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Filed pursuant to Rule 424(b)(5)
Registration Statement No. 333-219172

CALCULATION OF REGISTRATION FEE

Title of Securities to be Registered	Amount to be Registered	Proposed Maximum Offering Price Per Share	Proposed Maximum Aggregate Offering Price	Amount of Registration Fee(1)
Common Stock, $0.01 par value per share	5,822,785	$30.75	$179,050,638.75	$22,291.80

(1) Estimated in accordance with Rule 457(c) solely for purposes of calculating the registration fee. The maximum price per share and the maximum aggregate offering price are based on the average of the high and low sale price of the registrant's common stock as reported on The NASDAQ Capital Market on June 20, 2018.

PROSPECTUS SUPPLEMENT
(To Prospectus dated July 6, 2017)

5,063,292 Shares

Common Stock

We are offering 5,063,292 shares of our common stock.

Our common stock is listed on The Nasdaq Capital Market under the symbol "HRTX." On June 22, 2018, the last reported sale price of our common stock was $41.35 per share.

Investing in our securities involves certain risks. See "Risk Factors" beginning on Page S-12 of this prospectus supplement and in the accompanying prospectus, and in the other documents that are incorporated by reference and any related free writing prospectus, for certain risks you should consider. You should read the entire prospectus supplement and the accompanying prospectus, including any information incorporated by reference, carefully before you make your investment decision.

The underwriter has agreed to purchase 5,063,292 shares of our common stock from us at a price of $38.445 per share, which will result in approximately $194.7 million of net proceeds to us, before deducting estimated offering expenses payable by us. The underwriter may offer the shares of common stock from time to time to purchasers directly or through agents, or through brokers in brokerage transactions on The Nasdaq Capital Market, or to dealers in negotiated transactions, or in a combination of such methods of sale or otherwise, at a fixed price or prices, which may be changed, or at market prices prevailing at the time of sale, at prices related to such prevailing market prices or at negotiated prices. See "Underwriting."

The underwriter may also exercise its option to purchase up to an additional 759,493 shares of common stock from us, at a price of $38.445 per share, for 30 days after the date of this prospectus supplement.

Neither the U.S. Securities and Exchange Commission nor any other regulatory body has approved or disapproved of these securities or passed on the accuracy or adequacy of this prospectus supplement or the accompanying prospectus. Any representation to the contrary is a criminal offense.

The shares will be ready for delivery on or about June 28, 2018.

Sole Book-Running Manager

Jefferies

Prospectus Supplement dated June 25, 2018.

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You should rely only on the information contained in this prospectus supplement and the accompanying prospectus, including any information incorporated by reference, and in any free writing prospectus that we have authorized for use in connection with this offering. We have not, and the underwriter has not, authorized anyone to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. You should not assume that the information contained in this prospectus supplement and the accompanying prospectus, or in any free writing prospectus that we have authorized for use in connection with this offering, is accurate as of any date other that the date of those respective documents, or that information contained in any document incorporated by reference is accurate as of any date other than the date of the document incorporated by reference. Our business, financial condition, results of operations and prospects may have changed since those dates. We are not, and the underwriter is not, making offers to sell these securities in any jurisdiction in which an offer or solicitation is not authorized or permitted or in which the person making such offer or solicitation is not qualified to do so or to any person to whom it is unlawful to make such an offer or solicitation. You should read this prospectus supplement, the accompanying prospectus, including any information incorporated by reference, and any free writing prospectus that we have authorized for use in connection with this offering in their entirety before making an investment decision. You should also read and consider the information in the documents to which we have referred you in the sections entitled “Information Incorporated by Reference” and “Where You Can Find Additional Information.”

ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus form part of a registration statement on Form S-3 that we filed with the U.S. Securities and Exchange Commission (the "SEC") using a shelf registration process. This document contains two parts. The first part consists of this prospectus supplement, which provides you with specific information about this offering. The second part consists of the accompanying prospectus, which provides more general information, some of which may not apply to this offering. Generally, when we refer only to the "prospectus," we are referring to both parts combined. This prospectus supplement may add, update or change information contained in the accompanying prospectus. To the extent that any statement we make in this prospectus supplement is inconsistent with statements made in the accompanying prospectus, or any documents incorporated by reference, the statements made in this prospectus supplement will be deemed to modify or supersede those made in the accompanying prospectus, including the documents incorporated by reference therein. Information in any document we subsequently file that is incorporated by reference shall modify or supersede the information in the prospectus supplement, the accompanying prospectus and documents incorporated by reference prior to such subsequent filing.

In this prospectus supplement, "Heron," the "Company," "we," "us," and "our" and similar terms refer to Heron Therapeutics, Inc. References to our "common stock" refer to the common stock of Heron Therapeutics, Inc. Heron Therapeutics®, the Heron logo, SUSTOL®, CINVANTI® and Biochronomer® are our trademarks. All other trademarks appearing or incorporated by reference into this prospectus supplement are the property of their respective owners.

All references in this prospectus supplement to our financial statements include, unless the context indicates otherwise, the related notes.

The industry and market data and other statistical information contained in this prospectus supplement, the accompanying prospectus and the documents we incorporate by reference are based on management's own estimates, independent publications and reports by market research firms or other published independent sources and, in each case, are believed by management to be reasonable estimates. Although we believe these sources are reliable, we have not independently verified the information.

NOTE REGARDING FORWARD-LOOKING STATEMENTS

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

Factors that might cause these differences include the following:

- our ability to successfully commercialize, market and achieve market acceptance of SUSTOL® (granisetron) extended-release injection ("SUSTOL"), CINVANTI® (aprepitant) injectable emulsion ("CINVANTI") and future product candidates, including our positioning relative to competing products;
- estimates of the outcome of the commercial launch of CINVANTI;
- whether the HTX-011 Phase 2 and Phase 3 study results are indicative of the results in future studies;
- the timing of the New Drug Application ("NDA") submission to the U.S. Food and Drug Administration ("FDA") for HTX-011 and potential regulatory approval for and commercial launch of HTX-011;
- the potential market opportunities for SUSTOL, CINVANTI and HTX-011;
- our competitors' activities, including decisions as to the timing of competing product launches, generic entrants, pricing and discounting;
- whether safety and efficacy results of our clinical studies and other required tests for approval of our product candidates provide data to warrant progression of clinical trials, potential regulatory approval or further development of any of our product candidates;
- our ability to develop, acquire and advance product candidates into, and successfully complete, clinical studies, and our ability to submit for and obtain regulatory approval for product candidates, in our anticipated timing, or at all;
- our ability to meet the postmarketing study requirements within the FDA's mandated timelines and to obtain favorable results and comply with standard postmarketing requirements including U.S. federal advertising and promotion laws, federal and state anti-fraud and abuse laws, healthcare information privacy and security laws, safety information, safety surveillance and disclosure of payments or other transfers of value to healthcare professionals and entities for SUSTOL, CINVANTI or any of our product candidates;
- our ability to successfully develop and achieve regulatory approval for other future product candidates utilizing our proprietary Biochronomer® sustained-release drug delivery technology ("Biochronomer technology");
- our ability to establish key collaborations and vendor relationships 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 operate in non-U.S. jurisdictions in which we may choose to do business, including compliance with applicable regulatory requirements and laws;
- uncertainties associated with obtaining and enforcing patents to protect our products, and our ability to successfully defend ourselves against unforeseen third-party infringement claims;
- our estimates regarding our capital requirements; and
- our ability to obtain additional financing and raise capital as necessary to fund operations or pursue business opportunities.

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

This prospectus supplement may also contain estimates, projections and other information concerning our industry, our business and the markets for certain diseases, including data regarding the estimated size of those markets. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances reflected in this information.

PROSPECTUS SUMMARY

The following summary of our business highlights certain of the information contained elsewhere in or incorporated by reference into this prospectus supplement and the accompanying prospectus. Because this is only a summary, however, it does not contain all of the information that may be important to you. You should carefully read this prospectus supplement and the accompanying prospectus, including the documents incorporated by reference, which are described under "Information Incorporated By Reference" and "Where You Can Find Additional Information" in the accompanying prospectus. In particular, you should carefully consider the matters discussed in the section of this prospectus supplement titled "Risk Factors" and in the accompanying prospectus and periodic reports incorporated herein by reference.

Our Company

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

On August 9, 2016, our first commercial product, SUSTOL, was approved by the FDA. SUSTOL is indicated in combination with other antiemetics in adults for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic chemotherapy ("MEC") or anthracycline and cyclophosphamide ("AC") combination chemotherapy regimens. SUSTOL is an extended-release, injectable 5-HT_3 receptor antagonist that utilizes Heron's Biochronomer® polymer-based drug delivery technology to maintain therapeutic levels of granisetron for ³5 days. We commenced commercial sales of SUSTOL in the U.S. in October 2016.

On November 9, 2017, our second commercial product, CINVANTI, was approved by the FDA. CINVANTI, in combination with other antiemetic agents, is indicated in adults for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy ("HEC"), including high-dose cisplatin and nausea and vomiting associated with initial and repeat courses of MEC. CINVANTI is an intravenous formulation of aprepitant, a substance P/neurokinin-1 ("NK_1") receptor antagonist. CINVANTI is the only IV formulation of an NK_1 receptor antagonist indicated for the prevention of acute and delayed nausea and vomiting associated with HEC and nausea and vomiting associated with MEC that is free of polysorbate 80 or any other synthetic surfactant. We commenced commercial sales of CINVANTI in the U.S. in January 2018.

