

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

Form 10-K

(Mark One)

ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended December 31, 2014

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
(State or other jurisdiction of incorporation or organization)
123 SAGINAW DRIVE REDWOOD CITY, CA
(Address of principal executive offices)

94-2875566
(I.R.S. Employer Identification No.)
94063
(Zip Code)

Registrant's telephone number, including area code:
(650) 366-2626

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

<u>Title of each class:</u>	<u>Name of each exchange on which registered:</u>
Common Stock, par value \$0.01 per share	The NASDAQ Capital Market

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

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

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

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

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted 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 and post such files). Yes No

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§ 229.405 of this chapter) is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K.

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

Large accelerated filer Accelerated filer Non-accelerated filer Smaller reporting company
(Do not check if a smaller reporting company)

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

The aggregate market value of voting and non-voting common stock held by non-affiliates of the registrant as of June 30, 2014 totaled approximately \$162,634,000 based on the closing price of \$12.32 as reported by The NASDAQ Capital Market. As of March 2, 2015, there were 29,531,197 shares of the Company's common stock (\$0.01 par value) outstanding.

Documents Incorporated by Reference

Portions of the registrant's proxy statement related to its 2015 Annual Stockholders' Meeting to be filed subsequently are incorporated by reference into Part III of this Annual Report on Form 10-K. Except as expressly incorporated by reference, the registrant's proxy statement shall not be deemed to be part of this report.

[Table of Contents](#)

TABLE OF CONTENTS

[PART I](#)

Item 1.	Business	4
Item 1A.	Risk Factors	19
Item 1B.	Unresolved Staff Comments	42
Item 2.	Properties	42
Item 3.	Legal Proceedings	42
Item 4.	Mine Safety	42

[PART II](#)

Item 5.	Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities	43
Item 6.	Selected Financial Data	45
Item 7.	Management's Discussion and Analysis of Financial Condition and Results of Operations	46
Item 7A.	Quantitative and Qualitative Disclosures About Market Risk	54
Item 8.	Financial Statements and Supplementary Data	55
Item 9.	Changes in and Disagreements with Accountants on Accounting and Financial Disclosure	80
Item 9A.	Controls and Procedures	80
Item 9B.	Other Information	82

[PART III](#)

Item 10.	Directors, Executive Officers and Corporate Governance	83
Item 11.	Executive Compensation	83
Item 12.	Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters	83
Item 13.	Certain Relationships and Related Transactions, and Director Independence	84
Item 14.	Principal Accountant Fees and Services	84

[PART IV](#)

Item 15.	Exhibits, Financial Statement Schedules	85
	Signatures	86
	Exhibit Index	87

FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements within the meaning of the federal securities laws. You can identify forward-looking statements by the use of the words “believe,” “expect,” “anticipate,” “intend,” “estimate,” “project,” “will,” “should,” “may,” “plan,” “intend,” “assume” and other expressions which 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 the control of the Company. These risks, uncertainties and other factors may cause the actual results, performance or achievements of the Company to be materially different from the anticipated future results, performance or achievements expressed or implied by the forward-looking statements.

Factors that might cause these differences include the following:

- estimates of the timing of our resubmission of the New Drug Application (“NDA”) for SUSTOL[®] (granisetron injection, extended release), and potential regulatory approval for and commercial launch of SUSTOL;
- the anticipated progress of our research and development programs, including the initiation of new clinical trials and preclinical testing;
- if approved, the market conditions at commercial launch of SUSTOL or other future product candidates;
- our ability to successfully market, commercialize and achieve market acceptance for SUSTOL or other future product candidates, including our positioning relative to competing products;
- our ability to successfully develop and achieve regulatory approval for other future product candidates utilizing our proprietary Biochronomer[®] polymer-based drug delivery platform technology;
- our ability to establish key collaborations for our products and any other future 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 establish and maintain key vendor relationships necessary for the manufacture of our products;
- our ability to successfully operate in other non-U.S. jurisdictions in which we may choose to do business, including compliance with applicable regulatory requirements and laws;
- uncertainties associated with obtaining and enforcing patents to protect our products, and our ability to successfully defend ourselves against unforeseen third party infringement claims; and
- our estimates regarding our capital requirements and our needs for, and ability to obtain, additional financing.

These forward-looking statements were based on information, plans and estimates at the date of this Annual Report on Form 10-K, and 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. In addition, please see the “Risk Factors” section of this Annual Report on Form 10-K. These risk factors may be updated from time to time by our future filings under the Securities Exchange Act of 1934 (the “Exchange Act”). You should carefully review all information therein.

[Table of Contents](#)

PART I

In this report, all references to “Heron,” the “Company,” “we,” “our,” and “us,” refers to Heron Therapeutics, Inc., a Delaware corporation.

ITEM 1. BUSINESS.

Overview and Business Strategy

Heron Therapeutics, Inc. (formerly A.P. Pharma, Inc.) is a biotechnology company using its proprietary technology and innovative efforts to develop products to address unmet medical needs. Our product development efforts focus on identifying new delivery methods and formulations utilizing known compounds that may expand or extend the therapeutic effect or duration of action, or eliminate the drawbacks of current therapies. Our proprietary Biochronomer polymer-based drug delivery platform technology is designed to improve the therapeutic profile of injectable pharmaceuticals. We continue to evaluate other development programs, technologies or product candidates that may be complementary to or synergistic with our existing programs and product development goals.

Our Biochronomer technology, with which SUSTOL and certain of our other product candidates are formulated, consists of bioerodible polymers designed to release drugs over a defined period of time, depending on the medical need of a given therapeutic target. We have demonstrated that our Biochronomer technology can deliver drugs over periods varying from days to weeks and that the technology is potentially applicable to a range of therapeutic areas, including the prevention of chemotherapy-induced nausea and vomiting (“CINV”) and pain management, among others. Furthermore, we have completed comprehensive animal and human toxicology studies that have established that our Biochronomer polymers are well tolerated. Our lead product candidate, SUSTOL, is in development for the prevention of CINV following administration of chemotherapeutic agents. Our development programs include HTX-011 for the management of post-operative pain, HTX-019 for the prevention of CINV and HTX-003 for management of chronic pain and opioid addiction.

Clinical and Preclinical Development Programs

Our product candidates include the following:

Product Candidates	Target Indication	Development Status
SUSTOL (APF530)	Chemotherapy-induced nausea and vomiting	Phase 3
HTX-019	Chemotherapy-induced nausea and vomiting	Preclinical
HTX-011	Post-operative pain management	Phase 1
HTX-003	Chronic pain management, addiction	Preclinical

[Table of Contents](#)

SUSTOL (APF530) and Chemotherapy Induced Nausea and Vomiting

CINV

CINV is one of the most debilitating side effects of chemotherapy, often attributed as a leading cause of premature discontinuation of cancer treatment. Chemotherapeutic agents activate or destroy cells in the lining of the gut, releasing a neurotransmitter called serotonin. When serotonin binds to 5-hydroxytryptamine type 3 (“5-HT₃”) receptors the patient experiences nausea and vomiting. 5-HT₃ receptor antagonists inhibit the vomiting reflex by preventing serotonin from binding to 5-HT₃ receptors. 5-HT₃ receptor antagonists have been shown to be among the most effective treatments for CINV.

In its 2011 guidelines for prevention of CINV following the administration of moderately emetogenic chemotherapy (“MEC”) or highly emetogenic chemotherapy (“HEC”) agents, the American Society of Clinical Oncology (“ASCO”) recommends the use of 5-HT₃ receptor antagonists, often in combination with other agents such as corticosteroids or neurokinin-1 (“NK₁”) receptor antagonists (“ASCO 2011 CINV guidelines”). Approved 5-HT₃ receptor antagonists, such as granisetron, are currently available in oral and injectable formulations.

Patients suffering from CINV during the acute-onset phase, which occurs in the first 24 hours following administration of chemotherapy agents, have several treatment options among the currently available 5-HT₃ receptor antagonists. However, an unmet medical need exists for patients suffering from CINV during the delayed-onset phase, which typically occurs one to five days following administration of chemotherapy agents. For these patients, only one 5-HT₃ receptor antagonist is approved for prevention of delayed-onset CINV following administration of MEC agents, while none are approved for the prevention of delayed-onset CINV following the administration of HEC agents.

SUSTOL

Our lead investigational product candidate, APF530, which we intend to market as SUSTOL (granisetron injection, extended release), subject to regulatory approval, is being developed for the prevention of both acute- and delayed-onset CINV. The 5-HT₃ receptor antagonist granisetron was selected for SUSTOL because it is widely prescribed by physicians based on a well-established record of safety and efficacy. Injectable and oral formulations of granisetron are currently approved, but only for the treatment of acute-onset CINV. SUSTOL is formulated utilizing our proprietary Biochronomer technology and has been shown in clinical studies to maintain therapeutic drug levels of granisetron for up to five days with a single subcutaneous injection. In 2014, we initiated a Phase 3 clinical study with SUSTOL for the prevention of delayed-onset CINV following the administration of HEC agents (“HEC study”), which, if successful, would differentiate SUSTOL from the other 5-HT₃ receptor antagonists that are currently approved. We anticipate completing enrollment of our HEC study at the end of the first quarter of 2015.

Current CINV Therapies

In addition to granisetron (formerly marketed by Roche as KYTRIL® as oral and injectable formulations), currently available 5-HT₃ receptor antagonists include injectable palonosetron (ALOXI®; currently distributed and marketed by Eisai, Inc. in conjunction with Helsinn Healthcare), and ondansetron (formerly marketed by GlaxoSmithKline as ZOFTRAN®), which is available in oral and injectable formulations. NK₁ receptor antagonists are also administered for the prevention of CINV, often in combination with 5-HT₃ receptor antagonists to augment their therapeutic effect. Currently available NK₁ receptor antagonists include

[Table of Contents](#)

EMEND® (aprepitant) or EMEND® for injection (fosaprepitant), both marketed by Merck & Co. As shown in the table below, ALOXI is the only 5-HT₃ receptor antagonist approved for the prevention of delayed-onset CINV following administration of MEC agents, while none are approved for the prevention of delayed-onset CINV following administration of HEC agents. Generic versions of granisetron and ondansetron are currently available, and generic palonosetron may become available as soon as the fourth quarter of 2015. Industry estimates put CINV as affecting approximately 70–80% of patients undergoing cancer chemotherapy treatment, and according to Transparency Market Research, sales of therapeutics for the prevention of CINV approximated \$620 million in 2013. Sales of such therapeutics are expected to reach approximately \$1 billion in 2020.

5-HT₃ receptor antagonists approved by the U.S. Food and Drug Administration (“FDA”) include the following:

Chemotherapy Regimen	Acute-Onset CINV	Delayed-Onset CINV
Moderately Emetogenic	Granisetron Ondansetron Palonosetron (ALOXI)	Palonosetron (ALOXI)
Highly Emetogenic	Granisetron Ondansetron Palonosetron (ALOXI)	None

New Drug Application

In May 2009, we filed an NDA for SUSTOL with the FDA under Section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act. In March 2010, we received our first Complete Response Letter (“CRL”), which stated that the May 2009 NDA requesting approval of SUSTOL, could not be approved as it was initially submitted. The primary points raised in the initial CRL were related to the dosing system, certain identified deficiencies in the chemistry, manufacturing, and control (“CMC”) review, and the request we perform additional studies showing bioequivalence and metabolic rates and on human factors, and to perform a QT study. We met with the FDA in 2011 to clarify the comments and requests and subsequently performed additional work and data analyses which we believed addressed the concerns raised in the 2010 CRL. In September 2012, we resubmitted the NDA seeking approval for SUSTOL and in March 2013, the FDA issued a second CRL. The FDA identified several additional issues precluding the approval of the SUSTOL NDA resubmission, including further issues relating to the CMC review and deficiencies at certain of our contract manufacturers, and requested that we repeat human factors testing using commercially equivalent material, as well to provide data to allow reanalysis of our Phase 3 clinical results under the revised ASCO 2011 CINV guidelines. We believe that we have substantially addressed the issues raised in the March 2013 CRL, which will be reflected in our upcoming resubmission. We intend to include the results of our ongoing HEC study in the resubmission of our NDA for SUSTOL, which we anticipate filing mid-year 2015.

SUSTOL (APF530) Phase 3 Clinical Trials

Our Phase 3 HEC study for SUSTOL was initiated in 2014. This clinical trial is evaluating the efficacy of SUSTOL for the prevention of delayed-onset CINV following the administration of HEC agents. It is a prospective, randomized, placebo-controlled, double-blind, multicenter two-arm study of approximately 800 to 900 patients, comparing SUSTOL plus the NK₁ receptor

[Table of Contents](#)

antagonist fosaprepitant and corticosteroid dexamethasone to ondansetron plus fosaprepitant and dexamethasone. The primary objective of the study is to demonstrate the superiority of SUSTOL 500 mg (10 mg granisetron) given subcutaneously compared with ondansetron 0.15 mg/kg (up to 16 mg) given intravenously in the delayed-phase (>24-120 hours). The complete response rate (defined as no emesis and no use of rescue medications) in patients receiving highly emetogenic chemotherapy will be evaluated in accordance with the 2011 ASCO CINV guidelines. If SUSTOL is approved for delayed-onset CINV for patients undergoing highly emetogenic chemotherapy regimens, it would be the first injectable 5-HT₃ receptor antagonist approved for this indication.

In our pivotal Phase 3 clinical trial of SUSTOL, which was completed in 2008, we enrolled more than 1,300 patients and successfully demonstrated that SUSTOL's efficacy in preventing CINV was statistically non-inferior to that of ALOXI. The results from this study comprised the foundation for the original SUSTOL NDA. The study was designed to demonstrate the safety and efficacy of SUSTOL in the treatment of CINV following the administration of HEC or MEC agents and to establish an effective dose for SUSTOL. Four primary efficacy endpoints were selected: non-inferiority to ALOXI for the prevention of acute and delayed-onset CINV following administration of MEC agents, and acute-onset CINV following administration of HEC agents; and superiority for the prevention of delayed-onset CINV following administration of HEC agents.

The trial stratified patients into two groups, one receiving moderately and the other receiving highly emetogenic chemotherapeutic agents. In each emetogenic group, patients were randomized during Cycle 1 to receive SUSTOL high dose (10 mg granisetron), SUSTOL low dose (5 mg granisetron) or the currently approved dose of ALOXI. For up to three subsequent treatment cycles (Cycles 2–4), the patients were re-randomized to receive either of the two SUSTOL doses.

Patients in the 10 mg dose of SUSTOL achieved complete response rates numerically higher than, and statistically non-inferior to ALOXI across all four assessments. A pharmacokinetic analysis conducted in a sub-group of patients showed that a single SUSTOL 10 mg dose maintained blood levels of granisetron for the entire five-day period. Patients in the 5 mg dose of SUSTOL did not demonstrate non-inferiority to ALOXI for all endpoints and SUSTOL did not achieve the superiority endpoint for the delayed-onset CINV assessment following administration of HEC agents in either group. ALOXI is not FDA approved for the prevention of delayed-onset CINV following administration of HEC agents; therefore in order to receive FDA approval for this indication, we were required to demonstrate that SUSTOL was statistically superior to ALOXI. Collectively, the Phase 3 efficacy and safety data demonstrated that the 10 mg dose is the most effective dose and was therefore selected for the SUSTOL NDA.

SUSTOL was generally well tolerated, with a side effect profile consistent with previous human use of granisetron and only one serious adverse event reported was possibly attributed to SUSTOL. In Cycle 1, the data showed a low incidence of patients discontinuing therapy due to any adverse events (related or unrelated to study drugs): 0.5%, 0.9% and 0.9% in the moderately emetogenic patient group, and 2.0%, 3.5% and 1.2% in the highly emetogenic patient group for SUSTOL 5 mg, SUSTOL 10 mg and ALOXI, respectively. Further, of the patients completing the first cycle, 1,043 went on to receive a total of 2,374 additional doses of SUSTOL in Cycles 2 to 4. Of these patients, only 2 (or 0.2%) discontinued therapy due to treatment-related adverse events.

HTX-019 (NK₁ CINV Therapy)

In November 2014, we announced our development program for HTX-019. HTX-019 is a proprietary injectable formulation of aprepitant, an NK₁ receptor antagonist used in combination with 5-HT₃ receptor antagonists for the prevention of CINV. The HTX-019 formulation is distinguishable from the only injectable NK₁ receptor antagonist approved in the U.S. for the prevention

[Table of Contents](#)

of CINV, in that it does not contain polysorbate 80, which may cause hypersensitivity or other adverse reactions in some patients. We believe there is an unmet need for expanded options for NK₁ receptor antagonists, particularly those which may potentially reduce the risk of complications from hypersensitivity reactions. Subject to discussion with the FDA, we plan to develop HTX-019 utilizing the 505(b)(2) registration pathway.

HTX-011 (Post-Surgical Pain Management)

In November 2013, we initiated a development program targeting pain management. In recent years, the FDA has focused on approving drugs to successfully treat post-surgical pain, to reduce reliance on opioids, which can lead to post-surgical complications, extended hospitalization, as well as abuse and addiction. We believe there is significant opportunity for a non-opioid, sustained-release product targeting the post-surgical pain market. Our lead product candidate for this program is HTX-011, a combination of the local anesthetic bupivacaine and the anti-inflammatory meloxicam formulated utilizing our proprietary Biochronomer technology to release drug for up to 72 hours. We intend to evaluate this product in soft-tissue, nerve block, and orthopedic post-surgical settings. In the first quarter of 2015, we initiated a Phase 1 study to evaluate the safety of HTX-011 in healthy volunteers. Following the completion of the ongoing Phase 1 study, we plan to initiate additional Phase 1b/2 studies in 2015. According to Decision Resources, the post-surgical pain management market totaled approximately \$3.1 billion in 2012.

HTX-003 (Chronic Pain and Addiction)

In December 2014, we disclosed a second investigational product in our pain management program. HTX-003 is a long-acting formulation of buprenorphine for the treatment of chronic pain and opioid addiction. HTX-003 is formulated with our proprietary Biochronomer technology to deliver drug over 30 days with a single subcutaneous injection and accordingly is expected to have a low potential for patient abuse. We are presently evaluating our plans for further development for this product. According to EvaluatePharma, sales of treatments for the management of opioid addiction in the U.S. exceeded \$1 billion in 2013; however, the need remains for more effective treatments with less potential for abuse.

