# UNITED STATES
# SECURITIES AND EXCHANGE COMMISSION
**WASHINGTON, D.C. 20549**

# FORM 10-Q

☒ **QUARTERLY REPORT PURSUANT TO SECTION 13 OR 15 (d) OF THE SECURITIES EXCHANGE ACT OF 1934**

**For the quarterly period ended September 30, 2020**

**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** | **92121** |
| (Address of principal executive offices) | (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 |

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 number of shares of the registrant's common stock, par value $0.01 per share, outstanding as of October 29, 2020 was 90,855,254.

**HERON THERAPEUTICS, INC.**

**FORM 10-Q**
**FOR THE QUARTERLY PERIOD ENDED September 30, 2020**

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**PART I. FINANCIAL INFORMATION**

**ITEM 1. CONDENSED CONSOLIDATED FINANCIAL STATEMENTS**

**HERON THERAPEUTICS, INC.**

**Condensed Consolidated Balance Sheets**
(In thousands)

| | September 30, 2020 (Unaudited) | December 31, 2019 (See Note 2) |
|---|---|---|
| **ASSETS** | | |
| Current assets: | | |
| Cash and cash equivalents | $ 95,141 | $ 71,898 |
| Short-term investments | 163,005 | 319,074 |
| Accounts receivable, net | 33,654 | 39,879 |
| Inventory | 42,749 | 24,968 |
| Prepaid expenses and other current assets | 16,446 | 23,245 |
| Total current assets | 350,995 | 479,064 |
| Property and equipment, net | 21,741 | 19,618 |
| Right-of-use lease assets | 16,941 | 13,754 |
| Other assets | 346 | 346 |
| Total assets | $ 390,023 | $ 512,782 |
| **LIABILITIES AND STOCKHOLDERS' EQUITY** | | |
| Current liabilities: | | |
| Accounts payable | $ 12,067 | $ 2,758 |
| Accrued clinical and manufacturing liabilities | 40,718 | 34,614 |
| Accrued payroll and employee liabilities | 13,235 | 15,248 |
| Other accrued liabilities | 22,009 | 36,535 |
| Current lease liabilities | 2,912 | 1,926 |
| Convertible notes payable to related parties, net of discount | 6,637 | 5,624 |
| Total current liabilities | 97,578 | 96,705 |
| Non-current lease liabilities | 15,298 | 12,242 |
| Total liabilities | 112,876 | 108,947 |
| Stockholders' equity: | | |
| Common stock | 909 | 903 |
| Additional paid-in capital | 1,606,165 | 1,568,317 |
| Accumulated other comprehensive income | 540 | 85 |
| Accumulated deficit | (1,330,467) | (1,165,470) |
| Total stockholders' equity | 277,147 | 403,835 |
| Total liabilities and stockholders' equity | $ 390,023 | $ 512,782 |

*See accompanying notes.*

**HERON THERAPEUTICS, INC.**

**Condensed Consolidated Statements of Operations and Comprehensive Loss**
(Unaudited)
(In thousands, except per share amounts)

| | Three Months Ended September 30, | | Nine Months Ended September 30, | |
|---|---|---|---|---|
| | 2020 | 2019 | 2020 | 2019 |
| Revenues: | | | | |
| Net product sales | $ 19,965 | $ 42,624 | $ 68,033 | $ 110,885 |
| Operating expenses: | | | | |
| Cost of product sales | 7,170 | 17,195 | 26,797 | 45,745 |
| Research and development | 49,182 | 34,708 | 130,080 | 119,105 |
| General and administrative | 9,482 | 8,597 | 29,723 | 28,023 |
| Sales and marketing | 12,515 | 16,977 | 48,300 | 69,344 |
| Total operating expenses | 78,349 | 77,477 | 234,900 | 262,217 |
| Loss from operations | (58,384) | (34,853) | (166,867) | (151,332) |
| Other income, net | 156 | 1,258 | 1,870 | 4,503 |
| Net loss | (58,228) | (33,595) | (164,997) | (146,829) |
| Other comprehensive (loss) income: | | | | |
| Unrealized (losses) gains on short-term investments | (413) | (45) | 455 | 190 |
| Comprehensive loss | $ (58,641) | $ (33,640) | $ (164,542) | $ (146,639) |
| Basic and diluted net loss per share | $ (0.64) | $ (0.42) | $ (1.82) | $ (1.85) |
| Shares used in computing basic and diluted net loss per share | 90,849 | 79,940 | 90,671 | 79,308 |

*See accompanying notes.*

**HERON THERAPEUTICS, INC.**

**Condensed Consolidated Statements of Stockholders' Equity**
(Unaudited)
(In thousands)

| | Common Stock | | Additional Paid-In Capital | Accumulated Other Comprehensive Income (Loss) | Accumulated Deficit | Total Stockholders' Equity |
|---|---|---|---|---|---|---|
| | Shares | Amount | | | | |
| **Balance as of December 31, 2019** | 90,304 | $ 903 | $ 1,568,317 | $ 85 | $ (1,165,470) | $ 403,835 |
| Conversion benefit included in Convertible Notes issued | — | — | 108 | — | — | 108 |
| Issuance of common stock on exercise of stock options | 70 | — | 504 | — | — | 504 |
| Issuance of common stock on exercise of warrants | 268 | 3 | — | — | — | 3 |
| Stock-based compensation expense | — | — | 11,974 | — | — | 11,974 |
| Net loss | — | — | — | — | (51,579) | (51,579) |
| Net unrealized gain on short-term investments | — | — | — | 623 | — | 623 |
| Comprehensive loss | — | — | — | — | — | (50,956) |
| **Balance as of March 31, 2020** | 90,642 | 906 | 1,580,903 | 708 | (1,217,049) | 365,468 |
| Conversion benefit included in Convertible Notes issued | — | — | 109 | — | — | 109 |
| Issuance of common stock on exercise of stock options | 54 | 1 | 804 | — | — | 805 |
| Issuance of common stock under the employee stock purchase plan | 124 | 1 | 1,506 | — | — | 1,507 |
| Stock-based compensation expense | — | — | 11,114 | — | — | 11,114 |
| Net loss | — | — | — | — | (55,190) | (55,190) |
| Net unrealized gain on short-term investments | — | — | — | 245 | — | 245 |
| Comprehensive loss | — | — | — | — | — | (54,945) |
| **Balance as of June 30, 2020** | 90,820 | 908 | 1,594,436 | 953 | (1,272,239) | 324,058 |
| Conversion benefit included in Convertible Notes issued | — | — | 111 | — | — | 111 |
| Issuance of common stock on exercise of stock options | 35 | 1 | 523 | — | — | 524 |
| Stock-based compensation expense | — | — | 11,095 | — | — | 11,095 |
| Net loss | — | — | — | — | (58,228) | (58,228) |
| Net unrealized loss on short-term investments | — | — | — | (413) | — | (413) |
| Comprehensive loss | — | — | — | — | — | (58,641) |
| **Balance as of September 30, 2020** | 90,855 | $ 909 | $ 1,606,165 | $ 540 | $ (1,330,467) | $ 277,147 |

| | Common Stock | | Additional Paid-In Capital | Accumulated Other Comprehensive (Loss) Income | Accumulated Deficit | Total Stockholders' Equity |
|---|---|---|---|---|---|---|
| | Shares | Amount | | | | |
| **Balance as of December 31, 2018** | 78,174 | $ 782 | $ 1,330,186 | $ (87) | $ (960,721) | $ 370,160 |
| Conversion benefit included in Convertible Notes issued | — | — | 102 | — | — | 102 |
| Issuance of common stock on exercise of stock options | 732 | 7 | 6,532 | — | — | 6,539 |
| Stock-based compensation expense | — | — | 17,902 | — | — | 17,902 |
| Net loss | — | — | — | — | (63,012) | (63,012) |
| Net unrealized gain on short-term investments | — | — | — | 123 | — | 123 |
| Comprehensive loss | — | — | — | — | — | (62,889) |
| **Balance as of March 31, 2019** | 78,906 | 789 | 1,354,722 | 36 | (1,023,733) | 331,814 |
| Conversion benefit included in Convertible Notes issued | — | — | 103 | — | — | 103 |
| Issuance of common stock on exercise of stock options | 810 | 8 | 9,668 | — | — | 9,676 |
| Issuance of common stock under the Employee Stock Purchase Plan | 63 | 1 | 1,169 | — | — | 1,170 |
| Stock-based compensation expense | — | — | 12,706 | — | — | 12,706 |
| Net loss | — | — | — | — | (50,222) | (50,222) |
| Net unrealized gain on short-term investments | — | — | — | 112 | — | 112 |
| Comprehensive loss | — | — | — | — | — | (50,110) |
| **Balance as of June 30, 2019** | 79,779 | 798 | 1,378,368 | 148 | (1,073,955) | 305,359 |
| Issuance of common stock in public offerings, net | — | — | (110) | — | — | (110) |
| Conversion benefit included in Convertible Notes issued | — | — | 105 | — | — | 105 |
| Issuance of common stock on exercise of stock options | 251 | 2 | 4,022 | — | — | 4,024 |
| Stock-based compensation expense | — | — | 9,704 | — | — | 9,704 |
| Net loss | — | — | — | — | (33,595) | (33,595) |
| Net unrealized loss on short-term investments | — | — | — | (45) | — | (45) |
| Comprehensive loss | — | — | — | — | — | (33,640) |
| **Balance as of September 30, 2019** | 80,030 | $ 800 | $ 1,392,089 | $ 103 | $ (1,107,550) | $ 285,442 |

