Aquestive Therapeutics Announces Pivotal Study for Anaphylm™ (epinephrine) Sublingual Film Successfully Meets Primary and Secondary Endpoints and Provides Clinical Development Update Following FDA Meeting

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- *Anaphylm meets all predefined primary and secondary pharmacokinetic endpoints*
- *Anaphylm time to maximum concentration (Tmax) is consistently faster than autoinjectors*
- *Anaphylm exposure levels (AUC) are comparable to autoinjectors for 30 minutes after dosing*
- *Anaphylm is well-tolerated with no serious adverse events*
- *Company receives positive Type C meeting feedback from the U.S. Food and Drug Administration (FDA) regarding the clinical development of Anaphylm*
- *Company reaffirms goal of filing NDA before the end of 2024*

WARREN, N.J., March 14, 2024 (GLOBE NEWSWIRE) -- Aquestive Therapeutics, Inc. (NASDAQ: AQST), a pharmaceutical company advancing medicines to bring meaningful improvement to patients' lives through innovative science and delivery technologies, today released positive topline clinical data from its Phase 3 pivotal pharmacokinetic (PK) clinical study of Anaphylm™ (epinephrine) Sublingual Film and findings from the FDA Type C meeting. Anaphylm is the Company's first and only orally administered epinephrine prodrug product candidate under development for the treatment of severe life-threatening allergic reactions, including anaphylaxis.

"We are extremely pleased with the pivotal study results as well as our recent FDA interaction," said Daniel Barber, President and Chief Executive Officer of Aquestive. "When it comes to treating severe allergic reactions including anaphylaxis, we often hear from clinicians that rapid absorption of epinephrine at the first sign of symptoms is critical. Our pivotal study indicates that Anaphylm is comparable to the leading autoinjectors immediately following administration and our time to maximum concentration, or Tmax, is faster than the leading autoinjectors. We believe this performance is unprecedented among the alternate delivery options under development and are excited at the potential of Anaphylm as the only oral medicine for treatment of severe allergies."

"In addition, our recent discussions with the FDA remained consistent with our previous interactions," continued Mr. Barber. "We believe we have a clear understanding of the remaining clinical development steps necessary for a pre-NDA meeting with the FDA in the second half of the year. Our goal continues to be to file our NDA before the end of 2024 following completion of a positive pre-NDA meeting."

David Golden, M.D., a renowned expert on anaphylaxis and an allergy-immunology consultant at Sinai Hospital of Baltimore and Franklin Square Hospital in Baltimore, stated, "The data from the Anaphylm pivotal study build on the compelling data generated from the prior Anaphylm pilot studies. These latest study results show that the sublingual administration of epinephrine provides rapid and sustained levels of epinephrine similar to approved treatments. Anaphylm is a promising needle-free alternative to the current standard of care, allowing patients to easily carry and administer this life-saving medication."

Topline Data from Pivotal Phase 3 Study in Adults
The two-part, Phase 3, single-center, open-label, randomized study was designed to compare the PK and pharmacodynamics (PD) of single and repeat doses of Anaphylm versus single and repeat doses of the epinephrine intra-muscular (IM) injection and epinephrine autoinjectors (EpiPen® and Auvi-Q®) in healthy adult subjects. The primary endpoint was to compare the PK of epinephrine following the single administration of Anaphylm to the single administration of Adrenalin (epinephrine IM injection) and autoinjectors in healthy adult subjects. The secondary endpoints included evaluating PK sustainability following repeat administration and the safety and tolerability following single and repeat administrations versus epinephrine IM injection and epinephrine autoinjectors.

The single dose part of the Phase 3 study was designed as a four-period, four-treatment, four-sequence, comparative PK study with 64 enrolled adult subjects. As outlined in the presentation posted to the Company's website and filed with the SEC today, key findings from the single dosing part of the study included that Anaphylm:

- Achieved a geometric mean Cmax of 470 pg/mL bracketed by epinephrine autoinjectors AUVI-Q at 521 pg/mL and EpiPen at 469 pg/mL,
- Generated partial AUCs between (bracketed) autoinjectors and Adrenalin manual IM injection from 5 to 60 minutes
- Maintained a median Tmax of 12 minutes compared to 20 minutes for EpiPen, 30 minutes for AUVI-Q, and 50 minutes for Adrenalin,
- Produced a meaningful change from baseline pharmacodynamic measures of blood pressure and heart rate at the first tracked time point of 2 minutes, and
- Was consistently well tolerated with no SAEs.