Clinical Supplies and Manufacturing

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

With regard to our lead product candidate, SUSTOL, we use third-parties for each stage of the manufacturing process. We source the granisetron from independent suppliers. We use a different third-party supplier to manufacture our proprietary polymers and another third-party supplier formulates the components into the bulk drug product and completes the process by filling bulk drug product into syringes and packaging and labeling. To date, SUSTOL has been manufactured in small quantities

[Table of Contents](#)

for preclinical studies and clinical trials. If SUSTOL is approved for commercial sale, we will need to manufacture the product in larger quantities. Significant scale-up of manufacturing requires additional process development and validation studies, which the FDA must review and approve. We are currently in the process of completing this scale-up and validation work. If approved, the commercial success of SUSTOL, in the near-term, will be dependent upon the ability of our contract manufacturers to produce a product in commercial quantities at competitive costs of manufacture. If SUSTOL receives regulatory approval, we plan to scale-up manufacturing through our third-party manufacturers for SUSTOL with the objective of realizing important economies of scale. These scale-up activities will take time to implement, require additional capital investment, process development and validation studies, and FDA approval. We cannot guarantee that we will be successful in achieving competitive manufacturing costs through such scale-up activities.

Sales and Marketing

We are in the early stages of building our sales and marketing infrastructure necessary to commercialize SUSTOL in the U.S. on our own. We intend to establish a direct sales force if SUSTOL is approved. Because of the early stage of our other pharmaceutical development programs, we have not yet developed sales and marketing strategies for any other product candidates that we may successfully develop.

Customers and Distribution; Markets

We do not currently sell or distribute pharmaceutical products and consequently there is no market for our products.

Competition

The biotechnology and pharmaceutical industries are extremely competitive. Our potential competitors in the field are many in number and include major and mid-sized pharmaceutical and biotechnology companies. Many of our potential competitors have significantly more financial, technical and other resources than we do, which may give them a competitive advantage. In addition, they may have substantially more experience in effecting strategic combinations, in-licensing technology, developing drugs, obtaining regulatory approvals and manufacturing and marketing products. We cannot give any assurances that we can compete effectively with these other biotechnology and pharmaceutical companies.

Any products that we may develop or discover will compete in highly competitive markets. Our potential competitors in these markets may succeed in developing products that could render our product candidates obsolete or non-competitive. In addition, many of our competitors have significantly greater financial and other resources, and more experience than we do in the fields in which we may compete.

SUSTOL, if approved, is expected to face significant competition. In particular, competition may come from ALOXI (palonosetron), a 5-HT₃ receptor antagonist, and also generic versions of the product which may become available on the market as soon as October 2015 following expiration of the relevant patent. In addition to ALOXI and any future generic versions, SUSTOL will compete with generic forms of granisetron (formerly marketed as KYTRIL) and ondansetron (formerly marketed as ZOFTRAN). We are also aware of several companies that have developed, or are developing, both generic and new formulations of 5-HT₃ receptor antagonists including ProStrakan's SANCUSO[®] (granisetron transdermal patch) and Eisai's AKYNZEO[®], an oral combination product consisting of an NK₁ receptor antagonist and palonosetron, indicated for the

[Table of Contents](#)

treatment of acute-onset and delayed-onset CINV following the administration of both HEC and MEC agents. If we are able to successfully develop HTX-019 for the treatment of CINV, we will compete with other injectable products targeted towards this indication, such as EMEND for Injection (fosaprepitant).

With respect to our pain management program, in the event we are able to successfully develop HTX-011 for the treatment of post-surgical pain, we will compete with marketed products such as EXPAREL® (bupivacaine liposome injectable suspension), marketed by Pacira Pharmaceuticals, Inc.

Intellectual Property

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

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

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

We have filed a number of U.S. patent applications on inventions relating to the composition of a variety of polymers, specific products, product groups and processing technology. As of December 31, 2014, we had a total of 16 issued U.S. patents and an additional 42 issued (or registered) foreign patents. The patents on our Biochronomer technology expire between January 2016 and April 2026. The product SUSTOL is covered by patents granted in the United States and in foreign countries. Currently, the product SUSTOL is covered by six patents issued in the United States and by nine patents issued in foreign countries including Brazil, Canada, European Union (the "EU"), Japan, and Taiwan. U.S. patents covering SUSTOL have expiration dates ranging from January 2016 to September 2024; foreign patents covering SUSTOL have expiration dates ranging from January 2017 to September 2025. Granted patents include claims covering the product composition, methods of use and methods of preparation. Our policy is to actively seek patent protection in the United States 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.

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

[Table of Contents](#)

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

Government Regulation

Pharmaceutical Regulation

If and when we market any pharmaceutical products in the U.S., they will be subject to extensive government regulation. Likewise, if we seek to market and distribute any such products abroad, they would also be subject to extensive foreign government regulation.

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

See Item 1A. Risk Factors of this Annual Report on Form 10-K for a discussion of the factors that could adversely impact our development of commercial products and industry regulation.

Regulation in the United States

The FDA testing and approval process requires substantial time, effort and money. We cannot assure you that any of our products will ever obtain approval. The FDA approval process for new drugs includes, without limitation:

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

The FDA monitors the progress of trials conducted in the U.S. under an IND and may, at its discretion, re-evaluate, alter, suspend or terminate testing based on the data accumulated to that point and the FDA’s risk/benefit assessment with regard to the

[Table of Contents](#)

patients enrolled in the trial. The FDA may also withdraw approval for an IND for that drug if deemed warranted. Furthermore, even after regulatory approval is obtained, later discovery of previously unknown problems with a product may result in restrictions on the product or even complete withdrawal of the product from the market.

Preclinical Testing

Preclinical studies include laboratory evaluation of the product, as well as animal studies to assess the potential safety and effectiveness of the product. Most of these studies must be performed according to Good Laboratory Practices, a system of management controls for laboratories and research organizations to ensure the consistency and reliability of results. The results of the preclinical studies, together with manufacturing information and analytical data, are submitted to the FDA as part of an IND, which we are required to file before we can commence any clinical trials for our product candidates in the United States. Clinical trials may begin 30 days after an IND is received, unless the FDA raises concerns or questions about the conduct of the clinical trials. If concerns or questions are raised, an IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can proceed. We have filed and received approval for INDs in the U.S. and for an Investigational Medicinal Product Dossier ("IMPD") in the EU, and we may file additional INDs and IMPDs in the future. We cannot assure you that submission of any additional IND or IMPD for any of our preclinical product candidates will result in authorization to commence clinical trials.

Clinical Trials

Clinical trials involve the administration of the product candidate that is the subject of the trial to volunteers or patients under the supervision of a qualified principal investigator. Each clinical trial must be reviewed and approved by an independent institutional review board in the U.S. or ethics committee in the EU at each institution at which the study will be conducted. The institutional review board or ethics committee will consider, among other things, ethical factors, safety of human subjects and the possible liability of the institution arising from the conduct of the proposed clinical trial. Also, clinical trials in the U.S. must be performed according to good clinical practices, which are enumerated in FDA regulations and guidance documents.

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

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

In Phase 2 clinical trials, a drug is usually tested on a limited number of patients (generally up to several hundred) to preliminarily evaluate the efficacy of the drug for specific, targeted indications, determine dosage tolerance and optimal dosage, and identify possible adverse effects and safety risks.

In Phase 3 clinical trials, intended to support proof of concept and efficacy claims, a drug is usually tested on a larger number of patients (up to several thousand), in an expanded patient population and at multiple clinical sites.

[Table of Contents](#)

In Phase 4 clinical trials or other post-approval commitments, additional studies and patient follow-up are conducted to gain experience from the treatment of patients in the intended therapeutic indication. Additional studies and follow-up are also conducted to document a clinical benefit where drugs are approved under accelerated approval regulations and based on surrogate endpoints. In clinical trials, surrogate endpoints are alternative measurements of the symptoms of a disease or condition that are substituted for measurements of observable clinical symptoms. Failure to promptly conduct Phase 4 clinical trials and follow-up could result in expedited withdrawal of products approved under accelerated approval regulations.

We cannot assure you that any of our current or future clinical trials will result in approval to market our products.

Clinical Data Review and Approval in the U.S.

The data from the clinical trials, together with preclinical data and other supporting information that establishes a drug candidate's safety, are submitted to the FDA in the form of an NDA, or NDA supplement (for approval of a new indication if the product candidate is already approved for another indication). Under applicable laws and FDA regulations, each NDA submitted for FDA approval is usually given an internal administrative review within 60 days following submission of the NDA. If deemed complete, the FDA will "file" the NDA, thereby triggering substantive review of the application.

The FDA can refuse to file any NDA that it deems incomplete or not properly reviewable. The FDA has established internal substantive review goals of six months for priority NDAs (for drugs addressing serious or life threatening conditions for which there is an unmet medical need) and ten months for regular NDAs. The FDA, however, is not legally required to complete its review within these periods, and these performance goals may change over time. Moreover, in many cases, the outcome of the review, even if generally favorable, is not an actual approval, but a "complete response" that describes additional work that must be done before the NDA can be approved. The FDA's review of an NDA may involve review and recommendations by an independent FDA advisory committee. The FDA may deny approval of an NDA, or NDA supplement, if the applicable regulatory criteria are not satisfied, or it may require additional clinical data and/or additional Phase 3 clinical trials. Even if such data are submitted, the FDA may ultimately decide that the NDA or NDA supplement does not satisfy the criteria for approval.

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

Once issued, the FDA may withdraw product approval if ongoing regulatory standards are not met or if safety problems occur after the product reaches the market. In addition, the FDA may require testing and surveillance programs to monitor the safety or effectiveness of approved products which have been commercialized, and the FDA has the power to prevent or limit further

[Table of Contents](#)

marketing of a product based on the results of these post-marketing programs. The FDA may also request or require additional Phase 4 clinical trials after a product is approved. The results of Phase 4 clinical studies can confirm the effectiveness of a product candidate and can provide important safety information to augment the FDA's voluntary adverse drug reaction reporting system. Any products manufactured or distributed by us pursuant to FDA approvals would be subject to continuing regulation by the FDA, including record-keeping requirements and reporting of adverse experiences with the drug. Drug manufacturers and their subcontractors are required to register their establishments with the FDA and certain state agencies and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMPs, which impose certain procedural and documentation requirements upon us and our third-party manufacturers. We cannot be certain that we, or our present or future suppliers, will be able to comply with the cGMP regulations and other FDA regulatory requirements.

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

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

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

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

Section 505(b)(2) Applications

Some of our product candidates may be eligible for submission of applications for approval under the FDA's Section 505(b)(2) approval process, which generally requires less information than the NDAs described above. Section 505(b)(2) was enacted as part of the Drug Price Competition and Patent Term Restoration Act of 1984, also known as the Hatch-Waxman Act, and

[Table of Contents](#)

allows approval of NDAs that rely, at least in part, on studies that were not conducted by or for the applicant and to which the applicant has not obtained a right of reference. Such studies can be provided by published literature, or the FDA can rely on previous findings of safety and efficacy for a previously approved drug. Section 505(b)(2) applications may be submitted for drug products that represent a modification (e.g., a new indication or new dosage form) of an eligible approved drug. In such cases, the additional information in 505(b)(2) applications necessary to support the change from the previously approved drug is frequently provided by new studies submitted by the applicant. Because a Section 505(b)(2) application relies in part on previous studies or previous FDA findings of safety and effectiveness, preparing 505(b)(2) applications is generally less costly and time-consuming than preparing an NDA based entirely on new data and information from a full set of clinical trials. The law governing Section 505(b)(2) or FDA's current policies may change in such a way as to adversely affect our applications for approval that seek to utilize the Section 505(b)(2) approach. Such changes could result in additional costs associated with additional studies or clinical trials and delays.

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

Drug Enforcement Agency Regulation

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

Third-Party Payor Coverage and Reimbursement

Although none of our current product candidates have been approved or commercialized for any indication, if they are approved for marketing, commercial success of our product candidates will depend, in part, upon the availability of coverage and reimbursement from third-party payors at the federal, state and private levels. Government payor programs, including Medicare and Medicaid, private health care insurance companies and managed care plans have attempted to control costs by limiting coverage and the amount of reimbursement for particular procedures or drug treatments. The U.S. Congress and state

[Table of Contents](#)

legislatures, from time to time, propose and adopt initiatives aimed at cost containment. Ongoing federal and state government initiatives directed at lowering the total cost of health care will likely continue to focus on health care reform, the cost of prescription pharmaceuticals and on the reform of the Medicare and Medicaid payment systems. Examples of how limits on drug coverage and reimbursement in the United States may cause reduced payments for drugs in the future include:

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

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

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

Anti-Kickback, Fraud and Abuse and False Claims Regulation

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

Regulations under applicable federal and state healthcare laws and regulations include the federal health care programs' Anti-Kickback Law, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, in exchange for or to induce either the referral or purchase of any good or service for which payment may be made under federal health care programs such as the Medicare and Medicaid programs. In the event we receive marketing approval for a product, we will also be subject to scrutiny under 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,

[Table of Contents](#)

Medicaid, or other federal health care programs that are false or fraudulent. This false claims liability may attach in the event that a company is found to have knowingly submitted false average sales price, best price, or other pricing data to the government or to have unlawfully promoted its products.

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

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

Federal and State Sunshine Laws

In the event we receive approval of a product candidate for marketing, we will need to comply with federal "sunshine" laws that require transparency regarding financial arrangements with health care providers. This would include the reporting and disclosure requirements imposed by the PPACA on drug manufacturers regarding any "payment or transfer of value" made or distributed to physicians and teaching hospitals. The Physician Payments Sunshine Act contained within the PPACA requires manufacturers that participate in federal health care programs to begin collecting such information after a six-month period following commercial launch of a product. 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, and these laws may, unlike the federal law equivalent, require compliance at commercial launch.

Foreign Corrupt Practices Act

In addition, we may in the future be subject to the Foreign Corrupt Practices Act of 1997 ("FCPA"). The FCPA and other 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 U.S. Securities and Exchange Commission (the "SEC"). A determination that our operations or activities are not, or were not, in compliance with United States or foreign laws or regulations could result in the imposition of substantial fines, interruptions of business, loss of supplier, vendor or other third-party relationships, termination of necessary licenses and permits, and other legal or equitable sanctions. Other internal or government investigations or legal or regulatory proceedings, including lawsuits brought by private litigants, may also follow as a consequence.

Patient Privacy and Data Security

We are required to comply, as applicable, with numerous federal and state laws, including state security breach notification laws, state health information privacy laws and federal and state consumer protection laws, and to govern the collection, use

[Table of Contents](#)

and disclosure of personal information. Other countries also have, or are developing, laws governing the collection, use and transmission of personal information. In addition, most healthcare providers who may prescribe products we may sell in the future and from whom we may obtain patient health information are subject to privacy and security requirements under the Health Insurance Portability and Accountability Act of 1996 (“HIPAA”). 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. The legislative and regulatory landscape for privacy and data protection continues to evolve, and there has been an increasing amount of focus on privacy and data protection issues with the potential to affect our business, including recently enacted laws in a majority of states requiring security breach notification. These laws could create liability for us or increase our cost of doing business, and any failure to comply could result in harm to our reputation, and potentially fines and penalties.

Employees

As of March 2, 2015, we had 59 full-time employees, 40 of whom are involved in our research and development activities. We believe that we are able to attract skilled and experienced personnel, but competition for personnel is intense and there can be no assurance that we will be able to attract and retain the individuals needed. None of our employees are covered by a collective bargaining agreement and management considers relations with our employees to be good.

Company Information

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

On January 23, 2014, our common stock was approved for listing and began trading on The NASDAQ Capital Market under the symbol HRTX.

Our principal offices are located at 123 Saginaw Drive, Redwood City, California 94063. Our telephone number is (650) 366-2626. Our website address is www.herontx.com. We make available free of charge through our website our Annual Report on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC.

[Table of Contents](#)

ITEM 1A. RISK FACTORS.

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

Risks Related to our Business

We are substantially dependent upon the approval and success of our investigational product APF530, also referred to as SUSTOL.

The success of our business is dependent upon our ability to develop and commercialize our most advanced product candidate, APF530, which we intend to market as SUSTOL, subject to regulatory approval. We have invested a significant portion of our time and financial resources in the development of SUSTOL which has been studied in the prevention of acute-onset chemotherapy-induced nausea and vomiting ("CINV") in patients undergoing both moderately emetogenic chemotherapy ("MEC") and highly emetogenic chemotherapy ("HEC") and for the prevention of delayed-onset CINV for patients undergoing MEC. In 2014, we initiated a Phase 3 clinical study with APF530 for the prevention of delayed-onset CINV in patients receiving highly emetogenic chemotherapy ("HEC study"). We anticipate completing enrollment of the HEC study at the end of the first quarter of 2015. We intend to include the results of the study in the resubmission of our New Drug Application ("NDA") for SUSTOL, which we anticipate filing mid-year 2015. There can be no assurance that the HEC study will conclude on a timely basis, or that the results will be positive for us.

Our ability to generate revenue in the next one to two years and our future success, in large part, depends on the approval and successful commercialization of SUSTOL. We will not be able to commercialize SUSTOL until we obtain regulatory approval in the United States or foreign countries. In September 2012, we resubmitted the NDA seeking approval for APF530 with the U.S. Food and Drug Administration ("FDA"). In March 2013, we received a Complete Response Letter ("CRL") from the FDA pertaining to our resubmission of our NDA for APF530. A CRL also may request additional information, including additional pre-clinical or clinical data. Even if such additional information and data are submitted, the FDA may decide that the NDA still does not meet the standards for approval. In the CRL, the FDA identified several remaining issues that need to be addressed prior to approval of our NDA for APF530 including issues relating to: manufacturing of SUSTOL, the administration of SUSTOL and our analysis of efficacy data for SUSTOL under more recent guidelines classifying chemotherapy regimens. We believe we have substantially addressed the issues identified by the FDA in the CRL, although there can be no assurance that the FDA will agree. The FDA's review of our resubmission may not produce positive decisions as to whether:

- SUSTOL is safe and effective in its proposed use(s) and whether its benefits outweigh the risks;
- the proposed labeling for SUSTOL includes our desired product indications covering acute- and delayed-onset CINV, for use in both HEC and MEC regimens; and

[Table of Contents](#)

- the methods used in manufacturing SUSTOL and the controls used to maintain its quality are adequate to preserve chain of identity, strength, quality and purity.