*See accompanying notes.*

**HERON THERAPEUTICS, INC.**

**Condensed Consolidated Statements of Cash Flows**
(Unaudited)
(In thousands)

| | Nine Months Ended September 30, | |
|---|---|---|
| | **2020** | **2019** |
| **Operating activities:** | | |
| Net loss | $ (164,997) | $ (146,829) |
| Adjustments to reconcile net loss to net cash used for operating activities: | | |
| Stock-based compensation expense | 34,183 | 40,312 |
| Depreciation and amortization | 2,135 | 1,480 |
| Amortization of debt discount | 1,013 | 780 |
| Realized gain on available-for-sale securities | — | (8) |
| Amortization of premium (accretion of discount) on short-term investments | 39 | (3,264) |
| Impairment of property and equipment | 61 | 80 |
| Loss on disposal of property and equipment | — | 53 |
| Change in operating assets and liabilities: | | |
| Accounts receivable | 6,225 | (2,303) |
| Inventory | (17,781) | 14,860 |
| Prepaid expenses and other assets | 6,799 | (5,549) |
| Accounts payable | 9,309 | (15,236) |
| Accrued clinical and manufacturing liabilities | 6,104 | 1,603 |
| Accrued payroll and employee liabilities | (2,013) | (3,263) |
| Other accrued liabilities | (13,343) | 19,681 |
| Net cash used for operating activities | (132,266) | (97,603) |
| **Investing activities:** | | |
| Purchases of short-term investments | (92,040) | (287,579) |
| Maturities and sales of short-term investments | 248,525 | 395,406 |
| Purchases of property and equipment | (4,319) | (3,251) |
| Net cash provided by investing activities | 152,166 | 104,576 |
| **Financing activities:** | | |
| Net proceeds from sale of common stock | — | (110) |
| Proceeds from stock option exercises | 1,833 | 20,239 |
| Proceeds from purchases under the Employee Stock Purchase Plan | 1,507 | 1,170 |
| Proceeds from warrant exercises | 3 | — |
| Net cash provided by financing activities | 3,343 | 21,299 |
| Net increase in cash and cash equivalents | 23,243 | 28,272 |
| Cash and cash equivalents at beginning of year | 71,898 | 31,836 |
| Cash and cash equivalents at end of period | $ 95,141 | $ 60,108 |

*See accompanying notes.*

In this Quarterly Report on Form 10-Q, 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®, ZYNRELEF™ and Biochronomer® are our trademarks. All other trademarks appearing or incorporated by reference into this Quarterly Report on Form 10-Q are the property of their respective owners.

**1. Business**

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 (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. CINVANTI is under investigation for the treatment of Coronavirus Disease 2019 ("COVID-19") as a daily 2-minute IV injection when added to the current standard of care.

In September 2020, our third commercial product, ZYNRELEF (also known as HTX-011) was granted a marketing authorization by the European Commission ("EC"). ZYNRELEF is indicated for the treatment of somatic postoperative pain from small- to medium-sized surgical wounds in adults. The marketing authorization follows the European Medicines Agency's positive opinion from the Committee for Medicinal Products from Human Use in July 2020. The EC's centralized marketing authorization is valid for the 27 countries that are members of the European Union ("EU"), and the other countries in the European Economic Area ("EEA"). ZYNRELEF, a non-opioid, 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. We are currently assessing the evolving global environment for pharmaceuticals and developing a coordinated global marketing strategy, and at this time we anticipate making ZYNRELEF available to patients in Europe during the second half of 2021.

HTX-011 (ZYNRELEF in the EU and EEA) is an investigational agent in the United States and Canada. The FDA granted Breakthrough Therapy designation to HTX-011 and the New Drug Application ("NDA") received Priority Review designation. A Complete Response Letter ("CRL") was received from the FDA regarding the NDA for HTX-011 in June 2020. The CRL stated that the FDA is unable to approve the NDA in its present form based on the need for additional non-clinical information. Based on the complete review of the NDA, the FDA did not identify any clinical safety or efficacy issues or chemistry, manufacturing and controls issues. There are four non-clinical issues in the CRL, none of which relate to any observed toxicity. Three relate to confirming exposure of excipients in preclinical reproductive toxicology studies, and the fourth relates to changing the manufacturing release specification of the allowable level of an impurity based on animal toxicology coverage. In September 2020, we announced a successful Type A meeting with the FDA in which alignment was reached on the plans for our resubmission of the NDA for HTX-011 for the management of postoperative pain in the fourth quarter of 2020. Our New Drug Submission for HTX-011 for the management of postoperative was accepted by Health Canada in November 2019. We are working to respond to a list of questions received from Health Canada in July 2020, and we anticipate up to a 300-day review period following our responsive submission.

HTX-034, our next-generation product candidate for postoperative pain management, is an investigational non-opioid, fixed-dose combination, extended-release solution of the local anesthetic bupivacaine, the nonsteroidal anti-inflammatory drug meloxicam and an additional agent that further potentiates the activity of bupivacaine. HTX-034 is formulated in the same proprietary polymer as HTX-011 (ZYNRELEF in the EU and EEA). By combining two different mechanisms that each enhance the activity of the local anesthetic bupivacaine, HTX-034 is designed to provide superior and prolonged analgesia. Local administration of HTX-034 in a validated preclinical postoperative pain model resulted in sustained analgesia for 7 days. In May 2020, we initiated a Phase 1b/2 clinical study in patients undergoing bunionectomy of HTX-034. The study initiation followed clearance from the FDA of our Investigational New Drug application for HTX-034 for the treatment of postoperative pain.

As of September 30, 2020 we had $258.1 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 Quarterly Report on Form 10-Q is filed with the U.S. Securities and Exchange Commission ("SEC").

**2. Basis of Presentation**

The accompanying condensed consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the U.S. ("GAAP") for interim financial information and with the instructions to Form 10-Q and Article 10 of Regulation S-X. Accordingly, they do not include all of the information and disclosures required by GAAP for complete financial statements. In the opinion of management, all adjustments (consisting of normal recurring accruals) considered necessary for a fair presentation have been included. Operating results for the three and nine months ended September 30, 2020 are not necessarily indicative of the results that may be expected for other quarters or the year ending December 31, 2020. The condensed consolidated balance sheet as of December 31, 2019 has been derived from the audited financial statements as of that date, but does not include all of the information and disclosures required by GAAP. For more complete financial information, these condensed consolidated financial statements and the notes thereto should be read in conjunction with the audited financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2019, which was filed with the SEC on March 2, 2020.

**3. Accounting Policies**

***Principles of Consolidation***

The accompanying condensed 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 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 condensed 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 condensed 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 a control agreement in accordance with our Senior Secured Convertible Notes ("Convertible Notes") (see Note 8).

***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 |
|---|---|---|---|
| | Three Months Ended September 30, 2020 | Nine Months Ended September 30, 2020 | As of September 30, 2020 |
| Customer A | 43.3% | 42.8% | 53.9% |
| Customer B | 32.1% | 33.8% | 32.3% |
| Customer C | 22.8% | 21.7% | 12.8% |
| Total | 98.2% | 98.3% | 99.0% |

***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.

As of September 30, 2020 and December 31, 2019, we determined that an allowance for doubtful accounts was not required. For the three and nine months ended September 30, 2020 and 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.

***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 condensed 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 7).

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 condensed 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, the 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.

*Product Sales*

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

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 perform 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 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 product 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 the product 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 three and nine months ended September 30, 2020 were $20.0 million and $68.0 million, respectively, compared to $42.6 million and $110.9 million, respectively, for the same periods in 2019. For the three and nine months ended September 30, 2020, net products sales of CINVANTI were $19.8 million and $67.6 million, respectively, compared to $36.4 million and $97.6 million, respectively, for the same periods in 2019. For the three and nine months ended September 30, 2020, net product sales of SUSTOL were $0.2 million and $0.4 million, respectively, compared to $6.2 million and $13.3 million, respectively, for the same periods in 2019.

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 condensed consolidated balance sheets (in thousands):

| | Product Returns | Distributor Fees | Discounts, Rebates and Administrative Fees | Total |
|---|---|---|---|---|
| Balance at December 31, 2019 | $ 2,351 | $ 3,999 | $ 21,589 | $ 27,939 |
| Provision | 503 | 11,915 | 74,522 | 86,940 |
| Payments/credits | (134) | (12,600) | (83,799) | (96,533) |
| Balance at September 30, 2020 | $ 2,720 | $ 3,314 | $ 12,312 | $ 18,346 |

***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 income and represent the difference between our net loss and comprehensive 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 unaudited condensed 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):

| | September 30, | |
|---|---|---|
| | 2020 | 2019 |
| Stock options outstanding | 16,082 | 13,079 |
| Warrants outstanding | 220 | 640 |
| Shares of common stock underlying Convertible Notes outstanding | 9,370 | 8,860 |

***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 which did not have a material impact on our financial statement disclosures.