The repeat dosing part of the Phase 3 study was designed as a three-period, three-treatment, six sequence, comparative PK study with 36 enrolled adult subjects. As outlined in the presentation posted to the website and filed with the SEC, the key findings from the repeat dosing part of the Study included that Anaphylm:

- Maintains epinephrine plasma concentrations equal to or greater than existing injection products at all but 1 timepoint out to 2 hours,
- Demonstrated a median Tmax of 10 minutes after administration of the second dose,
- Exhibited consistent pharmacodynamics, and
- Was consistently well tolerated with no SAEs.

FDA Type C Meeting
The Company also successfully completed a Type C meeting with the FDA that addressed open items from the November 2022 End-of-Phase 2 meeting including addressing (1) the impact of any product hold time, (2) the potential for emesis (vomiting), and (3) the impact of potential mouth conditions such as angioedema (swelling).

In response to these questions, the FDA indicated that the Company has "adequately addressed" the FDA's previous concerns by removing product hold time from the administration instructions and provided additional information on how to characterize emesis in the Company's NDA submission.

Regarding mouth conditions, the FDA recommended administering Anaphylm after oral exposure to a known allergen and assessing PK performance thereunder. The Company will execute this study in the second quarter of 2024. This study will replace the Company's previously planned angioedema study.

The FDA noted that substantial progress had been made in the Anaphylm clinical development program and did not outline any new clinical development requirements. As expected, the FDA reiterated that, as with other epinephrine programs under development, concentrations of epinephrine above known EpiPen levels must be justified from a safety perspective, and PK sustainability remains a focus. Furthermore, the FDA recommended that Aquestive begin its pediatric study after completion of the remaining adult studies. The Company is aligned with this recommendation from the FDA. The FDA reserved judgement on the sufficiency of the Anaphylm clinical development program until completion of ongoing and planned studies, the results of which are expected to be presented at the pre-NDA meeting.

Table 1 provides an updated view on the expected clinical study dates.

Table 1: Anaphylm Clinical Study Timeline Status

Anticipated Timing	Pivotal PK Studies	Supportive PK Studies	FDA Meetings / Actions
Completed	Phase 3 PK Study Repeat Dose PK Study		Type C Meeting
Q1 2024		Temperature PK Study	
Q2 2024		Self-administration PK Study Allergen PK Study	
Q3 2024	Pediatric PK Study		
H2 2024			Pre-NDA Meeting

The next anticipated meeting with the FDA is the pre-NDA meeting targeted for the second half of 2024. Aquestive's goal is to file the NDA with the FDA before year end 2024.

A presentation containing additional information about this topline data and the Company's recent FDA Type C meeting is available on the Events and Presentations page within the Investor page of the Aquestive website.

About Anaphylaxis
Anaphylaxis is a serious systemic hypersensitivity reaction with that is rapid in onset and potentially fatal. As many as 49 million people in the United States are at chronic risk for anaphylaxis. Lifetime prevalence is at least 5%, or more than 16 million people in the United States. Direct costs of anaphylaxis have been estimated at $1.2 billion per year, with direct expenditures of $294 million for epinephrine, and indirect costs of $609 million. The frequency of hospital admissions for anaphylaxis has increased 500–700% in the last 10–15 years. Of patients who previously experienced anaphylaxis, 52% had never received an epinephrine auto-injector prescription, and 60% did not have an auto-injector currently available. The most common causes of anaphylaxis are foods (such as peanuts), venom from insect stings, and medications. Epinephrine injection is the current standard of treatment intended to reverse the severe manifestation of anaphylaxis, which may include skin rash, throat swelling, respiratory difficulty, gastrointestinal distress, and loss of consciousness.