Delays in obtaining regulatory approval for SUSTOL, or the issuance of another CRL by the FDA, would, among other consequences, delay the launch of SUSTOL and impact our ability to raise additional capital, which would have a material adverse effect on our business and financial condition.

If SUSTOL is approved, but does not attain market acceptance by healthcare professionals and patients, our business and results of operations will suffer.

Even if SUSTOL receives regulatory approval for commercial sale, the revenue that we may receive from the sale of SUSTOL may be less than expected and will depend on many factors that are outside of our control. Factors that may affect revenue from SUSTOL, if approved, include:

- the scope of our approved product label;
- 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;
- acceptance by institutional formulary committees;
- patient and physician satisfaction with the product;
- our ability to have SUSTOL manufactured at a commercial production level successfully and on a timely basis;
- the cost and availability of raw materials;
- the size of the potential market for the product;
- our ability to obtain adequate reimbursement from government and third-party payors;
- unfavorable publicity concerning the product or similar drugs;
- the introduction, availability and acceptance of competing treatments;
- adverse event information relating to the product;
- product liability litigation alleging injuries relating to the product;
- product labeling or product insert language required by the FDA or regulatory authorities in other countries;
- regulatory developments related to the manufacture or continued use of the product;

[Table of Contents](#)

- any post-approval study requirements and the results thereof;
- the extent and effectiveness of sales and marketing and distribution support for the product; and
- our competitors' activities, including decisions as to the timing of competing product launches, pricing and discounting.

Our revenue will be adversely affected if, due to these or other factors, our commercialization of SUSTOL does not achieve the acceptance and demand to sustain product revenue growth. If we are unable to successfully commercialize SUSTOL, we may not be able to earn sufficient revenues to continue our business.

We have yet to receive regulatory approval for a product utilizing our proprietary drug delivery technology.

Our Biochronomer® polymer-based drug delivery technology has not yet been proven through commercial approval, and successful launch, of a product utilizing this technology. We may not be able to substantiate the commercial viability of our drug delivery technology for a variety of reasons, including:

- the failure to receive regulatory approval of a drug utilizing the technology for delivery;
- the inability to show consistent results in the quality or quantity of product manufactured utilizing this delivery technology; and
- the inability to manufacture drugs using this delivery platform at a cost effective price.

In the event we are unable to demonstrate commercial success and viability of products utilizing this delivery technology, our prospects for success and growth would be significantly harmed.

We rely on third parties to do 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 date to oversee our clinical trials for APF530 and our other 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 organizations will perform their obligations at all times in a competent or timely fashion, and we must rigorously oversee their activities in order to place confidence in their conduction of these trials on our behalf. If the organizations 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 and our CROs are required to comply with current good clinical practices ("GCP"), which are regulations and guidelines enforced by the FDA, the Competent Authorities of the Member States of the European

[Table of Contents](#)

Economic Area and comparable foreign regulatory authorities. Regulatory authorities enforce GCP through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of our CROs fail to comply with applicable GCP, 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 assure that upon inspection by a given regulatory authority, such regulatory authority will determine that the HEC study or any other clinical trials comply with GCP requirements. In addition, the HEC study and any clinical trials must be conducted with product produced under GCP requirements. Failure to comply with these regulations may require us to repeat preclinical and clinical trials, which would delay the regulatory approval process.

Our CROs 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 on-going clinical, nonclinical 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 clinical data they obtain is compromised due to the failure to adhere to 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 fail to timely manufacture SUSTOL or fail to comply with stringent regulatory requirements we will face delays in our ability to obtain regulatory approval for SUSTOL.

We are dependent on single third-party manufacturers for the manufacture of our product candidates as well as on third parties for our supply chain, and if we experience problems with any of these third parties, the approval or manufacturing of SUSTOL or any of our product candidates could be delayed, which could harm our results of operations. To date, we have relied on third parties to manufacture and perform important pre-commercialization manufacturing activities for SUSTOL. As part of the process for obtaining regulatory approval, we must demonstrate that the facilities, equipment and processes used to manufacture SUSTOL are capable of consistently producing a product that meets all applicable quality criteria, and that is comparable to the product that was used in our clinical trials. We must also provide the FDA with information regarding the validation of the manufacturing facilities, equipment and processes of our third-party suppliers and manufacturers, and data supporting the stability of SUSTOL. If our third-party suppliers and manufacturers are not in compliance with current Good Manufacturing Practice ("cGMP") requirements, the approval by regulatory authorities for us to begin marketing a product may be delayed, existing product batches may be compromised, and we may experience delays in the availability of SUSTOL for commercial distribution.

For example, our most recent CRL from the FDA regarding our NDA resubmission for SUSTOL stated that the NDA could not be approved due to, among other issues, deficiencies observed during an inspection of the facilities used by our third-party suppliers and manufacturers to produce SUSTOL. If the FDA is not satisfied with our response and corrective actions taken by these third parties, we may be required to complete additional manufacturing development activities or provide other information to the FDA, which could cause substantial delays in obtaining regulatory approval for SUSTOL, increase our costs and have a material adverse effect on our business and financial condition.

[Table of Contents](#)

If our suppliers and contract manufacturers are unable to manufacture in commercially viable quantities, we could face delays in our ability to commercialize SUSTOL, and our costs will increase.

To date, APF530 has been manufactured primarily in small quantities for preclinical studies and clinical trials. If in the future APF530 or any of our product candidates are approved for commercial sale, we will need to be able to consistently manufacture our products in larger quantities. The commercial success of our products will be dependent upon the ability of our contract manufacturers to produce a product in commercial quantities at competitive costs of manufacture. If SUSTOL receives regulatory approval, we plan to scale-up manufacturing for SUSTOL in order to realize important economies of scale. These scale-up activities would take time to implement, require additional capital investment, process development and validation studies, and regulatory approval. We cannot guarantee that we will be successful in achieving competitive manufacturing costs through such scale-up activities.

We expect to depend on contract manufacturers for manufacturing any future products we develop, and 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 clinical or commercial quantities of any product. Our ability to develop and commercialize any products we may develop will depend in part on our ability to manufacture, or arrange for 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 of our contract manufacturers are at present our sole resource to manufacture certain key components of SUSTOL, and for products in preclinical testing in our research and development program. We may not be able to successfully negotiate long-term agreements with any of these third parties. Further, we may have difficulties with these relationships, and we may not be able to find replacement contract manufacturers on satisfactory terms or on a timely basis.

Further, we, along with our contract manufacturers, are required to comply with FDA requirements related to product testing, quality assurance, manufacturing and documentation. Our contract manufacturers may not be able to comply with the applicable FDA regulatory requirements. They may be required to pass an FDA preapproval inspection for conformity with cGMPs before we can obtain approval to manufacture our products and will be subject to ongoing, periodic, unannounced inspection by the FDA and corresponding state agencies to ensure strict compliance with cGMP, and other applicable government regulations and corresponding foreign standards. If we and our contract manufacturers fail to achieve and maintain high manufacturing standards in compliance with cGMP regulations, or fail to scale up manufacturing processes in a timely manner, we may experience manufacturing errors resulting in defective products that could be harmful to patients, product recalls or withdrawals, delays or interruptions of production or failures in product testing or delivery, delay or prevention of filing or approval of marketing applications for our products, cost overruns or other problems that could seriously harm our business. Not complying with FDA requirements could result in an enforcement action such as 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 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.

[Table of Contents](#)

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

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

Some of the critical materials and components used in manufacturing SUSTOL and our other product candidates are sourced from single suppliers. An interruption in the supply of a key material could significantly delay commercialization of SUSTOL, if approved, our research and development process or increase our expenses. 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 of 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.

If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to sell and market any products we may develop, we may be unable to generate product revenue.

We do not currently have an internal sales organization for the sale, marketing and distribution of SUSTOL, or for any other products we may develop. In order to successfully commercialize SUSTOL or any other product, we must build our sales, marketing, distribution and other non-technical capabilities or make arrangements with third parties to perform these services. The establishment and development of a sales organization to market SUSTOL and our other product candidates will be expensive and time consuming and could delay product launch, and we cannot be certain that we will be able to successfully develop this capacity. 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 may not become profitable.

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 technical personnel. Retaining our current employees and recruiting qualified scientific 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.

[Table of Contents](#)

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 or investments in strategic technologies, products, or businesses. Future acquisitions 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 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 technology and/or products sufficient to meet our objectives in undertaking the acquisition 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 programs and initiatives in pursuing an acquisition.

In connection with an acquisition, 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, and/or 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 the entry into collaborative agreements. We may not be able to enter into additional collaborative agreements or may not be able to negotiate commercially acceptable terms for these agreements.

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

If we do enter into such arrangements, we could be dependent upon 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'

[Table of Contents](#)

resources that will be devoted to our research activities related 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, among other activities, to:

- fund research and development activities with us;
- pay us fees upon 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 consume money 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.

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 \$315.2 million through December 31, 2014. Even if SUSTOL is approved, we expect to continue to generate substantial losses over at least the next several years as we:

- build a sales and marketing organization and commence commercialization of SUSTOL, if approved;
- 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 product candidates we may develop in the future; and
- engage in commercialization efforts with respect to any future approved product candidates.

To achieve and sustain profitability, we must, alone or with others, successfully develop, obtain regulatory approval for, manufacture, market and sell our products. If SUSTOL is approved for commercialization, we must successfully launch and commercialize the product. If SUSTOL is not approved, we will likely experience significant delays before we begin to recognize meaningful levels of revenue, if ever. We will incur substantial expenses in our efforts to develop and commercialize products and we may never generate sufficient revenue to become profitable or to sustain profitability.

[Table of Contents](#)

Additional capital may be needed 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.

At December 31, 2014, the Company had cash and cash equivalents in the amount of \$72.7 million. We believe that our current working capital is sufficient to fund operations through 2015, including pursuing regulatory approval to market SUSTOL, and completing Phase 1 human clinical studies commenced in 2015 relative to our HTX-011 and HTX-019 development programs and related preclinical activities. In the event we were to pursue clinical product development in other areas, potentially acquire other strategic assets, or begin to make significant investments in preparing for commercialization of SUSTOL, we would need to raise additional capital. If we are unable to obtain sufficient financing on acceptable terms or otherwise, we may be required to reduce or defer our activities. Our capital requirements going forward will depend on numerous factors, including: the scope, rate of progress, results and costs of preclinical testing and clinical trials, including completing our Phase 3 HEC Study; an approval decision by the FDA with respect to SUSTOL; the timing of and costs associated with the commercial launch of SUSTOL, if approved; the degree of commercial success of SUSTOL; the number and characteristics of product development programs we pursue and the pace of each program including the timing of clinical trials; the time, cost and outcome involved in seeking other regulatory approvals; scientific progress in our research and development programs; the magnitude and scope of our research and development programs; our ability to establish and maintain strategic collaborations or partnerships for research, development, clinical testing, manufacturing and marketing of our product candidates; the cost and timing of establishing sales, marketing and distribution capabilities if we commercialize products independently; the cost of establishing clinical and commercial supplies of our product candidates and any products that we may develop; and general market conditions.

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

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

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

- the status of regulatory approval of any pending applications with the FDA, 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 sales and marketing capabilities if we commercialize any products independently; and
- the cost of establishing supply arrangements for clinical and commercial development of our product candidates and any products that we may develop.

[Table of Contents](#)

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 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. 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 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 will have a material adverse effect on our business.

Provisions contained in our Convertible Notes limit our ability to incur additional indebtedness.

The Convertible Notes are secured by substantially all of our assets, including our cash 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 additional indebtedness or modifying the terms of existing indebtedness. The Convertible Notes also include events of default which include 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.

Risks Related to our Industry

Clinical 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 have incurred significant expenses in developing APF530 and, even if approved, it may not result in a commercially viable product. Before obtaining regulatory approvals for the commercial sale of any products, we, or our 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 SUSTOL and our other product candidates may not be predictive of the results of later stage clinical trials. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having progressed through preclinical studies and initial clinical trials. Our business, results of operations and financial condition may be materially adversely affected by any delays in, or termination of, our clinical trials. Factors impacting 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;

[Table of Contents](#)

- 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, resulting in increased costs; and
- 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 United States or similar regulatory authorities elsewhere in the world in a timely manner, if at all. If we fail to successfully develop and commercialize one or more of our product candidates, we may be unable to generate sufficient revenues to attain profitability and our reputation in the industry and in the investment community would likely be damaged, each of which would cause our stock price to decrease.

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

Before we can receive regulatory approval for the commercial sale of our potential products, the FDA and comparable authorities in non-U.S. jurisdictions require extensive preclinical safety testing and clinical trials to demonstrate their safety and efficacy. Significant delays in preclinical and clinical testing could materially impact our product development costs and delay regulatory approval of our product candidates. Completing clinical trials in a timely manner depends on, 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 institutional review board (“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;

[Table of Contents](#)

- delay or failure in obtaining clinical materials;
- delay or failure in recruiting and enrolling suitable subjects to participate in a trial;
- delay or failure in having subjects complete a trial or return 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;
- decision by the FDA, the IRB, comparable foreign regulatory entities, or recommendation 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 profile 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 are investigating. 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 their actual performance.

[Table of Contents](#)

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 SUSTOL or any of our other product candidates could be harmed, and our ability to generate product revenue will be delayed. Any delays in completing our clinical trials will increase our costs, slow down 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 any of our product candidates. Regulatory approval may also be delayed or revoked or may impose limitations on the indicated uses of a proposed product. If we are unable to obtain regulatory approval for SUSTOL or any of our other product candidates, our business will be substantially harmed.

The process for obtaining approval of a new drug is time consuming, subject to unanticipated delays and costs, and requires the commitment of substantial resources. The regulatory process is uncertain, can take many years and requires the expenditure of substantial resources. Any product that we or our collaborative partners develop must receive all necessary regulatory agency approvals or clearances before it may be marketed in the United States or other countries. Human pharmaceutical products are subject to rigorous preclinical and clinical testing and other requirements by the FDA in the United States and similar health authorities in foreign countries. We may not receive necessary regulatory approvals or clearances to market APF530 or any other product candidate 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 are susceptible to varying interpretations that could delay, limit or prevent regulatory agency approvals or clearances.

SUSTOL or any of our other 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;
- 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.

[Table of Contents](#)

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.

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 SUSTOL or any of our other product candidates from being marketed abroad.

In the event we pursue the right to market and sell SUSTOL or any other 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. 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 United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, 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 United States 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 United States 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 SUSTOL or any of our other product candidates receives regulatory approval, it 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 SUSTOL or any of our other product candidates, it would be 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 post-market information. Following initial regulatory approval of any drugs we may develop, including SUSTOL, we will be subject to continuing regulatory review, including review of adverse drug experiences and clinical results that are reported after our drug products become commercially available. This would include results from any post-marketing 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 be subject to periodic review and inspection by the FDA. If a

[Table of Contents](#)

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 be subject to ongoing FDA requirements for submission of safety and other post-market 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 United States 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. If SUSTOL is approved, we will also be 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.

We face intense competition from other companies developing products in the CINV indication, including those with potentially competitive delivery technologies.

SUSTOL, if approved, is expected to face significant competition. In particular, competition may come from ALOXI (palonosetron), a 5-hydroxytryptamine type 3 ("5-HT₃") receptor antagonist, and also generic versions of the product which may

[Table of Contents](#)

become available on the market as soon as October 2015 following expiration of the relevant patent. In addition to ALOXI and any future generic versions, SUSTOL will compete with generic forms of granisetron (formerly marketed as KYTRIL) and ondansetron (formerly marketed as ZOFRAN). We are also aware of several companies that have developed, or are developing, both generic and new formulations of 5-HT₃ receptor antagonists including ProStrakan's SANCUSO® (granisetron transdermal patch) and Eisai's AKYNZEO®, an oral combination product consisting of a neurokinin-1 receptor antagonist and palonosetron, indicated for the treatment of acute-onset and delayed-onset CINV following the administration of both HEC and MEC agents. If we are able to successfully develop HTX-019 for the treatment of CINV, we will compete with other injectable products targeted towards this indication, such as EMEND® for Injection (fosaprepitant).

With respect to our pain management program, in the event we are able to successfully develop HTX-011 for the treatment of post-surgical pain, we will compete with marketed products such as EXPAREL® (bupivacaine liposome injectable suspension), marketed by Pacira Pharmaceuticals, Inc.

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

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

Pricing for therapeutics can be extremely competitive, and strict formulary guidelines enforced by payors may create significant challenges in the acceptance and profitability of branded products. The market for generic products can be very lucrative, and 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 accordingly in the event of generic launch of products that may compete with those we may sell may significantly impact our potential revenues from such products. Upon the expiration or loss of patent protection for a branded product, or upon the "at-risk" launch (despite pending patent infringement litigation against the generic product) by a manufacturer of a generic version of a drug that may compete with one of our products, we could quickly lose a significant portion of our sales of that product. The inability for a branded product we may sell to successfully compete against generic products could negatively impact sales of our product, reduce our ability to grow our business, and could significantly harm our business prospects.

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

The continuing efforts of the United States 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

[Table of Contents](#)

revenues and gross margins to make the products we develop commercially viable. Our ability to commercialize any product candidates successfully will depend in part on the extent to which governmental authorities, private health insurers and other organizations establish appropriate reimbursement levels for the cost of such products and related treatments.

In certain foreign markets, the pricing of prescription pharmaceuticals is subject to government control. In the United States, 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 on the reform of the Medicare and Medicaid systems. The trend toward managed health care in the United States, which could significantly influence the purchase of health care services and products, as well as legislative proposals to reform health care, control pharmaceutical prices or reduce government insurance programs, may result in lower prices for our products, if 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.

If we cannot arrange for adequate third-party reimbursement for our products, our future revenue will suffer.