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, which did not have a material 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.

**4. 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 and 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 such assets were as follows (in thousands):

| | | Fair Value Measurements at Reporting Date Using | | |
|---|---|---|---|---|
| | Balance at September 30, 2020 | 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 | $ 88,144 | $ 88,144 | $ — | $ — |
| U.S. treasury bills and government agency obligations | 70,491 | 70,491 | — | — |
| U.S. corporate debt securities | 25,734 | — | 25,734 | — |
| Foreign corporate debt securities | 23,648 | — | 23,648 | — |
| U.S. commercial paper | 14,995 | — | 14,995 | — |
| Foreign commercial paper | 35,134 | — | 35,134 | — |
| Total | $ 258,146 | $ 158,635 | $ 99,511 | $ — |

| | | 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 | $ — |

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

As of September 30, 2020, cash equivalents included $7.0 million of available-for-sale securities with contractual maturities of three months or less. As of September 30, 2020, short-term investments included $163.0 million of available-for-sale securities with contractual maturities of three months to one year. 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. The money market funds as of September 30, 2020 and December 31, 2019 are included in cash and cash equivalents on the condensed consolidated balance sheets.

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, 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. Our Convertible Notes outstanding at September 30, 2020 do not have a readily available market value, however, the carrying value is considered to approximate its fair value.

**5. Short-term Investments**

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

| | September 30, 2020 | | | |
|---|---|---|---|---|
| | Amortized Cost | Gross Unrealized Gains | Gross Unrealized Losses | Estimated Fair Value |
| U.S. treasury bills and government agency obligations | $ 70,175 | $ 316 | $ — | $ 70,491 |
| U.S. corporate debt securities | 25,624 | 110 | — | 25,734 |
| Foreign corporate debt securities | 23,534 | 114 | — | 23,648 |
| U.S. commercial paper | 14,995 | — | — | 14,995 |
| Foreign commercial paper | 28,137 | — | — | 28,137 |
| Total | $ 162,465 | $ 540 | $ — | $ 163,005 |

| | 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 securities | 80,159 | 11 | — | 80,170 |
| Foreign corporate debt securities | 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 |

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 during the three and nine months ended September 30, 2020 and 2019.

Realized gains and losses associated with our available-for-sale securities, if any, are reported in the statements of operations and comprehensive loss. We did not recognize any realized gains or losses during the three months ended September 30, 2020 and 2019. We did not recognize any realized gains or losses during the nine months ended September 30, 2020. We recognized $8,000 of realized gains during the nine months ended September 30, 2019.

**6. Inventory**

Inventory consists of the following (in thousands):

| | September 30, 2020 | December 31, 2019 |
|---|---|---|
| Raw materials | $ 19,215 | $ 6,635 |
| Work in process | 12,098 | 12,571 |
| Finished goods | 11,436 | 5,762 |
| Total inventory | $ 42,749 | $ 24,968 |

As of September 30, 2020, total inventory included $39.7 million related to CINVANTI and $3.0 million related to SUSTOL. As of December 31, 2019, total inventory included $23.5 million related to CINVANTI and $1.5 million related to SUSTOL. In addition, cost of product sales for the three and nine months ended September 30, 2019 included charges of $1.7 million and $3.3 million, respectively, resulting from the write-off of short-dated SUSTOL inventory.

**7. Leases**

In December 2019, we amended our existing operating lease for laboratory and office space in San Diego, California to expand the office space by an additional 21,180 square feet ("Lease Amendment"). The Lease Amendment commenced on January 1, 2020 and expires on December 31, 2025. We have an option to extend the lease for an additional 5 years on expiration.

As of September 30, 2020, our operating lease for laboratory and office space in San Diego, California had a remaining lease term of 63 months.

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. The option to extend our operating lease in San Diego was not recognized as part of our lease liability and ROU lease assets. During the three and nine months ended September 30, 2020, we recognized $0.9 million and $2.9 million, respectively, of operating lease expense and we paid $1.0 million and $2.7 million, respectively, for our operating leases.

Future minimum lease payments under our operating leases as of September 30, 2020 are as follows (in thousands):

| | |
|---|---|
| 2020 | $ 966 |
| 2021 | 3,942 |
| 2022 | 4,058 |
| 2023 | 4,178 |
| 2024 | 4,274 |
| Thereafter | 4,379 |
| Total future minimum lease payments | $ 21,797 |
| Less: discount | (3,587) |
| **Total lease liabilities** | **$ 18,210** |

**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. 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 September 30, 2020, 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 nine months ended September 30, 2020, accrued interest of $0.3 million was paid-in-kind and rolled into the Convertible Note principal balance, which resulted in an additional debt discount of $0.3 million. For each of the three months ended September 30, 2020 and 2019, interest expense relating to the stated rate was $0.1 million. For the three months ended September 30, 2020, interest expense relating to the amortization of the debt discount was $0.4 million. For the three months ended September 30, 2019, interest expense relating to the amortization of the debt discount was $0.3 million. For each of the nine months ended September 30, 2020 and 2019, interest expense relating to the stated rate was $0.3 million. For the nine months ended September 30, 2020 and 2019, interest expense relating to the amortization of the debt discount was $1.0 million and $0.8 million, respectively.

As of September 30, 2020, the carrying value of the Convertible Notes was $6.6 million, which is comprised of the $7.5 million principal amount of the Convertible Notes outstanding, less debt discount of $0.9 million. As of September 30, 2020, the Convertible Notes were convertible into 9.4 million shares of our common stock.

## 9. Stockholders' Equity

### *Common Stock Offering*

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 nine months ended September 30, 2020, warrant holders exercised 267,870 warrants, which resulted in the issuance of 267,870 shares for net cash proceeds of $2,679. As of September 30, 2020, 195,574 warrants from the June 2014 public offering remain outstanding.

### *Stock Option Activity*

The following table summarizes the stock option activity for the nine months ended September 30, 2020:

| | Shares (in thousands) | Weighted-average Exercise Price | Weighted-average Remaining Contractual Term (Years) |
|---|---|---|---|
| Balance at December 31, 2019 | 16,665 | $ 20.47 | 7.87 |
| Granted | 316 | $ 18.32 | |
| Exercised | (159) | $ 11.54 | |
| Expired and forfeited | (740) | $ 21.92 | |
| Balance at September 30, 2020 | 16,082 | $ 20.45 | 7.06 |

For the nine months ended September 30, 2020, 159,000 shares of common stock were issued pursuant to the exercise of stock options, resulting in net proceeds of $1.8 million.

**Stock-based Compensation**

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):

| | Three Months Ended September 30, | | Nine Months Ended September 30, | |
|---|---|---|---|---|
| | 2020 | 2019 | 2020 | 2019 |
| Research and development | $ 4,612 | $ 4,365 | $ 14,580 | $ 14,123 |
| General and administrative | 3,277 | 2,939 | 10,012 | 10,333 |
| Sales and marketing | 3,206 | 2,400 | 9,591 | 15,856 |
| Total stock-based compensation expense | $ 11,095 | $ 9,704 | $ 34,183 | $ 40,312 |

As of September 30, 2020, there was $90.9 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 2.5 years.

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

| | September 30, | |
|---|---|---|
| | 2020 | 2019 |
| Risk-free interest rate | 0.9% | 2.1% |
| Dividend yield | 0.0% | 0.0% |
| Volatility | 67.3% | 67.4% |
| Expected life (years) | 6 | 6 |

We estimated the fair value of each purchase right granted under our 1997 Employee Stock Purchase Plan, as amended, at the beginning of each new offering period using the Black-Scholes option pricing model. There were no new offering periods during the three months ended September 30, 2020 and 2019.

**10. Income Taxes**

Deferred income tax assets and liabilities are recognized for temporary differences between financial statements and income tax carrying values using tax rates in effect for the years such differences are expected to reverse. Due to uncertainties surrounding our ability to generate future taxable income and consequently realize such deferred income tax assets, a full valuation allowance has been established. We continue to maintain a full valuation allowance against our deferred tax assets as of September 30, 2020.

The impact of an uncertain income tax position on the income tax return must be recognized at the largest amount that is more likely than not to be sustained upon audit by the relevant tax authority. An uncertain income tax position will be recognized when it is more likely than not of being sustained. The disclosures regarding an uncertain income tax position included in our Annual Report on Form 10-K for the year ended December 31, 2019, which was filed with the SEC on March 2, 2020, continue to be accurate for the three and nine months ended September 30, 2020.

**11. Subsequent Events**

In October 2020, we implemented changes to our organizational structure. In connection with the reorganization, we will provide employees one-time severance payments upon termination, continued benefits for a specified period of time, outplacement services and certain stock option modifications. We expect to incur total expenses of $5.6 million, $2.5 million of which is primarily for severance and $3.1 million for non-cash, stock-based compensation expense related to stock option modifications. We expect that the cash payments due under the reorganization will be substantially complete by the end of 2020.

## ITEM 2. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

The following discussion and analysis of our financial condition and results of operations should be read together with our condensed consolidated financial statements and related notes included in this Quarterly Report on Form 10-Q and the audited financial statements and related notes included in our Annual Report on Form 10-K for the year ended December 31, 2019, which was filed with the U.S. Securities and Exchange Commission ("SEC") on March 2, 2020.

