ACCELERON PHARMA INC
Form 8-K
December 03, 2018

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): December 1, 2018

ACCELERON PHARMA INC.
(Exact name of Registrant as specified in its charter)

Delaware	001-36065	27-0072226
(State or other jurisdiction of incorporation)	(Commission File Number)	(I.R.S. Employer Identification Number)

128 Sidney Street Cambridge, MA	02139
(Address of principal executive offices)	(Zip Code)

Registrant's telephone number, including area code: (617) 649-9200

Not Applicable
(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

o Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
o Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
o Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
o Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company o

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. o

Item 7.01 Regulation FD Disclosure.

On December 1, 2018, Acceleron Pharma Inc. ("Acceleron") and Celgene Corporation ("Celgene") announced results from the pivotal, phase 3 trial (BELIEVE) evaluating the safety and efficacy of luspatercept for the treatment of adults with beta-thalassemia-associated anemia who require regular red blood cell (RBC) transfusions. The data were presented by Maria Domenica Cappellini, M.D. in an oral session of the 60th American Society of Hematology (ASH) Annual Meeting and Exposition in San Diego, CA. A copy of the presentation is attached as Exhibit 99.1 to this Current Report on Form 8-K.

On December 2, 2018, Acceleron and Celgene announced results from the pivotal, phase 3 MEDALIST trial evaluating the efficacy and safety of investigational luspatercept to treat patients with ring sideroblast (RS+) myelodysplastic syndromes (MDS)-associated anemia who require red blood cell transfusions and who had failed, were intolerant to, or ineligible for erythropoietin therapy. Results were presented by Alan F. List, M.D. of the Moffitt Cancer Center during the Plenary Scientific Session at the 60th ASH Annual Meeting and Exposition in San Diego, CA. A copy of the presentation is attached as Exhibit 99.2 to this Current Report on Form 8-K.

On December 3, 2018, Acceleron will host a previously announced conference call and live audio webcast to review the MEDALIST and BELIEVE phase 3 trial presentations of luspatercept that were presented at the 60th ASH Annual Meeting and Exposition in San Diego, CA.

A copy of this slide presentation to be presented during the conference call and webcast on December 3, 2018 is attached as Exhibit 99.3 to this Current Report on Form 8-K.

The information contained in Item 7.01 of this Current Report on Form 8-K and Exhibits 99.1, 99.2, and 99.3 attached hereto are being furnished and shall not be deemed “filed” for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the “Exchange Act”) or for any other purpose, and shall not be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, regardless of any general incorporation language in any such filing, except as expressly set forth by specific reference in such a filing.

Item 8.01 Other Events.

BELIEVE Data

BELIEVE met the primary endpoint of erythroid response, defined as a ≥33% reduction in RBC transfusion burden (with a reduction of ≥ 2 units of RBC) during weeks 13-24 compared to the baseline 12-week interval prior to randomization. The study also included secondary endpoints that evaluated the impact of treatment on RBC transfusion burden. Mean change in transfusion burden from baseline to weeks 13-24 (luspatercept vs. placebo) was -1.35 RBC units.

RBC Transfusion Burden Reduction of ≥ 33% Response Rates[1]

Response Time Interval	Luspatercept	Placebo	P-value
Weeks 13-24	21.4% (48/224)	4.5% (5/112)	< 0.0001
Weeks 37-48	19.6% (44/224)	3.6% (4/112)	< 0.0001
Any 12 weeks during the entire treatment period	70.5% (158/224)	29.5% (33/112)	< 0.0001
Any 24 weeks during the entire treatment period	41.1% (92/224)	2.7% (3/112)	< 0.0001

RBC Transfusion Burden Reduction of ≥ 50% Response Rates[1]

Response Time Interval	Luspatercept	Placebo	P-value
Weeks 13-24	7.6% (17/224)	1.8% (2/112)	0.0303

Weeks 37-48	10.3% (23/224)	0.9% (1/112)	0.0017
Any 12 weeks during the entire treatment period	40.2% (90/224)	6.3% (7/112)	< 0.0001
Any 24 weeks during the entire treatment period	16.5% (37/224)	0.9% (1/112)	< 0.0001

[1]RBC transfusion burden reduction response rates are calculated versus baseline (i.e., the 12 weeks prior to randomization)

BELIEVE Safety Summary (Safety Population)

Grade 3 or higher treatment-emergent adverse events (TEAEs) were reported in 29.1% (65/223) of patients receiving luspatercept and 15.6% (17/109) of patients receiving placebo. Serious adverse events were reported in 15.2% (34/223) of patients receiving luspatercept and 5.5% (6/109) of patients receiving placebo. A TEAE of acute cholecystitis resulted in death in one placebo-treated patient (0.9%). No luspatercept-treated patients died due to TEAEs.

