ACCELERON PHARMA INC
Form 424B5
January 04, 2016

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Subject to completion, dated January 4, 2016

The information in this preliminary prospectus supplement is not complete and may be changed. A registration statement relating to our common stock has become effective under the Securities Act of 1933, as amended. This preliminary prospectus supplement and the accompanying prospectus are not an offer to sell these securities, and we are not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

Filed Pursuant to Rule 424(b)(5)
Registration No. 333-208845

PRELIMINARY PROSPECTUS SUPPLEMENT
(To prospectus dated January 4, 2016)

$150,000,000

Acceleron Pharma Inc.

COMMON STOCK

We are offering shares of our common stock with an aggregate public offering price of approximately $150,000,000.

Our common stock trades on the Nasdaq Global Market under the symbol "XLRN". On December 31, 2015, the last reported sale price of our common stock was $48.76 per share.

Our collaboration partner and one of our principal stockholders, Celgene, has indicated to us an intent to purchase our common stock in this offering at the public offering price, as described under "Underwriting" beginning on page S-43 of this prospectus supplement, in an amount that will result in Celgene increasing its holding to no more than 15% of our total outstanding common stock subsequent to the offering. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters could determine to sell more, less or no shares to this stockholder, and this stockholder could determine to purchase more, less or no shares in this offering.

Investing in our common stock involves risks. See "Risk Factors" beginning on page S-8 of this prospectus supplement, the accompanying prospectus and the other documents that are incorporated by reference herein.

	Per Share	***Total***
Public offering price	*$*	*$*

Underwriting discounts and commissions[(1)]	*$*	*$*
Proceeds, before expenses, to us	*$*	*$*

(1) *We have agreed to reimburse the underwriters for certain expenses incurred in connection with this offering. See "Underwriting."*

The underwriters also have the right to purchase up to an additional $22,500,000 in shares of common stock from us at the public offering price, less the underwriting discounts and commissions, at their option, within 30 days of the date of this prospectus supplement. If the underwriters exercise their option to purchase additional shares in full, the total underwriting discounts and commissions payable by us will be $10,350,000 and the total proceeds, before expenses, to us will be $162,150,000.

You should carefully read this prospectus supplement and the accompanying prospectus, together with the documents we incorporated by reference, before you invest in our stock.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus supplement or the accompanying prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The shares of common stock will be ready for delivery on or about January , 2016.

MORGAN STANLEY *LEERINK PARTNERS* *UBS INVESTMENT BANK*

JMP SECURITIES

The date of this prospectus supplement is January , 2016.

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Prospectus Supplement

Prospectus

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PRESENTATION OF INFORMATION

These offering materials consist of two documents: (1) this prospectus supplement, which describes the terms of the common stock that we are currently offering, and (2) the accompanying prospectus, which provides general information about us. The information in this prospectus supplement supersedes any inconsistent information included or incorporated by reference in the accompanying prospectus.

You should rely only on the information contained or incorporated by reference in this prospectus supplement and the accompanying prospectus and any relevant free writing prospectus. Neither we nor the underwriters have authorized anyone to provide you with information different from that contained in this prospectus supplement and the accompanying prospectus and any relevant free writing prospectus. If you receive any information not authorized by us or the underwriters, you should not rely on it. You should not assume that the information contained or incorporated by reference in this prospectus supplement or the accompanying prospectus or any relevant free writing prospectus is accurate as of any date other than its respective date.

We and the underwriters are offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where offers and sales are permitted. The distribution of this prospectus supplement, the accompanying prospectus or any free writing 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 supplement, the accompanying prospectus or any free writing prospectus must inform themselves about, and observe any restrictions relating to, the offering of the common stock and the distribution of this prospectus supplement, the accompanying prospectus and any free writing prospectus outside the United States. This prospectus supplement, the accompanying prospectus and any free writing prospectus do 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 supplement, the accompanying prospectus or any free writing prospectus by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

It is important for you to read and consider all of the information contained in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference in these documents in making your investment decision. We include cross-references in this prospectus supplement and the accompanying prospectus to captions in these materials where you can find additional related discussions. The table of contents in this prospectus supplement provides the pages on which these captions are located.

Unless the context otherwise requires, "Acceleron", the "Company", "we", "us", "our" and similar names refer to Acceleron Pharma Inc. and its wholly-owned subsidiary. When we refer to "you" we mean the holders of common stock offered hereby.

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NOTE REGARDING FORWARD LOOKING STATEMENTS

This prospectus supplement contains various "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act, which represent our expectations or beliefs concerning future events. Words such as "anticipate", "believe", "contemplate", "continue", "could", "estimate", "expect", "forecast", "goal", "intend", "may", "plan", "potential", "predict", "project", "should", "strategy", "target", "will", "would", "vision", or, in each case, the negative or other variations thereon or other similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

The forward-looking statements in this prospectus supplement include, among other things, statements regarding our intentions, beliefs, projections, outlook, analyses or current expectations concerning, among other things:

- our ongoing and planned preclinical studies and clinical trials;
- clinical trial data and the timing of results of our ongoing clinical trials;
- our plans to develop and commercialize dalantercept and ACE-083, and our and Celgene's plans to develop and commercialize luspatercept and sotatercept;
- the timing of, and our and Celgene's ability to, obtain and maintain regulatory approvals for our therapeutic candidates;
- our commercialization, marketing and manufacturing capabilities and strategy; and
- our estimates regarding our results of operations, financial condition, liquidity, capital requirements, prospects, growth and strategies.

