclasts. We began a Phase 1 clinical trial for FPA008 in October 2013 and expect preliminary data, including inflammation and bone turnover biomarker data, from the healthy volunteer portion of this trial by the end of 2014. We plan to begin dosing RA patients in this Phase 1 clinical trial by the end of 2014. We expect to commence clinical development of FPA008 in solid tumors in 2015.

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FPA144 is an antibody that inhibits FGF receptor 2b, or FGFR2b, and is being developed to treat patients with gastric cancer and potentially other solid tumors. In preclinical studies, FPA144 was highly effective in blocking the growth of gastric tumors that had abnormally high levels of FGFR2b. We plan to begin a Phase 1 clinical trial for FPA144 by the end of 2014. We plan to initially test escalating doses of FPA144 in patients with solid tumors and, after dose escalation, begin treating gastric cancer patients with *FGFR2* gene-amplified or FGFR2b over-expressing tumors.

The process of discovering targets for protein therapeutics has historically proven difficult and slow. There are more than 5,700 proteins in the body that represent potential protein therapeutic targets, but only about 30 are targeted by currently marketed protein drugs in cancer and inflammatory diseases. We spent seven years successfully developing a platform to improve and accelerate the protein therapeutic discovery process. Our platform is based on two components:

- a proprietary library of more than 5,700 human extracellular proteins that we believe is the most comprehensive collection of fully functional extracellular proteins available and is an abundant source of medically relevant novel targets for protein therapeutics; and
- proprietary and new technologies for producing and testing thousands of proteins at a time.

We believe our platform improves and accelerates the discovery of new protein targets and protein therapeutics because it can:

- identify novel medically relevant protein targets and protein therapeutics that have little or no previously known biological function or are not in the public domain and cannot easily be discovered by other methods;
- determine the best protein target among many alternatives for a particular disease by screening and comparing nearly all possible medically important targets simultaneously; and
- identify new targets more quickly and efficiently than previously possible because it can produce and test thousands of proteins at a time, rather than one or just a few at a time.

In the past several years we have used this platform to identify dozens of targets validated in rodent models and to build a growing pipeline of drug candidates. We have attracted numerous partnerships with leading biopharmaceutical companies, which have generated $274.7 million in funding for our business through September 30, 2014. Under the FP-1039 license and collaboration agreement with GSK, we are eligible to receive up to $435 million in contingent payments. We also have discovery collaborations with GSK, UCB Pharma, S.A., or UCB, and Bristol-Myers Squibb Company, or BMS, and are eligible to receive potential option exercise fees and contingent payments up to $124.3 million per target under the GSK muscle diseases collaboration, $193.8 million per target under the GSK respiratory diseases collaboration, $92.2 million per target under the UCB fibrosis and CNS collaboration and $300 million per target under our immuno-oncology collaboration with BMS. We believe our platform will continue to provide funding opportunities through product and discovery collaborations.

Our Corporate Information

We were incorporated under the laws of the State of Delaware in December 2001. Our principal executive offices are located at Two Corporate Drive, South San Francisco, California 94080, and our telephone number is (415) 365-5600.

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RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider and evaluate all of the information contained in this prospectus, any accompanying prospectus supplement and any free writing prospectus, and in the documents we incorporate by reference in this prospectus, before you decide to invest. In particular, you should carefully consider and evaluate the risks and uncertainties described in Part I Item 1A. Risk Factors of our most recent Quarterly Report on Form 10-Q, and any subsequent filings with the SEC that we file after the date of this prospectus, and all other information contained or incorporated by reference in this prospectus, as updated by our subsequent filings under the Exchange Act of 1934, as amended, which we refer to as the Exchange Act in this prospectus, and the risk factors and other information contained in the applicable prospectus supplement. Any of the risks and uncertainties set forth therein could materially and adversely affect our business, results of operations and financial condition, which in turn could materially and adversely affect the trading price or value of our common stock. As a result, you could lose all or part of your investment. Please also read carefully the section titled Special Note Regarding Forward-Looking Statements.

