UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM S-3 REGISTRATION STATEMENT

UNDER THE SECURITIES ACT OF 1933

HERON THERAPEUTICS, INC.

(Exact name of Registrant as specified in its charter)

4242 Campus Point Court, Suite 200

Delaware (State or other jurisdiction of incorporation or organization)

94-2875566 (I.R.S. Employe Identification Number)

San Diego, California 92121 (858) 251-4400 (Address, including zip code, and telephone number, including area code, of Registrant's principal executive offices)

> Ira Duarte **Executive Vice President, Chief Financial Officer** Heron Therapeutics, Inc. 4242 Campus Point Court, Suite 200 San Diego, California 92121 (858) 251-4400

(Name, address, including zip code, and telephone number, including area code, of agent for service)

Copies to:

Ryan A. Murr Branden C. Berns Gibson, Dunn & Crutcher LLP 555 Mission Street, Suite 3000 San Francisco, California 94105 Telephone: (415) 393-8200

Approximate date of commencement of proposed sale to the public: As soon as practicable after the effective date of this Registration Statement. If the only securities being registered on this Form are being offered pursuant to dividend or interest reinvestment plans, please check the following box: \Box If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, check the following box. If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. \Box If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. $\hfill\Box$ If this Form is a registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box. If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box. Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act. Accelerated filer Large accelerated filer Non-accelerated filer Smaller reporting company X П Emerging growth company If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 7(a)(2)(B) of the Securities Act. \Box The registrant hereby amends this registration statement on such date or dates as may be necessary to delay its effective date until the registrant shall file a further

amendment which specifically states that this registration statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933, as amended, or until the registration statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.

The information in this preliminary prospectus is not complete and may be changed. These securities may not be sold until the registration statement filed with the Securities and Exchange Commission is effective. This preliminary prospectus is not an offer to sell these securities, and it is not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

Subject to completion, dated August 23, 2023

Preliminary Prospectus



21,897,808 Shares of Common Stock

Pursuant to this prospectus, the selling stockholders identified herein (the "Selling Stockholders") are offering on a resale basis an aggregate of 21,897,808 shares of common stock, par value \$0.01 per share (the "Common Stock"), of Heron Therapeutics, Inc. ("Heron," "we," "our" or the "Company"), a Delaware corporation. All shares of Common Stock offered for resale hereby were deemed acquired by certain Selling Stockholders pursuant to a securities purchase agreement by and among the Company and the Selling Stockholders, dated July 21, 2023 (the "Purchase Agreement"), of which 20,734,917 shares are outstanding and held by the Selling Stockholders and 1,162,891 shares are issuable upon the exercise of pre-funded warrants (the "Pre-Funded Warrants") held by certain of the Selling Stockholders and issued pursuant to the Purchase Agreement. The shares of Common Stock issued and the Common Stock issuable upon the exercise of the Pre-Funded Warrants were sold pursuant to an exemption from the registration requirements of the Securities Act of 1933, as amended (the "Securities Act") provided in Section 4(a)(2) thereof and/or Rule 506 of Regulation D promulgated thereunder. We are registering the resale of the shares of Common Stock covered by this prospectus as required by the Purchase Agreement entered into by and among the Company and the Selling Stockholders.

We will not receive any of the proceeds from sales by the Selling Stockholders of the Common Stock. Upon any exercise of the Pre-Funded Warrants by payment of cash, however, we will receive the nominal cash exercise price paid by the holders of the Pre-Funded Warrants. We intend to use those proceeds, if any, for general corporate purposes.

The Selling Stockholders may sell or otherwise dispose of the Common Stock covered by this prospectus in a number of different ways and at varying prices. We provide more information about how the Selling Stockholders may sell or otherwise dispose of the Common Stock covered by this prospectus in the section entitled "Plan of Distribution" on page 13. Discounts, concessions, commissions and similar selling expenses attributable to the sale of Common Stock covered by this prospectus will be borne by the Selling Stockholders. We will pay all expenses (other than discounts, concessions, commissions and similar selling expenses) relating to the registration of the Common Stock with the Securities and Exchange Commission.

Our common stock is listed on The Nasdaq Capital Market under the symbol "HRTX." On August 21, 2023, the last reported sale price of our common stock on The Nasdaq Capital Market was \$1.73 per share.

Investing in shares of our common stock involves a high degree of risk. Before making any investment in these shares of our common stock, you should consider carefully the risks and uncertainties described in the section entitled "Risk Factors" beginning on page 6 of this prospectus.

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 securities are not being offered in any jurisdiction where the offer is not permitted.

The date of this prospectus is August 23, 2023

TABLE OF CONTENTS

| | Page |
|----------------------------------------------------------|------|
| Cautionary Note Regarding Forward-Looking Statements | 2 |
| Prospectus Summary | 4 |
| About the Company | 4 |
| <u>The Offering</u> | 5 |
| Risk Factors | 6 |
| <u>Use of Proceeds</u> | 7 |
| Description of Common Stock | 8 |
| <u>Selling Stockholders</u> | 10 |
| Plan of Distribution | 13 |
| <u>Legal Matters</u> | 16 |
| Experts | 16 |
| Where You Can Find More Information | 17 |
| <u>Incorporation of Certain Information by Reference</u> | 18 |
| | |

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the U.S. Securities and Exchange Commission (the "SEC") utilizing a shelf registration process. Under the shelf registration process, the Selling Stockholders may, from time to time, offer and sell the shares described in this prospectus in one or more offerings. Information about the Selling Stockholders may change over time.

This prospectus provides you with a general description of the shares the Selling Stockholders may offer. Each time the Selling Stockholders sell our shares using this prospectus, to the extent necessary and required by law, we will provide a prospectus supplement that will contain specific information about the terms of that offering, including the number of shares being offered, the manner of distribution, the identity of any underwriters or other counterparties and other specific terms related to the offering. The prospectus supplement may also add, update or change information contained in this prospectus. To the extent that any statement made in a prospectus supplement is inconsistent with statements made in this prospectus, the statements made in this prospectus will be deemed modified or superseded by those made in the prospectus supplement. You should read this prospectus, any applicable prospectus supplement and the information incorporated by reference in this prospectus before making an investment in shares of our common stock. See "Where You Can Find More Information" for more information.

Neither we nor the Selling Stockholders have authorized anyone to provide any information other than that contained in this prospectus or in any free writing prospectus prepared by or on behalf of us or to which we may have referred you. Neither we nor the Selling Stockholders take any responsibility for, nor can provide assurance as to the reliability of, any other information that others may give you. Neither we nor the Selling Stockholders have authorized any other person to provide you with different or additional information, and neither of us are making an offer to sell the shares in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus is accurate only as of the date on the front cover of this prospectus, regardless of the time of delivery of the prospectus or any sale of the ordinary shares. Our business, financial condition, results of operations and prospects may have changed since the date on the front cover of this prospectus.