By their nature, forward-looking statements involve risks and uncertainties because they relate to events, competitive dynamics, and industry change and depend on the economic circumstances that may or may not occur in the future or may occur on longer or shorter timelines than anticipated. We caution you that forward-looking statements are not guarantees of future performance and that our actual results of operations, financial condition and liquidity, and events in the industry in which we operate may differ materially from the forward-looking statements contained herein.

Any forward-looking statements that we make in this prospectus supplement speak only as of the date of such statement. You should read carefully the risk factors described in the section "Risk Factors" beginning on page S-8 of this prospectus supplement to better understand the risks and uncertainties inherent in our business and underlying any forward-looking statements.

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INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

We incorporate by reference in this prospectus supplement and the accompanying prospectus the documents listed below and any future filings we make with the Securities and Exchange Commission, or the SEC, under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act (in each case, other than those documents or the portions of those documents not deemed to be filed) until we have sold all of the securities to which this prospectus supplement relates. Any statement in a document incorporated by reference is an important part of this prospectus supplement and the accompanying prospectus. Any statement in a document incorporated by reference in this prospectus supplement and the accompanying prospectus will be deemed to be modified or superseded to the extent a statement contained in this prospectus supplement, the accompanying prospectus or any subsequently filed document that is incorporated by reference in this prospectus supplement and the accompanying prospectus modifies or supersedes such statement.

We incorporate by reference in this prospectus only the documents set forth below that have been previously filed with the SEC:

Our Annual Report on Form 10-K for the year ended December 31, 2014, filed March 2, 2015;

Our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2015, June 30, 2015 and September 30, 2015, filed with the SEC on May 7, 2015, August 6, 2015 and November 4, 2015, respectively;

Our Definitive Proxy Statement on Schedule 14A, filed with the SEC on April 17, 2015;

Our Current Reports on Form 8-K filed with the SEC on March 6, 2015, May 5, 2015 (as amended on May 6, 2015), June 9, 2015, June 15, 2015, September 11, 2015, October 23, 2015, December 10, 2015 and December 17, 2015; and

The description of our common stock contained in our Registration Statement on Form 8-A, filed September 9, 2013, including any amendments or reports filed for the purpose of updating such description.

We will provide without charge to each person to whom a copy of this prospectus supplement is delivered, upon the written or oral request of such person, a copy of any or all of the documents incorporated by reference (other than exhibits to those documents, unless the exhibits are specifically incorporated by reference into those documents). Requests should be directed to:

Acceleron Pharma Inc.
128 Sidney Street
Cambridge, Massachusetts 02139
(617) 649-9200

Copies of these filings are also available, without charge, through the "Investors & Media" section of our website (www.acceleronpharma.com) as soon as reasonably practicable after they are filed electronically with the SEC. The information contained on our website is not a part of this prospectus.

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WHERE YOU CAN FIND MORE INFORMATION

We file annual and quarterly reports, current reports, proxy statements, and other information with the SEC. We make these documents publicly available, free of charge, on our website at www.acceleronpharma.com as soon as reasonably practicable after filing such documents with the SEC.

You may read and copy any materials that we file with the SEC at its Public Reference Room, 100 F Street, N.E., Washington, D.C. 20549. You may obtain information on the operation of the Public Reference Room by calling the SEC at (800) 732-0330. Our filings are also available to the public from the website maintained by the SEC at http://www.sec.gov.

We have filed a Registration Statement on Form S-3 under the Securities Act with the SEC with respect to the securities being offered pursuant to this prospectus supplement. This prospectus supplement and the accompanying prospectus omit certain information contained in the Registration Statement on Form S-3, as permitted by the SEC. Refer to the Registration Statement on Form S-3, including the exhibits, for further information about us and the securities being offered pursuant to this prospectus supplement. Statements in this prospectus supplement and the accompanying prospectus regarding the provisions of documents filed with, or incorporated by reference in, the registration statement are not necessarily complete and each statement is qualified in all respects by that reference. Copies of all or any part of the registration statement, including the documents incorporated by reference or the exhibits, may be obtained upon payment of the prescribed rates at the offices of the SEC listed above and through the SEC's website.

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SUMMARY

This summary highlights selected information included or incorporated by reference in this prospectus supplement and the accompanying prospectus and does not contain all of the information that may be important to you. You should carefully review this entire prospectus supplement and the accompanying prospectus, including the risk factors and financial statements included and incorporated by reference in this prospectus supplement and the accompanying prospectus.

Our Business

Overview

We are a clinical stage biopharmaceutical company focused on the discovery, development and commercialization of novel therapeutic candidates that are based on the mechanisms that the human body uses to regulate the growth and repair of its cells and tissues. Our research focuses on key natural regulators of cellular growth and repair, particularly the Transforming Growth Factor-Beta, or TGF-ß protein superfamily. We believe that we are a leading company in discovering and developing therapeutic candidates that regulate cellular growth and repair. By combining our discovery and development expertise, including our proprietary knowledge of the TGF-ß superfamily, and our internal protein engineering and manufacturing capabilities, we have built a highly productive discovery and development platform that has generated innovative therapeutic candidates with novel mechanisms of action. These differentiated therapeutic candidates have the potential to significantly improve clinical outcomes for patients across many fields of medicine, and we have focused our discovery and development efforts on treatments for cancer and rare diseases.