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, including the documents incorporated by reference herein and therein, and any free writing prospectus that we have authorized for use in connection with this offering 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 that involve substantial risks and uncertainties. In some cases you can identify these statements by forward-looking words such as believe, may, will, estimate, continue, anticipate, intend, co project, plan, expect, or similar expressions, or the negative or plural of these words or expressions. Discussions containing these forward-looking statements may be found, among other places, in Business, Risk Factors and Management s Discussion and Analysis of Financial Condition and Results of Operations incorporated by reference from our most recent annual report on Form 10-K and in our most recent quarterly report on Form 10-Q filed with the SEC, as well as any amendments thereto reflected in subsequent filings with the SEC. These statements involve risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from the information expressed or implied by these forward-looking statements. These forward-looking statements include, but are not limited to, statements concerning the following:

- our estimates regarding our expenses, revenues, anticipated capital requirements and our needs for additional financing;
- our or our partners ability to advance drug candidates into, and successfully complete, clinical trials alone or in combination with other drugs;
- the timing of the initiation, progress and results of preclinical studies and research and development programs;
- our expectations regarding the potential safety, efficacy or clinical utility of our product candidates;
- the implementation, timing and likelihood of success of our plans to develop companion diagnostics for our product candidates;
- our ability to maintain and establish collaborations;
- the implementation of our business model, strategic plans for our business, drug candidates and technology;
- the scope of protection we establish and maintain for intellectual property rights covering our drug candidates and technology;

the size of patient populations targeted by products we or our partners develop and market adoption of our potential products by physicians and patients;

the timing or likelihood of regulatory filings and approvals;

developments relating to our competitors and our industry; and

our expectations regarding licensing, acquisitions and strategic operations.

In addition, you should refer to the Risk Factors section in the applicable prospectus supplement, or in any free writing prospectuses we may authorize for use in connection with a specific offering, for a discussion of other important factors, risks and uncertainties that may cause our actual results to differ materially from those expressed or implied by these forward-looking statements. Given these other important factors, risks and uncertainties, you should not place undue reliance on these forward-looking statements. Also, these forward-looking statements represent our estimates and assumptions only as of the date such forward-looking statements are made. You should carefully read this prospectus, together with the information incorporated herein by reference as described in the section titled Incorporation of Certain Information by Reference, completely and with the understanding that our actual future results may be materially different from what we expect. We can give no assurances that any of the events anticipated by the forward-looking statements will occur or, if any of them do, what impact they will have on our business, results of operations and financial condition.

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You should rely only on information contained or incorporated by reference in this prospectus, the registration statement of which this prospectus is a part, including the exhibits that we have filed with the registration statement, and the applicable prospectus supplement or in any free writing prospectuses we may authorize for use in connection with a specific offering. You should understand that our actual future results may be materially different from what we expect. We qualify all of the forward-looking statements in the foregoing documents by these cautionary statements.

Except as required by law, we undertake no obligation to update or revise any forward-looking statements to reflect new information or future events or developments. You should not assume that our silence over time means that actual events are bearing out as expressed or implied in such forward-looking statements. Before deciding to invest, you should carefully consider the risk factors discussed and incorporated by reference in this prospectus and any prospectus supplement or free writing prospectus and, if required, any post-effective amendment to the registration statement of which this prospectus is a part.

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USE OF PROCEEDS

Unless otherwise indicated in any prospectus supplement or free writing prospectus, the net proceeds from the sale of our common stock offered by this prospectus will be used for general corporate purposes and working capital requirements. As a result, unless otherwise indicated in the prospectus supplement, our management will have broad discretion to allocate the net proceeds of the offerings. Pending their ultimate use, we intend to invest the net proceeds in a variety of securities, including commercial paper, government and non-government debt securities and/or money market funds that invest in such securities.

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DESCRIPTION OF COMMON STOCK

The following describes the common stock that we may offer under this prospectus, including the material provisions of our amended and restated certificate of incorporation and our amended and restated bylaws, the registration rights agreement to which we and certain of our stockholders are parties and certain provisions of the General Corporation Law of the State of Delaware. Because the following is only a summary, it does not contain all of the information that may be important to you. For a complete description, you should refer to our amended and restated certificate of incorporation, amended and restated bylaws and registration rights agreement, copies of which have been filed with the SEC. See Where You Can Find More Information; Incorporation by Reference.

