Cumberland Pharmaceuticals Announces Initiative to Expand Availability of Caldolor® to Help Treat High Fevers Associated With Coronavirus Infections

March 31, 2020

- Caldolor® is the Only Injectable NSAID Product FDA Approved to Treat Fever
- Approved in Adult & Pediatric Patients (6 Months and Older) for Reduction of Fever

NASHVILLE, Tenn., March 31, 2020 /PRNewswire/ -- Cumberland Pharmaceuticals Inc. **(NASDAQ: CPIX)** a specialty pharmaceutical company, today announced a national initiative to support hospitals and clinics that use Caldolor® (*ibuprofen*) injection for the treatment of patients with fever, severe hyperthermia and other symptoms associated with COVID-19 infections.

Cumberland's initiative includes the availability of special supply and financial arrangements, including favorable pricing and payment terms for hospitals and clinics to help ensure timely access to Caldolor during this healthcare crisis. For more information regarding this special access, contact Jim Herman, Cumberland's Senior Vice President National Accounts at jherman@cumberlandpharma.com.

"Reducing a very high fever can be particularly important in certain patients infected by COVID-19 and we are removing logistical and financial obstacles that might stand in the way of quickly getting health care providers a very effective, fast-acting and safe fever-reducing drug. We stand ready to take further actions required to assure that medical providers have access to an uninterrupted supply of this critical medication," said A.J. Kazimi, Chief Executive Officer of Cumberland Pharmaceuticals.

Because of the potential dangers of a high fever, recent guidelines from the *Society of Critical Care Medicine* suggest that clinicians consider using pharmacologic agents for controlling fever in COIVD-19 patients.[1] High core body temperatures exceeding 101.3°F are associated with an increased incidence of convulsions, especially in children. Delirium can occur with temperatures between 103.1°F and 104.0°F, and coma with temperatures above 107.6°F.[2]

Eighty-eight percent of the patients in Wuhan, China infected with COVID-19 developed a fever during hospitalization. Of those patients, 26 percent were treated in an intensive care unit, and of those, approximately 60 percent developed respiratory failure and 31 percent developed shock. Prolonged hospital stays for those patients were not uncommon[3,4].

Some patients with high fevers are unable to swallow or retain oral antipyretic drugs and retain rectal suppositories.[5] Caldolor offers these patients relief and it is the only injectable nonsteroidal anti-inflammatory drug (NSAID) approved for the treatment of fever in the United States. Caldolor was first approved in 2009 for the reduction of fever in adults and children 6 months and older, as well as pain management for those age groups. The safety and effectiveness of IV ibuprofen has been investigated in 10 pre- and post-approval clinical studies involving nearly 2,000 subjects, resulting in a wealth of published clinical data and an outstanding safety database.

Furthermore, the definitive study of injectable ibuprofen for the treatment of fever – reported in the *New England Journal of Medicine* – found significant fever reduction, overall favorable outcome trends and no safety concerns in 455 patients. The double-blind, placebo-controlled trial evaluated large doses of injectable ibuprofen administered every six hours for up to 44 hours, and patients monitored for up to 30 days.[6] The World Health Organization has also recently issued new guidance that states there is no published or peer-reviewed data suggesting that use of ibuprofen leads to a worsening of COVID-19.[7]

Cumberland has also completed a multicenter study of Caldolor in newborns from birth to 6 months of age. Topline results from this newborn study indicated that the pharmacokinetics of the drug are similar to those in older children and adults, while no safety concerns were noted. This comes after the Company conducted clinical trials and received FDA approval in 2015 for children aged 6 months to 17 years old.

For more information on Caldolor, including important dosing and safety instructions, please see the product website and package insert at www.caldolor.com.

References:

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2. Kalil AC, Metersky ML, Klompas M, et al. Management of adults with hospital-acquired and ventilator-associated pneumonia: 2016 clinical practice guidelines by the Infectious Diseases Society of America and the American Thoracic Society. *Clin Infect Dis.* 2016;63(5):e61–111.
3. Zhou F, Ting Y, Roughui D, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *The Lancet. March 11, 2020*; DOI: https://doi.org/10.1016/S0140-6736(20)30566-3.
4. World Health Organization Situation Report from March 3, 2020.

