EPINEPHRINE DELIVERED VIA SUBLINGUAL FILM (ANAPHYLM™) ELICITS RAPID AND CONSISTENT PHARMACOKINETIC AND PHARMACODYNAMIC RESPONSES

Carl Kraus, MD[1], Stephen Wargacki, PhD[1], David Golden, MD[2], David Bernstein, MD[3], Matthew Greenhawt, MD[4]

[1]Aquestive Therapeutics, Inc, [2]Medstar Franklin Square Hospital, Baltimore, MD, [3]Cincinnati Children's Hospital Medical Center, University of Cincinnati, Cincinnati, OH, [4]Children's Hospital Colorado, University of Colorado, Aurora, CO

INTRODUCTION

- Epinephrine is the first-line treatment for anaphylaxis, typically administered via manual injection or auto-injector (e.g., EpiPen®, Auvi-Q®). While effective, real-world use is limited by needle phobia and the lack of on-hand availability, delaying treatment when seconds matter.
- Rapid administration is critical, yet barriers to injection use put patients at risk. A treatment that is fast-acting, easy to carry, and simple to use could improve real-world adherence and outcomes.
- Anaphylm (AQST-109, DESF) is a sublingual film containing a prodrug of epinephrine, designed as a needle-free, portable alternative for anaphylaxis treatment. Its novel delivery system enables rapid absorption via the oral mucosa, offering a breakthrough in ease of use and accessibility.
- Anaphylm is compact, discreet, and easily carried (e.g., wallet, pocket, mobile phone), potentiating an "always within reach" arrangement. Placed under the tongue, it dissolves quickly, providing a potential solution when treatment is needed.

OBJECTIVES

- To evaluate and compare the pharmacokinetics (PK) of epinephrine following a single administration of Anaphylm versus FDA-approved epinephrine products in healthy adult subjects, with the goal of demonstrating that Anaphylm achieves PK parameters within a targeted range – "bracketed" by auto-injectors and manual IM injection.

METHODS

KEY INCLUSION CRITERIA

- Healthy adult males and females aged 18 to 50 years with a body mass index (BMI) between 18 and 30 kg/m².

STUDY DESIGN

- This was a randomized, open-label, two-part study[a].
- Part B, the single dose evaluation, was a four-period, four-treatment, four-sequence, single administration study conducted in healthy adult volunteers.
- During this part, subjects received:
  - Anaphylm (sublingual): 12 mg
  - Epinephrine (manual IM injection): 1 mg/mL
  - EpiPen (auto-injector): 0.3 mg/0.3 mL
  - Auvi-Q (auto-injector): 0.3 mg/0.3 mL
- All subjects met standardized inclusion and exclusion criteria.

RESULTS

PK DATA

- Anaphylm administration resulted in PK profiles within the range of epinephrine auto-injectors (EAIs) and manual IM.
- Median T_{max} for Anaphylm was 12 minutes, faster than EpiPen (20 minutes), Auvi-Q (30 minutes), and manual IM (50 minutes) (**Table 1**).
- Partial AUC values for Anaphylm were consistently bracketed by EAI and manual IM values at 8- to 60- minutes post-dose (**Table 1**).

CONCLUSIONS

- **Anaphylm demonstrated faster and more consistent PK and PD profiles compared to EAIs and manual IM, with a median T_{max} of 12 minutes and a TE_{max} (SBP) of 8 minutes. These results suggest a rapid onset of action, which is critical in the management of anaphylaxis.**
- **Anaphylm exhibited the lowest variability in PD responses, supporting its potential for reliable and predictable epinephrine delivery. Reduced variability in drug effect may enhance confidence in its use during administration.**
- **Anaphylm achieved a median T_{max} faster than that of EpiPen, Auvi-Q, and manual IM, falling within a targeted PK range. These data suggest that Anaphylm may provide an absorption profile that balances speed of onset with sustained systemic exposure.**
- **As a needle-free, rapidly absorbed epinephrine formulation, Anaphylm represents a potential and novel alternative to current administration methods. Its PK profile, combined with ease of use, may help address known challenges associated with epinephrine treatment, including delays in administration and patient adherence.**

RESULTS (cont'd)

Table 1: Summary of PK Parameters

Treatment	GM C_{max} (pg/mL)	Median T_{max} (min)	IQR T_{max} (min)	GM $pAUC_{0\text{-}60min}$ (hr*pg/mL)
Anaphylm (Sublingual)	470.2	12.0	5.0	165.0
EpiPen (IM)	469.2	20.0	23.5	233.9
Auvi-Q (IM)	520.6	30.0	32.0	269.0
Epinephrine Injection (IM)	308.2	50.0	15.0	133.8

PD DATA

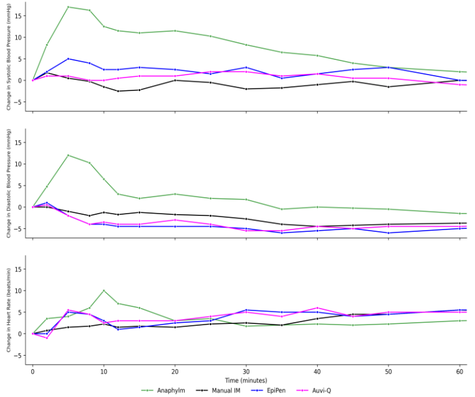
- Delivery of Anaphylm demonstrated rapid and clinically meaningful (>10mmHg and >10bpm) changes in SBP, DBP, and heart rate (HR) within 5 minutes post-dose (**Figure 1**).
- The PD response for Anaphylm supports consistency and is within the expected range, aligning with clinical standards for epinephrine.
- The fastest TE_{max} was observed with Anaphylm at 8 minutes (**Table 2**).

Table 2: SBP Parameters Within the First 60 Minutes

Treatment	Median E_{max} (ΔSBP mmHg)	Median TE_{max} (min)	IQR TE_{max} (min)
Anaphylm (Sublingual) (n = 64)	23.75	8.0	10.5
EpiPen (IM) (n = 63)	12.50	25.0	33.0
Auvi-Q (IM) (n = 61)	8.00	19.0	42.0
Epinephrine Injection (IM) (n = 62)	0.75	24.0	33.75

RESULTS (cont'd)

Figure 1: Median Change in SBP, DBP, and HR (0 to 60 Minutes)



SAFETY AND TOLERABILITY

- Anaphylm's safety profile was comparable to those of EAIs and manual IM.
- Most adverse events were consistent with known physiologic effects of epinephrine and were similar across treatment groups.
- There were no severe treatment-emergent adverse events (TEAEs) reported.
- All reported TEAEs were mild, transient, or resolved with minimal intervention.

REFERENCES

1. Shaker MS, Wallace DV, Golden DBK, et al. *J Allergy Clin Immunol.* 2020;145(4):1082-1123.

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DISCLOSURES

Drs. Golden, Bernstein, and Greenhawt are members of the advisory board and consultants to Aquestive Therapeutics, Inc. Drs. Kraus and Wargacki are employees of Aquestive Therapeutic, Inc.

[a] Results are focused on Anaphylm single dose (Part B). Part A of the study evaluated repeat doses.