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, and 10,000,000 shares of preferred stock, $0.001 par value. As of November 30, 2014, there were outstanding:

- 21,633,057 shares of common stock; and
- 2,756,741 shares of common stock subject to outstanding options.

As of November 30, 2014, we had 77 holders of record of our common stock. The actual number of stockholders is greater than this number of record holders, and includes stockholders who are beneficial owners, but whose shares are held in street name by brokers and other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

Common Stock

Voting Rights. Each holder of common stock is entitled to one vote for each share on all matters submitted to a vote of the stockholders. The affirmative vote of holders of substantially 66% of the voting power of all of the then-outstanding shares of capital stock, voting as a single class, will be required to amend certain provisions of our amended and restated certificate of incorporation, including provisions relating to amending our amended and restated bylaws, the classified board, the size of our board, removal of directors, director liability, vacancies on our board, special meetings, stockholder notices, actions by written consent and exclusive jurisdiction.

Dividends. Subject to preferences that may apply to any outstanding preferred stock, holders of our common stock are entitled to receive ratably any dividends that our board of directors may declare out of funds legally available for that purpose.

Liquidation. In the event of our liquidation, dissolution or winding up, holders of our common stock are entitled to share ratably in all assets remaining after payment of liabilities and the liquidation preference of any outstanding preferred stock.

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

Fully Paid and Nonassessable. All outstanding shares of our common stock are fully paid and non-assessable, and the shares of common stock to be issued upon completion of this offering will be fully paid and non-assessable.

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Registration Rights

Holders of 8,879,186 shares of our common stock have the right to demand that we file a registration statement or request that we cover their shares by a registration statement that we otherwise file, as described below.

Demand Registration Rights

The holders of a majority of the shares having demand registration rights may request that we register all or a portion of their shares of common stock for sale under the Securities Act. We will effect the registration as requested, unless, in the good faith judgment of our board of directors, such registration would be materially detrimental to the company and its stockholders and should be delayed. In addition, holders of the shares having demand registration rights may make unlimited requests that we register all or a portion of their common stock for sale under the Securities Act on Form S-3, or any successor form, so long as the aggregate price to the public in connection with any such offering is at least $1 million.

Incidental Registration Rights

In addition, if at any time we register any shares of our common stock, the holders of all shares having piggyback registration rights are entitled to notice of the registration and to include all or a portion of their shares of common stock in the registration.

Other Provisions

In the event that any registration in which the holders of registrable shares participate pursuant to the registration rights agreement is an underwritten public offering, the number of registrable shares to be included may, in specified circumstances, be limited due to market conditions.

For certain of these holders, we will pay all registration expenses, other than underwriting discounts and selling commissions, and the reasonable fees and expenses of a single special counsel for the selling stockholders related to any demand, piggyback and Form S-3 registration. The registration rights agreement contains customary cross-indemnification provisions, pursuant to which we must indemnify the selling stockholders in the event of material misstatements or omissions in the registration statement attributable to us, and they must indemnify us for material misstatements or omissions in the registration statement attributable to them. The demand, piggyback and Form S-3 registration rights described above will expire, with respect to a majority of the shares having registration rights, on September 23, 2017.

Anti-Takeover Provisions

Our Certificate of Incorporation and Bylaws

Our amended and restated certificate of incorporation and amended and restated bylaws include a number of provisions that may deter or impede unsolicited or hostile takeovers or changes of control or management. These provisions include:

Issuance of undesignated preferred stock. Our board of directors has the authority, without further action by the stockholders, to issue up to 10,000,000 shares of undesignated preferred stock with rights and preferences,

including voting rights, designated from time to time by our board of directors. The existence of authorized but unissued shares of preferred stock enables our board of directors to make it more difficult or to discourage an attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise.

Classified board. Our amended and restated certificate of incorporation provides for a classified board of directors consisting of three classes of directors, with staggered three-year terms. Only one class of directors

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will be elected at each annual meeting of our stockholders, with the other classes continuing for the remainder of their respective three-year terms. This provision may have the effect of delaying a change in control of our board.

Board of directors vacancies. Our amended and restated certificate of incorporation and amended and restated bylaws authorize only our board of directors to fill vacant directorships. In addition, the number of directors constituting our board of directors may be set only by resolution adopted by a majority vote of our entire board of directors. These provisions prevent a stockholder from increasing the size of our board of directors and gaining control of our board of directors by filling the resulting vacancies with its own nominees.