We have four internally discovered therapeutic candidates that are currently in clinical trials. Luspatercept, our lead program, and sotatercept, are partnered with Celgene Corporation, or Celgene. Celgene is conducting the Phase 3 clinical trials for luspatercept and is responsible for paying 100% of the development costs for all other clinical trials for luspatercept and sotatercept, including our ongoing earlier stage clinical trials for these therapeutic candidates. We may receive up to an additional $560 million of potential development, regulatory and commercial milestone payments and, if these therapeutic candidates are commercialized, we will receive a royalty on net sales in the low-to-mid 20% range. We will co-promote luspatercept and sotatercept, if approved, in North America for which our commercialization costs will be entirely funded by Celgene. We wholly own and are independently developing dalantercept, ACE-083 and our preclinical programs.

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Product Pipeline

Luspatercept

Luspatercept is designed to promote red blood cell production through a novel mechanism, and we are developing luspatercept to treat anemia and associated complications in patients with myelodysplastic syndromes, or MDS, and ß-thalassemia. In December 2015, Celgene initiated two Phase 3 clinical trials with luspatercept: one trial in patients with very low, low and intermediate risk MDS per the Revised International Prognostic Scoring System, the "MEDALIST" trial, and a second trial in regularly transfused patients with ß-thalassemia, the "BELIEVE" trial. We are also conducting two Phase 2 clinical trials of luspatercept for each of MDS and ß-thalassemia.

MDS

With respect to MDS, both our and Celgene's objective is to develop luspatercept as a treatment to increase hemoglobin levels and decrease red blood cell transfusion burden, with patients ultimately becoming transfusion independent. In addition to the Phase 3 clinical trial, we are currently conducting two Phase 2 clinical trials of luspatercept in patients with MDS. The first clinical trial is designed as a two-part trial, with an ascending dose part to evaluate the safety and efficacy in patients with low or intermediate risk MDS per the International Prognostic Scoring System, and an expansion part in which additional patients are enrolled at a selected dose level (3-month base study). We have currently completed enrollment in all of the dose escalation cohorts and we have completed enrollment of patients in the initial expansion cohort of the trial for a total of 58 patients. We have expanded the trial to include two additional cohorts of patients to further evaluate the effects of luspatercept in selected MDS patient populations. All patients enrolled in the base study are eligible to enroll in a second Phase 2 trial (extension study) that permits dosing with luspatercept for up to an additional two years. These trials are being conducted at sites in Germany.

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We believe that preliminary results from the long-term Phase 2 MDS extension study are encouraging. We presented these results, using a data cut-off date of August 31, 2015, at the 57th American Society of Hematology (ASH) Annual Meeting and Exposition in December 2015. As of the cut-off date, a total of 32 patients were treated in the extension study in which luspatercept was administered subcutaneously once every 3 weeks. Of these 32 patients, 13 had a low red blood cell (RBC) transfusion burden (LTB; < 4 units RBC/8 weeks) and 19 had a high transfusion burden (HTB; ≥4 units RBC/8 weeks). 59% of patients had been treated previously with erythropoiesis stimulating agents (ESA) and 19% of patients had previously been treated with lenalidomide. With regard to LTB patients, 9 of 13 (69%) LTB patients achieved the International Working Group (IWG) Hematologic Improvement Erythroid (HI-E) response criterion of a hemoglobin increase ≥1.5 g/dL for ≥8 weeks. With regard to HTB patients, 13 of 19 (68%) HTB patients achieved the IWG HI-E criterion of a reduction of ≥4 units RBC over 8 weeks, and 8 of 19 (42%) HTB patients treated with luspatercept achieved RBC transfusion independence for ≥8 weeks. An additional 3 of 3 (100%) LTB patients with 2 units/8 weeks at baseline achieved RBC transfusion independence for ≥8 weeks. A substantial majority of the patients in the Phase 2 trial had a bone marrow cell morphology referred to as ring sideroblasts and given the encouraging response rates in these patients, the Phase 3 trial has been designed to focus on patients with this particular cellular morphology. The most common adverse events observed in this extension study, which may be related to luspatercept, were bone pain, headache, hypotonia, myalgia and nausea. There were no drug-related serious adverse events.

The Phase 3 MDS MEDALIST trial targets patients with very low, low or intermediate risk MDS with ring sideroblasts who require RBC transfusions. The trial is double-blinded, placebo-controlled and will enroll an estimated 210 patients randomized 2:1, luspatercept versus placebo. In order to enroll in the trial, patients must be: refractory / intolerant to prior erythropoiesis stimulating agents (ESA) or ESA ineligible, ring sideroblast positive, receive a transfusion of at least 2 units of RBCs every 8 weeks confirmed for a minimum of 16 weeks with no consecutive 8-week period free from transfusion, and no prior lenalidomide, hypomethylating agents or immunosuppressive therapy. Patients are excluded from the study if they have del(5q) or secondary MDS. The primary endpoint for efficacy analysis will be the proportion of patients who become RBC-transfusion independent for a period of at least 8 weeks during the first 24 weeks of treatment.

ß-thalassemia

With respect to ß-thalassemia, both our and Celgene's objective is to develop luspatercept as a treatment to increase hemoglobin levels, decrease transfusion burden, decrease iron overload, improve symptoms associated with anemia, and alleviate other disease complications, such as leg ulcers. In addition to the Phase 3 clinical trial, we are currently conducting two Phase 2 clinical trials of luspatercept in patients with ß-thalassemia. The first clinical trial is designed as a two-part trial, with an ascending dose part to evaluate the safety and efficacy of luspatercept in patients with ß-thalassemia, and an expansion part in which additional patients are enrolled at a selected dose level (3-month base study). We have currently completed enrollment and treatment of all of the dose escalation cohorts as well as the expansion cohort of the trial. Patients enrolled in the initial 3-month trial are eligible to enroll in a second Phase 2 trial (extension study) that permits dosing with luspatercept for up to an additional two years. This trial is currently being conducted at sites in Italy and Greece.