HTX-011, which utilizes Heron's proprietary Biochronomer® polymer-based drug delivery technology, is an investigational, long-acting, extended-release formulation of the local anesthetic bupivacaine in a fixed-dose combination with the anti-inflammatory meloxicam for the management of postoperative pain. By delivering sustained levels of both a potent anesthetic and a local anti-inflammatory agent directly to the site of tissue injury, HTX-011 was designed to deliver superior pain relief while reducing the need for systemically administered pain medications such as opioids, which carry the risk of harmful side effects, abuse and addiction.

In March 2018, Heron reported positive topline results from EPOCH1 and EPOCH2, its pivotal Phase 3 studies of HTX-011 in bunionectomy and hernia repair, respectively. All primary and key secondary endpoints were achieved in these studies. Furthermore, HTX-011 is the only long-acting local anesthetic to demonstrate in Phase 3 studies significantly reduced pain and opioid use compared to bupivacaine solution, the current standard-of-care local anesthetic for postoperative pain control, through 72 hours. HTX-011 was well tolerated in both studies, with a safety profile comparable to placebo and bupivacaine solution. In June 2018, Heron reported positive topline results from its Phase 2b studies of HTX-011 in subjects undergoing total knee arthroplasty and

breast augmentation. HTX-011 was granted Fast Track designation by the FDA in the fourth quarter of 2017 and Breakthrough Therapy designation by the FDA in the second quarter of 2018. In the second half of 2018, Heron expects to submit an NDA to the FDA for HTX-011.

CINV Product Portfolio

SUSTOL

SUSTOL was our first commercial product. SUSTOL was approved by the FDA on August 9, 2016, and we commenced commercial sales in the U.S. in October 2016.

SUSTOL is indicated in combination with other antiemetics in adults for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of MEC or AC combination chemotherapy regimens. SUSTOL is an extended-release, injectable 5-hydroxytryptamine type 3 ("5-HT_3") receptor antagonist that utilizes our Biochronomer technology to maintain therapeutic levels of granisetron for ³5 days. The SUSTOL global Phase 3 development program was comprised of two, large, guideline-based clinical studies that evaluated SUSTOL's efficacy and safety in more than 2,000 patients with cancer. SUSTOL's efficacy in preventing nausea and vomiting was evaluated in both the acute phase (0-24 hours following chemotherapy) and the delayed phase (24-120 hours following chemotherapy).

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

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

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

CINVANTI

CINVANTI is our second commercial product. CINVANTI was approved by the FDA on November 9, 2017, and we commenced commercial sales in the U.S. in January 2018.

CINVANTI, in combination with other antiemetic agents, is indicated in adults for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of HEC including high-dose cisplatin and nausea and vomiting associated with initial and repeat courses of MEC.

CINVANTI is an intravenous formulation of aprepitant, an NK_1 receptor antagonist. CINVANTI is the first intravenous ("IV") formulation to directly deliver aprepitant, the active ingredient in EMEND® capsules. Aprepitant (including its prodrug, fosaprepitant) is the only single-agent NK_1 receptor antagonist to significantly

reduce nausea and vomiting in both the acute phase (0 – 24 hours after chemotherapy) and the delayed phase (24 – 120 hours after chemotherapy). CINVANTI is the only IV formulation of an NK_1 receptor antagonist indicated for the prevention of acute and delayed nausea and vomiting associated with HEC and nausea and vomiting associated with MEC that is free of polysorbate 80 or any other synthetic surfactant.

NK_1 receptor antagonists are typically used in combination with 5-HT3 receptor antagonists. The only other injectable NK_1 receptor antagonist currently approved in the U.S. for both acute and delayed CINV, EMEND® IV (fosaprepitant), contains polysorbate 80, a synthetic surfactant, which has been linked to hypersensitivity reactions, including anaphylaxis, and infusion site reactions. The CINVANTI formulation does not contain polysorbate 80 or any other synthetic surfactant. Our CINVANTI data has demonstrated the bioequivalence of CINVANTI to EMEND IV, supporting its efficacy for the prevention of both acute and delayed nausea and vomiting associated with HEC and nausea and vomiting associated with MEC. Results also showed CINVANTI was better tolerated in healthy volunteers than EMEND IV, with significantly fewer adverse events reported with CINVANTI.

Pain Management Product Portfolio

HTX-011

HTX-011, which utilizes our Biochronomer technology, is an investigational, long-acting, extended-release formulation of the local anesthetic bupivacaine in a fixed-dose combination with the anti-inflammatory meloxicam for the management of postoperative pain. By delivering sustained levels of both a potent anesthetic and a local anti-inflammatory agent directly to the site of tissue injury, HTX-011 was designed to deliver superior pain relief while reducing the need for systemically administered pain medications such as opioids, which carry the risk of harmful side effects, abuse and addiction.

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

Total Knee Arthroplasty — Study 209 Results

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

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

- The HTX-011 combination and HTX-011 alone resulted in reductions of 22% and 19%, respectively, in pain intensity measured at rest through 72 hours when compared to placebo ($p<0.0001$ and $p=0.0004$, respectively). These pain reductions from HTX-011 were also approximately double that of bupivacaine, which resulted in a reduction of 11%. The HTX-011 combination reduction was significantly better than that of bupivacaine through 72 hours ($p=0.0325$).
- With the more conservative assessment of pain with activity, the HTX-011 combination and HTX-011 alone resulted in reductions of 16% and 12%, respectively, in pain intensity measured with activity through 48 hours when compared to placebo ($p<0.0001$ and $p=0.0017$, respectively). These pain reductions from HTX-011 were significantly better than that of bupivacaine, which resulted in a reduction of 4% ($p=0.0012$ and $p=0.0366$, respectively). Both the HTX-011 combination and HTX-011 alone maintained control of pain with activity through 72 hours with a 15% ($p=0.0002$) and 11% ($p=0.0058$) reduction compared to placebo, respectively.
- The HTX-011 combination significantly reduced opioid use through 48 and 72 hours compared to placebo ($p=0.0091$ and $p=0.0253$, respectively).

Breast Augmentation — Study 211 Results

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

- HTX-011 400 mg administered by instillation into the surgical site and HTX-011 400 mg administered as a nerve block both resulted in reductions of 22% in pain intensity measured at rest through 24 hours when compared to placebo ($p=0.0023$ and $p=0.0055$, respectively). These pain reductions from HTX-011 were approximately triple that of bupivacaine administered as a nerve block, which resulted in a reduction of 8%. The HTX-011 400 mg instillation reduction was significantly better than that of bupivacaine ($p=0.0383$).
- With the more conservative assessment of pain with activity, HTX-011 400 mg instillation and HTX-011 400 mg nerve block resulted in reductions of 24% and 23%, respectively, in pain intensity measured with activity through 24 hours when compared to placebo ($p=0.0004$ and $p=0.0015$, respectively). These pain reductions from HTX-011 were approximately double that of bupivacaine administered as a nerve block, which resulted in a reduction of 12%.
- HTX-011 400 mg instillation and HTX-011 400 mg nerve block resulted in reductions in total opioid use of 33% and 26%, respectively, when compared to placebo ($p=0.0093$ and $p=0.0435$, respectively). These reductions from HTX-011 were approximately triple that of bupivacaine administered as a nerve block, which resulted in a reduction of 10%. The HTX-011 400 mg instillation reduction was significantly better than that of bupivacaine ($p=0.0455$).

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

HTX-011 was well tolerated in both studies, with a safety profile comparable to placebo and bupivacaine solution. There were no deaths and no clinically meaningful differences in overall adverse events, serious

adverse events, premature discontinuations due to adverse events, potential local anesthetic systemic toxicity related adverse events or wound healing.

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

In March 2018, we reported positive topline results from EPOCH1 and EPOCH2, our pivotal Phase 3 studies of HTX-011 in bunionectomy and hernia repair, respectively. All primary and key secondary endpoints were achieved in these studies. Furthermore, HTX-011 is the only long-acting local anesthetic to demonstrate in Phase 3 studies significantly reduced pain and opioid use compared to bupivacaine solution, the current standard-of-care local anesthetic for postoperative pain control, through 72 hours.

The primary and key secondary endpoints for both Phase 3 studies were identical. The primary endpoint was pain intensity as measured by the AUC 0-72 compared to placebo. Key secondary endpoints in order of evaluation were:

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

Bunionectomy — Study 301/EPOCH1 Results

EPOCH1 was a randomized, placebo- and active-controlled, double-blind, Phase 3 clinical study evaluating the efficacy and safety of locally administered HTX-011 at 60 mg compared to the standard dose of bupivacaine solution (50 mg) and placebo for post-operative pain control following bunionectomy surgery in 412 subjects. All primary and key secondary endpoints were achieved:

- There was a 27% reduction in pain intensity as measured by AUC 0-72 when comparing HTX-011 to placebo ($p<0.0001$);
- There was an 18% reduction in pain as measured by AUC 0-72 when comparing HTX-011 to bupivacaine solution ($p=0.0002$);
- Over 72 hours post-surgery, patients receiving HTX-011 consumed 37% less opioids than placebo patients ($p<0.0001$) and 25% less opioids than patients receiving bupivacaine solution ($p=0.0022$); and
- 29% of patients receiving HTX-011 required no opioid medication for 72 hours post-surgery compared to only 2% receiving placebo ($p<0.0001$) and 11% receiving the standard-of-care, bupivacaine solution ($p=0.0001$). These results parallel the significantly reduced incidence of severe pain in patients receiving HTX-011 compared to both placebo (36% reduction; $p<0.0001$) and bupivacaine (29% reduction; $p<0.0001$).