About Anaphylm™
Anaphylm is a polymer matrix-based epinephrine prodrug candidate product. The product is similar in size to a postage stamp, weighs less than an ounce, and begins to dissolve on contact. No water or swallowing is required for administration. The packaging for Anaphylm is thinner and smaller than an average credit card, can be carried in a pocket, and is designed to withstand weather excursions such as exposure to rain and/or sunlight. The tradename for AQST-109, "Anaphylm" has been conditionally approved by the United States Food and Drug Administration (FDA). Final approval of the Anaphylm proprietary name is conditioned on FDA approval of the product candidate.

About Aquestive Therapeutics
Aquestive is a pharmaceutical company advancing medicines to bring meaningful improvement to patients' lives through innovative science and delivery technologies. We are developing orally administered products to deliver complex molecules, providing novel alternatives to invasive and inconvenient standard of care therapies. Aquestive has five commercialized products marketed by its licensees in the U.S. and around the world, and is the exclusive manufacturer of these licensed products. The Company also collaborates with pharmaceutical companies to bring new molecules to market using proprietary, best-in-class technologies, like PharmFilm®, and has proven drug development and commercialization capabilities. Aquestive is advancing a late-stage proprietary product pipeline focused on treating diseases of the central nervous system and an earlier stage pipeline for the treatment of severe allergic reactions, including anaphylaxis. For more information, visit Aquestive.com and follow us on LinkedIn.

Forward-Looking Statements

Certain statements in this press release include “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995. Words such as “believe,” “anticipate,” “plan,” “expect,” “estimate,” “intend,” “may,” “will,” or the negative of those terms, and similar expressions, are intended to identify forward-looking statements. These forward-looking statements include, but are not limited to, statements regarding the advancement and related timing of our product candidate Anaphylm™ (epinephrine) Sublingual Film through clinical development and approval by the FDA, including expected clinical studies and clinical study dates, the timing of the pre-NDA meeting and Aquestive's goal of filing an NDA for Anaphylm before the end of 2024, the potential benefits Anaphylm could bring to patients, and other statements that are not historical facts.

These forward-looking statements are based on the Company’s current expectations and beliefs and are subject to a number of risks and uncertainties that could cause actual results to differ materially from those described in the forward-looking statements. Such risks and uncertainties include, but are not limited to, risks associated with the Company’s development work, including any delays or changes to the timing, cost and success of its product development activities and clinical trials for Anaphylm and our other product candidates, including the uncertain impact of the COVID-19 global pandemic; risk of the Company’s ability to generate sufficient data in its PK/PD comparability submission for FDA approval of Anaphylm; risk of the Company’s ability to address the FDA’s comments on the Company’s pivotal PK study protocol and other concerns identified in the FDA Type C meeting minutes for Anaphylm, including the risk that the FDA may require additional clinical studies for approval of Anaphylm; risk of delays in or the failure to receive FDA approval of Anaphylm; risk of the success of any competing products; risk inherent in commercializing a new product (including technology risks, financial risks, market risks and implementation risks, and regulatory limitations); risk of the rate and degree of market acceptance of our product candidates and our licensed products in the U.S. and abroad; risk of insufficient capital and cash resources, including insufficient access to available debt and equity financing and revenues from operations, to satisfy all of the Company’s short-term and longer term liquidity and cash requirements and other cash needs, at the times and in the amounts needed, including to fund future clinical development activities for Anaphylm and our other product candidates; risk of the size and growth of our product markets; risks of compliance with all FDA and other governmental and customer requirements for our manufacturing facilities; risks associated with intellectual property rights and infringement claims relating to the Company's products; risk of unexpected patent developments; uncertainties related to general economic, political (including the Ukraine and Israel wars and other acts of war and terrorism), business, industry, regulatory, financial and market conditions and other unusual items; and other risks and uncertainties affecting the Company described in the “Risk Factors” section and in other sections included in the Company’s Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, and Current Reports on Form 8-K filed with the U.S. Securities and Exchange Commission. Given those uncertainties, you should not place undue reliance on these forward-looking statements, which speak only as of the date made. All subsequent forward-looking statements attributable to the Company or any person acting on its behalf are expressly qualified in their entirety by this cautionary statement. The Company assumes no obligation to update forward-looking statements or outlook or guidance after the date of this press release whether as a result of new information, future events or otherwise, except as may be required by applicable law.

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