Stockholder action; special meetings of stockholders. Our amended and restated certificate of incorporation provides that our stockholders may not take action by written consent, but may only take action at annual or special meetings of our stockholders. Stockholders will not be permitted to cumulate their votes for the election of directors. Our amended and restated certificate of incorporation further provides that only the chairman of our board of directors or a majority of our board of directors may call special meetings of our stockholders.

Advance notice requirements for stockholder proposals and director nominations. Our amended and restated bylaws provide advance notice procedures for stockholders seeking to bring business before our annual meeting of stockholders or to nominate candidates for election as directors at our annual meeting of stockholders. Our amended and restated bylaws also specify certain requirements as to the form and content of a stockholder s notice. These provisions may make it more difficult for our stockholders to bring matters before our annual meeting of stockholders or to nominate directors at annual meetings of stockholders.

We designed these provisions to enhance the likelihood of continued stability in the composition of our board of directors and its policies, to discourage certain types of transactions that may involve an actual or threatened acquisition of us, and to reduce our vulnerability to an unsolicited acquisition proposal. We also designed these provisions to discourage certain tactics that may be used in proxy fights. However, these provisions could have the effect of discouraging others from making tender offers for our shares and, as a consequence, they may also reduce fluctuations in the market price of our shares that could result from actual or rumored takeover attempts.

Section 203 of the General Corporation Law of the State of Delaware

We are subject to Section 203 of the General Corporation Law of the State of Delaware, or DGCL, which prohibits a Delaware corporation from engaging in a business combination with any interested stockholder for a period of three years following the date the person became an interested stockholder, with the following exceptions:

before such date, the board of directors of the corporation approved either the business combination or the transaction that resulted in the stockholder becoming an interested holder;

upon completion of the transaction that resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction began, excluding for purposes of determining the voting stock outstanding (but not the outstanding voting stock owned by the interested stockholder) those shares owned (a) by persons who are

directors and also officers and (b) pursuant to employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; and

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

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In general, Section 203 defines business combination to include the following:

- any merger or consolidation involving the corporation and the interested stockholder;
- any sale, transfer, pledge or other disposition of 10% or more of the assets of the corporation involving the interested stockholder;
- subject to certain exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder;
- any transaction involving the corporation that has the effect of increasing the proportionate share of the stock or any class or series of the corporation beneficially owned by the interested stockholder; or
- the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits by or through the corporation.

In general, Section 203 defines an interested stockholder as an entity or person who, together with such entity s or person s affiliates and associates, beneficially owns, or is an affiliate of the corporation and within three years prior to the time of determination of interested stockholder status did own, 15% or more of the outstanding voting stock of the corporation.

A Delaware corporation may opt out of these provisions with an express provision in its certificate of incorporation. We have not opted out of these provisions, which may as a result discourage or prevent mergers or other takeover or change of control attempts of us.

Choice of Forum

Our amended and restated certificate of incorporation will provide that the Court of Chancery of the State of Delaware will be the exclusive forum for any derivative action or proceeding brought on our behalf, any action asserting a breach of fiduciary duty owed by any director, officer, employee or agent to us or our stockholders, any action asserting a claim against us arising pursuant to the DGCL or our certificate of incorporation or bylaws, any action to interpret, apply, enforce or determine the validity of our certificate of incorporation or bylaws, or any action asserting a claim against us that is governed by the internal affairs doctrine. However, several lawsuits involving other companies have been brought challenging the validity of choice of forum provisions in certificates of incorporation, and it is possible that a court could rule that such provision is inapplicable or unenforceable.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Computershare Trust Company, N.A.

Listing

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

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PLAN OF DISTRIBUTION

We may sell our common stock in any of the ways described below or in any combination or any other way set forth in an applicable prospectus supplement from time to time:

- to or through underwriters or dealers;
- through one or more agents; or
- directly to purchasers or to a single purchaser.

Each time we sell our common stock, we will provide a prospectus supplement (and any related free writing prospectus that we may authorize to be provided to you) that will describe the method of distribution and set forth the offering terms, including the name or names of any underwriters, dealers or agents, the purchase price and the proceeds to us, any over-allotment options under which underwriters may purchase additional common stock from us, any underwriting discounts, commissions and other items constituting underwriters discounts or commissions or agency fees and other items constituting underwriters or agents compensation and any securities exchanges on which our common stock may be listed.