For investors outside of the United States, neither we nor the Selling Stockholders have done anything that would permit the offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than in the United States. You are required to inform yourselves about and to observe any restrictions relating to the offering and the distribution of this prospectus outside of the United States.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

The information contained or incorporated by reference in 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. In some cases, you can identify forward-looking statements by the use of the words "believe," "expect," "anticipate," "intend," "estimate," "project," "will," "would," "could," "should," "may," "might," "plan," "assume" and other expressions that predict or indicate future events and trends and which do not relate to historical matters. All statements other than statements of historical facts contained or incorporated by reference in this prospectus, including statements regarding our future results of operations and financial position, business and commercialization strategy, products and product candidates, research pipeline, ongoing and planned preclinical studies and clinical trials, regulatory submissions and approvals, addressable patient population, research and development expenses, timing and likelihood of success, as well as plans and objectives of management for future operations, are forward-looking statements. You should not rely on forward-looking statements because they involve known and unknown risks, uncertainties and other factors, some of which are beyond our control. These risks, uncertainties and other factors may cause our actual results, performance or achievements to be materially different from our anticipated future results, performance or achievements expressed or implied by the forward-looking statements.

Factors that might cause these differences include the following:

- our ability to successfully commercialize, market and achieve market acceptance of ZYNRELEF® (bupivacaine and meloxicam) extended-release solution ("ZYNRELEF") in the United States ("U.S."), the European Union, the other countries in the European Economic Area, ("EEA"), and any other countries in which we receive applicable regulatory approvals, and of CINVANTI® (aprepitant) injectable emulsion ("CINVANTI"), SUSTOL® (granisetron) extended-release injection ("SUSTOL") and APONVIE® (aprepitant) injectable emulsion ("APONVIE") in the U.S. (collectively, our "Products"), and our positioning relative to products that now or in the future compete with our Products or product candidates;
- the timing of the U.S. Food and Drug Administration's ("FDA") review process, whether and to what degree the FDA approves our currently pending, and any future, supplemental New Drug Application ("sNDA") for ZYNRELEF to further expand the U.S. label, and our ability to capture the potential additional market opportunity for any expanded U.S. label;
- our ability to establish satisfactory pricing and obtain adequate reimbursement from government and third-party payors of our Products and product candidates that receive regulatory approvals;
- whether study results of our Products and product candidates are indicative of the results in future studies;
- the results of the commercial launch of APONVIE in the U.S.;
- the timing and results of the commercial launch of ZYNRELEF in Europe;
- the potential regulatory approval for and commercial launch of any product candidates, if approved;
- the potential market opportunities for our Products and any product candidates, if approved;
- our competitors' activities, including decisions as to the timing of competing product launches, generic entrants, pricing and discounting;
- whether safety and efficacy results of our clinical studies and other required tests for expansion of the indications for our Products and approval of our product candidates provide data to warrant progression of clinical trials, potential regulatory approval or further development of any of our Products or 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 Products or any of our product candidates;
- our ability to successfully develop and achieve regulatory approval for any product candidates utilizing our proprietary Biochronomer® drug delivery technology ("Biochronomer Technology");
- our ability to establish key collaborations and vendor relationships for our Products and product candidates;
- our ability to successfully develop and commercialize any technology that we may in-license or products we may acquire;
- · unanticipated delays due to manufacturing difficulties, supply constraints or changes in the regulatory environment;
- our ability to successfully operate in non-U.S. jurisdictions in which we may choose to do business, including compliance with applicable regulatory requirements and laws;
- uncertainties associated with obtaining and enforcing patents and trade secrets to protect our Products, our product Candidates, our Biochronomer Technology and our other technology, and our ability to successfully defend ourselves against unforeseen third-party infringement claims;
- · our estimates regarding our capital requirements;
- the impact of our restructuring activities, including the reduced headcount and external spend; and
- our ability to obtain additional financing and raise capital as necessary to fund operations or pursue business opportunities.

Our actual results and financial condition may differ materially from those indicated in the forward-looking statements as a result of the foregoing factors, as well as those identified in this prospectus under the heading "Risk Factors" and in the applicable prospectus supplement and under similar headings in the other documents incorporated by reference into this prospectus. Therefore, you should not rely unduly on any of these forward-looking statements. Forward-looking statements contained or incorporated by reference in this prospectus speak as of the date hereof and the Company does not undertake to update any of these forward-looking statements to reflect a change in its views or events or circumstances that occur after the date of this prospectus.

PROSPECTUS SUMMARY

The following summary highlights certain information contained elsewhere in this prospectus and the documents incorporated by reference herein. This summary provides an overview of selected information and does not contain all of the information you should consider in making your investment decision. Therefore, you should read the entire prospectus and the documents incorporated by reference herein carefully before investing in our securities. Investors should carefully consider the information set forth under "Risk Factors" beginning on page 6 of this prospectus and the financial statements and other information incorporated by reference in this prospectus. In this prospectus, unless otherwise noted, (1) the term "Heron" refers to Heron Therapeutics, Inc. and (2) the terms "Company," "we," "us," and "our" refer to our ongoing business operations.

ABOUT THE COMPANY

We are a commercial-stage biotechnology company focused on improving the lives of patients by developing and commercializing therapeutic innovations that improve medical care. Our advanced science, patented technologies, and innovative approach to drug discovery and development have allowed us to create and commercialize a portfolio of products that aim to advance the standard-of-care for acute care and oncology patients.

Our executive offices are 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. Information contained on, or accessible through, our website is not incorporated by reference in this prospectus. 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. We file our annual, quarterly and special reports, proxy statements and other information with the SEC. Our filings with the SEC are also available to the public on the SEC's website at http://www.sec.gov. Additional information regarding us, including our audited financial statements and descriptions of our business, is contained in the documents incorporated by reference in this prospectus. Our common stock is traded on The Nasdaq Capital Market under the symbol "HRTX."

THE OFFERING

Pursuant to this prospectus, the Selling Stockholders are offering on a resale basis an aggregate of 21,897,808 shares of Common Stock. All shares of Common Stock offered for resale hereby were acquired by certain Selling Stockholders pursuant to the Purchase Agreement by and among the Company and the Selling Stockholders, dated July 21, 2023, of which 20,734,917 shares are outstanding and held by the Selling Stockholders and 1,162,891 shares are issuable upon the exercise of the Pre-Funded Warrants held by certain of the Selling Stockholders and issued pursuant to the Purchase Agreement.