5. Morris P, Promes JT, Guntupalli KK, et al. A multi-center, randomized, double-blind, parallel, placebo-controlled trial to evaluate the efficacy, safety, and pharmacokinetics of intravenous ibuprofen for the treatment of fever in critically ill and non-critically ill adults. *Critical Care*. 2010; 14R125.
6. Bernard GR, Wheeler AP, Russell JA, et al. The Effects of Ibuprofen on Physiology and Survival of Patients with Sepsis. *NEJM*. 1997; 336:912-918.
7. World Health Organization (WHO) Guidelines on use of ibuprofen in treating symptoms associated with COVID-19 patients. Accessed March 29, 2020.

About Caldolor®

Caldolor is indicated in adults and pediatric patients 6 months and older for the management of mild to moderate pain and the management of moderate to severe pain as an adjunct to opioid analgesics, as well as the reduction of fever. Caldolor is contraindicated in patients with known hypersensitivity to ibuprofen or other NSAIDs, patients with a history of asthma or other allergic-type reactions after taking aspirin or other NSAIDs. Caldolor is contraindicated for use during the peri-operative period in the setting of coronary artery bypass graft (CABG) surgery. Caldolor should be used with caution in patients with prior history of ulcer disease or G.I. bleeding, in patients with fluid retention or heart failure, in the elderly, those with renal impairment, heart failure, liver impairment, and those taking diuretics or ACE inhibitors. Blood pressure should be monitored during treatment with Caldolor. For full prescribing information, including boxed warning, visit www.caldolor.com.

About Cumberland Pharmaceuticals

Cumberland Pharmaceuticals Inc. is a specialty pharmaceutical company focused on the delivery of high-quality prescription brands to improve patient care. The Company develops, acquires, and commercializes brands for the hospital acute care and gastroenterology market segments. The Company's portfolio of FDA approved brands includes:

- **Acetadote®** (*acetylcysteine*) Injection, for the treatment of acetaminophen poisoning;
- **Caldolor®** (*ibuprofen*) Injection, for the treatment of pain and fever;
- **Kristalose®** (*lactulose*) for Oral Solution, a prescription laxative, for the treatment of chronic and acute constipation;
- **Omeclamox®-Pak**, (*omeprazole, clarithromycin, amoxicillin*) for the treatment of Helicobacter pylori (*H. pylori*) infection and related duodenal ulcer disease;
- **Vaprisol®** (*conivaptan*) Injection, to raise serum sodium levels in hospitalized patients with euvolemic and hypervolemic hyponatremia;
- **Vibativ®** (*telavancin*) Injection, for the treatment of certain serious bacterial infections including hospital-acquired and ventilator-associated bacterial pneumonia, as well as complicated skin and skin structure infections;
- **RediTrex™** *(methotrexate)* Injection, for the treatment of active rheumatoid, juvenile idiopathic and severe psoriatic arthritis, as well as disabling psoriasis.

For more information on Cumberland's approved products, including full prescribing information, please visit the individual product websites, links to which can be found on the Company's website www.cumberlandpharma.com.

The Company has a series of Phase II clinical programs underway evaluating its ifetroban product candidates in patients with cardiomyopathy associated with Duchenne Muscular Dystrophy ("DMD"), Systemic Sclerosis ("SSc"), and Aspirin-Exacerbated Respiratory Disease ("AERD"), Hepatorenal Syndrome ("HRS") and Portal Hypertension ("P.H.").

Forward-Looking Statements

This press release contains forward-looking statements, which are subject to certain risks and reflect Cumberland's current views on future events based on what it believes are reasonable assumptions. No assurance can be given that these events will occur. As with any business, all phases of Cumberland's operations are subject to factors outside of its control, and any one or combination of these factors could materially affect Cumberland's results of operations. These factors include market conditions, competition, an inability of manufacturers to produce Cumberland's products on a timely basis or failure of manufacturers to comply with regulations applicable to pharmaceutical manufacturers, maintaining an effective sales and marketing infrastructure, natural disasters, public health epidemics, and other events beyond our control, as more fully discussed in the Company's most recent Form 10-K and subsequent 10-Qs as filed with the SEC. There can be no assurance that results anticipated by the Company will be realized or that they will have the expected effects. Readers are cautioned not to place undue reliance on forward-looking statements, which speak only as of the date hereof. The Company does not undertake any obligation to publicly revise these statements to reflect events after the date hereof.

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Investor Contact: Erin Gull, Corporate Relations, (615) 255-0068 or Media Contact: Jeff Bradford, the Bradford Group, (615) 515-4880