In both domestic and foreign markets, sales of our potential products, including SUSTOL, will depend in substantial part on the availability of adequate reimbursement from third-party payors such as government health administration authorities, private health insurers and other organizations. Third-party payors often challenge the price and cost-effectiveness of medical products and services and such pressure may increase in the future. Significant uncertainty exists as to the adequate reimbursement status of newly approved health care products. Any products we are able to successfully develop may not be reimbursable by third-party payors. In addition, our 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 before our products are approved for marketing and any such changes could further limit reimbursement. Reimbursement policies utilized by our collaborators or ourselves may be challenged by regulatory entities, with resultant fines, negative publicity and the need to implement changes that reduce the utilization of our products. If any products we develop do not receive adequate reimbursement, our revenue could be severely limited.

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

In the United States, upon commercial launch of a product, we will be subject to health care fraud and abuse regulation and enforcement by both the federal government and the states in which we conduct our business. Healthcare providers, physicians and third-party payors play a primary role in the recommendation and prescription of any product candidates for which we obtain 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 for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations include, but are not limited to, the following:

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

[Table of Contents](#)

- federal false claims laws which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other federal health care programs that are false or fraudulent. This false claims liability may attach in the event that a company is found to have knowingly submitted false average sales price, best price or other pricing data to the government or to have unlawfully promoted its products;
- federal “sunshine” laws that require transparency regarding financial arrangements with health care providers, such as the reporting and disclosure requirements imposed by the Patient Protection and Affordable Care Act (“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 payer, including commercial insurers.

The risk of being found in violation of these laws is increased by the fact that many of them have not been fully interpreted by the regulatory authorities or the courts, and their provisions are open to a variety of interpretations. Moreover, recent health care reform legislation has strengthened many of these laws. For example, 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.

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 required manufacturers that participate in federal health care programs to begin collecting such information after a six-month period following commercial launch of a product; however state law equivalents may require compliance at commercial launch.

In addition, we may in the future be subject to the Foreign Corrupt Practices Act of 1997 (“FCPA”). The FCPA and other 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 U.S. Securities and Exchange Commission. A determination that our operations or activities are not, or were not, in compliance with United States 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.

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.

[Table of Contents](#)

Any penalties, damages, fines, curtailment or restructuring of our operations could adversely affect our ability to operate our business and our financial results. Although compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, the risks cannot be entirely eliminated. Any action against us for violation of these laws or regulations, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. Moreover, achieving and sustaining compliance with applicable federal and state privacy, security and fraud laws may prove costly.

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 and 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, govern the collection, use and disclosure of personal information. Other countries also have, or are developing, laws governing the collection, use and transmission of personal information. In addition, most healthcare providers who may prescribe products we may sell in the future and from whom we may obtain patient health information are subject to privacy and security requirements under the Health Insurance Portability and Accountability Act of 1996 ("HIPAA"). 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. The legislative and regulatory landscape for privacy and data protection continues to

[Table of Contents](#)

evolve, and there has been an increasing amount of focus on privacy and data protection issues with the potential to affect our business, including recently enacted laws in a majority of states requiring security breach notification. These laws could create liability for us or increase our cost of doing business, and any failure to comply could result in harm to our reputation, and potentially fines and penalties.

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 such liability 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. At December 31, 2014, we had a total of 16 issued U.S. patents and an additional 42 issued (or registered) foreign patents. The patents on the bioerodible technologies expire between January 2016 and April 2026. The product SUSTOL is covered by patents in the United States and in foreign countries. Currently, the product SUSTOL is covered by six patents issued in the United States and by nine patents issued in foreign countries including Brazil, Canada, the EU, Japan, and Taiwan. U.S. patents covering SUSTOL have expiration dates ranging from January 2016 to September 2024; foreign patents covering SUSTOL have expiration dates ranging from January 2017 to September 2025. 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 United States are maintained in confidence for at

[Table of Contents](#)

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 which 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.

We also rely upon 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 United States 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. 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.

[Table of Contents](#)

If we are required to defend ourselves in a 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 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.

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.

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 testing, manufacture, marketing and sale of our products involve an inherent risk that product liability claims will be asserted against us. 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.

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, which is still pre-commercial and subject to more speculation by stock market investors.

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.

[Table of Contents](#)

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 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 outstanding Convertible Notes bear interest at a rate of 6% per annum, payable quarterly in cash or in kind, at the election of the holders of the Convertible Notes. The Convertible Notes are convertible into shares of our common stock at a rate of 1,250 shares for every \$1,000 of principal and accrued interest that is being converted. In the event the holders of the Convertible Notes were to opt to convert in full the outstanding principal and accrued interest due under the Convertible Notes as of December 31, 2014, we would be required to issue an aggregate of 6,676,845 million shares, representing approximately 23% of our outstanding shares, after giving effect to such conversion. This would result in substantial dilution of our existing stockholders.

Concentration in stockholder ownership could influence strategic actions.

Our directors, executive officers, principal stockholders and affiliated entities currently beneficially own or control a significant percentage of our outstanding common stock. In addition, certain of our principal stockholders hold outstanding warrants that are exercisable for additional shares of our common stock. As of December 31, 2014, Tang Capital Partners, LP and its affiliates’ (“TCP”) beneficial ownership in our common stock, as determined in accordance with Rule 13d-3 of the Exchange Act, was approximately 17%, excluding the exercise of outstanding warrants. In addition, TCP has the right to acquire 5,341,476 million shares upon conversion of the Convertible Notes. Kevin C. Tang, the Managing Director of Tang Capital Management, LLC, the general partner of Tang Capital Partners, LP, is also chairman of our board of directors.

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

[Table of Contents](#)

Future utilization of net operating loss carry-forwards may be impaired due to recent changes in ownership.

We believe our net operating losses and tax attributes may be subject to limitation under Section 382 of the Internal Revenue Code of 1986. As a result, our deferred tax assets, and related valuation allowance, have been reduced for the estimated impact of the net operating losses and credits that we currently estimate may expire unused. Utilization of our remaining net operating loss and research and development credit carry-forwards may still be subject to substantial annual limitations due to ownership change limitations provided by the Internal Revenue Code and similar state provisions for ownership changes after December 31, 2014, including those that may come in conjunction with future equity financings or market trades by our stockholders.

ITEM 1B. UNRESOLVED STAFF COMMENTS.

None.

ITEM 2. PROPERTIES.

We lease 26,067 square feet of laboratory, office and warehouse space in Redwood City, California under a lease expiring on November 30, 2016. In addition, we currently lease 1,400 square feet of office space in Stamford, Connecticut and 2,020 square feet of office space in San Diego, California. The lease for the Stamford office space was extended in 2014 for a three-month period ending on March 31, 2015. The lease for the San Diego office space was extended in 2014 for a six-month period ending on June 30, 2015. The annual rent expense for all properties is approximately \$1.3 million. We believe our facilities are adequate and suitable for our current needs, and that we will be able to obtain new or additional leased space in the future when necessary.

ITEM 3. LEGAL PROCEEDINGS.

We are not currently a party to any legal proceedings.

ITEM 4. MINE SAFETY DISCLOSURES.

Not applicable.

[Table of Contents](#)

PART II

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

Information About Our Common Stock

Shares of our common stock traded on the OTC Bulletin Board under the symbol "APPA.OB" until January 10, 2014. Our shares traded under the symbol "APPAD" following our one-for-twenty reverse stock split effective January 13, 2014. On January 23, 2014, our common stock was approved for listing and began trading on The NASDAQ Capital Market under the symbol "HRTX".

Set forth below are the high and low sales prices for our common stock for each full quarterly period within the two most recent fiscal years.

Year Ended December 31, 2014	High	Low
First Quarter	\$ 15.82	\$ 8.42
Second Quarter	\$ 15.50	\$ 10.02
Third Quarter	\$ 12.70	\$ 8.22
Fourth Quarter	\$ 10.49	\$ 6.51
Year Ended December 31, 2013	High	Low
First Quarter	\$ 17.80	\$ 5.60
Second Quarter	\$ 9.80	\$ 6.00
Third Quarter	\$ 10.00	\$ 6.40
Fourth Quarter	\$ 10.00	\$ 6.60

Stockholders

The number of record holders of our common stock as of March 2, 2015 was approximately 149.

Dividend Policy

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

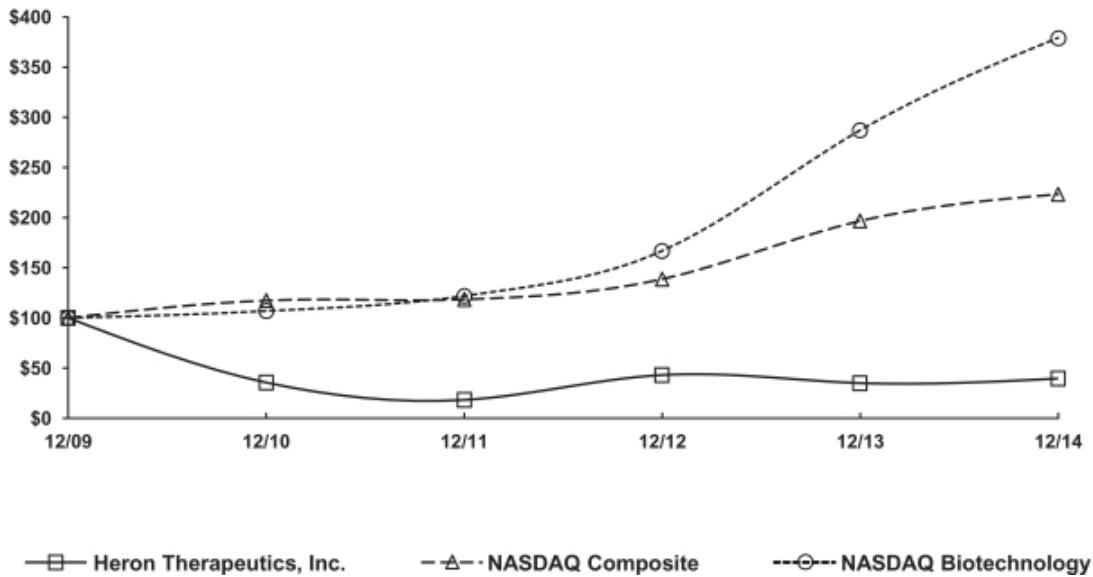
[Table of Contents](#)

Stock Performance Graph

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

The following graph shows the value of an investment of \$100 on December 31, 2009 in Heron Therapeutics, Inc. common stock, the NASDAQ Composite Index (U.S.) and the NASDAQ Biotechnology Index. All values assume reinvestment of the pretax value of dividends paid by companies included in these indices and are calculated as of December 31st of each year. Our common stock has traded on The NASDAQ Capital Market since January 2014. The comparisons shown in the graph are based upon historical data and we caution that the stock price performance shown in the graph is not indicative of, nor intended to forecast, the potential future performance of our stock.

COMPARISON OF 5 YEAR CUMULATIVE TOTAL RETURN*
Among Heron Therapeutics, Inc, the NASDAQ Composite Index
and the NASDAQ Biotechnology Index



* \$100 invested on 12/31/09 in stock or index, including reinvestment of dividends. Fiscal year ending December 31.

[Table of Contents](#)**ITEM 6. SELECTED FINANCIAL DATA.**

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

Years Ended December 31,
(In thousands, except per share amounts)

	2014	2013	2012	2011	2010
Statements of Operations Data:					
Revenues:					
Contract revenue	\$ —	\$ —	\$ —	\$ 646	\$ 1,301
Operating expenses:					
Research and development	54,833	32,516	15,174	8,207	7,264
General and administrative	19,728	21,941	8,657	3,501	3,971
Loss from operations	(74,561)	(54,457)	(23,831)	(11,062)	(9,934)
Gain on sale of interest in royalties	—	—	—	—	2,500
Other income (expense)	(1,806)	(826)	(599)	(373)	238
Loss from continuing operations	(76,367)	(55,283)	(24,430)	(11,435)	(7,196)
Gain (loss) from discontinued operations	—	—	1,082	(379)	(150)
Net loss	\$ (76,367)	\$ (55,283)	\$ (23,348)	\$ (11,814)	\$ (7,346)
Basic and diluted net loss per common share – loss from continuing operations	\$ (2.87)	\$ (3.42)	\$ (2.00)	\$ (1.90)	\$ (3.63)
Basic and diluted net loss per common share – net loss	\$ (2.87)	\$ (3.42)	\$ (1.91)	\$ (1.96)	\$ (3.70)
Weighted-average common shares outstanding used to calculate basic and diluted net loss per common share	26,569	16,163	12,223	6,013	1,984
Balance Sheet Data:					
Cash and cash equivalents	\$72,675	\$72,287	\$53,506	\$17,974	\$2,109
Working capital	60,112	65,933	49,936	14,547	941
Total assets	76,682	75,937	55,972	19,445	2,911
Long-term liabilities	—	—	—	—	35
Accumulated deficit	(315,237)	(238,870)	(183,587)	(160,239)	(148,425)
Total stockholders' equity	63,062	68,945	51,818	15,752	1,316

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

This Annual Report on Form 10-K contains forward-looking statements within the meaning of the federal securities laws. You can identify forward-looking statements by the use of the words "believe," "expect," "anticipate," "intend," "estimate," "project," "will," "should," "may," "plan," "intend," "assume" and other expressions which 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 the control of the Company. These risks, uncertainties and other factors may cause the actual results, performance or achievements of the Company to be materially different from the anticipated future results, performance or achievements expressed or implied by the forward-looking statements.

Factors that might cause these differences include the following:

- estimates of the timing of our resubmission of the New Drug Application ("NDA") for SUSTOL and potential regulatory approval for and commercial launch of SUSTOL;
- the anticipated progress of our research and development programs, including the initiation of new clinical trials and preclinical testing;
- if approved, the market conditions at commercial launch of SUSTOL or other future product candidates;
- our ability to successfully market, commercialize and achieve market acceptance for SUSTOL or other future product candidates, including our positioning relative to competing products;
- our ability to successfully develop and achieve regulatory approval for other future product candidates utilizing our proprietary Biochronomer polymer-based drug delivery platform technology;
- our ability to establish key collaborations for our products and any other future 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 establish and maintain key vendor relationships necessary for the manufacture of our products;
- our ability to successfully operate in other non-U.S. jurisdictions in which we may choose to do business, including compliance with applicable regulatory requirements and laws;
- uncertainties associated with obtaining and enforcing patents to protect our products, and our ability to successfully defend ourselves against unforeseen third party infringement claims; and
- our estimates regarding our capital requirements and our needs for, and ability to obtain, additional financing.

[Table of Contents](#)

These forward-looking statements were based on information, plans and estimates at the date of this Annual Report on Form 10-K, and 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. In addition, please see the "Risk Factors" section of this Annual Report on Form 10-K. These risk factors may be updated from time to time by our future filings under the Exchange Act. You should carefully review all information therein.

Introduction

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

- *Overview.* This section provides a general description of our business and operating expenses.
- *Critical accounting policies and estimates.* This section contains a discussion of the accounting policies that we believe are important to our financial condition and results of operations and that require significant judgment and estimates on the part of management in their application. In addition, all of our significant accounting policies, including the critical accounting policies and estimates, are summarized in Note 2 to the Financial Statements included in Item 8 of this Annual Report on Form 10-K.
- *Results of operations.* This section provides an analysis of our results of operations presented in the accompanying statements of operations by comparing the results for the year ended December 31, 2014 to the results for the year ended December 31, 2013 and comparing the results for the year ended December 31, 2013 to the results for the year ended December 31, 2012.
- *Liquidity and capital resources.* This section provides an analysis of our cash flows and a discussion of our outstanding commitments and contingencies that existed as of December 31, 2014. Included in this discussion is our financial capacity to fund our future commitments and a discussion of other financing arrangements.

Overview

Heron Therapeutics, Inc. (formerly A.P. Pharma, Inc.) is a biotechnology company using its proprietary technology and innovative efforts to develop products to address unmet medical needs. Our product development efforts focus on identifying new delivery methods and formulations utilizing known compounds that may expand or extend the therapeutic effect or duration of action, or eliminate the drawbacks of current therapies. Our proprietary Biochronomer polymer-based drug delivery platform technology is designed to improve the therapeutic profile of injectable pharmaceuticals. We continue to evaluate other development programs, technologies or product candidates that may be complementary to or synergistic with our existing programs and product development goals.

Research and Development Expense

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

[Table of Contents](#)

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

We expect our research and development expenses to increase in 2015 to support our ongoing research and development efforts for our product candidates, including the completion of our ongoing Phase 3 study for SUSTOL for the treatment of delayed-onset chemotherapy induced nausea and vomiting in patients undergoing highly emetogenic chemotherapy regimens ("HEC Study"), and the continued development of our other programs, including HTX-011 and HTX-019. The lengthy process of completing our clinical trials and seeking regulatory approval for our product candidates requires the expenditure of substantial resources. We do not expect SUSTOL, our lead product candidate, to be commercially available before 2016, if at all.

General and Administrative Expense

General and administrative expense primarily consists of salaries, stock-based compensation and other related costs for personnel in executive, finance and accounting, business development, investor relations, legal and human resource functions. Other general and administrative costs include professional fees for legal, information technology, accounting and other general corporate purposes, pre-commercialization costs and facility costs not otherwise included in research and development expense.

Other Income (Expense)

Other income (expense) primarily consists of interest expense and amortization of debt discount related to our Senior Secured Convertible Notes ("Convertible Notes"). In addition, other income (expense) includes impairment of fixed assets, gains (losses) from the disposal of fixed assets and interest income earned on our cash and cash equivalents.

Critical Accounting Policies and Estimates

The discussion and analysis of our financial condition and results of operations is based on our financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States. 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 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.

We believe the following critical accounting policies involve significant judgments and estimates used in the preparation of our financial statements.

[Table of Contents](#)

Accrued Clinical Liabilities

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

Income Taxes

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

We assess the likelihood that we will be able to recover our deferred tax assets. We consider all available evidence, both positive and negative, including our historical levels of income and losses, expectations and risks associated with estimates of future taxable income and ongoing prudent and feasible tax planning strategies in assessing the need for a valuation allowance. A valuation allowance is provided when it is more likely than not that the deferred tax assets will not be realized. At December 31, 2014, we established a valuation allowance to offset our net deferred tax assets due to the uncertainty of realizing future tax benefits from our net operating loss carryforwards and other deferred tax assets.

