# UNITED STATES
# SECURITIES AND EXCHANGE COMMISSION
# Washington, D.C. 20549

---

# FORM 8-K

---

## CURRENT REPORT

**Pursuant to Section 13 or 15(d)**
**of the Securities Exchange Act of 1934**

**Date of Report (Date of earliest event reported): February 28, 2022**

---

## AQUESTIVE THERAPEUTICS, INC.

(Exact name of registrant as specified in its charter)

---

| **Delaware** | **001-38599** | **82-3827296** |
|---|---|---|
| (State or Other Jurisdiction of Incorporation) | (Commission File Number) | (I.R.S. Employer Identification No.) |

**30 Technology Drive**
**Warren, NJ 07059**
(Address of Principal Executive Offices) (Zip Code)

**(908) 941-1900**
(Registrant's telephone number, including area code)

**Not Applicable**
(Former name or former address, if changed since last report)

---

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

| Title of each class | Trading Symbol(s) | Name of each exchange on which registered |
|---|---|---|
| Common Stock, par value $0.001 per share | AQST | Nasdaq Global Market |

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

**Item 8.01. Other Events.**

On February 28, 2022, Aquestive Therapeutics, Inc. (the "Company") issued a press release announcing that John Oppenheimer, M.D., FAAAAI, Clinical Professor of Medicine at UMDNJ Rutgers, Pulmonary and Allergy Associates NJ, presented a late breaking poster recapping topline data from a Phase 1 pharmacokinetic study of AQST-109 epinephrine oral film at the American Academy of Allergy, Asthma, and Immunology (AAAAI) annual meeting, which was held from February 25-28 in Phoenix, Arizona. At AAAAI, Dr. Oppenheimer presented a poster entitled "A Phase 1, Randomized Study Evaluating the Safety Tolerability, Pharmacokinetics (PK) and Pharmacodynamics (PD) of Single Ascending Doses of Epinephrine Prodrug 109 Sublingual Film (AQST-109) in Healthy Male Volunteers".

The full text of the press release and a copy of the Poster Presentation are filed as Exhibits 99.1 and 99.2, respectively, to this Current Report on Form 8-K and incorporated herein by reference; provided, however that information on or connected to the Company's website referenced in the Company's press release is expressly not incorporated by reference into or intended to be filed as a part of this Current Report on Form 8-K.

The press release attached as Exhibit 99.1 to this Current Report on Form 8-K includes "safe harbor" language pursuant to the Private Securities Litigation Reform Act of 1995, as amended, indicating that certain statements contained therein are "forward-looking" rather than historical.

The Poster Presentation is available on the Company's website located at www.aquestive.com, although the Company reserves the right to discontinue that availability at any time.

**Item 9.01. Financial Statements and Exhibits.**

(d) Exhibits.

| Exhibit Number | Description |
|---|---|
| 99.1 | Press Release of Aquestive Therapeutics, Inc. dated February 28, 2022 |
| 99.2 | AAAAI Poster Presentation of Aquestive Therapeutics, Inc. |
| 104 | Cover Page Interactive Data File (embedded within the Inline XBRL document) |

**SIGNATURE**

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

**Aquestive Therapeutics, Inc.**

Date: February 28, 2022

By: /s/ A. Ernest Toth, Jr.
A. Ernest Toth, Jr.
Chief Financial Officer

# Aquestive Therapeutics Presented Positive Topline Phase 1 Results for AQST-109 Epinephrine Oral Film at American Academy of Allergy, Asthma, and Immunology (AAAAI) Annual Meeting

WARREN, N.J., Feb. 28, 2022 (GLOBE NEWSWIRE) -- Aquestive Therapeutics, Inc. (NASDAQ: AQST), a pharmaceutical company advancing medicines to solve patients' problems with current standards of care and provide transformative products to improve their lives, presented a late breaking poster recapping positive topline data from a Phase 1 pharmacokinetic study of AQST-109 epinephrine oral film at the American Academy of Allergy, Asthma, and Immunology (AAAAI) annual meeting, which was held from February 25-28 in Phoenix, Arizona.