We believe the preliminary results from the Phase 2 clinical trials are encouraging. We presented these results, using a data cut-off date of September 25, 2015, at the 57th ASH Annual Meeting and Exposition in December 2015. As of the cut-off date, a total of 64 patients were treated in the dose escalation and expansion cohorts of this study, in which luspatercept was administered subcutaneously, once every 3 weeks. A total of 59 patients were evaluable for efficacy (5 patients were ongoing with <12 weeks treatment). Of these 59 patients, 31 were non-transfusion dependent and 28 were transfusion dependent. Specifically, 22 of 28 (79%) transfusion dependent patients had a ≥20% reduction in transfusion burden, 21 of 28 (75%) had a ≥33% reduction, and 16 of 28 (57%) had a ≥50% reduction over a 12-week period.

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A trend of reduction in liver iron concentration, or LIC, was observed in the majority of non-transfusion dependent patients with or without iron chelation therapy, and in the majority of transfusion dependent patients receiving iron chelation therapy. Improvement in quality of life in non-transfusion dependent patients correlated with increase in hemoglobin. Rapid healing of leg ulcers, a serious complication of ß-thalassemia, was observed in 3 patients, with 2 additional patients experiencing partial healing. The most common related adverse events were bone pain, myalgia, headache, arthralgia, musculoskeletal pain, asthenia, injection site pain, back pain and pain in jaw. There were no drug-related serious adverse events. 6 of 59 (10%) patients discontinued early with an associated adverse event: bone pain (2 patients) and arthralgia, asthenia, cerebrovascular accident and headache (1 patient each).

The Phase 3 ß-thalassemia BELIEVE trial targets adult ß-thalassemia patients who are regularly transfused. The trial is double-blinded and placebo-controlled and will enroll an estimated 300 patients randomized 2:1, luspatercept versus placebo. In order to enroll in the trial, patients must receive 6-20 units RBC transfused over the prior 24 weeks and have no transfusion-free period ≥ 35 days. Patients will be monitored for a 12-week prospective pre-treatment period to calculate baseline transfusion burden. The primary endpoint for efficacy analysis will be the proportion of patients with at least a 33% reduction in transfusion burden during weeks 13 to 24 of the trial compared to the 12 weeks preceding treatment.

Sotatercept

Sotatercept is designed to promote increases in red blood cells as well as bone mineral density. We and Celgene are developing sotatercept for the treatment of chronic kidney disease, or CKD, a disorder characterized by anemia and a mineral and bone disorder that leads to bone loss and cardiovascular disease. The mineral and bone disorder in these patients is not well-managed with current therapies. Studies in mice show that sotatercept may have beneficial effects on fibrotic damage to the kidney and on the development of calcified deposits that may contribute to the elevated risk of heart disease in CKD patients. Data from our ongoing Phase 2 clinical trial in patients with end-stage kidney disease shows that sotatercept may have positive effects on the mineral and bone disorder in these patients and may decrease the accumulation of vascular calcifications. We and Celgene are considering refocusing the sotatercept program on the treatment of patients with earlier, pre-dialysis kidney disease. We expect to meet with the FDA in the first half of 2016 to discuss the initiation of a clinical trial in pre-dialysis patients.

Dalantercept

Our third clinical stage therapeutic candidate, dalantercept, is designed to treat cancers by inhibiting blood vessel formation through a mechanism that is distinct from, and potentially synergistic with, the dominant class of cancer drugs that inhibit blood vessel formation, the vascular endothelial growth factor, or VEGF, pathway inhibitors. We are developing dalantercept primarily for use in combination with VEGF pathway inhibitors to produce better outcomes for cancer patients. Dalantercept in combination with axitinib, a tyrosine kinase inhibitor of the VEGF pathway, in Part 1 of the ongoing Phase 2 clinical trial, or the "DART" trial in patients with renal cell carcinoma, or RCC, produced clinical outcomes that exceed historical results with axitinib alone. We are currently conducting Part 2 of the DART trial, which is a double-blind, placebo-controlled trial, in which an estimated 130 patients are randomized to dalantercept plus axitinib or placebo plus axitinib. We expect to report on progression free survival from Part 2 of the DART trial by the end of 2016. In the open-label Part 1 and blinded Part 2 of the DART trial, the following serious adverse events have been reported as related to dalantercept, dalantercept or placebo (blinded Part 2), or both dalantercept and axitinib: fluid overload, dyspnea, epistaxis, renal injury, acute renal failure and hyponatremia. Non-serious adverse events associated with axitinib did not generally occur with higher than expected frequency or severity. In addition to the DART trial, we are conducting a clinical trial to evaluate the treatment of patients with advanced hepatocellular cancer (HCC) with a combination of dalantercept plus sorafenib, another tyrosine kinase inhibitor of the VEGF pathway. A total of 21 patients have been enrolled as of December 30, 2015. Five patients were initially treated with dalantercept

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0.6 mg/kg and sorafenib 400 mg; 4 of these patients discontinued within 6 weeks of treatment. Sixteen patients were treated with dalantercept 0.4 mg/kg and sorafenib 400 mg; 8 of these patients discontinued within 6 weeks of treatment and 1 within 12 weeks of treatment. Seven of the 16 patients dosed with 0.4 mg/kg dalantercept and sorafenib 400 mg remain in the trial after receiving between 1 and 18 weeks of treatment. In the first quarter of 2016, a safety review team will review the cumulative safety and efficacy data from this trial to determine whether additional patients should be enrolled. The preliminary data indicate a general lack of efficacy for the dalantercept plus sorafenib combination in the treatment of advanced HCC, and therefore we believe that it is unlikely that additional patients will be enrolled in the HCC trial.

