Filed pursuant to Rule 433 of the Securities Act of 1933
Issuer Free Writing Prospectus dated May 13, 2020
Relating to the Preliminary Prospectus dated May 12, 2020
Registration Statement File No. 333-238194

Oyster Point Pharma, Inc. has filed a registration statement on Form S-1 (File No. 333-238194), including a preliminary prospectus dated May 12, 2020, or the Preliminary Prospectus, with the Securities and Exchange Commission, or the SEC, for the offering to which this free writing prospectus relates. The Preliminary Prospectus can be accessed at https://www.sec.gov/Archives/edgar/data/1720725/000119312520140387/d844461ds1.htm. Before you invest, you should read the Preliminary Prospectus and any other documents that the Company has filed with the SEC for more information about the Company and the offering.

The information set forth below supplements or replaces, as applicable, the information contained in the Preliminary Prospectus. All page number references refer to page numbers in the Preliminary Prospectus, and references to "we," "us," "our," or "the Company" refer to Oyster Point Pharma, Inc.

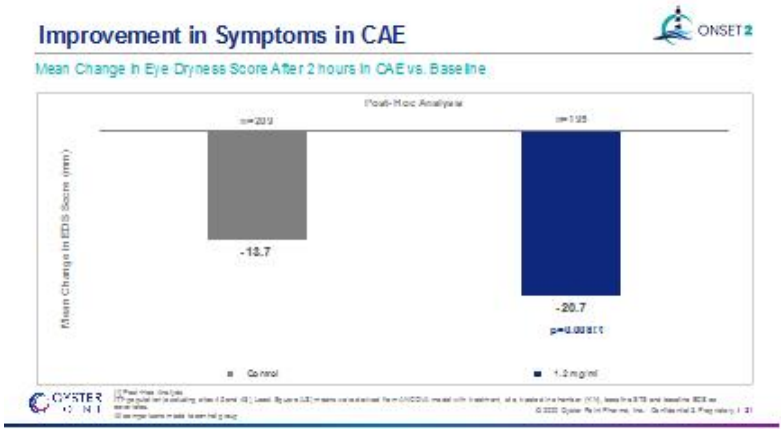
The following disclosure supplements and is hereby added to the disclosure at the end of page 7 of the Prospectus Summary.

On May 11, 2020, we reported top-line results from ONSET-2, a multicenter, randomized, double-masked, vehicle-controlled Phase 3 clinical trial designed to evaluate the safety and efficacy of OC-01 (varenicline) nasal spray for the signs and symptoms of dry eye disease (DED). The secondary endpoint of patient-reported symptoms of eye dryness in the Controlled Adverse Environment (CAE) at Week 4 was not statistically significant in either the 0.6 mg/ml or the 1.2 mg/ml dose groups. After conducting further post-hoc analyses of the data, we believe that there is a treatment benefit in the 1.2 mg/ml dose group that was not captured with the statistical method used for analysis of the endpoint. The statistical power for assessing this endpoint was negatively impacted by a decrease in the sample size, which we believe was due in part to subjects being unable to be assessed as a result of the COVID-19 pandemic. In addition, there were a number of subjects that did not meet the criteria for treatment in the CAE, thereby further reducing statistical power. Treatments in the CAE are only administered if a participant reports an Ocular Discomfort score of ^{3} 3 at two or more consecutive time points in at least one eye during CAE exposure, for participants with an Ocular Discomfort rating of 3 at baseline. Participants with an Ocular Discomfort rating of 4 at baseline for an eye must report an Ocular Discomfort rating of 4 for two additional consecutive measurements for that eye, not including the baseline measurement.

We believe that the loss of a number of subjects due to the COVID-19 pandemic and the number of subjects not meeting the treatment criteria could not have been anticipated when we designed our statistical model for this clinical trial. In addition, we believe that the reduction in the number of subjects not meeting the treatment criteria may be related to our enrollment of subjects with an EDS Score ranging from 0-100, which may have increased the number of subjects who were able to withstand the CAE for the entire 2-hour time period.

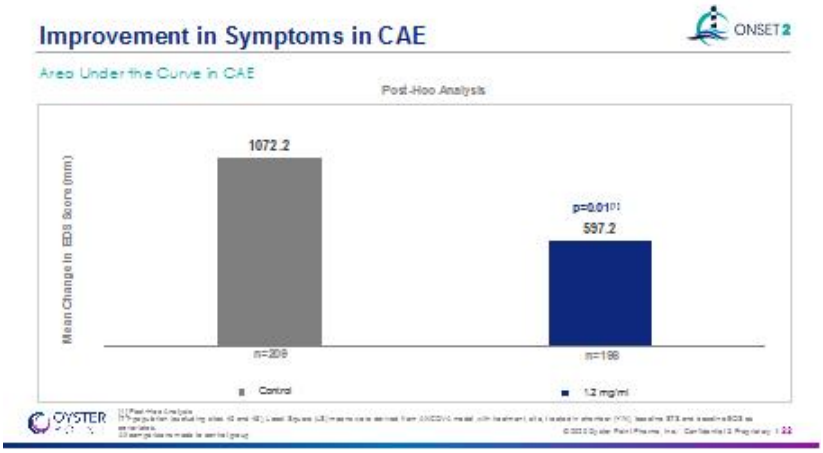
We believe that a post-hoc analysis that takes into account the entire 2-hour timeframe during which subjects were in the CAE and that measures the response of all subjects, whether or not they received treatment in the CAE, is relevant under these circumstances. One analysis method to evaluate the treatment effect in the context of the CAE is to build an ANCOVA model and calculate the Least Square (LS) means with treatment, site, treatment in chamber (Y/N), baseline Schirmer's Score and baseline EDS as covariates. The model compares the EDS at the 2-hour timepoint to the baseline EDS score, thereby