Grade 3 or 4 TEAEs in at least 1% of patients in either arm

	Luspatercept N= 223	Placebo N= 109
Anemia	3.1%	0.0%
Increased liver iron concentration	2.7%	0.9%
Hyperuricemia	2.7%	0.0%
Hypertension	1.8%	0.0%
Syncope	1.8%	0.0%
Back pain	1.3%	0.9%
Bone pain	1.3%	0.0%
Blood uric acid increased	1.3%	0.0%
Increased aspartate aminotransferase	1.3%	0.0%
Increase alanine aminotransferase	0.9%	2.8%
Thromboembolic events*	0.9%	0.0%

*All grades of thromboembolic events, including DVT, PE, portal vein thrombosis, ischemic stroke, thrombophlebitis, and superficial phlebitis were reported in 8 of 223 (3.6%) luspatercept-treated versus 1 of 109 (0.9%) placebo-treated patients

MEDALIST Data

MEDALIST met the primary endpoint of red blood cell transfusion independence (RBC-TI) for 8 or more weeks during the first 24 weeks of the study. Treatment with luspatercept resulted in a statistically significantly greater proportion of patients achieving RBC-TI ≥ 8 weeks compared to placebo. The study also found in secondary endpoints that treatment with luspatercept resulted in a statistically significant higher percentage of patients achieving RBC-TI of 12 or more weeks in the first 24 or 48 weeks of the study, as well as hematologic improvement-erythroid (HI-E) of 8 or more weeks.

Endpoints	Luspatercept	Placebo	P-Value
RBC-TI ≥8 weeks (weeks 1-24)	37.9% (58/153)	13.2% (10/76)	< 0.0001
RBC-TI ≥12 weeks (weeks 1-24)	28.1% (43/153)	7.9% (6/76)	0.0002
RBC-TI ≥12 weeks (weeks 1-48)	33.3% (51/153)	11.8% (9/76)	0.0003
HI-E ≥ 8 weeks (IWG 2006, weeks 1-24)	52.9% (81/153)	11.8% (9/76)	< 0.0001

MEDALIST Safety Summary

Treatment-emergent adverse events (TEAEs) of Grade 3 or 4 were reported in 42.5% (65/153) of patients receiving luspatercept and 44.7% (34/76) of patients receiving placebo. Progression to acute myeloid leukemia (AML) occurred in four patients, three patients (2.0%) receiving luspatercept and one patient (1.3%) receiving placebo. Five patients receiving luspatercept (3.3%) and four patients receiving placebo (5.3%) experienced one or more TEAE that resulted in death.

Most common TEAEs of any Grade in Greater than 10% of Patients in Either Arm

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	Luspatercept N=153	Placebo N=76
Fatigue	26.8%	13.2%
Diarrhea	22.2%	9.2%
Asthenia	20.3%	11.8%
Nausea	20.3%	7.9%
Dizziness	19.6%	5.3%
Back pain	19.0%	6.6%

Luspatercept is not approved in any region for any indication. The companies are planning regulatory application submissions of luspatercept in the United States and Europe in the first half of 2019.

About BELIEVE

BELIEVE is a phase 3, randomized, double blind, placebo-controlled multicenter study comparing luspatercept + best supportive care (BSC) versus placebo + BSC in adult beta-thalassemia patients who require regular RBC transfusions. The median age of the patients was 30 years in both treatment arms. 336 patients were randomized 2:1 to receive either luspatercept 1.0 mg/kg + BSC (224 patients) or placebo + BSC (112 patients) every 3 weeks for up to 48 weeks. Patients in the luspatercept + BSC arm were able to be titrated up to 1.25 mg/kg of luspatercept every 3 weeks. BSC was defined as RBC transfusions and iron chelation therapy to maintain each patient's baseline hemoglobin level. Crossover to the luspatercept treatment group was allowed after unblinding and assessment by an independent Data Safety Monitoring committee; patients receiving luspatercept + BSC will be followed for up to 3 years. The study was conducted at 65 sites in 15 countries.

About MEDALIST

MEDALIST is a phase 3, randomized, double blind, placebo-controlled, multi-center study evaluating the safety and efficacy of luspatercept in patients with very low-, low-, or intermediate-risk non-del(5q) myelodysplastic syndromes (MDS). All patients were RBC transfusion dependent and were either refractory or intolerant to prior erythropoiesis-stimulating agent (ESA) therapy, or were ESA naïve with endogenous serum erythropoietin ≥ 200 U/L, and had no prior treatment with disease modifying agents. The median age of the patients enrolled in the trial was 71 years in the luspatercept treatment group and 72 years in the placebo group. Median transfusion burden in both treatment arms was 5 RBC units/8 weeks. 229 patients were randomized to receive either luspatercept 1.0 mg/kg (153 patients) or placebo (76 patients) via subcutaneous injection once every 21 days. The study was conducted at 65 sites in 11 countries.

About Luspatercept

Luspatercept is a first-in-class erythroid maturation agent (EMA) that is believed to regulate late-stage red blood cell maturation. Acceleron and Celgene are jointly developing luspatercept as part of a global collaboration. Phase 3 clinical trials continue to evaluate the safety and efficacy of luspatercept in patients with MDS (the MEDALIST trial) and in patients with beta-thalassemia (the BELIEVE trial). A COMMANDS phase 3 trial in first-line, lower-risk, MDS patients, the BEYOND phase 2 trial in non-transfusion-dependent beta-thalassemia, and a phase 2 trial in myelofibrosis are ongoing. For more information, please visit www.clinicaltrials.gov.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

Exhibit Number Description of Exhibit

99.1	Slide presentation of BELIEVE data dated December 1, 2018
99.2	Slide presentation of MEDALIST data dated December 2, 2018
99.3	Slide presentation of Acceleron Pharma Inc. dated December 3, 2018

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

ACCELERON PHARMA INC.

By: /s/ John D. Quisel, J.D., Ph.D.
John D. Quisel, J.D., Ph.D.
Executive Vice President and Chief Business Officer

Date: December 3, 2018