ACE-083

Our fourth clinical stage therapeutic candidate, ACE-083, is designed to promote muscle growth and function in specific, targeted muscles. In 2014, we initiated a Phase 1 clinical trial with ACE-083 in healthy volunteers. ACE-083 has been well tolerated and no serious adverse events have been reported. Initial data from the Phase 1 trial showed that, at the highest dose level tested, ACE-083 generated a mean increase in muscle volume of approximately 14.5% in the treated muscle. We have completed enrollment for the ACE-083 Phase 1 clinical trial, and we expect to initiate a Phase 2 clinical trial with ACE-083 in patients with facioscapulohumeral dystrophy, or FSHD, in the second half of 2016.

Preclinical Programs

In addition to our clinical development activities, we are expanding our research capabilities in order to increase the rate at which our highly productive research group can identify and advance new, internally discovered, therapeutic candidates for clinical development. Our discovery efforts are primarily focused on identifying new protein therapeutic candidates from our IntelliTrap™ platform and identifying novel antibodies. We have selected our first IntelliTrap™ therapeutic candidate, ACE-2494, for pre-clinical evaluation and advancement to clinical trials by the end of 2016.

Risk Factors

An investment in our common stock involves a high degree of risk. Any of the factors set forth under "Risk Factors" may limit our ability to successfully execute our business strategy. You should carefully consider all of the information set forth in this prospectus and, in particular, should evaluate the specific factors set forth under "Risk Factors" beginning on page S-8 of this prospectus supplement and in our Annual Report on Form 10-K for the year ended December 31, 2014 in deciding whether to invest in our common stock.

Corporate Information

We were incorporated in the state of Delaware in June 2003 as Phoenix Pharma, Inc., and we subsequently changed our name to Acceleron Pharma Inc. and commenced operations in February 2004. Our principal executive offices are located at 128 Sidney Street, Cambridge, Massachusetts 02139, and our telephone number is (617) 649-9200. Our Internet website is *www.acceleronpharma.com*. The information on, or that can be accessed through, our website is not part of this prospectus, and you should not rely on any such information in making the decision whether to purchase our common stock.

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THE OFFERING

Issuer	Acceleron Pharma Inc.
Securities	3,076,292 shares of common stock based on assumed public offering price of $48.76 per share, the last reported sale price of our common stock on the NASDAQ Global Market on December 31, 2015 (or 3,537,735 shares if the underwriters exercise their option to purchase additional shares of common stock in full).
Common stock outstanding after this offering	36,273,941 shares of common stock based on assumed public offering price of $48.76 per share, the last reported sale price of our common stock on the NASDAQ Global Market on December 31, 2015 (assuming no exercise of the underwriters' option to purchase additional shares).
Public offering price per share	$
Use of proceeds	The net proceeds from this offering are estimated to be approximately $140.4 million (or approximately $161.6 million if the underwriters exercise their option to purchase additional shares in full), after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. We intend to use the net proceeds from this offering to conduct clinical trials and associated activities with ACE-083 and potential therapeutic candidates from our existing research pipeline, to further expand our research and development efforts to expand and advance our pipeline of earlier-stage programs, and for general and administrative expenses (including personnel-related costs), capital expenditures and working capital and other general corporate purposes. See "Use of Proceeds".
U.S. federal income tax consequences	For certain material U.S. federal income tax and estate tax consequences of the holding and disposition of shares of our common stock, see "Material U.S. Tax Considerations for Non-U.S. Holders".
NASDAQ Global Market symbol for our common stock	Our common stock is listed on the NASDAQ Global Market under the symbol "XLRN".

The number of shares of our common stock to be outstanding after the offering is based on 33,197,649 shares of our common stock outstanding as of September 30, 2015, and excludes:

- 3,327,582 shares of common stock issuable upon the exercise of stock options outstanding as of September 30, 2015, at a weighted-average exercise price of $18.57 per share;
- 398,015 shares of common stock issuable upon the exercise of warrants to purchase shares of common stock outstanding as of September 30, 2015, at a weighted-average exercise price of $5.87 per share;
- 524,150 shares of common stock issuable upon vesting of outstanding restricted stock units as of September 30, 2015;

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1,866,889 shares of common stock reserved for future issuance under our 2013 Equity Incentive Plan as of September 30, 2015; and

251,213 shares of common stock reserved for future issuance under our Employee Stock Purchase Plan as of September 30, 2015.

Except as otherwise indicated, all information in this prospectus supplement assumes:

no exercise by the underwriters of their option to purchase up to $22.5 million of additional shares of common stock in this offering; and

no exercise of stock options or warrants and no vesting of restricted stock units after September 30, 2015.

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RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the risks and uncertainties described below in addition to the other information included or incorporated by reference in this prospectus supplement before purchasing our common stock. If any of the following risks actually occurs, our business, financial condition or results of operations would likely suffer, possibly materially. In that case, the trading price of our common stock could fall, and you may lose all or part of the money you paid to buy our common stock. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties not presently known to us or that we currently believe to be immaterial may also adversely affect our business.

Risks Related to this Offering

Our stock price could be extremely volatile and, as a result, you may not be able to resell your shares at or above the price you paid for them.

