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Acasti Announces Preliminary Topline Results Met All Outcome Measures in the Pharmacokinetic Bridging Study for GTX-102, the Company's Drug Candidate for the Treatment of Ataxia Telangiectasia

LAVAL, Québec, Dec. 28, 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, announces that the preliminary topline results of the pharmacokinetic (PK) bridging study for GTX-102 met all outcome measures. The objectives of the study were to evaluate the bioavailability, pharmacokinetics, and safety of GTX-102, a novel, concentrated oral-mucosal metered spray of betamethasone in healthy volunteers. This new formulation is intended to improve the neurological symptoms of Ataxia Telangiectasia (A-T) in a pediatric population for which there are currently no FDA-approved therapies. GTX-102 can be sprayed conveniently over the tongue of A-T patients, who often have difficulties swallowing. This PK study was the next step in the proposed 505(b)(2) regulatory pathway for GTX-102.

Jan D'Alvise, Chief Executive Officer of Acasti, stated, "The completion of this PK bridging study is an important milestone in the advancement of our GTX-102 program designed to provide a new and convenient therapy for treating the chronic symptoms of A-T in children with this rare genetic disorder. We are very pleased to report the results of this study, which we expect will now support the advancement of the program directly into Phase 3. Currently there are no drugs approved for A-T, and we are pleased to report the topline findings of this pivotal study as we remain committed to bring this exciting and proprietary treatment to children who suffer from A-T."

This PK bridging study is a Phase 1, randomized, open-label, crossover study in healthy adult subjects to evaluate the comparative bioavailability, PK, and safety of GTX-102 administered as an oral spray compared to intramuscular (IM) betamethasone (which is expected to be the reference product for bridging purposes), and to an oral solution (OS) of betamethasone, which is available in Europe but not approved in the US. The betamethasone OS was shown to reduce neurological symptoms in children with A-T in a published multicenter, double-blind, randomized, placebo-controlled crossover trial conducted in Italy (Zannolli et al, 2012).

The primary objective of this PK bridging study was to evaluate and characterize the PK profile of GTX-102 as an oral spray. Details of the study design can be found on ClinicalTrials.gov (Identifier: NCT05531890).

A total of 48 healthy adult subjects (27 males and 21 females) were enrolled in this single

center, 5-treatment, 8-sequence, 2-period cross-over study. The 5 treatments assessed in the study were:

- GTX-102: low dose at 0.0125 mg/kg, medium dose at 0.05 mg/kg, and high dose at 0.1 mg/kg
- OS betamethasone at 0.1 mg/kg
- IM betamethasone at 0.1 mg/kg

Each subject received a single dose of 2 treatments in a cross-over fashion, in a randomized sequence over 2 treatment periods separated by 15 days. The dosing started on September 13, 2022 and ended on November 24, 2022. Betamethasone blood levels were compared between all treatment groups.

GTX-102 PK study outcome measures definitions and preliminary topline findings are as follows:

- Primary outcome measures and their definitions include:
  - $AUC_{0\text{-}72}$ is the area under the concentration time curve up to 72 hours post-dose
  - AUC_{∞} is the area under the concentration time curve extrapolated to infinity
  - C_{max} is the maximum concentration occurring between 0 hour to 72 hours after study drug administration.
- GTX-102 given at doses of 0.0125 (low), 0.5 (medium) or 0.1 (high) mg/kg, showed betamethasone blood concentrations that were highly predictable and consistent based on AUC and C_{max}, indicating good linearity and dose-proportionality.
- Following the high dose of GTX-102 (0.1 mg/kg), betamethasone blood concentrations were within the same range of exposure as IM betamethasone (0.1 mg/kg), based on AUC. The IM formulation of betamethasone will serve as a bridge for GTX-102 in the context of the proposed 505(b)(2) regulatory pathway.
- In addition, Betamethasone blood concentrations following the high dose of GTX-102 (0.1 mg/kg) were within the same range of exposure as OS betamethasone (0.1 mg/kg), based on AUC. This OS formulation was the same one that was used by Zannolli et al and may serve as a clinical comparator for further clinical development of GTX-102.
- There was statistically no significant difference ($p>0.05$) between GTX-102 (0.05 mg/kg) when comparing a fast rate of administration (each spray immediately following the preceding one) to a slow rate (1 spray/minute), as indicated by C_{max} and AUC. This is important because being able to use the fast or the slow rate of administration may provide greater flexibility for patients and caregivers.
- The Cmax of GTX-102 was within the same range of exposure as the OS, but the Cmax for the IM formulation was lower than both GTX-102 and the OS, as well as what has been reported previously for the IM in the literature. It is important to note that achieving bioequivalence with the IM was not an objective of this study, nor was it expected.
- No serious adverse events (AE) were reported during the study. AEs leading to study

discontinuation consisted of cough/fever/body pain/stuffy nose (1 case), Covid-19 (1 case) and elevated creatinine kinase (1 case), and all events occurred prior to receiving the second treatment. None were judged as being related to the study drugs by the investigator. The most frequent drug-related AE was mild headache (4 cases).

