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 11, 2019

Proteostasis Therapeutics, Inc.
(Exact name of registrant as specified in its charter)

Delaware	001-37695	20-8436652
(State or other jurisdiction of incorporation)	(Commission File Number)	(I.R.S. Employer Identification No.)

80 Guest Street, Suite 500 Boston, MA	02135
(Address of principal executive offices)	(Zip Code)

Registrant's telephone number, including area code (617) 225-0096
(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))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common stock, par value $0.001 per share	**PTI**	**The Nasdaq Global Market**

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 8.01 Other Events.

On December 11, 2019, the Company issued the press release attached hereto as Exhibit 99.1 announcing the following information:

Proteostasis Therapeutics, Inc. (NASDAQ:PTI), a clinical stage biopharmaceutical company dedicated to the discovery and development of groundbreaking therapies to treat cystic fibrosis (CF), today announced positive, initial *ex-vivo* results of PTI's proprietary cystic fibrosis transmembrane conductance regulator (CFTR) modulators, PTI-801, PTI-808, and PTI-428, in individuals with CF who are ineligible for the current standard of care CFTR modulator therapies due to their genotype. The data are part of a pan-European strategic initiative, known as HIT-CF (Human Individualized Therapy of CF), which seeks to accelerate the development of, and access to, personalized therapies for CF patients, beginning with those for whom no currently approved CFTR modulator therapy is indicated.

HIT-CF is sponsored by the European Commission Horizon 2020 program, in which CF-Europe, a patient organization representing more than 48,000 individuals with CF, collaborates and with the European Cystic Fibrosis Society Clinical Trial Network (ECFS-CTN), which is recruiting adult CF patients into the *ex-vivo* study through its 43 clinical trial centers. HIT-CF collects tissue samples from CF patients and develops organoids, or miniaturized organs, that are genetically identical to the patient donor, and share the same micro-anatomy as the organ from which they were derived.

As of today, rectal organoids from over 300 subjects have been collected for functional profiling and of those, 65 have been tested for response to PTI's investigational drugs. Early results support the initiation of enrollment of responding subjects into HIT-CF's clinical trial known as "CHOICES" (Crossover trial based on Human Organoid Individual response in CF - Efficacy Study), which is designed to evaluate the translation of organoid *ex-vivo* response to potential clinical benefit, such as changes in FEV_1 and sweat chloride. CHOICES, which is expected to initiate in mid-2020, will be the first ever personalized medicine-based study in CF, with initial data expected by the end of 2020. Fully funded by the HIT-CF, this trial is a placebo controlled, double blind, crossover study with an 8-week treatment period and 6 months of uninterrupted dosing. The results may serve as the basis for a potential Marketing Authorization Application with the European Medicines Agency (EMA) in 2021 through a novel regulatory pathway which is being pursued jointly by Proteostasis and HIT-CF. The CHOICES clinical study is part of PTI's broader clinical development strategy for its CFTR modulator candidates that is already separately funded for the common genotypes.

Results from the HIT-CF project to date will be presented at the Keystone Symposia on Tissue Organoids titled "Tissue Organoids as Models of Host Physiology and Pathophysiology of Disease (J1)" taking place on January 19-23, 2020 in Vancouver, BC, Canada.