**Poster Title:** A Phase 1, Randomized Study Evaluating the Safety Tolerability, Pharmacokinetics (PK) and Pharmacodynamics (PD) of Single Ascending Doses of Epinephrine Prodrug 109 Sublingual Film (AQST-109) in Healthy Male Volunteers
**Poster Number:** L37
**Presentation Time:** February 28, 2022, at 9:45 am MST

**Lead Author:** John Oppenheimer, M.D., FAAAAI, Clinical Professor of Medicine at UMDNJ Rutgers, Pulmonary and Allergy Associates NJ

**"**This poster presentation provides the opportunity to share our first-in-human data for AQST-109 to the international allergy community," stated John Oppenheimer, M.D., FAAAAI, Clinical Professor of Medicine at UMDNJ Rutgers, Pulmonary and Allergy Associates NJ. "Dosing with AQST-109 resulted in PK and PD responses that were within the expected therapeutic range. This is the first time it has been demonstrated that epinephrine can achieve therapeutic blood concentrations following sublingual administration. AQST-109 shows promise as a viable alternative to injection for the management of anaphylaxis. I look forward to further evaluation of this investigational medicine."

The webcast of Dr. Oppenheimer's presentation is available for viewing to registered attendees in the AAAAI Meeting Library.

**About AQST-109**
AQST-109 is a polymer matrix-based epinephrine prodrug administered as a sublingual film that is applied under the tongue for the rapid delivery of epinephrine. 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 AQST-109 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 Investigational New Drug Application (IND) was opened by the FDA on February 24, 2022. Separately, Health Canada provided clearance to continue our adaptive design crossover study. The Company expects to move forward with the manufacture of registration batches and to conduct pivotal studies for AQST-109 in 2022.

**About Aquestive Therapeutics**
Aquestive Therapeutics is a pharmaceutical company advancing medicines to solve patients' problems with current standards of care and provide transformative products to improve their lives. The Company has four approved and licensed products and commercialized one internally-developed proprietary product to date, Sympazan® (clobazam) oral film. The Company also has a commercial proprietary product pipeline focused on the treatment of diseases of the central nervous system, or CNS, and other unmet needs, and is developing orally administered complex molecules to provide alternatives to invasively administered standard of care therapies. The Company also collaborates with other pharmaceutical companies to bring new molecules to market using proprietary, best-in-class technologies, like PharmFilm®, and has proven capabilities for drug development and commercialization.

**Forward-Looking Statement**
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 AQST-109 through the regulatory and development pipeline and business strategies, market opportunities, and other statements that are not historical facts. These forward-looking statements are subject to the uncertain impact of the COVID-19 global pandemic on our business including with respect to our clinical trials including site initiation, patient enrollment and timing and adequacy of clinical trials; on regulatory submissions and regulatory reviews and approvals of our product candidates; pharmaceutical ingredient and other raw materials supply chain, manufacture, and distribution; sale of and demand for our products; our liquidity and availability of capital resources; customer demand for our products and services; customers' ability to pay for goods and services; and ongoing availability of an appropriate labor force and skilled professionals. Given these uncertainties, the Company is unable to provide assurance that operations can be maintained as planned prior to the COVID-19 pandemic.