Hernia Repair — Study 302/EPOCH2 Results

EPOCH2 was a randomized, placebo- and active-controlled, double-blind, Phase 3 clinical study evaluating the efficacy and safety of locally administered HTX-011 at 300 mg compared to the standard dose of bupivacaine solution (75 mg) and placebo for post-operative pain control following hernia repair surgery in 418 subjects. All primary and key secondary endpoints were achieved:

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

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

HTX-011 is the only long-acting anesthetic designed to address both postoperative pain and inflammation in a single administration at the surgical site. The unique synergy of bupivacaine and meloxicam in HTX-011 has consistently been shown to reduce pain over 72 hours significantly better than bupivacaine alone in multiple diverse surgical models. HTX-011 is administered as a single-dose application via needle-free syringe to directly coat the affected tissue within the surgical site prior to suturing, which makes HTX-011's route of administration faster, easier and potentially safer compared to numerous injections required with current local anesthetics.

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

Biochronomer Technology

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

Corporate Information

We have executive offices located at 4242 Campus Point Court, Suite 200, San Diego, California 92121, and our telephone number is (858) 251-4400. Our website address is *www.herontx.com.* We make our periodic

and current reports available on our website, free of charge, as soon as reasonably practicable after such material is electronically filed with, or furnished to, the SEC. No portion of our website is incorporated by reference into this prospectus supplement. The Company files annual, quarterly and special reports, proxy statements and other information with the SEC. You may read and copy any document filed by the Company at the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the public reference room. The Company's filings with the SEC are also available to the public on the SEC's web site at *http://www.sec.gov*. Additional information regarding the Company, including our audited financial statements and descriptions of our business, is contained in the documents incorporated by reference in this prospectus supplement. See "Information Incorporated by Reference" and "Where You Can Find Additional Information" in this prospectus supplement and the accompanying prospectus. Our common stock is listed on The Nasdaq Capital Market under the symbol "HRTX."

THE OFFERING

Common Stock We Are Offering Pursuant to this Prospectus Supplement	5,063,292 shares
Common Stock to be Outstanding after this Offering	70,107,490 shares
Option to Purchase Additional Shares	We have granted the underwriter an option for a period of 30 days from the date of this prospectus supplement to purchase up to 759,493 additional shares of common stock.
Use of Proceeds	We intend to use the net proceeds from this offering for the commercial launch of HTX-011, if approved by the FDA, the continued commercialization and marketing of SUSTOL and CINVANTI, our ongoing and future clinical trials, including further clinical studies for HTX-011, preclinical development work, other product development activities and general corporate purposes. See "Use of Proceeds."
The Nasdaq Capital Market Symbol	"HRTX"
Risk Factors	This investment involves a high degree of risk. You should read the "Risk Factors" section of this prospectus supplement and the accompanying prospectus and our most recent Annual Report on Form 10-K and any subsequent Quarterly Reports on Form 10-Q, incorporated by reference herein, for a discussion of factors to consider carefully before deciding to invest in shares of our common stock.

The number of shares of common stock shown above to be outstanding after this offering is based on the 65,044,198 shares outstanding as of March 31, 2018 and excludes:

- 12,905,851 shares of our common stock subject to options outstanding as of March 31, 2018 having a weighted average exercise price of $15.22 per share;
- 4,807,736 shares of our common stock that have been reserved for issuance in connection with future grants under our Amended and Restated 2007 Equity Plan (the "2007 Plan") as of March 31, 2018;
- 267,317 shares of our common stock that have been reserved for issuance under our Employee Stock Purchase Plan ("ESPP") as of March 31, 2018;
- 640,164 shares of our common stock that have been reserved for issuance upon exercise of outstanding warrants as of March 31, 2018, having a weighted average exercise price of $1.14 per share; and
- 8,102,702 shares of common stock issuable upon the conversion of outstanding principal due under outstanding secured convertible promissory notes as of March 31, 2018.

If the underwriter's option to purchase additional shares is exercised in full, we will issue and sell an additional 759,493 shares of our common stock and will have 70,866,983 shares outstanding after the offering.

Except as otherwise noted, all information in this prospectus supplement assumes no exercise of the underwriter's option to purchase additional shares of common stock.

RISK FACTORS

An investment in our common stock involves a high degree of risk. Before deciding whether to invest in our common stock, you should consider carefully the risks described below and discussed under the sections captioned "Risk Factors" contained in our Annual Report on Form 10-K for the year ended December 31, 2017, and any subsequent Quarterly Reports on Form 10-Q, which are incorporated by reference herein in their entirety, together with other information contained in or incorporated by reference in this prospectus supplement and in any free writing prospectus that we have authorized for use in connection with this offering. If any of these risks actually occurs, our business, financial condition, results of operations or prospects could be seriously harmed. This could cause the trading price of our common stock to decline, resulting in a loss of all or part of your investment.

Risks Related to Our Business

Topline data may not accurately reflect the complete results of a particular study or trial.

We may publicly disclose preliminary or topline data from our clinical studies such as the recent topline results for our clinical trials of HTX-011, which is based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the topline results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Topline data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, topline data should be viewed with caution until the final data are available.

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

A Fast Track designation by the FDA may not actually lead to a faster development or regulatory review or approval process.

HTX-011 has been granted a Fast Track designation from the FDA for local administration into the surgical site to reduce postoperative pain and the need for opioid analgesics for 72 hours. Fast Track designation is intended to facilitate the development and expedite the review of new therapies to treat serious conditions with unmet medical needs by providing sponsors with the opportunity for frequent interactions with the FDA. Obtaining a Fast Track designation does not change the standards for product approval, but may expedite the development or approval process. Even though the FDA has granted such designation for HTX-011, it may not actually result in faster clinical development or regulatory review or approval. Furthermore, such a designation does not increase the likelihood that HTX-011 will receive marketing approval in the United States.

Breakthrough Therapy designation from the FDA may not lead to a faster development or regulatory review or approval process, and it does not increase the likelihood that HTX-011 will receive marketing approval.

HTX-011 has been granted breakthrough therapy designation from the FDA for postoperative pain management. Breakthrough Therapy designation is designed to expedite the development and review of drugs that are intended to treat serious conditions and for which preliminary clinical evidence indicates substantial improvement over available therapies on clinically significant endpoint(s). The receipt of a breakthrough therapy designation for HTX-011 may not result in a faster development process, review or approval compared to drugs considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even though the FDA granted breakthrough designation, the FDA may later decide that HTX-011 no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

Risks Relating to this Offering

We will have broad discretion in the use of the net proceeds to us from this offering; we may not use the offering proceeds that we receive effectively.

Our management will have broad discretion in the application of the net proceeds to us from this offering, including for any of the purposes described in the section entitled “Use of Proceeds,” and you will not have the opportunity as part of your investment decision to assess whether the net proceeds are being used appropriately. Because of the number and variability of factors that will determine our use of the net proceeds to us from this offering, their ultimate use may vary from their currently intended use. The failure by our management to apply these funds effectively could harm our business. Pending their use, we may invest the net proceeds to us from this offering in investment-grade, interest-bearing securities. These investments may not yield a favorable return to our stockholders. See “Use of Proceeds.”

USE OF PROCEEDS

We estimate that the net proceeds from the sale of the shares of common stock that we are offering will be approximately $194.7 million, or approximately $223.9 million if the underwriter exercises in full its option to purchase up to 759,493 additional shares of common stock, after deducting the underwriting discounts, but before deducting estimated offering expenses payable by us.

We intend to use the net proceeds from this offering for the commercial launch of HTX-011, if approved by the FDA, the continued commercialization and marketing of SUSTOL and CINVANTI, our ongoing and future clinical trials, including further clinical studies for HTX-011, preclinical development work, other product development activities and general corporate purposes.

Pending the use of the net proceeds, we intend to invest the net proceeds in short-term, interest-bearing, investment-grade securities.

UNDERWRITING

We have entered into an underwriting agreement with Jefferies LLC with respect to the shares of common stock being offered hereby. Subject to the terms and conditions set forth in an underwriting agreement among us and the underwriter, the underwriter has agreed to purchase from us 5,063,292 shares of our common stock.

Subject to the terms and conditions set forth in the underwriting agreement, the underwriter has agreed to purchase all of the shares sold under the underwriting agreement if any of these shares are purchased.

We have agreed to indemnify the underwriter against certain liabilities, including liabilities under the Securities Act of 1933, as amended, and to contribute to payments the underwriter may be required to make in respect of those liabilities.

The underwriter is offering the shares, subject to prior sale, when, as and if issued to and accepted by it, subject to approval of legal matters by its counsel, including the validity of the shares, and other conditions contained in the underwriting agreement, such as the receipt by the underwriter of officer's certificates and legal opinions. The underwriter reserves the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Discounts.

