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

Form 10-K

(Mark One)

☑ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the fiscal year ended December 31, 2019

or

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the transition period from to

Commission file number: 001-33221

HERON THERAPEUTICS, INC.

(Exact name of registrant as specified in its charter)

DELAWARE	**94-2875566**
(State or other jurisdiction of incorporation or organization)	*(I.R.S. Employer Identification No.)*
4242 CAMPUS POINT COURT, SUITE 200 **SAN DIEGO, CA** *(Address of principal executive offices)*	**92121** *(Zip Code)*

Registrant's telephone number, including area code:
(858) 251-4400

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 $0.01 per share	HRTX	The Nasdaq Capital Market

Securities registered pursuant to Section 12(g) of the Act: None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☑ No ☐

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes ☐ No ☑

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☑ No ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☑ No ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	☑	Accelerated filer	☐
Non-accelerated filer	☐	Smaller reporting company	☐
		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. ☐

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☑

The aggregate market value of voting and non-voting common stock held by non-affiliates of the registrant as of June 28, 2019 totaled $1.4 billion based on the closing price of $18.59 as reported by The Nasdaq Capital Market. As of February 3, 2020, there were 90,374,284 shares of the Company's common stock ($0.01 par value) outstanding.

Documents Incorporated by Reference

Portions of the registrant's Definitive Proxy Statement related to its 2020 Annual Meeting of Stockholders' to be held on or about June 17, 2020 are incorporated by reference into Part III of this Annual Report on Form 10-K. Such Definitive Proxy Statement will be filed with the U.S. Securities and Exchange Commission within 120 days after the end of the fiscal year to which this report relates. Except as expressly incorporated by reference, the registrant's Definitive Proxy Statement shall not be deemed to be part of this report.

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FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements within the meaning of the federal securities laws. We make such forward-looking statements pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 and other federal securities laws. You can identify forward-looking statements by the use of the words “believe,” “expect,” “anticipate,” “intend,” “estimate,” “project,” “will,” “should,” “may,” “might,” “plan,” “assume” and other expressions that predict or indicate future events and trends and which do not relate to historical matters. You should not rely on forward-looking statements because they involve known and unknown risks, uncertainties and other factors, some of which are beyond our control. These risks, uncertainties and other factors may cause our actual results, performance or achievements to be materially different from our anticipated future results, performance or achievements expressed or implied by the forward-looking statements.

Factors that might cause these differences include the following:

- our ability to successfully commercialize, market and achieve market acceptance of CINVANTI® (aprepitant) injectable emulsion (“CINVANTI”), SUSTOL® (granisetron) extended-release injection (“SUSTOL”) and our product candidates, including HTX-011, and our positioning relative to competing products;
- our ability to establish satisfactory pricing and obtain adequate reimbursement from government and third-party payors of CINVANTI, SUSTOL and HTX-011, if approved, or any other products we may develop;
- whether study results of our products are indicative of the results in future studies;
- the potential regulatory approval for and commercial launch of HTX-011;
- the potential market opportunities for CINVANTI, SUSTOL and HTX-011, if approved;
- our competitors’ activities, including decisions as to the timing of competing product launches, generic entrants, pricing and discounting;
- whether safety and efficacy results of our clinical studies and other required tests for approval of our product candidates provide data to warrant progression of clinical trials, potential regulatory approval or further development of any of our product candidates;
- our ability to develop, acquire and advance product candidates into, and successfully complete, clinical studies, and our ability to submit for and obtain regulatory approval for product candidates in our anticipated timing, or at all;
- our ability to meet the postmarketing study requirements within the U.S. Food and Drug Administration’s (“FDA”) mandated timelines and to obtain favorable results and comply with standard postmarketing requirements, including U.S. federal advertising and promotion laws, federal and state anti-fraud and abuse laws, healthcare information privacy and security laws, safety information, safety surveillance and disclosure of payments or other transfers of value to healthcare professionals and entities for CINVANTI, SUSTOL or any of our product candidates;
- our ability to successfully develop and achieve regulatory approval for other future product candidates utilizing our proprietary Biochronomer® drug delivery technology (“Biochronomer Technology”);
- our ability to establish key collaborations and vendor relationships for our products and any other future products;
- our ability to successfully develop and commercialize any technology that we may in-license or products we may acquire;

- unanticipated delays due to manufacturing difficulties, supply constraints or changes in the regulatory environment;
- our ability to successfully operate in non-U.S. jurisdictions in which we may choose to do business, including compliance with applicable regulatory requirements and laws;
- uncertainties associated with obtaining and enforcing patents to protect our products, and our ability to successfully defend ourselves against unforeseen third-party infringement claims;
- our estimates regarding our capital requirements; and
- our ability to obtain additional financing and raise capital as necessary to fund operations or pursue business opportunities.

Any forward-looking statements in this Annual Report on Form 10-K reflect our current views with respect to future events or to our future financial performance and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. Factors that may cause actual results to differ materially from current expectations include, among other things, those listed under the section entitled “Risk Factors” in this Annual Report on Form 10-K. You should carefully review all of these factors. Given these uncertainties, you should not place undue reliance on these forward-looking statements. These forward-looking statements were based on information, plans and estimates as of the date of this Annual Report on Form 10-K, and except as required by law, we assume no obligation to update any forward-looking statements to reflect changes in underlying assumptions or factors, new information, future events or other changes. These risk factors may be updated by our future filings under the Securities Exchange Act of 1934 (“Exchange Act”). You should carefully review all information therein.

PART I

In this Annual Report on Form 10-K, all references to "Heron," the "Company," "we," "us," "our" and similar terms refer to Heron Therapeutics, Inc. and its wholly-owned subsidiary, Heron Therapeutics B.V., Heron Therapeutics®, the Heron logo, CINVANTI®, SUSTOL® and Biochronomer® are our trademarks. All other trademarks appearing or incorporated by reference into this Annual Report on Form 10-K are the property of their respective owners.

ITEM 1. BUSINESS.

Overview

We are a commercial-stage biotechnology company focused on improving the lives of patients by developing best-in-class treatments to address some of the most important unmet patient needs. We are developing novel, patient-focused solutions that apply our innovative science and technologies to already-approved pharmacological agents for patients suffering from pain or cancer.

In August 2016, our first commercial product, SUSTOL, was approved by the FDA. SUSTOL is indicated in combination with other antiemetics in adults for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic chemotherapy (MEC) or anthracycline and cyclophosphamide (AC) combination chemotherapy regimens. SUSTOL is an extended-release, injectable 5-hydroxytryptamine type 3 ("5-HT_3") receptor antagonist that utilizes our Biochronomer Technology to maintain therapeutic levels of granisetron for ≥5 days. We commenced commercial sales of SUSTOL in the U.S. in October 2016.

In November 2017, our second commercial product, CINVANTI was approved by the FDA. In October 2019, the FDA approved our supplemental New Drug Application ("sNDA") for CINVANTI to expand the indication and recommended dosage to include the 130 mg single-dose regimen for patients receiving moderately emetogenic cancer chemotherapy ("MEC"). CINVANTI, in combination with other antiemetic agents, is indicated in adults for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy (HEC) including high-dose cisplatin as a single-dose regimen, delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC) as a single-dose regimen, and nausea and vomiting associated with initial and repeat courses of MEC as a 3-day regimen. CINVANTI is an intravenous ("IV") formulation of aprepitant, a substance P/neurokinin-1 ("NK_1") receptor antagonist. CINVANTI is the first and only IV formulation of an NK_1 receptor antagonist indicated for the prevention of acute and delayed nausea and vomiting associated with HEC and nausea and vomiting associated with MEC that is free of synthetic surfactants, including polysorbate 80. We commenced commercial sales of CINVANTI in the U.S. in January 2018. In February 2019, the FDA approved our sNDA for CINVANTI, for IV use, which expanded the administration of CINVANTI beyond the initially approved administration method (a 30-minute IV infusion) to include a 2-minute IV injection.

HTX-011, an investigational agent, is a dual-acting, fixed-dose combination of the local anesthetic bupivacaine with a low dose of the nonsteroidal anti-inflammatory drug meloxicam. It is the first and only extended-release local anesthetic to demonstrate in Phase 3 studies significantly reduced pain and opioid use through 72 hours compared to bupivacaine solution, the current standard-of-care local anesthetic for postoperative pain control. HTX-011 was granted Fast Track designation from the FDA in the fourth quarter of 2017 and Breakthrough Therapy designation in the second quarter of 2018. Heron submitted a New Drug Application ("NDA") to the FDA for HTX-011 in October of 2018 and received Priority Review designation in December of 2018. A Complete Response Letter ("CRL") was received from the FDA regarding the NDA for HTX-011 on April 30, 2019 relating to Chemistry, Manufacturing and Controls ("CMC") and non-clinical information. No issues related to clinical efficacy or safety were noted. Heron resubmitted an NDA to the FDA for HTX-011 in September 2019. The Prescription Drug User Fee Act ("PDUFA") goal date is June 26, 2020. A Marketing Authorisation Application ("MAA") for HTX-011 was validated by the European Medicines Agency ("EMA") in March 2019 for review under the Centralised Procedure. Heron's New Drug Submission ("NDS") for HTX-011 for the management of postoperative pain was granted Priority Review status by Health Canada in October 2019 and accepted by Health Canada in November 2019.

HTX-034, our next-generation product candidate for postoperative pain management, is in development for postoperative pain via local application. Based on the positive results of preclinical studies in which HTX-034 demonstrated significant pain reduction for 7 days, we have initiated formal development of this next-generation postoperative pain management product candidate.

Chemotherapy-Induced Nausea and Vomiting ("CINV") Product Portfolio

SUSTOL

SUSTOL was our first commercial product. SUSTOL was approved by the FDA in August 2016, and we commenced commercial sales in the U.S. in October 2016.

SUSTOL is indicated in combination with other antiemetics in adults for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic chemotherapy (MEC) or anthracycline and cyclophosphamide (AC) combination chemotherapy regimens. SUSTOL is an extended-release, injectable 5-HT_3 receptor antagonist that utilizes our Biochronomer Technology to maintain therapeutic levels of granisetron for ≥5 days. The SUSTOL global Phase 3 development program was comprised of two, large, guideline-based clinical studies that evaluated SUSTOL's efficacy and safety in more than 2,000 patients with cancer. SUSTOL's efficacy in preventing nausea and vomiting was evaluated in both the acute phase (0–24 hours following chemotherapy) and the delayed phase (24–120 hours following chemotherapy).

SUSTOL is the first extended-release 5-HT_3 receptor antagonist approved for the prevention of acute and delayed nausea and vomiting associated with both MEC and AC combination chemotherapy regimens. A standard of care in the treatment of breast cancer and other cancer types, AC regimens are among the most commonly prescribed HEC regimens, as defined by both the National Comprehensive Cancer Network ("NCCN") and the American Society of Clinical Oncology ("ASCO").

In February 2017, the NCCN included SUSTOL as a part of its NCCN Clinical Practice Guidelines in Oncology for Antiemesis Version 1.2017. The NCCN has given SUSTOL a Category 1 recommendation, the highest-level category of evidence and consensus, for use in the prevention of acute and delayed nausea and vomiting in patients receiving HEC or MEC regimens. The guidelines now identify SUSTOL as a "preferred" agent for preventing nausea and vomiting following MEC. Further, the guidelines highlight the unique, extended-release formulation of SUSTOL.

In January 2018, a product-specific billing code, or permanent J-code ("J-code"), for SUSTOL became available. The new J-code was assigned by the Centers for Medicare and Medicaid Services ("CMS") and will help simplify the billing and reimbursement process for prescribers of SUSTOL.

CINVANTI

CINVANTI is our second commercial product. CINVANTI was approved by the FDA in November 2017, and we commenced commercial sales in the U.S. in January 2018. In October 2019, the FDA approved our sNDA for CINVANTI to expand the indication and recommended dosage to include the 130 mg single-dose regimen for patients receiving MEC.

CINVANTI, in combination with other antiemetic agents, is indicated in adults for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy (HEC) including high-dose cisplatin as a single-dose regimen, delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC) as a single-dose regimen, and nausea and vomiting associated with initial and repeat courses of MEC as a 3-day regimen.

CINVANTI is an IV formulation of aprepitant, an NK_1 receptor antagonist. CINVANTI is the first IV formulation to directly deliver aprepitant, the active ingredient in EMEND® capsules. Aprepitant (including its prodrug, fosaprepitant) is the only single-agent NK_1 receptor antagonist to significantly reduce nausea and vomiting in both the acute phase (0–24 hours after chemotherapy) and the delayed phase (24–120 hours after chemotherapy). CINVANTI is the first and only IV formulation of an NK_1 receptor antagonist indicated for the prevention of acute and delayed nausea and vomiting associated with HEC and nausea and vomiting associated with MEC that is free of synthetic surfactants, including polysorbate 80.

NK_1 receptor antagonists are typically used in combination with 5-HT_3 receptor antagonists. The only other injectable NK_1 receptor antagonist currently approved in the U.S. for both acute and delayed CINV, EMEND® IV (fosaprepitant), contains polysorbate 80, a synthetic surfactant, which has been linked to hypersensitivity reactions, including anaphylaxis, and infusion site reactions. The CINVANTI formulation does not contain polysorbate 80 or any other synthetic surfactant. Our CINVANTI data has demonstrated the bioequivalence of CINVANTI to EMEND IV, supporting its efficacy for the prevention of both acute and delayed nausea and vomiting associated with HEC and nausea and vomiting associated with MEC. Results also showed CINVANTI was better tolerated in healthy volunteers than EMEND IV, with significantly fewer adverse events (“AEs”) reported with CINVANTI.

In November 2018, a J-code for CINVANTI was assigned with an effective date of January 1, 2019. The new J-code was assigned by CMS and will help simplify the billing and reimbursement process for prescribers of CINVANTI.

In February 2019, the FDA approved our sNDA for CINVANTI, for IV use, which expanded the administration of CINVANTI beyond the initially approved administration method (a 30-minute IV infusion) to include a 2-minute IV injection.

Pain Management Product Portfolio

HTX-011

HTX-011, an investigational agent, is a dual-acting, fixed-dose combination of the local anesthetic bupivacaine with a low dose of the nonsteroidal anti-inflammatory drug meloxicam. It is the first and only extended-release local anesthetic to demonstrate in Phase 3 studies significantly reduced pain and opioid use through 72 hours compared to bupivacaine solution, the current standard-of-care local anesthetic for postoperative pain control. By delivering sustained levels of both a potent anesthetic and a local anti-inflammatory agent directly to the site of tissue injury, HTX-011 was designed to deliver superior pain relief while reducing the need for systemically administered pain medications such as opioids, which carry the risk of harmful side effects, abuse and addiction.

We submitted an NDA to the FDA for HTX-011 in October of 2018 and received Priority Review designation in December of 2018. A CRL was received from the FDA regarding the NDA for HTX-011 on April 30, 2019. The CRL stated that the FDA was unable to approve the NDA in its present form based on the need for additional CMC and non-clinical information. Based on the complete review of the NDA, the FDA did not identify any clinical efficacy or safety issues, and there was no requirement for further clinical studies or data analyses. In February 2020, we announced that the FDA extended the review period for the NDA for HTX-011 by up to three months. The new PDUFA goal date is June 26, 2020. The contract manufacturing site used to manufacture HTX-011 has been reinspected by the FDA with no Form 483 observations issued and with a recommendation by the FDA inspector for approval of the site. We have not been informed of any other manufacturing concerns.

In March 2019, the MAA for HTX-011 was validated by the EMA. Validation of the MAA confirms that the submission is complete and starts the EMA's Centralised Procedure. The EMA granted eligibility to the Centralised Procedure for HTX-011 based on it meeting the criteria of a medicinal product constituting a significant scientific innovation. The Centralised Procedure allows applicants to receive a marketing authorisation that is valid throughout the EU. An opinion from the EMA Committee for Medicinal Products for Human Use is anticipated in the second quarter of 2020.

In December 2019, the NDS for HTX-011 was granted Priority Review status and accepted by Health Canada. Health Canada's Priority Review status provides an accelerated 6-month review target for the NDS. A decision by Health Canada is anticipated in the third quarter of 2020.

In December 2019, data supporting the novel mechanism of action for the investigational agent HTX-011 were published online by the *Regional Anesthesia & Pain Medicine* ("RAPM") journal. The article, entitled "Mechanism of action of HTX-011: a novel, extended-release, dual-acting local anesthetic formulation for postoperative pain," also was published in the February 2020 print issue.

Recent Study Results

In October 2019, we reported positive topline results of a multi-center postoperative pain management study in which 51 patients undergoing total knee arthroplasty ("TKA") surgery received HTX-011 together with a scheduled postoperative regimen of generic oral analgesics (acetaminophen and celecoxib). Designed as a follow-on study to the Phase 2b study of HTX-011 in TKA (Study 209) that was completed in 2018, this study was designed to evaluate the decrease in pain and opioid use with HTX-011 when used together with a regimen of generic oral analgesics. In Study 209, HTX-011 significantly reduced pain and opioid use compared to placebo through 72 hours and significantly reduced pain compared to bupivacaine solution, the current standard-of-care local anesthetic for postoperative pain control, using a last observation carried forward ("LOCF") analysis. This study included the same multimodal, oral analgesic regimen as a prior published study with liposomal bupivacaine in TKA (Mont doi: 10.1016/j.arth.2017.07.024).

Topline results of this study include the following:

- Mean pain scores remained in the mild range through 72 hours post-surgery.
- Median consumption of opioids was 4-to-5 pills of oxycodone (22.5 morphine milligram equivalents) through 72 hours.
- 75% of patients were discharged from the hospital without a prescription for opioids.
- HTX-011, together with the multimodal, oral analgesic regimen, was well tolerated in this study. There were no deaths, serious adverse events ("SAEs") or premature discontinuations due to AEs.

In March 2019, we reported positive topline results of a multi-center postoperative pain management study in which 31 patients undergoing bunionectomy surgery received HTX-011 together with a regimen of generic over-the-counter ("OTC") oral analgesics (acetaminophen and ibuprofen). Designed as a follow-on study to the Phase 3 study in bunionectomy that investigated HTX-011 without the OTC analgesic regimen (EPOCH 1), this study was led by one of the lead investigators in the Phase 3 study and had the same entry criteria as the Phase 3 study. The goal of this study was to increase the proportion of patients who did not require opioids by combining HTX-011 with an OTC analgesic regimen. Topline results of this study include the following:

- 77% of patients receiving HTX-011 with the OTC analgesic regimen did not require opioids to manage their postoperative pain through 72 hours post-surgery, compared to 29%, 11% and 2% of patients receiving HTX-011, bupivacaine solution and placebo, respectively, in the Phase 3 study.
- 100% of patients receiving HTX-011 with the OTC analgesic regimen who were opioid-free through 72 hours remained opioid-free through 28 days post-surgery.
- The increase in patients who did not require opioids was associated with a large reduction in the percentage of patients experiencing severe pain. 29% of patients receiving HTX-011 with the OTC analgesic regimen experienced severe pain, compared to 53%, 76% and 83% of patients receiving HTX-011, bupivacaine solution and placebo, respectively, in the Phase 3 study.
- Over 72 hours post-surgery, patients receiving HTX-011 plus the OTC analgesic regimen consumed an average of only 1.6 morphine milligram equivalents ("MME"), which compares to 18.8 MME, 25.1 MME and 30.1 MME for patients receiving HTX-011, bupivacaine solution and placebo, respectively, in the Phase 3 study.
- HTX-011 was well tolerated with no SAEs associated with the addition of the OTC analgesic regimen.

In May 2019, we reported results of a multi-center postoperative pain management study in 93 patients that provides real-world evidence of opioid-free recovery in patients undergoing outpatient inguinal hernia repair surgery who received HTX-011 together with a scheduled background regimen of generic OTC oral analgesics (acetaminophen and ibuprofen). This study is the initial phase of the HOPE (Helping-Opioid-Prescription-Elimination) Project, which is designed to substantially reduce opioid prescriptions following surgery with HTX-011 as the foundation of a multimodal analgesic regimen. Currently, the average patient in the U.S. undergoing inguinal hernia repair surgery receives a discharge prescription for 30 opioid pills. Patients in this real-world outpatient study were discharged approximately 2–3 hours following surgery, and those who met pre-specified criteria were discharged without a prescription for opioid analgesics. The goal of this HOPE study was to provide real-world confirmation of the treatment algorithm developed in our Phase 3 hernia repair surgery follow-on study (Study 215), in which 90% of patients receiving HTX-011 with an OTC analgesic regimen remained opioid-free during a 72-hour inpatient assessment period, and to optimize the OTC analgesic regimen used with HTX-011. Topline results of this HOPE study include the following:

- 95% of patients receiving HTX-011 with the OTC analgesic regimen did not require opioids to manage their postoperative pain through recovery (Day 15).
- 91% of patients receiving HTX-011 with the OTC analgesic regimen were discharged without an opioid prescription, and none of these patients subsequently requested an opioid for postoperative pain.
- HTX-011 was well tolerated with no SAEs associated with the addition of the OTC analgesic regimen.
- Patients indicated an overall high satisfaction with the HTX-011-based analgesic regimen.

In January 2019, we reported positive topline results of Study 215, a multi-center postoperative pain management study in which 63 patients undergoing hernia repair surgery received HTX-011 together with a regimen of generic OTC oral analgesics (acetaminophen and ibuprofen). Designed as a follow-on to the Phase 3 study in hernia repair that investigated HTX-011 without the OTC analgesic regimen (EPOCH 2), this study included many of the same investigators and the same entry criteria as the Phase 3 study. The goal of this study was to increase the proportion of patients who did not require opioids by combining HTX-011 with a regimen of readily available, oral analgesics. Topline results of this study include the following:

- 90% of patients receiving HTX-011 with the OTC analgesic regimen did not require opioids to manage their postoperative pain through 72 hours post-surgery, compared to 51%, 40% and 22% of patients receiving HTX-011, bupivacaine solution and placebo, respectively, in the Phase 3 study.
- 81% of patients receiving HTX-011 with the OTC analgesic regimen who were opioid-free through 72 hours remained opioid-free through 28 days post-surgery.
- Over 72 hours post-surgery, patients receiving HTX-011 plus the OTC analgesic regimen consumed an average of only 0.9 MME, which compares to 10.8 MME, 14.5 MME and 17.5 MME for patients receiving HTX-011, bupivacaine and placebo, respectively, in the Phase 3 study.
- HTX-011 was well tolerated with no serious adverse events associated with the addition of the OTC analgesic regimen.

Pivotal Phase 3 Study Results

In March 2018, we reported positive topline results from EPOCH 1 and EPOCH 2, our pivotal Phase 3 studies of HTX-011 in bunionectomy and hernia repair, respectively. All primary and key secondary endpoints were achieved in these studies. Furthermore, HTX-011 is the only long-acting local anesthetic to demonstrate in Phase 3 studies significantly reduced pain and opioid use compared to bupivacaine solution, the current standard-of-care local anesthetic for postoperative pain control, through 72 hours.

The primary and key secondary endpoints for both Phase 3 studies were identical. The primary endpoint was pain intensity as measured by the Area Under the Curve (“AUC”) 0–72 compared to placebo. Key secondary endpoints in order of evaluation were:

- comparison of AUC 0–72 of pain intensity to bupivacaine solution;
- the total amount of opioid rescue medication consumption compared to placebo through 72 hours after surgery;
- the proportion of patients who received no opioid rescue medication after surgery compared to bupivacaine solution; and
- the total opioid consumption through 72 hours after surgery compared to bupivacaine.

Bunionectomy—Study 301/EPOCH 1 Results

EPOCH 1 was a randomized, placebo- and active-controlled, double-blind, Phase 3 clinical study evaluating the efficacy and safety of locally administered HTX-011 at 60 mg compared to the standard dose of bupivacaine solution (50 mg) and placebo for postoperative pain control following bunionectomy surgery in 412 subjects. All primary and key secondary endpoints were achieved:

- There was a 27% reduction in pain intensity as measured by AUC 0–72 when comparing HTX-011 to placebo ($p<0.0001$);
- There was an 18% reduction in pain as measured by AUC 0–72 when comparing HTX-011 to bupivacaine solution ($p=0.0002$);
- Over 72 hours post-surgery, patients receiving HTX-011 consumed 37% less opioids than placebo patients ($p<0.0001$) and 25% less opioids than patients receiving bupivacaine solution ($p=0.0022$); and

- 29% of patients receiving HTX-011 required no opioid medication for 72 hours post-surgery compared to only 2% receiving placebo ($p<0.0001$) and 11% receiving the standard-of-care, bupivacaine solution ($p=0.0001$). These results parallel the significantly reduced incidence of severe pain in patients receiving HTX-011 compared to both placebo (36% reduction; $p<0.0001$) and bupivacaine (29% reduction; $p<0.0001$).

In May 2019, the results from the pivotal Phase 3 EPOCH 1 bunionectomy study of HTX-011 were published online by the RAPM journal. The article, entitled "HTX-011 reduced pain intensity and opioid consumption versus bupivacaine HCl in bunionectomy: phase III results from the randomized EPOCH 1 study," also was published in the July 2019 print issue.

Hernia Repair—Study 302/EPOCH 2 Results

EPOCH 2 was a randomized, placebo- and active-controlled, double-blind, Phase 3 clinical study evaluating the efficacy and safety of locally administered HTX-011 at 300 mg compared to the standard dose of bupivacaine solution (75 mg) and placebo for postoperative pain control following hernia repair surgery in 418 subjects. All primary and key secondary endpoints were achieved:

- There was a 23% reduction in pain intensity as measured by AUC 0–72 when comparing HTX-011 to placebo ($p=0.0004$);
- There was a 21% reduction in pain as measured by AUC 0–72 when comparing HTX-011 to bupivacaine solution ($p<0.0001$);
- Over 72 hours post-surgery, patients receiving HTX-011 consumed 38% less opioids than placebo patients ($p=0.0001$) and 25% less opioids than patients receiving bupivacaine solution ($p=0.0240$); and
- 51% of patients receiving HTX-011 required no opioid medication for 72 hours post-surgery compared to only 22% receiving placebo ($p<0.0001$) and 40% receiving the standard-of-care, bupivacaine solution ($p=0.0486$). These results parallel the significantly reduced incidence of severe pain in patients receiving HTX-011 compared to both placebo (40% reduction; $p<0.0001$) and bupivacaine (19% reduction; $p=0.0372$).

In August 2019, the results from the Phase 3 EPOCH 2 hernia study of HTX-011 were published online in the journal, *Hernia*. The article, entitled "HTX-011 reduced pain intensity and opioid consumption versus bupivacaine HCI in herniorrhaphy: results of the phase 3 EPOCH 2 study," also was published in the December 2019 print issue.

HTX-011 was well tolerated in both Phase 3 studies, with a safety profile comparable to placebo and bupivacaine solution. There were no drug-related SAEs or discontinuations due to drug-related AEs in HTX-011-treated patients, and there were fewer opioid-related AEs in HTX-011-treated patients.

Phase 2b Study Results

In June 2018, we reported positive topline results from two completed Phase 2b studies of HTX-011: Study 209 (local administration in TKA) and Study 211 (instillation or pectoral pocket nerve block in breast augmentation). HTX-011 achieved the primary endpoints in both studies.

Total Knee Arthroplasty—Study 209 Results

Study 209 was a randomized, placebo- and active-controlled, double-blind, Phase 2b clinical study in patients undergoing primary unilateral TKA to evaluate the analgesic efficacy, safety and pharmacokinetics of locally administered HTX-011 into the surgical site. Following a dose-escalation phase, 222 patients were randomized to receive: (1) HTX-011 400 mg administered via instillation into the surgical site (HTX-011 alone); (2) HTX-011 400 mg administered via instillation into the surgical site with a low dose of ropivacaine injected into the posterior capsule (HTX-011 combination); (3) bupivacaine 125 mg administered via multiple injections into the surgical site; and (4) placebo. Ropivacaine and bupivacaine are generically available standard-of-care local anesthetics used in postoperative pain management. This study included a pre-specified hierarchical testing strategy for the primary and key secondary endpoints for the HTX-011 400 mg treatment groups. The primary endpoint was pain intensity as measured by the AUC from 0 to 48 hours post-surgery ("AUC 0–48") for HTX-011 compared to placebo. The key secondary endpoint was pain intensity as measured by the AUC from 0 to 72 hours post-surgery ("AUC 0–72") for HTX-011 compared to placebo. The primary and key secondary endpoints were achieved:

- The HTX-011 combination and HTX-011 alone resulted in reductions of 23% and 19%, respectively, in pain intensity measured at rest through 48 hours when compared to placebo ($p<0.0001$ and $p=0.0002$, respectively). These pain reductions from HTX-011 were approximately double that of bupivacaine, which resulted in a reduction of 11%. The HTX-011 combination reduction was significantly better than that of bupivacaine ($p=0.0212$).

- The HTX-011 combination and HTX-011 alone resulted in reductions of 22% and 19%, respectively, in pain intensity measured at rest through 72 hours when compared to placebo ($p<0.0001$ and $p=0.0004$, respectively). These pain reductions from HTX-011 were also approximately double that of bupivacaine, which resulted in a reduction of 11%. The HTX-011 combination reduction was significantly better than that of bupivacaine through 72 hours ($p=0.0325$).

- With the more conservative assessment of pain with activity, the HTX-011 combination and HTX-011 alone resulted in reductions of 16% and 12%, respectively, in pain intensity measured with activity through 48 hours when compared to placebo ($p<0.0001$ and $p=0.0017$, respectively). These pain reductions from HTX-011 were significantly better than that of bupivacaine, which resulted in a reduction of 4% ($p=0.0012$ and $p=0.0366$, respectively). Both the HTX-011 combination and HTX-011 alone maintained control of pain with activity through 72 hours with a 15% ($p=0.0002$) and 11% ($p=0.0058$) reduction compared to placebo, respectively.

- The HTX-011 combination significantly reduced opioid use through 48 and 72 hours compared to placebo ($p=0.0091$ and $p=0.0253$, respectively).

Breast Augmentation—Study 211 Results

Study 211 was a randomized, placebo- and active-controlled, double-blind, Phase 2b dose-finding study in patients undergoing augmentation mammoplasty to evaluate the analgesic efficacy, safety and pharmacokinetics of HTX-011 when administered by instillation into the surgical site or via ultrasound-guided lateral and medial pectoral nerve block before surgery. The study consisted of three cohorts comparing HTX-011 nerve block (60 mg, 120 mg, 240 mg) to the standard dose of bupivacaine 50 mg, administered as a nerve block, and placebo, and a final cohort comparing both HTX-011 400 mg administered by instillation and HTX-011 400 mg administered as a nerve block to the same two control groups. A total of 243 patients were enrolled. The primary endpoint was pain intensity as measured by the AUC from 0 to 24 hours post-surgery ("AUC 0–24") compared to placebo. The primary endpoint of the study was achieved:

- HTX-011 400 mg administered by instillation into the surgical site and HTX-011 400 mg administered as a nerve block both resulted in reductions of 22% in pain intensity measured at rest through 24 hours when compared to placebo (p=0.0023 and p=0.0055, respectively). These pain reductions from HTX-011 were approximately triple that of bupivacaine administered as a nerve block, which resulted in a reduction of 8%. The HTX-011 400 mg instillation reduction was significantly better than that of bupivacaine (p=0.0383).

- With the more conservative assessment of pain with activity, HTX-011 400 mg instillation and HTX-011 400 mg nerve block resulted in reductions of 24% and 23%, respectively, in pain intensity measured with activity through 24 hours when compared to placebo (p=0.0004 and p=0.0015, respectively). These pain reductions from HTX-011 were approximately double that of bupivacaine administered as a nerve block, which resulted in a reduction of 12%.

- HTX-011 400 mg instillation and HTX-011 400 mg nerve block resulted in reductions in total opioid use of 33% and 26%, respectively, when compared to placebo (p=0.0093 and p=0.0435, respectively). These reductions from HTX-011 were approximately triple that of bupivacaine administered as a nerve block, which resulted in a reduction of 10%. The HTX-011 400 mg instillation reduction was significantly better than that of bupivacaine (p=0.0455).

There was a strong correlation between pain reduction and the pharmacokinetics of HTX-011 in both studies.

HTX-011 was well tolerated in both Phase 2b studies, with a safety profile comparable to placebo and bupivacaine solution. There were no deaths and no clinically meaningful differences in overall AEs, SAEs, premature discontinuations due to AEs, potential local anesthetic systemic toxicity related AEs or wound healing.

Breakthrough Therapy Designation

In June 2018, we were granted Breakthrough Therapy designation for HTX-011 from the FDA for postoperative pain management. Breakthrough Therapy designation is designed to expedite the development and review of drugs that are intended to treat serious conditions and for which preliminary clinical evidence indicates substantial improvement over available therapies on clinically significant endpoint(s). Breakthrough Therapy designation was granted for HTX-011 based on the results of Phase 2 studies and two completed Phase 3 studies, which showed that HTX-011 produced significant reductions in both pain intensity and the need for opioids through 72 hours post-surgery compared to placebo and bupivacaine solution, the standard of care.

Fast Track Designation

In October 2017, we were granted Fast Track designation for HTX-011 from the FDA for local administration into the surgical site to reduce postoperative pain and the need for opioid analgesics for 72 hours. Fast Track designation is intended to facilitate the development and expedite the review of new therapies to treat serious conditions with unmet medical needs by providing sponsors with the opportunity for frequent interactions with the FDA.

Biochronomer Technology

Our proprietary Biochronomer Technology is designed to deliver therapeutic levels of a wide range of otherwise short-acting pharmacological agents over a period from days to weeks with a single administration. Our Biochronomer Technology consists of polymers that have been the subject of comprehensive animal and human toxicology studies that have shown evidence of the safety of the polymer. When administered, the polymers undergo controlled hydrolysis, resulting in a controlled, sustained release of the pharmacological agent encapsulated within the Biochronomer-based composition. Furthermore, our Biochronomer Technology is designed to permit more than one pharmacological agent to be incorporated, such that multimodal therapy can be delivered with a single administration.

Sales and Marketing

Our U.S.-based sales and marketing team consists of 77 employees as of February 3, 2020. The sales and marketing infrastructure includes a targeted, oncology sales force to establish relationships with a focused group of oncologists, oncology nurses and pharmacists. Additionally, the sales and marketing teams manage relationships with key accounts, such as managed care organizations, group purchasing organizations, hospital systems, oncology group networks, payors and government accounts. The sales force is supported by sales management, internal sales support, an internal marketing group and distribution support. We are currently building our U.S.-based sales and marketing team to support the commercialization of HTX-011, if approved.

Customers

CINVANTI is distributed in the U.S. through a limited number of specialty distributors ("Customers") that resell CINVANTI to healthcare providers and hospitals, the end users of CINVANTI. SUSTOL is distributed in the U.S. through a limited number of Customers that subsequently resell SUSTOL to healthcare providers, the end users of SUSTOL.

Competition

The biotechnology and pharmaceutical industries are extremely competitive. Our potential competitors are many in number and include major and mid-sized pharmaceutical and biotechnology companies. Many of our potential competitors have significantly more financial, technical and other resources than we do, which may give them a competitive advantage. In addition, they may have substantially more experience in effecting strategic combinations, in-licensing technology, developing drugs, obtaining regulatory approvals and manufacturing and marketing products. We cannot give any assurances that we can compete effectively with these other biotechnology and pharmaceutical companies. CINVANTI and SUSTOL compete in, and HTX-011 and any other products that we may develop or discover, if approved, will compete in, highly competitive markets. Our potential competitors in these markets may succeed in developing products that could render our products and product candidates obsolete or noncompetitive.

NK_1 receptor antagonists are also administered for the prevention of CINV, in combination with 5-HT_3 receptor antagonists, to augment the therapeutic effect of the 5-HT_3 receptor antagonist. CINVANTI faces significant competition. Currently available NK_1 receptor antagonists include: generic versions of EMEND® IV (fosaprepitant); EMEND® IV (fosaprepitant, marketed by Merck & Co); EMEND® (aprepitant, marketed by Merck & Co., Inc.); AKYNZEO® (palonosetron, a 5-HT_3 receptor antagonist, combined with netupitant, an NK_1 receptor antagonist, marketed by Eisai, Inc.); VARUBI® (rolapitant, marketed by TerSera Therapeutics LLC); and other products that include an NK_1 receptor antagonist that reach the market.

