Dear Stockholders,

We are making progress in advancing our mission to improve the lives of adult patients with acromegaly. During the past year, we achieved several important milestones, which provide us with greater optimism for oral octreotide capsules, conditionally trade-named MYCAPSSA, our product candidate in Phase 3 clinical trials for the maintenance treatment of adults with acromegaly.

**We reached a Special Protocol Assessment (SPA) agreement with the FDA** on a randomized, double-blinded and placebo-controlled 9-month Phase 3 clinical trial for MYCAPSSA. After many months of dialogue with the U.S. Food and Drug Administration, we announced the agreement in August 2017. This was a watershed moment for Chiasma, as the SPA indicated concurrence by the FDA with the adequacy and acceptability of specific, critical elements of the protocol for our CHIASMA OPTIMAL (Octreotide capsules vs. Placebo Treatment In MultinationAL centers) Phase 3 clinical trial. A SPA is a process by which an applicant and the FDA reach an agreement on the protocol design, endpoints and analysis of a Phase 3 clinical study prior to initiation, in order to determine if the study adequately addresses scientific and regulatory requirements for FDA approval. This mutually agreed-upon study was designed to address the efficacy concerns raised by the FDA in its Complete Response Letter in 2016. The written agreement with the FDA provided regulatory clarity of a clinical path forward for octreotide capsules in the U.S.

**We recently reached formal agreement with the FDA to redefine certain secondary endpoints** of the CHIASMA OPTIMAL Phase 3 clinical trial in May 2018. We believe this SPA modification agreement with the FDA favorably alters the mix of secondary endpoints to be reviewed by the agency in evaluating the totality of evidence of the treatment effect of octreotide capsules. Prior to the initiation of the trial, we estimated that a significant number of the placebo-treated patients in CHIASMA OPTIMAL may require injectable somatostatin analog rescue therapy. As such, the original fourth and fifth endpoints in the hierarchy of secondary endpoints (the change from screening to end of treatment in mean growth hormone and the change in IGF-1 from baseline to end of treatment) would have compared patients' response to octreotide capsules to patients' response on injectable somatostatin analog rescue therapy. Through the SPA Agreement Modification, these secondary endpoints have now been redefined to descriptive statistics only measured within each treatment group, and between-arm comparisons of these two descriptive measures will not be made. A new secondary endpoint measuring the proportion of patients requiring rescue treatment in each treatment arm during the nine-month, double-blind, placebo-controlled phase has been included as the fourth and final secondary endpoint in the hierarchy. This modification agreement is important, because the FDA has indicated it plans to consider the secondary endpoints in its evaluation of the totality of evidence of oral octreotide's treatment effect.

**We randomized the first patient in the CHIASMA OPTIMAL trial** in September 2017. In so doing, we met our previous guidance that enrollment in the study would begin during the second half of 2017. This was an important first step toward our goal of resubmitting a New Drug Application with the FDA, as we ramp toward the 50 acromegaly patients that will be required for enrollment by the SPA agreement. We estimate that we will release topline data from this trial by the end of 2019.

**We surpassed the midway point for randomization in our MPOWERED Phase 3 clinical trial.** MPOWERED (Maintenance of Acromegaly Patients with Octreotide Capsules Compared With Injections – Evaluation of REsponse Durability) is our international Phase 3 clinical trial of octreotide capsules to potentially support regulatory approval in the European Union. It is a global, randomized, open-label and active-controlled, 15-month trial being conducted under a protocol accepted by the European Medicines Agency. In September 2017, we announced that we had surpassed 50% patients randomized in the MPOWERED™ trial. We estimate we will release topline data from this trial in 2020.

**We recently reduced the total number of patients we believe will be required for enrollment into the MPOWERED trial.** When we initiated MPOWERED in 2016, we estimated up to 150 patients would be required to enter the 6-month run-in phase of the trial, in order to randomize 80 oral octreotide capsule responders to the 9-month comparator phase. But in March 2018, we announced we now estimate approximately 130 patients will be required to enter the 6-month run-in phase, in order to randomize 80 responders to the comparator phase. This is an encouraging milestone that may have important ramifications for the timing of MPOWERED's completion. We are encouraged by the reduced estimate, as it is the result of an aggregate higher patient response rate to octreotide capsules and lower withdrawal rate during the 6-month run-in phase than we had originally expected.

**We completed 2017 with approximately $66.9 million in cash and investments**, representing a cash burn of approximately $26.0 million during 2017. Based on our current plans, we expect that our existing cash and investments will be sufficient to fund our operations through our anticipated release of top-line data from the Phase 3 CHIASMA OPTIMAL trial by the end of 2019 and to support the MPOWERED trial in parallel.

As we look ahead, we are excited about the progress we are making in the development of MYCAPSSA. If approved, MYCAPSSA would become the first oral somatostatin analog in an injectable-only acromegaly treatment market. We expect to make significant headway this year toward completing recruitment of 50 patients in the CHIASMA OPTIMAL trial and randomizing a minimum of 80 responders to oral octreotide capsules in the MPOWERED trial.

Finally, thank you to our stockholders for your continued support of Chiasma. We strongly believe MYCAPSSA has the potential to be a new treatment option for adult patients with acromegaly, and we look forward to continuing this important mission.

Sincerely,

Mark Fitzpatrick
President and Chief Executive Officer
Chiasma, Inc.
May 18, 2018