protecting randomization. The results of this post-hoc analysis takes into account the full subject sample, regardless of whether subjects received treatment in the CAE, and takes into account the change in EDS score from the entire subject symptom experience during a full 2-hours in the CAE, as compared to their symptoms at 5 minutes after meeting treatment criteria and receiving treatment. The results of this analysis are displayed in the figure below:



The mean change from the 2-hour timepoint in the CAE compared to baseline resulted in a LS mean change from baseline EDS score of -20.7 mm, 95% CI -25.19 to -16.17 (p=0.008) in the 1.2 mg/ml dose group, compared to -13.7 mm in the control group. We interpret this post-hoc analysis as potentially demonstrating that, after 4 weeks of treatment with OC-01 versus placebo, and after 2-hours in the CAE, there is a significant improvement in EDS score when treated with 1.2 mg/ml OC-01 nasal spray compared to placebo.

To confirm this post-hoc analysis, we performed a second post-hoc analysis with an area under the curve (AUC) model using the data from Time 0 to Time 120 minutes within the CAE for the 1.2 mg/ml treatment group versus control. Similar to the method above, this analysis takes into account the full subject sample, regardless of whether subjects received treatment in the CAE, and takes into account the change in EDS score from the entire subject experience during a full 2-hours in the CAE. This assessment looks directly at the symptom score noted at the 2-hour time point in the CAE. The analysis method calculates LS means derived from an ANCOVA model with treatment, site, treated in chamber (Y/N), baseline STS and baseline EDS as covariates. The results are illustrated in the figure below:



The LS mean change over the 2-hour period was 597.2 mm, 95% CI 256.69 to 937.78 (p=0.0175) in the 1.2 mg/ml dose group, compared to 1072.2 mm in the control group. We believe this post-hoc analysis shows that after 2-hours in the CAE, AUC is statistically significantly smaller in subjects treated with 1.2 mg/ml OC-01 nasal spray, potentially indicating a protective benefit while the subject is in the CAE.

We intend to discuss the appropriateness of our original secondary endpoint analysis and our interpretation of the treatment benefit within the CAE of the 1.2 mg/ml dose group with the U.S. Food and Drug Administration (FDA) based on these post-hoc analyses in the context of our planned NDA submission.

The following risk factor on page 20 of the Preliminary Prospectus is hereby replaced in its entirety as follows.

OC-01 uses a novel and unproven therapeutic approach and mechanism of action to treat DED and therefore its efficacy and safety are difficult to predict, and there is no guarantee that OC-01 or any other product candidates will be approved by the FDA.

We are developing OC-01 as a preservative-free, aqueous nasal spray that will stimulate the lacrimal functional unit (LFU) to produce natural tear film. To our knowledge, OC-01 represents the first pharmacological treatment approach for DED that is aimed at stimulating the LFU. Other than with respect to data from studies and trials of OC-01 and OC-02, there is limited or no clinical evidence showing that natural tear film can be produced through the stimulation of the LFU. For instance, even though OC-01 has shown promising results in preclinical studies and clinical trials for the treatment of DED, we may not succeed in demonstrating safety and efficacy of OC-01 for other indications, including OLYMPIA, our upcoming Phase 2 clinical trial for NK. Advancing OC-01 as a novel product creates significant challenges for us, including:

- obtaining marketing approval;
- educating medical personnel, including eye care practitioners (ECPs), and patients regarding the potential efficacy and safety benefits, as well as the challenges, of incorporating our product candidates, if approved, into treatment regimens; and
- establishing the sales and marketing capabilities upon obtaining any marketing approvals to gain market acceptance.