The underwriter has agreed to purchase 5,063,292 shares of our common stock at a price of $38.445 per share, which will result in approximately $194.7 million of net proceeds to us before deducting estimated offering expenses payable by us. The underwriter may offer the shares of common stock from time to time to purchasers directly or through agents, or through brokers in brokerage transactions on The Nasdaq Capital Market, or to dealers in negotiated transactions, or in a combination of such methods of sale or otherwise, at a fixed price or prices, which may be changed, or at market prices prevailing at the time of sale, at prices related to such prevailing market prices or at negotiated prices. The difference between the price at which the underwriter purchases shares from us and the price at which the underwriter resells such shares may be deemed underwriting compensation. If the underwriter effects such transactions by selling shares of common stock to or through dealers, such dealers may receive compensation in the form of discounts or concessions from the underwriter and/or purchasers of shares of common stock for whom they may act as agents or to whom they may sell as principal. The expenses of the offering, not including the underwriting discounts, are estimated at $230,000 and are payable by us.

Option to Purchase Additional Shares

We have granted an option to the underwriter, exercisable for 30 days after the date of this prospectus supplement, to purchase up to 759,493 additional shares from us at a price of $38.445 per share.

No Sales of Similar Securities

We, our executive officers and directors have agreed, subject to specified exceptions, not to directly or indirectly:

- sell, offer, contract or grant any option to sell (including any short sale), pledge, transfer, establish an open "put equivalent position" within the meaning of Rule 16a-l(h) under the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or
- otherwise dispose of any shares of common stock, options or warrants to acquire shares of common stock, or securities exchangeable or exercisable for or convertible into shares of common stock currently or hereafter owned either of record or beneficially, or
- publicly announce an intention to do any of the foregoing for a period of 90 days after the date of this prospectus supplement without the prior written consent of Jefferies LLC.

This restriction terminates after the close of trading of the common stock on and including the 90th day after the date of this prospectus supplement.

Jefferies LLC may, in its sole discretion and at any time or from time to time before the termination of the 90-day period release all or any portion of the securities subject to lock-up agreements. Except for customary lock-up exceptions, including an exception allowing our directors and officers to make sales under preexisting 10b5-1 plans, there are no existing agreements between the underwriter and any of our shareholders who will execute a lock-up agreement, providing consent to the sale of shares prior to the expiration of the lock-up period; provided however, that the lock-up agreement for Kevin Tang, the Chairman of our Board of Directors, permits him to make gifts of securities subject to the lock-up agreement without requiring the recipient of such securities to execute a similar lock-up agreement.

The Nasdaq Capital Market Listing

The shares are listed on The Nasdaq Capital Market under the symbol “HRTX.”

Price Stabilization, Short Positions

Until the distribution of the shares is completed, SEC rules may limit the underwriter from bidding for and purchasing our common stock. However, the underwriter may engage in transactions that stabilize the price of the common stock, such as bids or purchases to peg, fix or maintain that price.

In connection with the offering, the underwriter may purchase and sell our common stock in the open market. These transactions may include short sales, purchases on the open market to cover positions created by short sales and stabilizing transactions. Short sales involve the sale by the underwriter of a greater number of shares than it is required to purchase in the offering. “Covered” short sales are sales made in an amount not greater than the underwriter’s option to purchase additional shares described above. The underwriter may close out any covered short position by either exercising its option to purchase additional shares or purchasing shares in the open market. In determining the source of shares to close out the covered short position, the underwriter will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the option granted to them. “Naked” short sales are sales in excess of such option. The underwriter must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriter is concerned that there may be downward pressure on the price of our common stock in the open market after pricing that could adversely affect investors who purchase in the offering. Stabilizing transactions consist of various bids for or purchases of shares of common stock made by the underwriter in the open market prior to the completion of the offering.

Similar to other purchase transactions, the underwriter’s purchases to cover the syndicate short sales may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock may be higher than the price that might otherwise exist in the open market. The underwriter may conduct these transactions on The Nasdaq Capital Market, in the over-the-counter market or otherwise.

Neither we nor the underwriter make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of our common stock. In addition, neither we nor the underwriter make any representation that it will engage in these transactions or that these transactions, once commenced, will not be discontinued without notice.

Passive Market Making

In connection with this Offering, the underwriter may also engage in passive market making transactions in our common stock on The Nasdaq Capital Market in accordance with Rule 103 of Regulation M under the

Exchange Act during a period before the commencement of offers or sales of shares of our common stock in this offering and extending through the completion of distribution. A passive market maker must display its bid at a price not in excess of the highest independent bid of that security. However, if all independent bids are lowered below the passive market maker's bid, that bid must then be lowered when specified purchase limits are exceeded. Passive market making may cause the price of our common stock to be higher than the price that otherwise would exist in the open market in the absence of those transactions. The underwriter is not required to engage in passive market making and, if commenced, may end passive market making activities at any time.

Electronic Distribution

In connection with the offering, the underwriter may distribute this prospectus supplement and the accompanying prospectus by electronic means, such as e-mail.

Other Relationships

The underwriter and its affiliates have engaged in, and may in the future engage in, investment banking and other commercial dealings in the ordinary course of business with us or our affiliates. They have received, or may in the future receive, customary fees for these transactions.

In addition, in the ordinary course of their business activities, the underwriter and its affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers. Such investments and securities activities may involve securities and/or instruments of ours or our affiliates. The underwriter and its affiliates may also make investment recommendations and/or publish or express independent research views in respect of such securities or financial instruments and may hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

Notice to Prospective Investors in the European Economic Area

In relation to each member state of the European Economic Area, no offer of shares of common stock which are the subject of the offering has been, or will be made to the public in that Member State, other than under the following exemptions under the Prospectus Directive:

A. to any legal entity which is a qualified investor as defined in the Prospectus Directive;

B. to fewer than 150, natural or legal persons (other than qualified investors as defined in the Prospectus Directive), subject to obtaining the prior consent of the underwriter for any such offer; or

C. in any other circumstances falling within Article 3(2) of the Prospectus Directive,

provided that no such offer of shares of common stock referred to in (a) to (c) above shall result in a requirement for the Company or the underwriter to publish a prospectus pursuant to Article 3 of the Prospectus Directive, or supplement a prospectus pursuant to Article 16 of the Prospectus Directive.

Each person located in a Member State to whom any offer of shares of common stock is made or who receives any communication in respect of any offer of ordinary shares, or who initially acquires any shares of common stock will be deemed to have represented, warranted, acknowledged and agreed to and with the underwriter and the Company that (1) it is a "qualified investor" within the meaning of the law in that Member State implementing Article 2(1)(e) of the Prospectus Directive; and (2) in the case of any shares of common stock acquired by it as a financial intermediary as that term is used in Article 3(2) of the Prospectus Directive, the shares of common stock acquired by it in the offer have not been acquired on behalf of, nor have they been acquired with a view to their offer or resale to, persons in any Member State other than qualified investors, as that term is defined in the Prospectus Directive, or in circumstances in which the prior consent of the underwriter has been given to the offer or resale; or where ordinary shares have been acquired by it on behalf of persons in any Member State other than qualified investors, the offer of those ordinary shares to it is not treated under the Prospectus Directive as having been made to such persons.

The Company, the underwriter and their respective affiliates will rely upon the truth and accuracy of the foregoing representations, acknowledgments and agreements.

This prospectus supplement has been prepared on the basis that any offer of shares of common stock in any Member State will be made pursuant to an exemption under the Prospectus Directive from the requirement to publish a prospectus for offers of shares of common stock. Accordingly, any person making or intending to make an offer in that Member State of shares of common stock which are the subject of the offering contemplated in this prospectus supplement may only do so in circumstances in which no obligation arises for the Company or the underwriter to publish a prospectus pursuant to Article 3 of the Prospectus Directive in relation to such offer. Neither the Company nor the underwriter have authorized, nor do they authorize, the making of any offer of shares of common stock in circumstances in which an obligation arises for the Company or the underwriter to publish a prospectus for such offer.

For the purposes of this provision, the expression an "offer of shares of common stock to the public" in relation to any shares of common stock in any Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the shares of common stock to be offered so as to enable an investor to decide to purchase or subscribe the shares of common stock, as the same may be varied in that Member State by any measure implementing the Prospectus Directive in that Member State, the expression "Prospectus Directive" means Directive 2003/71/EC (as amended) and includes any relevant implementing measure in each Member State.

The above selling restriction is in addition to any other selling restrictions set out below.

Notice to Prospective Investors in the United Kingdom

In addition, in the United Kingdom, this document is being distributed only to, and is directed only at, and any offer subsequently made may only be directed at persons who are "qualified investors" (as defined in the Prospectus Directive) (i) who have professional experience in matters relating to investments falling within Article 19 (5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended ("Order"), and/or (ii) who are high net worth companies (or persons to whom it may otherwise be lawfully communicated) falling within Article 49(2)(a) to (d) of the Order (all such persons together being referred to as "relevant persons"). This document must not be acted on or relied on in the United Kingdom by persons who are not relevant persons. In the United Kingdom, any investment or investment activity to which this document relates is only available to, and will be engaged in with, relevant persons.

Notice to Prospective Investors in Switzerland

The shares may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange ("SIX") or on any other stock exchange or regulated trading facility in Switzerland. This document has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland.

Neither this document nor any other offering or marketing material relating to the shares or the offering may be publicly distributed or otherwise made publicly available in Switzerland. Neither this document nor any other offering or marketing material relating to the offering, us or the shares has been or will be filed with or approved by any Swiss regulatory authority. In particular, this document will not be filed with, and the offer of shares will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA, and the offer of shares has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes ("CISA"). The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of shares.