Since our initial public offering in September 2013, the price of our common stock, as reported on the NASDAQ Global Market, or NASDAQ, has ranged from a low of $16.78 on November 8, 2013 to a high of $57.89 on January 22, 2014. In addition, the stock market in general has been highly volatile. As a result, the market price of our common stock is likely to be similarly volatile, and investors in our common stock may experience a decrease, which could be substantial, in the value of their stock, including decreases unrelated to our operating performance or prospects, and could lose part or all of their investment. The price of our common stock could be subject to wide fluctuations in response to a number of factors, including those described elsewhere in this prospectus and others such as:

- variations in our operating performance and the performance of our competitors;
- actual or anticipated fluctuations in our quarterly or annual operating results;
- publication of research reports by securities analysts about us or our competitors or our industry;
- our failure or the failure of our competitors to meet analysts' projections or guidance that we or our competitors may give to the market;
- additions and departures of key personnel;
- strategic decisions by us or our competitors, such as acquisitions, divestitures, spin-offs, joint ventures, strategic investments or changes in business strategy;
- the passage of legislation or other regulatory developments affecting us or our industry;
- speculation in the press or investment community;
- changes in accounting principles;
- terrorist acts, acts of war or periods of widespread civil unrest;

natural disasters and other calamities; and

changes in general market and economic conditions.

As we operate in a single industry, we are especially vulnerable to these factors to the extent that they affect our industry, or to a lesser extent our markets. In the past, securities class action litigation has often been initiated against companies following periods of volatility in their stock price. This type of litigation could result in substantial costs and divert our management's attention and resources, and could also require us to make substantial payments to satisfy judgments or to settle litigation.

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Your percentage ownership in us may be diluted by future issuances of capital stock, which could reduce your influence over matters on which stockholders vote.

Pursuant to the terms of our certificate of incorporation and amended and restated bylaws, our board of directors has the authority, without action or vote of our stockholders, to issue all or any part of our authorized but unissued shares of capital stock, including shares of our authorized but unissued preferred stock. Issuances of common stock or voting preferred stock would reduce your influence over matters on which our stockholders vote, and, in the case of issuances of preferred stock, would likely result in your interest in us being subject to the prior rights of holders of that preferred stock.

If you purchase shares in this offering, you will suffer immediate and substantial dilution.

If you purchase shares of our common stock in this offering, you will incur immediate and substantial dilution in the as adjusted net tangible book value of your stock of $41.26 per share as of September 30, 2015, based on assumed public offering price of $48.76 per share, the last reported sale price of our common stock on the NASDAQ Global Market on December 31, 2015, because the price that you pay will be substantially greater than the net tangible book value per share of the shares you acquire. You will experience additional dilution upon the exercise of options and warrants to purchase our common stock, as well as upon the vesting of outstanding restricted stock units, including those options currently outstanding and those granted in the future, and the issuance of restricted stock or other equity awards under our stock incentive plans. To the extent we raise additional capital by issuing equity securities, our stockholders will experience substantial additional dilution.

We have broad discretion to determine how to use the funds raised in this offering, and may use them in ways that may not enhance our operating results or the market price of our common stock.

Our management will have broad discretion over the use of proceeds from this offering, and we could spend the proceeds from this offering in ways our stockholders may not agree with or that do not yield a favorable return, if at all. We intend to use the net proceeds from this offering for the development of our product candidates and for other general corporate and working capital purposes. However, our use of these proceeds may differ substantially from our current plans. If we do not invest or apply the proceeds of this offering in ways that improve our operating results, we may fail to achieve expected financial results, which could cause the market price of our common stock to decline.

Our ability to use net operating loss and tax credit carryforwards and certain built-in losses to reduce future tax payments is limited by provisions of the Internal Revenue Code, and it is possible that certain transactions or a combination of certain transactions may result in material additional limitations on our ability to use our net operating loss and tax credit carryforwards.

As of December 31, 2014, we had U.S. federal and state net operating loss carryforwards, or NOL carryforwards, of $211.2 million and $165.0 million, respectively, available to reduce future taxable income, if any. These federal NOL carryforwards expire at various times through 2034 and the state NOL carryforwards expire at various times through 2034. These net operating losses have been fully offset by a valuation allowance due to uncertainties surrounding our ability to realize these tax benefits. In general, if we experience or have experienced a greater than 50 percent aggregate change in ownership of certain significant stockholders over a three-year period, or a Section 382 ownership change, utilization of our pre-change NOL carryforwards will be subject to an annual limitation under Section 382 of the Internal Revenue Code of 1986, as amended (the "Internal Revenue Code"), and similar state laws. Such limitations may result in expiration of a portion of the NOL carryforwards before utilization and may be substantial. If we experience a Section 382 ownership change in connection with this offering or as a result of future changes in our stock ownership, some of which changes are outside our control, the tax benefits related to the NOL carryforwards may be limited or lost.

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Risks Related to Our Financial Position and Need for Additional Capital

We have incurred net operating losses since our inception and anticipate that we will continue to incur substantial operating losses for the foreseeable future. We may never achieve or sustain profitability.

We have incurred net losses during most fiscal periods since our inception. As of September 30, 2015, we had an accumulated deficit of $280.4 million. We do not know whether or when we will become profitable. To date, we have not commercialized any products or generated any revenues from the sale of products, and we do not expect to generate any product revenues in the foreseeable future. Our losses have resulted principally from costs incurred in our discovery and development activities.

We anticipate that our expenses will increase in the future as we expand our discovery, research, development, manufacturing and commercialization activities. However, we also anticipate that these increased expenses will be partially offset by milestone payments we expect to receive under our agreements with Celgene and potentially by payments we may receive under new collaboration arrangements we may enter into with third parties for dalantercept, ACE-083 or other therapeutic candidates. If we do not receive the anticipated milestone payments or do not enter into partnerships for dalantercept, ACE-083 or other therapeutic candidates on acceptable terms, our operating losses will substantially increase over the next several years as we execute our plan to expand our discovery, research, development, manufacturing and commercialization activities. There can be no assurance that we will enter into a new collaboration or achieve milestones and, therefore, no assurance our losses will not increase prohibitively in the future.