This Quarterly Report on Form 10-Q 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," "could," "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") and SUSTOL® (granisetron) extended-release injection ("SUSTOL") in the United States, and ZYNRELEF™ in the European Union ("EU"), and the other countries in the European Economic Area ("EEA") (our "Products") and HTX-011 and HTX-034 (our "Product Candidates") and our positioning relative to competing products;
- our ability to establish satisfactory pricing and obtain adequate reimbursement from government and third-party payors of our Products and our Product Candidates, if approved, or any product candidates we may develop;
- whether study results of our Products and Product Candidates are indicative of the results in future studies;
- the commercial launch of ZYNRELEF in Europe and the potential regulatory approval for and commercial launch of our Product Candidates, if approved;
- the potential market opportunities for our Products and our Product Candidates, 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 our Product Candidates;
- 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 and trade secrets to protect our Products, our Product Candidates and our technology, and our ability to successfully defend ourselves against unforeseen third-party infringement claims;
- the extent of the impact of the ongoing Coronavirus Disease 2019 ("COVID-19") pandemic on our business;
- 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 Quarterly Report on Form 10-Q 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 Quarterly Report on Form 10-Q. 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 Quarterly Report on Form 10-Q, 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.

**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. CINVANTI is under investigation for the treatment of COVID-19 as a daily 2-minute IV injection when added to the current standard of care.

In September 2020, our third commercial product, ZYNRELEF (also known as HTX-011) was granted a marketing authorization by the European Commission ("EC"). ZYNRELEF is indicated for the treatment of somatic postoperative pain from small- to medium-sized surgical wounds in adults. The marketing authorization follows the European Medicines Agency's ("EMA") positive opinion from the Committee for Medicinal Products from Human Use ("CHMP") in July 2020. The EC's centralized marketing authorization is valid for the 27 countries that are members of the European Union ("EU"), and the other countries in the European Economic Area ("EEA"). ZYNRELEF, a non-opioid, 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. We are currently assessing the evolving global environment for pharmaceuticals and developing a coordinated global marketing strategy, and at this time we anticipate making ZYNRELEF available to patients in Europe during the second half of 2021.

HTX-011 (ZYNRELEF in the EU and EEA) is an investigational agent in the United States and Canada. The FDA granted Breakthrough Therapy designation to HTX-011 and the New Drug Application ("NDA") received Priority Review designation. A Complete Response Letter ("CRL") was received from the FDA regarding the NDA for HTX-011 in June 2020. The CRL stated that the FDA is unable to approve the NDA in its present form based on the need for additional non-clinical information. Based on the complete review of the NDA, the FDA did not identify any clinical safety or efficacy issues or chemistry, manufacturing and controls issues. There are four non-clinical issues in the CRL, none of which relate to any observed toxicity. Three relate to confirming exposure of excipients in preclinical reproductive toxicology studies, and the fourth relates to changing the manufacturing release specification of the allowable level of an impurity based on animal toxicology coverage. In September 2020, we announced a successful Type A meeting with the FDA in which alignment was reached on the plans for our resubmission of the NDA for HTX-011 for the management of postoperative pain in the fourth quarter of 2020. Our New Drug Submission ("NDS") for HTX-011 for the management of postoperative pain was accepted by Health Canada in November 2019. We are working to respond to a list of questions received from Health Canada in July 2020, and we anticipate up to a 300-day review period following our responsive submission.

HTX-034, our next-generation product candidate for postoperative pain management, is an investigational non-opioid, fixed-dose combination, extended-release solution of the local anesthetic bupivacaine, the nonsteroidal anti-inflammatory drug meloxicam and an additional agent that further potentiates the activity of bupivacaine. HTX-034 is formulated in the same proprietary polymer as HTX-011 (ZYNRELEF in the EU and EEA). By combining two different mechanisms that each enhance the activity of the local anesthetic bupivacaine, HTX-034 is designed to provide superior and prolonged analgesia. Local administration of HTX-034 in a validated preclinical postoperative pain model resulted in sustained analgesia for 7 days. In May 2020, we initiated a Phase 1b/2 clinical study in patients undergoing bunionectomy of HTX-034. The study initiation followed clearance from the FDA of our Investigational New Drug application for HTX-034 for the treatment of postoperative pain.

***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.

In July 2020, we announced the initiation of the GUARDS-1 Study, a Phase 2 clinical study evaluating CINVANTI in early hospitalized patients with COVID-19. GUARDS-1, also referred to as Study HTX-019-202, is a randomized, placebo-controlled, double-blinded, Phase 2 study designed to investigate the efficacy and safety of adding daily dosing of CINVANTI for 14 days as a 2-minute intravenous injection to standard of care to reduce mortality and the need for assisted ventilation in early hospitalized adult patients with a confirmed severe acute respiratory syndrome coronavirus 2 ("SARS-CoV-2") infection. The study will include up to approximately 100 adult patients who are hospitalized with a confirmed SARS-CoV-2 infection less than 24 hours prior to randomization. Heron's rationale for the investigation of CINVANTI for the treatment of COVID-19 is based on multiple potential mechanisms for activity, including decreasing the production and release of inflammatory cytokines to prevent the progression of lung injury to acute respiratory distress syndrome, decreasing severity of cough in patients with neurogenic cough, and antiviral activity. CINVANTI is approved for administration as a 2-minute intravenous injection. For these potential benefits, the plasma concentrations of aprepitant produced with the 2-minute intravenous injection of CINVANTI could provide a unique advantage over other methods of administration.

***Pain Management Product Portfolio***

**ZYNRELEF (HTX-011)**

ZYNRELEF, our third commercial product, was granted a marketing authorization by the EC in September 2020. ZYNRELEF is indicated for the treatment of somatic postoperative pain from small- to medium-sized surgical wounds in adults. The marketing authorization follows the EMA's positive opinion from the CHMP in July 2020. The EC's centralized marketing authorization is valid for the 27 countries that are members of the EU, and the other countries in the EEA. ZYNRELEF, a non-opioid, 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 are currently assessing the evolving global environment for pharmaceuticals and developing a coordinated global marketing strategy, and at this time we anticipate making ZYNRELEF available to patients in Europe during the second half of 2021.

HTX-011 (ZYNRELEF in the EU and EEA) is an investigational agent in the United States and Canada. The FDA granted Breakthrough Therapy designation to HTX-011 and the NDA received Priority Review designation. A CRL was received from the FDA regarding the NDA for HTX-011 in June 2020. The CRL stated that the FDA is unable to approve the NDA in its present form based on the need for additional non-clinical information. Based on the complete review of the NDA, the FDA did not identify any clinical safety or efficacy issues or chemistry, manufacturing and controls issues. There are four non-clinical issues in the CRL, none of which relate to any observed toxicity. Three relate to confirming exposure of excipients in preclinical reproductive toxicology studies, and the fourth relates to changing the manufacturing release specification of the allowable level of an impurity based on animal toxicology coverage. In September 2020, we announced a successful Type A meeting with the FDA in which alignment was reached on the plans for our resubmission of the NDA for HTX-011 for the management of postoperative pain in the fourth quarter of 2020.

In November 2019, the NDS for HTX-011 was accepted by Health Canada. We are working to respond to a list of questions received from Health Canada in July 2020, and we anticipate up to a 300-day review period following our responsive submission.

In December 2019, data supporting the novel mechanism of action for the investigational non-opioid 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.

Follow-on and Real-world Study Results

In October 2019, we reported positive topline results of a multi-center postoperative pain management study in which 51 patients undergoing 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 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.

In September 2020, the results from the EPOCH 2 follow-on hernia study of HTX-011 were published online by the *Surgery* journal. The article, entitled "Opioid-free recovery following herniorrhaphy with HTX-011 as the foundation of a multimodal analgesic regimen," also was published in the November 2020 print issue.

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).

In May 2020, the results from Study 209, a Phase 2b study of the investigational agent HTX-011 in primary unilateral total knee arthroplasty ("TKA") were published online by *The Journal of Arthroplasty*. The article, entitled "HTX-011 Reduced Pain and Opioid Use After Primary Total Knee Arthroplasty: Results of a Randomized Phase 2b Trial," also was published in the October 2020 print issue. All primary and key secondary endpoints in Study 209 were achieved, with HTX-011 demonstrating statistically significant reductions in pain intensity following surgery.

*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.

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.

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.

**HTX-034**

HTX-034, our next-generation product candidate for postoperative pain management, is an investigational non-opioid, fixed-dose combination, extended-release solution of the local anesthetic bupivacaine, the nonsteroidal anti-inflammatory drug meloxicam and an additional agent that further potentiates the activity of bupivacaine. HTX-034 is formulated in the same proprietary polymer as HTX-011 (ZYNRELEF in the EU and EEA). By combining two different mechanisms that each enhance the activity of the local anesthetic bupivacaine, HTX-034 is designed to provide superior and prolonged analgesia. Local administration of HTX-034 in a validated preclinical postoperative pain model resulted in sustained analgesia for 7 days.

