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): October 21, 2018

AEGLEA BIOTHERAPEUTICS, INC.
(Exact name of registrant as specified in its charter)

Delaware	001-37722	46-4312787
(State or other jurisdiction of incorporation)	(Commission File Number)	(IRS Employer Identification No.)

901 S. MoPac Expressway Barton Oaks Plaza One Suite 250 Austin, TX	78746
(Address of principal executive offices)	(Zip Code)

(512) 942-2935
(Registrant's telephone number, including area code)

(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:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ 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 ☒

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. ☒

Item 7.01 Regulation FD Disclosure.

On October 21, 2018, Aeglea BioTherapeutics, Inc. (the "Company") presented a poster at the European Society for Medical Oncology (ESMO) 2018 Congress in Munich, Germany, being held October 19-23, 2018 announcing clinical data for Pegzilarginase in advanced melanoma patients and issued a press release highlighting the clinical data shortly thereafter. A copy of the press release and presentation poster are attached as Exhibits 99.1 and 99.2 to this report, respectively. The presentation poster will also be available on the Company's website in the Events & Presentations section at www.aegleabio.com.

The information furnished with this report, including Exhibits 99.1 and 99.2, shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended ("Exchange Act"), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference into any other filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such a filing.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit Number	Description
99.1	Press Release issued by Aeglea BioTherapeutics, Inc., on October 22, 2018
99.2	Presentation Poster

SIGNATURE

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.

AEGLEA BIOTHERAPEUTICS, INC.

Date: October 22, 2018

By: /s/ Charles N. York II
Charles N. York II
Chief Financial Officer

Exhibit 99.1

Aeglea BioTherapeutics Announces Positive Interim Clinical Data for Pegzilarginase in Advanced Melanoma Patients at the European Society for Medical Oncology 2018 Congress

Pegzilarginase Monotherapy Demonstrates Anti-Tumor Activity

Austin, Texas, October 22, 2018 - Aeglea BioTherapeutics, Inc. (NASDAQ: AGLE), a clinical-stage biotechnology company that designs and develops innovative human enzyme therapeutics for patients with rare genetic diseases and cancer, today announced that it presented positive clinical data for pegzilarginase in melanoma patients at the European Society for Medical Oncology (ESMO) 2018 Congress in Munich, Germany. The poster, titled "Initial cohort expansion results of sustained arginine depletion with Pegzilarginase in melanoma patients in a phase 1 advanced solid tumor trial," was presented on October 21. Clinical data from the Company's ongoing Phase 1 clinical trial investigating pegzilarginase as a single agent includes expansion cohorts for cutaneous melanoma and uveal melanoma.

"This ongoing clinical study of pegzilarginase demonstrated single agent anti-tumor activity in what is a difficult-to-treat population of heavily pre-treated melanoma patients," said James Wooldridge, M.D., chief medical officer of Aeglea. "These findings are in line with expectations from our single agent preclinical studies. Given the significant synergies we observed in preclinical studies with immune checkpoint inhibitors, we look forward to data readouts from the Phase 1/2 combination clinical trial."

Data highlights from ESMO 2018:

- Pegzilarginase demonstrated single agent anti-tumor activity in patients with advanced melanoma
    - Of the 28 patients included in the two cohorts, there was one confirmed partial response (PR) and eight patients with stable disease (SD). Six patients remained on treatment at the time of the data cutoff.
    - Anti-tumor activity appeared greater in patients with tumors that lack ASS1 (argininosuccinate synthetase 1) expression, which is consistent with preclinical studies that suggest tumors lacking ASS1 expression are dependent on extracellular arginine for survival.
- Pegzilarginase rapidly and sustainably depleted plasma arginine with a manageable safety profile, treatment related adverse events were grade three or lower

