Heron Therapeutics Announces Financial Results for the Three and Twelve Months Ended December 31, 2021 and Highlights Recent Corporate Updates

February 28, 2022

- ZYNRELEF® has received 260 formulary approvals since initial launch in July 2021, with over a 90% hospital approval rate and over 60% of approvals have been for unrestricted usage -

- Over 300 unique accounts purchased ZYNRELEF with 70% of those accounts reordering the product -

- FDA approval received in December 2021 for a significant indication expansion of ZYNRELEF, now covering approximately 7 million procedures annually -

- CMS has issued a specific C-code in November 2021 for ZYNRELEF to support separate reimbursement for Medicare patients in the ASC setting of care -

- NDA Submission for HTX-019 for prevention of PONV in adults accepted by FDA with a PDUFA goal date of September 17, 2022 -

SAN DIEGO, Feb. 28, 2022 /PRNewswire/ -- Heron Therapeutics, Inc. (Nasdaq: HRTX), 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, today announced financial results for the three and twelve months ended December 31, 2021 and highlighted recent corporate updates.

Recent Corporate Updates

Acute Care Franchise

- **ZYNRELEF:**
  - The ZYNRELEF (bupivacaine and meloxicam) extended-release solution New Drug Application (NDA) was approved by the U.S. Food and Drug Administration (FDA) in May 2021. In December 2021, the FDA approved our supplemental New Drug Application (sNDA) for ZYNRELEF, which significantly expanded the indication statement, now covering approximately 7 million procedures annually. ZYNRELEF is currently indicated for use in adults for soft tissue or periarticular instillation to produce postsurgical analgesia for up to 72 hours after foot and ankle, small-to-medium open abdominal, and lower extremity total joint arthroplasty surgical procedures. The FDA also agreed to Heron's proposal for a second sNDA, planned for later this year, designed to further expand the indication statement.
  - ZYNRELEF became commercially available in the U.S. on July 1, 2021, and net product sales for the three and twelve months ended December 31, 2021 were $0.8 million and $2.9 million, respectively.
  - During the first two quarters of commercial launch ended December 31, 2021, over 300 unique accounts purchased ZYNRELEF with 70% of those accounts reordering the product. ZYNRELEF end-user (hospitals and ambulatory surgical centers (ASC)) demand units' volume sales increased by 126% in the fourth quarter over the prior quarter.
  - As of February 25, 2022, ZYNRELEF has received 260 formulary approvals, with over a 90% hospital approval rate, and over 60% of formulary approvals have been for unrestricted use. Over 100 additional formulary review meetings are scheduled through March 31, 2022.
  - Multiple commercial and Medicaid payers covering over 120 million lives have agreed to reimburse ZYNRELEF outside of the surgical bundle payment for surgeries performed in ASCs, with many of these covered lives also having their hospital outpatient procedures reimbursed outside the surgical bundle payment. Commercial and Medicaid payers represent more than 80% of our target patients in the outpatient setting. On November 2, 2021, we were issued a specific C-code (C9088) for separate reimbursement in the ASC setting of care effective January 1, 2022.
  - In the fourth quarter of 2021, Heron received FDA approval of two manufacturing supplements to the NDA for

ZYNRELEF to add a large-scale secondary supplier of our proprietary polymer and to add larger-scale manufacturing of ZYNRELEF. These approvals will allow for the manufacturing of millions of doses of ZYNRELEF annually at a significantly reduced cost of products sales.

- **NDA Submission for HTX-019 for Prevention of PONV in Adults Under Review:** A 505(b)(2) NDA for HTX-019 for the prevention of postoperative nausea and vomiting (PONV) in adults was submitted to the FDA in November 2021. The FDA accepted the NDA for filing and set a Prescription Drug User Fee Act (PDUFA) goal date of September 17, 2022.

Oncology Care Franchise

- **2021 Oncology Care Franchise Net Product Sales:** For the three and twelve months ended December 31, 2021, oncology care franchise net product sales were $19.9 million and $83.4 million, respectively, compared to $20.6 million and $88.6 million, respectively, for the same periods in 2020. During 2021, Heron's oncology care franchise net product sales have stabilized with moderate growth expected in 2022.

CINVANTI®

  - **Net Product Sales:** Net product sales of CINVANTI (aprepitant) injectable emulsion for the three and twelve months ended December 31, 2021 were $17.4 million and $73.5 million, respectively, compared to $20.3 million and $87.8 million, respectively, for the same periods in 2020.

  - In the fourth quarter of 2021, Heron received FDA approval of a manufacturing supplement to the NDA for CINVANTI to add larger-scale manufacturing of CINVANTI. This approval will significantly reduce the cost of products sales.

SUSTOL®

  - **Net Product Sales:** Net product sales of SUSTOL (granisetron) extended-release injection for the three and twelve months ended December 31, 2021 were $2.5 million and $9.9 million, respectively, compared to $0.3 million and $0.8 million, respectively, for the same periods in 2020.