To become and remain profitable, we or our partners must succeed in developing our therapeutic candidates, obtaining regulatory approval for them, and manufacturing, marketing and selling those products for which we or our partners may obtain regulatory approval. We or they may not succeed in these activities, and we may never generate revenue from product sales that is significant enough to achieve profitability. Even if we achieve profitability in the future, we may not be able to sustain profitability in subsequent periods. Our failure to become or remain profitable would depress our market value and could impair our ability to raise capital, expand our business, discover or develop other therapeutic candidates or continue our operations. A decline in the value of our company could cause you to lose all or part of your investment.

We will require substantial additional financing to achieve our goals, and a failure to obtain this necessary capital when needed could force us to delay, limit, reduce or terminate our product development or commercialization efforts.

As of September 30, 2015, our cash, cash equivalents and investments were $148.2 million. We believe that we will continue to expend substantial resources for the foreseeable future developing dalantercept, ACE-083 and new therapeutic candidates. These expenditures will include costs associated with research and development, potentially acquiring new technologies, conducting preclinical studies and clinical trials, potentially obtaining regulatory approvals and manufacturing products, as well as marketing and selling products approved for sale, if any. In addition, other unanticipated costs may arise. Because the outcome of our planned and anticipated clinical trials is highly uncertain, we cannot reasonably estimate the actual amounts necessary to successfully complete the development and commercialization of our therapeutic candidates.

Celgene pays development, manufacturing and commercialization and certain patent costs for sotatercept and luspatercept. Other than those costs, our future capital requirements depend on many factors, particularly in connection with the development of our other therapeutic candidates including dalantercept and ACE-083:

- the scope, progress, results and costs of researching and developing our other therapeutic candidates, and conducting preclinical studies and clinical trials;

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- the timing of, and the costs involved in, obtaining regulatory approvals for our other therapeutic candidates if clinical trials are successful;

- the cost of commercialization activities for our other therapeutic candidates, if any of these therapeutic candidates is approved for sale, including marketing, sales and distribution costs;

- the cost of manufacturing our other therapeutic candidates for clinical trials in preparation for regulatory approval and in preparation for commercialization;

- our ability to establish and maintain strategic partnerships, licensing or other arrangements and the financial terms of such agreements;

- the costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing patent claims, including litigation costs and the outcome of such litigation; and

- the timing, receipt, and amount of sales of, or royalties on, our future products, if any.

Based on our current operating plan, we believe that our current cash, cash equivalents and investments, together with the net proceeds from this offering and receipt of anticipated milestone payments will be sufficient to fund our projected operating requirements into the second half of 2019. However, our operating plan may change as a result of many factors currently unknown to us, and we may need additional funds sooner than planned. In addition, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe that we have sufficient funds for our current or future operating plans. Additional funds may not be available when we need them on terms that are acceptable to us, or at all. If adequate funds are not available to us on a timely basis, we may be required to delay, limit, reduce or terminate preclinical studies, clinical trials or other development activities for one or more of our therapeutic candidates or delay, limit, reduce or terminate our establishment of sales and marketing capabilities or other activities that may be necessary to commercialize our therapeutic candidates.

Raising additional capital may cause dilution to our existing stockholders, restrict our operations or require us to relinquish rights to our technologies or therapeutic candidates on unfavorable terms to us.

We may seek additional capital through a variety of means, including through private and public equity offerings and debt financings. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms may include liquidation or other preferences that adversely affect your rights as a stockholder. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take certain actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds through strategic partnerships with third parties, we may have to relinquish valuable rights to our technologies or therapeutic candidates, or grant licenses on terms that are not favorable to us. If we are unable to raise additional funds through equity or debt financing when needed, we may be required to delay, limit, reduce or terminate our product development or commercialization efforts for dalantercept, ACE-083 or any therapeutic candidates other than luspatercept or sotatercept, or grant rights to develop and market therapeutic candidates that we would otherwise prefer to develop and market ourselves.

Risks Related to Regulatory Review and Approval of Our Therapeutic Candidates

If we or our partners do not obtain regulatory approval for our current and future therapeutic candidates, our business will be adversely affected.

Our therapeutic candidates will be subject to extensive governmental regulations relating to, among other things, development, clinical trials, manufacturing and commercialization. In order to obtain regulatory approval for the commercial sale of any therapeutic candidates, we or our partners must demonstrate through extensive preclinical studies and clinical trials that the therapeutic candidate is safe

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and effective for use in each target indication. Clinical testing is expensive, time-consuming and uncertain as to outcome. We or our partners may gain regulatory approval for sotatercept, luspatercept, dalantercept, ACE-083 or any other therapeutic candidate in some but not all of the territories available or some but not all of the target indications or may receive approval with limited labeling or boxed warnings, resulting in limited commercial opportunity for the approved therapeutic candidates, or we or they may never obtain regulatory approval for these therapeutic candidates.

Delays in the commencement, enrollment or completion of clinical trials of our therapeutic candidates could result in increased costs to us as well as a delay or failure in obtaining regulatory approval, or prevent us from commercializing our therapeutic candidates on a timely basis, or at all.