Additionally, we believe that our deferred tax assets may have been limited in accordance with a provision of the Internal Revenue Code of 1986, whereby net operating loss and tax credit carryforwards available for use in a given period are limited upon the occurrence of certain events, including a significant change in ownership interests. As a result, our deferred tax assets and related valuation allowance were reduced for the estimated impact of the net operating losses and credits that may expire unused.

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

Stock-Based Compensation

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

[Table of Contents](#)

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

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

New Accounting Pronouncements

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

Results of Operations

Years Ended December 31, 2014 and 2013

Research and Development Expense

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

December 31,	2014	2013
SUSTOL-related costs	\$33,758	\$22,037
New product development related costs	6,761	800
Personnel and related costs	7,868	5,029
Stock-based compensation expense	3,329	2,562
Facility related costs	1,716	1,600
Other	1,401	488
Total research and development expense	\$54,833	\$32,516

For the year ended December 31, 2014, research and development expense increased to \$54.8 million compared to \$32.5 million for the year ended December 31, 2013. The increase was primarily a result of an increase in SUSTOL-related costs due to the ongoing Phase 3 HEC Study in 2014, manufacturing development costs and other SUSTOL-related activities. In addition, the increase in research and development expense was due to costs associated with new product development, including our pain management program targeting the relief of post-surgical pain. Finally, the increase in research and development expense was due to an increase in personnel and related costs of approximately \$2.8 million mainly due to additional personnel to support the increased development activities noted above, and an increase in non-cash, stock-based compensation expense of approximately \$0.8 million.

[Table of Contents](#)

General and Administrative Expense

For the year ended December 31, 2014, general and administrative expense decreased to \$19.7 million compared to \$21.9 million for the year ended December 31, 2013, primarily as a result of higher stock-based compensation expense in 2013 resulting from the resignation of our former chief executive officer in August 2013 and the hiring of new senior executives in May 2013. This decrease was partially offset by an increase in personnel and other costs in 2014 to support increased development efforts. For the year ended December 31, 2014, general and administrative expenses consist primarily of salaries and related expenses, professional fees, pre-commercialization costs and insurance expense.

Other Income (Expense)

Other income (expense) was (\$1.8 million) for the year ended December 31, 2014, compared to (\$0.8 million) for the year ended December 31, 2013. Other income (expense) increased in 2014 primarily due to the write-off of impaired manufacturing related equipment of approximately \$0.9 million (see Note 2 to the Financial Statements included in Item 8 of this Annual Report on Form 10-K for further details). The remainder of the balance consisted primarily of interest expense and amortization of debt discount related to our Convertible Notes, which was comparable between 2014 and 2013.

Years Ended December 31, 2013 and 2012

Research and Development

The major components of research and development expenses were as follows (in thousands):

December 31,	2013	2012
SUSTOL-related costs	\$22,037	\$ 8,419
New product development related costs	800	383
Personnel and related costs	5,029	2,603
Stock-based compensation expense	2,562	1,617
Facility related costs	1,600	1,099
Other	488	1,053
Total research and development expense	\$32,516	\$15,174

For the year ended December 31, 2013, research and development expense increased to \$32.5 million compared to \$15.2 million for the year ended December 31, 2012. This increase was primarily due to additional costs associated with addressing the issues raised by the FDA in the 2013 Complete Response Letter with respect to our NDA for SUSTOL, including validating our third-party manufacturing processes and increasing the scale of production. This increase was also due to additional personnel related costs, including stock-based compensation expense, to support these increased SUSTOL-related development activities.

[Table of Contents](#)

General and Administrative

For the year ended December 31, 2013, general and administrative expense increased to \$21.9 million compared to \$8.7 million for the year ended December 31, 2012. This increase was primarily due to increased personnel costs, consulting, professional fees, market research and pre-commercialization activities to support the continued development of SUSTOL. In addition, this increase was due to an increase in stock-based compensation resulting from the resignation of our former chief executive officer in August 2013 and the resulting hiring of new senior executives.

Other Income (Expense)

Other income (expense) was (\$0.8 million) for the year ended December 31, 2013, compared to (\$0.6 million) for the year ended December 31, 2012. Other income (expense) for both periods consisted primarily of interest expense and amortization of debt discount related to the Convertible Notes.

Discontinued Operations

Gain from discontinued operations was \$1.1 million in 2012, related to the reversal of a gross profit guaranty from a sale of certain technology rights in 2000.

Liquidity and Capital Resources

As of December 31, 2014, we had approximately \$72.7 million in cash and cash equivalents, compared to \$72.3 million in cash as of December 31, 2013. The net increase in cash and cash equivalents of approximately \$0.4 million was primarily due to the cash proceeds of approximately \$58.9 million received from the common stock offering completed in June 2014 and \$3.1 million from stock option exercises, offset by the use of cash to fund our continued development of SUSTOL and other product candidates, personnel costs and for other general corporate purposes.

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

In April 2011, we entered into definitive agreements for a convertible note financing of up to \$4.5 million. We received a total of approximately \$4.3 million, net of issuance costs.

In July 2011, we closed a unit financing where each unit consisted of one share of common stock and a warrant to purchase 0.5 shares of common stock; whereby we received approximately \$22.8 million of proceeds, net of issuance costs.

In July 2012, we closed a private placement of common stock whereby we received approximately \$50.5 million of proceeds, net of issuance costs.

In November 2013, we closed a public offering of common stock whereby we received approximately \$57.8 million of proceeds, net of issuance costs.

[Table of Contents](#)

In June 2014, we closed a public offering of common stock and pre-funded warrants whereby we received approximately \$58.9 million of proceeds, net of issuance costs.

We believe that our current working capital is sufficient to fund operations through 2015, including pursuing regulatory approval to market SUSTOL, and completing Phase 1 human clinical studies commenced in 2015 relative to our HTX-011 and HTX-019 development programs and related preclinical activities. In the event we were to pursue clinical product development in other areas, potentially acquire other strategic assets, or begin to make significant investments in preparing for commercialization of SUSTOL, we would need to raise additional capital. If we are unable to obtain sufficient financing on acceptable terms or otherwise, we may be required to reduce or defer our activities. Our capital requirements going forward will depend on numerous factors, including: the scope, rate of progress, results and costs of preclinical testing and clinical trials, including completing our Phase 3 HEC Study; an approval decision by the FDA with respect to SUSTOL; the timing of and costs associated with the commercial launch of SUSTOL, if approved; the degree of commercial success of SUSTOL; the number and characteristics of product development programs we pursue and the pace of each program including the timing of clinical trials; the time, cost and outcome involved in seeking other regulatory approvals; scientific progress in our research and development programs; the magnitude and scope of our research and development programs; our ability to establish and maintain strategic collaborations or partnerships for research, development, clinical testing, manufacturing and marketing of our product candidates; the cost and timing of establishing sales, marketing and distribution capabilities if we commercialize products independently; the cost of establishing clinical and commercial supplies of our product candidates and any products that we may develop; and general market conditions.

We may not be able to raise sufficient additional capital when we need it on favorable terms, or at all. The sale of additional equity in the future may be dilutive to our stockholders. If we are unable to obtain adequate funds on reasonable terms, we may be required to curtail operations significantly or to obtain funds by entering into financing, supply or collaboration agreements on unattractive terms.

We have no current means of generating material cash flows from operations. There can be no assurance that our product development efforts related to any of our product candidates will be successfully completed, that required regulatory approvals will be obtained, or that any products, if introduced, will be successfully marketed or achieve commercial acceptance. Until we can generate significant continuing revenues, we expect to satisfy our future cash needs through public or private equity offerings, debt financings and corporate collaboration and licensing arrangements. We cannot be certain that additional funding will be available to us on acceptable terms, or at all. Our ability to obtain new financing may be constrained by our failure to achieve significant business objectives, covenants contained in the Convertible Notes, and numerous other factors.

The following table summarizes our contractual obligations as of December 31, 2014.

	Payment due by period				
	Total	Less than 1 year	1-3 years	3-5 years	More than 5 years
			(In thousands)		
Operating lease obligations	\$ 1,589	\$ 867	\$ 722	\$ —	\$ —
Purchase obligations	877	877	—	—	—
Total	\$ 2,466	\$ 1,744	\$ 722	\$ —	\$ —

[Table of Contents](#)

The holders of the Convertible Notes may require prepayment of the Convertible Notes at any time at each holder's option (see Note 5 of Notes to Financial Statements included in Item 8 of this Annual Report on Form 10-K).

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

At December 31, 2014, purchase obligations primarily consisted of commitments with third-party manufacturers of materials to be used in our clinical and preclinical studies, as well as commitments with various vendors for clinical and preclinical studies. Approximately \$0.2 million of the total purchase obligations were not included in our financial statements for the year ended December 31, 2014. We intend to use our current financial resources to fund our commitments under these purchase obligations.

Off-Balance Sheet Arrangements

We have no off-balance sheet arrangements that have, or are reasonably likely to have, a current or future effect on our financial condition, expenses, results of operations, liquidity, capital expenditures or capital resources.

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

The primary objective of our investment activities is to preserve our capital to fund operations. Our exposure to market risk for changes in interest rates relates primarily to the increase or decrease in the amount of interest income we can earn. Our risk associated with fluctuating interest income is limited to our investments in interest rate-sensitive financial instruments. As of December 31, 2014, our cash equivalents consisted of investments in money market funds. 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.

[Table of Contents](#)

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA.

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors and Stockholders of
Heron Therapeutics, Inc.

We have audited the accompanying balance sheets of Heron Therapeutics, Inc. as of December 31, 2014 and 2013, and the related statements of operations, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2014. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements audited by us present fairly, in all material respects, the financial position of Heron Therapeutics, Inc. at December 31, 2014 and 2013, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2014, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), Heron Therapeutics, Inc.'s internal control over financial reporting as of December 31, 2014, based on criteria established in *Internal Control-Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission and our report dated March 12, 2015 expressed an unqualified opinion thereon.

/s/ OUM & Co. LLP

San Francisco, California
March 12, 2015

[Table of Contents](#)

HERON THERAPEUTICS, INC.
BALANCE SHEETS
(In thousands, except par value amounts)

December 31,	2014	2013
ASSETS		
Current assets:		
Cash and cash equivalents	\$ 72,675	\$ 72,287
Prepaid expenses and other current assets	1,057	638
Total current assets	73,732	72,925
Property and equipment, net	2,820	2,882
Other assets	130	130
Total assets	\$ 76,682	\$ 75,937
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	\$ 2,549	\$ 1,264
Accrued clinical liabilities	3,811	1,773
Accrued payroll and employee liabilities	2,731	2,566
Other accrued liabilities	2,931	364
Convertible notes payable to related parties, net of discount	1,598	1,025
Total current liabilities	13,620	6,992
Commitments and contingencies (see Note 5)		
Stockholders' equity:		
Preferred stock, \$0.01 par value: 2,500 shares authorized; no shares issued or outstanding at December 31, 2014 and 2013	—	—
Common stock, \$0.01 par value: 75,000 shares authorized; 29,227 and 23,572 shares issued and outstanding at December 31, 2014 and 2013, respectively	292	237
Additional paid-in capital	378,007	307,578
Accumulated deficit	(315,237)	(238,870)
Total stockholders' equity	63,062	68,945
Total liabilities and stockholders' equity	\$ 76,682	\$ 75,937

See accompanying Notes to Financial Statements.

[Table of Contents](#)

HERON THERAPEUTICS, INC.
STATEMENTS OF OPERATIONS
(In thousands, except per share amounts)

Years Ended December 31,	2014	2013	2012
Operating expenses:			
Research and development	\$ 54,833	\$ 32,516	\$ 15,174
General and administrative	19,728	21,941	8,657
Total operating expenses	74,561	54,457	23,831
Loss from operations	(74,561)	(54,457)	(23,831)
Other income (expense):			
Interest expense	(887)	(828)	(605)
Other income (expense), net	(919)	2	6
Total other income (expense)	(1,806)	(826)	(599)
Loss from continuing operations	(76,367)	(55,283)	(24,430)
Gain from discontinued operations	—	—	1,082
Net loss	<u>\$ (76,367)</u>	<u>\$ (55,283)</u>	<u>\$ (23,348)</u>
Basic and diluted net loss per share:			
Loss from continuing operations	\$ (2.87)	\$ (3.42)	\$ (2.00)
Net loss	<u>\$ (2.87)</u>	<u>\$ (3.42)</u>	<u>\$ (1.91)</u>
Shares used in computing basic and diluted net loss per share	26,569	16,163	12,223

See accompanying Notes to Financial Statements.

[Table of Contents](#)

HERON THERAPEUTICS, INC.
STATEMENTS OF STOCKHOLDERS' EQUITY
(In thousands)

	Common Stock		Additional Paid-In Capital	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount			
Balance, December 31, 2011	10,002	\$ 100	\$ 175,891	\$ (160,239)	\$ 15,752
Issuance of common stock in a private placement, net	5,100	51	50,440	—	50,491
Conversion benefit included in Convertible Notes issued	—	—	3,169	—	3,169
Issuance of common stock under Employee Stock Purchase Plan	4	—	22	—	22
Issuance of common stock upon exercise of warrants	5	1	(1)	—	—
Stock-based compensation expense	—	—	5,552	—	5,552
Fair value of warrants issued to non-employees	—	—	180	—	180
Net loss	—	—	—	(23,348)	(23,348)
Balance, December 31, 2012	15,111	152	235,253	(183,587)	51,818
Issuance of common stock in a public offering, net	7,706	77	57,725	—	57,802
Conversion benefit included in Convertible Notes issued	—	—	291	—	291
Issuance of common stock under Employee Stock Purchase Plan	6	1	33	—	34
Issuance of common stock upon exercise of stock options	537	5	2,788	—	2,793
Issuance of common stock upon exercise of warrants	212	2	598	—	600
Stock-based compensation expense	—	—	10,890	—	10,890
Net loss	—	—	—	(55,283)	(55,283)
Balance, December 31, 2013	23,572	237	307,578	(238,870)	68,945
Issuance of common stock and pre-funded warrants in a public offering, net	4,751	47	58,869	—	58,916
Conversion benefit included in Convertible Notes issued	—	—	309	—	309
Issuance of common stock under Employee Stock Purchase Plan	12	—	91	—	91
Issuance of common stock upon exercise of stock options	588	5	3,096	—	3,101
Issuance of common stock upon exercise of warrants	304	3	(3)	—	—
Stock-based compensation expense	—	—	8,067	—	8,067
Net loss	—	—	—	(76,367)	(76,367)
Balance, December 31, 2014	29,227	\$ 292	\$ 378,007	\$ (315,237)	\$ 63,062

See accompanying Notes to Financial Statements.

[Table of Contents](#)

HERON THERAPEUTICS, INC.
STATEMENTS OF CASH FLOWS
(In thousands)

Years Ended December 31,	2014	2013	2012
Operating activities:			
Net loss	\$(76,367)	\$(55,283)	\$(23,348)
Adjustments to reconcile net loss to net cash used for operating activities:			
Stock-based compensation	8,067	10,890	5,732
Depreciation and amortization	578	333	197
Amortization of debt discount	573	533	389
Gain from discontinued operations	—	—	(1,082)
Impairment loss on property and equipment	905	—	—
Loss on disposal of property and equipment	17	—	—
Change in operating assets and liabilities:			
Prepaid expense and other current assets	(419)	(54)	(318)
Accounts payable	1,285	(426)	984
Accrued clinical liabilities	2,038	1,127	92
Accrued payroll and employee liabilities	165	2,153	(149)
Other accrued liabilities	2,876	(36)	494
Net cash used for operating activities	(60,282)	(40,763)	(17,009)
Investing activities:			
Purchases of property and equipment	(1,438)	(1,685)	(972)
Net cash used for investing activities	(1,438)	(1,685)	(972)
Financing activities:			
Net proceeds from sale of common stock and/or pre-funded warrants	58,916	57,802	50,491
Proceeds from purchases under the Employee Stock Purchase Plan	91	34	22
Proceeds from stock option exercises	3,101	2,793	—
Proceeds from warrant exercises	—	600	—
Net proceeds from convertible note financing	—	—	3,000
Net cash provided by financing activities	62,108	61,229	53,513
Net increase in cash and cash equivalents	388	18,781	35,532
Cash and cash equivalents at beginning of year	72,287	53,506	17,974
Cash and cash equivalents at end of year	\$ 72,675	\$ 72,287	\$ 53,506
Supplemental disclosure of cash flow information:			
Interest paid	\$ —	\$ —	\$ —

See accompanying Notes to Financial Statements.

[Table of Contents](#)

HERON THERAPEUTICS, INC.
NOTES TO FINANCIAL STATEMENTS

1. Organization and Business

Heron Therapeutics, Inc. (formerly A.P. Pharma, Inc.) is a biotechnology company using its proprietary technology and innovative efforts to develop products to address unmet medical needs. Our product development efforts focus on identifying new delivery methods and formulations utilizing known compounds that may expand or extend the therapeutic effect or duration of action, or eliminate the drawbacks of current therapies. Our proprietary Biochronomer polymer-based drug delivery platform technology is designed to improve the therapeutic profile of injectable pharmaceuticals. We continue to evaluate other development programs, technologies or product candidates that may be complementary to or synergistic with our existing programs and product development goals.

Our Biochronomer technology, with which SUSTOL and certain of our other product candidates are formulated, consists of bioerodible polymers designed to release drugs over a defined period of time, depending on the medical need of a given therapeutic target. We have demonstrated that our Biochronomer technology can deliver drugs over periods varying from days to weeks and that the technology is potentially applicable to a range of therapeutic areas, including the prevention of chemotherapy-induced nausea and vomiting ("CINV") and pain management, among others. Furthermore, we have completed comprehensive animal and human toxicology studies that have established that our Biochronomer polymer is well tolerated. Our lead product candidate, SUSTOL, is in development for the prevention of CINV following administration of chemotherapeutic agents. Our development programs include HTX-011 for the management of post-operative pain, HTX-019 for the prevention of CINV and HTX-003 for management of chronic pain and opioid addiction.