Common Stock to be offered by the Selling

Stockholders:

 $20,\!734,\!917 \text{ shares of Common Stock and } 1,\!162,\!891 \text{ shares of Common Stock is suable}$

upon the exercise of Pre-Funded Warrants.

Common Stock outstanding prior to this offering: 140,759,276 shares.

Common Stock to be outstanding after this offering: 141,922,167 shares (assuming the exercise of all Pre-Funded Warrants).

Use of proceeds: We will not receive any of the proceeds from the sale by the Selling Stockholders of the

Common Stock. Upon any exercise of the Pre-Funded Warrants by payment of cash, however, we will receive the nominal cash exercise price paid by the holders of the

Pre-Funded Warrants. See " $\underline{\text{Use of Proceeds}}$ " on page 7 of this prospectus.

Risk factors: You should read the "Risk Factors" section beginning on page 6 of this prospectus for a

discussion of factors to consider carefully before deciding to invest in shares of our

common stock.

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

do not intend to apply for listing of the Pre-Funded Warrants on any securities exchange or

nationally recognized trading system.

RISK FACTORS

Investing in shares of our common stock involves a high degree of risk. Before investing in shares of our common stock, you should carefully consider the risks, uncertainties and assumptions contained in this prospectus and discussed under the heading "Risk Factors" included in our Annual Report on Form 10-K for the year ended December 31, 2022 and subsequent Quarterly Reports on Form 10-Q, which are on file with the SEC and are incorporated herein by reference, and which may be amended, supplemented or superseded from time to time by other reports we file with the SEC in the future, including any accompanying prospectus supplement and the documents incorporated by reference therein. Our business, financial condition, results of operations and future growth prospects could be materially and adversely affected by any of these risks. In these circumstances, the market price of our Common Stock could decline, and you may lose all or part of your investment.

USE OF PROCEEDS

We will not receive any of the proceeds from the sale of the shares of Common Stock by the Selling Stockholders. Some of the shares of Common Stock offered hereby are issuable upon the exercise of the Pre-Funded Warrants. Upon exercise of such Pre-Funded Warrants for cash, we will receive the nominal cash exercise price paid by the holders of the Pre-Funded Warrants. We intend to use those proceeds, if any, for general corporate purposes.

DESCRIPTION OF COMMON STOCK

The following is a description of our common stock. You should refer to our certificate of incorporation and our bylaws for the actual terms of our common 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 227,500,000 shares of capital stock of which 225,000,000 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 any dividends declared by the Board of Directors out of the funds legally available for payment of dividends. In the event of a liquidation, dissolution or winding up of the Company, holders of common stock will share ratably in all assets remaining after payment of liabilities and the liquidation preference of any outstanding preferred stock. Holders of common stock have no preemptive rights, no right to convert their common stock into any other securities, and no right to vote cumulatively for the election of directors. The outstanding shares of our common stock are fully paid and non-assessable.

As of July 25, 2023, 140,759,276 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."

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 Delaware General Corporation Law. 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 combinations" 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.

SELLING STOCKHOLDERS

The shares of Common Stock being offered by the Selling Stockholders are those previously issued to the Selling Stockholders and those issuable to the Selling Stockholders upon exercise of the Pre-Funded Warrants. The Selling Stockholders acquired the Common Stock and the Pre-Funded Warrants pursuant to the Purchase Agreement. We are registering the shares of Common Stock in order to permit the Selling Stockholders to offer the shares of Common Stock for resale from time to time. The Selling Stockholders may sell some, all or none of their shares of Common Stock. We do not know how long the Selling Stockholders will hold the Pre-Funded Warrants, whether any will exercise the Pre-Funded Warrants, and upon such exercise, how long such Selling Stockholders will hold the shares of Common Stock before selling them, and we currently have no agreements, arrangements or understandings with the Selling Stockholders regarding the sale of any of the shares of Common Stock. Except as otherwise disclosed in this registration statement, the Selling Stockholders have not had any material relationship with us within the past three years.

The table below lists the Selling Stockholders and other information regarding the beneficial ownership of the shares of Common Stock of each Selling Stockholder based on information supplied to us by the Selling Stockholders. The second column lists the number of shares of Common Stock beneficially owned by each Selling Stockholder, based on its ownership of the shares of Common Stock and Pre-Funded Warrants, as of the date such information was provided to us, assuming exercise of the Pre-Funded Warrants held by the Selling Stockholders on that date, without regard to any limitations on exercises. The third column lists the number shares of Common Stock being offered by this prospectus by the Selling Stockholders.

In accordance with the terms of the Purchase Agreement, this prospectus generally covers the resale of the sum of (i) the number of shares of Common Stock issued to the Selling Stockholders pursuant to the Purchase Agreement and (ii) the maximum number of shares of Common Stock issuable upon exercise of the Pre-Funded Warrants, determined as if the outstanding Pre-Funded Warrants were exercised in full as of the trading day immediately preceding the date this registration statement was initially filed with the SEC, each as of the trading day immediately preceding the applicable date of determination, without regard to any limitations on the exercise of the Pre-Funded Warrants. The fourth and fifth columns assume the sale of all of the shares of Common Stock offered by the Selling Stockholders pursuant to this prospectus. Except as noted below, beneficial ownership is determined in accordance with Section 13(d) of the Exchange Act and Rule 13d-3 thereunder. The beneficial ownership in the table below is based on 140,759,276 shares of our Common Stock actually outstanding as of July 25, 2023.