SUSTOL faces significant competition. Currently available 5-HT_3 receptor antagonists include: AKYNZEO® (palonosetron, a 5-HT_3 receptor antagonist, combined with netupitant, an NK_1 receptor antagonist, marketed by Helsinn Therapeutics (U.S.), Inc.); SANCUSO® (granisetron transdermal patch, marketed by ProStrakan Group Plc); and generic products including ondansetron (formerly marketed by GlaxoSmithKline plc as ZOFRAN), granisetron (formerly marketed by Hoffman-La Roche, Inc. as KYTRIL) and palonosetron (formerly marketed by Eisai in conjunction with Helsinn Healthcare S.A. as ALOXI). Currently, palonosetron is the only 5-HT_3 receptor antagonist other than SUSTOL that is approved for the prevention of delayed CINV associated with MEC regimens. SUSTOL is indicated in combination with other antiemetics in adults for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic chemotherapy (MEC) or anthracycline and cyclophosphamide (AC) combination chemotherapy regimens, which is considered to be a HEC regimen by the NCCN and ASCO. No other 5-HT_3 receptor antagonist is specifically approved for the prevention of delayed CINV associated with a HEC regimen.

If we are able to successfully develop HTX-011 for postoperative pain management, we will compete with MARCAINE™ (bupivacaine, marketed by Hospira, Inc.) and generic forms of bupivacaine; NAROPIN® (ropivacaine, marketed by Fresenius Kabi USA, LLC) and generic forms of ropivacaine; EXPAREL® (bupivacaine liposome injectable suspension, marketed by Pacira BioSciences, Inc.) and potentially other products in development for postoperative pain management that reach the market.

Manufacturing and Clinical Supplies

We do not own or operate manufacturing facilities for the production of commercial or clinical quantities of any product, including CINVANTI, SUSTOL or HTX-011. We currently rely on a small number of third-party manufacturers to produce compounds used in our product development and commercial activities and expect to continue to do so to meet the preclinical and clinical requirements of our potential products and for all of our commercial needs. We currently have long-term commercial supply agreements with certain third-party manufacturers. Our manufacturing and processing agreements require that all third-party contract manufacturers and processors produce active pharmaceutical ingredients and finished products in accordance with the FDA's current Good Manufacturing Practices ("cGMP") and all other applicable laws and regulations. We maintain confidentiality agreements with potential and existing manufacturers in order to protect our proprietary rights related to CINVANTI, SUSTOL, HTX-011, HTX-034 and our Biochronomer Technology.

Some of the critical materials and components used in manufacturing CINVANTI, SUSTOL, HTX-011 and HTX-034 are sourced from single suppliers. An interruption in the supply of a key material could significantly delay our research and development process or increase our expenses for commercialization or development of products. Specialized materials must often be manufactured for the first time for use in drug delivery technologies, or materials may be used in the technologies in a manner that is different from their customary commercial uses. The quality of materials can be critical to the performance of a drug delivery technology, so a reliable source that provides a consistent supply of materials is important. Materials or components needed for our drug delivery technologies may be difficult to obtain on commercially reasonable terms, particularly when relatively small quantities are required or if the materials traditionally have not been used in pharmaceutical products.

Intellectual Property

Our success will depend in large part on our ability to:

- obtain and maintain international and domestic patents and other legal protections for the proprietary technology, inventions and improvements we consider important to our business;
- prosecute and defend our patents;
- preserve our trade secrets; and
- operate without infringing the patents and proprietary rights of other parties.

We intend to continue to seek appropriate patent protection for the product candidates in our research and development programs and their uses by filing patent applications in the U.S. and other selected countries. We intend for these patent applications to cover, where possible, claims for composition of matter, medical uses, processes for preparation and formulations.

We have filed a number of U.S. patent applications on inventions relating to the composition of a variety of polymers, specific products, product groups and processing technology. As of December 31, 2019, we had a total of 29 issued U.S. patents and an additional 37 issued (or registered) foreign patents. The patents on the bioerodible technologies expire between May 2021 and March 2026. Currently, CINVANTI is covered by 6 patents issued in the U.S. with expiration dates of September 2035. Currently, SUSTOL is covered by 8 patents issued in the U.S. and by 31 patents issued in foreign countries including Austria, Belgium, Canada, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Japan, Luxembourg, Netherlands, Portugal, Spain, Sweden, Switzerland, Taiwan, and the United Kingdom. U.S. patents covering SUSTOL have expiration dates ranging from May 2021 to September 2024; foreign patents covering SUSTOL have expiration dates ranging from May 2021 to September 2025. HTX-011 is protected by ten patents issued in the U.S. and by 24 patents issued in foreign countries including Australia, Austria, Belgium, Canada, Denmark, Finland, France, Germany, Greece, Hong Kong, Ireland, Italy, Japan, Luxembourg, Mexico, Netherlands, Portugal, Spain, Sweden, Switzerland, Taiwan and the United Kingdom. U.S. patents covering HTX-011 have expiration dates ranging from May 2021 to April 2035; foreign patents covering HTX-011 have expiration dates ranging from May 2021 to March 2034. Our policy is to actively seek patent protection in the U.S. and to pursue equivalent patent claims in selected foreign countries, thereby seeking patent coverage for novel technologies and compositions of matter that may be commercially important to the development of our business. Granted patents include claims covering the product composition, methods of use and methods of preparation. Our existing patents may not cover future products, additional patents may not be issued and current patents, or patents issued in the future, may not provide meaningful protection or prove to be of commercial benefit.

Although we believe that our rights under patent applications we own provide a competitive advantage, the patent positions of pharmaceutical and biotechnology companies are highly uncertain and involve complex legal and factual questions. We may not be able to develop patentable products or processes, and may not be able to obtain patents from pending applications. Even if patent claims are allowed, the claims may not issue, or in the event of issuance, may not be sufficient to protect the technology owned by or licensed to us. Any patents or patent rights that we obtain may be circumvented, challenged or invalidated by our competitors.

We also rely on trade secrets, proprietary know-how and continuing innovation to develop and maintain our competitive position. We seek protection of these trade secrets, proprietary know-how and any continuing innovation, in part, through confidentiality and proprietary information agreements. However, these agreements may not provide meaningful protection for, or adequate remedies to protect, our technology in the event of unauthorized use or disclosure of information. Furthermore, our trade secrets may otherwise become known to, or be independently developed by, our competitors.

Government Regulation

Pharmaceutical Regulation

Pharmaceutical products that we market in the U.S. are subject to extensive government regulation. Likewise, if we receive approvals to market and distribute any such products abroad, they would also be subject to extensive foreign government regulation.

In the U.S., the FDA regulates pharmaceutical products. FDA regulations govern the testing, research and development activities, manufacturing, quality, storage, advertising, promotion, labeling, sale and distribution of pharmaceutical products. Accordingly, there is a rigorous process for the approval of new drugs and ongoing oversight of marketed products. We are also subject to foreign regulatory requirements governing clinical trials and drug products if products are tested or marketed abroad. The approval process outside the U.S. varies from jurisdiction to jurisdiction and the time required may be longer or shorter than that required for FDA approval.

Regulation in the U.S.

The FDA testing and approval process requires substantial time, effort and money. The FDA approval process for new drugs includes, without limitation:

- preclinical studies;
- submission in the U.S. of an Investigational New Drug application ("IND"), for clinical trials conducted in the U.S.;
- adequate and well-controlled human clinical trials to establish safety and efficacy of the product;
- submission and review of an NDA in the U.S.; and
- inspection of the facilities used in the manufacturing of the drug to assess compliance with the FDA's current cGMP regulations.

The FDA monitors the progress of trials conducted in the U.S. under an IND and may, at its discretion, re-evaluate, alter, suspend or terminate testing based on the data accumulated to that point and the FDA's risk/benefit assessment with regard to the patients enrolled in the trial. The FDA may also place a hold on one or more clinical trials conducted under an IND for a drug if it deems warranted. Furthermore, even after regulatory approval of an NDA is obtained, under certain circumstances, such as later discovery of previously unknown problems, the FDA can withdraw approval or subject the drug to additional restrictions.

Preclinical Testing

Preclinical studies include laboratory evaluation of the product and animal studies to assess the potential safety and effectiveness of the product. Most of these studies must be performed according to Good Laboratory Practices, a system of management controls for laboratories and research organizations to ensure the consistency and reliability of results.

An IND is the request for authorization from the FDA to administer an investigational new drug product to humans. The IND includes information regarding the preclinical studies, the investigational product's chemistry and manufacturing, supporting data and literature and the investigational plan and protocol(s). Clinical trials may begin 30 days after an IND is received, unless the FDA raises concerns or questions about the conduct of the clinical trials. If concerns or questions are raised, an IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can proceed. An IND must become effective before human clinical trials begin. We have filed INDs in the U.S. and Clinical Trial Applications ("CTAs") in the EU, and we may file additional INDs and CTAs in the future. We cannot assure that submission of any additional INDs or CTAs for any of our product candidates will result in authorization to commence clinical trials.

Clinical Trials

Clinical trials involve the administration of the product candidate that is the subject of the trial to volunteers or patients under the supervision of a qualified principal investigator and in accordance with a clinical trial protocol, which sets forth details, such as the study objectives, enrollment criteria and the safety and effectiveness criteria to be evaluated. Each clinical trial must be reviewed and approved at each institution at which the study will be conducted by an independent institutional review board ("IRB") in the U.S., referred to as an ethics committee in the EU and other markets or Research Ethics Board ("REB") in Canada. The IRB, ethics committee or REB (hereafter referred to as "IRB") will consider, among other things, ethical factors, safety of human subjects and the possible liability of the institution arising from the conduct of the proposed clinical trial. In addition, clinical trials in the U.S. and other regions must be performed according to good clinical practices, which are enumerated in FDA regulations and guidance documents. Some studies include oversight by an independent group of experts, known as a data safety monitoring board, which authorizes whether a study may move forward based on certain data from the study and may stop the clinical trial if it determines that there is an unacceptable safety risk for subjects or other grounds.

The FDA or other regulatory authorities may order the temporary, or permanent, discontinuation of a clinical trial at any time, or impose other sanctions, if it believes that the clinical trial is not being conducted in accordance with regulatory requirements or presents an unacceptable risk to the clinical trial patients. An IRB may also require the clinical trial at the site to be halted, either temporarily or permanently, for failure to comply with the IRB's requirements, or it may impose other conditions.

Clinical trials typically are conducted in sequential phases: Phases 1, 2, 3 and 4. The phases may overlap. The FDA may require that we suspend clinical trials at any time on various grounds, including if the FDA makes a finding that the subjects participating in the trial are being exposed to an unacceptable health risk.

In Phase 1 clinical trials, the investigational product is usually tested on a small number of healthy volunteers to determine safety, any adverse effects, proper dosage, absorption, metabolism, distribution, excretion and other drug effects. Follow-on Phase 1b clinical trials may also evaluate efficacy with respect to trial participants.

In Phase 2 clinical trials, the investigational product is usually tested on a limited number of patients (generally up to several hundred) to preliminarily evaluate the efficacy of the drug for specific, targeted indications, to determine dosage tolerance and optimal dosage, and to identify possible adverse effects and safety risks. Multiple Phase 2 clinical trials may be conducted to obtain information prior to beginning Phase 3 clinical trials.

In Phase 3 clinical trials, the investigational product is administered to an expanded patient population to confirm proof of concept and efficacy claims, provide evidence of clinical efficacy and to further test for safety, generally at multiple clinical sites.

In Phase 4 clinical trials or other post-approval commitments, additional studies and patient follow-up are conducted to gain experience from the treatment of patients in the intended therapeutic indication. The FDA and other regulatory authorities may require a commitment to conduct post-approval Phase 4 studies as a condition of approval. Additional studies and follow-up may be conducted to document a clinical benefit where drugs are approved under accelerated approval regulations and based on surrogate endpoints. In clinical trials, surrogate endpoints are alternative measurements of the symptoms of a disease or condition that are substituted for measurements of observable clinical symptoms. In the U.S., failure to timely conduct Phase 4 clinical trials and follow-up could result in withdrawal of approval for products approved under accelerated approval regulations.

Clinical Data Review and Approval in the U.S.

The data from the clinical trials, together with preclinical data and other supporting information that establishes a drug candidate's safety, are submitted to the FDA in the form of an NDA, or NDA supplement (for approval of a new indication if the product candidate is already approved for another indication). Under applicable laws and FDA regulations, the FDA reviews the NDA within 60 days of receipt of the NDA to determine whether the application will be accepted for filing based on the FDA's threshold determination that the NDA is sufficiently complete to permit substantive review. If deemed complete, the FDA will "file" the NDA, thereby triggering substantive review of the application. The FDA can refuse to file any NDA that it deems incomplete or not properly reviewable.

The FDA has established internal substantive review goals of 10 months for most NDAs. The FDA has various programs, including Breakthrough Therapy, Fast Track and Priority Review, which are intended to expedite or simplify the process for reviewing drugs, and/or provide for approval based on surrogate endpoints. Even if a drug qualifies for one or more of these programs, the FDA may later decide that the drug no longer meets the conditions for qualification or that the period for FDA review or approval will not be shortened. Generally, drugs that may be eligible for these programs are those for serious or life-threatening conditions, those with the potential to address unmet medical needs, and those that offer meaningful benefits over existing treatments. For example, Fast Track is a process designed to facilitate the development, and expedite the review, of drugs to treat serious diseases and fill an unmet medical need. The request may be made at the time of IND submission and generally no later than the pre-NDA meeting. The FDA will respond within 60 calendar days of receipt of the request. Priority Review designation, which is requested at the time of an NDA submission, is designed to give drugs that offer major advances in treatment or provide a treatment where no adequate therapy exists, an initial review within 6 months as compared to a standard review time of 10 months. Although Fast Track and Priority Review do not affect the standards for approval, the FDA will attempt to facilitate early and frequent meetings with a sponsor of a Fast Track designated drug and expedite review of the application for a drug designated for Priority Review. Accelerated approval provides an expedited approval of drugs that treat serious diseases and that fill an unmet medical need based on a surrogate endpoint. The FDA, however, is not legally required to complete its review within these periods, and these performance goals may change over time.

If the FDA approves the NDA, it will issue an approval letter authorizing the commercial marketing of the drug with prescribing information for specific indications. As a condition of NDA approval, the FDA may require a risk evaluation and mitigation strategy (“REMS”), to help ensure that the benefits of the drug outweigh the potential risks. REMS can include medication guides, communication plans for healthcare professionals, and elements to assure safe use. Additionally, the FDA will inspect the facility or the facilities at which the drug is manufactured. Moreover, product approval may require substantial post-approval testing and surveillance to monitor the drug’s safety or efficacy. Once granted, product approvals may be withdrawn if compliance with regulatory standards is not maintained or problems are identified following initial marketing. In many cases, the outcome of the review, even if generally favorable, is not an actual approval, but a “complete response” that generally outlines the deficiencies in the submission, which may require substantial additional testing or information before the FDA will reconsider the application. If, or when, those deficiencies have been addressed to the FDA’s satisfaction in a resubmission of the NDA, the FDA will issue an approval letter.

Satisfaction of FDA requirements or similar requirements of state, local and foreign regulatory agencies typically takes several years and requires the expenditure of substantial financial resources. Information generated in this process is susceptible to varying interpretations that could delay, limit or prevent regulatory approval at any stage of the process. Accordingly, the actual time and expense required to bring a product to market may vary substantially. Data obtained from clinical activities is not always conclusive and may be susceptible to varying interpretations, which could delay, limit or prevent regulatory approval. Success in early-stage clinical trials does not ensure success in later-stage clinical trials. Even if a product candidate receives regulatory approval, the approval may be significantly limited to specific disease states, patient populations and dosages, or have conditions placed on it that restrict the commercial applications, advertising, promotion or distribution of these products.

Once issued, the FDA may withdraw product approval if ongoing regulatory standards are not met or if safety problems occur after the product reaches the market. In addition, the FDA may require testing and surveillance programs to monitor the safety or effectiveness of approved products which have been commercialized, and the FDA has the power to prevent or limit further marketing of a product based on the results of these postmarketing programs. The FDA may also request or require additional Phase 4 clinical trials after a product is approved. The results of Phase 4 clinical trials can confirm the effectiveness of a product candidate and can provide important safety information to augment the FDA's voluntary adverse drug reaction reporting system. Any products manufactured or distributed by us pursuant to FDA approvals would be subject to continuing regulation by the FDA, including recordkeeping requirements and reporting of adverse experiences with the drug. Drug manufacturers and their subcontractors are required to register their establishments with the FDA and certain state agencies and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMPs, which impose certain procedural and documentation requirements on us and our third-party manufacturers.

In addition, both before and after approval is sought, we are required to comply with a number of FDA requirements. For example, we are required to report certain adverse reactions and production problems, if any, to the FDA, and to comply with certain limitations and other requirements concerning advertising and promotion for our products. In addition, quality control and manufacturing procedures must continue to conform to cGMP after approval, and the FDA periodically inspects manufacturing facilities to assess compliance with continuing cGMP. In addition, discovery of problems, such as safety problems, may result in changes in labeling or restrictions on a product manufacturer or NDA holder, including removal of the product from the market.

The FDA closely regulates the marketing and promotion of drugs. Approval may be subject to postmarketing surveillance and other recordkeeping and reporting obligations and involve ongoing requirements. Product approvals may be withdrawn if compliance with regulatory standards is not maintained or if problems occur following initial marketing. A company can make only those claims relating to safety and efficacy that are approved by the FDA. Failure to comply with these requirements can result in adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties.

Clinical Trial Conduct and Product Approval Regulation in Non-U.S. Jurisdictions

In addition to regulations in the U.S., we may be subject to a variety of foreign regulations governing clinical trials and commercial sales and distribution of our products. For example, our clinical trials conducted in the EU must be done under an Investigational Medicinal Product Dossier, and the oversight of an ethics committee. If we market our products in foreign countries, we also will be subject to foreign regulatory requirements governing marketing approval for pharmaceutical products. The requirements governing the conduct of clinical trials, product approval, pricing and reimbursement vary widely from country to country. Whether or not FDA approval has been obtained, approval of a product by the comparable regulatory authorities of foreign countries must be obtained before manufacturing or marketing the product in those countries. The approval process varies from country to country and the time required for such approvals may differ substantially from that required for FDA approval. There is no assurance that any future FDA approval of any of our product candidates will result in similar foreign approvals or vice versa. The process for clinical trials in other jurisdictions are similar, and trials are heavily scrutinized by the designated ethics committee.

Section 505(b)(2) Applications

Some of our product candidates may be eligible for submission of applications for approval under the FDA's Section 505(b)(2) approval process, which provides an alternate path to FDA approval for new or improved formulations or new uses of previously approved products. Section 505(b)(2) was enacted as part of the Drug Price Competition and Patent Term Restoration Act of 1984, also known as the Hatch-Waxman Act, and allows approval of NDAs that rely, at least in part, on studies that were not conducted by or for the applicant and to which the applicant has not obtained a right of reference. Such studies can be provided by published literature, or the FDA can rely on previous findings of safety and efficacy for a previously approved drug. If the 505(b)(2) applicant can establish that reliance on the FDA's previous approval is scientifically appropriate, it may eliminate the need to conduct certain preclinical studies or clinical trials of the new product. Section 505(b)(2) applications may be submitted for drug products that represent a modification (*e.g.*, a new indication or new dosage form) of an eligible approved drug. In such cases, the additional information in 505(b)(2) applications necessary to support the change from the previously approved drug is frequently provided by new studies submitted by the applicant. Because a Section 505(b)(2) application relies in part on previous studies or previous FDA findings of safety and effectiveness, preparing 505(b)(2) applications is generally less costly and time-consuming than preparing an NDA based entirely on new data and information from a full set of clinical trials. The FDA may approve the new product candidate for all, or some, of the label indications for which the referenced product has been approved, as well as for any new indication sought by the Section 505(b)(2) applicant. The law governing Section 505(b)(2) or FDA's current policies may change in such a way as to adversely affect our applications for approval that seek to utilize the Section 505(b)(2) approach. Such changes could result in additional costs associated with additional studies or clinical trials and delays.

The FDA provides that reviews and/or approvals of applications submitted under Section 505(b)(2) will be delayed in various circumstances. For example, the holder of the NDA for the listed drug may be entitled to a period of market exclusivity during which the FDA will not approve, and may not even review, a Section 505(b)(2) application from other sponsors. If the listed drug is claimed by one or more patents that the NDA holder has listed with the FDA, the Section 505(b)(2) applicant must submit a certification with respect to each such patent. If the 505(b)(2) applicant certifies that a listed patent is invalid, unenforceable or not infringed by the product that is the subject of the Section 505(b)(2) application, it must notify the patent holder and the NDA holder. If, within 45 days of providing this notice, the NDA holder sues the 505(b)(2) applicant for patent infringement, the FDA will not approve the Section 505(b)(2) application until the earlier of a court decision favorable to the Section 505(b)(2) applicant or the expiration of 30 months. The regulations governing marketing exclusivity and patent protection are complex, and it is often unclear how they will be applied in particular circumstances.

Drug Enforcement Agency Regulation

Our research and development processes involve the controlled use of hazardous materials, including chemicals. Some of these hazardous materials are considered to be controlled substances and subject to regulation by the U.S. Drug Enforcement Agency ("DEA"). Controlled substances are those drugs that appear on one of 5 schedules promulgated and administered by the DEA under the Controlled Substances Act ("CSA"). The CSA governs, among other things, the distribution, recordkeeping, handling, security and disposal of controlled substances. We must be registered by the DEA in order to engage in these activities, and we are subject to periodic and ongoing inspections by the DEA and similar state drug enforcement authorities to assess ongoing compliance with the DEA's regulations. Any failure to comply with these regulations could lead to a variety of sanctions, including the revocation, or a denial of renewal, of the DEA registration, injunctions or civil or criminal penalties.

Third-party Payor Coverage and Reimbursement

Commercial success of CINVANTI, SUSTOL and any of our other future products that are approved or commercialized for any indication will depend, in part, on the availability of coverage and reimbursement from third-party payors at the federal, state and private levels. Government payor programs, including Medicare and Medicaid, private health care insurance companies and managed care plans have attempted to control costs by limiting coverage and the amount of reimbursement for particular procedures or drug treatments. The U.S. Congress and state legislatures, from time to time, propose and adopt initiatives aimed at cost containment. Ongoing federal and state government initiatives directed at lowering the total cost of health care will likely continue to focus on health care reform, the cost of prescription pharmaceuticals and on the reform of the Medicare and Medicaid payment systems. Examples of how limits on drug coverage and reimbursement in the U.S. may cause reduced payments for drugs in the future include:

- changing Medicare reimbursement methodologies;
- fluctuating decisions on which drugs to include in formularies;
- revising drug rebate calculations under the Medicaid program or requiring that new or additional rebates be provided to Medicare, Medicaid and other federal or state healthcare programs; and
- reforming drug importation laws.

Some third-party payors also require pre-approval of coverage for new drug therapies before they will reimburse health care providers that use such therapies. While we cannot predict whether any proposed cost-containment measures will be adopted or otherwise implemented in the future, the announcement or adoption of these proposals could have a material adverse effect on our ability to obtain adequate prices for our current and future products and to operate profitably.

Reimbursement systems in international markets vary significantly by country and, within some countries, by region. Reimbursement approvals must be obtained on a country-by-country basis. In many foreign markets, including markets in which we hope to sell our products, the pricing of prescription pharmaceuticals is subject to government pricing control. In these markets, once marketing approval is received, pricing negotiations could take significant additional time. As in the U.S., the lack of satisfactory reimbursement or inadequate government pricing of any of our products would limit widespread use and lower potential product revenues.

Anti-kickback, Fraud and Abuse and False Claims Regulation

We are subject to health care fraud and abuse regulation and enforcement by both the federal government and the states in which we conduct our business. Healthcare providers, physicians and third-party payors play a primary role in the recommendation and prescription of CINVANTI, SUSTOL and any other product candidates for which we obtain marketing approval. Arrangements with third-party payors and customers may expose us to applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute our products for which we obtain marketing approval.

Regulations under applicable federal and state healthcare laws and regulations include the federal health care programs' Anti-Kickback Law, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, in exchange for or to induce either the referral or purchase of any good or service for which payment may be made under federal health care programs such as the Medicare and Medicaid programs. Remuneration has been broadly defined to include anything of value, including cash, improper discounts, and free or reduced-price items and services. Many states have similar laws that apply to their state health care programs as well as private payors. In addition, the False Claims Act ("FCA") imposes liability on persons who, among other things, present or cause to be presented false or fraudulent claims for payment by a federal health care program. The FCA has been used to prosecute persons submitting claims for payment that are inaccurate or fraudulent, that are for services not provided as claimed, or for services that are not medically necessary. Actions under the FCA may be brought by the Attorney General or as a *qui tam* action by a private individual in the name of the government. Violations of the FCA can result in significant monetary penalties and treble damages. The federal government is using the FCA, and the accompanying threat of significant liability, in its investigation and prosecution of pharmaceutical and biotechnology companies throughout the country, for example, in connection with the promotion of products for unapproved uses and other sales and marketing practices.

The risk of being found in violation of these laws is increased by the fact that many of them have not been fully interpreted by the regulatory authorities or the courts, and their provisions are open to a variety of interpretations. Moreover, recent health care reform legislation has strengthened many of these laws. For example, the Patient Protection and Affordable Care Act ("PPACA"), among other things, amends the intent requirement of the federal anti-kickback and criminal health care fraud statutes to clarify that a person or entity does not need to have actual knowledge of this statute or specific intent to violate it. In addition, PPACA provides that a claim including items or services resulting from a violation of the federal anti-kickback statute constitutes a false or fraudulent claim for purposes of the false claims statutes.

The continuing interpretation and application of these laws could have a material adverse impact on our business and our ability to compete should we commence marketing a product.

Federal and State Sunshine Laws

We must comply with federal and state "sunshine" laws, now known as Open Payments that require transparency regarding financial arrangements with health care providers. This would include the reporting and disclosure requirements imposed by the PPACA on drug manufacturers regarding any "payment or transfer of value" made or distributed to physicians and teaching hospitals. Failure to submit required information can result in civil monetary penalties. A number of states have laws that require the implementation of commercial compliance programs, impose restrictions on drug manufacturer marketing practices and/or require pharmaceutical companies to track and report payments, gifts and other benefits provided to physicians and other health care professionals and entities.

Foreign Corrupt Practices Act

We are subject to the Foreign Corrupt Practices Act of 1997 ("FCPA"). The FCPA and other similar anti-bribery laws in other jurisdictions, such as the U.K. Bribery Act, generally prohibit companies and their intermediaries from providing money or anything of value to officials of foreign governments, foreign political parties, or international organizations with the intent to obtain or retain business or seek a business advantage. Recently, there has been a substantial increase in anti-bribery law enforcement activity by U.S. regulators, with more frequent and aggressive investigations and enforcement proceedings by both the Department of Justice and the U.S. Securities and Exchange Commission ("SEC"). A determination that our operations or activities are not, or were not, in compliance with U.S. or foreign laws or regulations could result in the imposition of substantial fines, interruptions of business, loss of supplier, vendor or other third-party relationships, termination of necessary licenses and permits and other legal or equitable sanctions. Other internal or government investigations or legal or regulatory proceedings, including lawsuits brought by private litigants, may also follow as a consequence.

Patient Privacy and Data Security

We are required to comply, as applicable, with numerous federal and state laws, including state security breach notification laws, state health and personal information privacy laws and federal and state consumer protection laws, and to govern the collection, use and disclosure of personal information. For example, the California Consumer Privacy Act ("CCPA") became effective on January 1, 2020 and gave California residents expanded rights to access and require deletion of their personal information, opt out of certain personal information sharing and receive detailed information about how their personal information is used. Other countries also have, or are developing, laws governing the collection, use and transmission of personal information, such as the General Data Protection Regulation in the EU that became effective in May 2018 and the Personal Information Protection and Electronic Documents Act that became effective in Canada in April 2000. In addition, most healthcare providers who prescribe CINVANTI, SUSTOL or who may prescribe other products we may sell in the future and from whom we may obtain patient health information are subject to privacy and security requirements under the Health Insurance Portability and Accountability Act of 1996 ("HIPAA"), as amended by the Health Information Technology and Clinical Health Act, and its implementing regulations. We are not a HIPAA covered entity, do not intend to become one, and we do not operate as a business associate to any covered entities. Therefore, these privacy and security requirements do not apply to us. However, we could be subject to civil and criminal penalties if we knowingly obtain individually identifiable health information from a covered entity in a manner that is not authorized or permitted by HIPAA or for aiding and abetting the violation of HIPAA. The legislative and regulatory landscape for privacy and data protection continues to evolve, and there has been an increasing amount of focus on privacy and data protection issues with the potential to affect our business, including recently enacted laws in a majority of states requiring security breach notification. These laws could create liability for us or increase our cost

of doing business, and any failure to comply could result in harm to our reputation, and potentially fines and penalties.

In addition, state laws govern the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

Environmental, Health and Safety Laws

Our operations are subject to complex and increasingly stringent environmental, health and safety laws and regulations. Further, in the future, we may open manufacturing facilities that would likely be subject to environmental and health and safety authorities in the relevant jurisdictions. These authorities typically administer laws which regulate, among other matters, the emission of pollutants into the air (including the workplace), the discharge of pollutants into bodies of water, the storage, use, handling and disposal of hazardous substances, the exposure of persons to hazardous substances, and the general health, safety and welfare of employees and members of the public. Violations of these laws could subject us to strict liability, fines or liability to third parties.

Other Laws

We are subject to a variety of financial disclosure and securities trading regulations as a public company in the U.S., including laws relating to the oversight activities of the SEC and the regulations of The Nasdaq Capital Market, on which our shares are traded. We are also subject to various laws, regulations and recommendations relating to safe working conditions, laboratory practices and the experimental use of animals.

Employees

As of February 3, 2020, we had 231 employees, all of which were full-time employees; 124 are involved in research and development activities, 77 are involved in sales and marketing activities and 30 are involved in administration, human resources, finance, legal and information technology. None of our employees are covered by a collective bargaining agreement.

Company Information

We were founded in February 1983 as a California corporation under the name AMCO Polymerics, Inc. (“AMCO”). AMCO changed its name to Advanced Polymer Systems, Inc. (“APS”) in 1984 and was reincorporated in the state of Delaware in 1987. APS changed its name to A.P. Pharma, Inc. (“APP”) in May 2001. In January 2014, APP changed its name to Heron Therapeutics, Inc.

Our website address is *www.herontx.com*. We make our periodic and current reports available on our website, free of charge, as soon as reasonably practicable after such material is electronically filed with, or furnished to, the SEC. No portion of our website is incorporated by reference into this Annual Report on Form 10-K. We file our annual, quarterly and special reports, proxy statements and other information with the SEC. Our filings with the SEC are also available to the public on the SEC’s website at *http://www.sec.gov*. Additional information regarding us, including our audited financial statements and descriptions of our business, is contained in the documents incorporated by reference in this Annual Report on Form 10-K. Our common stock is traded on The Nasdaq Capital Market, under the symbol “HRTX.”

ITEM 1A. RISK FACTORS.

You should carefully consider the following information about risks and uncertainties that may affect us or our business, together with the other information appearing elsewhere in this Annual Report on Form 10-K. If any of the following events, described as risks, actually occur, our business, financial condition, results of operations and future growth prospects would likely be materially and adversely affected. In these circumstances, the market price of our common stock could decline, and you may lose all or part of your investment in our securities. An investment in our securities is speculative and involves a high degree of risk. You should not invest in our securities if you cannot bear the economic risk of your investment for an indefinite period of time and cannot afford to lose your entire investment.

Risks Related to Our Business

We are substantially dependent on the commercial success of CINVANTI, SUSTOL and HTX-011, if approved, and if CINVANTI, SUSTOL or HTX-011, if approved, do not attain market acceptance by healthcare professionals and patients, our business and results of operations will suffer.

The success of our business is substantially dependent on our ability to commercialize CINVANTI, SUSTOL and HTX-011, if approved. Although members of our management team have prior experience launching new drugs, CINVANTI and SUSTOL are the first two products that we have launched and, if HTX-011 is approved, it will be the third product that we launch.

Further, even if our sales organization performs as expected, the revenue that we may receive from the sales of CINVANTI, SUSTOL and HTX-011, if approved, may be less than anticipated due to factors that are outside of our control. These factors that may affect revenue include:

- the scope of our approved product labels;
- the perception of physicians and other members of the health care community of the safety and efficacy and cost-competitiveness relative to that of competing products;
- our ability to maintain successful sales, marketing and educational programs for certain physicians and other health care providers;
- our ability to raise patient and physician awareness of CINV associated with AC combination chemotherapy regimens, MEC or HEC and encourage physicians to look for incidence of CINV among patients;
- our ability to raise patient and physician awareness of the risks associated with using opioids for postoperative pain management and encourage physicians to consider utilizing a non-opioid alternative;
- the cost-effectiveness of our products;
- acceptance by institutional formulary committees;
- patient and physician satisfaction with our products;
- the size of the potential market for our products;
- our ability to obtain adequate reimbursement from government and third-party payors;
- unfavorable publicity concerning our products or similar products;

- the introduction, availability and acceptance of competing treatments, including competing generic products;
- AE information relating to our products or similar classes of drugs;
- product liability litigation alleging injuries relating to the products or similar classes of drugs;
- our ability to maintain and defend our patents for CINVANTI, SUSTOL and HTX-011;
- our ability to continue to have CINVANTI and SUSTOL manufactured at commercial production levels successfully and on a timely basis;
- our ability to scale up manufacturing of HTX-011 and continue to have HTX-011 manufactured at commercial production levels successfully and on a timely basis;
- the availability of raw materials necessary to manufacture CINVANTI, SUSTOL and HTX-011;
- our ability to access third parties to manufacture and distribute our products on acceptable terms or at all;
- regulatory developments related to the manufacture or continued use of our products;
- conduct of post-approval study requirements and the results thereof;
- the extent and effectiveness of sales and marketing and distribution support for our products;
- our competitors' activities, including decisions as to the timing of competing product launches, generic entrants, pricing and discounting; and
- any other material adverse developments with respect to the commercialization of our products.

Additionally, a CRL was received from the FDA regarding the NDA for HTX-011 on April 30, 2019. The CRL states that the FDA was unable to approve the NDA in its present form based on the need for additional CMC and non-clinical information. Based on the complete review of the NDA, the FDA did not identify any clinical safety or efficacy issues, and there was no requirement for further clinical studies or data analyses. In February 2020, we announced that the FDA extended the review period for the NDA for HTX-011 by up to three months. The new PDUFA goal date is June 26, 2020. The contract manufacturing site used to manufacture HTX-011 has been reinspected by the FDA with no Form 483 observations issued and with a recommendation by the FDA inspector for approval of the site. We have not been informed of any other manufacturing concerns. We cannot predict the outcome of any interactions that we might have with the FDA or when HTX-011 will receive marketing approval, if at all.

Our business will be adversely affected if, due to these or other factors, our commercialization of CINVANTI, SUSTOL or HTX-011, if approved, does not achieve the acceptance and demand necessary to sustain revenue growth. If we are unable to successfully commercialize CINVANTI, SUSTOL or HTX-011, if approved, our business and results of operations will suffer.

If we are unable to develop and maintain sales, marketing and distribution capabilities or enter into agreements with third parties to sell and market CINVANTI, SUSTOL, HTX-011, if approved, or any other products we may develop, our product sales may be adversely affected.

We have established an internal sales organization for the sale, marketing and distribution of CINVANTI, SUSTOL and HTX-011, if approved. In order to successfully commercialize any other products we may develop, we must increase our sales, marketing, distribution and other non-technical capabilities or make arrangements with third parties to perform these services. The development of a sales organization to market CINVANTI, SUSTOL, HTX-011, if approved, or any other products we may develop, is expensive and time consuming, and we cannot be certain that we will be able to successfully develop this capacity or that this function will execute as expected. If we are unable to establish adequate sales, marketing and distribution capabilities, whether independently or with third parties, we may not be able to generate product revenue and our business and results of operations will suffer.