Notice to Prospective Investors in the Dubai International Financial Centre

This prospectus supplement and the accompanying prospectus relate to an Exempt Offer in accordance with the Offered Securities Rules of the Dubai Financial Services Authority ("DFSA"). This prospectus supplement and the accompanying prospectus are intended for distribution only to persons of a type specified in the Offered Securities Rules of the DFSA. They must not be delivered to, or relied on by, any other person. The DFSA has no responsibility for reviewing or verifying any documents in connection with Exempt Offers. The DFSA has not approved this prospectus supplement and the accompanying prospectus nor taken steps to verify the information set forth therein and has no responsibility for this prospectus supplement and the accompanying prospectus. The shares to which this prospectus supplement and the accompanying prospectus relate may be illiquid and/or subject to restrictions on their resale. Prospective purchasers of the shares offered should conduct their own due diligence on the shares. If you do not understand the contents of this prospectus supplement and the accompanying prospectus you should consult an authorized financial advisor.

Notice to Prospective Investors in Australia

No placement document, prospectus, product disclosure statement or other disclosure document has been lodged with the Australian Securities and Investments Commission, in relation to the offering. This prospectus supplement and the accompanying prospectus do not constitute a prospectus, product disclosure statement or other disclosure document under the Corporations Act 2001 ("Corporations Act"), and do not purport to include the information required for a prospectus, product disclosure statement or other disclosure document under the Corporations Act.

Any offer in Australia of the shares may only be made to persons (Exempt Investors) who are "sophisticated investors" (within the meaning of section 708(8) of the Corporations Act), "professional investors" (within the meaning of section 708(11) of the Corporations Act) or otherwise pursuant to one or more exemptions contained in section 708 of the Corporations Act so that it is lawful to offer the shares without disclosure to investors under Chapter 6D of the Corporations Act.

The shares applied for by Exempt Investors in Australia must not be offered for sale in Australia in the period of 12 months after the date of allotment under the offering, except in circumstances where disclosure to investors under Chapter 6D of the Corporations Act would not be required pursuant to an exemption under section 708 of the Corporations Act or otherwise or where the offer is pursuant to a disclosure document which complies with Chapter 6D of the Corporations Act. Any person acquiring shares must observe such Australian on-sale restrictions.

This prospectus supplement and the accompanying prospectus contain general information only and do not take account of the investment objectives, financial situation or particular needs of any particular person. They do not contain any securities recommendations or financial product advice. Before making an investment decision, investors need to consider whether the information in this prospectus supplement and the accompanying prospectus is appropriate to their needs, objectives and circumstances, and, if necessary, seek expert advice on those matters.

Notice to Prospective Investors in Hong Kong

The shares have not been offered or sold and will not be offered or sold in Hong Kong, by means of any document, other than (a) to "professional investors" as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made under that Ordinance; or (b) in other circumstances which do not result in the document being a "prospectus" as defined in the Companies Ordinance (Cap. 32) of Hong Kong or which do not constitute an offer to the public within the meaning of that Ordinance. No advertisement, invitation or document relating to the shares has been or may be issued or has been or may be in the possession of any person for the purposes of issue, whether in Hong Kong or elsewhere, which is directed at, or the contents of which are

likely to be accessed or read by, the public of Hong Kong (except if permitted to do so under the securities laws of Hong Kong) other than with respect to shares which are or are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" as defined in the Securities and Futures Ordinance and any rules made under that Ordinance.

Notice to Prospective Investors in Japan

The shares have not been and will not be registered under the Financial Instruments and Exchange Law of Japan (Law No. 25 of 1948, as amended) and, accordingly, will not be offered or sold, directly or indirectly, in Japan, or for the benefit of any Japanese Person or to others for re-offering or resale, directly or indirectly, in Japan or to any Japanese Person, except in compliance with all applicable laws, regulations and ministerial guidelines promulgated by relevant Japanese governmental or regulatory authorities in effect at the relevant time. For the purposes of this paragraph, "Japanese Person" shall mean any person resident in Japan, including any corporation or other entity organized under the laws of Japan.

Notice to Prospective Investors in Singapore

This prospectus supplement and the accompanying prospectus have not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus supplement and the accompanying prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of shares may not be circulated or distributed, nor may the shares be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore ("SFA"), (ii) to a relevant person pursuant to Section 275(1), or any person pursuant to Section 275(1A), and in accordance with the conditions specified in Section 275, of the SFA, or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the shares are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

a) a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or

b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor,

securities (as defined in Section 239(1) of the SFA) of that corporation or the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the shares pursuant to an offer made under Section 275 of the SFA except:

a) to an institutional investor or to a relevant person defined in Section 275(2) of the SFA, or to any person arising from an offer referred to in Section 275(1A) or Section 276(4)(i)(B) of the SFA;

b) where no consideration is or will be given for the transfer;

c) where the transfer is by operation of law;

d) as specified in Section 276(7) of the SFA; or

e) as specified in Regulation 32 of the Securities and Futures (Offers of Investments) (Shares and Debentures) Regulations 2005 of Singapore.

Notice to Prospective Investors in Canada

This prospectus supplement constitutes an "exempt offering document" as defined in and for the purposes of applicable Canadian securities laws. No prospectus has been filed with any securities commission or similar

regulatory authority in Canada in connection with the offer and sale of the common stock. No securities commission or similar regulatory authority in Canada has reviewed or in any way passed upon this prospectus supplement or on the merits of the common stock and any representation to the contrary is an offence.

Canadian investors are advised that this prospectus supplement has been prepared in reliance on section 3A.3 of National Instrument 33-105 Underwriting Conflicts ("NI 33-105"). Pursuant to section 3A.3 of NI 33-105, this prospectus supplement is exempt from the requirement that the Company and the underwriter provide investors with certain conflicts of interest disclosure pertaining to "connected issuer" and/or "related issuer" relationships that may exist between the Company and the underwriter as would otherwise be required pursuant to subsection 2.1(1) of NI 33-105.

Resale Restrictions

The offer and sale of the common stock in Canada is being made on a private placement basis only and is exempt from the requirement that the Company prepares and files a prospectus under applicable Canadian securities laws. Any resale of the common stock acquired by a Canadian investor in this offering must be made in accordance with applicable Canadian securities laws, which may vary depending on the relevant jurisdiction, and which may require resales to be made in accordance with Canadian prospectus requirements, pursuant to a statutory exemption from the prospectus requirements, in a transaction exempt from the prospectus requirements or otherwise under a discretionary exemption from the prospectus requirements granted by the applicable local Canadian securities regulatory authority. These resale restrictions may under certain circumstances apply to resales of the common stock outside of Canada.

Representations of Purchasers

Each Canadian investor who purchases the common stock will be deemed to have represented to the Company and the underwriter(s) that the investor (i) is purchasing the common stock as principal, or is deemed to be purchasing as principal in accordance with applicable Canadian securities laws, for investment only and not with a view to resale or redistribution; (ii) is an "accredited investor" as such term is defined in section 1.1 of National Instrument 45-106 *Prospectus Exemptions* ("NI 45-106") or, in Ontario, as such term is defined in section 73.3(1) of the *Securities Act* (Ontario); and (iii) is a "permitted client" as such term is defined in section 1.1 of National Instrument 31-103 *Registration Requirements, Exemptions and Ongoing Registrant Obligations*.

Taxation and Eligibility for Investment

Any discussion of taxation and related matters contained in this prospectus supplement does not purport to be a comprehensive description of all of the tax considerations that may be relevant to a Canadian investor when deciding to purchase the common stock and, in particular, does not address any Canadian tax considerations. No representation or warranty is hereby made as to the tax consequences to a resident, or deemed resident, of Canada of an investment in the common stock or with respect to the eligibility of the common stock for investment by such investor under relevant Canadian federal and provincial legislation and regulations.

Rights of Action for Damages or Rescission

Securities legislation in certain of the Canadian jurisdictions provides certain purchasers of securities pursuant to an offering memorandum (such as this prospectus supplement), including where the distribution involves an "eligible foreign security" as such term is defined in Ontario Securities Commission Rule 45-501 *Ontario Prospectus and Registration Exemptions* and in Multilateral Instrument 45-107 *Listing Representation and Statutory Rights of Action Disclosure Exemptions*, as applicable, with a remedy for damages or rescission, or both, in addition to any other rights they may have at law, where the offering memorandum, or other offering document that constitutes an offering memorandum, and any amendment thereto, contains a "misrepresentation" as defined under applicable Canadian securities laws. These remedies, or notice with respect to these remedies,

must be exercised or delivered, as the case may be, by the purchaser within the time limits prescribed under, and are subject to limitations and defences under, applicable Canadian securities legislation. In addition, these remedies are in addition to and without derogation from any other right or remedy available at law to the investor.

Language of Documents

Upon receipt of this document, each Canadian investor hereby confirms that it has expressly requested that all documents evidencing or relating in any way to the sale of the securities described herein (including for greater certainty any purchase confirmation or any notice) be drawn up in the English language only. *Par la réception de ce document, chaque investisseur Canadien confirme par les présentes qu'il a expressément exigé que tous les documents faisant foi ou se rapportant de quelque manière que ce soit à la vente des valeurs mobilières décrites aux présentes (incluant, pour plus de certitude, toute confirmation d'achat ou tout avis) soient rédigés en anglais seulement.*

Notice to Prospective Investors in Israel

This document does not constitute a prospectus under the Israeli Securities Law, 5728-1968, or the Securities Law, and has not been filed with or approved by the Israel Securities Authority. In Israel, this prospectus is being distributed only to, and is directed only at, and any offer of the shares of common stock which are the subject of the offering is directed only at, (i) a limited number of persons in accordance with the Israeli Securities Law and (ii) investors listed in the first addendum, or the Addendum, to the Israeli Securities Law, consisting primarily of joint investment in trust funds, provident funds, insurance companies, banks, portfolio managers, investment advisors, members of the Tel Aviv Stock Exchange, underwriters, venture capital funds, entities with equity in excess of NIS 50 million and "qualified individuals," each as defined in the Addendum (as it may be amended from time to time), collectively referred to as qualified investors (in each case, purchasing for their own account or, where permitted under the Addendum, for the accounts of their clients who are investors listed in the Addendum). Qualified investors are required to submit written confirmation that they fall within the scope of the Addendum, are aware of the meaning of same and agree to it.