About Pegzilarginase in Cancer
Pegzilarginase is an enhanced human arginase that enzymatically degrades the amino acid arginine. In some cancers, tumor cells stop producing specific amino acids and must acquire them from the blood, making the tumor cells susceptible to starvation through depletion of those amino acids. Aeglea is developing pegzilarginase to exploit vulnerabilities in some cancers that lead to an increased dependency on extracellular arginine. Pegzilarginase targets these arginine dependent cancers by depleting blood arginine levels to below the normal range. Preclinical data demonstrated that the resulting arginine starvation inhibits proliferation, induces cell death, increases turnover of cell components and promotes anti-tumor immune responses. The Company's Phase 1 data in advanced solid tumors demonstrated that pegzilarginase was well tolerated at doses that produced marked and sustained reductions in blood arginine levels below the normal range.

About Aeglea BioTherapeutics
Aeglea is a clinical-stage biotechnology company that designs and develops innovative human enzyme therapeutics for patients with rare genetic diseases and cancer. The Company is developing pegzilarginase, its lead investigational therapy, for the treatment of Arginase 1 Deficiency, as monotherapy in arginine-dependent cancers and in combination with an immune checkpoint inhibitor for small cell lung cancer. In addition, Aeglea has an active research pipeline of other human enzyme-based approaches in both therapeutic areas. For more information, please visit http://aegleabio.com.

Safe Harbor / Forward Looking Statements
This press release contains "forward-looking" statements within the meaning of the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995. Forward-looking statements can be identified by words such as: "anticipate," "intend," "plan," "goal," "seek," "believe," "project," "estimate," "expect," "strategy," "future," "likely," "may," "should," "will" and similar

references. These statements are subject to numerous risks and uncertainties that could cause actual results to differ materially from what we expect. Examples of forward-looking statements include, among others, the potential therapeutic benefits and economic value of our lead product candidate or other product. Further information on potential risk factors that could affect our business and its financial results are detailed in our most recent Quarterly Report on Form 10-Q for the quarter ended June 30, 2018 filed with the Securities and Exchange Commission (SEC), and other reports as filed with the SEC. We undertake no obligation to publicly update any forward-looking statement, whether written or oral, that may be made from time to time, whether as a result of new information, future developments or otherwise.

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Exhibit 99.2

1269P

Abstract # 2668

Initial cohort expansion results of sustained arginine depletion with Pegzilarginase in melanoma patients in a phase 1 advanced solid tumor trial

Bartosz Chmielowski[1], Michael Gordon[2], Elizabeth I. Buchbinder[3], Ryan J. Sullivan[4], Justine V. Cohen[4], Brendan D. Curti[5], Diwakar Davar[6], Jade Homsi[7], Kimberly M. Komatsubara[8], Humberto Lara-Guerra[9], Susan E. Alters[9], Silvia Ferrati[9], Susan L. Potts[9], Stephen Eckert[9], Scott W. Rowlinson[9], James E. Wooldridge[9], Antoni Ribas[1], Richard D. Carvajal[8]

[1]Jonsson Comprehensive Cancer Center at UCLA, Los Angeles, CA, US; [2]HonorHealth Virginia G Piper Cancer Care Network, Scottsdale, AZ, US; [3]Dana-Farber Cancer Institute, Boston, MA, US; [4]Massachusetts General Hospital, Boston, MA, US; [5]Providence Caner Institute, Portland, OR, US; [6]University of Pittsburgh, Pittsburgh, PA, US; [7]UT Southwestern Medical Center, Dallas, TX, US; [8]Norbert Irving Comprehensive Cancer Center, New York, NY, US; [9]Aeglea Biotherapeutics, Austin, TX, US

Background

- Tumors without argininosuccinate synthetase 1 (ASS1) expression are dependent on extracellular arginine
- Pegzilarginase is an engineered human arginase I that depletes plasma arginine