If we cannot establish satisfactory pricing of CINVANTI, SUSTOL, HTX-011, if approved, or any other products we may develop that is also acceptable to the U.S. government, insurance companies, managed care organizations and other payors, or arrange for favorable reimbursement policies, our product sales may be adversely affected and our future revenue may suffer.

The continuing efforts of the U.S. government, insurance companies, managed care organizations and other payors of health care costs to contain or reduce costs of health care may adversely affect our ability to generate adequate revenues and gross margins to make CINVANTI, SUSTOL, HTX-011, if approved, or any other products we may develop commercially viable. Our ability to commercialize CINVANTI, SUSTOL, HTX-011, if approved, or any other products we may develop successfully will depend in part on the extent to which governmental authorities, private health insurers and other organizations establish appropriate reimbursement levels for the cost of such products and related treatments and for what uses reimbursement will be provided.

Adoption of CINVANTI, SUSTOL, HTX-011, if approved, or any other products we may develop by the medical community may be limited if third-party payors will not offer adequate coverage. In addition, third-party payors often challenge the price and cost-effectiveness of medical products and services and such pressure may increase in the future. In many cases, uncertainty exists as to the adequate reimbursement status of newly approved healthcare products. Accordingly, CINVANTI, SUSTOL, HTX-011, if approved, or any other products we may develop may not be reimbursable by certain third-party payors at the time of commercial launch and potentially for an extended period of time thereafter. In addition, products may not be considered cost-effective and adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize a profit.

Legislation and regulations affecting the pricing of pharmaceuticals may change and any such changes could further limit reimbursement. Cost control initiatives may decrease coverage and payment levels for CINVANTI, SUSTOL, HTX-011, if approved, or any other products we may develop and, in turn, the reimbursement that we receive. We are unable to predict all changes to the coverage or reimbursement methodologies that will be applied by private or government payors to CINVANTI, SUSTOL, HTX-011, if approved, or any other products we may develop. If CINVANTI, SUSTOL, HTX-011, if approved, or any other products we develop do not receive adequate reimbursement, our revenue could be severely limited.

In the U.S., given recent federal and state government initiatives directed at lowering the total cost of health care, the U.S. Congress and state legislatures will likely continue to focus on health care reform, reducing the cost of prescription pharmaceuticals and reforming the Medicare and Medicaid systems. For example, the PPACA encourages comparative effectiveness research. Any adverse findings for our products from such research may negatively impact reimbursement available for our products. Similarly, the SUPPORT for Patients and Communities Act (the "SUPPORT Act"), which was signed into law on October 24, 2018, encourages the prevention and treatment of opioid addiction and the development of non-opioid pain management treatments. Although it is too early to assess the impact of the SUPPORT Act, it could potentially increase competition for HTX-011, if approved, and have other negative impacts on our business. Economic pressure on state budgets may result in states increasingly seeking to achieve budget savings through mechanisms that limit coverage or payment for drugs. State Medicaid programs are increasingly asking manufacturers to pay supplemental rebates and requiring prior authorization by the state program for use of any drug for which supplemental rebates are not being paid. Further, the trend toward managed health care in the U.S., which could significantly influence the purchase of health care services and products, may result in lower prices for CINVANTI, SUSTOL, HTX-011, if approved, or any other products we may develop for marketing. While we cannot predict whether any legislative or regulatory proposals affecting our business will be adopted, the announcement or adoption of these proposals could have a material and adverse effect on our potential revenues and gross margins.

If we fail to comply with our reporting and payment obligations under U.S. governmental pricing and contracting programs, we could be subject to additional reimbursement requirements, penalties and fines, which could have a material adverse effect on our business, financial condition, and results of operations.

The Medicare program and certain government pricing programs, including the Medicaid drug rebate program, the Public Health Services' 340B drug pricing program, and the pricing program under the Veterans Health Care Act of 1992 impact the reimbursement we may receive from sales of CINVANTI, SUSTOL, HTX-011, if approved, or any other products that are approved for marketing. Pricing and rebate calculations vary among programs. The calculations are complex and are often subject to interpretation by manufacturers, governmental or regulatory agencies and the courts. We are required to submit a number of different pricing calculations to government agencies on a quarterly basis. Failure to comply with our reporting and payment obligations under U.S. governmental pricing and contracting programs may result in additional payments, penalties and fines due to government agencies, which may have a material adverse effect on our business, financial condition and results of operations.

Because the results of preclinical studies and clinical trials are not necessarily predictive of future results, we can provide no assurances that HTX-011 or any of our other product candidates will have favorable results in future studies or receive regulatory approval.

Positive results from preclinical studies or clinical trials should not be relied on as evidence that later or larger-scale studies will succeed. Even if our product candidates achieve positive results in early-stage preclinical studies or clinical studies, we will be required to demonstrate that these product candidates are safe and effective for use in Phase 3 studies before we can seek regulatory approvals for their commercial sale. Even if our early-stage preclinical studies or clinical studies achieve the specified endpoints, the FDA may determine that these data are not sufficient to allow the commencement of Phase 3 studies. There is an extremely high historical rate of failure of product candidates proceeding through clinical trials in our industry. There is no guarantee that the efficacy of any product candidates, including HTX-011, shown in early patient studies will be replicated or maintained in future studies and/or larger patient populations. Similarly, favorable safety and tolerability data seen in short-term studies might not be replicated in studies of longer duration and/or larger patient populations. If any product candidate demonstrates insufficient safety or efficacy in any preclinical study or clinical trial, we would experience potentially significant delays in, or be required to abandon, development of that product candidate. In addition, product candidates in Phase 3 studies may fail to show the desired safety and efficacy despite having progressed through preclinical and earlier stage clinical trials, which could delay, limit or prevent regulatory approval. Further, data obtained from pivotal clinical studies are susceptible to varying interpretations, which could delay, limit or prevent regulatory approval. Regulatory approval may also be delayed, limited or prevented by other factors. For example, a CRL was received from the FDA regarding the NDA for HTX-011 on April 30, 2019. The CRL stated that the FDA was unable to approve the NDA in its present form based on the need for additional CMC and non-clinical

information. Based on the complete review of the NDA, the FDA did not identify any clinical safety or efficacy issues, and there was no requirement for further clinical studies or data analyses. In February 2020, we announced that the FDA extended the review period for the NDA for HTX-011 by up to three months. The new PDUFA goal date is June 26, 2020. The contract manufacturing site used to manufacture HTX-011 has been reinspected by the FDA with no Form 483 observations issued and with a recommendation by the FDA inspector for approval of the site. We have not been informed of any other manufacturing concerns. Although the FDA inspector recommended approval of the contract manufacturing site used to manufacture HTX-011, other components of the FDA might have opinions that differ from that of any FDA inspector, and the FDA will make the ultimate decision regarding whether to approve the NDA for HTX-011. Even if we are successful in resolving some or all of the matters raised by the FDA in the CRL, there is significant risk that we will be unable to obtain FDA approval for HTX-011 on a timely basis or at all. If we delay or abandon our efforts to develop any of our product candidates, we may not be able to generate sufficient revenues to become profitable, and our reputation in the industry and in the investment community would likely be significantly damaged, each of which would cause our stock price to decrease significantly.

Interim, topline or preliminary data from our clinical trials that we announce or publish may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.

We may publicly disclose interim, topline, or preliminary data from our clinical trials, such as the results from our Phase 3b clinical trial of HTX-011 for patients undergoing total knee arthroplasty, which is based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a full analyses of all data related to the particular trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the interim, topline, or preliminary results that we report may differ from future results of the same trials, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Topline data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, topline data should be viewed with caution until the final data are available. We may also disclose interim data from our clinical trials. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Adverse differences between interim, topline or preliminary data and final data could significantly harm our business prospects.

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and our business in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure, and any information we determine not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise regarding a particular drug, product candidate or our business. If the interim, topline, or preliminary data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for and commercialize our product candidates, our business, operating results, prospects or financial condition may be harmed.

Although the FDA has granted Fast Track, Breakthrough Therapy and Priority Review designations to HTX-011, there can be no assurance that HTX-011 or any of our other future products that receive such designations will receive regulatory approval any sooner than other product candidates that do not have such designations, or at all.

In October 2017, we were granted Fast Track designation for HTX-011 from the FDA for local administration into the surgical site to reduce postoperative pain and the need for opioid analgesics for 72 hours. In June 2018, we were granted Breakthrough Therapy designation for HTX-011 from the FDA for postoperative pain management. In December 2018, we were granted Priority Review designation for HTX-011 from the FDA for postoperative pain management. Fast Track designation is intended to facilitate the development and expedite the review of new therapies to treat serious conditions with unmet medical needs by providing sponsors with the opportunity for frequent interactions with the FDA. Breakthrough Therapy designation is designed to expedite the development and review of drugs that are intended to treat serious conditions and for which preliminary clinical evidence indicates substantial improvement over available therapies on clinically significant endpoint(s). Priority Review designation is for drugs that, if approved, would be significant improvements in the safety or effectiveness of the treatment or prevention of serious conditions. Product candidates that receive Fast Track or Breakthrough Therapy designation may receive more frequent interactions with the FDA regarding the product candidate's development plan and clinical trials and may be eligible for the FDA's Rolling Review and Priority Review. Priority Review designation is intended to direct overall attention and resources of the FDA to the evaluation of such applications and means that the FDA's goal is to take action on such applications within 6 months, compared to 10 months under standard review. Despite receiving Fast Track, Breakthrough Therapy and Priority Review designations, we can provide no assurances that HTX-011 or any of our other future products that receive such designations will receive regulatory approval any sooner than other product candidates that do not have such designations, or at all. For example, despite receiving Fast Track designation, Breakthrough Therapy designation and Priority Review designation for HTX-011, a CRL was received from the FDA regarding the NDA for HTX-011 on April 30, 2019, and there is no guarantee that approval will be received in a timely manner, or at all. The FDA may also withdraw Fast Track or Breakthrough Therapy designations if it determines that HTX-011 or any of our other future products that receive such designations no longer meet the relevant criteria. In February 2020, we announced that the FDA extended the review period for the NDA for HTX-011 by up to three months. The new PDUFA goal date is June 26, 2020. The contract manufacturing site used to manufacture HTX-011 has been reinspected by the FDA with no Form 483 observations issued and with a recommendation by the FDA inspector for approval of the site. We have not been informed of any other manufacturing concerns. Although the FDA inspector recommended approval of the contract manufacturing site used to manufacture HTX-011, other components of the FDA might have opinions that differ from that of any FDA inspector, and the FDA will make the ultimate decision regarding whether to approve the NDA for HTX-011.

Although foreign regulatory authorities have given HTX-011 preferential designations intended to decrease the amount of time needed for regulatory approval, there can be no assurance that HTX-011 or any of our other future products that receive such designations will receive regulatory approval any sooner than other product candidates that do not have such designations, or at all.

In March 2019, the MAA for HTX-011 was validated by the EMA. Validation of the MAA confirms that the submission is complete and starts the EMA's Centralised Procedure. The EMA granted eligibility to the Centralised Procedure for HTX-011 based on it meeting the criteria of a medicinal product constituting a significant scientific innovation. The Centralised Procedure allows applicants to receive a marketing authorisation that is valid throughout the EU. In December 2019, the NDS for HTX-011 was granted Priority Review status and accepted by Health Canada. Health Canada's Priority Review status provided an accelerated 6-month review target for the NDS. A decision by Health Canada is anticipated in the third quarter of 2020. Despite receiving these designations, we can provide no assurances that HTX-011 or any of our other future products that receive such designations will receive regulatory approval any sooner than other product candidates that do not have such designations, or at all. Foreign regulatory authorities may also revoke designations previously given to our product candidates or elect to treat designated candidates in a manner different from what was originally indicated. Failure to realize the potential benefits of these designations could materially adversely affect our business, financial condition, cash flows and results of operations.

Our product platforms or product development efforts may not produce safe, efficacious or commercially viable products, and, if we are unable to develop new products, our business may suffer.

Our long-term viability and growth will depend on the successful development of products through our research and development activities. Product development is very expensive and involves a high degree of risk. Only a small number of research and development programs result in the commercialization of a product. Success in preclinical work or early-stage clinical trials does not ensure that later-stage or larger-scale clinical trials will be successful. Our ability to complete our clinical trials in a timely fashion depends in large part on a number of key factors, including protocol design, regulatory and IRB approval, the rate of patient enrollment in clinical trials and compliance with extensive current Good Clinical Practices ("cGCP").

In addition, because we fund the development of our product candidates, we may not be able to continue to fund all such development efforts to completion or to provide the support necessary to perform the clinical trials, obtain regulatory approvals, or market any approved products. If our drug delivery technologies or product development efforts fail to result in the successful development and commercialization of our product candidates, or if our new products do not perform as anticipated, such events could materially adversely affect our business, financial condition, cash flows and results of operations.

We rely on third parties to conduct our preclinical testing and conduct our clinical trials, and their failure to perform their obligations in a timely and competent manner may delay development and commercialization of our product candidates and our business could be substantially harmed.

We have used contract research organizations ("CROs") to oversee our clinical trials for CINVANTI, SUSTOL and HTX-011, and we expect to use the same or similar organizations for our future clinical trials and pipeline programs. There can be no assurance that these CROs will perform their obligations at all times in a competent or timely fashion, and we must rigorously oversee their activities in order to be confident in their conduct of these trials on our behalf. If the CROs fail to commit resources to our product candidates, our clinical programs related to our product candidates could be delayed, terminated or unsuccessful, and we may not be able to obtain regulatory approval for, or successfully commercialize, them. Different cultural and operational issues in foreign countries could cause delays or unexpected problems with patient enrollment or with the data obtained from those locations. If we experience significant delays in the progress of our clinical trials or experience doubts with respect to the quality of data derived from our clinical trials, we could face significant delays in gaining necessary product approvals.

We also rely on third parties to assist in conducting our preclinical studies in accordance with Good Laboratory Practices and the Animal Welfare Act requirements. We, our CROs and other third parties are required to comply with cGCP, which are regulations and guidelines enforced by the FDA, the Competent Authorities of the Member States of the European Economic Area and comparable foreign regulatory authorities. Regulatory authorities enforce cGCP through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of our CROs fail to comply with applicable cGCP, the clinical data generated in the clinical trials may be deemed unreliable, and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot be certain that on inspection by a given regulatory authority, such regulatory authority will determine that any of our ongoing or future clinical trials comply with cGCP. In addition, all of our clinical trials must be conducted with product produced under cGMP. Failure to comply with these regulations may require us to repeat preclinical and clinical trials, which would delay the regulatory approval process.

Our CROs and other third parties we may engage to support our development programs are not our employees, and, except for remedies available to us under our agreements with such CROs, we cannot control whether or not they devote sufficient time and resources to our ongoing clinical, non-clinical and preclinical programs. Outsourcing these functions involves risk that third parties may not perform to our standards, may not produce results in a timely manner, or may fail to perform at all. If CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines or if the quality or accuracy of the preclinical results or clinical data they obtain is compromised due to the failure to adhere to test requirements, our clinical protocols, regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. As a result, our results of operations and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenues could be delayed.

If our suppliers and contract manufacturers are unable to manufacture in commercially viable quantities, we could face delays in our ability to commercialize CINVANTI, SUSTOL, HTX-011 or any other products we may develop, our costs will increase and our product sales may be severely hindered.

If in the future any of our product candidates are approved for commercial sale, we will need to be able to consistently manufacture our products in larger quantities and be able to show equivalency to the FDA in the manufacture of our products at commercial scale as compared to development batch size. The commercial success of our products will be dependent on the ability of our contract manufacturers to produce a product in commercial quantities at competitive costs of manufacture in a process that is validated by the FDA. We have scaled-up manufacturing for CINVANTI and SUSTOL in order to realize important economies of scale, and these activities took time to implement, required additional capital investment, process development and validation studies and regulatory approval. We are in the process of scaling up manufacturing for HTX-011. We cannot guarantee that we will be successful in achieving competitive manufacturing costs through such scaled-up activities.

The manufacture of pharmaceutical products is a highly complex process in which a variety of difficulties may arise, including product loss due to material failure, equipment failure, vendor error, operator error, labor shortages, inability to obtain material, equipment or transportation, physical or electronic security breaches and natural disasters. Problems with manufacturing processes could result in product defects or manufacturing failures, which could require us to delay shipment of products or recall products previously shipped, or could impair our ability to expand into new markets or supply products in existing markets. We may not be able to resolve any such problems in a timely manner, if at all.

We depend on third-party suppliers and contract manufacturers to manufacture CINVANTI, SUSTOL and HTX-011, and we expect to do the same for any future products that we develop; if our contract manufacturers do not perform as expected, our business could suffer.

We do not own or operate manufacturing facilities for the production of commercial or clinical quantities of any product, including CINVANTI, SUSTOL and HTX-011. Our ability to successfully commercialize CINVANTI, SUSTOL and HTX-011, if approved, as well as any other products that we may develop, depends in part on our ability to arrange for and rely on other parties to manufacture our products at a competitive cost, in accordance with regulatory requirements, and in sufficient quantities for clinical testing and eventual commercialization. We currently rely on a small number of third-party manufacturers to produce compounds used in our product development activities and expect to continue to do so to meet the preclinical and clinical requirements of our potential products and for all of our commercial needs. Certain contract manufacturers are, at the present time (and are expected to be for the foreseeable future), our sole resource to manufacture certain key components of CINVANTI, SUSTOL and HTX-011, as well as key components for product candidates in clinical and preclinical testing in our research and development program. Although we entered into long-term commercial manufacturing agreements for the manufacture of CINVANTI, SUSTOL and HTX-011, and we have a long-term agreement for the manufacture of our Biochronomer Technology, we might not be able to successfully negotiate long-term agreements with any additional third parties, or we might not receive all required regulatory approvals to utilize such third parties, and, accordingly, we might not be able to reduce or remove our dependence on a single supplier for the commercial manufacturing of CINVANTI, SUSTOL and HTX-011, or any other products we may develop for marketing. We may have difficulties with these manufacturer relationships, and we may not be able to find

replacement contract manufacturers on satisfactory terms or on a timely basis. Our reliance on third-party suppliers and contract manufacturers also subjects our business to risks associated with geographic areas in which those parties reside, which could include natural disasters, pandemics, acts of war or terrorism, or resource shortages. Due to regulatory and technical requirements, we may have limited ability to shift production to a different third-party should the need arise. We cannot be certain that we could reach agreement on reasonable terms, if at all, with such a manufacturer. Even if we were to reach agreement, the transition of the manufacturing process to a different third-party could take a significant amount of time and money, and may not be successful.

Further, we, along with our contract manufacturers, are required to comply with FDA and foreign regulatory requirements related to product testing, quality assurance, manufacturing and documentation. Our contract manufacturers may not be able to comply with the applicable FDA or foreign regulatory requirements. They may be required to pass an FDA pre-approval inspection for conformity with cGMP before we can obtain approval to manufacture our products and will be subject to ongoing, periodic, unannounced inspection by the FDA and corresponding state agencies to ensure strict compliance with cGMP, and other applicable government regulations and corresponding foreign standards. If we and our contract manufacturers fail to achieve and maintain high manufacturing standards in compliance with cGMP, or fail to scale-up manufacturing processes in a timely manner, we may experience manufacturing errors resulting in defective products that could be harmful to patients, product recalls or withdrawals, delays or interruptions of production or failures in product testing or delivery, delay or prevention of filing or approval of marketing applications for our products, cost overruns or other problems that could seriously harm our business. For example, a CRL was received from the FDA regarding the NDA for HTX-011 on April 30, 2019. The CRL stated that the FDA was unable to approve the NDA in its present form based on the need for additional CMC and non-clinical information. Based on the complete review of the NDA, the FDA did not identify any clinical safety or efficacy issues, and there was no requirement for further clinical studies or data analyses. In February 2020, we announced that the FDA extended the review period for the NDA for HTX-011 by up to three months. The new PDUFA goal date is June 26, 2020. The contract manufacturing site used to manufacture HTX-011 has been reinspected by the FDA with no Form 483 observations issued and with a recommendation by the FDA inspector for approval of the site. We have not been informed of any other manufacturing concerns. Not complying with FDA or foreign regulatory requirements could result in an enforcement action, such as a product recall, or prevent commercialization of our product candidates and delay our business development activities. In addition, such failure could be the basis for the FDA or foreign regulators to issue a warning or untitled letter or take other regulatory or legal action, including recall or seizure, total or partial suspension of production, suspension of ongoing clinical trials, refusal to approve pending applications or supplemental applications, and potentially civil and/or criminal penalties depending on the matter.

CINVANTI, SUSTOL, HTX-011 or any of our other product candidates may be in competition with other products for access to the facilities of third parties. Consequently, CINVANTI, SUSTOL, HTX-011 or any of our other product candidates may be subject to manufacturing delays if our contractors give other companies' products greater priority than our products. For this and other reasons, our third-party contract manufacturers may not be able to manufacture CINVANTI, SUSTOL, HTX-011 or any of our other product candidates in a cost-effective or timely manner. If not manufactured in a timely manner, the clinical development of any of our product candidates or their submission for regulatory approval could be delayed, and our ability to deliver products to market on a timely basis could be impaired. This could increase our costs, cause us to lose revenue or market share and damage our reputation.

Certain of the components used in the manufacture of CINVANTI, SUSTOL, HTX-011 and our other product candidates are sourced from a single vendor.

Some of the critical materials and components used in manufacturing CINVANTI, SUSTOL, HTX-011 and our other product candidates are sourced from single suppliers. An interruption in the supply of a key material could significantly delay our research and development process or increase our expenses for commercialization or development products. Specialized materials must often be manufactured for the first time for use in drug delivery technologies, or materials may be used in the technologies in a manner different from their customary commercial uses. The quality of materials can be critical to the performance of a drug delivery technology, so a reliable source that provides a consistent supply of materials is important. Materials or components needed for our drug delivery technologies may be difficult to obtain on commercially reasonable terms, particularly when relatively small quantities are required or if the materials traditionally have not been used in pharmaceutical products. Our reliance on a single vendor for certain components used in the manufacturing of our products also subjects our business to risk associated with the geographic areas in which those single vendors reside, which could include natural disasters, pandemics, acts of war or terrorism, or resource shortages. Such an interruption could increase our costs and, to the extent it impairs our ability to have sufficient inventory, cause us to lose revenue or market share.

We have, or may have, significant inventory levels of drug products, and write-downs related to the impairment of those inventories may adversely impact or delay our profitability.

We have, or may have, significant inventory levels of drug products, and we may increase those inventory levels as we continue to commercialize our drug products. We determine inventory levels of drug products based on a variety of estimates, including timing of regulatory approval of our drug products, market demand for our drug products and those of our competitors, entrance of competing drug products, introduction of new, or changes in interpretations of, pharmaceutical regulation, and changes in healthcare provider and insurer reimbursement policies. These estimates are inherently difficult to make and may be inaccurate. We analyze our inventory levels and will write down inventory that has become obsolete. If our initial estimate of the appropriate inventory levels of drug products is or becomes inaccurate, write-downs of inventory may be required, which would be recorded as cost of product sales and thereby adversely impact or delay our profitability.

It is difficult to predict commercial demand for our drug products, and, if our estimates of demand are too low, it may adversely impact our ability to generate revenue and profits in the short term and our ability to establish and maintain a competitive position in the relevant markets where our drug products are sold, or may be sold, in the future.

Despite our efforts to maintain appropriate inventory levels of drug products, as we continue to commercialize our drug products, our estimates of appropriate inventory levels may not be accurate. If we fail to build up sufficient inventory levels to meet commercial demand, our ability to generate revenue and profits in the short term would be adversely impacted. Failure to meet demand may also cause us to lose market share to our competitors, which could materially adversely affect our business, financial condition, cash flows and results of operations. Given the time required to scale production and replenish inventory, our ability to correct for inaccurate estimates in a timely manner may be limited.

Similarly, if we are unable to ramp up production of prospective drug products to coincide with the regulatory approval of those products, our ability to generate revenue and profits in the short term would be adversely impacted. If our competitors are able to meet demand with their products before we are able to produce and sell inventory, our ability to gain market share will be adversely impacted, which could materially adversely affect our business, financial condition, cash flows and results of operations. In addition, if regulatory approval of any of our drug products comes earlier than anticipated, as a result of preferential designations designed to hasten the approval process or otherwise, and we have not built up sufficient inventory to meet commercial demand, our ability to generate additional revenue sooner as a result of those early approvals may be diminished.

We face intense competition from other companies developing products for the prevention of CINV or management of postoperative pain.

NK_1 receptor antagonists are also administered for the prevention of CINV, in combination with 5-HT_3 receptor antagonists, to augment the therapeutic effect of the 5-HT_3 receptor antagonist. CINVANTI faces significant competition. Currently available NK_1 receptor antagonists include: generic versions of EMEND® IV (fosaprepitant); EMEND® IV (fosaprepitant, marketed by Merck & Co); EMEND® (aprepitant, marketed by Merck & Co, Inc.); AKYNZEO® (palonosetron, a 5-HT_3 receptor antagonist, combined with netupitant, an NK_1 receptor antagonist, marketed by Eisai, Inc.); VARUBI® (rolapitant, marketed by TerSera Therapeutics LLC) and other products that include an NK_1 receptor antagonist that reach the market.

SUSTOL faces significant competition. Currently available 5-HT_3 receptor antagonists include: AKYNZEO® (palonosetron, a 5-HT_3 receptor antagonist, combined with netupitant, an NK_1 receptor antagonist, marketed by Helsinn Therapeutics (U.S.), Inc.); SANCUSO® (granisetron transdermal patch, marketed by ProStrakan Group Plc); and generic products including ondansetron (formerly marketed by GlaxoSmithKline plc as ZOFRAN), granisetron (formerly marketed by Hoffman-La Roche, Inc. as KYTRIL) and palonosetron (formerly marketed by Eisai in conjunction with Helsinn Healthcare S.A. as ALOXI). Currently, palonosetron is the only 5-HT_3 receptor antagonist other than SUSTOL that is approved for the prevention of delayed CINV associated with MEC regimens. SUSTOL is indicated in combination with other antiemetics in adults for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic chemotherapy (MEC) or anthracycline and cyclophosphamide (AC) combination chemotherapy regimens, which is considered to be a HEC regimen by the NCCN and ASCO. No other 5-HT_3 receptor antagonist is specifically approved for the prevention of delayed CINV associated with a HEC regimen.

If we are able to successfully develop HTX-011 for postoperative pain management, we will compete with MARCAINE™ (bupivacaine, marketed by Hospira, Inc.) and generic forms of bupivacaine; NAROPIN® (ropivacaine, marketed by Fresenius Kabi USA, LLC) and generic forms of ropivacaine; EXPAREL® (bupivacaine liposome injectable suspension, marketed by Pacira BioSciences, Inc.) and potentially other products in development for postoperative pain management that reach the market.

Small or early-stage companies and research institutions may also prove to be significant competitors, particularly through collaborative arrangements with large and established pharmaceutical companies. We will also face competition from these parties in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, and acquiring and in-licensing technologies and products complementary to our programs or potentially advantageous to our business. If any of our competitors succeed in obtaining approval from the FDA or other regulatory authorities for their products sooner than we do or for products that are more effective or less costly than ours, our commercial opportunity could be significantly reduced. Major technological changes can happen quickly in the biotechnology and pharmaceutical industries, and the development of technologically improved or different products or drug delivery technologies may make our product candidates or platform technologies obsolete or noncompetitive.

Our products may face competition from lower-cost generic products offered by our competitors.

Pricing for therapeutics can be extremely competitive, and strict formulary guidelines enforced by payors may create significant challenges in the acceptance and profitability of branded products. The market for generic products can be very lucrative, and it is dominated by companies that may have much larger distribution capabilities than we may have in the future. It can be very difficult to predict the timing of the launch of generic products given the commonality of litigation with manufacturers over anticipated patent expiration. Our inability to accurately foresee and plan for generic product launches that may compete with our products may significantly impact our potential revenues from such products. On the expiration or loss of patent protection for a branded product, or on the "at-risk" launch (despite pending patent infringement litigation against the generic product) by a manufacturer of a generic version of a drug that may compete with one of our products, we could quickly lose a significant portion of our sales of that product. The inability for a branded product we may sell to successfully compete against generic products could negatively impact sales of our product, reduce our ability to grow our business and significantly harm our business prospects.

For example, generic versions of EMEND® IV (fosaprepitant) launched in September 2019 following the expiration of the EMEND IV patents. As a result, we expect increased competition for CINVANTI, which could reduce CINVANTI sales and harm our business prospects. These and other risks related to the entry of generic product competing with CINVANTI are difficult to assess in terms of timing and impact on our operations and prospects.

Additionally, while we had expected that generic versions of ALOXI (palonosetron) would launch in September 2018 following the expiration of the ALOXI patents, a U.S. Court of Appeals for the Federal Circuit decision in May 2017 ruled in favor of a generic drug company challenging the ALOXI patents, thereby potentially accelerating the entry of generic versions of ALOXI (palonosetron). The Supreme Court granted certiorari in June 2018 and affirmed the Federal Circuit decision in January 2019. As a result of this litigation, generic versions of ALOXI (palonosetron) have entered the market and we have experienced increased competition for SUSTOL, which has reduced SUSTOL sales and may continue to negatively affect our future business prospects. These and other risks related to the entry of generic product competing with SUSTOL are difficult to assess in terms of timing and impact on our operations and prospects.

Our business and results of operations may suffer as a result of changes in our pricing or marketing strategies.

In an effort to remain competitive in the marketplace, we can determine, from time to time, to change our pricing or marketing strategies for our approved products, including by altering the amount or availability of discounts or rebates for any of our approved products. Any such changes could have short-term or long-term negative impacts on our revenues, which would cause our business and results of operations to suffer. For example, in October 2019, we eliminated the discounts on SUSTOL which reduced revenues. Price increases or changes to our marketing strategies may also negatively affect our reputation and our ability to secure and maintain reimbursement coverage for our approved products, which could result in decreased demand and cause our business and results of operations to suffer.

If we are unable to recruit and retain skilled employees, we may not be able to achieve our objectives.

We depend on a small number of key management and personnel. Retaining our current employees and recruiting qualified personnel to perform future research and development and commercialization work will be critical to our success. Competition is always present for highly skilled and experienced personnel, and an inability to recruit or retain sufficient skilled personnel could result in delays in our business growth and development and adversely impact our research and development or commercial activities. If we lose key members of our senior management team, we may not be able to find suitable replacements and our business may be harmed as a result.

Our business strategy may include acquisitions of other businesses, products or product licenses. We may not be able to successfully manage such activities.

We may engage in strategic transactions that could cause us to incur contingent liabilities, commitments or significant expense. In the course of pursuing strategic opportunities, we may evaluate potential acquisitions, licenses or investments in strategic technologies, products or businesses. Future acquisitions, licenses or investments could subject us to a number of risks, including, but not limited to:

- our inability to appropriately evaluate and take into consideration the potential uncertainties associated with the other party to such a transaction, including, but not limited to, the prospects of that party and their existing products or product candidates and regulatory approvals;
- difficulties associated with realizing the perceived potential for commercial success with respect to any acquired or licensed technology, product or business;
- our ability to effectively integrate any new technology, product and/or business including personnel, intellectual property or business relationships into our Company;
- our inability to generate revenues from acquired or licensed technology and/or products sufficient to meet our objectives in undertaking the acquisition or license or even to offset the associated acquisition and maintenance costs and/or assumption of liabilities; and
- the distraction of our management from our existing product development programs and initiatives in pursuing an acquisition or license.

In connection with an acquisition or license, we must estimate the value of the transaction by making certain assumptions that may prove to be incorrect, which could cause us to fail to realize the anticipated benefits of a transaction. Any strategic transaction we may pursue may not result in the benefits we initially anticipate, may result in costs that end up outweighing the benefits and may adversely impact our financial condition and be detrimental to our future business prospects.

Our business strategy may include entry into collaborative agreements. We may not be able to enter into collaborative agreements or may not be able to negotiate commercially acceptable terms for these agreements.

Our current business strategy may include the entry into collaborative agreements for the development and commercialization of our products and product candidates. The negotiation and consummation of these types of agreements typically involve simultaneous discussions with multiple potential collaborators and require significant time and resources from our officers, business development and research and development staff. In addition, in attracting the attention of pharmaceutical and biotechnology company collaborators, we compete with numerous other third parties with product opportunities as well as the collaborators' own internal product opportunities. We may not be able to consummate collaborative agreements, or we may not be able to negotiate commercially acceptable terms for these agreements.

If we do enter into such arrangements, we could be dependent on the subsequent success of these other parties in performing their respective responsibilities and the cooperation of our partners. Our collaborators may not cooperate with us or perform their obligations under our agreements with them. We cannot control the amount and timing of our collaborators' resources that will be devoted to researching our product candidates pursuant to our collaborative agreements with them. Our collaborators may choose to pursue existing or alternative technologies in preference to those being developed in collaboration with us.

Under agreements with any collaborators we may work with in the future, we may rely significantly on them to, among other activities:

- fund research and development activities with us;
- pay us fees on the achievement of milestones; and
- market for or with us any commercial products that result from our collaborations.

If we do not consummate collaborative agreements, we may use our financial resources more rapidly on our product development efforts, continue to defer certain development activities or forego the exploitation of certain geographic territories, any of which could have a material adverse effect on our business prospects. Further, we may not be successful in overseeing any such collaborative arrangements. If we fail to establish and maintain necessary collaborative relationships, our business prospects could suffer.

Natural disasters, pandemics, acts of war or terrorism, or resource shortages could disrupt our investigational drug candidate development and approved drug commercialization efforts and adversely affect results.

Our ongoing or planned clinical studies and approved drug commercialization efforts could be delayed or disrupted indefinitely on the occurrence of a natural disaster, pandemic, or acts of war or terrorism, or resource shortages. We are also vulnerable to damage from other disasters, such as power loss, fire, floods, hurricanes and similar events. For example, a natural disaster, pandemic, or act of war or terrorism, and the resulting damage could negatively impact enrollment and participation in our clinical studies, divert attention and resources at our research sites, cause unanticipated delays in the collection and receipt of data from our clinical studies, cause unanticipated delays in communications with, and any required approvals from, the FDA and other regulatory authorities, and cause unanticipated delays in the manufacturing and distribution of CINVANTI, SUSTOL, HTX-011 and any other products we may develop. If a significant disaster occurs, our ability to continue our operations could be seriously impaired and we may not have adequate insurance to cover any resulting losses. Any significant unrecoverable losses could seriously impair our operations and financial condition.

Risks Related to Our Financial Condition

We have a history of losses, we expect to generate losses in the near future, and we may never achieve or maintain profitability.

We have incurred significant operating losses and negative cash flows from operations and had an accumulated deficit of $1.2 billion through December 31, 2019. We expect to continue to generate substantial losses over at least the next several years as we:

- expand product development activities with respect to our product candidates;
- conduct preclinical development and clinical trials for our product candidates;
- pursue regulatory approvals for any current or future products; and
- engage in commercialization efforts for any future approved product candidates.

In addition, the amount we spend will impact our profitability. Our spending will depend, in part, on:

- the number of product candidates we pursue;
- the progress of our research and development programs for our product candidates, including clinical trials;

- the time and expense required to pursue FDA and/or non-U.S. regulatory approvals for our product candidates, whether such approvals are obtained and the scope of any approved product label;
- the cost of possible acquisitions of technologies, compounds, product rights or companies;
- the cost of obtaining licenses to use technology owned by others for proprietary products and otherwise;
- the time and expense required to prosecute, enforce and/or challenge patent and other intellectual property rights;
- the costs of potential litigation; and
- the costs associated with recruiting and compensating a highly skilled workforce in an environment where competition for such employees may be intense.

To achieve and sustain profitability, we must, alone or in cooperation with others, successfully develop, obtain regulatory approval for, manufacture, market and sell our products, including our current work commercializing CINVANTI and SUSTOL and our anticipated work commercializing HTX-011, if approved. We will incur substantial expenses in our efforts to develop and commercialize our products and we may never generate sufficient revenue to become profitable or to sustain profitability.

Additional capital may be needed in the future to enable us to implement our business plan, and we may be unable to raise capital, which would force us to limit or cease our operations and related product development programs.

