Distinguished Industry & Late-breaking Oral Abstracts - Session 1

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Phase 1 Evaluation of Sublingual Film: Pharmacokinetics/Pharmacodynamics Safety Tolerability in at Risk Pediatric Patients

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Background

- Pediatric risk for anaphylaxis is estimated at 1 to 761 per 100,000 person-years. [1]
- Epinephrine is the first-line treatment for anaphylaxis, commonly administered via auto-injector or manual injection.
- AQST-109 (Anaphylm) is a sublingual film containing a prodrug of epinephrine.
- A separate pivotal PK/PD study was conducted in healthy adults involving AQST-109 and injectable epinephrine products with biocomparability supported.
- This study aimed to generate data in pediatric subjects at high-risk for serious allergic reactions for comparison to the previously conducted adult study.

1. Wang Y, Allen KJ, Suaini NHA, McWilliam V, Peters RL, Koplin JJ. Allergy. 2019;74(6):1063-80..

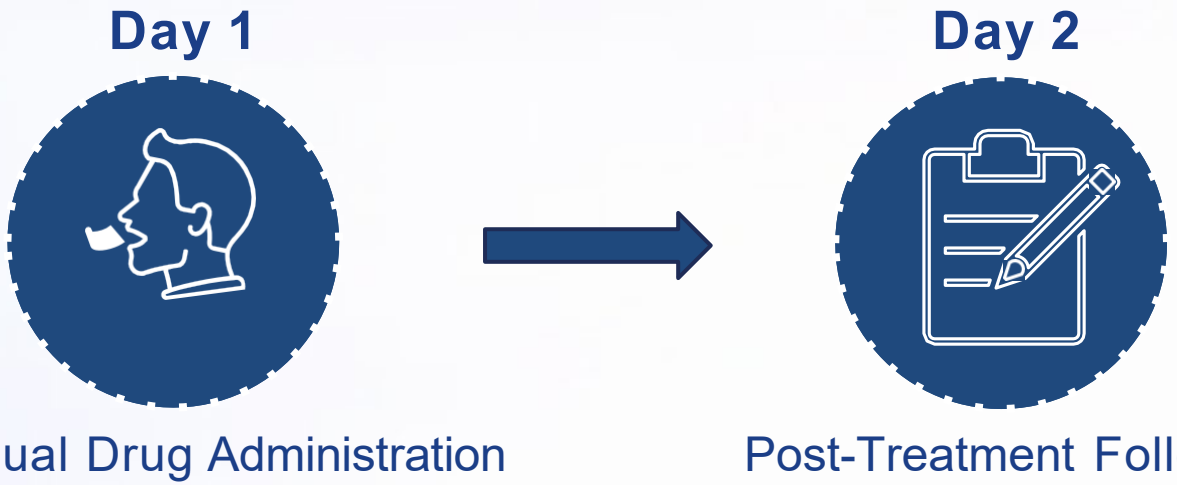
Study Design (N=32)

Phase 1, open-label, single-treatment study, multi-site study

32 participants between the ages of 7 and 17 years of age, weighing at least 30 kilograms (kg), with a history of allergic reactions and at high risk for serious allergic reactions received a single, 12 mg dose of AQST-109 sublingually

Objectives[1]:

- **Primary Endpoint**: Evaluate pharmacokinetics (PK) following administration of AQST-109 in pediatric participants aged 7–17 years, weighing ≥30 kg
- **Secondary Endpoint:** Maximum observed effects (E_{max}), area under the effect curve ($AUEC_{0-60}$) from time 0 to 60 minutes, and time to maximum effect (TE_{max}) for heart rate, systolic and diastolic blood pressure



Key: AUEC, area under the effect curve; E_{max}, maximum effect; TE_{max}, time to maximum effect.