In May 2020, we initiated a Phase 1b/2 clinical study in patients undergoing bunionectomy of HTX-034. The HTX-034 study is a randomized, active-controlled, double-blinded, Phase 1b/2 study in patients undergoing bunionectomy with an osteotomy and internal fixation. The study will evaluate the safety and efficacy of HTX-034 compared to bupivacaine solution, the current standard-of-care local anesthetic for postoperative pain control. The Phase 1b portion of the study is intended to select the optimal dose for the Phase 2 expansion portion.

***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.

***Critical Accounting Policies and Estimates***

The discussion and analysis of our financial condition and results of operations are based on our condensed 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 include: revenue recognition, investments, inventory, accrued clinical liabilities, income taxes, and stock-based compensation. There have been no material changes to our critical accounting policies and estimates disclosures included in our Annual Report on Form 10-K for the year ended December 31, 2019, which was filed with the SEC on March 2, 2020.

***Recent Accounting Pronouncements***

See Note 3 to the condensed consolidated financial statements included in Item 1 of this Quarterly Report on Form 10-Q.

***Results of Operations for the Three and Nine Months Ended September 30, 2020 and 2019***

*Net Product Sales*

Net product sales for the three and nine months ended September 30, 2020 were $20.0 million and $68.0 million, respectively, compared to $42.6 million and $110.9 million, respectively, for the same periods in 2019. For the three and nine months ended September 30, 2020, net product sales of CINVANTI were $19.8 million and $67.6 million, respectively, compared to $36.4 million and $97.6 million, respectively, for the same periods in 2019. For the three and nine months ended September 30, 2020, net product sales of SUSTOL were $0.2 million and $0.4 million, respectively, compared to $6.2 million and $13.3 million, respectively, for the same periods in 2019. On October 1, 2019, we made a business decision to discontinue all discounting of SUSTOL, which will continue to result in significantly lower SUSTOL net product sales in future periods. We expect the impact of the generic arbitrage to be resolved in 2020, with a return to growth for net product sales of both CINVANTI and SUSTOL in 2021 and beyond.

*Cost of Product Sales*

For the three and nine months ended September 30, 2020, cost of product sales was $7.2 million and $26.8 million, respectively, compared to $17.2 million and $45.7 million, respectively, for the same periods in 2019. 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 three and nine months ended September 30, 2019 included charges resulting from the write-off of short-dated SUSTOL inventory of $1.7 million and $3.3 million, respectively.

*Research and Development Expense*

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

| | Three Months Ended September 30, | | Nine Months Ended September 30, | |
|---|---|---|---|---|
| | 2020 | 2019 | 2020 | 2019 |
| HTX-011-related costs | $ 29,430 | $ 18,218 | $ 71,082 | $ 66,665 |
| HTX-034-related costs | 1,677 | 1,041 | 3,865 | 3,912 |
| CINVANTI-related costs | 2,271 | 261 | 5,210 | 3,900 |
| SUSTOL-related costs | 373 | 642 | 1,930 | 1,826 |
| Personnel costs and other expenses | 10,819 | 10,181 | 33,413 | 28,679 |
| Stock-based compensation expense | 4,612 | 4,365 | 14,580 | 14,123 |
| Total research and development expense | $ 49,182 | $ 34,708 | $ 130,080 | $ 119,105 |

For the three months ended September 30, 2020, research and development expense was $49.2 million, compared to $34.7 million for the same period in 2019. This increase was primarily due to increases in costs related to HTX-011 (ZYNRELEF in the EU and EEA) and CINVANTI of $11.2 million and $2.0 million, respectively.

For the nine months ended September 30, 2020, research and development expense was $130.1 million, compared to $119.1 million for the same period in 2019. This increase was primarily due to an increase in personnel costs and other expenses of $4.7 million, as well as costs related to HTX-011 (ZYNRELEF in the EU and EEA) and CINVANTI of $4.4 million and $1.3 million, respectively.

*General and Administrative Expense*

For the three and nine months ended September 30, 2020, general and administrative expense was $9.5 million and $29.7 million, respectively, compared to $8.6 million and $28.0 million for the same periods in 2019. This increase was primarily due to an increase in facility-related costs resulting from the expansion of our office space in San Diego, California.

*Sales and Marketing Expense*

For the three and nine months ended September 30, 2020, sales and marketing expense was $12.5 million and $48.3 million, respectively, compared to $17.0 million and $69.3 million, respectively, for the same periods in 2019. These decreases were primarily due to one-time costs associated with the retirement of our President in February 2019, including stock-based compensation expense for stock options. For the three months ended September 30, 2020, the decrease was also due to a decrease in costs to support the launch preparation activities for HTX-011 (ZYNRELEF in the EU and EEA). For the nine months ended September 30, 2020, the decrease was also due to a decrease in costs to support the ongoing commercialization of CINVANTI and SUSTOL.

*Other Income, Net*

For the three and nine months ended September 30, 2020, other income, net was $0.2 million and $1.9 million, respectively, compared to $1.3 million and $4.5 million, respectively, for the same periods in 2019. These decreases were primarily due to interest income earned on our short-term investments.

***Liquidity and Capital Resources***

As of September 30, 2020, we had cash, cash equivalents and short-term investments of $258.1 million, compared to $391.0 million as of December 31, 2019. 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 Quarterly Report on Form 10-Q is filed with the SEC.

Our net loss for the three and nine months ended September 30, 2020 was $58.2 million and $165.0 million, or $0.64 per share and $1.82 per share, respectively, compared to a net loss of $33.6 million and $146.8 million, or $0.42 per share and $1.85 per share, respectively, for the same periods in 2019.

Our net cash used for operating activities for the nine months ended September 30, 2020 was $132.3 million, compared to $97.6 million for the same period in 2019. The increase in net cash used for operating activities was primarily due to changes in working capital and an increase in net loss, partially offset by a decrease in stock-based compensation expense.

Our net cash provided by investing activities for the nine months ended September 30, 2020 was $152.2 million, compared to $104.6 million for the same period in 2019. The increase in cash provided by investing activities was primarily due to net maturities of short-term investments of $156.5 million for the nine months ended September 30, 2020, compared to $107.8 million for the same period in 2019.

Our net cash provided by financing activities for the nine months ended September 30, 2020 was $3.3 million, compared to $21.3 million for the same period in 2019. The decrease in cash provided by financing activities was due to a decrease of $18.4 million in net proceeds received from option exercises.

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***

In December 2019, we amended our existing operating lease for laboratory and office space in San Diego, California to expand the office space by an additional 21,180 square feet ("Lease Amendment"). The Lease Amendment commenced on January 1, 2020 and expires on December 31, 2025. We have an option to extend the lease for an additional 5 years on expiration. Pursuant to the Lease Amendment, we agreed to pay basic annual rent for the additional office space that increases incrementally over the term of the lease amendment from $0.9 million for the first 12 months (inclusive of rent abatements) to $1.3 million for the last 12 months, and such other amounts as set forth in the lease amendment.

We enter into agreements with clinical sites and clinical research organizations for the conduct of our clinical trials and contract manufacturing organizations for the manufacture and supply of preclinical, clinical and commercial materials and drug product. We make payments to these clinical sites and clinical research organizations based in part on the number of eligible patients enrolled and the length of their participation in the clinical trials and, in some cases, we are required to meet minimum purchase obligations under these agreements with contract manufacturing organizations. 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 agreements, contract research organization agreements and contract manufacturing 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 3. 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 September 30, 2020 and December 31, 2019. 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 4. CONTROLS AND PROCEDURES

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in our reports, filed under the Exchange Act, is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms, and that such information is accumulated and communicated to our management, including our principal executive officer and principal financial and accounting officer, as appropriate, to allow timely decisions regarding required disclosure. In designing and evaluating the disclosure controls and procedures, management recognized that any controls and procedures, no matter how well designed and operated, can provide only reasonable and not absolute assurance of achieving the desired control objectives. In reaching a reasonable level of assurance, management necessarily was required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures. In addition, the design of any system of controls also is based in part upon certain assumptions about the likelihood of future events, and there can be no assurance that any design will succeed in achieving its stated goals under all potential future conditions. Over time, a control may become inadequate because of changes in conditions or the degree of compliance with policies or procedures may deteriorate. Because of the inherent limitations in a cost-effective control system, misstatements due to error or fraud may occur and not be detected.

As required by Exchange Act Rule 13a-15(b), we carried out an evaluation under the supervision and with the participation of our management, including our principal executive officer and principal financial and accounting officer, of the effectiveness of the design and operation of our disclosure controls and procedures as of the end of the period covered by this report. Based on the foregoing, our principal executive officer and principal financial and accounting officer concluded that our disclosure controls and procedures were effective at the reasonable assurance level.

There were no changes in our internal control over financial reporting that occurred during the quarter covered by this report that materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

## PART II. OTHER INFORMATION

### ITEM 1. LEGAL PROCEEDINGS

From time to time, we may become subject to claims and litigations arising in the ordinary course of business. We are not a party to any material legal proceedings, nor are we aware of any material pending or threatened litigation.