Pegzilarginase mechanism of action

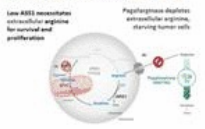

Figure 1 Urea cycle and Pegzilarginase

- Pegzilarginase alone:
  - Induced tumor autophagy,
  - Enhanced CD8+ T cell tumor infiltration
  - Demonstrated in vivo anti-tumor activity in PDx models with no or low expression of ASS1, including:
    - Melanoma
    - Small cell lung carcinoma
    - Large cell non-small cell lung carcinoma
    - Merkel carcinoma
- Pegzilarginase and immune checkpoint inhibitors were synergistic in syngeneic pre-clinical models

Study Methods

- Phase 1 dose escalation followed by expansion cohorts (NCT02561234)
- The MTD was 0.33 mg/kg IV once weekly[1]
- Expansion cohorts included patients with:
  - Unresectable, locally advanced or metastatic cutaneous melanoma (CM) that has relapsed, progressed, or unable to tolerate standard of care
  - Metastatic uveal melanoma (UM)
- We present the preliminary safety and activity of monotherapy pegzilarginase in pts with UM or CM treated at the MTD in either escalation or expansion cohorts

Study Design

Figure 2. Study Schema

Endpoints:

- Safety (CTCAE v4.0.3)
- Pharmacokinetics
- Plasma arginine
- Immunogenicity
- Tumor expression of ASS1 (ASS1 negative score=0)
- Preliminary efficacy (RECIST 1.1)

Results

Table 1. Demographics and Prior Therapy

Demographics	Cutaneous melanoma median (range) or n (%)	Uveal melanoma median (range) or n (%)
N	13	15
Age in years	72 (44-82)	68 (50-85)
Male : female	10 : 3	8 : 9
Race / Ethnicity		
White no Hispanic / Latino	12 (92.3 %)	15 (100 %)
Hispanic / Latino	1 (7.7 %)	0 (0 %)
Asian	0 (0 %)	0 (0 %)
Black / African American	0 (0 %)	0 (0 %)
Median prior systemic therapies	3 (1-5)	2 (0-5)
Investigator reported response to last prior therapy		
PD	10 (76.9 %)	7 (46.67)
SD	1 (7.7 %)	5 (33.3 %)
PR	0 (0 %)	0 (0 %)
CR	0 (0 %)	0 (0 %)
No prior systemic Tx	0 (0 %)	1 (6.7 %)
Not tolerated / Unknown	2 (15.4 %)	2 (13.3 %)
Patients with prior IO therapy		
Any line	13 (100 %)	12 (80 %)
Last line before enrollment	8 (48.2 %)	10 (66.7 %)
PD reported as best response to IO therapy	8/11 (82 %)	4/9 (56 %)

Table 2. Safety

Treatment Related[1] Adverse Events (TRAEs)	Grade 1-2 n (%)	Grade 3 n (%)
Any	16 (69.3 %)	6 (25.8 %)
Fatigue	11 (40.7 %)	1 (3.7 %)
Nausea	10 (37.0 %)	0
Diarrhea	8 (29.6 %)	1 (3.7 %)
Vomiting	7 (25.9 %)	1 (3.7 %)
Tremor	8 (29.6 %)	0
Glossodynia[2]	7 (25.9 %)	0
Gait disturbance	4 (14.8 %)	2 (7.4 %)
Decreased appetite	6 (22.2 %)	0
Dizziness	6 (22.2 %)	0
Rash[3]	6 (22.2 %)	0
Asthenia	3 (11.1 %)	1 (3.7 %)
Dysgeusia	4 (14.8 %)	0
Neutropenia	2 (7.4 %)	1 (3.7%)
Dehydration	2 (7.4 %)	1 (3.7 %)
Anemia	3 (11.1 %)	0
Leukopenia	3 (11.1 %)	0
AST increased	3 (11.1 %)	0
Oropharyngeal pain	3 (11.1 %)	0
Muscular weakness	3 (11.1 %)	0
Pruritus	3 (11.1 %)	0
Weight loss	3 (11.1 %)	0
Abdominal pain	3 (11.1 %)	0
Failure to thrive	0	1 (3.7 %)
Fall	0	1 (3.7 %)
Hypophosphataemia	0	1 (3.7 %)