Safe Harbor

To the extent that statements in this release are not historical facts, they are forward-looking statements reflecting the current beliefs and expectations of management made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Words such as "aim," "may," "will," "expect," "anticipate," "estimate," "intend," and similar expressions (as well as other words or expressions referencing future events, conditions or circumstances) are intended to identify forward-looking statements. Examples of forward-looking statements made in this release include, without limitation, statements regarding the expected presentation at an upcoming conference. Forward-looking statements made in this release involve substantial risks and uncertainties that could cause actual results to differ materially from those expressed or implied by the forward-looking statements, and we, therefore cannot assure you that our plans, intentions, expectations or strategies will be attained or achieved. Such risks and uncertainties include, without limitation, our expectations regarding our participation in HIT-CF's pan-European strategic initiative, the potential of our proprietary combination therapies for the treatment of CF, the potential benefit of our proprietary combination therapies to patients, expected timing of patient enrollment in, data from, the completion of, and reporting top line results of our clinical studies and cohorts for our clinical programs, including our planned Phase 2 program and initiation of a pivotal or registrational study, the possibility final or future results from our drug candidate trials (including, without limitation, longer duration studies) do not achieve positive results or are materially and negatively different from or not indicative of the preliminary results reported by the Company (noting that these results are based on a small number of patients and small data set), uncertainties inherent in the execution and completion of clinical trials (including, without limitation, the possibility that FDA or other regulatory agency comments delay, change or do not permit trial commencement, or intended label, or the FDA or other regulatory agency requires us to run cohorts sequentially or conduct additional cohorts or pre-clinical or clinical studies), in the enrollment of CF patients in our clinical trials in a competitive clinical environment, in the timing of availability of trial data, in the results of the clinical trials, in possible adverse events from our trials, in the actions of regulatory agencies, in the endorsement, if any, by therapeutic development arms of CF patient advocacy groups (and the maintenance thereof), in the commercialization and acceptance of new therapies, and those set forth in our Annual Report on Form 10-K for the year ended December 31, 2018, our Quarterly Report on Form10-Q for the quarter ended September 30, 2019 and our other SEC filings. We assume no obligation to update or revise any forward-looking statements, whether as a result of new information, future events or otherwise.

The above information is not an admission as to the materiality of any information therein. The Company undertakes no duty or obligation to update or revise the information contained in this report, although it may do so from time to time as its management believes is appropriate. Any such updating may be made through the filing of other reports or documents with the SEC, through press releases or through other public disclosures.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	Exhibit Name
99.1	Press Release, filed herewith.

EXHIBIT INDEX

Exhibit No.	Exhibit Name
99.1	Press Release, filed herewith.

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.

Date: December 11, 2019

PROTEOSTASIS THERAPEUTICS, INC.

By: /s/ Meenu Chhabra
Meenu Chhabra
President and Chief Executive Officer

Exhibit 99.1

Proteostasis Therapeutics to Initiate First Ever Personalized Medicine-Based Clinical Trial, CHOICES, in European CF Patients with Genotypes Ineligible for Approved CFTR Modulators

Ongoing Ex-Vivo Study Supports Initiation of Clinical Trial in 2020 with Potential to Serve as the Basis for an MAA in 2021

BOSTON, Mass. – December 11, 2019 – Proteostasis Therapeutics, Inc. (NASDAQ:PTI), a clinical stage biopharmaceutical company dedicated to the discovery and development of groundbreaking therapies to treat cystic fibrosis (CF), today announced positive, initial *ex-vivo* results of PTI's proprietary cystic fibrosis transmembrane conductance regulator (CFTR) modulators, PTI-801, PTI-808, and PTI-428, in individuals with CF who are ineligible for the current standard of care CFTR modulator therapies due to their genotype. The data are part of a pan-European strategic initiative, known as HIT-CF (Human Individualized Therapy of CF), which seeks to accelerate the development of, and access to, personalized therapies for CF patients, beginning with those for whom no currently approved CFTR modulator therapy is indicated.

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As of today, rectal organoids from over 300 subjects have been collected for functional profiling and of those, 65 have been tested for response to PTI's investigational drugs. Early results support the initiation of enrollment of responding subjects into HIT-CF's clinical trial known as "CHOICES" (Crossover trial based on Human Organoid Individual response in CF - Efficacy Study), which is designed to evaluate the translation of organoid *ex-vivo* response to potential clinical benefit, such as changes in FEV_1 and sweat chloride. CHOICES, which is expected to initiate in mid-2020, will be the first ever personalized medicine-based study in CF, with initial data expected by the end of 2020. Fully funded by the HIT-CF, this trial is a placebo controlled, double blind, crossover study with an 8-week treatment period and 6 months of uninterrupted dosing. The results may serve as the basis for a potential Marketing Authorization Application with the European Medicines Agency (EMA) in 2021 through a novel regulatory pathway which is being pursued jointly by Proteostasis and HIT-CF. The CHOICES clinical study is part of PTI's broader clinical development strategy for its CFTR modulator candidates that is already separately funded for the common genotypes.