### 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 Quarterly Report on Form 10-Q. 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 and HTX-034, if approved, and if these products and product candidates 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 and SUSTOL (together with ZYNRELEF™ in the European Union, and the other countries in the European Economic Area, our "Products") and HTX-011 and HTX-034, if approved (our "Product Candidates") in the United States ("U.S."). 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 and HTX-034 are approved in the U.S., they will be the third and fourth products that we launch in the U.S., respectively. ZYNRELEF, approved for commercial sale in the European Union ("EU"), and the other countries in the European Economic Area ("EEA"), would be our first product to be made commercially available in Europe. HTX-011, if approved in Canada, would be our first product to be made commercially available in Canada.

Further, even if our sales organization performs as expected, the revenue that we may receive from the sales of our Products and our Product Candidates, 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 and our Product Candidates;
- acceptance by institutional formulary committees;
- patient and physician satisfaction with our Products and our Product Candidates;
- the size of the potential market for our Products and our Product Candidates;
- our ability to obtain adequate reimbursement from government and third-party payors;

- unfavorable publicity concerning our Products, our Product Candidates or similar products;
- the introduction, availability and acceptance of competing treatments, including competing generic products;
- adverse event information relating to our Products, our Product Candidates or similar classes of drugs;
- product liability litigation alleging injuries relating to our Products, our Product Candidates or similar classes of drugs;
- our ability to maintain and defend our patents and trade secrets for our Products, our Product Candidates and our proprietary Biochronomer® drug delivery technology ("Biochronomer Technology");
- 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 (ZYNRELEF in the EU and EEA) and HTX-034 and continue to have HTX-011 (ZYNRELEF in the EU and EEA) manufactured at commercial production levels successfully and on a timely basis;
- the availability of raw materials necessary to manufacture our Products and our Product Candidates;
- our ability to access third parties to manufacture and distribute our Products and our Product Candidates on acceptable terms or at all;
- regulatory developments related to the manufacture or continued use of our Products and our Product Candidates;
- conduct of post-approval study requirements and the results thereof;
- the extent and effectiveness of sales and marketing and distribution support for our Products and our Product Candidates;
- the extent of the impact of the ongoing Coronavirus Disease 2019 ("COVID-19") pandemic on our business;
- 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 and our Product Candidates.

Additionally, a Complete Response Letter ("CRL") was received from the U.S. Food and Drug Administration ("FDA") regarding the New Drug Application ("NDA") for HTX-011 on June 26, 2020. The CRL states that the FDA was unable to approve the NDA in its present form based on the need for additional non-clinical information. Based on the complete review of the NDA, the FDA did not identify any clinical safety or efficacy issues or Chemistry Manufacturing and Controls ("CMC") issues. There are four non-clinical issues in the CRL, none of which relate to any observed toxicity. Three relate to confirming exposure of excipients in preclinical reproductive toxicology studies, and the fourth relates to changing the manufacturing release specification of the allowable level of an impurity based on animal toxicology coverage. 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 our Products and our Product Candidates does not achieve the acceptance and demand necessary to sustain revenue growth. If we are unable to successfully commercialize our Products and our Product Candidates 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 our Products, our Product Candidates or any other products we may develop, our sales may be adversely affected.***

We have established an internal sales organization for the sale, marketing and distribution of our Products and our Product Candidates in the U.S. In order to successfully commercialize ZYNRELEF in the EU and EEA, HTX-011 in Canada, and 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 our Products, our Product Candidates 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.

Our internal sales organization does not have expertise launching products on an international level and, therefore, we may not be able to successfully commercialize our Products and our Product Candidates outside of the U.S. In order to commercialize our Products and our Product Candidates 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. If we decide to seek the assistance of third parties with international expertise to help commercialize our Products and our Product Candidates outside of the U.S., we may not be successful in finding willing third parties and, even if we are able to find willing third parties, they might not be able to successfully obtain the approvals and take the steps needed to commercialize our Products and our Product Candidates. If we decide to commercialize our Products or our Product Candidates outside of the U.S. without the assistance of third parties with international expertise, it may take longer than expected to obtain the approvals and take the steps needed to commercialize such Products or Product Candidates. As a result, we may decide to delay or abandon development efforts in certain markets. Any such delay or abandonment may have an adverse effect on the benefits otherwise expected from marketing our Products or our Product Candidates in foreign countries.

***If we cannot establish satisfactory pricing of our Products, our Product Candidates 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 our Products, our Product Candidates or any other products we may develop commercially viable. Our ability to commercialize our Products, our Product Candidates 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 our Products, our Product Candidates 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, our Products, our Product Candidates 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 our Products, our Product Candidates 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 our Products, our Product Candidates or any other products we may develop. If our Products, our Product Candidates 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 Patient Protection and Affordable Care Act ("PPACA") encourages comparative effectiveness research. Any adverse findings for our Products or Product Candidates from such research may negatively impact reimbursement available for our Products or our Product Candidates. Similarly, the SUPPORT for Patients and Communities Act ("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 and HTX-034, if approved, and have other negative impacts on our business. In addition to these initiatives, proposals are being discussed that would tie the prices of U.S. pharmaceuticals to the cost of pharmaceuticals in other countries, governmental drug pricing task forces have been formed with the goal of combating the increased costs of prescription pharmaceuticals and several states in the U.S. have introduced legislation to require pharmaceutical companies to disclose their costs to justify the prices of their products. Additionally, on September 13, 2020, an Executive Order was signed furthering these initiatives, creating a "most-favored-nation" policy and directing the U.S. Secretary of Health and Human Services to develop and implement rulemaking and payment plans that would limit the amount paid by Medicare for certain pharmaceutical products to the lowest prices (after certain adjustments) of such products paid in certain other countries. As evidenced by proposals and initiatives such as these, low prices of our Products or our Product Candidates in foreign jurisdictions may have a negative impact on the prices of our Products or our Product Candidates in the U.S. For example, if legislation is passed or regulations are adopted that tie the prices of U.S. pharmaceuticals to the cost of pharmaceuticals in other countries and if ZYNRELEF is subject to pricing regulations in the EU or in other countries in which it is approved that keep its price low in those jurisdictions, then this could lower the potential price of the product in the U.S., thereby limiting the revenue we would be able to generate from it. Additionally, on September 24, 2020, the FDA published a final rule establishing a legal framework for the importation of certain prescription drugs from Canada with the stated purpose of achieving a significant reduction in the cost of covered products to the American consumer while posing no additional risk to the public's health and safety (the "Importation Rule"). Although it is too early to assess the impact of the Importation Rule, it could potentially reduce U.S. revenues for any of our Products or Product Candidates that are also approved in Canada and potentially 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, our Product Candidates 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 our Products, our Product Candidates or any other products that are approved for marketing in the U.S. 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, HTX-034, CINVANTI for the treatment of COVID-19 or any of our other future 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 or other future 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 of our Product Candidates, including HTX-011 and any other future product candidates, 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 or other future 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 June 26, 2020. The CRL stated that the FDA was unable to approve the NDA in its present form based on the need for additional non-clinical information. Based on the complete review of the NDA, the FDA did not identify any clinical safety or efficacy issues or CMC issues. There are four non-clinical issues in the CRL, none of which relate to any observed toxicity. Three relate to confirming exposure of excipients in preclinical reproductive toxicology studies, and the fourth relates to changing the manufacturing release specification of the allowable level of an impurity based on animal toxicology coverage. 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 or other future 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.

***Our evaluation of CINVANTI for the treatment of COVID-19 is at an early stage, and development of CINVANTI for the treatment of COVID-19 will require extensive testing and funding.***

In July 2020, we announced the initiation of the GUARDS-1 Study, a Phase 2 clinical study evaluating CINVANTI in early hospitalized patients with COVID-19. GUARDS-1, also referred to as Study HTX-019-202, is a randomized, placebo-controlled, double-blinded, Phase 2 study designed to investigate the efficacy and safety of adding daily dosing of CINVANTI for 14 days as a 2-minute intravenous injection to standard of care to reduce mortality and the need for assisted ventilation in early hospitalized adult patients with a confirmed SARS-CoV-2 infection. Our clinical development program for CINVANTI as a potential treatment option for patients with COVID-19 is in early stages, and we may be unable to demonstrate that CINVANTI successfully treats the virus in a timely manner, if at all. We are also committing financial resources and personnel to these developmental efforts, which may cause delays in or otherwise negatively impact our other development programs, despite uncertainties surrounding the longevity and extent of COVID-19 as a global health concern. Our business could be negatively impacted by our allocation of significant resources to a global health threat that is unpredictable and could rapidly dissipate or against which our drug, if developed, may not be partially or fully effective. In addition, another party may be successful in producing a more efficacious drug or other treatment for COVID-19, which may lead to the diversion of funding away from us and toward other companies or lead to decreased demand for our potential treatment.

***Government entities may take actions that directly or indirectly have the effect of limiting opportunities for CINVANTI as a treatment for COVID-19.***

Various government entities, including the U.S. government, are offering incentives, grants and contracts to encourage additional investment by commercial organizations into preventative and therapeutic agents against COVID-19, which may have the effect of increasing the number of competitors and/or providing advantages to competitors. Accordingly, there can be no assurance that we will be able to successfully establish a competitive market share if we ultimately receive regulatory approval for CINVANTI as a treatment for COVID-19. COVID-19 treatments may also be subject to government pricing controls, which could adversely affect the profitability of any COVID-19 treatment we are able to develop and commercialize.