- **2022 Oncology Care Franchise Net Product Sales Guidance:** Heron currently expects the first quarter of 2022 net product sales for the oncology care franchise in the range of $20 million to $22 million. The Company is not providing full-year 2022 financial guidance at this time due to the uncertainty around the COVID-19 pandemic and its impact on patient care.

"2021 was a tremendous year for Heron. The approval and successful commercial launch of ZYNRELEF was a game-changing milestone for patients, healthcare providers, and pain management. We are extremely pleased with the very positive feedback from patients and surgeons about the benefits of ZYNRELEF, which has resulted in a high reorder rate. With our new broader label for ZYNRELEF and the recent rapid decline of COVID, we expect to significantly expand ZYNRELEF's commercial footprint this year," said Barry Quart, Pharm.D., Chairman and Chief Executive Officer of Heron. "In oncology care, our CINV portfolio has stabilized and is poised for sales growth in 2022."

Financial Results

Net product sales for the three and twelve months ended December 31, 2021 were $20.7 million and $86.3 million, respectively, compared to $20.6 million and $88.6 million, respectively, for the same periods in 2020.

Heron's net loss for the three and twelve months ended December 31, 2021 was $54.6 million and $220.7 million, or $0.54 per share and $2.24 per share, respectively, compared to $62.3 million and $227.3 million, or $0.68 per share and $2.50 per share, respectively, for the same periods in 2020. Net loss for the three and twelve months ended December 31, 2021 included non-cash, stock-based compensation expense of $12.9 million and $46.9 million, respectively, compared to $16.0 million and $50.2 million, respectively, for the same periods in 2020.

As of December 31, 2021, Heron had cash, cash equivalents and short-term investments of $157.6 million, compared to $208.5 million as of December 31, 2020. Net cash used for operating activities for the year ended December 31, 2021 was $203.4 million, compared to $184.8 million for the same period in 2020. The increase in our net cash used for operating activities was primarily due to changes in working capital related to the launch of ZYNRELEF in July 2021, including manufacturing of commercial inventory. We expect net cash used for operating activities of $44 million to $48 million in the first quarter of 2022. We anticipate that our net cash usage will continue to moderate lower throughout 2022 as net product sales increase and we realize cost savings from anticipated larger-scale manufacturing.

Conference Call and Webcast

Heron will host a conference call and webcast on February 28, 2022 at 4:30 p.m. ET. The conference call can be accessed by dialing 877-311-5906 for domestic callers and 281-241-6150 for international callers. Please provide the operator with the passcode 9276143 to join the conference call. The conference call will also be available via webcast under the Investor Relations section of Heron's website at www.herontx.com. An archive of the teleconference and webcast will also be made available on Heron's website for 60 days following the call.

About ZYNRELEF for Postoperative Pain

ZYNRELEF is the first and only dual-acting local anesthetic that delivers a fixed-dose combination of the local anesthetic bupivacaine and a low dose

of nonsteroidal anti-inflammatory drug meloxicam. ZYNRELEF is the first modified-release local anesthetic to be classified by the FDA as an "extended-release" product because ZYNRELEF is also the first and only extended-release local anesthetic to demonstrate in Phase 3 studies significantly reduced pain and significantly increased proportion of patients requiring no opioids through the first 72 hours following surgery compared to bupivacaine solution, the current standard-of-care local anesthetic for postoperative pain control. ZYNRELEF was initially approved by the FDA in May 2021 for use in adults for soft tissue or periarticular instillation to produce postsurgical analgesia for up to 72 hours after bunionectomy, open inguinal herniorrhaphy and total knee arthroplasty. In December 2021, the FDA approved an expansion of ZYNRELEF's indication. ZYNRELEF is now indicated in adults for soft tissue or periarticular instillation to produce postsurgical analgesia for up to 72 hours after foot and ankle, small-to-medium open abdominal, and lower extremity total joint arthroplasty surgical procedures. Safety and efficacy have not been established in highly vascular surgeries, such as intrathoracic, large multilevel spinal, and head and neck procedures. In September 2020, the European Commission granted a marketing authorization for ZYNRELEF for the treatment of somatic postoperative pain from small- to medium-sized surgical wounds in adults. As of January 1, 2021, ZYNRELEF is approved in 31 European countries including the countries of the European Union and European Economic Area and the United Kingdom.

Please see full prescribing information, including Boxed Warning, at www.ZYNRELEF.com.

About HTX-019 for PONV

HTX-019 is an IV injectable emulsion formulation designed to directly deliver aprepitant, the active ingredient in EMEND® (aprepitant) capsules, which is the only substance P/neurokinin-1 (NK_1) receptor antagonist (RA) to be approved in the U.S. for the prevention of PONV in adults.

The FDA-approved dose of oral EMEND is 40 mg for PONV prevention, which is given within 3 hours prior to induction of anesthesia for surgery. In a Phase 1 clinical trial, 32 mg of HTX-019 as a 30-second IV injection was demonstrated to be bioequivalent to oral aprepitant 40 mg. The NDA for HTX-019 for PONV was submitted in November 2021 and the FDA set a PDUFA goal date of September 17, 2022.