Under the terms of the Pre-Funded Warrants held by the Selling Stockholders, a Selling Stockholder may not exercise such securities to the extent such exercise would cause such Selling Stockholder, together with its affiliates and attribution parties, to beneficially own a number of shares of common stock which would exceed 4.99% (the "Maximum Percentage") of our then-outstanding common stock following such exercise, excluding for purposes of such determination shares of Common Stock issuable upon exercise of the Pre-Funded Warrants that have not been exercised. By written notice to the Company, the Selling Stockholders may from time to time increase or decrease the Maximum Percentage to any other percentage not in excess of 19.99% specified in such notice; provided, that any increase in the Maximum Percentage will not be effective until the 61st day after such notice is delivered us. The number of shares in the second and third columns do not reflect this limitation. The

Selling Stockholders may sell all, some or none of their shares of Common Stock in this offering. See "Plan of Distribution."

| | | | Shares Beneficially Owned After the Offering | | | |
|--------------------------------------------------------------|--------------------------------------------------------------------------|------------------------------------------------------|-------------------------------------------------|----------------------------------------------------------|--|--|
| Selling Stockholder | Number of Shares Beneficially Owned Prior to the Offering | Number of Shares to be Sold in the Offering | Number of Shares | Percentage of Total Outstanding Common Stock | | |
| Entities Affiliated with Rubric Capital Management LP(1) | 26,713,503 | 14,963,503 | 11,750,000 | 8.3% | | |
| Velan Capital Master Fund, LP ⁽²⁾ | 8,149,635 | 3,649,635 | 4,500,000 | 3.2% | | |
| Hercules Capital Inc. ⁽³⁾ | 364,963 | 364,963 | _ | — % | | |
| Entities Affiliated with Clearline Capital LP ⁽⁴⁾ | 5,797,615 | 2,919,707 | 2,877,908 | 2.0% | | |

- (1) The shares reported under "Shares of Common Stock Beneficially Owned Prior to the Offering" consist of (i) 22,651,982 shares of Common Stock held by Rubric Capital Master Fund LP, (ii) 2,118,381 shares of Common Stock held by Blackstone CSP-MST FMAP Fund and (iii) 1,943,140 shares of Common Stock held by BEMAP Master Fund Ltd. (collectively, the "Rubric Funds"). The Rubric Funds are managed or sub-managed by Rubric Capital Management LP is Rubric Capital Management GP LLC. The managing member of Rubric Capital Management GP LLC is David Rosen. Mr. Rosen may be deemed to have shared voting and investment power of the securities managed or sub-managed, as applicable, by Rubric Capital Management LP. Mr. Rosen disclaims beneficial ownership of such securities, except to the extent of his pecuniary interest therein. The address of the Selling Stockholders is 155 E 44th St, New York, NY 10017. Rubric Capital Management LP is party to that certain Cooperation Agreement dated February 21, 2023 by and among Heron Therapeutics. Inc. and Velan Capital Management LP attached as Exhibit 10.1 to that certain Current Report filed by the Company on Form 8-K with the Securities and Exchange Commission on February 22, 2023.
- The shares reported under "Shares of Common Stock Beneficially Owned Prior to the Offering" consist of (i) 6,986,744 shares of Common Stock and (ii) 1,162,891 Pre-Funded Warrants to purchase Common Stock. The Pre-Funded Warrants are exercisable immediately and will expire when exercised in full, however, the pre-funded warrants cannot be exercised by the Selling Stockholder if, after giving effect thereto, the Selling Stockholder (together with its affiliates) would beneficially own, as determined in accordance with Section 13(d) of the Securities Exchange Act of 1934, as amended, more than 4.99% of the outstanding shares of Common Stock. Such ownership limitation may be increased upon 61 days' notice to the Company. Velan Capital Holdings LLC ("Velan GP"), as the general partner of the Selling Stockholder, may be deemed to beneficially own the shares beneficially owned by the Selling Stockholder. Velan Capital Investment Management LP ("Velan Capital"), as the investment manager of the Selling Stockholder, may be deemed to beneficially own the shares beneficially owned by the Selling Stockholder. Velan Capital Management LLC ("Velan IM GP"), as the general partner of Velan Capital, may be deemed to beneficially own the shares beneficially owned by the Selling Stockholder. Balaji Venkataraman, as a Managing Member of each of Velan GP and Velan IM GP, may be deemed to beneficially own the shares beneficially owned by the Selling Stockholder. Adam Morgan, as a Managing Member of each of Velan GP and Velan IM GP, may be deemed to beneficially own the shares beneficially owned by the Selling Stockholder. Adam Morgan has served as Chairman of the board of directors of the Company since April 2023, and as a director since February 2023. The address of the Selling Stockholder is 1055 Powers Place, Suite B, Alpharetta, Georgia, 30009. Velan Capital Management LP is party to that certain Cooperation Agreement dated February 21, 2023 by and among Heron Therapeutics. Inc. and Rubric Capital Management LP attached as Exhibit 10.1 to that certain Current Report filed by the Company on Form 8-K with the Securities and Exchange Commission on February 22, 2023.

- (3) The shares reported under "Shares of Common Stock Beneficially Owned Prior to the Offering" consist of 364,963 shares of Common Stock. In August 2023, the Selling Stockholder, along with certain affiliates of the Selling Stockholder, entered into a secured credit facility with the Company, providing the Company with an aggregate gross principal amount of up to \$50.0 million in loans, subject to certain terms and conditions; the Selling Stockholder has been granted a first priority lien security interest in all the assets (with a few exceptions) of the Company as collateral for such credit facility. The address of the Selling Stockholder is 400 Hamilton Ave., Ste 310, Palo Alto, CA 94301.
- (4) The shares reported under "Shares of Common Stock Beneficially Owned Prior to the Offering" consist of (i) 4,552,332 shares of Common Stock held by Clearline Capital Partners LP, and (ii) 1,245,283 shares of Common Stock held by Clearline Capital Partners Master Fund LP (collectively, the "Clearline Funds"). The Clearline Funds are managed or sub-managed by Clearline Capital LP, as applicable. The general partner of Clearline Capital LP is Clearline Capital GP LLC. The managing member of Clearline Capital GP LLC is Marc Majzner. Mr. Majzner may be deemed to have shared voting and investment power of the securities managed or sub-managed, as applicable, by Clearline Capital LP.

 Mr. Majzner disclaims beneficial ownership of such securities, except to the extent of his pecuniary interest therein. The address of the Selling Stockholders is 950 3rd Ave, 23rd Floor, New York, NY 10022.

PLAN OF DISTRIBUTION

We are registering the Common Stock and the Common Stock issuable upon exercise of Pre-Funded Warrants (collectively, the "Shares") previously issued in the private placement to permit the resale of these shares of Common Stock by the Selling Stockholders thereof from time to time after the date of this prospectus. We will not receive any of the proceeds from the resale by the Selling Stockholders of the Shares. We will bear all fees and expenses incident to our obligation to register the Shares.

The Selling Stockholders, which shall include donees, pledgees, transferees or other successors-in-interest selling Shares or interests in Shares received after the date of this prospectus from a Selling Stockholder as a gift, pledge, partnership distribution or other transfer, may, from time to time, sell, transfer or otherwise dispose of any or all of their Shares or interests in shares of Common Stock on any stock exchange, market or trading facility on which the shares are traded or in private transactions. These dispositions may be at fixed prices, at prevailing market prices at the time of sale, at prices related to the prevailing market price, at varying prices determined at the time of sale, or at negotiated prices.