***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 similar designations in the U.S. or in any other regulatory jurisdictions 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 similar designations in the U.S. or in any other regulatory jurisdictions 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 June 26, 2020, and there is no guarantee that approval will be received in a timely manner, or at all. The FDA or any foreign regulatory authorities may also withdraw or revoke Fast Track, Breakthrough Therapy, or similar designations, or elect to treat designated candidates in a manner different from what was originally indicated, if they determine that HTX-011 or any of our other future products that receive such designations no longer meet the relevant criteria. 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 Institutional Review Board ("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 or provide selected services for our clinical trials for our Products and our Product Candidates, 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 current Good Manufacturing Practices ("cGMP"). Failure to comply with these regulations may require us to repeat preclinical and clinical trials, which would increase our related expenses and 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 our Products, our Product Candidates 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 such Product Candidates in larger quantities and be able to show equivalency to the FDA, and foreign regulatory authorities, in the manufacture of such Product Candidates at commercial scale as compared to development batch size. The commercial success of our Products and our Product Candidates 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 (ZYNRELEF in the EU and EEA). 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 or man-made 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 our Products and our Product Candidates, 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 our Products and our Product Candidates. Our ability to successfully commercialize our Products and our Product Candidates, 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 our Products and our Product Candidates, 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 our Products and our Product Candidates, 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 our Products, our Product Candidates 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 or man-made disasters, including epidemics, 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 our Product Candidates 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 Product Candidates, cost overruns or other problems that could seriously harm our business. 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.

Our Products, our Product Candidates and any other products we may develop may be in competition with other products for access to the facilities of third parties. Consequently, our Products, our Product Candidates and any other products we may develop may be subject to manufacturing delays if our contractors give other companies' products greater priority than ours. For this and other reasons, our third-party contract manufacturers may not be able to manufacture our Products, our Product Candidates and any other products we may develop 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 our Products, our Product Candidates and our other product candidates are sourced from a single vendor.***

Some of the critical materials and components used in manufacturing our Products, our Product Candidates 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 and our Product Candidates also subjects our business to risk associated with the geographic areas in which those single vendors reside, which could include natural or man-made disasters, including 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 Products and our Product Candidates. 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 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 Products are sold, or may be sold, in the future.***

Despite our efforts to maintain appropriate inventory levels of our Products, as we continue to commercialize our 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 Product Candidates to coincide with the regulatory approval of those Product Candidates, 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 Product Candidates 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, management of postoperative pain or treatment of COVID-19.***

CINVANTI faces significant competition. $NK_1$ receptor antagonists are 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. 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. At present, VEKLURY® (remdesivir, marketed by Gilead in the U.S.) is the only treatment approved for COVID-19. If we are able to successfully develop CINVANTI for the treatment of COVID-19, we will potentially also compete with: ACTEMRA® (tocilizumab, marketed by Genentech, Inc., a member of the Roche Group); Jakafi®/Jakavi® (ruxolitinib, marketed in the U.S. by Incyte Corporation and outside of the U.S. by Novartis AG); ILARIS® (canakinumab, marketed by Novartis AG); tradipitant (an $NK_1$ receptor antagonist currently under investigation by Vanda Pharmaceuticals Inc. pursuant to an exclusive worldwide license agreement with Eli Lilly and Company and not approved anywhere globally for any use); gimsilumab (a GM-CSF mAb, under investigation for acute lung injury, or ARDS (including cytokine storm), and not approved anywhere globally for any use); CM4620-IE (a CRAC channel inhibitor being developed by CalciMedica for pancreatitis and SIRs and not approved anywhere globally for any use); CERC-002 (an anti-LIGHT fully human mAb being investigated for Crohn's disease and ARDS by Cerecor, and not approved anywhere globally for any use); Lenzilumab (a GM-CSF mAb being developed by Humanigen for CarT, GvHD, CMML, eosinophilic asthma, and not approved anywhere globally for any use); TJM2/TJ003234 (a GM-CSF mAb under development by i-Mab Biopharma for cytokine storm in severe COVID-19, and not approved anywhere globally for any use); and potentially other products in development for the treatment of COVID-19 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.

ZYNRELEF and HTX-034, if successfully developed for postoperative pain management in the EU, will face significant competition in the EU. Currently there are numerous generic local anesthetics and other non-opioids for postoperative pain management available in the EU, and other products in development for postoperative pain management may also reach the EU market. For example, in September 2020 the EMA's CHMP adopted a positive opinion, recommending the granting of a marketing authorization for EXPAREL® (bupivacaine liposome injectable suspension, marketed by Pacira BioSciences, Inc. in the U.S.) for postsurgical analgesia, and the EC is expected to adopt a final decision in November 2020.

If we are able to successfully develop HTX-011 or HTX-034 for postoperative pain management in the U.S., we will compete with MARCAINE™ (bupivacaine hydrochloride injection, solution, marketed by Pfizer 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.); Xaracoll® (bupivacaine HCl) implant, marketed by Innocoll Pharmaceuticals Limited); ANJESO® (meloxicam) injection, marketed by Baudax Bio, Inc.); OFIRMEV® (acetaminophen) injection, marketed by Mallinckrodt Pharmaceuticals; and potentially other products in development for postoperative pain management that reach the U.S. market.

If we are able to successfully develop HTX-011 or HTX-034 for postoperative pain management in Canada, we will compete with MARCAINE™ (bupivacaine hydrochloride injection, solution, marketed by Pfizer Inc.); SENSORCAINE® (bupivacaine and epinephrine injection, marketed by Aspen Pharmacare Canada); NAROPIN® (ropivacaine and hydrochloride, marketed by Aspen Pharmacare Canada); and potentially other products in development for postoperative pain management that reach the Canadian market, including potentially EXPAREL® (bupivacaine liposome injectable suspension, marketed by Pacira BioSciences, Inc. in the U.S.), for which a New Drug Submission was validated by Health Canada and for which an approval is anticipated by the end of 2020.

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 product candidates sooner than we do for our Product Candidates 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 and our Product Candidates 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 and our Product Candidates may significantly impact our potential revenues from such Products and Product Candidates. 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 or Product Candidate. The inability for a branded Product or Product Candidate we may sell to successfully compete against generic products could negatively impact sales of our Product or Product Candidate, 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 our 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.

***Our business, financial condition, results of operations and growth could be harmed by the effects of the ongoing COVID-19 pandemic and actions taken in response to the COVID-19 pandemic.***

We are subject to risks related to public health crises such as the global pandemic associated with the novel coronavirus and the associated disease. We are unable to accurately predict the full impact that the ongoing COVID-19 pandemic will have on our results of operations, cash flows and financial condition. We may experience disruptions that could severely impact our business, clinical trials and preclinical studies, such as:

- decreased sales of our Products and our Product Candidates;
- fewer individuals undertaking or completing cancer treatments and elective surgeries, whether due to contracting COVID-19, self-isolating or quarantining to lower the risk of contracting COVID-19, or being unable to access care as a result of healthcare providers tending to COVID-19 patients;
- our third-party contract manufacturers not being able to maintain adequate (in amount and quality) supply to support the commercial sale of our Products and our Product Candidates, or the clinical development of our Product Candidates due to staffing shortages, production slowdowns or stoppages and disruptions in delivery systems;
- delays and difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff, delays or difficulties in enrolling patients or maintaining enrolled patients in our clinical trials and failure of our CROs to perform all or a part of their obligations;
- interruption or delays in the operations of the FDA and comparable foreign regulatory agencies, which may impact regulatory review and approval timelines;

- limitations on our employee resources, and those of our business partners, that would otherwise be focused on the conduct of our business in all aspects, including because of sickness of employees or members of their families and inherent difficulties involved with transitioning to and maintaining a remote working structure amidst a global pandemic; and

- disruption to global financial markets, which could reduce our ability to access capital and negatively affect our liquidity.

These and other factors arising from the COVID-19 pandemic could result in us not being able to maintain market position or increase market penetration for our Products and our Product Candidates, and could result in our inability to meet development milestones for our Product Candidates, each of which would harm our business, financial condition, results of operations and growth. In addition, the COVID-19 pandemic and actions taken in response to it by governments, businesses and individuals may give rise to or amplify the other risks discussed under this section entitled "Risk Factors."

***Natural or man-made disasters, including epidemics, 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 or man-made disaster, including an epidemic, pandemic, or acts of war or terrorism, or resource shortages. For example, COVID-19 has caused a decline in, and suspensions of, elective surgeries, which negatively impacts our ability to conduct our clinical trials and, if it continues, could decrease the potential market opportunities for ZYNRELEF in Europe and HTX-011 and HTX-034, if approved, in the U.S. or other markets. We are also vulnerable to damage from other disasters, such as power loss, fire, floods, hurricanes and similar events. For example, a natural or man-made disaster, including an epidemic, 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, European Medicines Agency, United Kingdom's Medicines and Healthcare Products Regulatory Agency, Health Canada, and other regulatory authorities, and cause unanticipated delays in the manufacturing and distribution of our Products, our Product Candidates 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 $1.3 billion through September 30, 2020. 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 Product Candidates; 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 our Products and our anticipated work commercializing our Product Candidates. We will incur substantial expenses in our efforts to develop and commercialize our Products and our Product Candidates 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 September 30, 2020, we had cash, cash equivalents and short-term investments of $258.1 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 our Product Candidates in the U.S. and making ZYNRELEF and our Product Candidates commercially available outside of the U.S.; the degree of commercial success of our Products and our Product Candidates; the scope, rate of progress, results and costs of preclinical testing and clinical trials; the timing and cost to manufacture our Products and our Product Candidates; 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 other products that we may develop; the extent of the impact of the ongoing COVID-19 pandemic on our business; 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 our Products and our Product Candidates;
- 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;
- the cost of establishing supply arrangements for clinical and commercial development of our Products, our Product Candidates and any other products that we may develop; and
- the extent of the impact of the ongoing COVID-19 pandemic on our business.