As of December 31, 2019, we had cash, cash equivalents and short-term investments of $391.0 million. Historically, we have financed our operations, including technology and product research and development, primarily through sales of our common stock and debt financings. Our capital requirements going forward will depend on numerous factors, including but not limited to: the costs associated with the commercial launch of HTX-011, if approved; the degree of commercial success of CINVANTI, SUSTOL and HTX-011, if approved; the scope, rate of progress, results and costs of preclinical testing and clinical trials; the timing and cost to manufacture our products; the number and characteristics of product development programs we pursue and the pace of each program, including the timing of clinical trials; the time, cost and outcome involved in seeking other regulatory approvals; scientific progress in our research and development programs; the magnitude and scope of our research and development programs; our ability to establish and maintain strategic collaborations or partnerships for research, development, clinical testing, manufacturing and marketing of our product candidates; the cost and timing of establishing sales, marketing and distribution capabilities if we commercialize products independently; the cost of establishing clinical and commercial supplies of our product candidates and any products that we may develop; and general market conditions.

We may not be able to raise additional capital when needed or desired, or we may need to raise additional capital on unfavorable terms, which could result in dilution to existing stockholders.

We may not be able to raise sufficient additional capital when needed on favorable terms, or at all. If we are unable to obtain adequate funds, we may be required to curtail significantly or cease our operations.

The timing and degree of any future capital requirements will depend on many factors, including:

- our ability to successfully commercialize, market and achieve market acceptance of CINVANTI, SUSTOL and HTX-011, if approved;
- the status of regulatory approval of any pending applications with the FDA, or other regulators, as the case may be, and the costs involved with pursuing regulatory approvals;

- the number and characteristics of product development programs we pursue and the pace of each program;
- the scope, rate of progress, results and costs of preclinical testing and clinical trials;
- our ability to establish and maintain strategic collaborations or partnerships for research, development, clinical testing, manufacturing and marketing of our product candidates;
- the cost and timing of establishing or enlarging sales and marketing capabilities; and
- the cost of establishing supply arrangements for clinical and commercial development of our product candidates and any products that we may develop.

If we issue additional equity securities or securities convertible into equity securities to raise funds, our stockholders will suffer dilution of their investment, and such issuance may adversely affect the market price of our common stock.

Any new debt financing we enter into may involve covenants that restrict our operations. These restrictive covenants may include, among other things, limitations on borrowing and specific restrictions on the use of our assets, as well as prohibitions on our ability to create liens, pay dividends, redeem capital stock or make investments. Our Senior Secured Convertible Notes ("Convertible Notes") also include restrictions on our use of cash and financial activities, and are secured by liens on substantially all of our assets. In the event that additional funds are obtained through arrangements with collaborative partners, these arrangements may require us to relinquish rights to some of our technologies, product candidates or products on terms that are not favorable to us or require us to enter into a collaboration arrangement that we would otherwise seek to develop and commercialize ourselves. If adequate funds are not available, we may default on our indebtedness, be required to delay, reduce the scope of, or eliminate one or more of our product development programs and reduce personnel-related and other costs, which would have a material adverse effect on our business.

Provisions contained in our debt instruments limit our ability to incur additional indebtedness.

The Convertible Notes are secured by substantially all of our assets, including our bank and investment accounts, and the terms of the Convertible Notes require us to seek approval from the holders of the Convertible Notes before taking certain actions, including incurring certain additional indebtedness or modifying the terms of certain existing indebtedness. The Convertible Notes also contain provisions that trigger events of default on any default of our financial obligations under certain material contracts we may enter into. In addition, potential third-party lenders may be unwilling to subordinate new debt to the Convertible Notes. As a result, we may not be able to raise funds through the issuance of debt in the future, which could impair our ability to finance our business obligations or pursue business expansion initiatives.

We could be exposed to significant product liability claims that could be time-consuming and costly to defend, divert management attention and adversely impact our ability to obtain and maintain insurance coverage.

The administration of drugs in humans, whether in clinical studies or commercially, carries the inherent risk of product liability claims whether or not the drugs are actually the cause of an injury. CINVANTI, SUSTOL, our product candidates and products that we may commercially market in the future may cause, or may appear to have caused, injury or dangerous drug reactions, and we may not learn about or understand those effects until the product or product candidate has been administered to patients for a prolonged period of time.

Although we are insured against such risks up to an annual aggregate limit in connection with clinical trials and commercial sales of our products, our present product liability insurance may be inadequate and may not fully cover the costs of any claim or any ultimate damages we might be required to pay. Product liability claims or other claims related to our products, regardless of their outcome, could require us to spend significant time and money in litigation or to pay significant damages. Any successful product liability claim may prevent us from obtaining adequate product liability insurance in the future on commercially desirable or reasonable terms. In addition, product liability coverage may cease to be available in sufficient amounts or at an acceptable cost. An inability to obtain sufficient insurance coverage at an acceptable cost or otherwise to protect against potential product liability claims could prevent or inhibit the commercialization of our products. A product liability claim could also significantly harm our reputation and delay market acceptance of our products.

If any of our services providers are characterized as employees, we would be subject to employment and tax withholding liabilities and other additional costs.

We rely on independent third parties to provide certain services to us. We structure our relationships with these outside services providers in a manner that we believe results in an independent contractor relationship, not an employee relationship. An independent contractor is generally distinguished from an employee by his or her degree of autonomy and independence in providing services. A high degree of autonomy and independence is generally indicative of an independent contractor relationship, while a high degree of control is generally indicative of an employment relationship. Tax or other regulatory authorities may challenge our characterization of services providers as independent contractors both under existing laws and regulations and under laws and regulations adopted in the future. We are aware of a number of judicial decisions and legislative proposals that could bring about major changes in the way workers are classified, including the California legislature's recent passage of California Assembly Bill 5, which California Governor Gavin Newsom signed into law in September 2019 ("AB 5"). AB 5 purports to codify the holding of the California Supreme Court's unanimous decision in Dynamex Operations West, Inc. v. Superior Court of Los Angeles, which introduced a new test for determining worker classification that is widely viewed as expanding the scope of employee relationships and narrowing the scope of independent contractor relationships. While AB 5 exempts certain licensed health care professionals, including physicians and psychologists, not all of our independent contractors work in exempt occupations. Given AB 5's recent passage, there is no guidance from the regulatory authorities charged with its enforcement and there is a significant degree of uncertainty regarding its application. In addition, AB 5 has been the subject of widespread national discussion and it is possible that other jurisdictions might enact similar laws. As a result, there is significant uncertainty regarding what the state, federal and foreign worker classification regulatory landscape will look like in future years. The current economic climate indicates that the debate over worker classification will continue for the foreseeable future. If such regulatory authorities or state, federal or foreign courts were to determine that our services providers are employees and not independent contractors, we would, among other things, be required to withhold income taxes, to withhold and pay Social Security, Medicare and similar taxes, to pay unemployment and other related payroll taxes, and to provide certain employee benefits. We could also be liable for unpaid past taxes and other costs and subject to penalties. As a result, any determination that the services providers we characterize as independent contractors are our employees could have a material adverse effect on our business, financial condition and results of operations.

The investment of our cash is subject to risks, which may cause losses or adversely affect the liquidity of these investments and our results of operations, liquidity and financial condition.

Our investments of cash, cash equivalents and short-term investments are subject to general credit, liquidity, market and interest rate risks, which have been and may, in the future, be exacerbated by a U.S. and/or global financial crisis. We may realize losses in the fair value of certain of our investments or a complete loss of these investments if the credit markets tighten, which would have an adverse effect on our results of operations, liquidity and financial condition.

Risks Related to Our Industry

Drug development involves a lengthy and expensive process with an uncertain outcome, and results of earlier studies and trials may not be predictive of future trial results.

Conducting clinical trials is a lengthy, time-consuming and expensive process. For example, we incurred significant expenses in developing CINVANTI and SUSTOL, with no guarantees that doing so would result in a commercially viable product. Before obtaining regulatory approvals for the commercial sale of any products, we, or our potential partners, must demonstrate through preclinical testing and clinical trials that our product candidates are safe and effective for their intended uses in humans. We have incurred and will continue to incur substantial expense and devote a significant amount of time to preclinical testing and clinical trials.

The outcome of clinical testing is inherently uncertain. Failure can occur at any time during the clinical trial process. The results of preclinical studies and early clinical trials of product candidates may not be predictive of the results of later-stage clinical trials. In addition, regulations are not static, and regulatory agencies, including the FDA, alter their staff, interpretations and practices and may in the future impose more stringent requirements than are currently in effect, which may adversely affect our planned drug development and/or our commercialization efforts. Satisfying regulatory requirements typically takes a significant number of years and can vary substantially based on the type, complexity and novelty of the product candidate. Our business, results of operations and financial condition may be materially adversely affected by any delays in, or termination of, our clinical trials. Factors that could impede our ability to generate commercially viable products through the conduct of clinical trials include:

- insufficient funds to conduct clinical trials;
- the inability to find partners, if necessary, for support, including research, development, manufacturing or clinical needs;
- the failure of tests or studies necessary to submit an NDA, such as clinical studies, bioequivalence studies in support of a 505(b)(2) regulatory filing, or stability studies;
- the failure of clinical trials to demonstrate the safety and efficacy of our product candidates to the extent necessary to obtain regulatory approvals;
- the failure by us or third-party investigators, CROs, or other third parties involved in the research to adhere to regulatory requirements applicable to the conduct of clinical trials;
- the failure of preclinical testing and early clinical trials to predict results of later clinical trials;
- any delay in completion of clinical trials caused by a regional disturbance where we or our collaborative partners are enrolling patients in clinical studies, such as a pandemic, terrorist activities, or war, political unrest, a natural disaster or any other reason or event, resulting in increased costs;
- any delay in obtaining advice from the FDA or similar regulatory authorities; and
- the inability to obtain regulatory approval of our product candidates following completion of clinical trials, or delays in obtaining such approvals.

There can be no assurance that if our clinical trials are successfully initiated and completed we will be able to obtain approval by the FDA in the U.S. or similar regulatory authorities elsewhere in the world in a timely manner, if at all. For example, a CRL was received from the FDA regarding the NDA for HTX-011 on April 30, 2019, stating that it was unable to approve the application in its current form based on the need for additional CMC and non-clinical information. Based on the complete review of the NDA, the FDA did not identify any clinical safety or efficacy issues, and there was no requirement for further clinical studies or data analyses. In February 2020, we announced that the FDA extended the review period for the NDA for HTX-011 by up to three months. The new PDUFA goal date is June 26, 2020. The contract manufacturing site used to manufacture HTX-011 has been reinspected by the FDA with no Form 483 observations issued and with a recommendation by the FDA inspector for approval of the site. We have not been informed of any other manufacturing concerns. Even if we are successful in resolving some or all of the matters raised by the FDA in the CRL, there is significant risk that we will be unable to obtain FDA approval for HTX-011 on a timely basis or at all. If we fail to successfully develop and commercialize one or more of our product candidates, we may be unable to generate sufficient revenues to attain profitability, and our reputation in the industry and in the investment community would likely be damaged, each of which would cause our stock price to decrease.

Delays in clinical testing could increase our costs and delay our ability to obtain regulatory approval and commercialize our product candidates.

Before we can receive regulatory approval for the commercial sale of our potential products, the FDA and comparable authorities in non-U.S. jurisdictions require extensive preclinical safety testing and clinical trials to demonstrate their safety and efficacy. Significant delays in preclinical and clinical testing could materially impact our product development costs and delay regulatory approval of our product candidates. Our ability to complete clinical trials in a timely manner could be impacted by, among other factors:

- delay or failure in reaching agreement with the FDA or comparable foreign regulatory authority on a trial design that we are able to execute;
- delay or failure in obtaining authorization to commence a trial or inability to comply with conditions imposed by a regulatory authority regarding the scope or design of a clinical study;
- delay or failure in reaching agreement on acceptable terms with prospective CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- delay or failure in obtaining IRB approval or the approval of other reviewing entities, including comparable foreign entities, to conduct a clinical trial at each site;
- withdrawal of clinical trial sites from our clinical trials as a result of changing standards of care or the ineligibility of a site to participate in our clinical trials;
- delay or failure in obtaining clinical materials;
- delay or failure in recruiting and enrolling suitable subjects to participate in a trial;
- delay or failure of subjects completing a trial or returning for post-treatment follow-up;
- clinical sites and investigators deviating from trial protocol, failing to conduct the trial in accordance with regulatory requirements, or dropping out of a trial;
- inability to identify and maintain a sufficient number of trial sites, many of which may already be engaged in other clinical trial programs, including some that may be for the same indication;
- failure of our third-party clinical trial managers to satisfy their contractual duties or meet expected deadlines;

- delay or failure in adding new clinical trial sites;
- ambiguous or negative interim results or results that are inconsistent with earlier results;
- feedback from the FDA, the IRB, data safety monitoring boards or comparable foreign entities, or results from earlier stage or concurrent preclinical and clinical studies that might require modification to the protocol;
- decisions by the FDA, the IRB, comparable foreign regulatory entities, or recommendations by a data safety monitoring board or comparable foreign regulatory entity to suspend or terminate clinical trials at any time for safety issues or for any other reason;
- unacceptable risk-benefit profiles or unforeseen safety issues or adverse side effects;
- failure to demonstrate a benefit from using a drug;
- manufacturing issues, including problems with manufacturing or obtaining from third parties sufficient quantities of a product candidate for use in clinical trials; and
- changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial.

Patient enrollment, a significant factor in the timing of clinical trials, is affected by many factors including the size and nature of the patient population, the proximity of subjects to clinical sites, the eligibility criteria for the trial, the design of the clinical trial, the ability to obtain and maintain patient consents, whether enrolled subjects drop out before completion, competing clinical trials and clinicians' and patients' perceptions as to the potential advantages of the drug being studied in relation to other available therapies, including any new drugs that may be approved for the indications we investigate. Furthermore, we rely on CROs and clinical trial sites to ensure the proper and timely conduct of our clinical trials and while we have agreements governing their activities, we have limited influence over CROs' actual performance.

Our failure to successfully establish, recruit for, and oversee our clinical trials could delay our product development efforts and negatively impact our business. If we experience delays in the completion of any ongoing study, the commercial prospects of HTX-011 or any of our other product candidates could be harmed, and our ability to generate product revenue will be delayed. Any delays in completing our clinical trials will increase our costs, slow our product candidates' development and approval process and jeopardize our ability to commence product sales and generate revenues. Any of these occurrences may harm our business, financial condition and prospects significantly.

We may not obtain regulatory approval for our product candidates in development. Regulatory approval may also be delayed or revoked or may impose limitations on the indicated uses of a proposed product. If we are unable to obtain regulatory approval for our product candidates in development, our business will be substantially harmed.

The process for obtaining regulatory approval of a new drug is time-consuming, is subject to unanticipated delays and costs and requires the commitment of substantial resources. Any product that we or our potential future collaborative partners develop must receive all necessary regulatory agency approvals or clearances before it may be marketed in the U.S. or other countries. Human pharmaceutical products are subject to rigorous preclinical and clinical testing and other requirements by the FDA in the U.S. and similar health authorities in foreign countries. We may not receive necessary regulatory approvals or clearances to market our product candidates currently in development in the U.S. or in other jurisdictions, as a result of changes in regulatory policies prior to approval or other events. Additionally, data obtained from preclinical and clinical activities, or from stability or bioequivalence studies, are susceptible to varying interpretations that could delay, limit or prevent regulatory agency approvals or clearances.

Our product candidates could fail to receive regulatory approval from the FDA or a comparable foreign regulatory authority for many reasons, including:

- disagreement with the design or implementation of our clinical trials;
- failure to demonstrate that the product candidate is safe and effective for its proposed indication;
- failure of clinical trial results to meet the level of statistical significance required for approval;
- the failure of third parties to manage and conduct the trials or perform necessary oversight to meet expected deadlines or to comply with regulatory requirements;
- failure to demonstrate that the product candidate's clinical and other benefits outweigh its safety risks;
- disagreement with our interpretation of data from preclinical studies or clinical trials;
- the insufficiency of data collected from clinical trials to support the submission and filing of an NDA or other submission or to obtain regulatory approval;
- disapproval of the manufacturing processes or facilities of third-party manufacturers with whom we contract for clinical and commercial supplies; and
- changes in approval policies or regulations that render our preclinical and clinical data insufficient for approval.

The FDA or a comparable non-U.S. regulatory authority may require additional preclinical or clinical data to support approval, such as confirmatory studies and other data or studies to address questions or concerns that may arise during the FDA review process. Regulatory approval may also be delayed, limited or prevented by other factors. For example, a CRL was received from the FDA regarding the NDA for HTX-011 on April 30, 2019. The CRL stated that the FDA was unable to approve the NDA in its present form based on the need for additional CMC and non-clinical information. Based on the complete review of the NDA, the FDA did not identify any clinical safety or efficacy issues, and there was no requirement for further clinical studies or data analyses. In February 2020, we announced that the FDA extended the review period for the NDA for HTX-011 by up to three months. The new PDUFA goal date is June 26, 2020. The contract manufacturing site used to manufacture HTX-011 has been reinspected by the FDA with no Form 483 observations issued and with a recommendation by the FDA inspector for approval of the site. We have not been informed of any other manufacturing concerns. Although the FDA inspector recommended approval of the contract manufacturing site used to manufacture HTX-011, other components of the FDA might have opinions that differ from that of any FDA inspector, and the FDA will make the ultimate decision regarding whether to approve the NDA for HTX-011. Even if we are successful in resolving some or all of the matters raised by the FDA in the CRL, there is significant risk that we will be unable to obtain FDA approval for HTX-011 on a timely basis or at all. Additionally, in 2013, 2018 and 2019, the U.S. federal government entered shutdowns suspending services deemed non-essential as a result of the failure by Congress to enact regular appropriations. Our development and commercialization activities could be harmed or delayed by a similar shutdown of the U.S. federal government in the future, which may significantly delay the FDA's ability to timely review and process any submissions we have filed or may file or cause other regulatory delays, which could have a material adverse effect on our business.

Even if granted, regulatory approvals may include significant limitations on the uses for which products may be marketed. Failure to comply with applicable regulatory requirements can, among other things, result in warning letters, imposition of civil penalties or other monetary payments, delay in approving or refusal to approve a product candidate, suspension or withdrawal of regulatory approval, product recall or seizure, operating restrictions, interruption of clinical trials or manufacturing, injunctions and criminal prosecution.

In addition, the marketing and manufacturing of products are subject to continuing FDA review, and later discovery of previously unknown problems with a product, its manufacture or its marketing may result in the FDA requiring further clinical research or restrictions on the product or the manufacturer, including withdrawal of the product from the market.

Failure to obtain regulatory approval in international jurisdictions would prevent CINVANTI, SUSTOL, HTX-011 or any other products we may develop from being marketed abroad.

In the event we pursue the right to market and sell CINVANTI, SUSTOL, HTX-011 or any other products we may develop in jurisdictions other than the U.S., we would be required to obtain separate marketing approvals and comply with numerous and varying regulatory requirements in each foreign country. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the U.S. generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the U.S., it is required that the product be approved for reimbursement before the product can be approved for sale in that country. In the event we choose to pursue them, we may not obtain approvals from regulatory authorities outside the U.S. on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the U.S. does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. If we are unable in the future to obtain approval of a product candidate by regulatory authorities in non-U.S. jurisdictions, the commercial prospects of that product candidate may be significantly diminished and our business prospects could decline.

Even if our product candidates in development receive regulatory approval, they may still face future development and regulatory difficulties. If we fail to comply with continuing federal, state and foreign regulations, we could lose our approvals to market drugs, and our business would be seriously harmed.

Even if we obtain regulatory approval for our product candidates in development, they remain subject to ongoing requirements of the FDA and comparable foreign regulatory authorities, including requirements related to manufacturing, quality control, further development, labeling, packaging, storage, distribution, safety surveillance, import, export, advertising, promotion, recordkeeping, and reporting of safety and other postmarket information. Following initial regulatory approval for drugs we develop, including CINVANTI, SUSTOL or any other products we may develop, we remain subject to continuing regulatory review, including review of adverse drug experiences and clinical results that may be reported after drug products become commercially available. This would include results from any postmarketing tests or continued actions required as a condition of approval. The manufacturer and manufacturing facilities we use to make any of our drug candidates will also be subject to periodic review and inspection by the FDA. If a previously unknown problem or problems with a product or a manufacturing and laboratory facility used by us is discovered, the FDA or foreign regulatory agency may impose restrictions on that product or on the manufacturing facility, including requiring us to withdraw the product from the market. Any changes to an approved product, including the way it is manufactured or promoted, often require FDA approval before the product, as modified, can be marketed. We and our contract manufacturers will also be subject to ongoing FDA requirements for submission of safety and other postmarket information. If we and our contract manufacturers fail to comply with applicable regulatory requirements, a regulatory agency may:

- issue warning letters;
- impose civil or criminal penalties;
- suspend or withdraw our regulatory approval;
- suspend or terminate any of our ongoing clinical trials;

- refuse to approve pending applications or supplements to approved applications filed by us;
- impose restrictions on our operations;
- close the facilities of our contract manufacturers; or
- seize or detain products or require a product recall.

The occurrence of any event or penalty described above may inhibit our ability to commercialize our products and generate revenue.

Additionally, such regulatory review covers a company's activities in the promotion of its drugs, with significant potential penalties and restrictions for promotion of drugs for an unapproved use or other inappropriate sales and marketing activities. Advertising and promotion of any product candidate that obtains approval in the U.S. will be heavily scrutinized by the FDA, the Department of Justice, and the Department of Health and Human Services' Office of Inspector General. Violations of applicable advertising and promotion laws and regulations, including promotion of products for unapproved (or off-label) uses, are subject to enforcement letters, inquiries and investigations and civil and criminal sanctions by the FDA. We are also required to submit information on our open and completed clinical trials to public registries and databases; failure to comply with these requirements could expose us to negative publicity, fines and penalties that could harm our business. We are also required to comply with the requirements to submit to governmental authorities information on payments to physicians and certain other third parties; failure to comply with these requirements could expose us to negative publicity, fines and penalties that could harm our business.

The commercial use of our products may cause unintended side effects or adverse reactions, or incidents of misuse may occur, which could adversely affect our business.

We cannot predict whether any commercial use of our product candidates, once approved, will produce undesirable or unintended side effects that have not been evident in clinical trials conducted for such product candidates to date. Additionally, incidents of product misuse may occur. These events, including the reporting of adverse safety events, among others, could result in product recalls, product liability actions or withdrawals or additional regulatory controls (including additional regulatory scrutiny and requirements for additional labeling), all of which could have a material adverse effect on our business, financial condition, cash flows and results of operations.

If we cannot establish pricing of our product candidates acceptable to the U.S. or foreign governments, insurance companies, managed care organizations and other payors, or arrange for favorable reimbursement policies, our product sales will be severely hindered.

The continuing efforts of the U.S. and foreign governments, insurance companies, managed care organizations and other payors of health care costs to contain or reduce costs of health care may adversely affect our ability to generate adequate revenues and gross margins to make the products we develop commercially viable. Our ability to commercialize any product candidates successfully will depend in part on the extent to which governmental authorities, private health insurers and other organizations establish appropriate reimbursement levels for the cost of such products and related treatments and for what uses reimbursement will be provided.

In the U.S., given recent federal and state government initiatives directed at lowering the total cost of health care, the U.S. Congress and state legislatures will likely continue to focus on health care reform, reducing the cost of prescription pharmaceuticals and reforming the Medicare and Medicaid systems. For example, the PPACA encourages comparative effectiveness research. Any adverse findings for our products from such research may negatively impact reimbursement available for our products. Similarly, the SUPPORT Act, which was signed into law on October 24, 2018, encourages the prevention and treatment of opioid addiction and the development of non-opioid pain management treatments. Although it is too early to assess the impact of the SUPPORT Act, it could potentially increase competition for HTX-011, if approved, and have other negative impacts on our business. Economic pressure on state budgets may result in states increasingly seeking to achieve budget savings through mechanisms that limit coverage or payment for drugs. State Medicaid programs are increasingly asking manufacturers to pay supplemental rebates and requiring prior authorization by the state program for use of any drug for which supplemental rebates are not being paid. Further, the trend toward managed health care in the U.S., which could significantly influence the purchase of health care services and products, may result in lower prices for our products, once approved for marketing. While we cannot predict whether any legislative or regulatory proposals affecting our business will be adopted, the announcement or adoption of these proposals could have a material and adverse effect on our potential revenues and gross margins.

The pharmaceutical industry is subject to significant regulation and oversight pursuant to anti-kickback laws, false claims statutes and anti-corruption laws, which may result in significant additional expense and limit our ability to commercialize our products. In addition, any failure to comply with these regulations could result in substantial fines or penalties.

We are subject to health care fraud and abuse regulations that are enforced by both the federal government and the states in which we conduct our business. Healthcare providers, physicians and third-party payors play a primary role in the recommendation and prescription of any product with marketing approval. Our future arrangements with third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute our products with marketing approval. Restrictions under applicable federal and state healthcare laws and regulations include, but are not limited to, the following:

- the Federal health care programs' Anti-Kickback Law, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, in exchange for or to induce either the referral of an individual for, or the purchase, lease, order or recommendation of, any good or service for which payment may be made under federal health care programs such as the Medicare and Medicaid programs;

- federal false claims laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid or other federal health care programs that are false or fraudulent. This false claims liability may attach in the event that a company is found to have knowingly submitted false average sales price, best price or other pricing data to the government or to have unlawfully promoted its products;

- federal "sunshine" laws, now known as Open Payments, that require transparency regarding financial arrangements with health care providers, such as the reporting and disclosure requirements imposed by the PPACA on drug manufacturers regarding any "payment or transfer of value" made or distributed to physicians and teaching hospitals; and

- state law equivalents of each of the above federal laws, such as anti-kickback and false claims laws, which may apply to items or services reimbursed by any third-party payor, including commercial insurers.

The risk of being found in violation of these laws is increased by the fact that many of them have not been fully interpreted by the regulatory authorities or the courts, and their provisions are open to a variety of interpretations. Moreover, recent health care reform legislation has strengthened many of these laws. For example, the PPACA, among other things, amends the intent requirement of the federal anti-kickback and criminal health care fraud statutes to clarify that a person or entity does not need to have actual knowledge of this statute or specific intent to violate it. In addition, PPACA provides that a claim including items or services resulting from a violation of the federal anti-kickback statute constitutes a false or fraudulent claim for purposes of the false claims statutes. Finally, some states, such as California, Massachusetts and Vermont, mandate implementation of commercial compliance programs to ensure compliance with these laws.

In addition, a number of states have laws that require pharmaceutical companies to track and report payments, gifts and other benefits provided to physicians and other health care professionals and entities. Similarly, the federal Physician Payments Sunshine Act within PPACA requires pharmaceutical companies to report to the federal government certain payments to physicians and teaching hospitals. The Physician Payments Sunshine Act provisions require manufacturers that participate in federal health care programs to begin collecting such information after a 6-month period following commercial launch of a product; however, state law equivalents may require compliance beginning at commercial launch.

In addition, we may in the future be subject to the FCPA. The FCPA and similar anti-bribery laws in other jurisdictions generally prohibit companies and their intermediaries from providing money or anything of value to officials of foreign governments, foreign political parties, or international organizations with the intent to obtain or retain business or seek a business advantage. Recently, there has been a substantial increase in anti-bribery law enforcement activity by U.S. regulators, with more frequent and aggressive investigations and enforcement proceedings by both the Department of Justice and the SEC. A determination that our operations or activities are not, or were not, in compliance with U.S. or foreign laws or regulations could result in the imposition of substantial fines, interruptions of business, loss of supplier, vendor or other third-party relationships, termination of necessary licenses and permits, and other legal or equitable sanctions. Other internal or government investigations or legal or regulatory proceedings, including lawsuits brought by private litigants, may also follow as a consequence.

Changes in laws affecting the healthcare industry could also adversely affect our revenues and profitability, including new laws, regulations or judicial decisions, or new interpretations of existing laws, regulations or decisions related to patent protection and enforcement, healthcare availability, and product pricing and marketing. Changes in FDA regulations and regulations issued by other regulatory agencies inside and outside of the U.S., including new or different approval requirements, timelines and processes, may also delay or prevent the approval of product candidates, require additional safety monitoring, labeling changes, restrictions on product distribution or other measures that could increase our costs of doing business and adversely affect the market for our products. The enactment in the U.S. of healthcare reform, new legislation or implementation of existing statutory provisions on importation of lower-cost competing drugs from other jurisdictions and legislation on comparative effectiveness research are examples of previously enacted and possible future changes in laws that could adversely affect our business.

If our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, exclusion from government-funded healthcare programs, like Medicare and Medicaid, and the curtailment or restructuring of our operations. Any penalties, damages, fines, curtailment or restructuring of our operations could adversely affect our ability to operate our business and our financial results. Although compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, the risks cannot be entirely eliminated. Any action against us for violation of these laws or regulations, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. Moreover, achieving and sustaining compliance with applicable federal and state privacy, security and fraud laws may prove costly.

We may incur significant liability if it is determined that we are promoting the "off-label" use of drugs or promoting in a non-truthful and misleading way.

We are prohibited from promoting CINVANTI, SUSTOL or any other products we may develop for "off-label" uses or promoting in a non-truthful and misleading way that are not described in its labeling and that differ from the uses approved by the FDA. Physicians may prescribe drug products for off-label uses, and such off-label uses are common across medical specialties. The FDA and other regulatory agencies do not regulate a physician's choice of treatments. However, they do restrict pharmaceutical companies and their sales representatives' dissemination of information concerning off-label use. The FDA and other regulatory agencies actively enforce regulations prohibiting promotion of products for off-label uses and the promotion of products for which marketing authorization has not been obtained. A company that is found to have promoted products for off-label uses may be subject to significant liability, including civil and administrative remedies as well as criminal sanctions. Notwithstanding the regulatory restrictions on off-label promotion, the FDA and other regulatory authorities allow companies to engage in truthful, non-misleading, and non-promotional scientific exchanges concerning their products.

The FDA or other regulatory authorities may conclude that we have violated applicable laws, rules or regulations, and we may therefore be subject to significant liability, including civil and administrative remedies, as well as criminal sanctions. Such enforcement actions could cause us reputational harm and divert the attention of our management from our business operations. Likewise, our distribution and contracting partners and those providing vendor support services may also be the subject of regulatory investigations involving, or remedies or sanctions for, off-label promotion of CINVANTI, SUSTOL or any other products we may develop, which may adversely impact sales of CINVANTI, SUSTOL or any other products we may develop or trigger indemnification obligations. These consequences, could, in turn, have a material adverse effect on our business, financial condition and results of operations and could cause the market value of our common shares to decline.

Health care reform could increase our expenses and adversely affect the commercial success of our products.

The PPACA includes numerous provisions that affect pharmaceutical companies. For example, the PPACA seeks to expand healthcare coverage to the uninsured through private health insurance reforms and an expansion of Medicaid. The PPACA also imposes substantial costs on pharmaceutical manufacturers, such as an increase in liability for rebates paid to Medicaid, new drug discounts that must be offered to certain enrollees in the Medicare prescription drug benefit and an annual fee imposed on all manufacturers of brand prescription drugs in the U.S. The PPACA also requires increased disclosure obligations—including those required under the "sunshine" laws—and an expansion of an existing program requiring pharmaceutical discounts to certain types of hospitals and federally subsidized clinics and contains cost-containment measures that could reduce reimbursement levels for pharmaceutical products. These and other aspects of the PPACA, including the regulations that may be imposed in connection with the implementation of the PPACA, could increase our expenses and adversely affect our ability to successfully commercialize our products and product candidates.

Our employees may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could have a material adverse effect on our business.

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional failures to comply with FDA regulations or similar regulations of comparable foreign regulatory authorities, provide accurate information to the FDA or comparable foreign regulatory authorities, comply with manufacturing standards we have established, comply with federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable foreign regulatory authorities, report financial information or data accurately, or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of significant fines or other sanctions.

We are subject to certain data privacy and security requirements, which are very complex and difficult to comply with at times. Any failure to ensure adherence to these requirements could subject us to fines, penalties and damage our reputation.

We are required to comply, as applicable, with numerous federal and state laws, including state security breach notification laws, state health information privacy laws and federal and state consumer protection laws, which govern the collection, use and disclosure of personal information. For example, the CCPA became effective on January 1, 2020 and gave California residents expanded rights to access and require deletion of their personal information, opt out of certain personal information sharing and receive detailed information about how their personal information is used. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that may increase data breach litigation. Although the CCPA includes exemptions for certain clinical trials data, and HIPAA-protected health information, the law may increase our compliance costs and potential liability with respect to other personal information we collect about California residents. The CCPA has prompted a number of proposals for new federal and state privacy legislation. Other countries also have, or are developing, laws governing the collection, use and transmission of personal information, such as the General Data Protection Regulation in the EU that became effective in May 2018 and the Personal Information Protection and Electronic Documents Act that became effective in Canada in April 2000. These laws and similar laws adopted in the future could increase our potential liability, increase our compliance costs and adversely affect our business. In addition, most healthcare providers who may prescribe products we sell and from whom we may obtain patient health information are subject to privacy and security requirements under HIPAA. We are not a HIPAA covered entity, do not intend to become one, and we do not operate as a business associate to any covered entities. Therefore, these privacy and security requirements do not apply to us. However, we could be subject to criminal penalties if we knowingly obtain individually identifiable health information from a covered entity in a manner that is not authorized or permitted by HIPAA or for aiding and abetting the violation of HIPAA. We are unable to predict whether our actions could be subject to prosecution in the event of an impermissible disclosure of health information to us. These laws could create liability for us or increase our cost of doing business, and any failure to comply could result in harm to our reputation and potentially fines and penalties.

Security breaches and other disruptions could compromise our information and expose us to liability, which would cause our business and reputation to suffer.

In the ordinary course of our business, we collect and store sensitive data, including intellectual property, our proprietary business information and that of our suppliers, as well as personally identifiable information of clinical trial participants and employees. Similarly, our third-party providers possess certain of our sensitive data. The secure maintenance of this information is critical to our operations and business strategy. Despite our security measures, our information technology and infrastructure may be vulnerable to attacks by hackers or breached due to employee error, malfeasance or other disruptions. Any such breach could compromise our networks and the information stored there could be accessed, publicly disclosed, lost or stolen. The legislative and regulatory landscape for privacy and data protection continues to evolve, and there has been an increasing amount of focus on privacy and data protection issues with the potential to affect our business, including recently enacted laws in a majority of states requiring security breach notification. Thus, any access, disclosure or other loss of information, including our data being breached at our partners or third-party providers, could result in legal claims or proceedings and liability under laws that protect the privacy of personal information, disrupt our operations and damage our reputation, which could adversely affect our business. Although we are insured against such risks up to an annual aggregate limit, our cyber liability insurance may be inadequate and may not fully cover the costs of any claim or any ultimate damages we might be required to pay. Any successful cyber liability claim may prevent us from obtaining adequate cyber liability insurance in the future on commercially desirable or reasonable terms. In addition, cyber liability coverage may cease to be available in sufficient amounts or at an acceptable cost. An inability to obtain sufficient cyber coverage at an acceptable cost or otherwise to protect against potential cyber liability claims could prevent or inhibit the development or commercialization of our products. A cyber liability claim could also significantly harm our reputation and delay market acceptance of our products.

Our use of hazardous materials could subject us to liabilities, fines and sanctions.

Our laboratory and clinical testing sometimes involve use of hazardous, radioactive or otherwise toxic materials. We are subject to federal, state and local laws and regulations governing how we use, manufacture, handle, store and dispose of these materials.

Although we believe that our safety procedures for handling and disposing of such materials comply in all material respects with all federal, state and local regulations and standards, there is always the risk of accidental contamination or injury from these materials. In the event of an accident, we could be held liable for any damages that result, and we could also be subject to fines and penalties and such liability and costs could exceed our financial resources. If we fail to comply with these regulations and standards or with the conditions attached to our operating licenses, the licenses could be revoked, and we could be subjected to criminal sanctions and substantial financial liability or be required to suspend or modify our operations. Compliance with environmental and other laws may be expensive and current or future regulations may impair our product development efforts.

Risks Related to Our Intellectual Property

If we are unable to adequately protect or enforce our intellectual property rights, we may lose valuable assets or incur costly litigation to protect our rights.