The Selling Stockholders may use any one or more of the following methods when disposing of the Shares or interests therein:

- on any national securities exchange or quotation service on which the securities may be listed or quoted at the time of sale;
- ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;
- block trades in which the broker-dealer will attempt to sell the Shares as agent, but may position and resell a portion of the block as principal to facilitate the transaction;
- purchases by a broker-dealer as principal and resale by the broker-dealer for its own account;
- an exchange distribution in accordance with the rules of the applicable exchange;
- · privately negotiated transactions;
- short sales;
- through the writing or settlement of options or other hedging transactions, whether through an options exchange or otherwise;
- through agreements between broker-dealers and the Selling Stockholders to sell a specified number of such Shares at a stipulated price per Share:
- a combination of any such methods of sale; and
- any other method permitted by applicable law.

The Selling Stockholders may, from time to time, pledge or grant a security interest in some or all of the Shares owned by them and, if they default in the performance of their secured obligations, the pledgees or secured parties may offer and sell the Shares, from time to time, under this prospectus, or under an amendment to this prospectus under Rule 424(b) or other applicable provision of the Securities Act amending the list of Selling Stockholders to include the pledgee, transferee or other successors in interest as Selling Stockholders under this prospectus. The Selling Stockholders also may transfer the Shares in other circumstances, in which case the pledgees, transferees or other successors in interest will be the selling beneficial owners for purposes of this prospectus.

In connection with the sale of our Common Stock or interests therein, the Selling Stockholders may enter into hedging transactions with broker-dealers or other financial institutions, which may in turn engage in short sales of the Common Stock in the course of hedging the positions they assume. The Selling Stockholders may

also sell shares of our Common Stock short and deliver these securities to close out their short positions, or loan or pledge the Common Stock to broker-dealers that in turn may sell these securities. The Selling Stockholders may also enter into options or other transactions with broker-dealers or other financial institutions or the creation of one or more derivative securities which require the delivery to each such broker-dealer or other financial institution of Shares offered by this prospectus, which Shares such broker-dealer or other financial institution may resell pursuant to this prospectus (as supplemented or amended to reflect such transaction).

The aggregate proceeds to the Selling Stockholders from the sale of the Common Stock offered by them will be the purchase price of the Common Stock less discounts or commissions, if any. Each of the Selling Stockholders reserves the right to accept and, together with its agents from time to time, to reject, in whole or in part, any proposed purchase of Common Stock to be made directly or through agents. We will not receive any of the proceeds from this offering.

The Selling Stockholders also may resell all or a portion of the Shares in open market transactions in reliance upon Rule 144 under the Securities Act, provided that they meet the criteria and conform to the requirements of that rule.

There can be no assurance that any Selling Stockholder will sell any or all of the Shares registered pursuant to the registration statement, of which this prospectus forms a part.

The Selling Stockholders and any underwriters, broker-dealers or agents that participate in the sale of the Common Stock or interests therein may be "underwriters" within the meaning of Section 2(11) of the Securities Act. Any discounts, commissions, concessions or profit they earn on any resale of the Shares may be underwriting discounts and commissions under the Securities Act. Selling Stockholders who are "underwriters" within the meaning of Section 2(11) of the Securities Act will be subject to the prospectus delivery requirements of the Securities Act.

To the extent required, the shares of our Common Stock to be sold, the names of the Selling Stockholders, the respective purchase prices and public offering prices, the names of any agents, dealer or underwriter, and any applicable commissions or discounts with respect to a particular offer will be set forth in an accompanying prospectus supplement or, if appropriate, a post-effective amendment to the registration statement that includes this prospectus.

In order to comply with the securities laws of some states, if applicable, the Common Stock may be sold in these jurisdictions only through registered or licensed brokers or dealers. In addition, in some states the Common Stock may not be sold unless it has been registered or qualified for sale or an exemption from registration or qualification requirements is available and is complied with.

We have advised the Selling Stockholders that the anti-manipulation rules of Regulation M under the Exchange Act may apply to sales of Shares in the market and to the activities of the Selling Stockholders and their affiliates. In addition, to the extent applicable, we will make copies of this prospectus (as it may be supplemented or amended from time to time) available to the Selling Stockholders for the purpose of satisfying the prospectus delivery requirements of the Securities Act. The Selling Stockholders may indemnify any broker-dealer that participates in transactions involving the sale of the Shares against certain liabilities, including liabilities arising under the Securities Act.

We are required to pay all fees and expenses incident to the registration of our securities. We have agreed to indemnify the Selling Stockholders against liabilities, including liabilities under the Securities Act and state securities laws, relating to the registration of the Shares offered by this prospectus. Once sold under the registration statement, of which this prospectus forms a part, the Shares will be freely tradable in the hands of persons other than our affiliates.

We have agreed with the Selling Stockholders to keep the registration statement of which this prospectus constitutes a part effective until the earlier of (1) such time as all of the Shares covered by this prospectus have been disposed of pursuant to and in accordance with the registration statement or (2) the date on which all of the Shares may be sold without restriction pursuant to Rule 144 of the Securities Act.

LEGAL MATTERS

Certain legal matters relating to the issuance of the securities offered by this prospectus will be passed upon for us by Gibson, Dunn & Crutcher LLP, San Francisco, California.

EXPERTS

WithumSmith+Brown, PC, an independent registered public accounting firm, has audited our consolidated financial statements as of and for the periods ended December 31, 2022, and December 31, 2021, as set forth in its reports, which are incorporated by reference in this prospectus and elsewhere in the registration statement upon the authority of said firm as experts in auditing and accounting.

Our consolidated financial statements are incorporated by reference in reliance on such reports, given on the authority of such firms as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

We are required to file annual, quarterly and current reports, proxy statements and other information with the SEC. The SEC maintains an Internet site that contains all reports and other information that we file electronically with the SEC. The address of that website is www.sec.gov. Copies of certain information filed by us with the SEC are also available on our website at www.herontx.com. Our website is not a part of this prospectus and is not incorporated by reference in this prospectus, and you should not consider the contents of our website in making an investment decision with respect to our common stock.