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. Our Products, our Product Candidates and other 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") and Assembly Bill 2257, which went into effect in September 2020 and amended certain portions of AB 5 ("AB 2257"). AB 5 and AB 2257 are often referred to collectively simply as 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 little 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 our Products, 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, national or global disturbance where we or our collaborative partners are enrolling patients in clinical studies, such as a pandemic (including COVID-19), terrorist activities, or war, political unrest, a natural or man-made 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 June 26, 2020, stating that it was unable to approve the application in its current form based on the need for additional non-clinical information. Based on the complete review of the NDA, the FDA did not identify any clinical safety or efficacy issues or CMC issues. There are four non-clinical issues in the CRL, none of which relate to any observed toxicity. Three relate to confirming exposure of excipients in preclinical reproductive toxicology studies, and the fourth relates to changing the manufacturing release specification of the allowable level of an impurity based on animal toxicology coverage. 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 significantly damaged, each of which would cause our stock price to significantly 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 Product Candidates, 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 CINVANTI for the treatment of COVID-19, HTX-011, HTX-034 or any of our other future 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 Product Candidate. 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 June 26, 2020. The CRL stated that the FDA was unable to approve the NDA in its present form based on the need for additional non-clinical information. Based on the complete review of the NDA, the FDA did not identify any clinical safety or efficacy issues or CMC issues. There are four non-clinical issues in the CRL, none of which relate to any observed toxicity. Three relate to confirming exposure of excipients in preclinical reproductive toxicology studies, and the fourth relates to changing the manufacturing release specification of the allowable level of an impurity based on animal toxicology coverage. 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 our Products, our Product Candidates or any other products we may develop from being marketed abroad.***

In the event we pursue the right to market and sell our Products, our Product Candidates 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 our Products and 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 related to our Products 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 Products 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 and Product Candidates we develop commercially viable. Our ability to commercialize any Products or 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 Product Candidates 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 and HTX-034, if approved, and have other negative impacts on our business. In addition to these initiatives, proposals are being discussed that would tie the prices of U.S. pharmaceuticals to the cost of pharmaceuticals in other countries, governmental drug pricing task forces have been formed with the goal of combating the increased costs of prescription pharmaceuticals and several states in the U.S. have introduced legislation to require pharmaceutical companies to disclose their costs to justify the prices of their products. Additionally, on September 13, 2020, an Executive Order was signed furthering these initiatives, creating a "most-favored-nation" policy and directing the U.S. Secretary of Health and Human Services to develop and implement rulemaking and payment plans that would limit the amount paid by Medicare for certain pharmaceutical products to the lowest prices (after certain adjustments) of such products paid in certain other countries. As evidenced by proposals and initiatives such as these, low prices of our Products and Product Candidates in foreign jurisdictions may have a negative impact on the prices of our Products and Product Candidates in the U.S. For example, if legislation is passed or regulations are adopted that tie the prices of U.S. pharmaceuticals to the cost of pharmaceuticals in other countries and if ZYNRELEF is subject to pricing regulations in the EU or in other countries in which it is approved that keep its price low in those jurisdictions, then this could lower the potential price of the product in the U.S., thereby limiting the revenue we would be able to generate from it. Additionally, on September 24, 2020, the FDA published the Importation Rule. Although it is too early to assess the impact of the Importation Rule, it could potentially reduce U.S. revenues for any of our Products or Product Candidates that are also approved in Canada and potentially 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 and our Product Candidates, 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 and our Product Candidates. 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 the federal government and the states in which we conduct our business, as well as foreign jurisdictions in which we may conduct business. Healthcare providers, physicians and third-party payors play a primary role in the recommendation and prescription of any drug 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 and Product Candidates with marketing approval. Restrictions under applicable federal, state and foreign 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 drug 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; and

- increasingly complex standards for complying with foreign laws and regulations, including those of the EU, that may differ substantially from country to country and may conflict with corresponding U.S. laws and regulations.

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 drug product; however, state law equivalents may require compliance beginning at commercial launch.

In addition, we are subject to the Foreign Corrupt Practices Act of 1977 (the “FCPA”). In September 2020, ZYNRELEF was granted marketing authorization by the EC, our first such foreign regulatory approval. We are currently assessing the evolving global environment for pharmaceuticals and developing a coordinated global marketing strategy, and at this time we anticipate making ZYNRELEF available to patients in Europe during the second half of 2021. 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 drug 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 our 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 and our Product Candidates. 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, state and foreign 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 our Products, our Products Candidates 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 our Products, our Product Candidates or any other products we may develop, which may adversely impact sales of our Products, our Product Candidates 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, our Product Candidates and any other product candidates we may develop.***

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, our Product Candidates and any other product candidates we may develop.

***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 California Consumer Privacy Act of 2018 ("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 protected health information under the Health Insurance Portability and Accountability Act of 1996 and the Privacy Rule adopted pursuant thereto ("HIPAA"), 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 financial losses and 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, our Product Candidates, or any other product candidates we may develop. A cyber liability claim could also significantly harm our reputation and delay market acceptance of our Products, our Product Candidates, or any other product candidates we may develop.

***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 September 30, 2020, we had a total of 31 issued U.S. patents and an additional 45 issued (or registered) foreign patents. The patents on the bioerodible technologies expire between May 2021 and March 2026. Currently, CINVANTI is covered by 7 patents issued in the U.S. with expiration dates of September 2035 and by one patent issued in Japan. Currently, SUSTOL is covered by 8 patents issued in the U.S. and by 35 patents issued in foreign countries including Austria, Belgium, Canada, Denmark, Finland, France, Germany, Greece, Hong Kong, 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 (ZYNRELEF in the EU and EEA) is protected by 11 patents issued in the U.S. and by 25 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 (ZYNRELEF in the EU and EEA) have expiration dates ranging from May 2021 to April 2035. HTX-034 is protected by 8 patents issued in the U.S. and by 7 patents issued in foreign countries including Australia, Canada, Japan, Mexico and Taiwan. U.S. patents covering HTX-034 have expiration dates ranging from March 2034 to April 2035; foreign patents covering HTX-034 have expiration dates ranging from March 2034 to April 2035. 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, our Product Candidates or our 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, our Product Candidates, or any other product candidates we may develop. 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, our Product Candidates, or any other product candidates we may develop 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, our Product Candidates, or any other product candidates we may develop. 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, our Product Candidates, or any other product candidates we may develop. 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, our Product Candidates, or any other product candidates we may develop.

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 September 30, 2020, we would be required to issue an aggregate of approximately 9.4 million shares, representing 9.3% of our outstanding shares, after giving effect to such conversion. This would result in substantial dilution of our existing stockholders.

***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 2. UNREGISTERED SALES OF EQUITY SECURITIES AND USE OF PROCEEDS**

None.

**ITEM 3. DEFAULTS UPON SENIOR SECURITIES**

None.

**ITEM 4. MINE SAFETY DISCLOSURES**

Not applicable.

**ITEM 5. OTHER INFORMATION**

None.

**ITEM 6. EXHIBITS**

| Exhibit Number | Description |
|---|---|
| 31.1 | Certification of Principal Executive Officer Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002 |
| 31.2 | Certification of Principal Financial and Accounting Officer 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 | 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 Extension Definition |
| 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 included as Exhibit 101) |

**SIGNATURES**

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

Heron Therapeutics, Inc.

Date: November 5, 2020

/s/ Barry Quart

Barry Quart, Pharm.D.
Chief Executive Officer
(As Principal Executive Officer)

/s/ Lisa Peraza

Lisa Peraza
Vice President, Chief Accounting Officer
(As Principal Financial and Accounting Officer)

**EXHIBIT 31.1**

**SECTION 302 CERTIFICATION**

I, Barry Quart, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q 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: November 5, 2020

/s/ Barry Quart

Barry Quart, Pharm.D.
Chief Executive Officer
(As Principal Executive Officer)

**EXHIBIT 31.2**

**SECTION 302 CERTIFICATION**

I, Lisa Peraza, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q 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: November 5, 2020

/s/ Lisa Peraza

Lisa Peraza
Vice President, Chief Accounting Officer
(As Principal Financial and Accounting 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 her capacity as Vice President, Chief Accounting Officer, respectively, 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 Quarterly Report of the Registrant on Form 10-Q for the quarter ended September 30, 2020 (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 quarter and the results of operations of the Registrant for such quarter.

Date: November 5, 2020

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

/s/ Lisa Peraza
Lisa Peraza
Vice President, Chief Accounting Officer
(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.