Our lead investigational product candidate, APF530, which we intend to market as SUSTOL (granisetron injection, extended release), subject to regulatory approval, is being developed for the prevention of both acute- and delayed-onset CINV. The 5-hydroxytryptamine type 3 ("5-HT₃") receptor antagonist granisetron was selected for SUSTOL because it is widely prescribed by physicians based on a well-established record of safety and efficacy. Injectable and oral formulations of granisetron are currently approved, but are only for the treatment of acute-onset CINV. SUSTOL is formulated utilizing our proprietary Biochronomer technology and has been shown in clinical studies to maintain therapeutic drug levels of granisetron for up to five days with a single subcutaneous injection. In 2014, we initiated a Phase 3 clinical study with SUSTOL for the prevention of delayed-onset CINV following the administration of highly emetogenic agents ("HEC study"), which, if successful, would differentiate SUSTOL from the other 5-HT₃ receptor antagonists that are currently approved. We anticipate completing enrollment of our HEC study at the end of the first quarter of 2015.

In May 2009, we filed a New Drug Application ("NDA") for SUSTOL with the U.S Food and Drug Administration ("FDA") under Section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act. In March 2010, we received our first Complete Response Letter ("CRL"), which stated that the May 2009 NDA requesting approval of SUSTOL, could not be approved as it was initially submitted. The primary points raised in the initial CRL were related to the dosing system, certain identified deficiencies in the chemistry, manufacturing, and control ("CMC") review, and the request we perform additional studies showing bioequivalence and metabolic rates and on human factors, and to perform a QT study. We met with the FDA in 2011 to clarify the comments and requests and subsequently performed additional work and data analyses which we believed addressed the concerns raised in the 2010 CRL. In September 2012, we resubmitted the NDA seeking approval for SUSTOL and in March 2013, the FDA issued a second CRL. The FDA identified several additional issues precluding the approval of the SUSTOL NDA resubmission, including further issues relating to the CMC review and deficiencies at certain of our contract manufacturers,

[Table of Contents](#)

HERON THERAPEUTICS, INC.
NOTES TO FINANCIAL STATEMENTS

and requested that we repeat human factors testing using commercially equivalent material, as well to provide data to allow reanalysis of our Phase 3 clinical results under the revised ASCO 2011 CINV guidelines. We believe that we have substantially addressed the issues raised in the March 2013 CRL, which will be reflected in our upcoming resubmission. We intend to include the results of our ongoing HEC study in the resubmission of our NDA for SUSTOL, which we anticipate filing mid-year 2015.

In November 2013, we initiated a development program targeting pain management. In recent years, the FDA has focused on approving drugs to successfully treat post-surgical pain, to reduce reliance on opioids, which can lead to post-surgical complications, extended hospitalization, as well as abuse and addiction. We believe there is significant opportunity for a non-opioid, sustained-release product targeting the post-surgical pain market. Our lead product candidate for this program is HTX-011, a combination of the local anesthetic bupivacaine and the anti-inflammatory meloxicam formulated utilizing our proprietary Biochronomer technology to release drug for up to 72 hours. We intend to evaluate this product in soft-tissue, nerve block, and orthopedic post-surgical settings. In the first quarter of 2015, we initiated a Phase 1 study to evaluate the safety of HTX-011 in healthy volunteers. Following the completion of the ongoing Phase 1 study, we plan to initiate additional Phase 1b/2 studies in 2015.

In November 2014, we announced our development program for HTX-019. HTX-019 is a proprietary injectable formulation of aprepitant, a neurokinin-1 ("NK₁") receptor antagonist used in combination with 5-HT₃ receptor antagonists for the prevention of CINV. The HTX-019 formulation is distinguishable from the only injectable NK₁ receptor antagonist approved in the U.S. for the prevention of CINV, in that it does not contain polysorbate 80, which may cause hypersensitivity or other adverse reactions in some patients. We believe there is an unmet need for expanded options for NK₁ receptor antagonists, particularly those which may potentially reduce the risk of complications from hypersensitivity reactions. Subject to discussion with the FDA, we plan to develop HTX-019 utilizing the 505(b)(2) registration pathway.

In December 2014, we disclosed a second investigational product in our pain management program. HTX-003 is a long-acting formulation of buprenorphine for the treatment of chronic pain and opioid addiction. HTX-003 is formulated with our Biochronomer technology to deliver drug over 30 days with a single subcutaneous injection and accordingly is expected to have a low potential for patient abuse. We are presently evaluating our plans for further development for this product.

In January 2014, we changed our name from A.P. Pharma, Inc. to Heron Therapeutics, Inc. Effective January 13, 2014, we effected a 1-for-20 reverse split of our outstanding common stock ("Reverse Stock Split") (See Note 7).

Liquidity

We have incurred significant operating losses and negative cash flows from operations and we have an accumulated deficit of \$315.2 million as of December 31, 2014. Since 2011, we completed a total of five rounds of equity and/or convertible debt financings, which provided us with cash of approximately \$194.3 million, net of issuance costs, to fund operations (see Notes 5 and 6). As of December 31, 2014, we had cash and cash equivalents on hand of \$72.7 million.

We believe that our current working capital is sufficient to fund operations through 2015, including pursuing regulatory approval to market SUSTOL, and completing Phase 1 human clinical studies commenced in 2015 relative to our HTX-011 and HTX-019 development programs and related preclinical activities. In the event we were to pursue clinical product development in other

[Table of Contents](#)

HERON THERAPEUTICS, INC.
NOTES TO FINANCIAL STATEMENTS

areas, potentially acquire other strategic assets, or begin to make significant investments in preparing for commercialization of SUSTOL, we would need to raise additional capital. If we are unable to obtain sufficient financing on acceptable terms or otherwise, we may be required to reduce or defer our activities. Our capital requirements going forward will depend on numerous factors, including: the scope, rate of progress, results and costs of preclinical testing and clinical trials, including completing our HEC Study; an approval decision by the FDA with respect to SUSTOL; the timing of and costs associated with the commercial launch of SUSTOL, if approved; the degree of commercial success of SUSTOL; the number and characteristics of product development programs we pursue and the pace of each program including the timing of clinical trials; the time, cost and outcome involved in seeking other regulatory approvals; scientific progress in our research and development programs; the magnitude and scope of our research and development programs; our ability to establish and maintain strategic collaborations or partnerships for research, development, clinical testing, manufacturing and marketing of our product candidates; the cost and timing of establishing sales, marketing and distribution capabilities if we commercialize products independently; the cost of establishing clinical and commercial supplies of our product candidates and any products that we may develop; and general market conditions.

We may not be able to raise sufficient additional capital when we need it on favorable terms, or at all. The sale of additional equity in the future may be dilutive to our stockholders. If we are unable to obtain adequate funds on reasonable terms, we may be required to curtail operations significantly or to obtain funds by entering into financing, supply or collaboration agreements on unattractive terms.

2. Summary of Significant Accounting Policies

Use of Estimates

The preparation of financial statements in conformity with accounting principles generally accepted in the United States (“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 critical accounting policies that involve significant judgment and estimates include accrued clinical liabilities, income taxes and stock-based compensation. Actual results could differ materially from those estimates.

Reclassifications

Certain amounts in the 2013 financial statements have been reclassified to conform to the 2014 presentation.

Cash and Cash Equivalents

Cash and cash equivalents consist of cash and highly liquid investments with original maturities from purchase date of three months or less. Our bank accounts have been placed under a control agreement in accordance with our Senior Secured Convertible Notes (“Convertible Notes”).

Fair Value of Financial Instruments

Financial instruments, including cash and cash equivalents, receivables, 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

[Table of Contents](#)

HERON THERAPEUTICS, INC.
NOTES TO FINANCIAL STATEMENTS

because of the short-term maturity of these instruments. Our Convertible Notes outstanding at December 31, 2014 do not have a readily available ascertainable market value, however, the carrying value is considered to approximate its fair value (see Note 3 for further details regarding the fair value of financial instruments).

Concentration of Credit Risk

Cash and cash equivalents are financial instruments which 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, certificates of deposit or United States government and agency obligations. 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.

Property and Equipment

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

Impairment of Long-Lived Assets

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

Accrued Clinical Liabilities

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

Research and Development Expenses

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

[Table of Contents](#)

HERON THERAPEUTICS, INC.
NOTES TO FINANCIAL STATEMENTS

Patent Costs

We incur fees of outside legal counsel in connection with filing and maintaining its various patent applications. All patent costs are expensed as incurred and included in general and administrative expense in the Statements of Operations.

Stock-Based Compensation Expense

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

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

Warrants

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

Income Taxes

Accounting Standard Codification No. 740, *Accounting for Uncertainty in Income Taxes*, clarifies the accounting for uncertain tax positions. This provision requires that we recognize the impact of a tax position in our financial statements if the position is more likely than not to be sustained upon examination and on the technical merits of the position. The total amount of unrecognized tax benefits as of December 31, 2014 was \$120,000 which, if recognized, would affect other tax accounts, primarily deferred taxes in future periods, and would not affect our effective tax rate since we maintain a full valuation allowance against its deferred tax assets (see Note 8 for further details).

Comprehensive Income (Loss)

Comprehensive income (loss) is defined as the change in equity during a period from transactions and other events and circumstances from non-owner sources. Our comprehensive net loss for all periods presented was comprised solely of our net loss and there were no other changes in equity from non-owner sources.

Earnings per Share

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

[Table of Contents](#)

HERON THERAPEUTICS, INC.
NOTES TO FINANCIAL STATEMENTS

Because we have incurred a net loss for all periods presented in the statements of operations, outstanding stock options, warrants and common stock underlying Convertible Notes are not included in the computation of net loss per share because their effect would be anti-dilutive.

The following table includes the number of outstanding stock options, warrants and common stock underlying Convertible Notes not included in the computation as of the dates shown below (in thousands):

As of December 31,	2014	2013	2012
Stock options outstanding	7,918	6,356	4,324
Warrants outstanding	4,108	3,969	4,219
Common stock underlying Convertible Notes outstanding	6,677	6,291	5,927

Recent Accounting Pronouncements

In January 2015, the Financial Accounting Standards Board (“FASB”) issued Accounting Standards Update (“ASU”) No. 2015-01, *Income Statement—Extraordinary and Unusual Items (Subtopic 225-20)* (“ASU 2015-01”). ASU 2015-01 eliminates the concept of extraordinary items from GAAP. ASU 2015-01 will save time and reduce costs for preparers because they will not have to assess whether a particular event or transaction event is extraordinary (even if they ultimately would conclude it is not). This also alleviates uncertainty for preparers, auditors, and regulators because auditors and regulators no longer will need to evaluate whether a preparer treated an unusual and/or infrequent item appropriately. FASB concluded that ASU 2015-01 will not result in a loss of information because although ASU 2015-01 will eliminate the requirements in Subtopic 225-20 for reporting entities to consider whether an underlying event or transaction is extraordinary, the presentation and disclosure guidance for items that are unusual in nature or occur infrequently will be retained and will be expanded to include items that are both unusual in nature and infrequently occurring. The amendments in ASU 2015-01 are effective for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2015. A reporting entity may apply the amendments prospectively. A reporting entity also may apply the amendments retrospectively to all prior periods presented in the financial statements. Early adoption is permitted provided that the guidance is applied from the beginning of the fiscal year of adoption. We plan to adopt the provisions on ASU 2015-01 in the first quarter of 2016. We do not expect the adoption of this ASU to have a material impact on our results of operations or financial condition.

In August 2014, FASB issued ASU No. 2014-15, *Presentation of Financial Statements – Going Concern (Subtopic 205-40)* (“ASU 2014-15”). ASU 2014-15 requires management to assess an entity’s ability to continue as a going concern by incorporating and expanding upon certain principles that are currently in U.S. auditing standards. Specifically, the amendments (1) provide a definition of the term substantial doubt, (2) require an evaluation every reporting period including interim periods, (3) provide principles for considering the mitigating effect of management’s plans, (4) require certain disclosures when substantial doubt is alleviated as a result of consideration of management’s plans, (5) require an express statement and other disclosures when substantial doubt is not alleviated, and (6) require an assessment for a period of one year after the date that the financial statements are issued (or available to be issued). The amendments in ASU 2014-15 are effective for the annual period ending after December 15, 2016, and for annual periods and interim periods thereafter. Early adoption is permitted. We plan to adopt the provisions on ASU 2014-15 in 2016. We do not expect the adoption of this ASU to have a material impact on our results of operations or financial condition.

[Table of Contents](#)

HERON THERAPEUTICS, INC.
NOTES TO FINANCIAL STATEMENTS

In June 2014, FASB issued ASU No. 2014-12, *Compensation – Stock Compensation (Topic 718)* (“ASU 2014-12”). ASU 2014-12 requires that a performance target that affects vesting and that could be achieved after the requisite service period be treated as a performance condition. ASU 2014-12 is effective for annual periods and interim periods within those annual periods beginning after December 15, 2015. Earlier adoption is permitted. The amendments in ASU 2014-12 may either be applied (a) prospectively to all awards granted or modified after the effective date or (b) retrospectively to all awards with performance targets that are outstanding as of the beginning of the earlier annual period presented in the financial statements and to all new or modified awards thereafter. We plan to adopt the provisions of ASU 2014-12 in the first quarter of 2016. We do not expect the adoption of this ASU to have a material impact on our results of operations or financial condition.

In July 2013, the FASB issued ASU No. 2013-11, *Presentation of an Unrecognized Tax Benefit When a Net Operating Loss Carryforward, a Similar Tax Loss, or a Tax Credit Carryforward Exists* (“ASU 2013-11”). This update provides explicit guidance on the financial statement presentation of an unrecognized tax benefit when a net operating loss carryforward, a similar tax loss, or a tax credit carryforward exists. We adopted this guidance in 2014 and it did not have a material impact on our financial condition, results of operations or related financial statement disclosures.

3. Fair Value Measurements

Fair value is defined as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Valuation techniques used to measure fair value must maximize the use of observable inputs and minimize the use of unobservable inputs. The fair value hierarchy based on three levels of inputs, of which the first two are considered observable and the last unobservable, that may be used to measure fair value, is as follows:

- Level 1 — 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.

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 not elected not to apply the fair value option to our financial assets and liabilities.

[Table of Contents](#)

HERON THERAPEUTICS, INC.
NOTES TO FINANCIAL STATEMENTS

We consider the carrying amount of cash and cash equivalents, receivables, prepaid expenses and other current assets, accounts payable and accrued liabilities to be representative of their respective fair values because of the short-term nature of those instruments. For the year ended December 31, 2014, we did not hold any investment securities and our cash equivalents consisted of money market funds. We did not hold any cash equivalents or investment securities during the year ended December 31, 2013.

4. Balance Sheet Details

Property and Equipment

Property and equipment is comprised of the following (in thousands):

December 31,	2014	2013
Scientific equipment	\$ 4,793	\$ 4,371
Computer equipment and software	1,133	1,080
Furniture, fixtures and office equipment	351	344
Leasehold improvements	1,376	1,360
	7,653	7,155
Less: accumulated depreciation and amortization	(4,833)	(4,273)
	<u>\$ 2,820</u>	<u>\$ 2,882</u>

Depreciation and amortization expense for the years ended December 31, 2014, 2013 and 2012 was approximately \$578,000, \$333,000 and \$197,000, respectively.

During the year ended December 31, 2014, we recognized \$905,000 as an impairment loss due to the write-down of a piece of manufacturing-related equipment. In March 2013, we received a CRL from the FDA which included issues to address related to our manufacturing process. As such, we made changes to our supply chain which in turn made this piece of manufacturing-related equipment no longer of use. As of December 31, 2014, the estimated fair value of the equipment was approximately \$115,000 which was based on our experience with the resale of used manufacturing equipment and the value of similar used equipment currently available for sale.

Accrued Payroll and Employee Liabilities and Other Accrued Expense

Accrued payroll and employee liabilities and other accrued expense consisted of the following (in thousands):

December 31,	2014	2013
Accrued employee salaries and benefits	\$ 719	\$ 796
Accrued bonuses	2,012	1,770
Total accrued payroll and employee liabilities	<u>\$2,731</u>	<u>\$2,566</u>

[Table of Contents](#)

HERON THERAPEUTICS, INC.
NOTES TO FINANCIAL STATEMENTS

December 31,	2014	2013
Accrued professional fees	\$ 1,775	\$ 69
Accrued accounts payable	886	26
Deferred rent	105	131
Other accrued liabilities	165	138
Total other accrued expense	<u>\$2,931</u>	<u>\$364</u>

5. Commitments and Contingencies

Leases

We lease 26,067 square feet of laboratory, office and warehouse space in Redwood City, California under a lease expiring on November 30, 2016. In addition, we currently lease 1,400 square feet of office space in Stamford, Connecticut and 2,020 square feet of office space in San Diego, California. The lease for the Connecticut office space was extended in 2014 for a three-month period ending on March 31, 2015. The lease for the San Diego office space was extended in 2014 for a six-month period ending on June 30, 2015. We believe our facilities are adequate and suitable for our current needs, and we will be able to obtain new or additional leased space in the future when necessary. We also lease certain office equipment under operating lease arrangements.

Annual future minimum lease payments as of December 31, 2014 are as follows (in thousands):

Years ended December 31,	Operating Leases
2015	\$ 867
2016	722
2017	—
2018	—
2019	—
Thereafter	—
Total	<u>\$ 1,589</u>

Rent expense under all operating leases totaled approximately \$1,381,000, \$967,000 and \$580,000 for the years ended December 31, 2014, 2013 and 2012, respectively.

Clinical Development Agreements

We have entered into agreements with various vendors for the research and development of product candidates, which are generally cancellable anytime at our option. Under the terms of these agreements, the vendors provide a variety of services including conducting preclinical development, research, manufacturing clinical compounds, enrolling and recruiting patients, monitoring studies, data analysis and regulatory filing assistance. Payments under these agreements typically include fees for services and reimbursement of expenses. In addition, under certain agreements, we are subject to penalties in the event we permanently discontinue performance under these agreements.

[Table of Contents](#)

HERON THERAPEUTICS, INC.
NOTES TO FINANCIAL STATEMENTS

Purchase Obligations

At December 31, 2014, purchase obligations of approximately \$877,000 primarily consisted of commitments with third-party manufacturers of materials to be used in our clinical and pre-clinical studies, as well as commitments with various vendors for clinical and preclinical studies. Approximately \$218,000 of the total purchase obligations were not included in our financial statements for the year ended December 31, 2014.

