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Acasti Pharma Announces Preliminary Topline Results Met All Primary Outcome Measures in the Single Dose Pharmacokinetic Study for GTX-101, the Company's Drug Candidate for the Treatment of Postherpetic Neuralgia (PHN)

LAVAL, Québec, Dec. 22, 2022 (GLOBE NEWSWIRE) -- Acasti Pharma Inc. ("Acasti" or the "Company") (Nasdaq: ACST and TSX-V: ACST), a late-stage, specialty pharma company advancing three clinical stage drug candidates addressing rare and orphan diseases, today announced that preliminary topline results for its single-dose, pharmacokinetic (PK) bridging study to evaluate the relative bioavailability of GTX-101 compared to the reference listed drug in the U.S., bupivacaine subcutaneous injectable, met all primary outcome measures for the study. The final clinical study report is anticipated to be received by the Company in the first half of 2023. This PK study was the next step in the proposed 505(b)(2) regulatory pathway for GTX-101 and provides important information on the dose and dosing frequency in humans for future planned clinical studies.

GTX-101 is a novel formulation of bupivacaine hydrochloride (HCl) for topical administration via a bio-adhesive, film-forming polymer, for relief of pain associated with Postherpetic Neuralgia (PHN), a persistent and often debilitating neuropathic pain caused by nerve damage from the varicella zoster virus (shingles), which may persist for months and even years. The potential benefits of GTX-101 could include faster onset of action and a longer duration of pain relief as compared to the lidocaine patch. GTX-101 can be conveniently sprayed on the skin wherever the pain is located, and based on the PK profile of bupivacaine, the Company believes that GTX-101 may only need to be applied once or twice a day to the affected area for 24/7 pain relief, although this dosing schedule will need to be confirmed in future clinical studies. Based on this product profile, and assuming a successful development program, the Company believes GTX-101 has the potential to be a game-changer as a non-opioid alternative to the lidocaine patch for PHN patients who suffer from this debilitating pain.

Jan D'Alvise, Chief Executive Officer of Acasti, stated, "We are very pleased to report that GTX-101 met all primary outcome measures in this study, and it moves us one step closer to bringing this exciting new treatment alternative to patients who suffer from PHN. The completion of this PK study for GTX-101 is yet another major accomplishment achieved by the Acasti team in 2022, and based on these successful results, the next step for this program is a multiple ascending dose study in healthy subjects to potentially be followed by an efficacy assessment study (Phase 2) in PHN patients."

D'Alvise continued, "We now have multiple drugs in the clinic that are progressing on schedule towards important key milestones. We continue to expect to report topline results for our PK bridging study for GTX-102, our novel formulation of betamethasone for children with Ataxia Telangiectasia (A-T) before the end of December 2022. Also, the FDA has now granted Acasti a Type C meeting in late January to confirm our proposed Phase 3 safety study design for GTX-104 and clarify their requirements to submit our NDA under section 505(b)(2). We look forward to updating you on these important milestones as they are achieved."

The Single Dose PK study for GTX-101 was a Phase 1, Randomized, Single-Dose, 4-Cohort, Parallel study to evaluate the pharmacokinetics, dose proportionality, safety and tolerability of GTX-101 (bupivacaine hydrochloride metered dose spray) and subcutaneous injectable bupivacaine in 48 healthy subjects. The primary objective was to assess the pharmacokinetics of 3 dose levels of GTX-101 (50, 100, and 200 mg) given as a single-dose topical application (metered spray). Details of the study design can be found on ClinicalTrials.gov, Identifier: NCT05517486.

The study enrolled 48 healthy adult subjects (24 males/24 females, mean age = 36 years), in 12 subjects per cohort. Subjects in Cohorts 1, 2, and 3 received GTX-101 as either 5, 10, or 20 sprays (50, 100, or 200 mg, respectively). Subjects in Cohort 4 received a single 10 mg subcutaneous injection of the active control. It is important to note that one of the secondary objectives of this study was to compare the bioavailability of these two very different modes of administration. The first subject / first dose was administered on July 26th and the dosing phase of the study was completed on August 21st, 2022.

Following GTX-101 topical administration, bupivacaine is expected to diffuse into the skin and act locally, while a limited fraction of bupivacaine is expected to diffuse into the systemic circulation as measured in the blood. This circulating level of bupivacaine in the blood stream is not anticipated to contribute significantly to the analgesic effect but should be monitored to avoid any risk of toxicity.

GTX-101 PK Study Outcome Definitions and Preliminary Topline Findings Are as Follows:

- Primary outcome measures and their definitions include:
  - C_{max} is the maximum concentration occurring at T_{max} between 0 hour to 240 hours after study drug administration.
  - T_{max} is the time of maximum concentration between 0 hour to 240 hours after study drug administration.
  - AUC_{last} is the area under the concentration time curve from the time of last dosing to the time of last quantifiable concentration.
  - AUC_{∞} is the area under the concentration time curve extrapolated to infinity.
  - T_{half} is the time required for the plasma concentration to decrease by 50%.
- The median time to reach the maximum concentration of bupivacaine in plasma (T_{max}) following GTX-101 single-dose topical applications of 50, 100 and 200 mg ranged between 18 to 24 hours depending on dose, while the median T_{max} following the

subcutaneous injection of 10 mg of bupivacaine was only 23 minutes. This finding suggests that the bupivacaine delivered by GTX-101 remains in the skin for a long period of time, potentially inducing prolonged analgesic effect in the sprayed area.