We have filed a registration statement, of which this prospectus is a part, covering the shares of Common Stock offered hereby. As allowed by SEC rules, this prospectus does not include all of the information contained in the Registration Statement and the included exhibits, financial statements and schedules. You are referred to the Registration Statement, the included exhibits, financial statements and schedules for further information. 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. This prospectus is qualified in its entirety by such other information.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to "incorporate by reference" the information we have filed with them, which means that we can disclose important information to you by referring you to those documents. The information we incorporate by reference is an important part of this prospectus, and information that we file later with the SEC will automatically update and supersede this information. The documents we are incorporating by reference are:

- Our Annual Report on Form 10-K for the year ended December 31, 2022, filed with the SEC on March 29, 2023;
- The information specifically incorporated by reference into our Annual Report on Form 10-K from our <u>Definitive Proxy Statement</u> on Schedule 14A, filed with the SEC on May 1, 2023;
- Our Quarterly Reports on Form 10-Q for the periods ended March 31, 2023 and June 30, 2023, filed with the SEC, respectively, on <u>May 11, 2023</u> and <u>August 14, 2023</u>;
- Our Current Reports on Form 8-K, filed with the SEC on <u>February 22, 2023</u>, <u>April 3, 2023</u>, <u>April 20, 2023</u>, <u>June 12, 2023</u>, <u>June 23, 2023</u> and July 24, 2023; and
- The description of the Company's common stock contained in Amendment No. 3 to that certain registration statement on <u>Form 8-A</u>, 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 document that is not deemed filed under such provisions, (1) on or after the date of filing of the registration statement containing this prospectus and prior to the effectiveness of the registration statement and (2) 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 and will be automatically updated and, to the extent described above, supersede information contained or incorporated by reference in this prospectus and previously filed documents that are incorporated by reference in this prospectus.

Nothing in this prospectus shall be deemed to incorporate information furnished but not filed with the SEC pursuant to Item 2.02, 7.01 or 9.01 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 the prospectus is delivered a copy of any or all of the reports or documents incorporated by reference herein (other than exhibits to such documents, unless such exhibits are specifically incorporated by reference herein). You may request a copy of these filings, at no cost, by writing or telephoning us at the following address: Heron Therapeutics, Inc., 4242 Campus Point Court, Suite 200, San Diego, California 92121 Attention: Investor Relations, telephone: (858) 251-4400. We maintain a website at www.herontx.com. You may access our definitive proxy statements on Schedule 14A, annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and periodic amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act with the SEC free of charge at our website as soon as reasonably practicable after such material is electronically filed with, or furnished to, the SEC. The information contained in, or that can be accessed through, our website is not incorporated by reference in, and is not part of, this prospectus. We have not authorized anyone 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.

Heron Therapeutics, Inc.



Up to 21,897,808 Shares of Common Stock

PROSPECTUS

August 23, 2023

PART II

Information Not Required in Prospectus

ITEM 14. OTHER EXPENSES OF ISSUANCE AND DISTRIBUTION

The following table sets forth the fees and expenses payable in connection with the registration of the Common Stock hereunder. All amounts other than the SEC registration fees are estimates.

| <u>Item</u> | Amount to be paid |
|-------------------------------------|----------------------|
| SEC registration fees | \$ 3,885 |
| Legal fees and expenses | 250,000 |
| Accounting fees and expenses | 8,000 |
| Printing and miscellaneous expenses | 30,000 |
| Total | \$ 291,885 |

ITEM 15. INDEMNIFICATION OF DIRECTORS AND OFFICERS

Section 145(a) of the Delaware General Corporation Law provides, in general, that a corporation may indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative (other than an action by or in the right of the corporation), because he or she is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, against expenses (including attorneys' fees), judgments, fines and amounts paid in settlement actually and reasonably incurred by the person in connection with such action, suit or proceeding, if he or she acted in good faith and in a manner he or she reasonably believed to be in or not opposed to the best interests of the corporation and, with respect to any criminal action or proceeding, had no reasonable cause to believe his or her conduct was unlawful.

Section 145(b) of the Delaware General Corporation Law provides, in general, that a corporation may indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action or suit by or in the right of the corporation to procure a judgment in its favor because the person is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, against expenses (including attorneys' fees) actually and reasonably incurred by the person in connection with the defense or settlement of such action or suit if he or she acted in good faith and in a manner he or she reasonably believed to be in or not opposed to the best interests of the corporation, except that no indemnification shall be made with respect to any claim, issue or matter as to which he or she shall have been adjudged to be liable to the corporation unless and only to the extent that the Court of Chancery or other adjudicating court determines that, despite the adjudication of liability but in view of all of the circumstances of the case, he or she is fairly and reasonably entitled to indemnity for such expenses which the Court of Chancery or other adjudicating court shall deem proper.

Section 145(g) of the Delaware General Corporation Law provides, in general, that a corporation may purchase and maintain insurance on behalf of any person who is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise against any liability asserted against such person and incurred by such person in any such capacity, or arising out of his or her status as such, whether or not the corporation would have the power to indemnify the person against such liability under Section 145 of the Delaware General Corporation Law.

The Company's certificate of incorporation provides that, to the extent permitted by applicable law, the Company's directors shall not be personally liable to the Company or its stockholders for monetary damages for

any breach of fiduciary duty as directors of the Company. The Company's certificate of incorporation eliminates the personal liability of directors to the fullest extent permitted by the Delaware General Corporation Law and, together with the Company's bylaws, provides that the Company shall fully indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action, suit, arbitration, alternate dispute resolution mechanism, inquiry, investigation, administrative hearing or other proceeding (whether civil, criminal, administrative, arbitrative or investigative) by reason of the fact that such person is or was a director or officer of the Company, or is or was serving at the request of the Company as a director or officer of another corporation, partnership, limited liability company, joint venture, trust, employee benefit plan, foundation, association, organization or other legal entity, against expenses (including attorneys' fees), judgments, damages, liabilities, losses, penalties, excise taxes, fines and amounts paid in settlement actually and reasonably incurred by such person in connection with such action, suit, arbitration, alternate dispute resolution mechanism, inquiry, investigation, administrative hearing or other proceeding.

The Company has also entered into agreements to indemnify its directors and certain officers in addition to the indemnification provided for in the Company's certificate of incorporation and bylaws. These agreements, among other things, indemnify the Company's directors and certain of its officers for certain expenses (including attorneys' fees), judgments, fines and settlement amounts incurred by such person in any action or proceeding, including any action by or in the right of the Company, on account of services as a director or officer of the Company or as a director or officer, of any subsidiary of the Company, or as a director or officer of any other company or enterprise that the person provides services to at the request of the Company. We also maintain an insurance policy that covers certain liabilities of directors and officers of our Company arising out of claims based on acts or omissions in their capacities as directors or officers.