We cannot guarantee that OC-01 or any of our other future product candidates will be approved by the FDA. Product candidates in later-stage clinical trials often fail to demonstrate sufficient safety and efficacy to the satisfaction of the FDA, EMA and other comparable foreign regulatory authorities despite having successfully progressed through preclinical studies and other clinical trials. In some instances, there can be significant variability in safety and efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial protocols, differences in size and type of the patient populations, differences in and adherence to the dosing regimen and other trial protocols and the rate of dropout among clinical trial participants. For example, although OC-01 met the primary endpoint in ONSET-2 in both the 1.2 mg/ml and 0.6 mg/ml dose groups, OC-01 nasal spray did not meet the secondary endpoint for patient-reported symptoms of eye dryness in a Controlled Adverse Environment (CAE) and other secondary endpoints in either dose group. Following completion of ONSET-2, we conducted additional analyses on a post-hoc basis of the data from our ONSET-2 study to support our planned NDA submission. We may also conduct additional post-hoc analyses on the results of clinical trials in the future. Post-hoc analyses performed after unmasking trial results can result in the introduction of bias, may not be predictive of success in any future clinical trials and are given less weight by regulatory authorities than pre-specified analyses. Additionally, we cannot guarantee that the safety profile of OC-01 in healthy volunteers and patients with DED will be replicated in trials and studies for other indications, such as NK. Assessments of efficacy can vary widely for a particular participant, and from participant to participant and site to site within a clinical trial. This subjectivity can increase the uncertainty of, and adversely impact, our clinical trial outcomes. In addition, participants treated with OC-01 may also be treated with other investigational drugs, prescription drugs or even over-the-counter treatments following the treatment period of our OC-01 studies, any of which with OC-01 may also be treated with other investigational drugs,

prescription drugs or even over-the-counter treatments following the treatment period of our OC-01 studies, any of which can cause side effects or adverse events that are unrelated to our product candidate, but which are observed during the long-term safety follow-up for OC-01. The occurrence of such side effects or adverse events could have a negative impact on OC-01's safety profile.

The following risk factor beginning on page 49 of the Preliminary Prospectus is hereby replaced in its entirety as follows.

The regulatory approval processes of the FDA, EMA and other comparable foreign regulatory authorities are lengthy, time consuming and inherently unpredictable. If we are ultimately unable to obtain regulatory approval for our product candidates, we will be unable to generate product revenue and our business will be substantially harmed.

The time required to obtain approval by the FDA, EMA and other comparable foreign regulatory authorities is unpredictable, typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the type, complexity and novelty of the product candidates involved. In addition, approval policies, regulations or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions, which may cause delays in the approval or the decision not to approve an application. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other data. Even if we eventually complete clinical testing and receive approval of any regulatory filing for our product candidates, the FDA, EMA and other comparable foreign regulatory authorities may approve our product candidates for a more limited indication or a narrower patient population than we originally requested. For example, the fact that OC-01 did not achieve certain secondary endpoints in ONSET-2 could have an adverse effect on our ability to obtain our desired label for OC-01, if approved. We have not submitted for, or obtained, regulatory approval for any product candidate, and it is possible that none of our existing product candidates or any product candidates we may seek to develop in the future will ever obtain regulatory approval.

Further, development of our product candidates and/or regulatory approval may be delayed for reasons beyond our control. For example, a U.S. federal government shutdown or budget sequestration, such as ones that occurred during 2013, 2018 and 2019, or diversion of resources to currently handle the COVID-19 public health emergency and pandemic may result in significant reductions to the FDA's budget, employees and operations, which may lead to slower response times and longer review periods, potentially affecting our ability to progress development of our product candidates or obtain regulatory approval for our product candidates. In addition, the impact of COVID-19 may cause the FDA to allocate additional resources to product candidates focused on treating related illnesses, which could lead to longer approval processes for our product candidates. Moreover, some of our analyses of the ONSET-2 clinical trial data are post-hoc analyses and, although we believe that these post-hoc analyses can provide additional information regarding results from this clinical trial, retrospective analyses can result in the introduction of bias and may be given less weight by the FDA, including for purposes of determining whether to accept our NDA for filing or approving our NDA. Finally, our competitors may file citizens' petitions with the FDA in an attempt to persuade the FDA that our product candidates, or the clinical trials that support their approval, contain deficiencies. Such actions by our competitors could delay or even prevent the FDA from approving any of our NDAs.

Applications for our product candidates could fail to receive regulatory approval for many reasons, including the following:

- the FDA, EMA or other comparable foreign regulatory authorities may disagree with the design, implementation or results of our clinical trials;
- the FDA, EMA or other comparable foreign regulatory authorities may determine that our product candidates are not safe and effective, only moderately effective or have undesirable or unintended side effects, toxicities or other characteristics that preclude our obtaining marketing approval or prevent or limit commercial use;

- the population studied in the clinical trial may not be sufficiently broad or representative to assure efficacy and safety in the full population for which we seek approval;
- the FDA, EMA or other comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials of our product candidates may not be sufficient to support the submission of an NDA, or other submission or to obtain regulatory approval in the United States or elsewhere;
- we may be unable to demonstrate to the FDA, EMA or other comparable foreign regulatory authorities that a product candidate's risk-benefit ratio for its proposed indication is acceptable;
- the FDA, EMA or other comparable foreign regulatory authorities may fail to approve the manufacturing processes, test procedures and specifications or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and
- the approval policies or regulations of the FDA, EMA or other comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

This lengthy approval process, as well as the unpredictability of the results of clinical trials, may result in our failing to obtain regulatory approval to market any of our product candidates, which could materially affect our business, financial condition, results of operations and growth prospects.

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