These forward-looking statements are based on our 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 our product development activities and clinical trials for AQST-109 and our other product candidates; risk of delays in U.S. Food and Drug Administration (FDA) approval of AQST-109, Libervant™ (diazepam) Buccal Film, and our other drug candidates or failure to receive approval; ability to address the concerns identified in the FDA's Complete Response Letter dated September 25, 2020 regarding the New Drug Application for Libervant; risk of our ability to demonstrate to the FDA "clinical superiority" within the meaning of the FDA regulations of Libervant relative to FDA-approved diazepam rectal gel and nasal spray products including by establishing a major contribution to patient care within the meaning of FDA regulations relative to the approved products as well as risks related to other potential pathways or positions which are or may in the future be advanced to the FDA to overcome the seven year orphan drug exclusivity granted by the FDA for the approved nasal spray product of a competitor in the U.S. and there can be no assurance that we will be successful; risk that a competitor obtains FDA orphan drug exclusivity for a product with the same active moiety as any of our other drug products for which we are seeking FDA approval and that such earlier approved competitor orphan drug blocks such other product candidates in the U.S. for seven years for the same indication; risk in obtaining market access for other reasons; risk inherent in commercializing a new product (including technology risks, financial risks, market risks and implementation risks and regulatory limitations); risk of development of our sales and marketing capabilities; risk of sufficient capital and cash resources, including access to

available debt and equity financing and revenues from operations, to satisfy all of our short-term and longer term cash requirements and other cash needs, at the times and in the amounts needed; risk of failure to satisfy all financial and other debt covenants and of any default; short-term and long-term liquidity and cash requirements, cash funding and cash burn; risk related to government claims against Indivior for which we license, manufacture and sell Suboxone® and which accounts for the substantial part of our current operating revenues; risks related to the outsourcing of certain marketing and other operational and staff functions to third parties; risk of the rate and degree of market acceptance of our product and product candidates; the success of any competing products, including generics; 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; the impact of existing and future legislation and regulatory provisions on product exclusivity; legislation or regulatory actions affecting pharmaceutical product pricing, reimbursement or access; claims and risks that may arise regarding the safety or efficacy of the Company's products and product candidates; risk of loss of significant customers; risks related to legal proceedings and associated costs, including patent infringement matters challenging third party at risk generic sale of our proprietary products, and other investigative and antitrust litigation matters; changes in government laws and regulations; risk of product recalls and withdrawals; uncertainties related to general economic, political, business, industry, regulatory and market conditions and other unusual items; and other uncertainties affecting the Company described in the “Risk Factors” section and in other sections included in our Annual Report on Form 10 K, in our Quarterly Reports on Form 10-Q, and in our Current Reports on Form 8-K filed with the Securities Exchange Commission (SEC). 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 us or any person acting on our 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.



**Investor Inquiries**
ICR Westwicke
Stephanie Carrington
stephanie.carrington@westwicke.com
646-277-1282

# (L37) A Phase 1, Randomized Study Evaluating the Safety Tolerability, Pharmacokinetics (PK) and Pharmacodynamics (PD) of Single Ascending Doses of Epinephrine Prodrug 109 Sublingual Film (AQST-109) in Healthy Male Volunteers

John Oppenheimer MD FAAAAI[1], Steve Wargacki PhD[2], Rajesh Kainthan PhD[2], Cathie Leister[3] , Shawn Berg[3], Ayman Kafal PhD[2], Gary Slatko MD [2]

[1]UMDNJ Rutgers University School of Medicine, [2]Aquestive Therapeutics, [3]Independent Consultant

## INTRODUCTION

- Although epinephrine has been in use for more than a century, epinephrine auto injectors (EAI) are often under utilized due to various factors including needle phobia, delayed administration and failure to carry[1].
- Obstacles for patients and caregivers include incorrect use and lack of response. Incorrect use and delayed injection of epinephrine have been reported as primary reasons for lack of response in the treatment of anaphylaxis[2].
- Incorrect use of epinephrine injectors has also resulted in needle injuries. Lack of response to epinephrine has also been associated with the malfunction of the auto-injectors[2,3].
- Consequently, a different treatment modality could address significant unmet need resulting from deficiencies of auto-injectors and improve patient access, usage, and therapeutic response[4].
- To date, alternative delivery routes for epinephrine have failed to produce the speed and observed plasma levels (Cmax) produced by the Standard of Care (EpiPen).
- Aquestive Therapeutics is developing a sublingual (SL) film containing AQST-109 (a prodrug of Epinephrine) delivered using PharmFilm technology[5].
- The targeted indication for AQST-109 is the same as that for Epinephrine injection in the emergency treatment of Type 1 allergic reactions, including anaphylaxis.
- The target formulation and dose for AQST-109 is one that results in exposure that is comparable to that of commonly used epinephrine IM injections, such as 0.3 mg EpiPen®.
- This study demonstrates important safety and tolerability of AQST-109 and provides the PK/PD information of tested formulations that will define the eventual dose and the final formulation for a future bioequivalence study with epinephrine IM injection (such as EpiPen®).