ITEM 16. EXHIBITS AND FINANCIAL STATEMENT SCHEDULES

Exhibits

| Exhibit Number | Description |
|-------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 3.1 | Certificate of Incorporation, as amended through July 29, 2009 (incorporated by reference to our Quarterly Report on Form 10-Q for the quarter ended June 30, 2009, as Exhibit 3.1, filed on August 4, 2009). |
| 3.2 | <u>Certificate of Amendment of Certificate of Incorporation (incorporated by reference to our Current Report on Form 8-K, as Exhibit 3.1, filed on June 30, 2011).</u> |
| 3.3 | <u>Certificate of Amendment to the Certificate of Incorporation (incorporated by reference to our Current Report on Form 8-K, as Exhibit 3.1, filed on January 13, 2014).</u> |
| 3.4 | <u>Certificate of Amendment to the Certificate of Incorporation (incorporated by reference to our Post-Effective Amendment to its Registration Statement on Form 8-A/A, filed on July 6, 2017).</u> |
| 3.5 | Certificate of Amendment to the Certificate of Incorporation (incorporated by reference to our Annual Report on Form 10-K for the year ended December 31, 2018, as Exhibit 3.6, filed on February 22, 2019). |
| 3.6 | Certificate of Amendment to the Certificate of Incorporation (incorporated by reference to our Current Report on Form 8-K, as Exhibit 3.1, filed on June 12, 2023). |
| 3.7 | Amended and Restated Bylaws (incorporated by reference to our Current Report on Form 8-K, as Exhibit 3.1, filed on February 8, 2019). |
| 4.1 | Common Stock Certificate (incorporated by reference to our Registration on Form S-3 (Registration No. 333-162968), as Exhibit 4.1, filed on November 6, 2009). |

- 5.1 Opinion of Gibson, Dunn & Crutcher LLP.**
- 23.1 Consent of Independent Registered Public Accounting Firm (WithumSmith+Brown, PC).**
- 23.2 Consent of Gibson, Dunn & Crutcher LLP (included in legal opinion filed as Exhibit 5.1).**
- 24.1 <u>Power of Attorney (included on the signature page hereto).</u>
- 107 <u>Filing Fee Table.**</u>
- ** Filed herewith.

ITEM 17. UNDERTAKINGS

The undersigned Registrant hereby undertakes:

- (a) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:
- (i) To include any prospectus required by section 10(a)(3) of the Securities Act of 1933;
- (ii) To reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than 20% change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective registration statement; and
- (iii) To include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement;

Provided, *however*, that Paragraphs (a)(i), (ii), and (iii) of this section do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the Commission by the registrant pursuant to section 13 or section 15(d) of the Securities Exchange Act of 1934 that are incorporated by reference in the registration statement, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of the registration statement.

- (b) That, for the purpose of determining any liability under the Securities Act of 1933, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof;
- (c) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering;
 - (d) That, for the purpose of determining liability under the Securities Act of 1933 to any purchaser:
 - (i) Each prospectus filed by the Registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the registration statement as of the date the filed prospectus was deemed part of and included in the registration statement; and

- (ii) Each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5), or (b)(7) as part of a registration statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(1)(i), (vii), or (x) for the purpose of providing the information required by section 10(a) of the Securities Act of 1933 shall be deemed to be part of and included in the registration statement as of the earlier of the date such form of prospectus is first used after effectiveness or the date of the first contract of sale of securities in the offering described in the prospectus. As provided in Rule 430B, for liability purposes of the issuer and any person that is at that date an underwriter, such date shall be deemed to be a new effective date of the registration statement relating to the securities in the registration statement to which that prospectus relates, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof. Provided, however, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such effective date, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such effective date.
- (e) That, for the purpose of determining liability of the registrant under the Securities Act of 1933 to any purchaser in the initial distribution of the securities: The undersigned registrant undertakes that in a primary offering of securities of the undersigned registrant pursuant to this registration statement, regardless of the underwriting method used to sell the securities to the purchaser, if the securities are offered or sold to such purchaser by means of any of the following communications, the undersigned registrant will be a seller to the purchaser and will be considered to offer or sell such securities to such purchaser:
 - (i) Any preliminary prospectus or prospectus of the undersigned registrant relating to the offering required to be filed pursuant to Rule 424;
 - (ii) Any free writing prospectus relating to the offering prepared by or on behalf of the undersigned registrant or used or referred to by the undersigned registrant;
 - (iii) The portion of any other free writing prospectus relating to the offering containing material information about the undersigned registrant or its securities provided by or on behalf of the undersigned registrant; and
 - (iv) Any other communication that is an offer in the offering made by the undersigned registrant to the purchaser.

The undersigned Registrant hereby undertakes that, for purposes of determining any liability under the Securities Act of 1933, each filing of the Registrant's annual report pursuant to section 13(a) or section 15(d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefit plan's annual report pursuant to section 15(d) of the Securities Exchange Act of 1934) that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

Insofar as indemnification for liabilities arising under the Securities Act, as amended, may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the SEC such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of

appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

The undersigned Registrant hereby undertakes that:

- (i) For purposes of determining any liability under the Securities Act of 1933, the information omitted from the form of prospectus filed as part of this registration statement in reliance upon Rule 430A and contained in a form of prospectus filed by the Registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act of 1933 shall be deemed to be part of this registration statement as of the time it was declared effective.
- (ii) For the purpose of determining any liability under the Securities Act of 1933, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in San Diego, California, on August 23, 2023.

HERON THERAPEUTICS, INC.

By: /s/ Ira Duarte

Ira Duarte

Executive Vice President, Chief Financial Officer

KNOW ALL PERSONS BY THESE PRESENTS, that each individual whose signature appears below hereby constitutes and appoints Craig Collard and Ira Duarte, and each of them acting individually, as his or her true and lawful attorney-in-fact and agent, with full power of substitution, for him or her and in his or her name, place and stead, in any and all capacities, to sign this registration statement and any and all amendments thereto, including post-effective amendments, and to file the same, with all exhibits thereto, any related registration filed pursuant to Rule 462(b) under the Securities Act of 1933, as amended, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorney-in-fact and agent, full power and authority to do and perform each and every act and thing requisite and necessary to be done in and about the premises, as fully to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all the said attorney-in-fact and agent or his or her substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, this registration statement has been signed by the following persons in the capacities and on the dates indicated.