About CINVANTI for Chemotherapy Induced Nausea and Vomiting (CINV) Prevention

CINVANTI, in combination with other antiemetic agents, is indicated in adults for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy (HEC) including high-dose cisplatin as a single-dose regimen, delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC) as a single-dose regimen, and nausea and vomiting associated with initial and repeat courses of MEC as a 3-day regimen. CINVANTI is an IV formulation of aprepitant, an NK_1 RA.

CINVANTI is the first IV formulation to directly deliver aprepitant, the active ingredient in EMEND® capsules. Aprepitant (including its prodrug, fosaprepitant) is the only single-agent NK_1 RA 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). The FDA-approved dosing administration included in the U.S. prescribing information for CINVANTI include 100 mg or 130 mg administered as a 30-minute IV infusion or a 2-minute IV injection.

Please see full prescribing information at www.CINVANTI.com.

About SUSTOL for CINV Prevention

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

Please see full prescribing information at www.SUSTOL.com.

About Heron Therapeutics, Inc.

Heron Therapeutics, Inc. is a commercial-stage biotechnology company focused on improving the lives of patients by developing best-in-class treatments to address some of the most important unmet patient needs. 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. For more information, visit www.herontx.com.

Forward-looking Statements

This news release contains "forward-looking statements" as defined by the Private Securities Litigation Reform Act of 1995. Heron cautions readers that forward-looking statements are based on management's expectations and assumptions as of the date of this news release and are subject to certain risks and uncertainties that could cause actual results to differ materially, including, but not limited to, the potential additional market opportunity for the ZYNRELEF expanded U.S. label; the timing and results of studies for the further expansion of the U.S. label for ZYNRELEF; the timing of the commercial launch of ZYNRELEF in Europe; the potential market opportunities for ZYNRELEF in the U.S. and Europe; the timing of the NDA review process for HTX-019 and whether the FDA approves HTX-019; the net product sales guidance for the oncology care franchise; the expected future balances of Heron's cash, cash equivalents and short-term investments; the expected duration over which Heron's cash, cash equivalents and short-term investments balances will fund its operations; the extent of the impact of the ongoing COVID-19 pandemic on our business; and other risks and uncertainties identified in the Company's filings with the U.S. Securities and Exchange Commission. Forward-looking statements reflect our analysis only on their stated date, and Heron takes no obligation to update or revise these statements except as may be required by law.

Heron Therapeutics, Inc.
Consolidated Statements of Operations
(In thousands, except per share amounts)

	Three Months Ended December 31,		Twelve Months Ended December 31,	
	2021	2020	2021	2020
	(Unaudited)			
Revenues:				
Net product sales	$ 20,655	$ 20,605	$ 86,346	$ 88,638
Operating expenses:				
Cost of product sales	10,941	9,392	46,021	36,189
Research and development	28,877	44,453	130,821	174,533
General and administrative	9,887	12,503	40,153	42,226
Sales and marketing	24,487	15,553	87,179	63,853
Total operating expenses	74,192	81,901	304,174	316,801
Loss from operations	(53,537)	(61,296)	(217,828)	(228,163)
Other income (expense), net	(1,109)	(985)	(2,855)	885
Net Loss	$ (54,646)	$ (62,281)	$ (220,683)	$ (227,278)
Basic and diluted net loss per share	$ (0.54)	$ (0.68)	$ (2.24)	$ (2.50)
Shares used in computing basic and diluted net loss per share	101,978	91,081	98,471	90,774

Heron Therapeutics, Inc.
Consolidated Balance Sheets
(in thousands)

	December 31, 2021	December 31, 2020
ASSETS		
Current assets:		
Cash and cash equivalents	$ 90,541	$ 105,138
Short-term investments	67,039	103,353
Accounts receivable, net	35,499	41,850
Inventory	48,382	41,905
Prepaid expenses and other current assets	12,962	21,950
Total current assets	254,423	314,196
Property and equipment, net	23,734	22,737
Right-of-use lease assets	9,829	16,277
Other assets	17,720	346
Total assets	$ 305,706	$ 353,556
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 3,803	$ 525
Accrued clinical and manufacturing liabilities	23,716	49,962
Accrued payroll and employee liabilities	15,263	13,597
Other accrued liabilities	25,859	28,369
Current lease liabilities	2,417	2,997
Convertible notes payable to related parties, net of discount	—	7,053
Total current liabilities	71,058	102,503
Non-current lease liabilities	7,996	14,561
Non-current convertible notes payable, net	149,082	—
Total liabilities	228,136	117,064
Stockholders' equity:		
Common stock	1,020	913
Additional paid-in capital	1,689,987	1,628,070
Accumulated other comprehensive income (loss)	(6)	257
Accumulated deficit	(1,613,431)	(1,392,748)
Total stockholders' equity	77,570	236,492
Total liabilities and stockholders' equity	$ 305,706	$ 353,556

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