Our success will depend in part on our ability to obtain patents and maintain trade secret protection, as well as successfully defending these patents against challenges, while operating without infringing the proprietary rights of others. We have filed a number of U.S. patent applications on inventions relating to the composition of a variety of polymers, specific products, product groups and processing technology. As of December 31, 2019, we had a total of 29 issued U.S. patents and an additional 37 issued (or registered) foreign patents. The patents on the bioerodible technologies expire between May 2021 and March 2026. Currently, CINVANTI is covered by 6 patents issued in the U.S. with expiration dates of September 2035. Currently, SUSTOL is covered by 8 patents issued in the U.S. and by 31 patents issued in foreign countries including Austria, Belgium, Canada, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Japan, Luxembourg, Netherlands, Portugal, Spain, Sweden, Switzerland, Taiwan, and the United Kingdom. U.S. patents covering SUSTOL have expiration dates ranging from May 2021 to September 2024; foreign patents covering SUSTOL have expiration dates ranging from May 2021 to September 2025. HTX-011 is protected by 10 patents issued in the U.S. and by 24 patents issued in foreign countries including Australia, Austria, Belgium, Canada, Denmark, Finland, France, Germany, Greece, Hong Kong, Ireland, Italy, Japan, Luxembourg, Mexico, Netherlands, Portugal, Spain, Sweden, Switzerland, Taiwan and the United Kingdom. U.S. patents covering HTX-011 have expiration dates ranging from May 2021 to April 2035; foreign patents covering HTX-011 have expiration dates ranging from May 2021 to March 2034. Our policy is to actively seek patent protection in the U.S. and to pursue equivalent patent claims in selected foreign countries, thereby seeking patent coverage for novel technologies and compositions of matter that may be commercially important to the development of our business. Granted patents include claims covering the product composition, methods of use and methods of preparation. Our existing patents may not cover future products, additional patents may not be issued and current patents, or patents issued in the future, may not provide meaningful protection or prove to be of commercial benefit.

The patent positions of pharmaceutical companies, including ours, are uncertain and involve complex legal and factual questions. In addition, the coverage claimed in a patent application can be significantly reduced before the patent is issued. Consequently, our patent applications may not issue into patents, and any issued patents may not provide sufficient protection for our product candidates or provide sufficient protection to afford us a commercial advantage against competitive technologies or may be held invalid if challenged or circumvented. Patent applications in the U.S. are maintained in confidence for at least 18 months after their filing. Consequently, we cannot be certain that the patent applications we are pursuing will lead to the issuance of any patent or be free from infringement or other claims from other parties. Our competitors may also independently develop products similar to ours or design around or otherwise circumvent patents issued to us or licensed by us. In addition, the laws of some foreign countries may not protect our proprietary rights to the same extent as U.S. laws.

We may enter into collaborative agreements that may subject us to obligations that must be fulfilled and require us to manage complex relationships with third parties. In the future, if we are unable to meet our obligations or manage our relationships with our collaborators under these agreements our revenue may decrease. The loss or diminution of our intellectual property rights could result in a decision by our third-party collaborators to terminate their agreements with us. In addition, these agreements are generally complex and contain provisions that could give rise to legal disputes, including potential disputes concerning ownership of intellectual property and data under collaborations. Such disputes can lead to lengthy, expensive litigation or arbitration, requiring us to divert management time and resources to such dispute.

Because the patent positions of pharmaceutical and biotechnology companies involve complex legal and factual questions, enforceability of patents cannot be predicted with certainty. The ultimate degree of patent protection that will be afforded to products and processes, including ours, in the U.S., remains uncertain and is dependent on the scope of protection decided on by the patent offices, courts and lawmakers in these countries. The America Invents Act, which was enacted in 2011 and reformed certain patent laws in the U.S., may create additional uncertainty. Patents, if issued, may be challenged, invalidated or circumvented. As more products are commercialized using our proprietary product platforms, or as any product achieves greater commercial success, our patents become more likely to be subject to challenge by potential competitors.

We also rely on trade secrets, technical know-how and continuing technological innovation to develop and maintain our competitive position. We require our employees, consultants, advisors and collaborators to execute appropriate confidentiality and assignment-of-inventions agreements with us. These agreements typically provide that all materials and confidential information developed or made known to the individual during the course of the individual's relationship with us is to be kept confidential and not disclosed to third parties except in specific circumstances, and that all inventions arising out of the individual's relationship with us shall be our exclusive property. These agreements may be breached, and in some instances, we may not have an appropriate remedy available for breach of the agreements. Furthermore, our competitors may independently develop substantially equivalent proprietary information and techniques, reverse engineer our information and techniques, or otherwise gain access to our proprietary technology. We may be unable to meaningfully protect our rights in trade secrets, technical know-how and other non-patented technology. We may have to resort to litigation to protect our intellectual property rights, or to determine their scope, validity or enforceability. In addition, interference proceedings declared by the U.S. Patent and Trademark Office may be necessary to determine the priority of inventions with respect to our patent applications. Enforcing or defending our proprietary rights is expensive, could cause diversion of our resources and may not prove successful. In addition, courts outside the U.S. may be less willing to protect trade secrets. Costly and time-consuming litigation could be necessary to seek to enforce and determine the scope of our proprietary rights. Any failure to enforce or protect our rights could cause us to lose the ability to exclude others from using our technology to develop or sell competing products.

We may infringe on the intellectual property rights of others, and any litigation could force us to stop developing or selling potential products and could be costly, divert management attention and harm our business.

We must be able to develop products without infringing the proprietary rights of other parties. Because the markets in which we operate involve established competitors with significant patent portfolios, including patents relating to the composition of a variety of polymers, specific products, product groups and processing technology, it could be difficult for us to use our technologies or develop products without infringing the proprietary rights of others. Therefore, there is risk that third parties may make claims of infringement against our products or technologies. We may not be able to design around the patented technologies or inventions of others, and we may not be able to obtain licenses to use patented technologies on acceptable terms, or at all. If we cannot operate without infringing the proprietary rights of others, we will not be able to develop or commercialize some or all of our product candidates, and consequently will not be able to earn product revenue.

There is considerable uncertainty within the pharmaceutical industry about the validity, scope and enforceability of many issued patents in the U.S. and elsewhere in the world. We cannot currently determine the ultimate scope and validity of patents that may be granted to third parties in the future or which patents might be asserted to be infringed by any future manufacture, use or sale of our products. In part as a result of this uncertainty, there has been, and we expect that there may continue to be, significant litigation in the pharmaceutical industry regarding patents and other intellectual property rights. We may have to enforce our intellectual property rights against third parties who infringe our patents and other intellectual property or challenge our patent or trademark applications. For example, in the U.S., putative generics of innovator drug products (including products in which the innovation comprises a new drug delivery method for an existing product, such as the drug delivery market occupied by us) may file Abbreviated New Drug Applications ("ANDA") and, in doing so, certify that their products either do not infringe the innovator's patents or that the innovator's patents are invalid. This often results in litigation between the innovator and the ANDA applicant. This type of litigation is commonly known as "Paragraph IV" litigation in the U.S. These litigations could result in new or additional generic competition to any of our products that may be marketed in the future and a potential reduction in product revenue.

If we are required to defend ourselves in a patent-infringement lawsuit, we could incur substantial costs, and the lawsuit could divert management attention, regardless of the lawsuit's merit or outcome. These legal actions could seek damages and seek to enjoin testing, manufacturing and marketing of the accused product or process. In addition to potential liability for significant damages, we could be required to redesign affected products or obtain a license to continue to manufacture or market the accused product or process and any license required under any such patent may not be made available to us on acceptable terms, if at all. Competitors may sue us as a way of delaying the introduction of our products. Any litigation, including any interference or derivation proceedings to determine priority of inventions, oppositions or other post-grant review proceedings to patents in the U.S. or in countries outside the U.S., or litigation against our partners may be costly and time-consuming and could harm our business. We expect that litigation may be necessary in some instances to determine the validity and scope of certain of our proprietary rights. Litigation may be necessary in other instances to determine the validity, scope and/or non-infringement of certain patent rights claimed by third parties to be pertinent to the manufacture, use or sale of our products. Ultimately, the outcome of such litigation could adversely affect the validity and scope of our patent or other proprietary rights or hinder our ability to manufacture and market our products.

Periodically, we review publicly available information regarding the development efforts of others in order to determine whether these efforts may violate our proprietary rights. We may determine that litigation is necessary to enforce our proprietary rights against others. Such litigation could result in substantial expense, regardless of its outcome, and may not be resolved in our favor.

Risks Related to Our Common Stock

The price of our common stock has been and may continue to be volatile.

The stock markets, in general, and in particular with respect to biotech and life sciences companies, have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. These broad market fluctuations may adversely affect the trading price of our common stock. In addition, the limited trading volume of our stock may contribute to its volatility. Our stock price may be particularly volatile given the stage of our business.

In the past, following periods of volatility in the market price of a particular company's securities, litigation has often been brought against that company. If litigation of this type is brought against us, it could be extremely expensive and divert management's attention and our Company's resources.

Our certificate of incorporation, our bylaws and Delaware law contain provisions that could discourage another company from acquiring us and may prevent attempts by our stockholders to replace or remove our current management.

Provisions of Delaware law, our certificate of incorporation and our bylaws may discourage, delay or prevent a merger or acquisition that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. In addition, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace or remove our Board of Directors. These provisions include authorizing the issuance of "blank check" preferred stock without any need for action by stockholders.

In addition, Section 203 of Delaware General Corporation Law, which is applicable to us, may discourage, delay or prevent a change in control of our Company by prohibiting stockholders owning in excess of 15% of our outstanding voting stock from merging or combining with us, unless certain approvals are obtained.

Conversion of our Convertible Notes would result in substantial dilution for our existing stockholders.

Our Convertible Notes bear interest at a rate of 6% per annum, payable quarterly in cash or in kind, at the election of the holders of the Convertible Notes. The Convertible Notes are convertible into shares of our common stock at a rate of 1,250 shares for every $1,000 of principal and accrued interest that is being converted. In the event the holders of the Convertible Notes were to opt to convert in full the outstanding principal and accrued interest due under the Convertible Notes as of December 31, 2019, we would be required to issue an aggregate of approximately 9.0 million shares, representing 9.0% of our outstanding shares, after giving effect to such conversion. This would result in substantial dilution of our existing stockholders.

Concentration in stockholder ownership could influence strategic actions.

Our directors, executive officers, principal stockholders and affiliated entities currently beneficially own or control a significant percentage of our outstanding common stock. Based on information set forth in an amended Schedule 13D filed with the SEC on January 7, 2020, the beneficial ownership in our common stock, as determined in accordance with Rule 13d-3 of the Exchange Act, of Tang Capital Partners, LP ("TCP") was approximately 3.4 million shares of common stock, or 3.8% of our outstanding shares of common stock on December 31, 2019. In addition, as of December 31, 2019, TCP has the right to acquire approximately 7.2 million shares of common stock on conversion of the Convertible Notes; TCP can acquire up to approximately 5.7 million of the foregoing shares of common stock without providing 61 days' notice.

Such a substantial concentration of common stock ownership or control could significantly influence corporate actions on various strategic matters, including, for example, receptivity to collaborations and merger or sale overtures to the extent that stockholder approval is required for such transactions. Further, covenants contained in the Convertible Notes would require approval from the noteholders for any change of control transaction we might consider. Accordingly, we may only be able to pursue transactions that are supported by these large stockholders. In addition, the conversion of the Convertible Notes, the exercise of these warrants, or the sale by our current stockholders of a substantial number of shares, or the expectation that such exercises or sales may occur, could significantly reduce the market price of our common stock.

Future utilization of net operating loss carryforwards or research and development credit carryforwards may be impaired due to recent changes in ownership.

We believe our net operating loss and research and development credit carryforwards, and certain other tax attributes, may be subject to limitation under Section 382 of the Internal Revenue Code of 1986 ("IRC"). As a result, our deferred tax assets, and related valuation allowance, have been reduced for the estimated impact of the net operating loss and research and development credit carryforwards that we currently estimate may expire, unused. Utilization of our remaining net operating loss and research and development credit carryforwards may still be subject to substantial annual limitations due to ownership change limitations provided by the IRC and similar state provisions for ownership changes after December 31, 2018, including those that may come in conjunction with future equity financings or market trades by our stockholders.

Our business could be negatively affected as a result of the actions of activist stockholders.

Proxy contests have been waged against many companies in the biopharmaceutical industry over the last few years. If faced with a proxy contest, we may not be able to respond successfully to the contest, which would be disruptive to our business. Even if we are successful, our business could be adversely affected by a proxy contest involving us because:

- responding to proxy contests and other actions by activist stockholders can be costly and time-consuming, disrupting operations and diverting the attention of management and employees, and can lead to uncertainty;
- perceived uncertainties as to future direction may result in the loss of potential acquisitions, collaborations or in-licensing opportunities, and may make it more difficult to attract and retain qualified personnel and business partners; and
- if individuals are elected to our Board of Directors with a specific agenda, it may adversely affect our ability to effectively implement our strategic plan in a timely manner and create additional value for our stockholders.

These actions could cause the market price of our common stock to experience periods of volatility.

If we identify a material weakness in our internal control over financial reporting, our ability to meet our reporting obligations and the trading price of our common stock could be negatively affected.

A material weakness is a deficiency, or a combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of our financial statements will not be prevented or detected on a timely basis. Accordingly, a material weakness increases the risk that the financial information we report contains material errors.

We regularly review and update our internal controls, disclosure controls and procedures and corporate governance policies. In addition, we are required under the Sarbanes-Oxley Act of 2002 to report annually on our internal control over financial reporting. Any system of internal controls, however well designed and operated, is based in part on certain assumptions and can provide only reasonable, not absolute, assurances that the objectives of the system are met. If we, or our independent registered public accounting firm, determine that our internal controls over financial reporting are not effective, or we discover areas that need improvement in the future, these shortcomings could have an adverse effect on our business and financial results.

If we cannot conclude that we have effective internal control over our financial reporting, or if our independent registered public accounting firm is unable to provide an unqualified opinion regarding the effectiveness of our internal control over financial reporting, investors could lose confidence in the reliability of our financial statements. Failure to comply with reporting requirements could also subject us to sanctions and/or investigations by the SEC, The Nasdaq Capital Market or other regulatory authorities.

Because we do not anticipate paying any cash dividends on our common stock in the foreseeable future, capital appreciation, if any, will be the source of gain for our stockholders.

We have never declared or paid cash dividends on our common stock. We currently intend to retain all of our current and future earnings to finance the growth and development of our business. As a result, capital appreciation, if any, of our common stock will be the sole source of gain for our stockholders for the foreseeable future.

ITEM 1B. UNRESOLVED STAFF COMMENTS.

None.

ITEM 2. PROPERTIES.

As of December 31, 2019, we had an operating lease for 52,148 square feet of laboratory and office space in San Diego, California, with a lease term that expires on December 31, 2025. In January 2020, we expanded our space in San Diego, with the addition of 21,180 square feet of office space. The lease of the additional space began on January 1, 2020 and expires on December 31, 2025. We also leased 26,067 square feet of laboratory, office and warehouse space in Redwood City, California and 1,898 square feet of office space in Jersey City, New Jersey. The lease for the Redwood City space expired on May 31, 2019. The lease for the Jersey City office space expired on December 31, 2019.

ITEM 3. LEGAL PROCEEDINGS.

We are not currently a party to any material legal proceedings.

On June 3, 2019, a purported federal securities class action complaint was filed against the Company, its Chief Executive Officer and Chief Financial Officer by Jimmy Wong, individually and on behalf of all others similarly situated (“Plaintiff”), in the United States District Court for the Southern District of California (“Complaint”). On November 21, 2019, the Plaintiff voluntarily dismissed the Complaint, without prejudice, as to all defendants.

ITEM 4. MINE SAFETY DISCLOSURES.

Not applicable.

PART II

ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES.

Information About Our Common Stock

Shares of our common stock are traded on The Nasdaq Capital Market, under the symbol "HRTX."

Stockholders

The number of record holders of our common stock as of February 3, 2020 was 108.

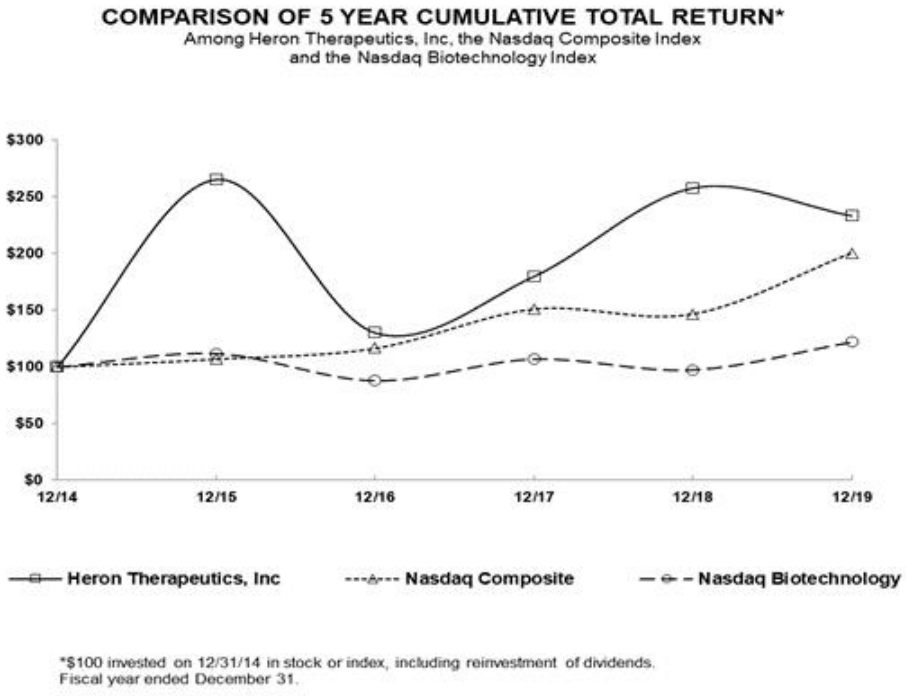
Dividend Policy

We have never paid dividends on our common stock. We currently intend to retain all available funds and any future earnings for use in the operation and expansion of our business, and we do not anticipate paying any cash dividends in the foreseeable future.

Stock Performance Graph

The following is not deemed "filed" with the SEC and is not to be incorporated by reference into any filing we make under the Securities Act of 1933, as amended, or under the Exchange Act, whether made before or after the date hereof and irrespective of any general incorporation by reference language in such filing.

The following graph shows the value of an investment of $100 on December 31, 2014 in Heron Therapeutics, Inc. common stock, the Nasdaq Composite Index (U.S.) and the Nasdaq Biotechnology Index. All values assume reinvestment of the pretax value of dividends paid by companies included in these indices and are calculated as of December 31st of each year. Our common stock has traded on The Nasdaq Capital Market since January 2014. The comparisons shown in the graph are based on historical data and we caution that the stock price performance shown in the graph is not indicative of, nor intended to forecast, the potential future performance of our stock.



	12/14	12/15	12/16	12/17	12/18	12/19
Heron Therapeutics, Inc.	$ 100.00	$ 265.41	$ 130.22	$ 179.92	$ 257.85	$ 233.60
Nasdaq Composite Index	100.00	106.96	116.45	150.96	146.67	200.49
Nasdaq Biotechnology Index	100.00	111.77	87.91	106.92	97.45	121.92

Issuer Purchases of Securities

None.

Unregistered Sales of Equity Securities and Use of Proceeds

None.

ITEM 6. SELECTED FINANCIAL DATA.

The following Selected Financial Data should be read in conjunction with "Management's Discussion and Analysis of Financial Condition and Results of Operations" included in Item 7 and the Consolidated Financial Statements and Notes included in Item 8 of this Annual Report on Form 10-K.

	Years Ended December 31,				
	2019	2018	2017	2016	2015
	(In thousands, except per share amounts)				
Statements of Operations Data:					
Revenues:					
Net product sales	$ 145,968	$ 77,474	$ 30,767	$ 1,279	$ —
Operating expenses:					
Cost of product sales	61,619	27,512	4,588	35	—
Research and development	167,382	140,032	138,582	103,125	61,183
General and administrative	37,897	29,263	25,554	21,366	18,395
Sales and marketing	89,764	64,604	56,601	47,668	17,347
Loss from operations	(210,694)	(183,937)	(194,558)	(170,915)	(96,925)
Other income (expense), net	5,945	5,097	(2,926)	(2,228)	(666)
Net loss	$ (204,749)	$ (178,840)	$ (197,484)	$ (173,143)	$ (97,591)
Basic and diluted net loss per common share	$ (2.50)	$ (2.44)	$ (3.65)	$ (4.56)	$ (2.95)
Shares used in computing basic and diluted net loss per share	81,779	73,193	54,040	37,925	33,081
Balance Sheet Data:					
Cash and cash equivalents	$ 71,898	$ 31,836	$ 144,583	$ 13,414	$ 75,180
Short-term investments	319,074	300,535	27,796	37,724	55,986
Working capital	382,359	355,229	124,892	23,410	115,016
Total assets	512,782	462,179	234,307	67,482	137,845
Promissory note payable to related party	—	—	25,000	50,000	—
Non-current lease liabilities	12,242	—	—	—	—
Accumulated deficit	(1,165,470)	(960,721)	(783,455)	(585,971)	(412,828)
Total stockholders' equity (deficit)	403,835	370,160	131,136	(21,251)	118,110

ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS.

You should read the following discussion and analysis of our financial condition and results of operations together with our audited financial statements and the related notes and other financial information included elsewhere in this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report on Form 10-K, including information with respect to our plans and strategy for our business, include forward-looking statements that involve risks and uncertainties. You should review the "Risk Factors" included in Item 1A of this Annual Report on Form 10-K for a discussion of important factors that could cause our actual results to differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Introduction

Management's discussion and analysis of financial condition and results of operations is provided as a supplement to the Consolidated Financial Statements and Notes, included in Item 8 of this Annual Report on Form 10-K, to help provide an understanding of our financial condition, the changes in our financial condition and our results of operations. Our discussion is organized as follows:

- *Overview.* This section provides a general description of our business and operating expenses.
- *Critical accounting policies and estimates.* This section contains a discussion of the accounting policies that we believe are important to our financial condition and results of operations and that require significant judgment and estimates on the part of management in their application. In addition, all of our significant accounting policies, including the critical accounting policies and estimates, are summarized in Note 2 to the Consolidated Financial Statements included in Item 8 of this Annual Report on Form 10-K.
- *Results of operations.* This section provides an analysis of our results of operations presented in the accompanying consolidated statements of operations and comprehensive loss by comparing the results for the year ended December 31, 2019 to the results for the year ended December 31, 2018, and comparing the results for the year ended December 31, 2018 to the results for the year ended December 31, 2017.
- *Liquidity and capital resources.* This section provides an analysis of our cash flows and a discussion of our outstanding commitments and contingencies that existed as of December 31, 2019. Included in this discussion is our financial capacity to fund our future commitments and a discussion of other financing arrangements.

Overview

Heron Therapeutics, Inc. ("Company," "Heron" or "we") is a commercial-stage biotechnology company focused on improving the lives of patients by developing best-in-class treatments to address some of the most important unmet patient needs. We are developing novel, patient-focused solutions that apply our innovative science and technologies to already-approved pharmacological agents for patients suffering from pain or cancer.

In August 2016, our first commercial product, SUSTOL (granisetron) extended-release injection ("SUSTOL"), was approved by the U.S. Food and Drug Administration ("FDA"). SUSTOL is indicated in combination with other antiemetics in adults for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic chemotherapy (MEC) or anthracycline and cyclophosphamide (AC) combination chemotherapy regimens. SUSTOL is an extended-release, injectable 5-hydroxytryptamine type 3 receptor antagonist that utilizes our proprietary Biochronomer drug delivery technology to maintain therapeutic levels of granisetron for ≥5 days. We commenced commercial sales of SUSTOL in the U.S. in October 2016.

In November 2017, our second commercial product, CINVANTI (aprepitant) injectable emulsion ("CINVANTI") was approved by the FDA. In October 2019, the FDA approved our supplemental New Drug Application ("sNDA") for CINVANTI to expand the indication and recommended dosage to include the 130 mg single-dose regimen for patients receiving moderately emetogenic cancer chemotherapy ("MEC"). CINVANTI, in combination with other antiemetic agents, is indicated in adults for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy (HEC) including high-dose cisplatin as a single-dose regimen, delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC) as a single-dose regimen, and nausea and vomiting associated with initial and repeat courses of MEC as a 3-day regimen. CINVANTI is an intravenous ("IV") formulation of aprepitant, a substance P/neurokinin-1 ("NK_1") receptor antagonist. CINVANTI is the first and only IV formulation of an NK_1 receptor antagonist indicated for the prevention of acute and delayed nausea and vomiting associated with HEC and nausea and vomiting associated with MEC that is free of synthetic surfactants, including polysorbate 80. We commenced commercial sales of CINVANTI in the U.S. in January 2018. In February 2019, the FDA approved our sNDA for CINVANTI, for IV use, which expanded the administration of CINVANTI beyond the initially approved administration method (a 30-minute IV infusion) to include a 2-minute IV injection.

HTX-011, an investigational agent, is a dual-acting, fixed-dose combination of the local anesthetic bupivacaine with a low dose of the nonsteroidal anti-inflammatory drug meloxicam. It is the first and only extended-release local anesthetic to demonstrate in Phase 3 studies significantly reduced pain and opioid use through 72 hours compared to bupivacaine solution, the current standard-of-care local anesthetic for postoperative pain control. HTX-011 was granted Fast Track designation from the FDA in the fourth quarter of 2017 and Breakthrough Therapy designation in the second quarter of 2018. Heron submitted a New Drug Application ("NDA") to the FDA for HTX-011 in October of 2018 and received Priority Review designation in December of 2018. A Complete Response Letter ("CRL") was received from the FDA regarding the NDA for HTX-011 on April 30, 2019 relating to chemistry, manufacturing and controls and non-clinical information. No issues related to clinical efficacy or safety were noted. Heron resubmitted an NDA to the FDA for HTX-011 in September 2019. The Prescription Drug User Fee Act goal date is June 26, 2020. A Marketing Authorisation Application for HTX-011 was validated by the European Medicines Agency in March 2019 for review under the Centralised Procedure. Heron's New Drug Submission for HTX-011 for the management of postoperative pain was granted Priority Review status by Health Canada in October 2019 and accepted by Health Canada in November 2019.

HTX-034, our next-generation product candidate for postoperative pain management, is in development for postoperative pain via local application. Based on the positive results of preclinical studies in which HTX-034 demonstrated significant pain reduction for 7 days, we have initiated formal development of this next-generation postoperative pain management product candidate.

Net Product Sales

Net product sales include revenue recognized for sales of CINVANTI and SUSTOL to a limited number of specialty distributors ("Customers"), less applicable sales allowances. See the "Critical Accounting Policies and Estimates" section of this Annual Report on Form 10-K for further details on our revenue recognition policy.

Cost of Product Sales

Cost of product sales relates to the costs to produce, package and deliver CINVANTI and SUSTOL to our Customers. These costs include raw materials, labor, manufacturing and quality control overhead, and depreciation of equipment, as well as shipping and distribution costs. See the "Critical Accounting Policies and Estimates" section of this Annual Report on Form 10-K for further details on our inventory policy.

Research and Development Expense

All costs of research and development are expensed in the period incurred. Research and development expense primarily consists of salaries and related costs for personnel, stock-based compensation expense, fees paid to outside service providers and consultants, facilities costs and materials used in the clinical and preclinical trials and research and development.

At this time, due to the risks inherent in the clinical trial process, we are unable to estimate with any certainty the costs we will incur in the continued development of our product candidates. Other than costs for outsourced services associated with our clinical programs, we generally do not track research and development expense by project; rather, we track such expense by the type of cost incurred.

We expect research and development expense to significantly increase in 2020 to support our ongoing research and development efforts for our product candidates, including HTX-011 and HTX-034, clinical and manufacturing costs, and costs for postmarketing requirements for CINVANTI and SUSTOL. The lengthy process of completing our clinical trials and seeking regulatory approval for our product candidates requires the expenditure of substantial resources.

General and Administrative Expense

General and administrative expense primarily consists of salaries, stock-based compensation expense and other related costs for personnel in executive, finance and accounting, information technology, legal and human resource functions. Other general and administrative expense includes professional fees for legal, investor relations, accounting and other general corporate purposes, facility costs and insurance not otherwise included in research and development expense. We expect general and administrative expense in 2020 to remain consistent with 2019.

Sales and Marketing Expense

Sales and marketing expense primarily consists of salaries and related costs for personnel, stock-based compensation expense and other related costs for sales operations, marketing and market access. Other sales and marketing costs include professional fees and commercialization costs related to launch preparation activities for HTX-011 and ongoing costs related to CINVANTI and SUSTOL. We expect sales and marketing expense to significantly increase in 2020 to support the launch of HTX-011, if approved. The commercial launch process requires the expenditure of substantial resources.

Other Income (Expense), Net

Other income (expense), net primarily consists of interest income earned on our cash, cash equivalents and short-term investments, and other income resulting from the disgorgement of short-swing profits arising from the sales of our common stock by a beneficial owner pursuant to Section 16(b) of the Securities and Exchange Act of 1934 (“Exchange Act”). In addition, other income (expense), net includes interest expense on the Subordinated Secured Promissory Note (“Promissory Note”), as well as interest expense and amortization of debt discount related to our Senior Secured Convertible Notes (“Convertible Notes”), and gains (losses) from the disposal of fixed assets.

Critical Accounting Policies and Estimates

The discussion and analysis of our financial condition and results of operations are based on our consolidated financial statements, which have been prepared in accordance with accounting principles generally accepted in the U.S. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, revenues and expenses, and related disclosure of contingent assets and liabilities. We evaluate our estimates on an ongoing basis, including those related to revenue recognition, investments, inventory, accrued clinical liabilities, income taxes and stock-based compensation. We base our estimates on historical experience and on assumptions that we believe to be reasonable under the circumstances, the results of which form the basis of making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ materially from these estimates under different assumptions or conditions.

Our critical accounting policies used in the preparation of our consolidated financial statements involve significant judgments and estimates and include the following:

Revenue Recognition

Product Sales

CINVANTI is distributed in the U.S. through a limited number of Customers that resell CINVANTI to healthcare providers and hospitals, the end users of CINVANTI. SUSTOL is distributed in the U.S. through a limited number of Customers that resell SUSTOL to healthcare providers, the end users of SUSTOL.

Adoption of Topic 606

On January 1, 2018, we adopted the Financial Accounting Standards Board ("FASB") Accounting Standards Update No. 2014-09, *Revenue from Contracts with Customers* ("Topic 606") using the modified retrospective approach applied to those contracts that were not completed as of January 1, 2018. Results from reporting periods beginning after January 1, 2018 are presented under Topic 606, while prior period amounts are not adjusted and continue to be reported in accordance with our historical accounting under the FASB Accounting Standards Codification Topic 605, *Revenue Recognition* ("Topic 605"). Prior to the adoption of Topic 606, we recognized product sales as revenue to the extent that our Customers had resold our products to end users (sell-through approach). With the adoption of Topic 606, we recognize product sales as revenue when our products are sold to our Customers (sell-in approach). Product sales under both Topic 605 and 606 are reported net of product sales allowances, which include product returns.

Revenue is recognized in an amount that reflects the consideration we expect to receive in exchange for our products. To determine revenue recognition for contracts with customers within the scope of Topic 606, we performed the following 5 steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations of the contract(s); (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract(s); and (v) recognize revenue when (or as) we satisfy the performance obligations.

Product Sales Allowances

We recognize product sales allowances as a reduction of product sales in the same period the related revenue is recognized. Product sales allowances are based on amounts owed or to be claimed on the related sales. These estimates take into consideration the terms of our agreements with Customers, historical product returns, rebates or discounts taken, the shelf life of the product and specific known market events, such as competitive pricing and new product introductions. If actual future results vary from our estimates, we may need to adjust these estimates, which could have an effect on product sales and earnings in the period of adjustment. Our product sales allowances include:

- Product Returns—We allow our Customers to return product for credit for up to 12 months after its product expiration date. As such, there may be a significant period of time between the time the product is shipped and the time the credit is issued on returned product.
- Distributor Fees—We offer contractually determined discounts to our Customers. These discounts are paid no later than two months after the quarter in which product was shipped.
- Group Purchasing Organization ("GPO") Discounts and Rebates—We offer cash discounts to GPO members. These discounts are taken when the GPO members purchase CINVANTI or SUSTOL from our Customers, who then charge back to us the discount amount. Additionally, we offer volume and contract-tier rebates to GPO members. Rebates are based on actual purchase levels during the quarterly rebate purchase period.
- GPO Administrative Fees—We pay administrative fees to GPOs for services and access to data. These fees are based on contracted terms and are paid after the quarter in which the product was purchased by the GPOs' members.

- Medicaid Rebates—We participate in Medicaid rebate programs, which provide assistance to certain low-income patients based on each individual state's guidelines regarding eligibility and services. Under the Medicaid rebate programs, we pay a rebate to each participating state, generally within three months after the quarter in which CINVANTI or SUSTOL was sold.

We believe our estimated allowance for product returns requires a high degree of judgment and is subject to change based on our experience and certain quantitative and qualitative factors. We believe our estimated allowances for distributor fees, GPO discounts, rebates and administrative fees and Medicaid rebates do not require a high degree of judgment because the amounts are settled within a relatively short period of time.

Our product sales allowances and related accruals are evaluated each reporting period and adjusted when trends or significant events indicate that a change in estimate is appropriate. Changes in product sales allowance estimates could materially affect our results of operations and financial position.

Investments

We invest in various types of securities, including U.S. treasury bills and government agency obligations, corporate debt securities and commercial paper. As of December 31, 2019, we had $319.1 million in short-term investments which were classified as Level 1 or 2 within the fair value hierarchy. Fair values determined by Level 1 inputs utilize quoted prices in active markets for identical assets. Fair values determined by Level 2 inputs utilize data points that are observable such as quoted prices for similar assets, quoted prices in markets that are not active or other inputs that are observable. These securities have been initially valued at the transaction price and subsequently valued utilizing a third-party service provider who assesses the fair value using inputs other than quoted prices that are observable either directly or indirectly, such as yield curve, volatility factors, credit spreads, default rates, loss severity, current market and contractual prices for the underlying instruments or debt, broker and dealer quotes, as well as other relevant economic measures. We perform certain procedures to corroborate the fair value of these holdings, and in the process, we apply judgment and estimates that if changed, could significantly affect our statements of financial positions.

Inventory

Inventory is stated at the lower of cost or estimated net realizable value on a first-in, first-out, or FIFO, basis. We periodically analyze our inventory levels and write down inventory that has become obsolete, inventory that has a cost basis in excess of its estimated realizable value and inventory quantities that are in excess of expected sales requirements as cost of product sales. The determination of whether inventory costs will be realizable requires estimates by management. If actual market conditions are less favorable than projected by management, additional write-downs of inventory may be required, which would be recorded as cost of product sales.

Accrued Clinical Liabilities

We accrue clinical costs based on work performed, which relies on estimates of the progress of the clinical trials and the related expenses incurred. Clinical trial related contracts vary significantly in duration, and may be for a fixed amount, based on the achievement of certain contingent events or deliverables, a variable amount based on actual costs incurred, capped at a certain limit or contain a combination of these elements. Revisions are recorded to research and development expense in the period in which the facts that give rise to the revision become known. Historically, revisions have not resulted in material changes to research and development expense; however, a modification in the protocol of a clinical trial or cancellation of a clinical trial could result in a material charge to our results of operations.

Income Taxes

We make certain estimates and judgments in determining income tax expense for financial statement purposes. These estimates and judgments occur in the calculation of certain deferred tax assets and liabilities, which arise from differences in the timing of recognition of revenue and expense for tax and financial statement purposes. As part of the process of preparing our consolidated financial statements, we are required to estimate our income taxes for each of the jurisdictions in which we operate. This process involves estimating our current tax exposure under the most recent tax laws and assessing temporary differences resulting from differing treatment of items for tax and financial statement purposes.