1. Aquestive Therapeutics, data on file.

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Sample Demographics

- 37 participants screened and enrolled across seven sites
- 32 eligible participants were administered AQST-109
  - 3 were excluded for clinically significant ECG or vital sign abnormalities, and 2 were excluded based on weight parameters falling outside the 5th and 95th percentiles by age[1]

Characteristic	Overall (n=32)
Median age yrs (range)	13.0 (8-17)
Male (%)	20 (62.5)
Median weight kg (range)	47.15 (30.2-73.8)
Median BMI kg/m^2 (range)	18.70 (14.7-24.6)

1. Aquestive Therapeutics, data on file.

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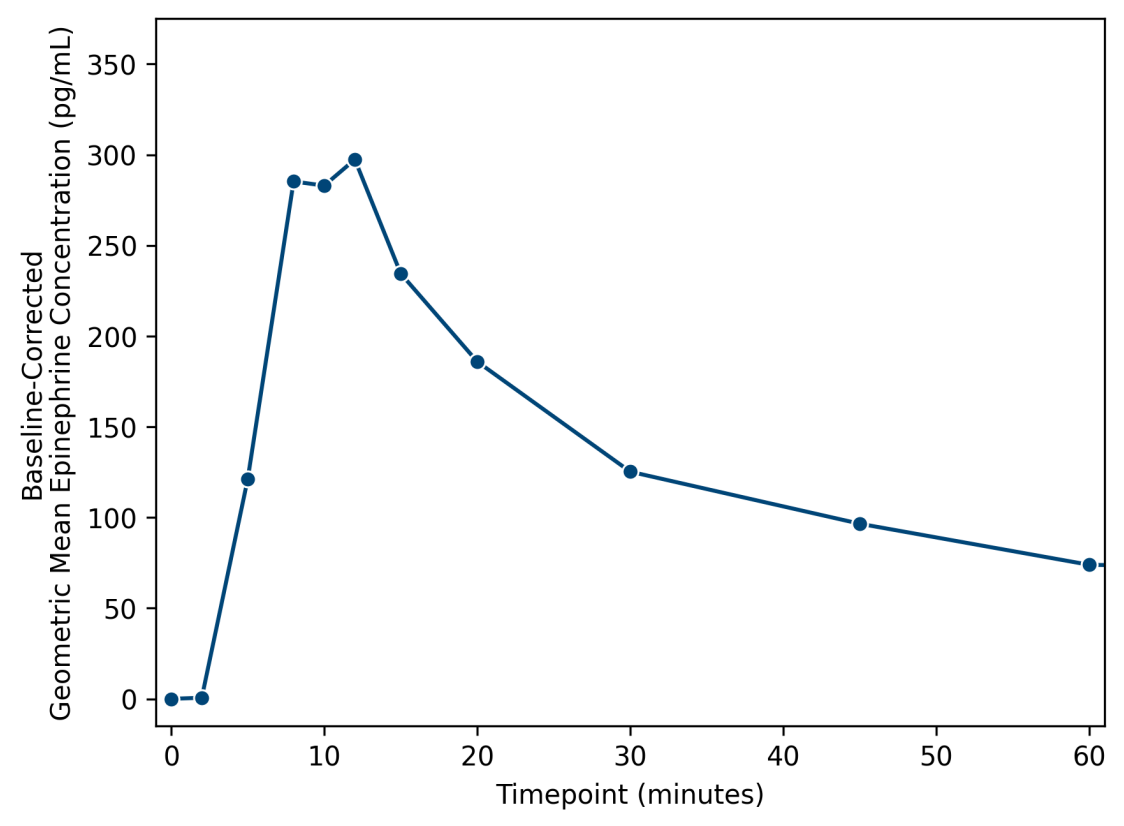
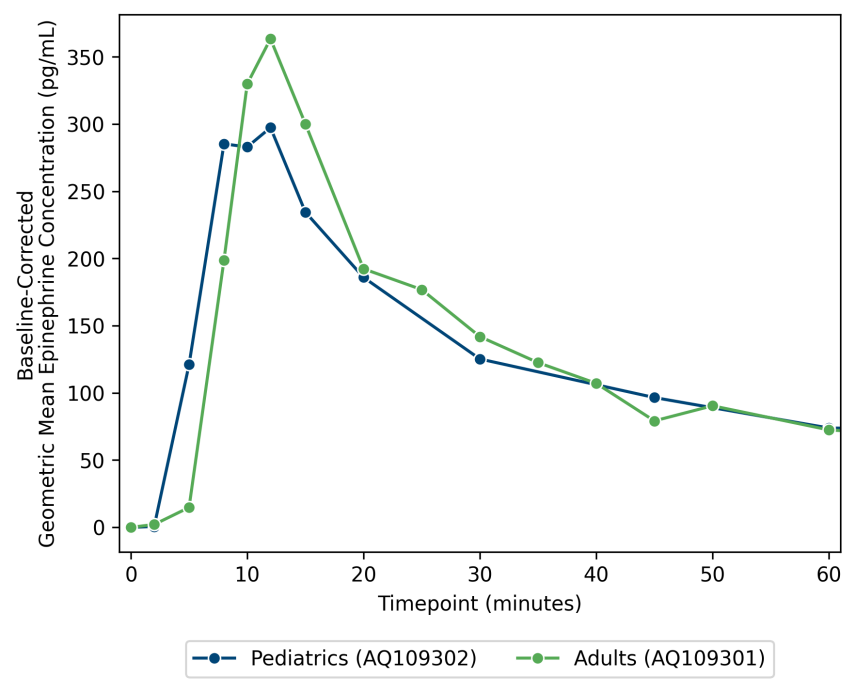
Pharmacokinetics