Results from the HIT-CF project to date will be presented at the Keystone Symposia on Tissue Organoids titled "Tissue Organoids as Models of Host Physiology and Pathophysiology of Disease (J1)" taking place on January 19-23, 2020 in Vancouver, BC, Canada.

"Proteostasis is honored to have been invited to participate in the HIT-CF project and is the only company in the group with a combination of novel CFTR modulators being tested *ex-vivo*. We are very enthusiastic about the progress of the study," said Geoffrey Gilmartin, M.D., M.M.Sc., Chief Medical Officer of Proteostasis Therapeutics. "In Europe alone, there are

more than 2,300 adult patients whose genotypes render them ineligible for approved CFTR modulators and exclude them from participating in clinical trials with this drug class. This project's proposed personalized medicine approach is paving a potential new way to develop and provide access to novel CFTR modulators for patients with the most dire need for treatment options that target the cause of the disease. Additionally, based on an individual patient's disease phenotype and not just the genetic designation, this approach could also create a new path towards more effective treatment for all people with CF."

"The inequality in access to CFTR modulators is an acute problem across Europe where 1 in 5 individuals do not have a F508del mutation. In addition, drug reimbursement policies are leading to an ever-growing gap between patients who do, and those who do not have effective treatment options," said Christiane De Boeck, Work Package Leader at HIT-CF, and Former President of ECFS. "AtHIT-CF Europe, we believe that novel strategies such as personalized medicine and development of new treatment options are central to addressing the inequality of access across the continent. We are thrilled with these initial results and look forward to providing additional updates."

About Organoids

Organoids are cell cultures that grow in a culture dish and look similar to the organ from which they are derived. Because organoids are made from stem cells, they contain the same mutations as the person from whom the biopsies are derived. Investigational drugs which target the basic defect of CF can be used in an organoid system to evaluate rare mutations where the drugs may have a positive effect.

Unlike *in vitro* systems such as human bronchial epithelial (HBE) cells, which are derived from lungs that have been removed from CF patients, or the engineered, rat-derived FRT cell line, the latter has resulted in false positive clinical results, rectal organoids are cultured from tissues obtained through a minimally invasive and painless procedure from donors who then become eligible to participate in a clinical study. Organoids can provide valuable insights for donors, including their likelihood of achieving improvements in pulmonary function and reductions in sweat chloride concentration with CFTR modulators based on the *ex-vivo* response to those drugs.[1]

About HIT-CF Europe

HIT-CF Europe is a research project which aims to provide better treatment and better lives for people with cystic fibrosis (CF) and rare mutations. To achieve this, drug candidates are first tested on patient-derived organoids in qualified laboratories across Europe. Subsequently, based on the measured signal in the organoids, a smaller group of patients will be invited to participate in a clinical trial with one or more investigational molecules from a participating pharmaceutical company.

All participating centers are part of the European Cystic Fibrosis Society – Clinical Trial Network(ECFS-CTN). The project has received funding from the European Union's Horizon 2020 research and innovation program under grant agreement number 755021. For more information, visit www.hitcf.org.

About Proteostasis Therapeutics, Inc.

Proteostasis Therapeutics, Inc. is a clinical stage biopharmaceutical company developing small molecule therapeutics to treat cystic fibrosis and other diseases caused by dysfunctional protein processing. Headquartered in Boston, MA, the Proteostasis Therapeutics team focuses on identifying therapies that restore protein function. For more information, visit www.proteostasis.com.

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1 Berkers et al, Rectal Organoids Enable Personalized Treatment of Cystic Fibrosis Cell Reports 26, 1701–1708, February 12, 2019