We assess the likelihood that we will be able to recover our deferred tax assets. In doing so, we consider all available evidence, both positive and negative, including our historical levels of income and losses, expectations and risks associated with estimates of future taxable income and ongoing prudent and feasible tax planning strategies. A valuation allowance is provided when it is more likely than not that the deferred tax assets will not be realized. At December 31, 2019, we established a valuation allowance to offset our deferred tax assets due to the uncertainty of realizing future tax benefits from our net operating loss carryforwards and other deferred tax assets.

Should there be a change in our ability to recover our deferred tax assets, we would recognize a benefit to our tax provision in the period in which we determine that it is more likely than not that we will recover our deferred tax assets.

Stock-based Compensation

We generally grant stock-based payment awards under our stockholder-approved, stock-based compensation plans. We have granted, and may in the future grant, stock options and restricted stock awards to employees, directors, consultants and advisors under our Amended and Restated 2007 Equity Incentive Plan. In addition, all of our employees are eligible to participate in our 1997 Employee Stock Purchase Plan, as amended, which enables employees to purchase common stock at a discount through payroll deductions. Prior to our relisting on The Nasdaq Capital Market in January 2014, we issued non-plan stock option grants to certain employees, as set forth under Item 12 of this Annual Report on Form 10-K. These non-plan stock option grants were registered with the U.S. Securities and Exchange Commission (“SEC”) on Form S-8.

We estimate the fair value of stock options granted using the Black-Scholes option pricing model. This fair value is then amortized over the requisite service periods of the awards. The Black-Scholes option pricing model requires the input of subjective assumptions, including each option’s expected life and price volatility of the underlying stock. Expected volatility is based on our historical stock price volatility. The expected life of employee stock options represents the average of the contractual term of the options and the weighted-average vesting period, as permitted under the simplified method.

As stock-based compensation expense is based on awards ultimately expected to vest, it has been reduced for estimated forfeitures. Forfeitures are estimated at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates. Forfeitures are estimated based on historical experience. Changes in assumptions used under the Black-Scholes option pricing model could materially affect our net loss and net loss per share.

Recent Accounting Pronouncements

See Note 2 to the Consolidated Financial Statements included in Item 8 of this Annual Report on Form 10-K.

Results of Operations

Years Ended December 31, 2019 and 2018

Net Product Sales

Net product sales for the year ended December 31, 2019 were $146.0 million, compared to $77.5 million for the same period in 2018. For the year ended December 31, 2019, net product sales of CINVANTI were $132.2 million, compared to $56.2 million for the same period in 2018. For the year ended December 31, 2019, net product sales of SUSTOL were $13.8 million, compared to $21.3 million for the same period in 2018. On October 1, 2019, we made a business decision to discontinue all discounting of SUSTOL which will result in significantly lower SUSTOL net product sales in future periods.

Cost of Product Sales

For the year ended December 31, 2019, cost of product sales was $61.6 million, compared to $27.5 million for the same period in 2018. Cost of product sales primarily included raw materials, labor and overhead related to the manufacturing of CINVANTI and SUSTOL, as well as shipping and distribution costs. In addition, cost of product sales for the years ended December 31, 2019 and 2018 included charges resulting from the write-off of short-dated SUSTOL inventory of $3.3 million and $1.8 million, respectively.

Prior to FDA approval, $1.4 million of costs to manufacture CINVANTI were recorded to research and development expense in prior periods. By March 31, 2018, all CINVANTI units that were manufactured prior to FDA approval had been sold. We began capitalizing raw materials, labor and overhead related to the manufacturing of CINVANTI following FDA approval.

Research and Development Expense

Research and development expense consisted of the following (in thousands):

	December 31,	
	2019	2018
HTX-011-related costs	$ 95,256	$ 81,855
HTX-034-related costs	5,714	—
CINVANTI-related costs	4,632	7,336
SUSTOL-related costs	2,409	3,811
Personnel costs and other expenses	40,169	33,341
Stock-based compensation expense	19,202	13,689
Total research and development expense	$ 167,382	$ 140,032

For the year ended December 31, 2019, research and development expense was $167.4 million, compared to $140.0 million for the same period in 2018. This increase was primarily due to an increase in costs related to HTX-011 and HTX-034 of $13.4 million and $5.7 million, respectively, as well as personnel costs and other expenses of $6.8 million and stock-based compensation expense of $5.5 million, partially offset by decreases in costs related to CINVANTI and SUSTOL of $2.7 million and $1.4 million, respectively.

General and Administrative Expense

For the year ended December 31, 2019, general and administrative expense was $37.9 million, compared to $29.3 million for the same period in 2018. This increase was primarily due to an increase in personnel costs and other expenses to support our increased development and commercialization efforts and an increase in stock-based compensation expense.

Sales and Marketing Expense

For the year ended December 31, 2019, sales and marketing expense was $89.8 million, compared to $64.6 million for the same period in 2018. This increase was primarily due to costs to support the launch preparation activities for HTX-011. In addition, the increase was related to one-time costs associated with the retirement of our President in February 2019, including $8.4 million of stock-based compensation expense for stock option modifications.

Other Income (Expense), Net

For the year ended December 31, 2019, other income (expense), net was $5.9 million, compared to $5.1 million for the same period in 2018. This increase was primarily due to interest income earned on our short-term investments, as well as a decrease in interest expense due to the repayment of the Promissory Note in August 2018, partially offset by other income resulting from the disgorgement of short-swing profits arising from the sales of our common stock by a beneficial owner pursuant to Section 16(b) of the Exchange Act in September 2018.

Results of Operations

Years Ended December 31, 2018 and 2017

Net Product Sales

Net Product Sales for the year ended December 31, 2018 were $77.5 million, compared to $30.8 million for the same period in 2017.

For the year ended December 31, 2018, net product sales of CINVANTI were $56.2 million. There was no comparable activity in 2017, as we commenced commercial sales of CINVANTI in the U.S. in January 2018.

For the year ended December 31, 2018, net product sales of SUSTOL were $21.3 million under the new revenue recognition standard, Topic 606, which we adopted on January 1, 2018. For the year ended December 31, 2018, net product sales of SUSTOL would have been $21.0 million under the prior revenue recognition standard Topic 605. For the year ended December 31, 2017, net product sales of SUSTOL were $30.8 million.

Cost of Product Sales

For the year ended December 31, 2018, cost of product sales was $27.5 million, compared to $4.6 million for the same period in 2017. Cost of product sales primarily included raw materials, labor and overhead related to the manufacturing of CINVANTI and SUSTOL, as well as shipping and distribution costs. In addition, cost of product sales included a one-time charge of $1.8 million resulting from the write-off of short-dated SUSTOL inventory.

Prior to FDA approval, $1.4 million of costs to manufacture CINVANTI were recorded to research and development expense in prior periods. By March 31, 2018, all CINVANTI units that were manufactured prior to FDA approval had been sold. We began capitalizing raw materials, labor and overhead related to the manufacturing of CINVANTI following FDA approval.

Research and Development Expense

Research and development expense consisted of the following (in thousands):

	December 31,	
	2018	2017
HTX-011-related costs	$ 81,855	$ 78,092
CINVANTI-related costs	7,336	15,649
SUSTOL-related costs	3,811	7,390
Personnel costs and other expenses	33,341	26,139
Stock-based compensation expense	13,689	11,312
Total research and development expense	$ 140,032	$ 138,582

For the year ended December 31, 2018, research and development expense was $140.0 million, compared to $138.6 million for the same period in 2017. The increase in research and development expense was primarily due to personnel costs and other expenses of $7.2 million, costs related to HTX-011 of $3.8 million and stock-based compensation expense of $2.4 million, partially offset by a decrease in costs related to CINVANTI and SUSTOL of $8.3 million and $3.6 million, respectively.

General and Administrative Expense

For the year ended December 31, 2018, general and administrative expense was $29.3 million, compared to $25.6 million for the same period in 2017. The increase in general and administrative expense was primarily due to facility-related costs, as well as personnel costs to support our increased development and commercialization efforts.

Sales and Marketing Expense

For the year ended December 31, 2018, sales and marketing expense was $64.6 million, compared to $56.6 million for the same period in 2017. The increase in sales and marketing expense was primarily due to costs to support the commercialization of CINVANTI and SUSTOL, as well as market research and planning for HTX-011.

Other Income (Expense), Net

For the year ended December 31, 2018, other income (expense), net was $5.1 million, compared to ($2.9) million for the same period in 2017. The increase in other income (expense), net was primarily due to interest income earned on our short-term investments and other income resulting from the disgorgement of short-swing profits arising from the sales of our common stock by a beneficial owner pursuant to Section 16(b) of the Exchange Act. A portion of this increase was also a result of a decrease in interest expense due to the repayment of the Promissory Note in August 2018 (see Note 8 to our Consolidated Financial Statements).

Liquidity and Capital Resources

As of December 31, 2019, we had cash, cash equivalents and short-term investments of $391.0 million, compared to $332.4 million as of December 31, 2018. Based on our current operating plan and projections, we believe that existing cash, cash equivalents and short-term investments will be sufficient to meet our anticipated cash requirements for at least one year from the date this Annual Report on Form 10-K is filed with the SEC.

Our net loss for the year ended December 31, 2019 was $204.7 million, or $2.50 per share, compared to a net loss of $178.8 million, or $2.44 per share, for the same period in 2018.

Our net cash used for operating activities for the year ended December 31, 2019 was $124.6 million, compared to $191.8 million for the same period in 2018. The decrease in net cash used for operating activities was primarily due to changes in working capital associated with the launch of CINVANTI in 2018 and an increase in stock-based compensation expense, partially offset by an increase in net loss.

Our net cash used for investing activities for the year ended December 31, 2019 was $21.8 million, compared to $278.6 million for the same period in 2018. The decrease in cash used for investing activities was primarily due to a decrease in net purchases of short-term investments from $269.4 million for the year ended December 31, 2018 to $14.6 million for the year ended December 31, 2019.

Our net cash provided by financing activities for the year ended December 31, 2019 was $186.4 million, compared to $357.6 million for the same period in 2018. The decrease in cash provided by financing activities was due primarily to a decrease in net proceeds received from public offerings of our common stock from $363.1 million for the year ended December 31, 2018 to $162.2 million for the year ended December 31, 2019, partially offset by $25.0 million for the repayment of the Promissory Note in August 2018.

Historically, we have financed our operations, including technology and product research and development, primarily through sales of our common stock and debt financings.

Contractual Obligations

The following table summarizes our contractual obligations as of December 31, 2019 (in thousands):

	Payments due by period				
	Total	Less than 1 year	1–3 years	3–5 years	More than 5 years
Operating lease obligations	$ 17,509	$ 2,724	$ 5,689	$ 5,999	$ 3,097
Capital expenditures	11,065	11,065	—	—	—
Purchase obligations	65,784	65,784	—	—	—
Total	$ 94,358	$ 79,573	$ 5,689	$ 5,999	$ 3,097

As of December 31, 2019, we had an operating lease for 52,148 square feet of laboratory and office space in San Diego, California, with a lease term that expires on December 31, 2025. In January 2020, we expanded our space in San Diego, with the addition of 21,180 square feet of office space. The lease of the additional space began on January 1, 2020 and expires on December 31, 2025. We have one 5-year option to renew this lease on expiration. We also leased 26,067 square feet of laboratory, office and warehouse space in Redwood City, California and 1,898 square feet of office space in Jersey City, New Jersey. The lease for the Redwood City space expired on May 31, 2019. The lease for the Jersey City office space expired on December 31, 2019. For the year ended December 31, 2019, rent expense for all properties was $3.0 million.

At December 31, 2019, capital expenditures consisted of non-cancellable commitments for equipment related to scale-up activities at our third-party manufacturers. Total capital expenditures of $10.1 million were not included in our consolidated financial statements for the year ended December 31, 2019. We intend to use our current financial resources to fund our commitments under the capital expenditure obligations.

At December 31, 2019, purchase obligations primarily consisted of non-cancellable commitments with third-party manufacturers in connection with the manufacturing of HTX-011, CINVANTI and SUSTOL, as well as commitments with various vendors for sales and marketing support. Total purchase obligations of $40.9 million were not included in our consolidated financial statements for the year ended December 31, 2019. We intend to use our current financial resources to fund our commitments under these purchase obligations.

The holders of the Convertible Notes may also require prepayment of such notes at any time at each holder’s option (see Notes to Consolidated Financial Statements included in this Annual Report on Form 10-K). As of December 31, 2019, $7.2 million aggregate principal amount of the Convertible Notes were outstanding.

We enter into agreements with clinical sites and clinical research organizations for the conduct of our clinical trials. We make payments to these sites and organizations based in part on the number of eligible patients enrolled and the length of their participation in the clinical trials. Under certain of these agreements, we may be subject to penalties in the event that we prematurely terminate these agreements. At this time, due to the variability associated with clinical site and contract research organization agreements, we are unable to estimate with certainty the future costs we will incur. We intend to use our current financial resources to fund our obligations under these commitments.

Off–Balance Sheet Arrangements

We are not involved in any “off–balance sheet arrangements” within the meaning of the rules of the SEC.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK.

The primary objective of our investment activities is to preserve our capital to fund operations. Our exposure to market risk for changes in interest rates relates primarily to the increase or decrease in the amount of interest income we can earn on our investment portfolio. Our risk associated with fluctuating interest income is limited to our investments in interest rate-sensitive financial instruments. Under our current policies, we do not use interest rate derivative instruments to manage this exposure to interest rate changes. We mitigate default risk by investing in short-term investment grade securities, such as treasury-backed money market funds, U.S. treasury and agency securities, corporate debt securities and commercial paper. As a result of the generally short-term nature of our investments, a 50-basis point movement in market interest rates would not have a material impact on the fair value of our portfolio as of December 31, 2019 and 2018. While changes in our interest rates may affect the fair value of our investment portfolio, any gains or losses are not recognized in our consolidated statements of operations and comprehensive loss until the investment is sold or if a reduction in fair value is determined to be a permanent impairment. Our debt obligations on our Convertible Notes carry a fixed interest rate and, as a result, we are not exposed to interest rate risk on our convertible debt. We seek to ensure the safety and preservation of our invested principal by limiting default risk, market risk and reinvestment risk. We do not have any material foreign currency obligations or other derivative financial instruments.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA.

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

Stockholders and Board of Directors
Heron Therapeutics, Inc.
San Diego, California

Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated balance sheets of Heron Therapeutics, Inc. (the "Company") as of December 31, 2019 and 2018, the related consolidated statements of operations and comprehensive loss, stockholders' equity (deficit), and cash flows for each of the three years in the period ended December 31, 2019, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2019 and 2018, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2019**,** in conformity with accounting principles generally accepted in the United States of America.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) ("PCAOB"), the Company's internal control over financial reporting as of December 31, 2019, based on criteria established in *Internal Control – Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission ("COSO") and our report dated March 2, 2020 expressed an unqualified opinion thereon.

Changes in Accounting Principles

As discussed in Note 6 to the consolidated financial statements, the Company has changed its method of accounting for leases in 2019 due to the adoption of Financial Accounting Standards Board (United States) Accounting Standard Codification Topic No. 842, *Leases.*

As discussed in Note 5 to the consolidated financial statements, the Company has changed its method of accounting for revenue in 2018 due to the adoption of Financial Accounting Standards Board (United States) Accounting Standard Codification Topic No. 606, *Revenue from Contracts with Customers.*

Basis for Opinion

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's consolidated financial statements based on our audits. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud.

Our audits included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

Critical Audit Matter

The critical audit matter communicated below is a matter arising from the current period audit of the consolidated financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the consolidated financial statements; and (2) involved our especially challenging, subjective, or complex judgments. The communication of critical audit matters does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matters below, providing separate opinions on the critical audit matter or on the accounts or disclosures to which it relates.

Revenues from Contracts with Customers

Description of the Matter—Product Returns

As discussed in Note 5 to the consolidated financial statements, the Company earns its revenue through the sale of its products, CINVANTI and SUSTOL, to specialty distributors. Such revenue totaled $146.0 million for the year ended December 31, 2019. The amount of revenue recognized is net of product sales allowances for product returns, distributor fees, group purchase organization fees, discounts and rebates, and Medicare rebates, which totaled $162.2 million for the year ended December 31, 2019. The allowances are recorded in the same period that the related revenue is recognized and create variability for consideration that the Company expects to receive. Management's estimated allowance for product returns requires a high degree of judgment and is subject to change based on various quantitative and qualitative factors. Accordingly, extensive audit effort and a high degree of auditor judgment were needed to evaluate management's estimates and assumptions used in the determination of product returns.

How We Addressed the Matter in Our Audit

We tested the effectiveness of internal control over financial reporting that relate to the Company's processes for estimating product returns.

We evaluated the significant accounting policies relating to product returns, as well as management's application of the policies, for appropriateness and reasonableness.

We selected a sample of customer transactions and performed the following procedures for each selection:

- Obtained and read contract source documents and management's contract analyses.
- Evaluated whether the selected estimates were applied consistently across similar arrangements.
- Tested the reasonableness of management's assumptions by comparing them to historical data, peer group information, and, where available, subsequent product returns.
- Where management used actual shipments and returns to estimate product returns, we tested the third-party reports used by management for completeness and accuracy.

We tested the mathematical accuracy of management's calculation of revenue, net of product sales allowances, including product returns, and the associated timing of revenue recognition, in the consolidated financial statements.

/s/ OUM & CO. LLP

San Francisco, California
March 2, 2020

We have served as the Company's auditor since 2006.

HERON THERAPEUTICS, INC.

CONSOLIDATED BALANCE SHEETS

(In thousands, except par value amounts)

	December 31, 2019	December 31, 2018
ASSETS		
Current assets:		
Cash and cash equivalents	$ 71,898	$ 31,836
Short-term investments	319,074	300,535
Accounts receivable, net	39,879	64,652
Inventory	24,968	39,032
Prepaid expenses and other current assets	23,245	11,193
Total current assets	479,064	447,248
Property and equipment, net	19,618	14,677
Right-of-use lease assets	13,754	—
Other assets	346	254
Total assets	$ 512,782	$ 462,179
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 2,758	$ 16,863
Accrued clinical and manufacturing liabilities	34,614	24,470
Accrued payroll and employee liabilities	15,248	13,397
Other accrued liabilities	36,535	32,715
Current lease liabilities	1,926	—
Convertible notes payable to related parties, net of discount	5,624	4,574
Total current liabilities	96,705	92,019
Non-current lease liabilities	12,242	—
Total liabilities	108,947	92,019
Commitments and contingencies (see Note 6)		
Stockholders' equity:		
Preferred stock, $0.01 par value: 2,500 shares authorized; no shares issued or outstanding at December 31, 2019 and 2018	—	—
Common stock, $0.01 par value: 150,000 shares authorized; 90,304 and 78,174 shares issued and outstanding at December 31, 2019 and 2018, respectively	903	782
Additional paid-in capital	1,568,317	1,330,186
Accumulated other comprehensive income (loss)	85	(87)
Accumulated deficit	(1,165,470)	(960,721)
Total stockholders' equity	403,835	370,160
Total liabilities and stockholders' equity	$ 512,782	$ 462,179

See accompanying Notes to Consolidated Financial Statements.

HERON THERAPEUTICS, INC.

CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS

(In thousands, except per share amounts)

	Years Ended December 31,		
	2019	**2018**	**2017**
Revenues:			
Net product sales	$ 145,968	$ 77,474	$ 30,767
Operating expenses:			
Cost of product sales	61,619	27,512	4,588
Research and development	167,382	140,032	138,582
General and administrative	37,897	29,263	25,554
Sales and marketing	89,764	64,604	56,601
Total operating expenses	356,662	261,411	225,325
Loss from operations	(210,694)	(183,937)	(194,558)
Other income (expense), net:			
Interest income	7,259	5,965	1,049
Interest expense	(1,472)	(2,672)	(3,937)
Other income (expense)	158	1,804	(38)
Total other income (expense), net	5,945	5,097	(2,926)
Net loss	(204,749)	(178,840)	(197,484)
Other comprehensive loss:			
Unrealized gains (losses) on short-term investments	172	(77)	7
Comprehensive loss	$ (204,577)	$ (178,917)	$ (197,477)
Basic and diluted net loss per share	$ (2.50)	$ (2.44)	$ (3.65)
Shares used in computing basic and diluted net loss per share	81,779	73,193	54,040

See accompanying Notes to Consolidated Financial Statements.

HERON THERAPEUTICS, INC.

CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY (DEFICIT)

(In thousands)

	Common Stock		Additional Paid-In Capital	Accumulated Other Comprehensive (Loss) Income	Accumulated Deficit	Total Stockholders' Equity (Deficit)
	Shares	Amount				
Balance, December 31, 2016	39,355	394	564,343	(17)	(585,971)	(21,251)
Issuance of common stock in public offerings, net	23,822	238	306,041	—	—	306,279
Conversion benefit included in Convertible Notes issued	—	—	369	—	—	369
Issuance of common stock under Employee Stock Purchase Plan	77	1	988	—	—	989
Issuance of common stock on exercise of stock options	1,351	13	11,450	—	—	11,463
Issuance of common stock on exercise of warrants	4	—	—	—	—	—
Issuance of warrants	—	—	226	—	—	226
Stock-based compensation expense	—	—	30,538	—	—	30,538
Net loss	—	—	—	—	(197,484)	(197,484)
Net unrealized gain on short-term investments	—	—	—	7	—	7
Comprehensive loss	—	—	—	—	—	(197,477)
Balance, December 31, 2017	64,609	$ 646	$ 913,955	$ (10)	$ (783,455)	$ 131,136
Cumulative effect of adoption of new accounting standard	—	—	—	—	1,574	1,574
Issuance of common stock in public offerings, net	11,963	120	363,008	—	—	363,128
Conversion benefit included in Convertible Notes issued	—	—	392	—	—	392
Issuance of common stock under Employee Stock Purchase Plan	72	1	1,178	—	—	1,179
Issuance of common stock on exercise of stock options	1,530	15	18,286	—	—	18,301
Stock-based compensation expense	—	—	33,367	—	—	33,367
Net loss	—	—	—	—	(178,840)	(178,840)
Net unrealized loss on short-term investments	—	—	—	(77)	—	(77)
Comprehensive loss	—	—	—	—	—	(178,917)
Balance, December 31, 2018	78,174	$ 782	$ 1,330,186	$ (87)	$ (960,721)	$ 370,160
Issuance of common stock in public offerings, net	9,857	99	162,052	—	—	162,151
Conversion benefit included in Convertible Notes issued	—	—	416	—	—	416
Issuance of common stock under Employee Stock Purchase Plan	126	1	2,108	—	—	2,109
Issuance of common stock on exercise of stock options	1,983	20	22,144	—	—	22,164
Issuance of common stock on exercise of warrants	132	1	—	—	—	1
Issuance of common stock on conversion of Convertible Notes	32	—	—	—	—	—
Stock-based compensation expense	—	—	51,411	—	—	51,411
Net loss	—	—	—	—	(204,749)	(204,749)
Net unrealized loss on short-term investments	—	—	—	172	—	172
Comprehensive loss	—	—	—	—	—	(204,577)
Balance, December 31, 2019	90,304	$ 903	$ 1,568,317	$ 85	$ (1,165,470)	$ 403,835

See accompanying Notes to Consolidated Financial Statements.

HERON THERAPEUTICS, INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS

(In thousands)

	Years Ended December 31,		
	2019	**2018**	**2017**
Operating activities:			
Net loss	$ (204,749)	$ (178,840)	$ (197,484)
Adjustments to reconcile net loss to net cash used for operating activities:			
Stock-based compensation expense	51,411	33,367	30,538
Depreciation and amortization	2,044	1,513	1,531
Amortization of debt discount	1,050	890	773
Accretion of discount on short-term investments	(3,730)	(3,412)	(278)
Realized gain on available-for-sale investments	(8)	—	—
Impairment of property and equipment	107	72	—
Loss on disposal of property and equipment	62	29	39
Change in operating assets and liabilities:			
Accounts receivable	24,773	(22,778)	(39,914)
Prepaid expenses and other assets	(12,052)	(7,482)	3
Inventory	14,064	(29,122)	(4,768)
Accounts payable	(14,105)	(1,906)	11,955
Accrued clinical and manufacturing liabilities	10,144	(3,614)	13,713
Accrued payroll and employee liabilities	1,851	4,537	446
Deferred revenue	—	—	1,664
Other accrued liabilities	4,558	14,941	11,482
Net cash used for operating activities	(124,580)	(191,805)	(170,300)
Investing activities:			
Purchases of short-term investments	(477,035)	(497,104)	(121,570)
Maturities and sales of short-term investments	462,406	227,700	131,783
Purchases of property and equipment	(7,154)	(9,171)	(2,553)
Proceeds from the sale of property and equipment	—	25	78
Net cash (used for) provided by investing activities	(21,783)	(278,550)	7,738
Financing activities:			
Net proceeds from sale of common stock and/or pre-funded warrants	162,151	363,128	306,279
Proceeds from purchases under the Employee Stock Purchase Plan	2,109	1,179	989
Proceeds from stock option exercises	22,164	18,301	11,463
Proceeds from warrant exercises	1	—	—
Repayment of promissory note payable to related party	—	(25,000)	(25,000)
Net cash provided by financing activities	186,425	357,608	293,731
Net increase (decrease) in cash and cash equivalents	40,062	(112,747)	131,169
Cash and cash equivalents at beginning of year	31,836	144,583	13,414
Cash and cash equivalents at end of year	$ 71,898	$ 31,836	$ 144,583
Supplemental disclosure of cash flow information:			
Interest paid	$ —	$ 1,183	$ 2,789
Cumulative effect of adoption of new accounting standard	$ —	$ 1,574	$ —

See accompanying Notes to Consolidated Financial Statements.

1. Organization and Business

Heron Therapeutics, Inc. ("Company," "Heron" or "we") is a commercial-stage biotechnology company focused on improving the lives of patients by developing best-in-class treatments to address some of the most important unmet patient needs. We are developing novel, patient-focused solutions that apply our innovative science and technologies to already-approved pharmacological agents for patients suffering from pain or cancer.

In August 2016, our first commercial product, SUSTOL (granisetron) extended-release injection ("SUSTOL"), was approved by the U.S. Food and Drug Administration ("FDA"). SUSTOL is indicated in combination with other antiemetics in adults for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic chemotherapy (MEC) or anthracycline and cyclophosphamide (AC) combination chemotherapy regimens. SUSTOL is an extended-release, injectable 5-hydroxytryptamine type 3 receptor antagonist that utilizes our proprietary Biochronomer drug delivery technology to maintain therapeutic levels of granisetron for ≥5 days. We commenced commercial sales of SUSTOL in the U.S. in October 2016.

In November 2017, our second commercial product, CINVANTI (aprepitant) injectable emulsion ("CINVANTI") was approved by the FDA. In October 2019, the FDA approved our supplemental New Drug Application ("sNDA") for CINVANTI to expand the indication and recommended dosage to include the 130 mg single-dose regimen for patients receiving moderately emetogenic cancer chemotherapy ("MEC"). CINVANTI, in combination with other antiemetic agents, is indicated in adults for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy (HEC) including high-dose cisplatin as a single-dose regimen, delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC) as a single-dose regimen, and nausea and vomiting associated with initial and repeat courses of MEC as a 3-day regimen. CINVANTI is an intravenous ("IV") formulation of aprepitant, a substance P/neurokinin-1 ("NK_1") receptor antagonist. CINVANTI is the first and only IV formulation of an NK_1 receptor antagonist indicated for the prevention of acute and delayed nausea and vomiting associated with HEC and nausea and vomiting associated with MEC that is free of synthetic surfactants, including polysorbate 80. We commenced commercial sales of CINVANTI in the U.S. in January 2018. In February 2019, the FDA approved our sNDA for CINVANTI, for IV use, which expanded the administration of CINVANTI beyond the initially approved administration method (a 30-minute IV infusion) to include a 2-minute IV injection.

HTX-011, an investigational agent, is a dual-acting, fixed-dose combination of the local anesthetic bupivacaine with a low dose of the nonsteroidal anti-inflammatory drug meloxicam. It is the first and only extended-release local anesthetic to demonstrate in Phase 3 studies significantly reduced pain and opioid use through 72 hours compared to bupivacaine solution, the current standard-of-care local anesthetic for postoperative pain control. HTX-011 was granted Fast Track designation from the FDA in the fourth quarter of 2017 and Breakthrough Therapy designation in the second quarter of 2018. Heron submitted a New Drug Application ("NDA") to the FDA for HTX-011 in October of 2018 and received Priority Review designation in December of 2018. A Complete Response Letter was received from the FDA regarding the NDA for HTX-011 on April 30, 2019 relating to chemistry, manufacturing and controls and non-clinical information. No issues related to clinical efficacy or safety were noted. Heron resubmitted an NDA to the FDA for HTX-011 in September 2019. The Prescription Drug User Fee Act goal date is June 26, 2020. A Marketing Authorisation Application for HTX-011 was validated by the European Medicines Agency in March 2019 for review under the Centralised Procedure. Heron's New Drug Submission for HTX-011 for the management of postoperative pain was granted Priority Review status by Health Canada in October 2019 and accepted by Health Canada in November 2019.

HTX-034, our next-generation product candidate for postoperative pain management, is in development for postoperative pain via local application. Based on the positive results of preclinical studies in which HTX-034 demonstrated significant pain reduction for 7 days, we have initiated formal development of this next-generation postoperative pain management product candidate.

As of December 31, 2019, we had $391.0 million in cash, cash equivalents and short-term investments. We have incurred significant operating losses and negative cash flows from operations. Management believes that the Company's existing cash, cash equivalents and short-term investments will be sufficient to meet the Company's anticipated cash requirements for at least one year from the date this Annual Report on Form 10-K is filed with the U.S. Securities and Exchange Commission ("SEC").

2. Summary of Significant Accounting Policies

Principles of Consolidation

The accompanying consolidated financial statements include the accounts of Heron Therapeutics, Inc. and its wholly-owned subsidiary, Heron Therapeutics B.V., which was organized in the Netherlands in March 2015. Heron Therapeutics B.V. has no operations and no material assets or liabilities, and there have been no significant transactions related to Heron Therapeutics B.V. since its inception.

Use of Estimates

The preparation of financial statements in conformity with accounting principles generally accepted in the U.S. ("GAAP") requires management to make estimates and assumptions that affect the amounts reported in the financial statements and disclosures made in the accompanying notes to the financial statements. Our significant accounting policies that involve significant judgment and estimates include revenue recognition, investments, inventory and the related reserves, accrued clinical liabilities, income taxes and stock-based compensation. Actual results could differ materially from those estimates.

Cash, Cash Equivalents and Short-term Investments

Cash and cash equivalents consist of cash and highly liquid investments with contractual maturities of three months or less from the original purchase date.

Short-term investments consist of securities with contractual maturities of greater than three months from the original purchase date. Securities with contractual maturities greater than one year are classified as short-term investments on the consolidated balance sheets, as we have the ability, if necessary, to liquidate these securities to meet our liquidity needs in the next 12 months. We have classified our short-term investments as available-for-sale securities in the accompanying consolidated financial statements. Available-for-sale securities are stated at fair market value, with net changes in unrealized gains and losses reported in other comprehensive loss and realized gains and losses included in other income (expense), net. The cost of securities sold is based on the specific identification method. Interest and dividends on securities classified as available-for-sale are included in interest income.

Our bank and investment accounts have been placed under control agreements in accordance with our Senior Secured Convertible Notes ("Convertible Notes") (see Note 8).

Fair Value of Financial Instruments

A company may elect to use fair value to measure accounts and loans receivable, available-for-sale and held-to-maturity securities, equity method investments, accounts payable, guarantees and issued debt. Other eligible items include firm commitments for financial instruments that otherwise would not be recognized at inception and non-cash warranty obligations where a warrantor is permitted to pay a third party to provide the warranty goods or services. If the use of fair value is elected, any upfront costs and fees related to the item such as debt issuance costs must be recognized in earnings and cannot be deferred. The fair value election is irrevocable and generally made on an instrument-by-instrument basis, even if a company has similar instruments that it elects not to measure based on fair value. Unrealized gains and losses on existing items for which fair value has been elected are reported as a cumulative adjustment to beginning retained earnings and any changes in fair value are recognized in earnings. We have elected to not apply the fair value option to our financial assets and liabilities.

Financial instruments, including cash and cash equivalents, receivables, inventory, prepaid expenses, other current assets, accounts payable and accrued expenses, are carried at cost, which is considered to be representative of their respective fair values because of the short-term maturity of these instruments. Short-term available-for-sale investments are carried at fair value (see Note 3). Our Convertible Notes outstanding at December 31, 2019 do not have a readily available ascertainable market value, however, the carrying value is considered to approximate its fair value.

Concentration of Credit Risk

Cash, cash equivalents and short-term investments are financial instruments that potentially subject us to concentrations of credit risk. We deposit our cash in financial institutions. At times, such deposits may be in excess of insured limits. We may also invest our excess cash in money market funds, U.S. government and agencies, corporate debt securities and commercial paper. We have established guidelines relative to our diversification of our cash investments and their maturities in an effort to maintain safety and liquidity. These guidelines are periodically reviewed and modified to take advantage of trends in yields and interest rates.

Our products are distributed in the U.S. through a limited number of specialty distributors and full line wholesalers (collectively, "Customers") that resell our products to healthcare providers and hospitals, the end users.

The following table includes the percentage of net product sales and accounts receivable balances for our three major Customers, each of which comprised 10% or more of our net product sales:

	Net Product Sales	Accounts Receivable
	Year Ended December 31, 2019	As of December 31, 2019
Customer A	40.9%	48.9%
Customer B	39.5%	38.6%
Customer C	17.4%	11.7%
Total	97.8%	99.2%

Accounts Receivable, Net

Accounts receivable are recorded at the invoice amount, net of an allowance for doubtful accounts. The allowance for doubtful accounts reflects accounts receivable balances that are believed to be uncollectible. In estimating the allowance for doubtful accounts, we consider: (1) our historical experience with collections and write-offs; (2) the credit quality of our Customers and any recent or anticipated changes thereto; and (3) the outstanding balances and past due amounts from our Customers.

We offered extended payment terms to our Customers in connection with our product launches of SUSTOL and CINVANTI in October 2016 and January 2018, respectively, in anticipation of the timing in reimbursement by government and commercial payers. Effective January 2018, we shortened payment terms to certain of our SUSTOL Customers. Effective January 2019, we shortened payment terms to our CINVANTI Customers. As of December 31, 2019, extended payment terms given to our Customers were evaluated in accordance with GAAP and did not impact the collectability of accounts receivables.

As of December 31, 2019, we determined that an allowance for doubtful accounts was not required. For the year ended December 31, 2019, we did not write-off any accounts receivable balances.

Inventory

Inventory is stated at the lower of cost or estimated net realizable value on a first-in, first-out, or FIFO, basis. We periodically analyze our inventory levels and write down inventory that has become obsolete, inventory that has a cost basis in excess of its estimated realizable value and inventory quantities that are in excess of expected sales requirements as cost of product sales. The determination of whether inventory costs will be realizable requires estimates by management. If actual market conditions are less favorable than projected by management, additional write-downs of inventory may be required, which would be recorded as cost of product sales.

Property and Equipment

Property and equipment is stated at cost less accumulated depreciation and amortization. Depreciation is calculated on a straight-line basis over the estimated useful lives of the assets (generally 5 years). Leasehold improvements are stated at cost and amortized on a straight-line basis over the shorter of the estimated useful life of the asset or the lease term.

Impairment of Long-Lived Assets

If indicators of impairment exist, we assess the recoverability of the affected long-lived assets by determining whether the carrying value of such assets can be recovered through undiscounted future operating cash flows. If impairment is indicated, we measure the amount of such impairment by comparing the carrying value of the asset to the fair value of the asset and record the impairment as a reduction in the carrying value of the related asset with a corresponding charge to operating expenses. Estimating the undiscounted future operating cash flows associated with long-lived assets requires judgment and assumptions that could differ materially from actual results.