LEGAL MATTERS

Gibson, Dunn & Crutcher LLP of San Francisco, California will pass on the validity of the shares of common stock offered hereby. Latham & Watkins LLP of San Diego, California is counsel to the underwriter in connection with this offering.

EXPERTS

OUM & Co. LLP, an independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2017, as set forth in their report, which is incorporated by reference in this prospectus supplement and elsewhere in the registration statement. Our consolidated financial statements are incorporated by reference in reliance on OUM & Co. LLP's report, given on their authority as experts in accounting and auditing.

INFORMATION INCORPORATED BY REFERENCE

The SEC allows the Company to "incorporate by reference" the information that is filed by the Company with the SEC, which means that the Company can disclose important information to you by referring you to those documents. The documents incorporated by reference are:

1. The Company's Annual Report on Form 10-K for the year ended December 31, 2017;
2. The information specifically incorporated by reference in the Company's Annual Report on Form 10-K for the year ended December 31, 2017 from the Company's Definitive Proxy Statement on Schedule 14A relating to the Company's 2018 Annual Meeting of Stockholders, which was filed with the SEC on April 30, 2018;
3. The Company's Quarterly Report on Form 10-Q for the quarterly period ended March 31, 2018;
4. The Company's Current Reports on Form 8-K filed with the SEC on April 3, 2018, June 22, 2018 and June 25, 2018; and
5. The description of the Company's common stock contained in Amendment No. 3 to that certain registration statement on Form 8-A, filed with the SEC on July 6, 2017 pursuant to Section 12 of the Exchange Act, including any amendment or report filed for the purpose of updating that description.

All documents we file with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act, except as to any portion of any report or documents that is not deemed filed under such provisions, on or after the date of this prospectus supplement until the earlier of the date on which all of the securities registered hereunder have been sold or the registration statement of which this prospectus supplement is a part has been withdrawn, shall be deemed incorporated by reference in this prospectus supplement and to be a part of this prospectus supplement from the date of filing of those documents.

Any statement contained in a document incorporated or deemed to be incorporated by reference herein shall be deemed to be modified or superseded, for purposes of this prospectus supplement, to the extent that a statement contained in or omitted from this prospectus supplement, or in any other subsequently filed document that also is or is deemed to be incorporated by reference herein, modifies or supersedes such statement. Any such statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this prospectus supplement. Nothing in this prospectus supplement shall be deemed to incorporate information furnished but not filed with the SEC pursuant to Item 2.02 or Item 7.01 of Form 8-K.

Upon written or oral request, we will provide, without charge, to each person, including any beneficial owner, to whom a copy of this prospectus supplement is delivered, upon such person's written or oral request, a copy of any and all of the information incorporated by reference in this prospectus supplement, other than exhibits to such documents, unless such exhibits are specifically incorporated by reference into the information that this prospectus supplement incorporates. Requests should be directed to the Secretary at Heron Therapeutics, Inc., 4242 Campus Point Court, Suite 200, San Diego, California 92121, telephone number (858) 251-4400. You may also find these documents in the "Investor Relations" section of our website, *www.herontx.com*. The information on our website is not incorporated into this prospectus supplement. We have authorized no one to provide you with any information that differs from that contained in this prospectus supplement. Accordingly, you should not rely on any information that is not contained in this prospectus supplement. You should not assume that the information in this prospectus is accurate as of any date other than the date of the front cover of this prospectus supplement.

WHERE YOU CAN FIND ADDITIONAL INFORMATION

The Company is subject to the informational requirements of the Exchange Act, and in accordance therewith, files annual, quarterly and special reports, proxy statements and other information with the SEC. You may read and copy any document filed by the Company at the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the public reference room. The Company's filings with the SEC are also available to the public at the SEC's web site at *http://www.sec.gov*. Statements contained in this prospectus supplement as to the contents of any contract or other document are not necessarily complete, and in each instance we refer you to the copy of the contract or document filed as an exhibit to the registration statement, each such statement being qualified in all respects by such reference.

PROSPECTUS

Common Stock
Preferred Stock
Warrants

Under this prospectus, we or any selling stockholder may offer and sell from time to time, in one or more offerings, an indeterminate number of shares of our common stock, preferred stock, and warrants or any combination thereof, separately, together or in series. The warrants may be convertible into or exercisable or exchangeable for common stock or preferred stock and the preferred stock may be convertible into or exchangeable for common stock. Each time securities are offered or sold pursuant to this prospectus, we will describe in a prospectus supplement the securities being offered and sold, as well as the specific terms of the securities.

Our common stock is listed on The NASDAQ Capital Market under the symbol “HRTX.” On July 5, 2017, the last reported sale price on The NASDAQ Capital Market was $14.00 per share.

You should read this prospectus, any prospectus supplement and the documents incorporated by reference in this prospectus and any prospectus supplement carefully before you invest. This prospectus may not be used to offer or sell any of our common stock, preferred stock or warrants unless accompanied by a prospectus supplement.

We or any selling stockholder may offer these securities in amounts, at prices and on terms determined at the time of offering. We or any selling stockholder may sell the securities directly to investors, through agents we select, or through underwriters and dealers we select. See “Plan of Distribution” in this prospectus. Each prospectus supplement will provide the amount, price, terms and plan of distribution relating to the securities to be sold pursuant to such prospectus supplement. If agents, underwriters or dealers are used to sell the securities, we will name them and describe their compensation in a prospectus supplement or sales agreement prospectus.

Investing in our securities involves certain risks. See “Risk Factors” beginning on Page 5 of this prospectus and in the applicable prospectus supplement and any related free writing prospectus, and in the other documents that are incorporated by reference into this prospectus or the applicable prospectus supplement, for certain risks you should consider. You should read the entire prospectus carefully before you make your investment decision.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this prospectus is July 6, 2017

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You should rely only on the information contained or incorporated by reference into this prospectus and any prospectus supplement or any free writing prospectus that we may provide to you. We have not authorized anyone to provide you with different information. You must not rely upon any unauthorized information or representation. You should not assume that the information contained in this prospectus or any applicable prospectus supplement is accurate as of any date other than the date on the front cover of the prospectus or the prospectus supplement or that the information contained in any document incorporated by reference is accurate as of any date other than the date of the document incorporated by reference. Our business, financial condition, results of operations and prospects may have changed since those dates. We are not making offers to sell the securities in any jurisdiction in which an offer or solicitation is not authorized or permitted or in which the person making such offer or solicitation is not qualified to do so or to anyone to whom it is unlawful to make an offer or solicitation.

ABOUT THIS PROSPECTUS

This prospectus is part of an automatic shelf registration statement that we filed with the Securities and Exchange Commission, or the SEC, as a "well-known seasoned issuer" as defined in Rule 405 under the Securities Act of 1933, as amended, or the Securities Act. Under this shelf registration statement, we and/or selling stockholders may offer shares of our common stock and preferred stock, various series of warrants to purchase common stock or preferred stock, or any combination thereof, from time to time in one or more offerings under this prospectus at prices and on terms to be determined by market conditions at the time of offering. This prospectus only provides you with a general description of the securities we and/or selling stockholders may offer. Each time we and/or selling stockholders offer a type or series of securities under this prospectus, we will provide a prospectus supplement to this prospectus that will contain more specific information about the securities being offered and specific terms of the offering. We may also authorize one or more free writing prospectuses to be provided to you that may contain material information relating to these offerings. This prospectus may not be used to sell our securities unless accompanied by a prospectus supplement. Each such prospectus supplement and any related free writing prospectus that we may authorize to be provided to you may also add, update or change information contained in this prospectus or in documents incorporated by reference into this prospectus. If there is any inconsistency between the information in this prospectus and the applicable prospectus supplement or related free writing prospectus, you should rely on the prospectus supplement or any related free writing prospectus we may authorize to be provided to you. We urge you to carefully read this prospectus, any applicable prospectus supplement and any related free writing prospectus, together with the information incorporated herein by reference as described under the headings "Information Incorporated by Reference" and "Where You Can Find Additional Information" before you invest in our securities.

Neither we nor any selling stockholder have authorized anyone to provide you with information in addition to or different from that contained in this prospectus, any applicable prospectus supplement and any related free writing prospectus. We take no responsibility for, and can provide no assurances as to the reliability of, any information not contained in this prospectus, any applicable prospectus supplement or any related free writing prospectus that we may authorize to be provided to you. This prospectus is an offer to sell only the securities offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. You should assume that the information in this prospectus, any applicable prospectus supplement or any related free writing prospectus is accurate only as of the date on the front of the document (unless the information specifically indicates that another date applies) and that any information incorporated by reference is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of this prospectus, any applicable prospectus supplement or any related free writing prospectus, or any sale of a security.