| Signature | Title | Date |
|------------------------------------------------------------------|---------------------------------------------------------------------------------|-----------------|
| /s/ Craig Collard Craig Collard | Chief Executive Officer and Director (Principal Executive Officer) | August 23, 2023 |
| /s/ Ira Duarte Ira Duarte | Executive Vice President, Chief Financial Officer (Principal Financial Officer) | August 23, 2023 |
| /s/ Lisa Peraza Lisa Peraza | Vice President, Chief Accounting Officer (Principal Accounting Officer) | August 23, 2023 |
| /s/ Adam Morgan Adam Morgan | Chairman of the Board of Directors | August 23, 2023 |
| /s/ Sharmila Dissanaike Sharmila Dissanaike, M.D., FACS, FCCM | Director | August 23, 2023 |
| /s/ Craig Johnson Craig Johnson | Director | August 23, 2023 |
| /s/ Kevin Kotler Kevin Kotler | Director | August 23, 2023 |
| /s/ Susan Rodriguez Susan Rodriguez | Director | August 23, 2023 |
| /s/ Christian Waage Christian Waage | Director | August 23, 2023 |

GIBSON DUNN

Gibson, Dunn & Crutcher LLP

555 Mission Street San Francisco, CA 94105-0921 Tel 415.393.8200 www.gibsondunn.com

August 23, 2023

Heron Therapeutics, Inc. 4242 Campus Point Court, Suite 200 San Diego, California 92121

Re: Heron Therapeutics, Inc.

Registration Statement on Form S-3

Ladies and Gentlemen:

We have examined the Registration Statement on Form S-3 (the "Registration Statement") of Heron Therapeutics, Inc., a Delaware corporation (the "Company"), filed with the Securities and Exchange Commission (the "Commission") pursuant to the Securities Act of 1933, as amended (the "Securities Act"), in connection with the resale from time to time by the selling stockholders identified in the Registration Statement (the "Selling Stockholders") of up to (i) 20,734,917 shares (the "Shares") of the Company's common stock, par value \$0.01 per share ("Common Stock") and (ii) 1,162,891 shares (the "Pre-Funded Warrant Shares") of Common Stock that are issuable upon exercise of pre-funded warrants (the "Pre-Funded Warrants") that were acquired by the Selling Stockholders in connection with a July 25, 2023 private placement transaction.

In arriving at the opinion expressed below, we have examined originals, or copies certified or otherwise identified to our satisfaction as being true and complete copies of the originals, of specimen common stock certificates, the Pre-Funded Warrants and such other documents, corporate records, certificates of officers of the Company and of public officials and other instruments as we have deemed necessary or advisable to enable us to render the opinions set forth below. In our examination, we have assumed without independent investigation the genuineness of all signatures, the legal capacity and competency of all natural persons, the authenticity of all documents submitted to us as originals and the conformity to original documents of all documents submitted to us as copies.

Based upon the foregoing, and subject to the assumptions, exceptions, qualifications and limitations set forth herein, we are of the opinion that (i) the Shares are validly issued, fully paid and non-assessable and (ii) the Pre-Funded Warrant Shares, when issued by the Company against payment therefor in accordance with the terms of the Pre-Funded Warrants, will be validly issued, fully paid and non-assessable.

We consent to the filing of this opinion as an exhibit to the Registration Statement, and we further consent to the use of our name under the caption "<u>Legal Matters</u>" in the Registration Statement and the prospectus that forms a part thereof. In giving these consents, we do not thereby admit that we are within the category of persons whose consent is required under Section 7 of the Securities Act or the Rules and Regulations of the Commission.

Very truly yours,

/s/ Gibson, Dunn & Crutcher LLP

Beijing • Brussels • Century City • Dallas • Denver • Dubai • Frankfurt • Hong Kong • Houston • London • Los Angeles • Munich New York • Orange County • Palo Alto • Paris • San Francisco • São Paulo • Singapore • Washington, D.C.

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in the Prospectus constituting a part of this Registration Statement on Form S-3 of our report dated March 29, 2023, relating to the consolidated financial statements of Heron Therapeutics, Inc. appearing in the entity's Annual Report on Form 10-K for the year ended December 31, 2022.

We also consent to the reference to us under the caption "Experts" in the Prospectus.

/s/ WithumSmith+Brown, PC

San Francisco, California August 23, 2023

Calculation of Filing Fee Tables

FORM S-3

(Form Type)

Heron Therapeutics, Inc.

(Exact Name of Registrant as Specified in its Charter)

Table 1: Newly Registered and Carry Forward Securities

| | Security Type | Security Class Title | Fee Calculation or Carry Forward Rule | Amount Registered | Proposed Maximum Offering Price Per Unit | Maximum Aggregate Offering Price | Fee Rate | Amount of Registration Fee | Carry Forward Form Type | Carry Forward File Number | Carry Forward Initial effective date | Filing Fee Previously Paid In Connection with Unsold Securities to be Carried Forward |
|----------------------------|-----------------------------|---------------------------------------------|---------------------------------------------------|----------------------|------------------------------------------------------|-------------------------------------------|-------------|----------------------------------|----------------------------------|------------------------------------|--------------------------------------------------|---------------------------------------------------------------------------------------|
| | Newly Registered Securities | | | | | | | | | | | |
| Fees to Be | | Common stock, par value \$0.01 per | | | | | | | | | | |
| Paid | Equity | share ⁽¹⁾ | Rule 457(c) | 21,897,808(2) | \$1.61 ⁽³⁾ | \$35,255,470 ⁽³⁾ | 0.00011020 | \$3,885 | | | | |
| Fees Previously Paid | N/A | N/A | N/A | N/A | N/A | N/A | | N/A | | | | |
| | | | | Ca | arry Forwa | rd Securities | | | | | | • |
| Carry Forward | NI/A | NI/A | N/A | N/A | | NT/A | | | NI/A | NI/A | NI/A | NI/A |
| Securities | N/A | N/A | | | | N/A | | ¢2.00= | N/A | N/A | N/A | N/A |
| | | Total Offering Amounts | | | \$35,255,470 | | \$3,885 | | | | | |
| | Total Fees Previously Paid | | | | | | _ | | | | | |
| | Total Fee Offsets | | | | | | | <u> </u> | | | | |
| | Net Fee Due | | | | | | | \$3,885 | | | | |

- (1) Pursuant to Rule 416 under the Securities Act of 1933, as amended (the "Securities Act"), this registration statement also covers such an indeterminate amount of shares of common stock as may become issuable to prevent dilution resulting from stock splits, stock dividends and similar events.
- (2) Consists of 20,734,917 shares of common stock and 1,162,891 shares of common stock issuable upon the exercise of pre-funded warrants.
- (2) Estimated solely for the purpose of calculating the registration fee, based on the average of the high and low prices of the shares of common stock on The Nasdaq Capital Market on August 17, 2023 (such date being within five business days of the date that this registration statement was first filed with the Securities and Exchange Commission, in accordance with Rule 457(c) under the Securities Act).