AQST-109 pharmacokinetics were observed to be similar in adult and pediatric patients aged 7-17 years and weighing 30 kilograms or more[1]





PK Parameter	Pediatric	Adult
C_{max} (pg/mL)	568.6	470.2
T_{max} (min)	10.0	12.0

- Cross-study comparison of PK suggests ***no statistical difference*** between adults and pediatrics*

1. Aquestive Therapeutics, data on file. *Statistical analyses involved 2-sample t-tests on natural log transformed values assuming unequal variances. Cmax is provided as geometric mean. Tmax is provided as median.

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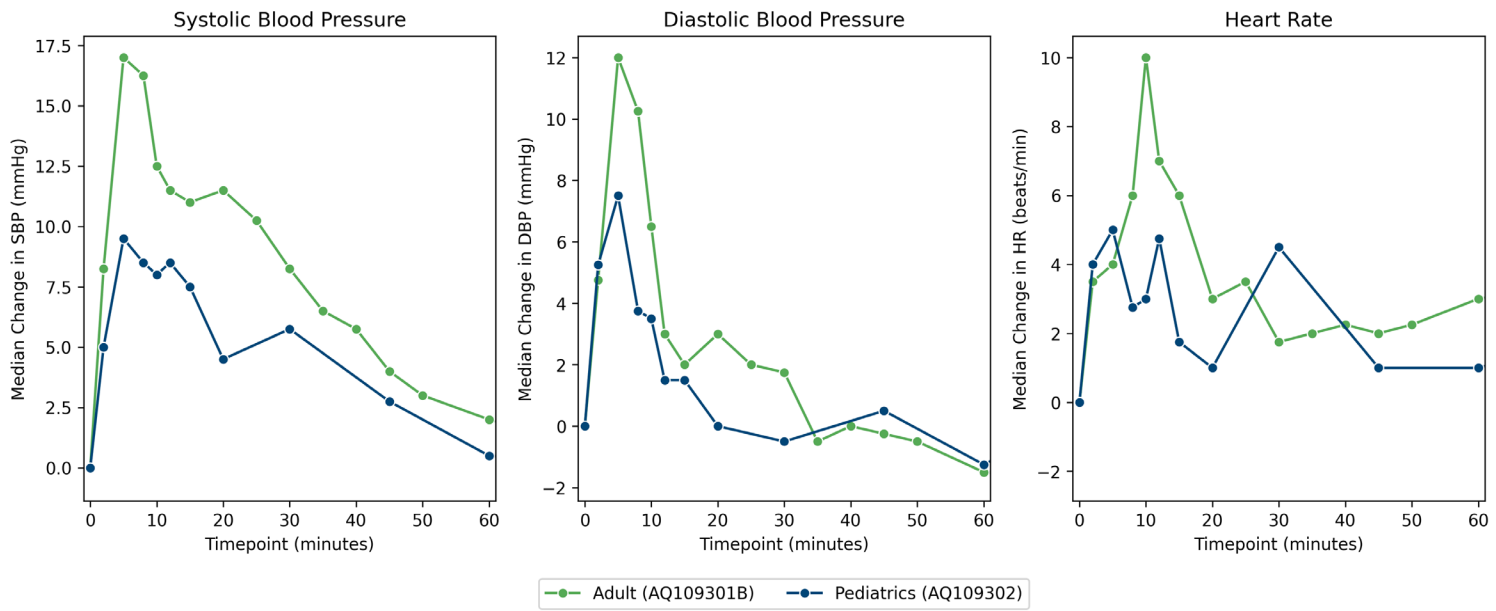
Pharmacodynamics