- The exposure to bupivacaine based on C_{max} and AUC_{∞} following GTX-101 topical application as a single-dose of 50, 100 and 200 mg, increased with increasing dose. This was predictable and expected.
- The systemic exposure to bupivacaine following a 200mg dose of GTX-101 was:
    - Approximately 29-fold less than a single subcutaneous dose of 10mg of bupivacaine based on C_{max} and,
    - Approximately 6-fold less than a single subcutaneous dose of 10mg of bupivacaine based on AUC_{∞}.
    - These results are predicted to correspond to an increased safety margin for GTX-101 with regards to toxicity risk.
- The mean half-life (T_{half}) following GTX-101 single-dose topical application of 50, 100 and 200 mg ranged between 24 to 37 hours depending on dose, suggesting a slow elimination and potentially long duration of effect, while the mean T_{half} following the subcutaneous injection of 10 mg of bupivacaine was only 8 hours.
- Adverse events judged as related to the study drug by the investigator were (1 case each):
    - Following GTX-101 topical application: headache (3%) and numbness (3%) at the sprayed area, and
    - Following bupivacaine subcutaneous injection: dizziness (8%) and nausea (8%).

In conclusion, this Single Dose PK study was conducted successfully, and it achieved all its primary outcome measures. The data provides Acasti with key information to help characterize the PK parameters, and safety and tolerability of GTX-101, and supports additional future clinical development. The full clinical study report will be received in the first half of calendar 2023, and the company intends to eventually publish this data.

Based on market research with more than 250 physicians, the Company believes that a significant unmet need exists for treating these patients with PHN. Approximately 40% of patients that are prescribed the standard of care, which includes oral gabapentin and lidocaine patches, experience insufficient pain relief. Gabapentin does not work well for this indication, it can cause unpleasant side effects, and was recently added to the controlled substance list in several states due to a tendency for abuse. The lidocaine patches are difficult to use as they fall off and can cause skin sensitivity and irritation, especially in older individuals, and depending on their placement, are inconvenient, uncomfortable, and unattractive. Given these issues with the oral and patch alternatives, many PHN patients end up being prescribed opioids, which given the abuse potential, physicians want to avoid at all costs.

About PHN

Postherpetic neuralgia (PHN) is neuropathic pain caused due to damage by the varicella zoster virus. After a primary varicella infection (chickenpox), the varicella zoster virus can

remain persistent but clinically latent in the sensory nerve ganglia for many years before being reactivated and becoming manifest clinically as herpes zoster (shingles). Despite healing for herpes zoster, the pain may persist for months or even years and this PHN is the most common and debilitating complication of herpes zoster.

Postherpetic neuralgia is associated with significant loss of function and reduced quality of life, particularly in the elderly, and is highly resistant to treatment. Since PHN is often resistant to pharmacologic treatments, a multimodal analgesic treatment strategy is often used to balance the efficacy and tolerability of the medication regimen, the side effects of which can be limiting and can themselves compromise quality of life and patient compliance. Postherpetic neuralgia occurs most commonly in the elderly, in whom a large number of drugs are often prescribed, and so the use of a long-acting topical analgesic with minimal risk of systemic toxicity, would be advantageous.

Current treatment of PHN most often consists of oral gabapentin (first line) and prescription lidocaine patches (second line), and refractory cases may be prescribed opioids to address persistent pain. Gabapentin and opioid abuse have continued to proliferate, and lidocaine patches are suboptimal for many reasons. Prescription lidocaine patches are only approved for PHN, and the market is currently made up of both branded and generic offerings. It is estimated that PHN affects approximately 120,000 patients per year in the United States. According to the third-party report commissioned by Acasti, the total addressable market for GTX-101 could be as large as $2.5 billion, consisting of approximately $200 million for PHN pain and $2.3 billion for non-PHN pain.

About Acasti

Acasti is a late-stage specialty pharma company with drug delivery technologies and drug candidates addressing rare and orphan diseases. Acasti's novel drug delivery technologies have the potential to improve the performance of currently marketed drugs by achieving faster onset of action, enhanced efficacy, reduced side effects, and more convenient drug delivery—all which could help to increase treatment compliance and improve patient outcomes. Acasti's three lead clinical assets have each been granted Orphan Drug Designation by the FDA, which provide the assets with seven years of marketing exclusivity post-launch in the United States, and additional intellectual property protection with over 40 granted and pending patents. Acasti's lead clinical assets target underserved orphan diseases: (i) GTX-104, an intravenous infusion targeting Subarachnoid Hemorrhage (SAH), a rare and life-threatening medical emergency in which bleeding occurs over the surface of the brain in the subarachnoid space between the brain and skull; (ii) GTX-102, an oral mucosal spray targeting Ataxia-telangiectasia (A-T), a progressive, neurodegenerative genetic disease that primarily affects children, causing severe disability, and for which no treatment currently exists; and (iii) GTX-101, a topical spray targeting PHN.

For more information, please visit: https://www.acasti.com/en.

Forward-Looking Statements

Statements in this press release that are not statements of historical or current fact constitute "forward-looking information" within the meaning of Canadian securities laws and "forward-looking statements" within the meaning of the U.S. Private Securities Litigation Reform Act of 1995, as amended, Section 27A of the Securities Act of 1933, as amended,

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Acasti Contact:
Jan D'Alvise
Chief Executive Officer
Tel: 450-686-4555
Email: info@acasti.com
www.acasti.com

Investor Relations:
Robert Blum
Lytham Partners, LLC
602-889-9700
ACST@lythampartners.com

acasti

Source: Acasti Pharma, Inc.