ZYNRELEF® Label Expansion Approved

December 09, 2021

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Forward-Looking Statements

This presentation contains "forward-looking statements" as defined by the Private Securities Litigation Reform Act of 1995. We caution investors that forward-looking statements are based on management's expectations and assumptions as of the date of this presentation, and involve substantial risks and uncertainties that could cause our clinical development programs, future results, performance or achievements to differ significantly from those expressed or implied by the forward-looking statements. These risks and uncertainties include, but are not limited to, those associated with: the timing of the commercial launch of ZYNRELEF in Europe; the potential market opportunity for ZYNRELEF in the US and Europe; the potential additional market opportunity for the expanded U.S. label; the timing and results of studies for the further expansion of the U.S. label for ZYNRELEF; the timing and results of studies for the HTX-034 development program; the timing of the FDA's review process and whether the FDA approves the NDA for HTX-019 for prevention of postoperative nausea and vomiting; 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 Coronavirus Disease 2019 (COVID-19) pandemic on our business; and other risks and uncertainties identified in the Company's filings with the Securities and Exchange Commission. Forward-looking statements reflect our analysis only on their stated date, and we take no obligation to update or revise these statements except as may be required by law.

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ZYNRELEF NEW Approved Expanded Indications

Indications

ZYNRELEF contains bupivacaine, an amide local anesthetic, and meloxicam, a nonsteroidal anti-inflammatory drug (NSAID), and is 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.

Limitations of Use

Safety and efficacy have not been established in highly vascular surgeries, such as intrathoracic, large multilevel spinal, and head and neck procedures.

Successful FDA Interactions Resulted in Expansion of ZYNRELEF Label

- In a little over two months, the FDA approved our supplemental NDA to significantly expand ZYNRELEF indications to include foot and ankle, small-to-medium open abdominal, and lower extremity total joint arthroplasty surgical procedures.
  - Significantly expands the commercial opportunity to ~7 million procedures
  - Significantly improves the opportunity for therapeutic substitution
- FDA has agreed to contents of a second supplemental NDA to further expand the indications to orthopedic and soft tissue surgical procedures
  - Submission targeted for 2H2022
  - Expanded broad claim structure designed to cover the full 14 million target procedures

ZYNRELEF Launch Update

- ZYNRELEF sales off to a fast start and growing rapidly:
  - 270 unique ordering accounts
  - 58% reordering (excellent feedback from surgeons regarding clinical results with ZYNRELEF)
  - Reimbursement for ZYNRELEF outside the surgical bundle is now up to 120 million commercial and Medicaid covered lives in the ASC setting of care
- Growth expected to significantly accelerate with the approval of the expanded label for ZYNRELEF
- FDA approved manufacturing supplement to NDA to add large-scale supplier of our proprietary polymer.
  - Approval received in under 4 months
  - Allows for polymer batch size sufficient to manufacture millions of doses of ZYNRELEF annually at a significantly reduced cost of goods

Clinical Studies Needed for sNDA #2 to Obtain Broadest Label Underway

- Study 220 C-section: enrollment in Group #1 (300 mg) completed and only one additional patient to enroll in Group #2 (400 mg)

- AMAZE Study:
  - Abdominoplasty – recruiting 30 patients
  - Total Shoulder Arthroplasty – recruiting 30 patients

- Study 221 Spine: protocol finalized, recruiting 30 patients

- sNDA #2 on target for 2H2022

Important Safety Information for Patients

Important Safety Information

ZYNRELEF contains an NSAID (non-steroidal anti-inflammatory drug), a type of medicine which:

- **can increase the risk of a heart attack or stroke that can lead to death. This risk increases with higher doses and longer use of an NSAID.**
- **cannot be used during heart bypass surgery**
- **can increase the risk of gastrointestinal bleeding, ulcers, and tears.**

ZYNRELEF should also not be used:

- if you are allergic to any component of ZYNRELEF, similar local anesthetics, aspirin or other NSAIDs (such as ibuprofen or naproxen), or have had an asthma attack, hives, or other allergic reaction after taking any of these medicines.
- as a paracervical block, during childbirth.

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Important Safety Information for Patients (cont)

The most common side effects of ZYNRELEF are constipation, vomiting, and headache.

The medicines in ZYNRELEF (a local anesthetic and an NSAID) may affect the nervous and cardiovascular system; may reduce the effects of some blood pressure medications; should be avoided if you have severe heart failure; may cause adverse effects on cartilage; may cause liver or kidney problems, a rare blood disorder or life-threatening skin or allergic reactions; may harm your unborn baby if received at 20 weeks of pregnancy or later; and may cause low red blood cells (anemia).

Tell your healthcare provider about all your medical conditions and about all the medicines you take including prescription or over-the-counter medicines, vitamins, or herbal supplements to discuss if ZYNRELEF is right for you.

Talk to your healthcare provider for medical advice about side effects. Report side effects to Heron at 1-844-437-6611 or to FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

The information provided here is not comprehensive.

Please see full Prescribing Information, including Boxed Warning

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