AQST-109 pharmacodynamics were observed to be similar in adult and pediatric subjects aged 7-17 years and weighing 30 kilograms or more[1]



Pediatric Participants		
Parameter	**Unit**	**Overall Change**
Systolic Blood Pressure*		
E_{max}	mmHg	15.4 (12.3)
TE_{max} (median)	min	11.0
$AUEC_{0-60}$	h*mmHg	8.7 (8.6)
Diastolic Blood Pressure*		
E_{max}	mmHg	9.8 (13.6)
TE_{max} (median)	min	8.0
$AUEC_{0-60}$	h*mmHg	3.6 (6.0) [n=31]
Heart Rate*		
E_{max}	bpm	12.5 (17.3)
TE_{max} (median)	min	12.0
$AUEC_{0-60}$	h*bpm	5.9 (7.8) [n=31]

Key: AUEC, area under the effect curve; E_{max}, maximum effect; TE_{max}, time to maximum effect.

1. Aquestive Therapeutics, data on file. Pediatric Study CSR. *Values for Emax and AUEC are mean (SD).

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Safety Summary (Patient Reported Events)

AE's reported by at least 5% of pediatric patients after single dose[1]

System Organ Class Preferred Term	Overall (N=32) (n) [2]
Any drug-related TEAE	84.4% (27)
General disorders and administration site conditions	
Hypoaesthesia [3]	12.5% (4)
Paraesthesia [3]	12.5% (4)
Discomfort	12.5% (4)
Pain	6.3% (2)
Gastrointestinal disorders	
Nausea	12.5% (4)
Vomiting	9.4% (3)
Abdominal pain upper	6.3% (2)

1. Aquestive Therapeutics, data on file. 2. Participants are only counted once per treatment for each row in the column "Participants (%)". 3. Hypoaesthia and paraesthesia thought to be related to the numbing effects of the permeation enhancer.

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Safety Summary (Clinician-Observed Events)

Solicited AE's reported by PIs in at least 5% of pediatric patients after single dose[1]

Preferred Term	Overall (N=32)	Symptomatic	Asymptomatic
	% subjects (n) [2]	% events (n) [2]	
Administration site conditions			
Exfoliation	28.1% (9)	18.7% (6)	9.4% (3)
Erythema	18.8% (6)	6.3% (2)	12.5% (4)
Pallor	15.6% (5)	3.1% (1)	12.5% (4)
Ulcer	9.4% (3)	3.1% (1)	6.3% (2)
Total Events	23	10	13

- AEs were clinician-observed during routine oral mouth checks
- 57% (13/23) of clinician-observed events were asymptomatic
- All but one of the clinician-observed were asymptomatic or mild in severity
- Only 1 out of the 3 ulcerative events was mildly symptomatic

1. Aquestive Therapeutics, data on file. 2. Participants are only counted once per treatment for each row in the column "Participants (%)".

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Conclusions

- These findings support PK comparability between pediatric and adult populations.
- Transient increases in SBP, DBP and HR were observed in this pediatric study, consistent with adult data and known pharmacological actions of epinephrine.
- Safety results were consistent with the adult population.

Acknowledgements

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Thank You