We cannot guarantee that clinical trials will be conducted as planned or completed on schedule, if at all. A failure of one or more clinical trials can occur at any stage of testing. Events that may prevent successful or timely commencement, enrollment or completion of clinical development include:

- delays by us or our current or future partners in reaching a consensus with regulatory agencies on trial design;
- delays in reaching agreement on acceptable terms with prospective clinical research organizations, or CROs, and clinical trial sites;
- delays in obtaining required Institutional Review Board, or IRB, approval at each clinical trial site;
- delays in recruiting suitable patients to participate in clinical trials;
- imposition of a clinical hold by regulatory agencies for any reason, including safety or manufacturing concerns or after an inspection of clinical operations or trial sites;
- failure by CROs, other third parties or us or our current or future partners to adhere to clinical trial requirements;
- failure to perform in accordance with the FDA's good clinical practices, or GCP, or applicable regulatory guidelines in other countries;
- delays in the testing, validation, manufacturing and delivery of the therapeutic candidates to the clinical sites;
- delays caused by patients not completing participation in a trial or not returning for post-treatment follow-up;
- clinical trial sites or patients dropping out of a trial;
- occurrence of serious adverse events in clinical trials that are associated with the therapeutic candidates that are viewed to outweigh its potential benefits; or
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols.

Delays, including delays caused by the above factors, can be costly and could negatively affect our or Celgene's ability to complete a clinical trial. If we or Celgene are not able to successfully complete clinical trials, we will not be able to obtain regulatory approval and will not be able to commercialize our therapeutic candidates.

There is a high risk of clinical failure at any stage of clinical development, and we may never succeed in developing marketable products or generating product revenue.

Our encouraging preclinical and clinical results to date for sotatercept, luspatercept, dalantercept and ACE-083 are not necessarily predictive of the results of our ongoing or future clinical trials. Promising

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results in preclinical studies of a drug candidate may not be predictive of similar results in humans during clinical trials, and successful results from early clinical trials of a drug candidate may not be replicated in later and larger clinical trials or in clinical trials for different indications. If the results of our or our current or future partners' ongoing or future clinical trials are inconclusive with respect to the efficacy of our therapeutic candidates or if we or they do not meet the clinical endpoints with statistical significance or if there are safety concerns or adverse events associated with our therapeutic candidates, we or our partner may be prevented or delayed in obtaining marketing approval for our therapeutic candidates. In addition, data obtained from trials and studies are susceptible to varying interpretations, and regulators may not interpret our data as favorably as we do, which may delay or prevent regulatory approval. Alternatively, even if we or our partners obtain regulatory approval, that approval may be for indications or patient populations that are not as broad as intended or desired or may require labeling that includes significant use or distribution restrictions or safety warnings. We or our partners may also be required to perform additional or unanticipated clinical trials to obtain approval or be subject to additional post-marketing testing requirements to maintain regulatory approval. In addition, regulatory authorities may withdraw their approval of a product or impose restrictions on its distribution, such as in the form of a risk evaluation and mitigation strategy.

If we or our current or future partners fail to obtain regulatory approval in jurisdictions outside the United States, we and they will not be able to market our products in those jurisdictions.

We and our current or future partners intend to market our therapeutic candidates, if approved, in international markets. Such marketing will require separate regulatory approvals in each market and compliance with numerous and varying regulatory requirements. The approval procedures vary from country-to-country and may require additional testing. Moreover, the time required to obtain approval may differ from that required to obtain FDA approval. In addition, in many countries outside the United States, a therapeutic candidate must be approved for reimbursement before it can be approved for sale in that country. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one foreign regulatory authority does not ensure approval by regulatory authorities in other foreign countries or by the FDA. The foreign regulatory approval process may include all of the risks associated with obtaining FDA approval. We or our current or future partners may not obtain foreign regulatory approvals on a timely basis, if at all. We or our partners may not be able to file for regulatory approvals and may not receive necessary approvals to commercialize our products in any market.

We and Celgene regularly request and receive guidance from the FDA and foreign regulators regarding the design or conduct of clinical trials with our therapeutic candidates. This guidance is not binding on these agencies and could change substantially and unpredictably, potentially in a way that makes our clinical trials or our path to regulatory approval longer, more expensive or otherwise more difficult.

Any guidance that we or Celgene receive from the FDA or foreign regulators regarding the design or conduct of our clinical trials is not necessarily indicative of what these regulators will eventually require from us or Celgene to obtain regulatory approval of our therapeutic candidates. These regulators typically caution that any guidance received from them represents their then-current thinking, does not create or confer any rights to us or Celgene, and does not operate to bind the regulator. If later guidance that we or Celgene receive from the FDA or foreign regulators regarding our clinical trial design or conduct is materially different than the current guidance we have received from these regulators, we may need to change our clinical development plans and it may take longer, be more expensive or otherwise be more difficult to obtain FDA or foreign regulatory approval of our therapeutic candidates and our business may be materially harmed.

We undertake no obligation to disclose guidance that we or Celgene may receive from the FDA or foreign regulators. Any guidance from the FDA or foreign regulators that we may disclose publicly speaks

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only as of the date of such disclosure. We undertake no obligation to update any disclosure we make regarding regulator guidance to reflect additional regulatory guidance received after the date of such disclosure or to reflect the occurrence of unanticipated events that may affect the guidance.

Even if we or our current or future partners receive regulatory approval for our therapeutic candidates, such products will be subject to ongoing regulatory review, which may result in significant additional expense. Additionally, our therapeutic candidates, if approved, could be subject to labeling and other restrictions, and we or our current or future partners may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our products.

Any regulatory approvals that we or our current or future partners receive for our therapeutic candidates may also be subject to limitations on the approved indicated uses for which the product may be marketed or to conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials, and surveillance to monitor safety and efficacy. In addition, if the FDA approves any of our therapeutic candidates, the manufact