We may use one or more underwriters in the sale of our common stock, in which case the common stock will be acquired by the underwriter or underwriters for their own account and may be resold from time to time in one or more transactions either:

- 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; or
- at negotiated prices.

We may directly solicit offers to purchase our common stock. Agents designated by us from time to time may also solicit offers to purchase our common stock. Any agent designated by us, who may be deemed to be an underwriter as that term is defined in the Securities Act, involved in the offer or sale of our common stock will be named, and any commissions payable by us to such agent will be set forth in the prospectus supplement.

If a dealer is utilized in the sale of our common stock, we will sell the offered securities to the dealer, as principal. The dealer, who may be deemed to be an underwriter as that term is defined in the Securities Act, may then resell our common stock to the public at varying prices to be determined by the dealer at the time of resale.

If an underwriter is, or underwriters are, used in the sale, we will execute an underwriting agreement with the underwriters at the time of sale to the underwriters. The names of the underwriters will be set forth in the prospectus supplement, which will be used by the underwriters to make resales of our common stock to the public. In connection with the sale our common stock, the underwriters may be deemed to have received compensation from us in the form of underwriting discounts or commissions and may also receive commissions from purchasers of our common stock for whom they may act as agents. Underwriters may also sell our common stock to or through dealers, and the dealers may receive compensation in the form of discounts, concessions or commissions from the underwriters and/or commissions from the purchasers for whom they may act as agents.

If so indicated in the applicable prospectus supplement, we will authorize underwriters, dealers or other persons to solicit offers by certain institutions to purchase our common stock from us at the public offering price set forth in the applicable prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on a future date or dates. Institutions with which these contracts may be made include commercial and savings banks, insurance companies, pension funds, investment companies, educational and charitable

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institutions and others. The obligations of any purchasers under any delayed delivery contract will not be subject to any conditions except that:

- the purchase of our common stock shall not at the time of delivery be prohibited under the laws of the jurisdiction to which the purchaser is subject, and
- if our common stock is also being sold to underwriters, we will have sold to the underwriters our common stock not sold for delayed delivery.

The underwriters, dealers and other persons will not have any responsibility in respect of the validity or performance of such contracts. The prospectus supplement relating to the contracts will set forth the price to be paid for our common stock pursuant to the contracts, the commission payable for solicitation of the contracts and the date or dates in the future for delivery of our common stock pursuant to the contracts.

Unless otherwise set forth in the applicable prospectus supplement, the obligations of underwriters to purchase our common stock will be subject to certain conditions precedent and such underwriters will be obligated to purchase all of our common stock, if any shares of our common stock are purchased. In connection with the offering of our common stock, we may grant to the underwriters an option to purchase additional shares of our common stock to cover over-allotments at the offering price, with an additional underwriting commission, as may be set forth in the accompanying prospectus supplement. If we grant any over-allotment option, the terms of such over-allotment option will be set forth in the prospectus supplement.

Underwriters, dealers, remarketing firms and agents may be entitled, under agreements that they may enter into with us, to indemnification by us against certain civil liabilities, including liabilities under the Securities Act, or to contribution with respect to payments which they may be required to make in respect thereof and may engage in transactions with, or perform services for, us in the ordinary course of business.

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 our common stock 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 common stock originally sold by the dealer is purchased in a covering transaction to cover short positions. Those activities may cause the price of our common stock to be higher than it would otherwise be. If commenced, the underwriters may discontinue any of the activities at any time.

The specific terms of any lock-up provisions in respect of any given offering will be described in the applicable prospectus supplement.

The underwriters, dealers and agents may engage in transactions with us, or perform services for us, in the ordinary course of business for which they receive compensation.

The anticipated date of delivery of our common stock will be set forth in the applicable prospectus supplement relating to each offer.