Leases

In February 2016, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("ASU") No. 2016-02, *Leases (Topic 842)* ("ASU 2016-02"), which provides principles for the recognition, measurement, presentation and disclosure of leases for both lessees and lessors. In July 2018, the FASB issued ASU No. 2018-11, *Leases (Topic 842): Targeted Improvements* and ASU No. 2018-10, *Codification Improvements to Topic 842, Leases*. ASU 2016-02 and the subsequent modifications are identified as the FASB Accounting Standards Codification ("ASC") Topic 842 ("Topic 842"). Topic 842 requires lessees to classify leases as either finance or operating based on whether or not the lease is effectively a financed purchase. Lease expense is recognized over the term of the lease using an effective interest method for finance leases and on a straight-line basis over the lease term for operating leases. A lessee is also required to record a right-of-use ("ROU") lease asset and a lease liability for all leases with a lease term greater than 12 months. Leases with a term of 12 months or less will be accounted for similar to historical guidance for operating leases under the FASB ASC Topic 840, *Leases*. We adopted Topic 842 on January 1, 2019 using the alternative transition method allowed under ASU No. 2018-11. We elected the package of practical expedients permitted under the transition guidance, which allowed us to carryforward our historical assessments of: (i) whether a contract is or contains a lease; (ii) lease classification; and (iii) initial direct costs. We elected a policy of not recording leases on the balance sheet when the lease term is 12 months or less. The adoption of Topic 842 had a substantial impact on the consolidated balance sheet with the recognition of lease liabilities and corresponding ROU lease assets. There was no material impact on our results of operations or liquidity (see Note 6).

We determine if an agreement is a lease or contains lease components at inception. Operating leases are recorded as lease liabilities with corresponding ROU lease assets on the consolidated balance sheets. ROU lease assets represent our right to use the underlying assets over the lease term, and lease liabilities represent the present value of our obligation to make lease payments arising from the lease. Lease liabilities are recognized at the lease commencement based on the present value of lease payments over the lease term. As most of our leases do not provide an implicit rate, we use our incremental borrowing rate based on the information available at the commencement date in determining the present value of lease payments. We use the implicit rate when readily determinable. The ROU lease assets equal the lease liabilities, less unamortized lease incentives, unamortized initial direct costs and the cumulative difference between rent expense and amounts paid under the lease. The lease term includes any option to extend or terminate the lease when it is reasonably certain that we will exercise that option. Lease expense is recognized on a straight-line basis over the lease term. We have lease agreements with both lease and non-lease components, which are generally accounted for separately.

Revenue Recognition

In May 2014, FASB issued ASU No. 2014-09, *Revenue from Contracts with Customers* ("Topic 606"). Topic 606 is based on the principle that revenue should be recognized to depict the transfer of promised goods or services to customers in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. In the first quarter of 2018, we adopted Topic 606 using the modified retrospective approach. Under this approach, incremental disclosures are provided to present each financial statement line item for 2018 under the prior standard. As a result of the adoption of Topic 606, we recorded a cumulative adjustment to accumulated deficit of $1.6 million on January 1, 2018. This adjustment reflects the acceleration of $2.9 million in gross product sales less $1.1 million in product sales allowances and $0.2 million in cost of product sales (see Note 5).

Accrued Clinical Liabilities

We accrue clinical costs based on work performed, which relies on estimates of the progress of the trials and the related expenses incurred. Clinical trial related contracts vary significantly in duration, and may be for a fixed amount, based on the achievement of certain contingent events or deliverables, a variable amount based on actual costs incurred, capped at a certain limit or contain a combination of these elements. Revisions are recorded to research and development expense in the period in which the facts that give rise to the revision become known. Historically, revisions have not resulted in material changes to research and development expense; however, a modification in the protocol of a clinical trial or cancellation of a clinical trial could result in a material charge to our results of operations.

Research and Development Expense

All costs of research and development are expensed in the period incurred. Research and development expense primarily consists of personnel and related costs, stock-based compensation expense, fees paid to outside service providers and consultants, facilities costs and materials used in clinical and preclinical trials and research and development.

Patent Costs

We incur outside legal fees in connection with filing and maintaining our various patent applications. All patent costs are expensed as incurred and are included in general and administrative expense in the consolidated statements of operations and comprehensive loss.

Stock-Based Compensation Expense

We estimate the fair value of stock-based payment awards using the Black-Scholes option pricing model. This fair value is then amortized using the straight-line single-option method of attributing the value of stock-based compensation to expense over the requisite service periods of the awards. The Black-Scholes option pricing model requires the input of complex and subjective assumptions, including each option's expected life and price volatility of the underlying stock.

As stock-based compensation expense is based on awards ultimately expected to vest, it has been reduced for estimated forfeitures. Forfeitures are estimated at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates. Forfeitures are estimated based on historical data.

Warrants

We have issued warrants to purchase shares of our common stock in conjunction with certain equity financings or in exchange for services. The terms of the warrants were evaluated to determine the appropriate classification as equity or a liability.

Income Taxes

We recognize the impact of a tax position in our consolidated financial statements if the position is more likely than not to be sustained on examination and on the technical merits of the position. The total amount of unrecognized tax benefits, if recognized, would affect other tax accounts, primarily deferred taxes in future periods, and would not affect our effective tax rate, since we maintain a full valuation allowance against our deferred tax assets (see Note 10). We recognize interest and penalties related to income tax matters in income tax expense.

Comprehensive Loss

Comprehensive loss is defined as the change in equity during a period from transactions and other events and circumstances from non-owner sources. Net changes in unrealized gains and losses on available-for-sale securities are included in other comprehensive loss and represent the difference between our net loss and comprehensive net loss for all periods presented.

Net Loss per Share

Basic net loss per share is calculated by dividing the net loss by the weighted-average number of common shares outstanding for the period, without consideration of common stock equivalents. Diluted net loss per share is computed by dividing the net loss by the weighted-average number of common shares and common stock equivalents outstanding for the period determined using the treasury stock method. For purposes of this calculation, stock options, warrants and shares of common stock underlying Convertible Notes are considered to be common stock equivalents and are included in the calculation of diluted net loss per share only when their effect is dilutive.

Because we have incurred a net loss for all periods presented in the consolidated statements of operations and comprehensive loss, the following common stock equivalents were not included in the computation of net loss per share because their effect would be anti-dilutive (in thousands):

	December 31,		
	2019	2018	2017
Stock options outstanding	16,665	15,265	13,463
Warrants outstanding	508	640	620
Shares of common stock underlying Convertible Notes outstanding	8,960	8,473	7,983

Recent Accounting Pronouncements

Adopted in 2020

In August 2018, the FASB issued ASU No. 2018-13, *Fair Value Measurement (Topic 820) - Disclosure Framework - Changes to the Disclosure Requirements for Fair Value Measurement* (“ASU 2018-13”), which is designed to improve the effectiveness of disclosures by removing, modifying and adding disclosures related to fair value measurements. In the first quarter of 2020, we adopted the provisions of ASU 2018-13 and we have substantially completed our assessment of the impact on our financial statement disclosures. We do not expect the adoption of ASU 2018-13 to have a significant impact on our consolidated financial statements.

In June 2016, the FASB issued ASU No. 2016-13, *Financial Instruments - Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments* ("ASU 2016-13"), which amends the impairment model by requiring entities to use a forward-looking approach based on expected losses to estimate credit losses on certain types of financial instruments, including trade receivables and available-for-sale debt securities. In May 2019, the FASB issued ASU No. 2019-05, *Financial Instruments - Credit Losses (Topic 326): Targeted Transition Relief* ("ASU 2019-05"), which amends ASU 2016-13 by providing entities with an option to irrevocably elect the fair value option to be applied on an instrument-by-instrument basis for eligible financial instruments that are within the scope of Topic 326. The fair value option election does not apply to held-to-maturity debt securities. On January 1, 2020, we adopted the provisions of ASU 2016-13 and we have substantially completed our assessment based on the composition of our portfolio of financial instruments and current and forecasted economic conditions as of January 1, 2020. We are continuing to finalize our calculations for credit losses and to establish processes and internal controls that may be required to comply with ASU 2016-13. We do not expect the adoption of ASU 2016-13 to have a significant impact on our results of operations, financial condition or internal controls.

Not Yet Adopted

In December 2019, the FASB issued ASU No. 2019-12, *Income Taxes (Topic 740)* ("ASU 2019-12"), which is intended to simplify the accounting for income taxes by eliminating certain exceptions related to the approach for intraperiod tax allocation, the methodology for calculating income taxes in an interim period and the recognition of deferred tax liabilities for outside basis differences. ASU 2019-12 also simplifies aspects of the accounting for franchise taxes and enacted changes in tax laws or rates. ASU 2019-12 is effective for fiscal years beginning after December 15, 2020, including interim periods within those fiscal years. Early adoption is permitted. Adoption of ASU 2019-12 requires certain changes to be made prospectively and other changes to be made retrospectively. We plan to adopt the provisions of ASU 2019-12 in the first quarter of 2021, and we are currently evaluating the impact on our results of operations, financial condition and internal controls.

3. Fair Value Measurements

Fair value is defined as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Valuation techniques used to measure fair value must maximize the use of observable inputs and minimize the use of unobservable inputs. The FASB ASC Topic 820, *Fair Value Measurements & Disclosures*, establishes a fair value hierarchy which prioritizes the inputs used in measuring fair value as follows:

- Level 1—Observable inputs such as quoted prices in active markets for identical assets or liabilities.
- Level 2—Inputs other than Level 1 that are observable, either directly or indirectly, such as quoted prices for similar assets or liabilities; quoted prices in markets that are not active; or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities.
- Level 3—Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities.

We measure cash, cash equivalents and short-term investments at fair value on a recurring basis. The fair values of these such assets were as follows (in thousands):

	Fair Value Measurements at Reporting Date Using			
	Balance at December 31, 2019	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Cash and money market funds	$ 56,931	$ 56,931	$ —	$ —
U.S. treasury bills and government agency obligations	140,626	140,626	—	—
U.S. corporate debt securities	80,170	—	80,170	—
Foreign corporate debt securities	23,203	—	23,203	—
U.S. commercial paper	32,801	—	32,801	—
Foreign commercial paper	57,241	—	57,241	—
Total	$ 390,972	$ 197,557	$ 193,415	$ —

	Fair Value Measurements at Reporting Date Using			
	Balance at December 31, 2018	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Cash and money market funds	$ 22,751	$ 22,751	$ —	$ —
U.S. treasury bills and government agency obligations	59,741	$ 59,741	$ —	$ —
U.S. corporate debt securities	59,087	—	59,087	—
Foreign corporate debt securities	5,046	—	5,046	—
U.S. commercial paper	61,885	—	61,885	—
Foreign commercial paper	123,861	—	123,861	—
Total	$ 332,371	$ 82,492	$ 249,879	$ —

We have not transferred any investment securities between the three levels of the fair value hierarchy.

As of December 31, 2019, cash equivalents included $15.0 million of available-for-sale securities with contractual maturities of three months or less. As of December 31, 2019, short-term investments included $279.7 million of available-for-sale securities with contractual maturities of three months to one year and $39.4 million of available-for-sale securities with contractual maturities greater than one year. As of December 31, 2018, cash equivalents included $9.1 million of available-for-sale securities with contractual maturities of three months or less, and short-term investments included $300.5 million of available-for-sale securities with contractual maturities of three months to one year. The money market funds as of December 31, 2019 and 2018 are included in cash and cash equivalents on the consolidated balance sheets.

4. Balance Sheet Details

Short-Term Investments

The following is a summary of our short-term investments (in thousands):

	December 31, 2019			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
U.S. treasury bills and government agency obligations	$ 140,567	$ 59	$ —	$ 140,626
U.S. corporate debt	80,159	11	—	80,170
Foreign corporate debt	23,188	15	—	23,203
U.S. commercial paper	32,801	—	—	32,801
Foreign commercial paper	42,274	—	—	42,274
Total	$ 318,989	$ 85	$ —	$ 319,074

	December 31, 2018			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
U.S. treasury bills and government agency obligations	$ 59,747	$ —	$ (6)	$ 59,741
U.S. corporate debt securities	59,164	—	(77)	59,087
Foreign corporate debt securities	5,041	5	—	5,046
U.S. commercial paper	52,800	—	—	52,800
Foreign commercial paper	123,870	—	(9)	123,861
Total	$ 300,622	$ 5	$ (92)	$ 300,535

The amortized cost of debt securities is adjusted for amortization of premiums and accretion of discounts to maturity. We regularly monitor and evaluate the realizable value of our marketable securities. We did not recognize any impairment losses for the years ended December 31, 2019 and 2018.

Unrealized gains and losses associated with our investments are reported in accumulated other comprehensive loss. For the years ended December 31, 2019 and 2017, we recorded $172,000 and $7,000, respectively, in net unrealized gains associated with our short-term investments. For the year ended December 31, 2018, we recorded $77,000 in net unrealized losses associated with our short-term investments.

Realized gains and losses associated with our investments, if any, are reported in the statements of operations and comprehensive loss. We recognized $8,000 in realized gains during the year ended December 31, 2019. We did not recognize any realized gains or losses during the years ended December 31, 2018 and 2017.

Inventory

Inventory consists of the following (in thousands):

	December 31,	
	2019	2018
Raw materials	$ 6,635	$ 10,112
Work in process	12,571	20,604
Finished goods	5,762	8,316
Total inventory	$ 24,968	$ 39,032

As of December 31, 2019, total inventory included $23.5 million related to CINVANTI and $1.5 million related to SUSTOL. As of December 31, 2018, total inventory included $32.3 million related to CINVANTI and $6.7 million related to SUSTOL. In addition, cost of product sales for the years ended December 31, 2019 and 2018 included charges of $3.3 million and $1.8 million, respectively, resulting from the write-off of short-dated SUSTOL inventory.

Property and Equipment

Property and equipment, net consists of the following (in thousands):

	December 31,	
	2019	2018
Scientific equipment	$ 24,603	$ 18,077
Leasehold improvements	206	1,783
Computer equipment and software	1,314	1,190
Furniture, fixtures and office equipment	1,520	1,722
Property and equipment, gross	27,643	22,772
Less: accumulated depreciation and amortization	(8,025)	(8,095)
Property and equipment, net	$ 19,618	$ 14,677

Depreciation and amortization expense for the years ended December 31, 2019, 2018 and 2017 was $2.0 million, $1.5 million and $1.5 million, respectively. As of December 31, 2019 and 2018, $13.5 million and $10.3 million of property and equipment, respectively, was in process and not depreciated during the respective years.

Accrued Payroll and Employee Liabilities and Other Accrued Liabilities

Accrued payroll and employee liabilities consist of the following (in thousands):

	December 31,	
	2019	2018
Accrued employee salaries and benefits	$ 3,047	$ 2,330
Accrued bonuses	9,545	9,139
Accrued vacation	2,656	1,928
Total accrued payroll and employee liabilities	$ 15,248	$ 13,397

Other accrued liabilities consist of the following (in thousands):

	December 31,	
	2019	2018
Accrued product sales allowances	$ 27,939	$ 25,503
Accrued consulting and professional fees	7,742	5,768
Deferred rent	—	780
Accrued accounts payable	310	224
Other accrued liabilities	544	440
Total other accrued liabilities	$ 36,535	$ 32,715

5. Revenue Recognition

Product Sales

CINVANTI is distributed in the U.S. through a limited number of Customers that resell CINVANTI to healthcare providers and hospitals, the end users of CINVANTI. SUSTOL is distributed in the U.S. through a limited number of Customers that resell SUSTOL to healthcare providers, the end users of SUSTOL.

Adoption of Topic 606

On January 1, 2018, we adopted Topic 606 using the modified retrospective approach applied to those contracts that were not completed as of January 1, 2018. Results from reporting periods beginning after January 1, 2018 are presented under Topic 606, while prior period amounts are not adjusted and continue to be reported in accordance with our historical accounting under the FASB ASC Topic 605, *Revenue Recognition* (“Topic 605”). Prior to the adoption of Topic 606, we recognized product sales as revenue to the extent that our Customers had resold our products to end users (sell-through approach). With the adoption of Topic 606, we recognize product sales as revenue when our products are sold to our Customers (sell-in approach). Product sales under both Topic 605 and 606 are reported net of product sales allowances, which include product returns.

Revenue is recognized in an amount that reflects the consideration we expect to receive in exchange for our products. To determine revenue recognition for contracts with customers within the scope of Topic 606, we performed the following 5 steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations of the contract(s); (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract(s); and (v) recognize revenue when (or as) we satisfy the performance obligations.

The following table shows the reconciliation of assets and liabilities disclosed in our Annual Report on Form 10-K for the year ended December 31, 2017, as adjusted, due to the modified retrospective adoption of Topic 606 on January 1, 2018 (in thousands):

	As Reported Under Topic 605	Effect of Change	As Adjusted Under Topic 606
Inventory	$ 10,108	$ (198)	$ 9,910
Other accrued liabilities	17,175	991	18,166
Deferred revenue	2,763	(2,763)	—
Accumulated deficit	(783,455)	1,574	(781,881)

The following table shows the consolidated financial statement line items as if revenue from contracts with customers had been accounted for under Topic 605 (in thousands, except per share data):

	As Reported Under Topic 606	Effect of Change	As Calculated Under Topic 605
Consolidated Balance Sheet as of December 31, 2018:			
Inventory	$ 39,032	$ 2,181	$ 41,213
Other accrued liabilities	32,715	(7,195)	25,520
Deferred revenue	—	14,010	14,010
Accumulated deficit	(960,721)	(4,634)	(965,355)
Consolidated Statement of Operations for the Year Ended December 31, 2018:			
Net product sales	$ 77,474	$ (5,043)	$ 72,431
Cost of product sales	27,512	(1,983)	25,529
Loss from operations	(183,937)	(3,060)	(186,997)
Net loss	(178,840)	(3,060)	(181,900)
Basic and diluted net loss per share	(2.44)	(0.05)	(2.49)
Consolidated Statement of Cash Flows for the Year Ended December 31, 2018:			
Net loss	$ (178,840)	$ (3,060)	$ (181,900)
Adjustments to reconcile net loss to net cash used in operating activities:			
Inventory	(29,122)	(1,983)	(31,105)
Other accrued liabilities	14,941	(6,204)	8,737
Deferred revenue	—	11,247	11,247

Product Sales Allowances

We recognize product sales allowances as a reduction of product sales in the same period the related revenue is recognized. Product sales allowances are based on amounts owed or to be claimed on the related sales. These estimates take into consideration the terms of our agreements with Customers, historical product returns, rebates or discounts taken, the shelf life of the product and specific known market events, such as competitive pricing and new product introductions. If actual future results vary from our estimates, we may need to adjust these estimates, which could have an effect on product sales and earnings in the period of adjustment. Our product sales allowances include:

- Product Returns—We allow our Customers to return product for credit for up to 12 months after its product expiration date. As such, there may be a significant period of time between the time the product is shipped and the time the credit is issued on returned product.
- Distributor Fees—We offer contractually determined discounts to our Customers. These discounts are paid no later than two months after the quarter in which product was shipped.
- Group Purchasing Organization ("GPO") Discounts and Rebates—We offer cash discounts to GPO members. These discounts are taken when the GPO members purchase CINVANTI or SUSTOL from our Customers, who then charge back to us the discount amount. Additionally, we offer volume and contract-tier rebates to GPO members. Rebates are based on actual purchase levels during the quarterly rebate purchase period.
- GPO Administrative Fees—We pay administrative fees to GPOs for services and access to data. These fees are based on contracted terms and are paid after the quarter in which the product was purchased by the GPOs' members.
- Medicaid Rebates—We participate in Medicaid rebate programs, which provide assistance to certain low-income patients based on each individual state's guidelines regarding eligibility and services. Under the Medicaid rebate programs, we pay a rebate to each participating state, generally within three months after the quarter in which CINVANTI or SUSTOL was sold.

We believe our estimated allowance for product returns requires a high degree of judgment and is subject to change based on our experience and certain quantitative and qualitative factors. We believe our estimated allowances for distributor fees, GPO discounts, rebates and administrative fees and Medicaid rebates do not require a high degree of judgment because the amounts are settled within a relatively short period of time.

Our product sales allowances and related accruals are evaluated each reporting period and adjusted when trends or significant events indicate that a change in estimate is appropriate. Changes in product sales allowance estimates could materially affect our results of operations and financial position.

Net product sales for the year ended December 31, 2019 were $146.0 million, compared to $77.5 million for the same period in 2018. For the year ended December 31, 2019, net products sales of CINVANTI were $132.2 million, compared to $56.2 million for the same period in 2018. For the year ended December 31, 2019, net product sales of SUSTOL were $13.8 million, compared to $21.3 million for the same period in 2018.

The following table provides a summary of activity with respect to our product returns, distributor fees and discounts, rebates and administrative fees, which are included in other accrued liabilities on the consolidated balance sheets (in thousands):

	Product Returns	Distributor Fees	Discounts, Rebates and Administrative Fees	Total
Balance at December 31, 2018	$ 947	$ 2,813	$ 21,743	$ 25,503
Provision	2,960	18,934	140,305	162,199
Payments/credits	(1,556)	(17,748)	(140,459)	(159,763)
Balance at December 31, 2019	$ 2,351	$ 3,999	$ 21,589	$ 27,939

6. Commitments and Contingencies

Leases

As of December 31, 2019, we had an operating lease for 52,148 square feet of laboratory and office space in San Diego, California, with a lease term that expires on December 31, 2025. In January 2020, we expanded our space in San Diego, with the addition of 21,180 square feet of office space. The lease of the additional space began on January 1, 2020 and expires on December 31, 2025. We have one 5-year option to renew this lease on expiration.

We leased 26,067 square feet of laboratory, office and warehouse space in Redwood City, California. The lease for the Redwood City space expired on May 31, 2019. On March 15, 2018, we entered into a sublease agreement for the Redwood City property. The sublease agreement expired on May 31, 2019. We also leased 1,898 square feet of office space in Jersey City, New Jersey. The lease for the Jersey City office space expired on December 31, 2019. We believe our facilities are adequate and suitable for our current needs and that we will be able to obtain new or additional leased space in the future when necessary.

On January 1, 2019, on the adoption of Topic 842, we recognized initial ROU lease assets of $13.7 million and initial lease liabilities of $14.5 million. Our weighted-average remaining lease term for our operating leases was 6 years. The option to extend our lease in San Diego was not recognized as part of our lease liability and ROU lease assets. During the year ended December 31, 2019, we recognized $3.0 million of operating lease expense and paid $3.4 million for our operating leases.

Annual future minimum lease payments as of December 31, 2019 are as follows (in thousands):

Year ended December 31:		
2020	$	2,724
2021		2,804
2022		2,885
2023		2,969
2024		3,030
Thereafter		3,097
Total future minimum lease payments		17,509
Less: discount		(3,341)
Total lease liabilities	$	14,168

On January 1, 2020, we recognized an initial ROU lease asset of $5.1 million, an unamortized lease incentive of $0.6 million and a lease liability of $5.7 million related to the additional space leased in San Diego, California. We have agreed to pay a basic annual rent for the additional office space that increases incrementally over the term of the lease from $0.9 million for the first 12 months of the lease (inclusive of certain rent abatements) to $1.3 million for the last 12 months of the lease, and such other amounts as set forth in the lease.

Rent expense under all operating leases totaled $3.1 million, $3.2 million and $3.1 million for the years ended December 31, 2019, 2018 and 2017, respectively.

Clinical Development Agreements

We enter into agreements with clinical sites and clinical research organizations for the conduct of our clinical trials. We make payments to these sites and organizations based in part on the number of eligible patients enrolled and the length of their participation in the clinical trials. Under certain of these agreements, we may be subject to penalties in the event that we prematurely terminate these agreements. At this time, due to the variability associated with clinical site and contract research organization agreements, we are unable to estimate with certainty the future costs we will incur. We intend to use our current financial resources to fund our obligations under these commitments.

7. Realignment of Goals and Objectives and New Development Focus

Following the approval of SUSTOL and consistent with our transition into a commercial-stage biotechnology company, we realigned our goals and objectives and refocused our development efforts to the area of postoperative pain management. On September 30, 2016, the Board of Directors accepted the resignations of three executive officers, and these executive officers and other employees directly affected by the realignment and refocusing were provided with one-time severance payments on termination, continued benefits for a specified period of time and outplacement assistance.

The total expense for these activities was $9.4 million, $5.5 million of which is primarily for severance and $3.9 million of which is for non-cash, stock-based compensation expense. The total expense was recognized between September 30, 2016 and December 31, 2017. As of December 31, 2018, we had paid all of the cash severance charges.

In March 2018, we shut down operations at our Redwood City facility and entered into a sublease agreement for the remainder of the lease term. The fair value of the cease-use liability was calculated using the remaining lease payments, offset by future sublease payments, deferred rent amortization and prepaid rent amounts. In the first quarter of 2018, we recorded expense of $0.5 million to general and administrative expense as a loss on the lease.

We have accounted for these expenses in accordance with the FASB ASC Topic 420, *Exit or Disposal Cost Obligations*.

8. Secured Notes to Related Party

Convertible Notes

In April 2011, we entered into a securities purchase agreement for a private placement of up to $4.5 million in Convertible Notes with certain investors, including Tang Capital Partners, LP (“TCP”). TCP is controlled by Tang Capital Management, LLC (“TCM”). The manager of TCM is Kevin Tang, who served as a director at the time and currently serves as the Chairman of our Board of Directors. At the time of issuance, the terms of the Convertible Notes were determined by our independent directors to be no less favorable than terms that would be obtained in an arm’s length financing transaction. We received a total of $4.3 million, net of issuance costs, from the issuance of these Convertible Notes.

The Convertible Notes are secured by substantially all of our assets, including placing our bank and investment accounts under a control agreement. The Convertible Notes bear interest at 6% per annum, payable quarterly in cash or in additional principal amount of Convertible Notes, at the election of the purchasers. The Convertible Notes mature on May 2, 2021; however, the holders of the Convertible Notes may require prepayment of the Convertible Notes at any time, at each holder’s option.

The Convertible Notes are convertible into shares of our common stock at a rate of 1,250 shares for every $1,000 of outstanding principal due under the Convertible Notes. There is no right to convert the Convertible Notes to the extent that, after giving effect to such conversion, the holder would beneficially own in excess of 9.99% of our outstanding common stock. Each holder of the Convertible Notes can increase or decrease this beneficial ownership conversion limit by written notice to us, which will not be effective until 61 days after delivery of the notice.

As of December 31, 2019, we were in compliance with all covenants under the Convertible Notes. On the occurrence of an event of default under the Convertible Notes, the holders of the Convertible Notes have the right to require us to redeem all or a portion of their Convertible Notes.

In 2011, we filed a registration statement with the SEC to register for resale 3.5 million shares underlying the Convertible Notes. The registration statement was declared effective on July 29, 2011. The Convertible Note holders have agreed to waive their right to require us to maintain the effectiveness of the registration statement and to register the additional shares underlying the Convertible Notes until they provide notice otherwise.

The Convertible Notes contain an embedded conversion feature that was in-the-money on the issuance dates. Based on an effective fixed conversion rate of 1,250 shares for every $1,000 of principal and accrued interest due under the Convertible Notes, the total conversion benefit at issuance exceeded the loan proceeds. Therefore, a debt discount was recorded in an amount equal to the face value of the Convertible Notes on the issuance dates, and we began amortizing the resultant debt discount over the respective 10-year term of the Convertible Notes. During the year ended December 31, 2019, accrued interest of $0.4 million was paid-in-kind and rolled into the Convertible Note principal balance, which resulted in an additional debt discount of $0.4 million. For the years ended December 31, 2019, 2018 and 2017, interest expense relating to the stated rate was $0.4 million for each of the three periods. Interest expense relating to the amortization of the debt discount was $1.1 million, $0.9 million and $0.8 million, respectively.

As of December 31, 2019, the carrying value of the Convertible Notes was $5.6 million, which is comprised of the $7.2 million principal amount of the Convertible Notes outstanding, less a debt discount of $1.6 million. As of December 31, 2019, the Convertible Notes were convertible into 9.0 million shares of our common stock.

Promissory Note

In August 2016, we entered into the Subordinated Secured Promissory Note ("Promissory Note") with TCP whereby TCP agreed to lend us up to $100.0 million. The Promissory Note had a two-year term and bore interest at a rate of 8% per annum. The first close of $50.0 million occurred on August 5, 2016. The second close of an additional $50.0 million was not drawn and expired prior to the draw down. There were no fees, no warrants and no equity conversion features associated with this transaction. The Promissory Note was secured by a second-priority lien on substantially all of our assets. TCP is controlled by TCM. The manager of TCM is Kevin Tang, who serves as the Chairman of our Board of Directors. The terms of the Promissory Note were determined by our independent directors to be no less favorable than terms that would be obtained in an arm's length financing transaction.

For the years ended December 31, 2018 and 2017, interest expense was $1.2 million and $2.8 million, respectively. In August 2018, we paid the remaining obligation under the Promissory Note, which included $25.0 million of outstanding principal and $0.2 million of accrued interest. As of December 31, 2018, there were no remaining obligations under the Promissory Note.

9. Stockholders' Equity

2017 Common Stock Offerings

In January 2017, we sold 14.1 million shares of our common stock at a public offering price of $12.20 per share. We received total net proceeds of $163.7 million (net of $8.8 million in issuance costs) from the sale of the common stock.

In December 2017, we sold 9.7 million shares of our common stock at a public offering price of $15.50 per share. We received total net proceeds of $142.6 million (net of $7.4 million in issuance costs) from the sale of the common stock.

2018 Common Stock Offerings

In April 2018, we sold 6.9 million shares of our common stock at a public offering price of $26.00 per share. We received total net cash proceeds of $168.7 million (net of $10.7 million in issuance costs) from the sale of the common stock.

In June 2018, we sold 5.1 million shares of our common stock at a public offering price of $39.50 per share. We received total net cash proceeds of $194.4 million (net of $5.6 million in issuance costs) from the sale of the common stock.

2019 Common Stock Offerings

In October 2019, we sold 9.9 million shares of our common stock at a public offering price of $17.50 per share. We received total net cash proceeds of $162.2 million (net of $10.3 million in issuance costs) from the sale of the common stock.

Public Offering Warrants

In June 2014, as a component of our public offering, we sold 600,000 pre-funded warrants to purchase shares of our common stock. The pre-funded warrants have an exercise price of $0.01 per share and expire on June 30, 2021. During the year ended December 31, 2017, warrant holders exercised 4,426 warrants under the cashless exercise provision in each such holder's warrant, which resulted in the net issuance of 4,423 shares of common stock and no net cash proceeds to us. During the year ended December 31, 2019, warrant holders exercised 132,130 warrants, which resulted in the issuance of 132,130 shares for net cash proceeds of $1,321. As of December 31, 2019, 463,444 warrants from the June 2014 public offering remain outstanding.

Common Stock Reserved for Future Issuance

Shares of our common stock reserved for future issuance as of December 31, 2019 were as follows (in thousands):

	Number of Shares
Stock options outstanding	16,665
Stock options available for grant	4,971
Employee Stock Purchase Plan	370
Warrants outstanding	508
Shares of common stock underlying Convertible Notes outstanding (see Note 8)	8,960
Total shares reserved for future issuance	31,474

Employee Stock Purchase Plan

In 1997, our stockholders approved our Employee Stock Purchase Plan ("ESPP") at which time a maximum of 10,000 shares of common stock were available for issuance. In December 2007, May 2009, June 2011, May 2014, May 2015, June 2016, June 2017 and June 2019, our stockholders authorized increases in the number of shares reserved for issuance under the ESPP by 5,000, 10,000, 25,000, 25,000, 100,000, 100,000, 200,000 and 300,000 shares, respectively, for a total of 775,000 shares reserved at December 31, 2019. Under the terms of the ESPP, employees can elect to have up to a maximum of 10% of their base earnings withheld to purchase shares of our common stock. The purchase price of the stock is 85% of the lower of the closing prices for our common stock on either: (i) the first trading day in the enrollment period, as defined in the ESPP, in which the purchase is made, or (ii) the purchase date. The length of the enrollment period is 6 months. Enrollment dates are the first business day of May and November. Under the ESPP, we issued 125,727, 71,499, and 77,283 shares in 2019, 2018 and 2017, respectively. The weighted-average exercise price per share of the purchase rights exercised during 2019, 2018 and 2017 was $16.77, $16.48 and $12.80, respectively. As of December 31, 2019, 404,909 shares of common stock have been issued under the ESPP and 370,091 shares of common stock are available for future issuance.

Stock Option Plans

We currently have one stock option plan from which we can grant options and restricted stock awards to employees, officers, directors and consultants. In December 2007, the stockholders approved our 2007 Equity Incentive Plan ("2007 Plan") at which time a maximum of 150,000 shares of common stock were available for grant. In May 2010, June 2011, May 2014, May 2015, June 2016, June 2017 and June 2019, our stockholders approved amendments to our 2007 Plan to increase the maximum number of shares of common stock available for grant by 100,000, 4,500,000, 1,750,000, 4,300,000, 3,000,000, 5,000,000 and 7,000,000 shares of common stock, respectively, resulting in an aggregate of 25,800,000 shares of common stock authorized for issuance as of December 31, 2019. At December 31, 2019, there were 4,971,026 shares available for future grant under the 2007 Plan. Any shares that are issuable on exercise of options granted that expire, are cancelled or that we receive pursuant to a net exercise of options are available for future grant and issuance.

In 2014, 2013 and 2012, we granted options to certain employees outside of our stockholder approved stock option plans. All options to purchase our common stock were granted with an exercise price that equals fair market value of the underlying common stock on the grant dates and expire no later than 10 years from the date of grant. The options are exercisable in accordance with vesting schedules that generally provide for them to be fully vested and exercisable 4 years after the date of grant, provided, however, that we have also issued stock options awards that are subject to performance vesting requirements. All stock option grants issued outside of our stockholder approved plans have been registered on Form S-8 with the SEC.

The following table summarizes the stock option activity:

	Outstanding Options	
	Number of Shares	Weighted-Average Exercise Price
Balance at December 31, 2016	11,845,376	$ 14.44
Granted	4,300,621	$ 16.17
Exercised	(1,350,605)	$ 8.49
Cancelled	(1,332,428)	$ 20.06
Balance at December 31, 2017	13,462,964	$ 15.03
Granted	4,052,011	$ 26.83
Exercised	(1,529,509)	$ 11.97
Cancelled	(720,859)	$ 17.98
Balance at December 31, 2018	15,264,607	$ 18.33
Granted	4,933,480	$ 24.21
Exercised	(1,983,221)	$ 11.18
Cancelled	(1,550,226)	$ 23.26
Balance at December 31, 2019	16,664,640	$ 20.47

For the year ended December 31, 2019, options cancelled (included in the above table) consisted of 1,021,453 options forfeited with a weighted-average exercise price of $20.91 and 528,773 options expired with a weighted-average exercise price of $27.81.

As of December 31, 2019, options exercisable have a weighted-average remaining contractual term of 6.3 years. The total intrinsic value of stock option exercises, which is the difference between the exercise price and closing price of our common stock on the date of exercise, during the years ended December 31, 2019 and 2018 was $25.0 million and $31.4 million, respectively. As of December 31, 2019 and 2018, the total intrinsic value of options outstanding and exercisable was $56.3 million and $75.7 million, respectively.

	Years Ended December 31,					
	2019		2018		2017	
	Options	Weighted-Average Exercise Price	Options	Weighted-Average Exercise Price	Options	Weighted-Average Exercise Price
Exercisable at end of year	7,436,379	$ 17.02	6,523,093	$ 14.83	5,446,586	$ 13.25
Options vested or expected to vest	15,962,432	$ 20.31	14,449,017	$ 18.11	12,854,571	$ 14.98

Exercise prices and weighted-average remaining contractual lives for the options outstanding as of December 31, 2019 were:

Options Outstanding	Range of Exercise Prices	Weighted-Average Remaining Contractual Life (in years)	Weighted-Average Exercise Price	Options Exercisable	Weighted-Average Exercise Price of Options Exercisable
3,027,881	$5.20–$13.00	4.97	$ 10.16	2,720,921	$ 9.84
3,834,655	$13.05–$17.00	7.42	16.23	2,326,188	16.17
1,623,707	$17.05–$24.55	8.01	20.10	704,338	20.48
2,336,151	$24.97	8.93	24.97	644,066	24.97
3,877,880	$25.02	9.95	25.02	—	—
1,940,366	$25.06–$38.75	7.58	30.48	1,032,365	30.38
24,000	$39.00	8.56	39.00	8,501	39.00
16,664,640		7.58	20.47	7,436,379	17.02

On December 31, 2019, we had reserved 16,664,640 shares of common stock for future issuance on exercise of outstanding options granted under the 2007 Plan, as well as the non-plan grants.