- Based on this data, Acasti will work with our clinical experts and FDA to determine the best final dosing regimen for GTX-102 to incorporate into our Phase 3 study design.

D'Alvise concluded, "With the completion of this important comparative PK bridging study, we are confident that the expected final development step for GTX-102 will be to conduct a Phase 3 safety and efficacy trial in A-T patients using a treatment regimen similar to the one already proved effective by Zannolli, et al. We plan to request a Type B meeting with the FDA following the receipt of the full PK study dataset sometime in calendar H1 2023 to confirm the proposed Phase 3 study design. If all proceeds as planned, the Phase 3 study is expected to be initiated in the second half of calendar 2023. If the Phase 3 program meets the primary endpoints, an NDA filing for GTX-102 under Section 505(b)(2) is expected to follow."

About A-T

A-T is a progressive, genetic, neurodegenerative disorder that primarily effects young children, causing severe disability, impairment of the immune system and an increasing susceptibility to infections and cancer. The hallmark symptoms of A-T are cerebellar ataxia and other motor dysfunction, and dilated blood vessels (telangiectasia) that occur in the sclera of the eyes and on the skin. Children begin to experience balance and coordination problems when they begin to walk (toddler age), and ultimately become wheelchair bound in their second decade of life. In pre-adolescence (age 5-8 years), patients experience oculomotor apraxia, dysarthria, and dysphagia. They often develop compromised immune systems and are at increased risk of developing respiratory tract infections and cancer (typically lymphomas and leukemia). Patients typically die by age 25 years from complications of lung disease or cancer.

A-T is diagnosed through a combination of clinical assessments, laboratory analysis, and genetic testing. There is no known treatment to slow disease progression, and treatments that are used are strictly aimed at symptoms (e.g., physical, occupational or speech therapy for neurologic issues), or conditions secondary to the disease (e.g., antibiotics for lung infections, chemotherapy for cancer, etc.).

A market research study commissioned by Acasti found that A-T affects approximately 4,300 patients per year in the United States and has a potential total addressable market of $150 million, based on the number of treatable patients (as disclosed in Acasti's most recently filed quarterly report on Form 10-Q).

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 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.

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, and Section 21E of the Securities Exchange Act of 1934, as amended (collectively, "forward looking statements"). Such forward looking statements involve known and unknown risks, uncertainties, and other unknown factors that could cause the actual results of Acasti to be materially different from historical results or from any future results expressed or implied by such forward-looking statements. In addition to statements which explicitly describe such risks and uncertainties, readers are urged to consider statements containing the terms "believes," "belief," "expects," "intends," "anticipates," "potential," "should," "may," "will," "plans," "continue", "targeted" or other similar expressions to be uncertain and forward looking. Readers are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date of this press release. The forward-looking statements in this press release are based upon Acasti's current expectations and involve assumptions that may never materialize or may prove to be incorrect. Actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of various risks and uncertainties, including, without limitation: (i) the success and timing of each of the planned Type B meeting with the FDA and the anticipated Phase 3 safety and efficacy trial for GTX-102, (ii) the success and timing of regulatory submissions of the PK bridging study and Phase 3 safety study protocol for GTX-104, and Acasti's other pre-clinical and clinical trials; (iii) regulatory requirements or developments; (iv) changes to clinical trial designs and regulatory pathways; (v) legislative, regulatory, political and economic developments, and (vi) the effects of COVID-19 on clinical programs and business operations. The foregoing list of important factors that could cause actual events to differ from expectations should not be construed as exhaustive and should be read in conjunction with statements that are included herein and elsewhere, including the risk factors detailed in documents that have been and may be filed by Acasti from time to time with the Securities and Exchange Commission. All forward-looking statements contained in this press release speak only as of the date on which they were made. Acasti undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made, except as required by applicable securities laws. Neither NASDAQ, the TSXV nor its Regulation Services Provider (as that term is defined in

the policies of the TSXV) accepts responsibility for the adequacy or accuracy of this release.

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