## OBJECTIVES

Primary objective

- The primary objective of this study was to assess the safety and tolerability of AQST-109 across 4 film formulations ranging from 3 mg up to 24 mg, in healthy young male volunteers.

Secondary objectives

- To assess the PK of AQST-109 and epinephrine following SL administration as a function of dose as well as across the 4 film formulations.
- To compare descriptively the PK and PD (Heart Rate, Systolic and Diastolic Blood Pressure) following SL administration of the 4 formulations of AQST-109.

## METHODS

### STUDY DESIGN

- This was a two-center, Phase 1, Open label, randomized, SAD, safety-tolerability, PK, and PD study of AQST-109 SL drops and 4 SL film formulations of AQST-109 in young healthy male volunteers under fasting conditions.

## METHODS

- In two sequential cohorts (Cohorts 1 and 2), each consisting of 6 subjects, single ascending doses of 0.6 and 1.2 mg of AQST-109 drops are administered in a SL fashion. Subsequently, 6 additional subjects are assigned to receive a 3 mg Film dose of AQST-109 (Cohort 3). Finally, 24 subjects are randomized into 1 of 4 cohorts (Cohorts 4 to 7), corresponding to 4 different film formulations of AQST-109.
- Cohort 4 receives the same formulation as the one used in Cohort 3: Formulation 1. Cohorts 5, 6, and 7 receive new formulations: Formulations 2, 3, and 4, respectively.
- Cohorts 4 to 7, each consisting of 6 subjects, initially receive the AQST-109 film at the 6 mg dose.
- A sample size of 6 subjects per dose level for each cohort is judged adequate to estimate AQST-109 and epinephrine PK parameters for selection of the next dose level and for assessment of safety and tolerability.
- The twenty-four subjects returned to receive single ascending SL doses up to 24 mg in a sequential fashion.
- Dose escalation stopping criteria were predefined as:
  - Two or more TEAE's determined to be moderate in severity or above
  - Average peak plasma concentrations exceeding 30% of the target level Cmax of 520 pg/mL, thus, values greater than 676 pg/mL, would be considered as a stopping value

**Figure 1: Study design**


## ANALYSIS

- Formulation 2 met the predefined stopping criteria after the 12mg dose. Formulation 1 met the stopping criteria after the 18 mg dose. Formulations 3 and 4 were escalated through 18mg but stopped without further escalation as study objectives were met.
- For this specific analysis, subjects that received either AQST-109 Formulation 1 (F1) or Formulation 2 (F2) at the 12 mg dosage strength were selected.
- Safety and tolerability data was reported using descriptive statistics
- PK analysis was performed using Phoenix® WinNonlin®. Inferential statistical analyses was performed using SAS® according to FDA guidelines.
- Subjects were monitored for adverse events and local tolerability. PK and PD measurements (systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR) were taken pre-dose and frequently post-dose to 8 hours.
- EpiPen® data from a previous study was used as a historical comparator.

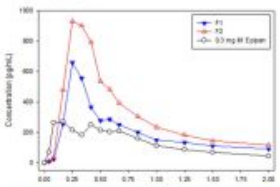
## RESULTS - PK

- All formulations and dosage strengths evaluated in this study were well tolerated. No serious AE's were observed and local administration site AE's were mild and self-resolving.
- Dosing with F1 at 12mg resulted in a geometric mean Cmax and AUC0-t of 552 pg/mL and 634 hr*pg/mL respectively (Table 1).
- Dosing with F2 at 12 mg resulted in a geometric mean Cmax and AUC0-t of 762 pg/mL and 803 hr*pg/mL respectively (Table 1).
- The median Tmax for both formulations was 15 minutes.
- By comparison, EpiPen dosing resulted in a geometric mean Cmax and AUC0-t of 341 pg/mL and 326 hr*pg/mL respectively.
- Figure 2 further illustrates the plasma concentration data over time following administration of the 2 formulations and 0.3 mg IM EpiPen, with F1 and F2 showing narrower span than Epipen.