Valuation and Expense Information

The following table summarizes stock-based compensation expense related to stock-based payment awards granted pursuant to all of our equity compensation arrangements (in thousands):

	December 31,		
	2019	2018	2017
Research and development	$ 19,202	$ 13,689	$ 11,312
General and administrative	13,564	9,630	9,469
Sales and marketing	18,645	10,048	9,757
Total stock-based compensation expense	$ 51,411	$ 33,367	$ 30,538

As of December 31, 2019, there was $128.7 million of total unrecognized compensation cost related to non-vested, stock-based payment awards granted under all of our equity compensation plans and all non-plan option grants. Total unrecognized compensation cost will be adjusted for future changes in estimated forfeitures. We expect to recognize this compensation cost over a weighted-average period of 3.0 years.

We estimated the fair value of each option grant and ESPP purchase right on the date of grant using the Black-Scholes option pricing model with the following weighted-average assumptions:

Options:

	December 31,		
	2019	2018	2017
Risk-free interest rate	1.8%	2.8%	2.1%
Dividend yield	—%	—%	—%
Volatility	66.5%	70.4%	74.0%
Expected life (years)	6	6	6

ESPP:

	December 31,		
	2019	2018	2017
Risk-free interest rate	1.9%	2.4%	1.2%
Dividend yield	—%	—%	—%
Volatility	52.1%	59.7%	50.0%
Expected life (months)	6	6	6

The weighted-average fair value of options granted was $14.70, $17.24 and $10.61 for the years ended December 31, 2019, 2018 and 2017, respectively.

The weighted-average fair value of shares purchased through the ESPP was $5.94, $9.95 and $4.51 for the years ended December 31, 2019, 2018 and 2017, respectively.

The risk-free interest rate assumption is based on observed interest rates on U.S. Treasury debt securities with maturities close to the expected term of our employee and director stock options and ESPP purchases.

The dividend yield assumption is based on our history and expectation of dividend payouts. We have never paid dividends on our common stock, and we do not anticipate paying dividends in the foreseeable future.

We used our historical stock price to estimate volatility.

The expected life of employee and director stock options represents the average of the contractual term of the options and the weighted-average vesting period, as permitted under the simplified method. We have elected to use the simplified method, as we do not have enough historical exercise experience to provide a reasonable basis on which to estimate the expected term. The expected life for the ESPP purchase rights is 6 months, which represents the length of each purchase period.

10. Income Taxes

For the years ended December 31, 2019, 2018 and 2017, we did not record a provision for income taxes due to a full valuation allowance against our deferred tax assets.

The difference between the provision for income taxes and income taxes computed using the effective U.S. federal statutory rate is as follows (in thousands):

	December 31,		
	2019	2018	2017
Tax at statutory federal rate	$ (42,997)	$ (37,557)	$ (67,145)
State tax, net of federal benefit	(9,823)	(6,527)	(6,203)
Research and development credits	(4,855)	(4,775)	(5,962)
Stock-based compensation expense	2,906	(2,059)	3,151
Non-deductible compensation	4,720	901	—
Change in valuation allowance	49,479	50,834	3,241
Impact of the 2017 Tax Act	—	—	74,361
Other	570	(817)	(1,443)
Provision for income taxes	$ —	$ —	$ —

Deferred income tax assets and liabilities arising from differences between accounting for financial statement purposes and tax purposes, less valuation allowance at year-end are as follows (in thousands):

	December 31,	
	2019	2018
Deferred tax assets:		
Net operating loss carryforward	$ 210,301	$ 172,113
Research and development credits	42,490	35,670
Stock-based compensation	15,628	11,905
Lease liabilities	3,487	—
Other	3,818	3,171
Total gross deferred tax assets	275,724	222,859
Deferred tax liabilities:		
Right-of-use lease assets	(3,385)	—
Total gross deferred tax liabilities	(3,385)	—
Valuation allowance	(272,339)	(222,859)
Net deferred tax assets	$ —	$ —

We have established a valuation allowance to offset net deferred tax assets as of December 31, 2019 and 2018 due to the uncertainty of realizing future tax benefits from such assets.

As of December 31, 2019, we had federal, California and other state net operating loss (“NOL”) carryforwards of $865.2 million, $125.9 million and $1.1 billion, respectively. The federal NOL carryforwards consist of $549.7 million generated before January 1, 2018, which will begin to expire in 2021, and $315.5 million that can be carried forward indefinitely, but are subject to the 80% taxable income limitation. The state NOL carryforwards will begin to expire in 2028.

As of December 31, 2019, we had federal and state research and development credit carryforwards of $33.7 million and $15.8 million, respectively. The federal research and development credit carryforwards will begin to expire in 2022. The state research and development credit carryforwards can be carried forward indefinitely.

Internal Revenue Code ("IRC") Section 382 and 383 places a limitation on the amount of taxable income that can be offset by NOL and credit carryforwards after a change in control (generally greater than 50% change in ownership within a three-year period) of a loss corporation. California has similar rules. Generally, after a change in control, a loss corporation cannot deduct NOL and credit carryforwards in excess of the IRC Section 382 and 383 limitation. We have performed an IRC Section 382 and 383 analysis and determined there were ownership changes in 2007, 2011 and 2013. We are currently in the process of completing the IRC Section 382 and 383 analysis for 2019. The limitation in the federal and state NOL and research and development credit carryforwards reduce the deferred tax assets, which are further offset by a full valuation allowance. The limitation can result in the expiration of the NOLs and research and development credit carryforwards available as of December 31, 2019.

We file U.S. and state income tax returns with varying statutes of limitations. The tax years from 2001 to 2019 remain open to examination due to the carryover of unused NOL carryforwards and tax credits.

The Tax Cuts and Jobs Act of 2017 ("2017 Tax Act") was enacted in December 2017. The 2017 Tax Act, among other things, reduced the U.S. federal corporate tax rate from 35% to 21%, effective January 1, 2018, required companies to pay a one-time transition tax on earnings of certain foreign subsidiaries that were previously tax deferred and created new taxes on certain foreign earnings. We revalued our deferred tax assets as of December 31, 2017 based on a U.S. federal tax rate of 21%, which resulted in a reduction to our deferred tax assets of $74.3 million fully offset by a reduction to the valuation allowance. We were not required to pay a one-time transition tax on earnings of our foreign subsidiary as the foreign subsidiary has an accumulated deficit. In addition, the Global Intangible Low-taxed Income provision, as defined in the 2017 Tax Act, is not applicable given the Company's controlled foreign corporations incurred losses for the years ended December 31, 2018 and 2019.

In December 2017, the SEC staff issued Staff Accounting Bulletin No. 118 ("SAB 118"), which provided guidance for the tax effects of the 2017 Tax Act. SAB 118 provided a measurement period that should not extend beyond one year from the 2017 Tax Act's enactment date for companies to complete the accounting under ASC 740. In accordance with SAB 118, we must have reflected the income tax effects of those aspects of the 2017 Tax Act for which the accounting under ASC 740 was complete. To the extent that our accounting for certain income tax effects of the 2017 Tax Act was incomplete, but we were able to determine a reasonable estimate, we were required to record a provisional estimate in our financial statements. If were not able to determine a provisional estimate to be included in our financial statements, we should have continued to apply ASC 740 on the basis of the provisions of the tax laws that were in effect immediately before the enactment of the Tax Act. We completed our analysis of the 2017 Tax Act's income tax effects. In accordance with SAB 118, the 2017 Tax Act-related income tax effects that we initially reported as provisional estimates were refined as additional analysis was performed. Our analysis was completed in the fourth quarter of 2018 and there was no material impact to our consolidated balance sheets or statements of operations and comprehensive loss.

A reconciliation of our unrecognized tax benefits is as follows (in thousands):

	Year Ended December 31,		
	2019	2018	2017
Balance at beginning of year	$ 2,385	$ 120	$ 120
Additions for tax positions of prior years	147	—	—
Additions based on tax positions related to current year	2,252	2,265	—
Balance at end of year	$ 4,784	$ 2,385	$ 120

Due to our valuation allowance, the $4.8 million of unrecognized tax benefits would not affect the effective tax rate, if recognized. It is the Company's practice to recognize interest and penalties related to income tax matters in income tax expense. As of December 31, 2019, we had no accrued interest and penalties related to uncertain tax positions. We do not expect any material changes to the estimated amount of liability associated with our uncertain tax positions within the next 12 months.

11. Other Income (Expense), Net

In 2018, we recorded $1.9 million in income to other income (expense), net resulting from the disgorgement of short-swing profits arising from the sales of our common stock by a beneficial owner pursuant to Section 16(b) of the Securities and Exchange Act of 1934.

12. Employee Benefit Plan

We have a defined contribution 401(k) plan ("Plan") covering substantially all of our employees. In the past three calendar years, we made matching cash contributions equal to 50% of each participant's contribution during the Plan year up to a maximum amount equal to the lesser of 3% of each participant's annual compensation or $8,400, $8,250 and $8,100 for the years ended December 31, 2019, 2018 and 2017, respectively. Such amounts were recorded as expense in the corresponding years. We may also contribute additional discretionary amounts to the Plan as we determine. For the years ended December 31, 2019, 2018 and 2017, we contributed $1.0 million, $0.7 million and $0.6 million, respectively, to the Plan. No discretionary contributions have been made to the Plan since its inception.

13. Summary of Quarterly Consolidated Financial Data (Unaudited)

The following is a summary of the unaudited quarterly results of operations for the years ended December 31, 2019 and 2018:

	2019			
	First Quarter	Second Quarter	Third Quarter	Fourth Quarter
	(In thousands, except per share amounts)			
Revenues:				
Net product sales	$ 31,602	$ 36,659	$ 42,624	$ 35,083
Cost of product sales	(14,962)	(13,588)	(17,195)	(15,874)
Gross Profit	16,640	23,071	25,429	19,209
Operating expenses:				
Research and development	42,972	41,425	34,708	48,277
General and administrative	9,648	9,778	8,597	9,874
Sales and marketing	28,720	23,647	16,977	20,420
Loss from operations	(64,700)	(51,779)	(34,853)	(59,362)
Other income, net	1,688	1,557	1,258	1,442
Net loss	$ (63,012)	$ (50,222)	$ (33,595)	$ (57,920)
Basic and diluted net loss per share	$ (0.80)	$ (0.63)	$ (0.42)	$ (0.65)

	2018			
	First Quarter	Second Quarter	Third Quarter	Fourth Quarter
	(In thousands, except per share amounts)			
Revenues:				
Net product sales	$ 11,567	$ 17,277	$ 19,786	$ 28,844
Cost of product sales	(3,133)	(5,231)	(7,576)	(11,572)
Gross Profit	8,434	12,046	12,210	17,272
Operating expenses:				
Research and development	39,561	30,159	30,421	39,891
General and administrative	7,028	6,209	7,288	8,738
Sales and marketing	13,835	14,531	16,281	19,957
Loss from operations	(51,990)	(38,853)	(41,780)	(51,314)
Other expense, net	(275)	183	3,434	1,755
Net loss	$ (52,265)	$ (38,670)	$ (38,346)	$ (49,559)
Basic and diluted net loss per share	$ (0.81)	$ (0.54)	$ (0.49)	$ (0.63)

ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE.

None.

ITEM 9A. CONTROLS AND PROCEDURES.

(a) Disclosure Controls and Procedures; Changes in Internal Control Over Financial Reporting

Our management, with the participation of our principal executive and principal financial and accounting officers, has evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934 ("Exchange Act")) as of December 31, 2019. Based on this evaluation, our principal executive and principal financial and accounting officers concluded that our disclosure controls and procedures were effective as of December 31, 2019.

During the first quarter of 2019, we implemented certain internal controls in connection with our adoption of the Financial Accounting Standards Board's Accounting Standards Update No. 2016-02 *Leases (Topic 842)*. In doing so, we have modified and enhanced our internal control over financial reporting (as such term is defined in Exchange Act Rule 13a-15(f)) during the period covered by this Annual Report on Form 10-K as a result of the implementation of these new processes and systems. Other than the above-mentioned changes, there have been no significant changes in our internal control over financial reporting that occurred during the period covered by this Annual Report on Form 10-K that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

(b) Management Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Internal control over financial reporting is defined in Rule 13a-15(f) and Rule 15d-15(f) promulgated under the Exchange Act as a process designed by, or under the supervision of, our principal executive and principal financial officers and effected by our Board of Directors, management and other personnel, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with accounting principles generally accepted in the U.S. and includes those policies and procedures that:

- pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of our assets;
- provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with accounting principles generally accepted in the U.S., and that receipts and expenditures are being made only in accordance with authorizations of our management and directors; and
- provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of our assets that could have a material effect on our financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2019. In making this assessment, our management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission in *Internal Control-Integrated Framework (2013)*.

Based on our assessment, management concluded that, as of December 31, 2019, our internal control over financial reporting was effective based on those criteria.

The independent registered public accounting firm that audited the consolidated financial statements that are included in this Annual Report on Form 10-K has issued an audit report on our internal control over financial reporting. The report appears below.

(c) Report of Independent Registered Public Accounting Firm on Internal Control Over Financial Reporting

Stockholders and Board of Directors
Heron Therapeutics, Inc.
San Diego, California

Opinion on Internal Control over Financial Reporting

We have audited Heron Therapeutics, Inc.'s (the "Company's") internal control over financial reporting as of December 31, 2019, based on criteria established in *Internal Control – Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission (the "COSO criteria"). In our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2019, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) ("PCAOB"), the consolidated balance sheets of the Company as of December 31, 2019 and 2018, the related consolidated statements of operations and comprehensive loss, stockholders' equity (deficit), and cash flows for each of the three years in the period ended December 31, 2019, and the related notes and our report dated March 2, 2020 expressed an unqualified opinion thereon.

Basis for Opinion

The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting, included in the accompanying Item 9A.(b), *Management Report on Internal Control over Financial Reporting*. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit of internal control over financial reporting in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audit also included performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

Definition and Limitations of Internal Control over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

/s/ OUM & CO. LLP

San Francisco, California
March 2, 2020

ITEM 9B. OTHER INFORMATION.

None.

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE.

Information required by this item will be contained in our Definitive Proxy Statement for our 2020 Annual Meeting of Stockholders, to be filed pursuant to Regulation 14A with the SEC within 120 days of December 31, 2019. Such information is incorporated herein by reference.

We have adopted a Code of Ethics that applies to our Principal Executive Officer, Principal Financial and Accounting Officer, and to all of our other officers, directors and employees. The Code of Ethics is available in the Corporate Governance section of the Investor Resources page on our website at *www.herontx.com*. We intend to disclose future waivers or material amendments to certain provisions of our Code of Ethics on the above-referenced website within 4 business days following the date of such waiver or amendment.

ITEM 11. EXECUTIVE COMPENSATION.

Information required by this item will be contained in our Definitive Proxy Statement for our 2020 Annual Meeting of Stockholders, to be filed pursuant to Regulation 14A with the SEC within 120 days of December 31, 2019. Such information is incorporated herein by reference.

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS.

Information required by this item will be contained in our Definitive Proxy Statement for our 2020 Annual Meeting of Stockholders, to be filed pursuant to Regulation 14A with the SEC within 120 days of December 31, 2019. Such information is incorporated herein by reference.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE.

Information required by this item will be contained in our Definitive Proxy Statement for our 2020 Annual Meeting of Stockholders, to be filed pursuant to Regulation 14A with the SEC within 120 days of December 31, 2019. Such information is incorporated herein by reference.

ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES.

Information required by this item will be contained in our Definitive Proxy Statement for our 2020 Annual Meeting of Stockholders, to be filed pursuant to Regulation 14A with the SEC within 120 days of December 31, 2019. Such information is incorporated herein by reference.

PART IV

ITEM 15. EXHIBITS, FINANCIAL STATEMENT SCHEDULES.

1. Consolidated Financial Statements.

   The consolidated financial statements and supplementary data set forth in Part II of the Annual Report on Form 10-K are included herein.

2. Consolidated Financial Statement Schedules.

   These schedules are omitted because they are not required, or are not applicable, or the required information is shown in the consolidated financial statements or notes thereto.

3. Exhibits.

   The exhibits listed in the accompanying Exhibit Index are incorporated by reference herein or filed as part of this Annual Report on Form 10-K.

EXHIBIT INDEX

Exhibit	Document Description
3.1	Certificate of Incorporation, as amended through July 29, 2009 (incorporated by reference to our Quarterly Report on Form 10-Q for the quarter ended June 30, 2009, as Exhibit 3.1, filed on August 4, 2009)
3.2	Certificate of Amendment of Certificate of Incorporation (incorporated by reference to our Current Report on Form 8-K, as Exhibit 3.1, filed on June 30, 2011)
3.3	Certificate of Amendment to the Certificate of Incorporation (incorporated by reference to our Current Report on Form 8-K, as Exhibit 3.1, filed on January 13, 2014)
3.4	Certificate of Amendment to the Certificate of Incorporation (incorporated by reference to our Company's Post-Effective Amendment to its Registration Statement on Form 8-A/A, filed on July 6, 2017)
3.5	Certificate of Amendment of Certificate of Incorporation (incorporated by reference to our Annual Report on Form 10-K for the year ended December 31, 2018, as Exhibit 3.6, filed on February 22, 2019)
3.6	Amended and Restated Bylaws (incorporated by reference to our Current Report on Form 8-K, as Exhibit 3.1, filed on February 8, 2019)
4.1	Common Stock Certificate (incorporated by reference to our Registration on Form S-3 (Registration No. 333-162968), as Exhibit 4.1, filed on November 6, 2009)
4.2	Form of Warrant to Purchase Shares of Common Stock (incorporated by reference to our Current Report on Form 8-K, as Exhibit 4.1, filed on June 27, 2014)
4.3	Form of Warrant to Purchase Shares of Common Stock (incorporated by reference to our Current Report on Form 8-K, as Exhibit 10.3, filed on October 22, 2009)
4.4	Amended and Restated Certificate of Designation, Preferences, and Rights of Series A Preferred Stock (incorporated by reference to our Current Report on Form 8-K, as Exhibit 3.C, filed on December 19, 2006)
4.5	Description of the Registrant's Securities Registered Pursuant to Section 12 of the Securities Exchange Act of 1934
10.1*	1997 Employee Stock Purchase Plan, as amended to date (incorporated by reference to our Definitive Proxy Statement on Schedule 14A, as Exhibit B, filed on April 26, 2019)
10.2	Lease Agreement between the Company and Metropolitan Life Insurance Company for lease of the Company's offices in Redwood City dated as of November 7, 1997 (incorporated by reference to our Annual Report on Form 10-K for the year ended December 31, 1997, as Exhibit 10-E, filed on March 30, 1998)
10.3*	Amended and Restated 2007 Equity Incentive Plan (incorporated by reference to our Definitive Proxy Statement on Schedule 14A, as Exhibit A, filed on April 26, 2019)
10.4*	Form of 2007 Equity Incentive Plan Stock Option Agreement (incorporated by reference to our Registration on Form S-8 (Registration No. 333-148660), as Exhibit 4.3, filed on January 14, 2008)
10.5*	Form of 2007 Equity Incentive Plan Restricted Stock Unit Agreement (incorporated by reference to our Registration on Form S-8 (Registration No. 333-148660), as Exhibit 4.4, filed on January 14, 2008)
10.6*	Form of 2007 Equity Incentive Plan Restricted Stock Award Agreement (incorporated by reference to our Annual Report on Form 10-K for the year ended December 31, 2007, as Exhibit 10-O, filed on March 31, 2008)
10.7*	Form of Indemnification Agreement (incorporated by reference to our Annual Report on Form 10-K for the year ended December 31, 2007, as Exhibit 10-S, filed on March 31, 2008)
10.8	Registration Rights Agreement, dated as of October 22, 2009, by and among the Company and the purchasers listed therein (incorporated by reference to our Current Report on Form 8-K, as Exhibit 10.2, filed on October 22, 2009)
10.9	Securities Purchase Agreement, dated as of April 24, 2011, by and among the Company and the purchasers listed therein (incorporated by reference to our Current Report on Form 8-K, as Exhibit 10.1, filed on April 28, 2011)
10.10	Form of Senior Secured Convertible Note due 2021 (incorporated by reference to our Current Report on Form 8-K, as Exhibit 10.2, filed on April 28, 2011)
10.11	Securities Agreement, dated as of April 24, 2011, by and between the Company and Tang Capital Partners, LP, as Agent for the Purchasers (incorporated by reference to our Current Report on Form 8-K, as Exhibit 10.3, filed on April 28, 2011)

10.12	Second Amendment to Lease, dated as of April 1, 2011, by and between the Company and Metropolitan Life Insurance Company (incorporated by reference to our Current Report on Form 8-K, as Exhibit 10.4, filed on April 28, 2011)
10.13	Securities Purchase Agreement, dated June 29, 2011, by and between the Company and the purchasers listed on Schedule I thereto (incorporated by reference to our Current Report on Form 8-K, as Exhibit 10.1, filed on June 30, 2011)
10.14	Amendment to Senior Secured Convertible Note Due 2021, dated June 29, 2011, by and between the Company and the purchasers named in the Securities Purchase Agreement, dated April 24, 2011, (incorporated by reference to our Current Report on Form 8-K, as Exhibit 10.2, filed on June 30, 2011)
10.15	Third Amendment to Lease, dated as of July 28, 2011, by and between the Company and Metropolitan Life Insurance Company (incorporated by reference to our Current Report on Form 8-K, as Exhibit 10.1, filed on August 3, 2011)
10.16	Registration Rights Agreement, dated July 25, 2012, by and between the Company and the purchasers named therein (incorporated by reference to our Current Report on Form 8-K, as Exhibit 10.2, filed on July 25, 2012)
10.17*	Executive Employment Agreement, dated May 1, 2013, by and between the Company and Barry D. Quart, Pharm.D. (incorporated by reference to our Quarterly Report on Form 10-Q for the quarter ended March 31, 2013, as Exhibit 10-AI, filed on May 10, 2013)
10.18*	Executive Employment Agreement, dated May 1, 2013, by and between the Company and Robert H. Rosen (incorporated by reference to our Quarterly Report on Form 10-Q for the quarter ended March 31, 2013, as Exhibit 10-AJ filed on May 10, 2013)
10.19	Form of Non-Qualified Stock Option Agreement (incorporated by reference to our Quarterly Report on Form 10-Q for the quarter ended June 30, 2013, as Exhibit 10-AL, filed on August 8, 2013)
10.20*	Amendment to Executive Employment Agreement, dated May 1, 2013, as amended on April 22, 2015, by and between the Company and Dr. Barry Quart (incorporated by reference to our Quarterly Report on Form 10-Q for the quarter ended March 31, 2015, as Exhibit 10.1, filed on May 8, 2015)
10.21*	Amendment to Executive Employment Agreement, dated May 1, 2013, as amended on April 22, 2015, by and between the Company and Robert Rosen (incorporated by reference to our Quarterly Report on Form 10-Q for the quarter ended March 31, 2015, as Exhibit 10.2, filed on May 8, 2015)
10.22+	SUSTOL® (granisetron, extended release) Injection Commercial Manufacturing Services Agreement – Finished Final Drug Product, dated May 27, 2015, by and between the Company and Lifecore Biomedical, LLC) (incorporated by reference to our Current Report on Form 8-K, as Exhibit 10.1, filed on May 29, 2015)
10.23+	Commercial Supply Agreement, dated December 8, 2015, by and between the Company and SAFC, Inc. (incorporated by reference to our Annual Report on Form 10-K/A Amendment No. 1 for the year ended December 31, 2015, as Exhibit 10.36, filed on December 23, 2016)
10.24	Fourth Amendment to Lease, dated as of April 11, 2016, by and between the Company and Metropolitan Life Insurance Company (incorporated by reference to our Current Report on Form 8-K, as Exhibit 10.1, filed on April 15, 2016)
10.25*	Executive Employment Agreement, dated January 28, 2016, by and between the Company and Kimberly Manhard (incorporated by reference to our Quarterly Report on Form 10-Q for the quarter ended March 31, 2016, as Exhibit 10.1, filed on May 5, 2016)
10.26	Security Agreement, dated as of August 5, 2016, by and among the Company, Tang Capital Partners, LP and TC Management Services, LLC (incorporated by reference to our Quarterly Report on Form 10-Q for the quarter ended September 30, 2016, as Exhibit 10.1, filed on November 8, 2016)
10.27	Subordinated Secured Promissory Note, dated August 5, 2016, by and between the Company and Tang Capital Partners, LP (incorporated by reference to our Quarterly Report on Form 10-Q for the quarter ended September 30, 2016, as Exhibit 10.2, filed on November 8, 2016)
10.28	Lease Agreement, dated October 18, 2016, by and between the Company and AP3-SD1 Campus Point LLC (incorporated by reference to our Quarterly Report on Form 10-Q for the quarter ended September 30, 2016, as Exhibit 10.3, filed on November 8, 2016)
10.29	Waiver, dated January 18, 2017, between the Company and Tang Capital Partners, LP (incorporated by reference to our Current Report on Form 8-K, as Exhibit 10.1, filed on January 24, 2017)
10.30	First Amendment to Lease, dated March 15, 2017, by and between the Company and AP3-SD1 Campus Point LLC (incorporated by reference to our Current Report on Form 8-K, as Exhibit 10.1, filed on March 17, 2017)

10.31*	Executive Employment Agreement, dated April 24, 2017, by and between the Company and Robert E. Hoffman (incorporated by reference to our Quarterly Report on Form 10-Q for the quarter ended June 30, 2017, as Exhibit 10.1, filed on August 9, 2017)
10.32	Second Amendment to Lease, dated May 8, 2018, by and between the Company and AP3-SD1 Campus Point LLC (incorporated by reference to our Quarterly Report on Form 10-Q for the quarter ended March 31, 2018, as Exhibit 10.1, filed on May 10, 2018)
10.33	Waiver, dated March 28, 2018, between the Company and Tang Capital Partners, LP (incorporated by reference to our Current Report on Form 8-K, as Exhibit 10.1, filed on April 3, 2018)
10.34*	Executive Employment Agreement, dated July 15, 2019, by and between the Company and John Poyhonen (incorporated by reference to our Quarterly Report on Form 10-Q for the quarter ended June 30, 2019, as Exhibit 10.1, filed on August 5, 2019)
10.35	Third Amendment to Lease, dated December 19, 2019, by and between the Company and ARE-SD Region No. 61, LLC (incorporated by reference to our Current Report on Form 8-K, as Exhibit 10.1, filed on December 20, 2019)
23.1	Consent of Independent Registered Public Accounting Firm (OUM & Co. LLP)
24.1	Power of Attorney (included on the signature page hereto)
31.1	Certification Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
31.2	Certification Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
32.1	Certification Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
101.INS	Inline XBRL Instance Document – the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document
101.SCH	Inline XBRL Taxonomy Extension Schema Document
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document
104	Cover Page Interactive Data File (embedded within the Inline XBRL document and contained in Exhibit 101)

* Management contract or compensatory plan, contract or arrangement.

\+ Confidential treatment has been requested with respect to certain portions of the exhibit, which portions have been omitted and filed separately with the U.S. Securities and Exchange Commission.

ITEM 16. FORM 10-K SUMMARY.

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

HERON THERAPEUTICS, INC.

DATE: March 2, 2020 BY: /s/ BARRY QUART

Barry Quart, Pharm.D.

President and Chief Executive Officer

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS that each individual whose signature appears below constitutes and appoints Barry Quart and Robert Hoffman as his or her true and lawful attorney-in-fact and agent, with full power of substitution, for him or her and in his or her name, place and stead, in any and all capacities, with respect to this annual report and any and all amendments thereto, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorney-in-fact and agent, full power and authority to do and perform each and every act and thing requisite and necessary to be done in and about the premises, as fully to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all the said attorney-in-fact and agent or his or her substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the Registrant in the capacities and on the dates indicated.

Signature	Title	Date
/s/ BARRY QUART Barry Quart, Pharm. D.	President, Chief Executive Officer and Director *(Principal Executive Officer)*	March 2, 2020
/s/ ROBERT HOFFMAN Robert Hoffman	Chief Financial Officer and Senior Vice President, Finance *(Principal Financial and Accounting Officer)*	March 2, 2020
/s/ KEVIN TANG Kevin Tang	Chairman of the Board of Directors	March 2, 2020
/s/ STEPHEN DAVIS Stephen Davis	Director	March 2, 2020
/s/ CRAIG JOHNSON Craig Johnson	Director	March 2, 2020
/s/ KIMBERLY MANHARD Kimberly Manhard	Executive Vice President, Drug Development and Director	March 2, 2020
/s/ JOHN POYHONEN John Poyhonen	Executive Vice President, Chief Commercial Officer and Director	March 2, 2020
/s/ CHRISTIAN WAAGE Christian Waage	Director	March 2, 2020

Exhibit 4.5

DESCRIPTION OF THE REGISTRANT'S SECURITIES REGISTERED PURSUANT TO SECTION 12 OF THE SECURITIES EXCHANGE ACT OF 1934

As of the date of the Annual Report on Form 10-K of which this exhibit is a part, Heron Therapeutics, Inc. (the "Company" or "we" or "our") has one class of security registered under Section 12 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"): our common stock, par value $0.01 per share ("common stock").

Description of Common Stock

The following description of our common stock is a summary and does not purport to be complete. It is subject to and qualified in its entirety by reference to our Certificate of Incorporation, as amended (the "certificate of incorporation") and our Amended and Restated Bylaws (the "bylaws"), each of which are incorporated by reference as an exhibit to the Annual Report on Form 10-K of which this exhibit is a part. We encourage you to read our certificate of incorporation, our bylaws and the applicable provisions of the Delaware General Corporation Law (the "DGCL") for additional information.

General

Authorized Shares. We are authorized to issue up to 150,000,000 shares of common stock.

Voting Rights. The holders of our common stock are entitled to one vote per share on all matters to be voted upon by the stockholders. When a quorum is present at any meeting of our stockholders, the affirmative vote of a majority of the votes properly cast on the matter (excluding any abstentions or broker non-votes) will be the act of the stockholders with respect to all matters other than the contested election of directors (which will be elected by a plurality of all votes properly cast), or as otherwise provided in the bylaws, the certificate of incorporation or a preferred stock designation, or as otherwise required by law.

Dividends. Subject to preferences that may be applicable to any outstanding preferred stock, the holders of our common stock are entitled to receive ratably all dividends, if any, as may be declared form time to time by our Board of Directors out of the funds legally available.

Other Rights. In the event of the liquidation, dissolution or winding up of the Company, the holders of our common stock are entitled to share ratably in all assets remaining after payment of liabilities, subject to prior distribution rights of preferred stock, if any, then outstanding. The common stock has no preemptive or conversion rights. There are no redemption or sinking fund provisions applicable to the common stock. All outstanding shares of common stock are fully paid and non-assessable.

Transfer Agent and Registrar. The transfer agent and registrar for our common stock is Computershare Trust Company N.A.

Listing. Our common stock is currently listed on The Nasdaq Capital Market under the symbol "HRTX".

Certain Provisions Affecting Control of the Company

Certificate of Incorporation and Bylaw Provisions. Some provisions of the DGCL and our certificate of incorporation and bylaws contain provisions that could make the following transactions more difficult:

- acquisition of us by means of a tender offer;
- acquisition of us by means of a proxy contest or otherwise; or
- removal of our incumbent officers and directors.

These provisions, summarized below, are intended to discourage coercive takeover practices and inadequate takeover bids and to promote stability in our management. These provisions are also designed to encourage persons seeking to acquire control of us to first negotiate with our Board of Directors.

Undesignated Preferred Stock. The ability to authorize undesignated preferred stock makes it possible for our Board of Directors to issue one or more series of preferred stock with voting or other rights or preferences that could impede the success of any attempt to change control of us. These and other provisions may have the effect of deferring hostile takeovers or delaying changes in control or management of our company.

Advance Notice Procedures. The advance notice procedures in our bylaws with regard to stockholder proposals relating to the nomination of candidates for election as directors or new business to be brought before meetings of our stockholders provide that notice of stockholder proposals must be timely given in writing to our corporate secretary prior to the meeting at which the action is to be taken. Generally, to be timely, notice must be received at our principal executive offices not less than 90 days nor more than 120 days prior to the first anniversary date of the annual meeting for the preceding year. Our bylaws specify the requirements as to form and content of all such stockholder notices. These requirements may have the effect of precluding stockholders from bringing proposals relating to the nomination of candidates for election as directors or new business before the stockholders at an annual or special meeting.

Delaware Anti-Takeover Statute. We are subject to Section 203 of the DGCL. This law prohibits a publicly held Delaware corporation from engaging in any business combination with any interested stockholder for a period of three years following the date that the stockholder became an interested stockholder unless:

- prior to the date of the transaction, the board of directors of the corporation approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;
- upon consummation of the transaction that resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the number of shares outstanding those shares owned by persons who are directors and also officers and by employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; or
- on or subsequent to the date of the transaction, the business combination is approved by the board of directors and authorized at an annual or special meeting of stockholders, and not by written consent, by the affirmative vote of at least two-thirds of the outstanding voting stock which is not owned by the interested stockholder.

Section 203 of the DGCL defines “business combination” to include:

- any merger or consolidation involving the corporation and the interested stockholder;
- any sale, transfer, pledge or other disposition of 10% or more of the corporation’s assets involving the interested stockholder;
- in general, any transaction that results in the issuance or transfer by the corporation of any of its stock to the interested stockholder; or
- the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits provided by or through the corporation.

In general, Section 203 of the DGCL defines an “interested stockholder” as an entity or person beneficially owning 15% or more of the outstanding voting stock of the corporation and any entity or person affiliated with or controlling or controlled by the entity or person.

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in the Registration Statements on Form S-3 (No. 333-219172) and Form S-8 (Nos. 333-35151, 333-90428, 333-118546, 333-127574, 333-137954, 333-148660, 333-162610, 333-167515, 333-176365, 333-176366, 333-190549, 333-198853, 333-202588, 333-206165, 333-214503, 333-219830 and 333-233023) of Heron Therapeutics, Inc. of our reports dated February 27, 2020 relating to the consolidated financial statements and the effectiveness of Heron Therapeutics, Inc.'s internal control over financial reporting, which appear in this Annual Report on Form 10-K.

/s/ OUM & CO. LLP

San Francisco, California
March 2, 2020

Exhibit 31.1

CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Barry Quart, certify that:

1. I have reviewed this Annual Report on Form 10-K of Heron Therapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 2, 2020

By: /s/ Barry Quart
Barry Quart, Pharm.D.
President and Chief Executive Officer
(As Principal Executive Officer)

Exhibit 31.2

CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Robert Hoffman, certify that:

1. I have reviewed this Annual Report on Form 10-K of Heron Therapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 2, 2020

By: /s/ Robert Hoffman
Robert Hoffman
Chief Financial Officer and
Senior Vice President, Finance
(As Principal Financial Officer)

Exhibit 32.1

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

Each of the undersigned, in his capacity as Chief Executive Officer and Chief Financial Officer, as applicable, of Heron Therapeutics, Inc. (the "Registrant"), hereby certifies, for purposes of 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, to the best of his knowledge that:

- the Annual Report of the Registrant on Form 10-K for the year ended December 31, 2019 (the "Report"), which accompanies this certification, fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
- the information contained in the Report fairly presents, in all material respects, the financial condition of the Registrant at the end of such year and the results of operations of the Registrant for such year.

Dated: March 2, 2020

/s/ Barry Quart
Barry Quart, Pharm.D.
President and Chief Executive Officer
(As Principal Executive Officer)

/s/ Robert Hoffman
Robert Hoffman
Chief Financial Officer and Senior Vice President, Finance
(As Principal Financial and Accounting Officer)

This certification accompanies the Report to which it relates, is not deemed to be filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of Heron Therapeutics, Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of the Report), irrespective of any general incorporation language contained in such filing.

Note: A signed original of this written statement required by Section 906 has been provided to Heron Therapeutics, Inc. and will be retained by Heron Therapeutics, Inc. and furnished to the Securities and Exchange Commission or its staff upon request.