Total number of patients included in safety analysis = 27
[1] Treatment-related Adverse Events (TRAEs ≥15% or Grade 3)
[2] Glossodynia, oral pain or oropharyngeal pain
[3] Macular, maculo-papular, or acneiform

- No Grade ≥ 4 TRAEs were reported
- No infusion reactions were reported following 276 infusions
- Three patients experienced treatment-related, serious Grade 3 AEs: 1) Asthenia and failure to thrive, 2) vomiting, and 3) dehydration
- Anti-drug antibody (ADA) analysis (N=27 pts):
  - 5 anti-pegzilarginase ADA
    - 4 pre-existing (3 specific to Arg 1)
    - 1 emergent specific to Arg 1
  - 4 anti-PEG ADAs; 3 pre-existing, 1 unknown
  - All titers were low (highest in 1 patient ~ 1:320)
- No apparent effects of ADA on PK, arginine reduction, or safety

Table 3. Pharmacokinetics

Cohort	Cycle	$T_{1/2}$ (hr) mean (s.d.)	Cmax (µg/mL) mean (s.d.)	AUC_{0-168} (hr*µg/mL) mean (s.d.)
Cutaneous Melanoma	1	46 (4.6)	7.44 (1.3)	422 (116)
	2	45.5 (5.4)	7.22 (0.8)	382 (51.3)
Uveal Melanoma	1	41 (7.4)	8.23 (1.5)	366 (96.7)
	2	47.5 (6.1)	8.22 (2.2)	478 (161)

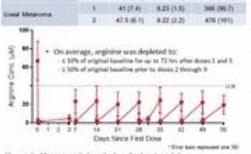

Figure 3. Plasma arginine during Cycles 1 and 2

Time on Study and Best Objective Response*

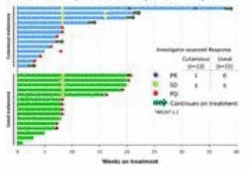

Figure 4. Time on treatment and best response observed

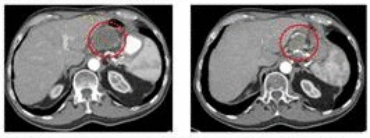

Figure 6. Pre-/Post-treatment CT scans in a patient with cutaneous melanoma and confirmed PR

Efficacy (RECIST 1.1)

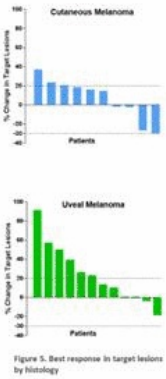

Figure 5. Best response in target lesions by histology

Efficacy by ASS1 Expression

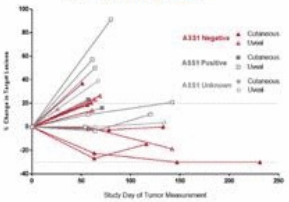

Figure 7. Time course of percent change in target lesions

Conclusions

- Pegzilarginase monotherapy demonstrated anti-tumor activity in heavily pre-treated patients with melanoma
  - One confirmed PR at Week 20 and 8 patients with SD at Week 8 or later
  - Anti-tumor activity appeared greater in tumors lacking ASS1 expression consistent with pre-clinical PDx findings
- As previously reported, pegzilarginase rapidly and sustainably depleted plasma arginine with a manageable safety profile
- These results, combined with pre-clinical evidence of synergy with immune checkpoint inhibitors, support further clinical evaluation of pegzilarginase in immunotherapy combinations

References, Support and Disclosures
[1]Patil et al. Oncogene (2018), 37(18): 1-16
[2]Aghelio et al. Cancer Res (2018), 78(13 sup): 869
[3]Yasco et al. Cancer Res (2018), 78(13 sup): CT030
Support: Aeglea Biotherapeutics Inc. and the Cancer Prevention and Research Institute of Texas (Grant # DP140031)
Disclosures: All Aeglea employees have an equity interest in Aeglea Biotherapeutics, Inc.