**Table 1: Baseline-Corrected Plasma Epinephrine PK After AQST-109 and 0.3mg IM EpiPen**

| PK Parameter | AQST-109 F1, 12mg (N=6) | AQST-109 F2, 12mg (N=6) | 0.3mg IM EpiPen (N=12) |
|---|---|---|---|
| $C_{max}$ (pg/mL) | 552 | 762 | 341 |
| Median $T_{max}$ (minutes) (minimum, maximum) | 15 (15-25) | 15 (10-35) | 22 (5-66) |
| AUC 0-t (hr*pg/mL) | 634 | 803 | 326 |

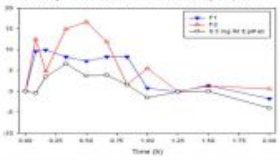
**Figure 2: Mean Baseline-Corrected Plasma Epinephrine Concentration over Time Following Administration of AQST-109 and 0.3mg IM EpiPen**




## RESULTS- PD

- Figure 3 shows SBP changes over time following administration of F1, F2 and 0.3 mg IM EpiPen.
- AQST-109 shows a similar change from baseline systolic blood pressure when compared to EpiPen, with F2 presenting slightly larger variations over time.
- The data suggests a similar timing and magnitude of the hemodynamic effect from epinephrine without regard for the route of administration.

**Figure 3: Mean Change from Baseline SBP over Time Following Administration of AQST-109 and 0.3mg IM EpiPen**




## CONCLUSION

- Dosing with AQST-109 resulted in Cmax and Tmax values comparable to published data for auto-injectors. Similarly, PD resulted in comparable changes to injected epinephrine.
- AQST-109 SL film demonstrated consistent Tmax values in a tighter range than reported for injectable epinephrine.
- AQST-109 SL film formulations were safe and well-tolerated across all formulations and all dose levels.
- This is the first time it has been demonstrated that epinephrine could achieve therapeutic plasma concentrations following sublingual administration.
- AQST-109 sublingual film shows promise as a novel alternative for the treatment of anaphylaxis.

## REFERENCES

1. Camiscioli CC, Dupuis R, Grieves A, et al. A behavioral economics intervention to encourage epinephrine-carrying among food allergic adults: a randomized controlled trial. Ann Allergy Asthma Immunol. 2019;119(3):234-240
2. Prince BT, Mikkol I, Slukus DR. Underuse of epinephrine for the treatment of anaphylaxis: missed opportunities. J Asthma Allergy. 2018;11:143-151
3. Glassberg et al. J Ann Allergy Asthma Immunol 126 (2021) 175e179
4. Posner L, Camargo CA Jr. Drug Healthc Patient Saf. 2017;9:9-18
5. Strains PER et al. J Allergy Clin Immunol. 2010;125(2):419-423.e4.
6. Aquestive Therapeutics. Investigator's Brochure. Edition Number: 1.0. Released 16 February 2021.

## ACKNOWLEDGMENTS

Sponsored by Aquestive Therapeutics, Inc. Editorial support was provided by Cat Tuong Nguyen, MD, PhD of Cat Tuong Nguyen Inc. and funded by Aquestive Therapeutics, Inc.

## DISCLOSURES

John Oppenheimer is a member of the Advisory board and has served as a consultant for Aquestive Therapeutics, Inc. Shawn Berg and Cathie Leister serve as a paid consultant to Aquestive Therapeutics, Inc. Steve Wargacki, Rajesh Kainthan, Ayman Kafal and Gary Slatko are employees of Aquestive Therapeutics, Inc.