6. Senior Secured Convertible Notes to Related Parties

In April 2011, we entered into a Securities Purchase Agreement for a private placement of up to \$4.5 million in Convertible Notes. 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 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 principal and accrued interest due under the Convertible Notes. There is no right to convert the Convertible Notes to the extent that, after giving effect to such conversion, the holder would beneficially own in excess of 9.99% of our outstanding common stock. Each holder of the Convertible Notes can increase or decrease this beneficial ownership conversion limit by written notice to us, which will not be effective until 61 days after delivery of the notice.

As of December 31, 2014, we were in compliance with all covenants under the Convertible Notes. Upon 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.

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

The Convertible Notes contain an embedded conversion feature that was in-the-money on the issuance dates. Based on an effective fixed conversion rate of 1,250 shares for every \$1,000 of principal and accrued interest due under the Convertible Notes, the total conversion benefit at issuance exceeded the loan proceeds. Therefore, a debt discount was recorded in an amount equal to the face value of the Convertible Notes on the issuance dates and we began amortizing the resultant debt discount over the respective 10-year term of the Convertible Notes. During the year ended December 31, 2014, accrued interest of approximately \$309,000 was paid-in-kind and rolled into the Note principal balance, which resulted in an additional debt discount of approximately \$309,000. For the year ended December 31, 2014, 2013 and 2012, interest expense relating to the stated rate was approximately \$314,000, \$295,000 and \$216,000, respectively, and interest expense relating to the amortization of the debt discount was approximately \$573,000, \$533,000 and \$389,000, respectively.

[Table of Contents](#)

HERON THERAPEUTICS, INC.
NOTES TO FINANCIAL STATEMENTS

As of December 31, 2014, the carrying value of the Convertible Notes was approximately \$1,598,000, which is comprised of the \$5,341,000 principal amount of the Convertible Notes outstanding, less debt discount of \$3,743,000. If the \$5,341,000 principal amount of Convertible Notes is converted, we would issue 6,676,845 shares of our common stock.

7. Stockholders' Equity

Amendments to Articles of Incorporation – Reverse Stock Split

Effective January 13, 2014, we amended our Certificate of Incorporation to change our name to Heron Therapeutics, Inc. and to effect a 1-for-20 reverse split of our outstanding common stock. The name change and Reverse Stock Split were approved by our stockholders on September 19, 2013. As a result of the Reverse Stock Split, we amended our Certificate of Incorporation to reduce the total authorized shares of our common stock from 1,500,000,000 to 75,000,000 shares.

2011 Private Placement

In June 2011, we sold 8.0 million shares of our common stock for net proceeds of \$22.8 million (net of approximately \$1.2 million in issuance costs). For each share purchased, the investors received one warrant to purchase 0.5 shares of common stock at an exercise price of \$3.60 per share. The warrants were immediately exercisable and expire on July 1, 2016. The warrants may be exercised for cash only, or, if a registration statement is not then effective and available for the resale of the shares of common stock issuable upon exercise of the warrants, by surrender of such warrant, or a portion of such warrant, by way of cashless exercise. There is no right to exercise the warrants to the extent that, after giving effect to such exercise the holder would beneficially own in excess of 9.99% of our outstanding shares of common stock or such other limit as may be designated by any particular purchaser. Each holder of the warrants can amend or waive the foregoing limitation by written notice to us, with such waiver taking effect only upon the expiration of a 61-day notice period.

On July 29, 2011, we filed a registration statement with the SEC to register for resale the shares and the shares of common stock issuable upon the exercise of the warrants. The registration statement was declared effective on August 4, 2011. We are obligated to maintain the effectiveness of the registration statement until the investors are able to sell shares and the shares of common stock underlying the warrants without limitation or restriction under Rule 144 of the Securities Act of 1933, as amended ("Rule 144"). There is currently only one investor who is an affiliate of ours and is therefore not able to sell without limitation under Rule 144, and that investor has agreed to waive its right to require us to maintain the effectiveness of the registration statement until it provides notice otherwise.

During the year ended December 31, 2014, warrant holders exercised 460,706 warrants under the cashless exercise provision in the warrant agreement, which resulted in the net issuance of 303,614 shares of common stock and no net cash proceeds to us. During the year ended December 31, 2013, we received \$0.6 million for cash exercises of these warrants. During the year ended December 31, 2012, warrant holders exercised 7,500 warrants under the cashless exercise provision in the warrant agreement, which resulted in the net issuance of 5,034 shares of common stock and no net cash proceeds to us.

[Table of Contents](#)

HERON THERAPEUTICS, INC.
NOTES TO FINANCIAL STATEMENTS

2012 Private Placement

In July 2012, we sold approximately 5.1 million shares of our common stock at a purchase price of \$10.50 per share, resulting in net proceeds of approximately \$50.5 million (net of approximately \$3.1 million in issuance costs). On August 24, 2012, we filed a registration statement with the SEC to register these shares for resale. The registration statement was declared effective on September 6, 2012.

2013 Common Stock Offering

In November 2013, we sold approximately 7.7 million shares of our common stock at a public offering price of \$8.00 per share. We received total net proceeds of approximately \$57.8 million (net of approximately \$3.9 million in issuance costs). The offering was made pursuant to an effective registration statement, which was previously filed with the SEC and was declared effective.

2014 Common Stock Offering

In June 2014, we sold approximately 4.8 million shares of our common stock at a public offering price of \$11.75 per share. In addition, as a component of the offering, we sold 600,000 pre-funded warrants to purchase shares of our common stock at a public offering price of \$11.74 per share. The pre-funded warrants have an exercise price of \$0.01 per share and are exercisable for seven years from the date of issuance. We received total net proceeds of approximately \$58.9 million (net of approximately \$4.0 million in issuance costs) from the sale of the common stock and the pre-funded warrants. The offering was made pursuant to an effective registration statement, which was previously filed with the SEC and was declared effective.

Common Stock Reserved for Future Issuance

Shares of Company common stock reserved for future issuance at December 31, 2014 were as follows:

	Number of Shares
Stock options outstanding	7,918,004
Stock options available for grant	1,333,212
Employee stock purchase plan	29,893
Warrants outstanding	4,108,147
Common stock underlying Convertible Notes outstanding	6,676,845
Total shares reserved for future issuance	<u>20,066,101</u>

[Table of Contents](#)

HERON THERAPEUTICS, INC.
NOTES TO FINANCIAL STATEMENTS

Warrants

The following table summarizes the warrants outstanding as of December 31, 2014:

	Number of Shares Outstanding	Exercise Price	Expiration Date
Issued to private placement investors in October 2009	198,860	\$ 17.60	01/07/2015
Issued to private placement investors in July 2011	3,289,287	\$ 3.60	07/01/2016
Issued in a public offering in June 2014	600,000	\$ 0.01	06/30/2021
Other	20,000	\$ 13.80	08/01/2015
Total warrants outstanding	4,108,147		

The weighted-average exercise price of warrants outstanding as of December 31, 2014 was \$3.80.

Employee Stock Purchase Plan

In 1997 our stockholders approved our Employee Stock Purchase Plan (the "ESPP"). In December 2007, May 2009, June 2011 and May 2014, our stockholders authorized increases in the number of shares reserved for issuance under the ESPP by 5,000, 10,000, 25,000 and 25,000 shares, respectively, for a total of 75,000 shares reserved at December 31, 2014. Under the terms of the ESPP, employees can elect to have up to a maximum of 10% of their base earnings withheld to purchase our common stock. The purchase price of the stock is 85% of the lower of the closing prices for our common stock on: (i) the first trading day in the enrollment period, as defined in the ESPP, in which the purchase is made, or (ii) the purchase date. The length of the enrollment period is six months. Enrollment dates are the first business day of May and November and the first enrollment date was April 30, 1997. Approximately 24% of eligible employees participated in the ESPP in 2014. Under the ESPP, we issued 12,028, 5,630 and 4,270 shares in 2014, 2013 and 2012, respectively. The weighted-average exercise price per share of the purchase rights exercised during 2014, 2013 and 2012 was \$7.59, \$6.12 and \$5.21, respectively. As of December 31, 2014, 45,107 shares of common stock have been issued under the ESPP and 29,893 shares of common stock are available for future issuance.

Stock Option Plans

We currently have one stock option plan from which we can grant options and restricted stock awards to employees, officers, directors and consultants. In December 2007, the stockholders approved our 2007 Equity Incentive Plan (the "2007 Plan") at which time a maximum of 150,000 shares of common stock were available for grant. In May 2010, June 2011 and May 2014, our stockholders approved amendments to our 2007 Plan to increase the maximum number of shares of common stock available for grant by 100,000, 4,500,000 and 1,750,000 shares of common stock, respectively, resulting in an aggregate of 6,500,000 shares of common stock authorized for issuance as of December 31, 2014. At December 31, 2014, there were 1,333,212 shares available for future grant under the 2007 Plan. Any shares that are issuable upon exercise of options granted that expire, are cancelled, or are received back by us pursuant to a net exercise of options, are available for future grant and issuance.

[Table of Contents](#)

HERON THERAPEUTICS, INC.
NOTES TO FINANCIAL STATEMENTS

We also granted stock options and restricted stock awards under the 2002 Stock Incentive Plan (the "2002 Plan") in prior years. The remaining shares available to be granted under the 2002 Plan expired in February 2012.

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

A summary of our stock option activity and related data follows:

	Outstanding Options	
	Number	Weighted-
	of Shares	Average
		Exercise
		Price
Balance at December 31, 2011	2,505,283	\$ 6.13
Granted	1,874,246	11.61
Exercised	—	—
Cancelled	(55,655)	9.56
Balance at December 31, 2012	4,323,874	8.46
Granted	4,256,971	8.08
Exercised	(537,029)	5.20
Cancelled	(1,688,135)	9.45
Balance at December 31, 2013	6,355,681	8.22
Granted	3,181,001	9.40
Exercised	(756,593)	6.34
Cancelled	(862,085)	9.88
Balance at December 31, 2014	<u>7,918,004</u>	\$ 8.69

For the year ended December 31, 2014, option holders exercised 756,593 stock options, a portion of which were exercised under the cashless exercise provision of the 2007 Plan, resulting in the net issuance of 587,997 shares of common stock and cash proceeds to us of approximately \$3.1 million.

For the year ended December 31, 2014, options cancelled (included in the above table) consisted of 806,507 options forfeited with a weighted-average exercise price of approximately \$9.06 and 55,578 options expired with a weighted-average exercise price of approximately \$21.64.

[Table of Contents](#)

HERON THERAPEUTICS, INC.
NOTES TO FINANCIAL STATEMENTS

As of December 31, 2014, options exercisable have a weighted-average remaining contractual term of 6.3 years. The total intrinsic value of stock option exercises, which is the difference between the exercise price and closing price of our common stock on the date of exercise, during the years ended December 31, 2014 and 2013, was approximately \$3,377,000 and \$1,720,000, respectively. There were no exercises during the year ended December 31, 2012. As of December 31, 2014 and 2013, the total intrinsic value of options outstanding and exercisable was approximately \$14,654,000 and \$4,943,000, respectively, which is the difference between the exercise price and closing price of our common stock.

Years Ended December 31,	2014		2013		2012	
	Options	Weighted-Average Exercise Price	Options	Weighted-Average Exercise Price	Options	Weighted-Average Exercise Price
Exercisable at end of year	2,237,901	\$ 9.01	1,770,597	\$ 8.67	1,142,099	\$ 7.98
Options vested or expected to vest	7,841,074	\$ 8.69	6,292,296	\$ 8.22	4,283,344	\$ 8.45

Exercise prices and weighted-average remaining contractual lives for the options outstanding as of December 31, 2014 were:

Options Outstanding	Range of Exercise Prices	Weighted-Average Remaining Contractual Life (in years)	Weighted-Average Exercise Price	Options Exercisable	Weighted-Average Exercise Price of Options Exercisable
953,090	\$ 3.80 – \$ 7.00	5.92	\$ 5.78	662,840	\$ 5.34
2,511,808	\$ 7.20	8.01	7.20	531,578	7.20
2,428,458	\$ 7.61 – \$ 9.05	9.12	8.87	204,669	8.95
1,991,338	\$ 9.20 – \$ 15.40	7.42	11.27	805,504	12.09
33,310	\$15.41 – \$139.20	1.05	36.97	33,310	36.97
<u>7,918,004</u>	<u>\$ 3.80 – \$139.20</u>	<u>7.92</u>	<u>8.69</u>	<u>2,237,901</u>	<u>9.01</u>

At December 31, 2014, we had reserved 7,918,004 shares of common stock for future issuance upon exercise of outstanding options granted under the 2002 and 2007 Plans, as well as the non-plan grants.

[Table of Contents](#)

HERON THERAPEUTICS, INC.
NOTES TO FINANCIAL STATEMENTS

Valuation and Expense Information

The following table summarizes stock-based compensation expense related to stock-based payment awards granted pursuant to all of our equity compensation arrangements for the years ended December 31, 2014, 2013 and 2012 (in thousands):

December 31,	2014	2013	2012
Research and development	\$3,329	\$ 2,562	\$1,617
General and administrative	4,738	8,328	4,115
Stock-based compensation expense included in operating expenses	<u>\$8,067</u>	<u>\$10,890</u>	<u>\$5,732</u>

As of December 31, 2014, there was \$34,073,000 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 2.6 years.

For the years ended December 31, 2014, 2013, and 2012, we estimated the fair value of each option grant and ESPP purchase right on the date of grant using the Black-Scholes option pricing model with the following weighted-average assumptions:

Options:

December 31,	2014	2013	2012
Risk-free interest rate	1.9%	1.1%	0.8%
Dividend yield	—%	—%	—%
Volatility	99.0%	104.2%	106.2%
Expected life (years)	6.0	6.0	5.5

ESPP:

December 31,	2014	2013	2012
Risk-free interest rate	0.1%	0.1%	0.2%
Dividend yield	—%	—%	—%
Volatility	53.8%	76.0%	77.9%
Expected life (years)	0.5	0.5	0.5

The weighted-average fair value of options granted was \$7.40, \$6.53 and \$9.21 for the years ended December 31, 2014, 2013 and 2012, respectively.

The weighted-average fair value of shares purchased through the ESPP was \$3.06, \$3.01 and \$4.00 for the years ended December 31, 2014, 2013 and 2012, respectively.

[Table of Contents](#)

HERON THERAPEUTICS, INC.
NOTES TO FINANCIAL STATEMENTS

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

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

We used our historical stock price to estimate volatility.

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

8. Income Taxes

For the years ended December 31, 2014, 2013 and 2012, we did not record a provision for income taxes because we have incurred operating losses for all three years.

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

December 31,	2014	2013
Deferred tax assets:		
Net operating loss carryforward	\$ 59,513	\$ 31,834
Research and development credits	7,667	4,792
Stock-based compensation	5,128	4,124
Other, net	964	487
Total deferred tax assets	73,272	41,237
Valuation allowance for net deferred tax assets	(73,272)	(41,237)
Net deferred taxes	\$ —	\$ —

Taxes on income vary from the statutory federal income tax rate applied to earnings before tax on income as follows (in thousands):

December 31,	2014	2013	2012
Statutory federal income tax rate of 34%	\$(25,965)	\$(18,796)	\$(7,937)
Stock-based compensation expense	551	513	176
NOL not benefitted	25,085	17,983	7,551
Other, net	329	300	210
Provision for taxes	\$ —	\$ —	\$ —

[Table of Contents](#)

HERON THERAPEUTICS, INC. NOTES TO FINANCIAL STATEMENTS

A valuation allowance is provided when it is more likely than not that the deferred tax assets will not be realized. We have established a valuation allowance to offset net deferred tax assets at December 31, 2014, and 2013 due to the uncertainty of realizing future tax benefits from our net operating loss carryforwards and other deferred tax assets. The net change in the total valuation allowance for the year ended December 31, 2014 and 2013 was an increase of approximately \$32,035,000 and \$22,038,000, respectively.

At December 31, 2014, we had federal and California state net operating loss carryforwards of approximately \$149,573,000 and \$148,402,000, respectively, expiring beginning in 2018 for federal and 2015 for California state purposes. At December 31, 2014, we had federal and California state research credit carryforwards of approximately \$4,676,000 and \$4,493,000, respectively, expiring beginning in 2022 for federal. The California state credits can be carried forward indefinitely.

Internal Revenue Code section 382 places a limitation on the amount of taxable income that can be offset by net operating ("NOL") carryforwards after a change in control (generally greater than 50% change in ownership) of a loss corporation. California has similar rules. Generally, after a control change, a loss corporation cannot deduct NOL carryforwards in excess of the Section 382 limitation. We have performed an IRC Section 382 analysis and determined there were ownership changes in 2007, 2011, and 2013. There may be further ownership changes after December 31, 2014. The limitation in the Federal and state carryforwards associated with the NOL and credit carryforwards reduce the deferred tax assets, which are further offset by a full valuation allowance. The limitation can result in the expiration of the NOLs and credit carryforwards available as of December 31, 2014 before utilization.

We adopted the ASC Topic 740 provisions regarding Uncertainty in Income Taxes as of January 1, 2009. For benefits to be realized, a tax position must be more likely than not to be sustained upon examination. The amount recognized is measured as the largest amount of benefit that is greater than 50 percent likely of being realized upon settlement.

As of December 31, 2014, we had unrecognized tax benefits of \$120,000, and the amount that would impact our effective tax rate, before the consideration of the valuation allowance, is \$120,000.

It is our policy to recognize interest and penalties related to income tax matters in income tax expense. As of December 31, 2014, we had no accrued interest and penalties related to uncertain tax positions.

We file U.S. and state income tax returns with varying statutes of limitations. The tax years from 1997 to 2014 remain open to examination due to the carryover of unused net operating losses and tax credits.

We do not expect any material changes to the estimated amount of liability associated with its uncertain tax positions within the next 12 months.