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

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LEGAL MATTERS

The legal validity of the common stock offered by this prospectus will be passed upon for us by Hogan Lovells US LLP, Menlo Park, California. 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

Ernst & Young LLP, an independent registered public accounting firm, has audited our financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2013, as set forth in their report, which is incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP s report, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We are currently subject to the reporting requirements of the Exchange Act, and in accordance therewith file periodic reports, proxy statements and other information with the SEC. You may read and copy (at prescribed rates) any such 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 operation of the public reference room. Our SEC filings are also available to you on the SEC s website at www.sec.gov and in the Investors section of our website at www.fiveprime.com. Our website and the information contained on that site, or connected to that site, are not incorporated into and are not a part of this prospectus.

This prospectus and any prospectus supplement are part of a registration statement that we filed with the SEC and do not contain all of the information in the registration statement. The full registration statement may be obtained from the SEC or us, as provided below. Forms of the indenture and other documents establishing the terms of the offered securities are or may be filed as exhibits to the registration statement. Statements in this prospectus or any prospectus supplement about these documents are summaries and each statement is qualified in all respects by reference to the document to which it refers. You should refer to the actual documents for a more complete description of the relevant matters. You may inspect a copy of the registration statement at the SEC s Public Reference Room in Washington, D.C. or through the SEC s website, as provided above.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC s rules allow us to incorporate by reference information into this prospectus, which means that we can disclose important information to you by referring you to another document filed separately with the SEC. The information incorporated by reference is deemed to be part of this prospectus, and subsequent information that we file with the SEC will automatically update and supersede that information. Any statement contained in a previously filed document incorporated by reference will be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained in this prospectus modifies or replaces that statement.

We incorporate by reference our 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, including those made after the date of the initial filing of the registration statement of which this prospectus is a part and prior to effectiveness of such registration statement, until we file a post-effective amendment that indicates the termination of the offering of the securities made by this prospectus and will become a part of this prospectus from the date that such documents are filed

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with the SEC. We are not, however, incorporating by reference any documents or portions thereof, whether specifically listed below or filed in the future, that are not deemed filed with the SEC, including any information furnished pursuant to Items 2.02 or 7.01 of Form 8-K or related exhibits furnished pursuant to Item 9.01 of Form 8-K.

This prospectus and any accompanying prospectus supplement incorporate by reference the documents set forth below that have previously been filed with the SEC:

- our Annual Report on Form 10-K for the year ended December 31, 2013, which was filed with the SEC on March 26, 2014;
- our Quarterly Reports on Form 10-Q for the fiscal quarters ended: (i) March 31, 2014, as filed with the SEC on May 12, 2014, and as amended by Form 10-Q/A as filed with the SEC on August 26, 2013; (ii) June 30, 2014, as filed with the SEC on August 7, 2014; and (iii) September 30, 2014, as filed with the SEC on November 12, 2014;
- our Current Reports on Form 8-K, which were filed with the SEC on January 23, 2014, March 19, 2014, May 20, 2014, October 2, 2014, October 23, 2014, November 14, 2014 (two reports), November 18, 2014 and November 24, 2014; and
- the description of our common stock contained in our registration statement on Form 8-A, which was filed on September 16, 2013, including any amendments or reports filed for the purpose of updating the description.

All filings filed by us pursuant to the Exchange Act after the date of the initial filing of the registration statement of which this prospectus is a part and prior to effectiveness of the registration statement shall be deemed to be incorporated by reference into this prospectus.

Any statement contained in a document incorporated by reference in this prospectus shall 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 that also is or is deemed to be incorporated by reference in this prospectus modifies or supersedes such statement. Any statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this prospectus.

You may obtain copies of any of these filings by contacting us at the address and telephone number indicated below or by contacting the SEC as described above in the section titled Where You Can Find More Information. Documents incorporated by reference are available from us without charge, excluding all exhibits unless an exhibit has been specifically incorporated by reference into this prospectus, by requesting them in writing or by telephone at:

Five Prime Therapeutics, Inc.

Attention: Aron Knickerbocker, Chief Business Officer

Two Corporate Drive

South San Francisco, California 94080

(415) 365-5750

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3,410,000 Shares

Five Prime Therapeutics, Inc.

Common Stock

PROSPECTUS SUPPLEMENT

Joint Book-Running Managers

Citigroup **Leerink Partners** **Wells Fargo Securities**

Co-Managers

Guggenheim Securities **Oppenheimer & Co.**

January 6, 2015