This prospectus contains summaries of certain provisions contained in some of the documents described herein, but reference is made to the actual documents for complete information. All of the summaries are qualified in their entirety by the actual documents. Copies of some of the documents referred to herein have been filed, will be filed or will be incorporated by reference as exhibits to the registration statement of which this prospectus is a part, and you may obtain copies of those documents as described below under the heading "Where You Can Find Additional Information."

NOTE REGARDING FORWARD-LOOKING STATEMENTS

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

Factors that might cause these differences include the following:

- our ability to successfully commercialize, market and achieve market acceptance of SUSTOL® (granisetron) extended-release injection ("SUSTOL") and for future product candidates, including our positioning relative to competing products;
- estimates of the outcomes of our New Drug Application ("NDA") submission to the U.S. Food and Drug Administration ("FDA") for CINVANTI™ (HTX-019) ("CINVANTI") and potential regulatory approval for and commercial launch of CINVANTI;
- any limitations or unfavorable warning or cautionary language that the FDA may ultimately impose on the label for CINVANTI;
- the potential market opportunities for SUSTOL, CINVANTI and HTX-011;
- our competitors' activities, including decisions as to the timing of competing product launches, generic entrants, pricing and discounting;
- whether safety and efficacy results of our clinical trials and other required tests for approval of our product candidates provide data to warrant progression of clinical trials, potential regulatory approval or further development of any of our product candidates;
- our ability to meet the post-marketing study requirements within the FDA's mandated timelines and to obtain favorable results and comply with standard post-marketing requirements including U.S. federal advertising and promotion laws, federal and state anti-fraud and abuse laws, healthcare information privacy and security laws, safety surveillance, and disclosure of payments or other transfers of value to healthcare professionals and entities for SUSTOL or any of our product candidates;
- our ability to successfully develop and achieve regulatory approval for other future product candidates utilizing our proprietary Biochronomer® sustained-release drug delivery technology;
- our ability to establish key collaborations and vendor relationships 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 operate in non-U.S. jurisdictions in which we may choose to do business, including compliance with applicable regulatory requirements and laws;
- uncertainties associated with obtaining and enforcing patents to protect our products, and our ability to successfully defend ourselves against unforeseen third-party infringement claims;

- our estimates regarding our capital requirements; and
- our ability to obtain additional financing and raise capital as necessary to fund operations or pursue business opportunities.

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

This prospectus may also contain estimates, projections and other information concerning our industry, our business, and the markets for certain diseases, including data regarding the estimated size of those markets. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances reflected in this information.

ABOUT THE COMPANY

Unless the context requires otherwise, in this Prospectus, the "Company," "Heron" "we," "us" and "our" refer to Heron Therapeutics, Inc.

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

Our common stock is listed on The NASDAQ Capital Market under the symbol "HRTX."

We were founded in February 1983 as a California corporation under the name AMCO Polymerics, Inc., or AMCO. AMCO changed its name to Advanced Polymer Systems, Inc. in 1984 and was reincorporated in the state of Delaware in 1987. We changed our name to A.P. Pharma, Inc. in May 2001 and changed our name from A.P. Pharma, Inc. to Heron Therapeutics, Inc. in January 2014. Our executive offices are located at 4242 Campus Point Court, Suite 200, San Diego, California 92121 and our telephone number is (858) 251-4400. Additional information regarding our company, including our audited financial statements and descriptions of our business, is contained in the documents incorporated by reference in this prospectus. See "Where You Can Find Additional Information" on page 13 and "Information Incorporated by Reference" beginning on page 13.

RISK FACTORS

Investing in our securities involves a high degree of risk. Before you decide whether to purchase any of our securities, in addition to the other information, documents or reports included in or incorporated by reference into this prospectus and any accompanying prospectus supplement or other offering materials, you should carefully consider the risk factors in the section entitled “Risk Factors” in any prospectus supplement to this prospectus as well as in our most recent Annual Report on Form 10-K and any subsequent Quarterly Reports on Form 10-Q, which are incorporated by reference into this prospectus and any prospectus supplement in their entirety, as the same may be amended, supplemented or superseded from time to time by our filings under the Exchange Act. For additional information, see the section entitled “Where You Can Find Additional Information.” These risks could materially and adversely affect our business, results of operations, financial condition and prospects and could result in a partial or complete loss of your investment.

USE OF PROCEEDS

We intend to use the net proceeds we receive from the sale of securities as set forth in the applicable prospectus supplement. Unless otherwise set forth in a prospectus supplement, we will not receive any proceeds from the sale of securities by any selling stockholder.

RATIO OF EARNINGS TO FIXED CHARGES

If we offer preference equity securities under this prospectus, then we will, if required at that time, provide a ratio of combined fixed charges and preference dividends to earnings in the applicable prospectus supplement for such offering or in a document that we file with the SEC and incorporate by reference in the future.

DESCRIPTION OF SECURITIES

Description of Capital Stock

The following is a description of our common stock and a summary of our preferred stock. You should refer to our certificate of incorporation and our bylaws for the actual terms of our capital stock. Copies of our certificate of incorporation and bylaws may be obtained as described under the heading “Where You Can Find Additional Information” in this prospectus.

We are authorized to issue up to 102,500,000 shares of capital stock of which 100,000,000 shares are of common stock, par value $0.01 per share, and 2,500,000 shares are of preferred stock, par value $0.01 per share.

Common Stock

The holders of common stock are entitled to one vote per share on all matters to be voted upon by the stockholders. Subject to preferences that may be applicable to any outstanding preferred stock, the holders of common stock are entitled to receive ratably all dividends, if any, as may be declared form time to time by our Board of Directors out of the funds legally available. In the event of the liquidation, dissolution or winding up of the Company, the holders of our common stock are entitled to share ratably in all assets remaining after payment of liabilities, subject to prior distribution rights of preferred stock, if any, then outstanding. The common stock has no preemptive or conversion rights. There are no redemption or sinking fund provisions applicable to the common stock. All outstanding shares of common stock are fully paid and non-assessable, and the shares of common stock to be issued upon completion of this offering will be fully paid and non-assessable.

As of April 17, 2017, 53,696,906 shares of our common stock were issued and outstanding.

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

Listing. Our common stock is currently listed on The NASDAQ Capital Market under the symbol “HRTX.”

Preferred Stock

Under our certificate of incorporation, our Board of Directors has the authority, without further action by stockholders, to designate up to 2,500,000 shares of preferred stock in one or more series and to fix the rights, preferences, privileges, qualifications and restrictions granted to or imposed upon the preferred stock, including dividend rights, conversion rights, voting rights, rights and terms of redemption, liquidation preference and sinking fund terms, any or all of which may be greater than the rights of the common stock.

As of April 17, 2017, no shares of preferred stock were issued and outstanding.

If we issue preferred stock, we will fix the rights, preferences, privileges, qualifications and restrictions of the preferred stock of each series that we sell under this prospectus and applicable prospectus supplements in the certificate of designations relating to that series. If we issue preferred stock, we will incorporate by reference into the registration statement of which this prospectus is a part the form of any certificate of designations that describes the terms of the series of preferred stock we are offering before the issuance of the related series of preferred stock. We urge you to read the prospectus supplement and any free writing prospectus related to any series of preferred stock we may offer, as well as the complete certificate of designations that contains the terms of the applicable series of preferred stock.

Certain Provisions Affecting Control of Heron Therapeutics

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

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

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

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

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

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

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

Section 203 defines “business combination” to include:

- any merger or consolidation involving the corporation and the interested stockholder;
- any sale, transfer, pledge or other disposition of 10% or more of our assets involving the interested stockholder;

- in general, any transaction that results in the issuance or transfer by us of any of our stock to the interested stockholder; or
- the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits provided by or through the corporation.

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

Description of Warrants

General Description of Warrants

We may issue warrants for the purchase of common stock, preferred stock or any combination of these securities. Warrants may be issued independently or together with other securities and may be attached to or separate from any offered securities. Each series of warrants will be issued under a separate warrant agreement to be entered into between a warrant agent and us. The warrant agent will act solely as our agent in connection with the warrants and will not have any obligation or relationship of agency or trust for or with any holders or beneficial owners of warrants. The following outlines some of the general terms and provisions of the warrants that we may issue from time to time. Additional terms of the warrants and the applicable warrant agreement will be set forth in the applicable prospectus supplement. The following description, and any description of the warrants included in a prospectus supplement, may not be complete and is subject to and qualified in its entirety by reference to the terms and provisions of the applicable warrant agreement, which we will file with the SEC in connection with any offering of warrants.

Stock Warrants

The prospectus supplement relating to a particular issue of warrants exercisable for common stock or preferred stock will describe the terms of the common stock warrants and preferred stock warrants, including the following:

- the title of the warrants;
- the offering price for the warrants, if any;
- the aggregate number of the warrants;
- the designation and terms of the common stock or preferred stock that may be purchased upon exercise of the warrants;
- if applicable, the designation and terms of the securities that the warrants are issued with and the number of warrants issued with each security;
- if applicable, the date from and after which the warrants and any securities issued with the warrants will be separately transferable;
- the number of shares and price of common stock or preferred stock that may be purchased upon exercise of a warrant;
- the dates on which the right to exercise the warrants commences and expires;
- if applicable, the minimum or maximum amount of the warrants that may be exercised at any one time;
- if applicable, a discussion of material U.S. federal income tax considerations;
- anti-dilution provisions of the warrants, if any;

- redemption or call provisions, if any, applicable to the warrants; and
- any additional terms of the warrants, including terms, procedures and limitations relating to the exchange and exercise of the warrants.