December 31,	2014	2013
	(in thousands)	
Unrecognized tax benefit:		
Beginning of period	\$ 120	\$ 120
Current year changes	—	—
Prior year changes	—	—
End of Period	\$ 120	\$ 120

[Table of Contents](#)

HERON THERAPEUTICS, INC.
NOTES TO FINANCIAL STATEMENTS

9. Employee Benefit Plan

We have a defined contribution 401K plan (the "Plan") covering substantially all of our employees. In the past three calendar years, we made matching cash contributions equal to 50% of each participant's contribution during the Plan year up to a maximum amount equal to the lesser of 3% of each participant's annual compensation or \$7,800, \$7,650 and \$7,500 for the years 2014, 2013 and 2012, respectively. Such amounts were recorded as expense in the corresponding years. We may also contribute additional discretionary amounts to the Plan as we may determine. For the years ended December 31, 2014, 2013 and 2012, we contributed to the Plan approximately \$181,000, \$134,000 and \$71,000, respectively. No discretionary contributions have been made to the Plan since its inception.

10. Discontinued Operations

For the year ended December 31, 2012, we recognized a gain from discontinued operations of approximately \$1.1 million related to the reversal of a gross profit guaranty from our sale of certain technology in 2000.

11. Summary of Quarterly Financial Data (unaudited)

The following is a summary of the unaudited quarterly results of operations for the years ended December 31, 2014 and 2013:

(In thousands, except per share amounts)

2014	First Quarter	Second Quarter	Third Quarter	Fourth Quarter
Operating expenses:				
Research and development	\$ 11,628	\$ 14,279	\$ 14,731	\$ 14,195
General and administrative	5,694	4,512	4,222	5,300
Loss from operations	(17,322)	(18,791)	(18,953)	(19,495)
Interest income	—	—	—	3
Interest expense	(216)	(220)	(224)	(227)
Other expense	—	—	(17)	(905)
Net loss	<u>\$ (17,538)</u>	<u>\$ (19,011)</u>	<u>\$ (19,194)</u>	<u>\$ (20,624)</u>
Basis and diluted net loss per share	<u>\$ (0.74)</u>	<u>\$ (0.78)</u>	<u>\$ (0.66)</u>	<u>\$ (0.71)</u>

[Table of Contents](#)

HERON THERAPEUTICS, INC.
NOTES TO FINANCIAL STATEMENTS

(In thousands, except per share amounts)

2013	First Quarter	Second Quarter	Third Quarter	Fourth Quarter
Operating expenses:				
Research and development	\$ 7,065	\$ 10,748	\$ 6,165	\$ 8,538
General and administrative	5,687	4,461	6,500	5,293
Loss from operations	(12,752)	(15,209)	(12,665)	(13,831)
Interest income	1	1	—	—
Interest expense	(202)	(205)	(209)	(212)
Net loss	<u>\$ (12,953)</u>	<u>\$ (15,413)</u>	<u>\$ (12,874)</u>	<u>\$ (14,043)</u>
Basis and diluted net loss per share	<u>\$ (0.85)</u>	<u>\$ (1.01)</u>	<u>\$ (0.84)</u>	<u>\$ (0.75)</u>

[Table of Contents](#)

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

None.

ITEM 9A. CONTROLS AND PROCEDURES.

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

Our management, with the participation of our principal executive and principal financial and accounting officers, has evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934 (the "Exchange Act")) as of December 31, 2014. Based on this evaluation, our principal executive and principal financial and accounting officers concluded that our disclosure controls and procedures were effective as of December 31, 2014.

There was no change in our internal control over financial reporting during the quarter ended December 31, 2014 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

(b) Management Report on Internal Control Over Financial Reporting

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

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

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

[Table of Contents](#)

Our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2014. In making this assessment, our management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission in Internal Control-Integrated Framework (2013 Framework).

Based on our assessment, management concluded that, as of December 31, 2014, our internal control over financial reporting was effective based on those criteria.

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

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

The Board of Directors and Stockholders of
Heron Therapeutics, Inc.

We have audited Heron Therapeutics, Inc.'s internal control over financial reporting as of December 31, 2014, based on criteria established in *Internal Control – Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission (the COSO criteria). Heron Therapeutics, Inc.'s management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying *Management Report on Internal Control Over Financial Reporting* included in Item 9A. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit.

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

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

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

[Table of Contents](#)

In our opinion, Heron Therapeutics, Inc. maintained, in all material respects, effective internal control over financial reporting as of December 31, 2014, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the balance sheets of Heron Therapeutics, Inc. as of December 31, 2014 and 2013, and the related statements of operations, stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2014, and our report dated March 12, 2015, expressed an unqualified opinion thereon.

/s/ OUM & Co. LLP
San Francisco, California
March 12, 2015

ITEM 9B. OTHER INFORMATION.

None.

[Table of Contents](#)

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE.

Information required by this item will be contained in our Definitive Proxy Statement for our 2015 Annual Meeting of Stockholders, to be filed pursuant to Regulation 14A with the SEC within 120 days of December 31, 2014. Such information is incorporated herein by reference.

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

ITEM 11. EXECUTIVE COMPENSATION.

Information required by this item will be contained in our Definitive Proxy Statement for our 2015 Annual Meeting of Stockholders, to be filed pursuant to Regulation 14A with the SEC within 120 days of December 31, 2014. Such information is incorporated herein by reference.

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

Additional information required by this item will be contained in our Definitive Proxy Statement for our 2015 Annual Meeting of Stockholders, to be filed pursuant to Regulation 14A with the SEC within 120 days of December 31, 2014. Such information is incorporated herein by reference.

Securities Authorized for Issuance Under Equity Compensation Plans

The following table contains information regarding our equity compensation plans as of December 31, 2014.

	Number of Securities to be Issued upon Exercise of Outstanding Options	Weighted- Average Exercise Price of Outstanding Options	Number of Securities Remaining Available for Future Issuance under Equity Compensation Plans (Excluding Securities Reflected in the First Column)
Equity compensation plans approved by security holders			
Stock option and awards plans (1)	4,064,883	\$ 9.16	1,333,212
Employee stock purchase plan	—	—	29,893
Equity compensation plans not approved by security holders (2)	3,853,121	\$ 8.19	—
Total	7,918,004	\$ 8.69	1,363,105

[Table of Contents](#)

- (1) Consists of awards granted under the 2002 Plan and the 2007 Plan.
- (2) Consists of non-plan grants made to certain employees in 2013 and 2014. These grants were made with the same terms as stock option grants made under the 2007 Plan.

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

Information required by this item will be contained in our Definitive Proxy Statement for our 2015 Annual Meeting of Stockholders, to be filed pursuant to Regulation 14A with the SEC within 120 days of December 31, 2014. Such information is incorporated herein by reference.

ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES.

Information required by this item will be contained in our Definitive Proxy Statement for our 2015 Annual Meeting of Stockholders, to be filed pursuant to Regulation 14A with the SEC within 120 days of December 31, 2014. Such information is incorporated herein by reference.

[Table of Contents](#)

PART IV

ITEM 15. EXHIBITS, FINANCIAL STATEMENT SCHEDULES.

1. Financial Statements.

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

2. Financial Statement Schedules.

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

3. Exhibits.

The exhibit index attached to this report is incorporated by reference herein.

[Table of Contents](#)

EXHIBIT INDEX

FORM 10-K ANNUAL REPORT

Exhibit Number	Document Description
3.1	Certificate of Incorporation, as amended through July 29, 2009 (Incorporated by reference to our Quarterly Report on Form 10-Q for the quarter ended June 30, 2009, as Exhibit 3.1, filed on August 4, 2009)
3.2	Bylaws (Incorporated by reference to our Registration Statement on Form S-1 (Registration No. 33-15429), as an Exhibit)
3.3	Amended and Restated Certificate of Designation, Preferences, and Rights of Series A Preferred Stock (Incorporated by reference to our Current Report on Form 8-K, as Exhibit 3.C, filed on December 19, 2006)
3.4	Certificate of Amendment of Certificate of Incorporation (Incorporated by reference to our Current Report on Form 8-K, as Exhibit 3.1, filed on June 30, 2011)
3.5	Certificate of Amendment of Certificate of Incorporation (Incorporated by reference to our Current Report on Form 8-K, as Exhibit 3.1, filed on January 13, 2014)
4.1	Common Stock Certificate (Incorporated by reference to our Registration on Form S-3 (Registration No. 333-162968), as Exhibit 4.1, filed on November 6, 2009)
4.2	Form of Warrant to Purchase Shares of Common Stock (Incorporated by reference to our Current Report on Form 8-K, as Exhibit 10.3, filed on October 22, 2009)
10.1*	1997 Employee Stock Purchase Plan, as amended to date (Incorporated by reference to our Definitive Proxy on Schedule 14A, as Exhibit B, filed on April 24, 2014)
10.2	Lease Agreement between Registrant and Metropolitan Life Insurance Company for lease of Registrant's offices in Redwood City dates as of November 17, 1997 (Incorporated by reference to our Annual Report on Form 10-K for the year ended December 31, 1997, as Exhibit 10-E, filed on March 30, 1998)
10.3*	2002 Equity Incentive Plan dated June 13, 2002 (Incorporated by reference to our Registration on Form S-8 (Registration No. 333-90428), as Exhibit 99.1, filed on June 13, 2002)
10.4*	Form of Amended and Restated 2007 Equity Incentive Plan (Incorporated by reference to our Definitive Proxy on Schedule 14A, as Exhibit A, filed on April 24, 2014)
10.5*	Form of 2007 Equity Incentive Plan Stock Option Agreement (Incorporated by reference to our Registration on Form S-8 (Registration No. 333-148660), as Exhibit 4.3, filed on January 14, 2008)
10.6*	Form of 2007 Equity Incentive Plan Restricted Stock Unit Agreement (Incorporated by reference to our Registration on Form S-8 (Registration No. 333-148660), as Exhibit 4.4, filed on January 14, 2008)
10.7*	Form of 2007 Equity Incentive Plan Restricted Stock Award Agreement (Incorporated by reference to our Annual Report on Form 10-K for the year ended December 31, 2007, as Exhibit 10-O, filed on March 31, 2008)

Table of Contents

<u>Exhibit Number</u>	<u>Document Description</u>
10.8*	Form of 2002 Equity Incentive Plan Stock Option Agreement (Incorporated by reference to our Annual Report on Form 10-K for the year ended December 31, 2007, as Exhibit 10-P, filed on March 31, 2008)
10.9*	Form of Indemnification Agreement (Incorporated by reference to our Annual Report on Form 10-K for the year ended December 31, 2007, as Exhibit 10-S, filed on March 31, 2008)
10.10	Securities Purchase Agreement, dated as of October 19, 2009, by and among the Registrant and the purchasers listed therein (Incorporated by reference to our Current Report on Form 8-K, as Exhibit 10.1, filed on October 22, 2009)
10.11	Registration Rights Agreement, dated as of October 22, 2009, by and among the Registrant and the purchasers listed therein (Incorporated by reference to our Current Report on Form 8-K, as Exhibit 10.2, filed on October 22, 2009)
10.12	Securities Purchase Agreement, dated as of April 24, 2011, by and among the Company and the purchasers listed therein (Incorporated by reference to our Current Report on Form 8-K, as Exhibit 10.1, filed on April 28, 2011)
10.13	Form of Senior Secured Convertible Note due 2021 (Incorporated by reference to our Current Report on Form 8-K, as Exhibit 10.2, filed on April 28, 2011)
10.14	Securities Agreement, dated as of April 24, 2011, by and between the Company and Tang Capital Partners, LP, as Agent for the Purchasers (Incorporated by reference to our Current Report on Form 8-K, as Exhibit 10.3, filed on April 28, 2011)
10.15	Second Amendment to Lease, effective as of April 1, 2011, by and between the Company and Metropolitan Life Insurance Company (Incorporated by reference to our Current Report on Form 8-K, as Exhibit 10.4, filed on April 28, 2011)
10.16*	Management Retention Agreement, dated as of April 25, 2011, by and between the Company and Michael A. Adam (Incorporated by reference to our Current Report on Form 8-K, as Exhibit 10.6, filed on April 28, 2011)
10.17	Securities Purchase Agreement, dated June 29, 2011, by and between the Company and the purchasers listed on Schedule I thereto (Incorporated by reference to our Current Report on Form 8-K, as Exhibit 10.1, filed on June 30, 2011)
10.18	Amendment to Senior Secured Convertible Note Due 2021, dated June 29, 2011, by and between the Company and the purchasers named in the Securities Purchase Agreement, dated April 24, 2011, by and among the Company and the purchasers listed therein (Incorporated by reference to our Current Report on Form 8-K, as Exhibit 10.2, filed on June 30, 2011)
10.19	Third Amendment to Lease, effective as of July 28, 2011, by and between the Company and Metropolitan Life Insurance Company (Incorporated by reference to our Current Report on Form 8-K, as Exhibit 10.1, filed on August 3, 2011)

Table of Contents

<u>Exhibit Number</u>	<u>Document Description</u>
10.20	Securities Purchase Agreement, dated July 25, 2012, by and between the Company and the purchasers named therein (Incorporated by reference to our Current Report on Form 8-K, as Exhibit 10.1, filed on July 25, 2012)
10.21	Registration Rights Agreement, dated July 25, 2012, by and between the Company and the purchasers named therein (Incorporated by reference to our Current Report on Form 8-K, as Exhibit 10.2, filed on July 25, 2012)
10.22*	Management Retention Agreement as of December 3, 2012, by and between the Company and Mark S. Gelder, M.D. (Incorporated by reference to our Annual Report on Form 10-K for the year ended December 31, 2012, as Exhibit 10-AH, filed on March 1, 2013)
10.23*	Executive Employment Agreement, dated May 1, 2013, by and between the Company and Barry D. Quart, Pharm.D. (Incorporated by reference to our Quarterly Report on Form 10-Q for the quarter ended March 31, 2013, as Exhibit 10-AI, filed on May 10, 2013)
10.24*	Executive Employment Agreement, dated May 1, 2013, by and between the Company and Robert H. Rosen (Incorporated by reference to our Quarterly Report on Form 10-Q for the quarter ended March 31, 2013, as Exhibit 10-AJ filed on May 10, 2013)
10.25*	Executive Employment Agreement, dated May 1, 2013, by and between the Company and Stephen Davis (Incorporated by reference to our Quarterly Report on Form 10-Q for the quarter ended March 31, 2013, as Exhibit 10-AK, filed on May 10, 2013)
10.26	Form of Non-Qualified Stock Option Agreement (Incorporated by reference to our Quarterly Report on Form 10-Q for the quarter ended June 30, 2013, as Exhibit 10-AL, filed on August 8, 2013)
10.27*	Amendment to Management Retention Agreement, dated as of April 25, 2011, as amended May 29, 2013 (as amended, the Retention Agreement) (Incorporated by reference to our Quarterly Report on Form 10-Q for the quarter ended June 30, 2013, as Exhibit 10-AM, filed on August 8, 2013)
10.28*	Offer Letter dated November 10, 2012 between the Company and Mark S. Gelder, M.D. (Incorporated by reference to our Annual Report on Form 10-K for the year ended December 31, 2013, as Exhibit 10-AE, filed on March 7, 2014)
10.29*	Offer Letter dated October 16, 2013 between the Company and Brian G. Drazba (Incorporated by reference to our Annual Report on Form 10-K for the year ended December 31, 2013, as Exhibit 10-AF, filed on March 7, 2014)
10.30*	Management Retention Agreement as of October 23, 2013, by and between the Company and Brian G. Drazba (Incorporated by reference to our Annual Report on Form 10-K for the year ended December 31, 2013, as Exhibit 10-AG, filed on March 7, 2014)
10.31*	Executive Employment Agreement, dated November 1, 2013, by and between the Company and Paul Marshall (Incorporated by reference to our Annual Report on Form 10-K for the year ended December 31, 2013, as Exhibit 10-AH, filed on March 7, 2014)

[Table of Contents](#)

<u>Exhibit Number</u>	<u>Document Description</u>
23.1	Consent of Independent Registered Public Accounting Firm (OUM & Co. LLP)
24.1	Power of Attorney (included in signature page hereto)
31.1	Certification Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
31.2	Certification Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
32.1	Certification Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
101.INS	XBRL Instance Document
101.SCH	XBRL Taxonomy Extension Schema Document
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	XBRL Taxonomy Extension Label Linkbase Document
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document

* Management contract or compensatory plan, contract or arrangement.

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in the Registration Statements on Form S-1 (Nos. 333-174288 and 333-175905), Form S-3 (Nos. 333-162968, 333-167890, 333-183549, 333-195928, and 333-198862), and Form S-8 (Nos. 333-35151, 333-90428, 333-118546, 333-127574, 333-137954, 333-148660, 333-162610, 333-167515, 333-176365, 333-176366, 333-190549, 333-198853, and 333-202588) of Heron Therapeutics, Inc. of our reports dated March 12, 2015 relating to the financial statements and the effectiveness of Heron Therapeutics, Inc.'s internal control over financial reporting, which appear in this Annual Report on Form 10-K.

/s/ OUM & CO. LLP

San Francisco, California

March 12, 2015

SECTION 302 CERTIFICATION

I, Barry D. Quart, certify that:

1. I have reviewed this Annual Report on Form 10-K of Heron Therapeutics, Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
 - a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
 - b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
 - c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
 - d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
 - a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
 - b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 13, 2015

/s/ Barry D. Quart

Barry D. Quart, Pharm.D.

Chief Executive Officer

SECTION 302 CERTIFICATION

I, Brian G. Drazba, certify that:

1. I have reviewed this Annual Report on Form 10-K of Heron Therapeutics, Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
 - a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
 - b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
 - c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
 - d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
 - a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
 - b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 13, 2015

/s/ Brian G. Drazba

Brian G. Drazba

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

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

Each of the undersigned, in his capacity as Chief Executive Officer and Chief Financial Officer, 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 Annual Report of the Registrant on Form 10-K for the year ended December 31, 2014 (the "Report"), which accompanies this certification, fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
- the information contained in the Report fairly presents, in all material respects, the financial condition of the Registrant at the end of such year and the results of operations of the Registrant for such year.

Dated: March 13, 2015

/s/ Barry D. Quart

Barry D. Quart, Pharm.D.
Chief Executive Officer

/s/ Brian G. Drazba

Brian G. Drazba
Vice President, Finance and
Chief Financial 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.