Exercise of Warrants

Each warrant will entitle the holder of the warrant to purchase at the exercise price set forth in the applicable prospectus supplement the number of shares of common stock or preferred stock being offered. Holders may exercise warrants at any time up to the close of business on the expiration date set forth in the applicable prospectus supplement. After the close of business on the expiration date, unexercised warrants will be void. Holders may exercise warrants as set forth in the prospectus supplement relating to the warrants being offered.

Until a holder exercises the warrants to purchase any securities underlying the warrants, the holder will not have any rights as a holder of the underlying securities by virtue of ownership of warrants.

SELLING STOCKHOLDERS

Selling stockholders are persons or entities that, directly or indirectly, have acquired or will from time to time acquire from us, our securities. Such selling stockholders may be parties to registration rights agreements with us, or we otherwise may have agreed or will agree to register their securities for resale. The initial purchasers of our securities, as well as their transferees, pledgees, donees or successors, all of whom we refer to as "selling stockholders," may from time to time offer and sell our securities pursuant to this prospectus, any applicable prospectus supplement or post-effective amendment.

Information regarding the beneficial ownership of our securities by a selling stockholder, the number of securities being offered by a selling stockholder and the number of securities beneficially owned by a selling stockholder after the applicable offering, where applicable, will be set forth in a prospectus supplement or in a post-effective amendment. The applicable prospectus supplement or post-effective amendment will also disclose whether any of the selling stockholders has held any position or office with, has been employed by or otherwise has had a material relationship with us during the three years prior to the date of the applicable prospectus supplement or post-effective amendment.

PLAN OF DISTRIBUTION

We may sell the securities covered by this prospectus from time to time in one or more offerings. Registration of the securities covered by this prospectus does not mean, however, that those securities will necessarily be offered or sold.

We may sell the securities separately or together:

- through one or more underwriters or dealers in a public offering and sale by them;
- directly to investors; or
- through agents.

We may sell the securities from time to time:

- in one or more transactions at a fixed price or prices, which may be changed from time to time;
- at market prices prevailing at the times of sale;
- at prices related to such prevailing market prices; or
- at negotiated prices.

We will describe the method of distribution of the securities issued pursuant to this prospectus and the terms of the offering in the applicable prospectus supplement. Discounts or concessions allowed or re-allowed or paid to dealers may be changed from time to time.

If underwriters are used in the sale of any securities, the securities will be acquired by the underwriters for their own account and may be resold from time to time in one or more transactions described above. The securities may be either offered to the public through underwriting syndicates represented by managing underwriters, or directly by underwriters. Generally, the underwriters' obligations to purchase the securities will be subject to conditions precedent and the underwriters will be obligated to purchase all of the securities if they purchase any of the securities. We may use underwriters with whom we have a material relationship. We will describe in the applicable prospectus supplement, naming the underwriter, the nature of any such relationship.

We may authorize underwriters, dealers or agents to solicit offers by certain purchasers to purchase the securities from us at the public offering price set forth in the applicable prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on a specified date in the future. The contracts will be subject only to those conditions set forth in the applicable prospectus supplement, and the applicable prospectus supplement will set forth any commissions we pay for solicitation of these contracts.

Underwriters, dealers and agents may be entitled to indemnification by us against certain civil liabilities, including liabilities under the Securities Act, or to contribution with respect to payments made by the underwriters, dealers or agents, under agreements between us and the underwriters, dealers and agents.

We may grant underwriters who participate in the distribution of securities an option to purchase additional securities to cover over-allotments, if any, in connection with the distribution.

Underwriters, dealers or agents may receive compensation in the form of discounts, concessions or commissions from us or our purchasers, as their agents in connection with the sale of securities. These underwriters, dealers or agents may be considered to be underwriters under the Securities Act. As a result, discounts, commissions or profits on resale received by the underwriters, dealers or agents may be treated as underwriting discounts and commissions. The applicable prospectus supplement will identify any such underwriter, dealer or agent and describe any compensation received by them from us. Any initial public offering price and any discounts or concessions allowed or re-allowed or paid to dealers may be changed from time to time.

Unless otherwise specified in the applicable prospectus supplement, all securities we offer, other than common stock, will be new issues of securities with no established trading market. Any underwriters may make a market in these securities, but will not be obligated to do so and may discontinue any market making at any time without notice. Any common stock sold pursuant to a prospectus supplement will be listed for trading on The NASDAQ Capital Market or other principal market for our common stock. We may apply to list any series of preferred stock or warrants on an exchange, but we are not obligated to do so. Therefore, there may not be liquidity or a trading market for any series of securities.

Any underwriter may engage in over-allotment transactions, stabilizing transactions, short-covering transactions and penalty bids in accordance with Regulation M under the Exchange Act. Over-allotment involves sales in excess of the offering size, which create a short position. Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum. Short covering transactions involve purchases of the securities in the open market after the distribution is completed to cover short positions. Penalty bids permit the underwriters to reclaim a selling concession from a dealer when the securities originally sold by the dealer are purchased in a covering transaction to cover short positions. Those activities may cause the price of the securities to be higher than it would otherwise be. If commenced, the underwriters may discontinue any of the activities at any time. We make no representation or prediction as to the direction or magnitude of any effect that such transactions may have on the price of the securities. For a description of these activities, see the information under the heading “Underwriting” or “Plan of Distribution” in the applicable prospectus supplement.

Underwriters, broker-dealers or agents who may become involved in the sale of the common stock may engage in transactions with and perform other services for us in the ordinary course of their business for which they receive compensation.

E XPERTS

OUM & Co. LLP, an independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2016, as set forth in their report, which is incorporated by reference in this prospectus and elsewhere in the registration statement. Our consolidated financial statements are incorporated by reference in reliance on OUM & Co. LLP’s report, given on their authority as experts in accounting and auditing.

LEGAL MATTERS

The legality of the issuance of the securities being offered hereby and the binding nature of any warrants being offered hereby is being passed upon by Gibson, Dunn & Crutcher LLP, San Francisco, California.

INFORMATION INCORPORATED BY REFERENCE

The SEC allows the Company to "incorporate by reference" the information that is filed by the Company with the SEC, which means that the Company can disclose important information to you by referring you to those documents. The documents incorporated by reference are:

1. The Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2016;
2. Portions of our Definitive Proxy Statement on Schedule 14A filed with the SEC on April 26, 2017 that have been incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2016;
3. The Company's Quarterly Report on Form 10-Q for the quarter ended March 31, 2017;
4. The Company's Current Reports on Form 8-K filed with the SEC on January 24, 2017, March 17, 2017, April 3, 2017, April 24, 2017, and June 13, 2017; and
5. The description of the Company's common stock contained in the registration statement on Form 8-A, as amended, filed with the SEC on January 22, 2014 pursuant to Section 12(b) of the Exchange Act, including any amendment or report filed for the purpose of updating that description.

All documents we file with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act, except as to any portion of any report or documents that is not deemed filed under such provisions, on or after the date of this prospectus until the earlier of the date on which all of the securities registered hereunder have been sold or the registration statement of which this prospectus is a part has been withdrawn, shall be deemed incorporated by reference in this prospectus and to be a part of this prospectus from the date of filing of those documents.

Any statement contained in a document incorporated or deemed to be incorporated by reference herein shall be deemed to be modified or superseded, for purposes of this prospectus, to the extent that a statement contained in or omitted from this prospectus, or in any other subsequently filed document that also is or is deemed to be incorporated by reference herein, modifies or supersedes such statement. Any such statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this prospectus. Nothing in this prospectus shall be deemed to incorporate information furnished, but not filed, with the SEC pursuant to Item 2.02 or Item 7.01 of Form 8-K.

Upon written or oral request, we will provide, without charge, to each person, including any beneficial owner, to whom a copy of this prospectus is delivered, upon such person's written or oral request, a copy of any and all of the information incorporated by reference in this prospectus, other than exhibits to such documents, unless such exhibits are specifically incorporated by reference into the information that this prospectus incorporates. Requests should be directed to the Secretary at Heron Therapeutics, Inc., 4242 Campus Point Court, Suite 200, San Diego, California 92121, telephone number (858) 251-4400. You may also find these documents in the "Investor Relations" section of our website, *www.herontx.com*. The information on our website is not incorporated into this prospectus. We have authorized no one to provide you with any information that differs from that contained in this prospectus. Accordingly, you should not rely on any information that is not contained in this prospectus. You should not assume that the information in this prospectus is accurate as of any date other than the date of the front cover of this prospectus.

WHERE YOU CAN FIND ADDITIONAL INFORMATION

The Company is subject to the informational requirements of the Exchange Act, and in accordance therewith, files annual, quarterly and special reports, proxy statements and other information with the SEC. You may read and copy any document filed by the Company at the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549.

Please call the SEC at 1-800-SEC-0330 for further information on the public reference room. The Company's filings with the SEC are also available to the public at the SEC's Internet web site at *http://www.sec.gov*. Statements contained in this prospectus as to the contents of any contract or other document are not necessarily complete, and in each instance we refer you to the copy of the contract or document filed as an exhibit to the registration statement, each such statement being qualified in all respects by such reference.

5,063,292 Shares

Common Stock

PROSPECTUS SUPPLEMENT

Jefferies

June 25, 2018