



Adrenaverse™ Prodrug Platform  
**Investor Day**

September 27, 2024

# Disclaimer

This presentation and the accompanying oral commentary have been prepared by Aquestive Therapeutics, Inc. (“Aquestive”, the “Company”, “our” or “us”) and contains 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 U.S. Food and Drug Administration (FDA), including the timing of submission of supporting and pediatric clinical studies, holding a pre-New Drug Application (NDA) meeting with the FDA and filing the NDA for Anaphylm with the FDA, and the following launch of Anaphylm, if approved by the FDA; that the results of the Company’s clinical studies for Anaphylm are sufficient to support submission of the NDA for approval of Anaphylm by the FDA; that Anaphylm will be the first and only oral administration of epinephrine and accepted as an alternative to existing standards of care, if Anaphylm is approved by the FDA; the advancement and related timing of our product candidate Libervant™ (diazepam) Buccal Film for the indicated epilepsy patient population aged between six and eleven years through clinical development and FDA regulatory approval and the following launch of Libervant for this patient population if approved by the FDA; the approval for U.S. market access of Libervant for the labeled patient population aged six years and older and overcoming the orphan drug market exclusivity of an FDA approved nasal spray product of another company extending to January 2027 for these epilepsy patients six years of age and older; the advancement, growth and related timing of our Adrenaverse™ pipeline of epinephrine prodrug product candidates, including AQST-108 (epinephrine) Topical Gel (and potential alternative indications), through clinical development including design and timing of clinical studies including those necessary to support the targeted indication of Alopecia areata for AQST-108, and holding a pre-investigational new drug application meeting (IND) with the FDA, and the following launch of AQST-108, if approved by the FDA; the commercial opportunity of Libervant, Anaphylm, AQST-108 and our other product candidates, including potential revenues (including projected peak annual sales) generated from commercialization of these products and product candidates should these product candidates be approved by the FDA; our ability to price AQST-108 competitively and to leverage our commercial, distribution and manufacturing capabilities and infrastructure for AQST-108 and other product candidates, if approved by the FDA; the potential growth of our patent portfolio including the extension of patent protection for AQST-108 should the pending patents be approved by the U.S. Patent and Trademark Office (PTO); the potential benefits our products and product candidates could bring to patients; and business strategies, market opportunities, and other statements that are not historical facts.

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 our development work, including any delays or changes to the timing, cost and success of our product development activities and clinical trials and plans, including those relating to Anaphylm (including for pediatric patients), AQST-108, and the Company’s other product candidates; risks associated with the Company’s distribution work for Libervant, including any delays or changes to the timing, cost and success of Company’s distribution activities and expansion of market access to patients aged two to five for Libervant; risk of delays in advancement of the regulatory approval process through the FDA of our product candidates, including the filing of the respective NDAs, including for Anaphylm, AQST-108, Libervant for patients aged between six and eleven and other product candidates, or failure to receive FDA approval at all of any of these product candidates; risk of the Company’s ability to generate sufficient clinical data for approval of our product candidates, including with respect to our 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 future clinical trials 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 the success of any competing products; risk that we may not overcome the seven year orphan drug market exclusivity granted by the FDA for the approved nasal spray product of another company in the U.S. in order for Libervant to be granted U.S. market access for patients aged six years and older until the expiration of the orphan drug market exclusivity period of the nasal spray product due to expire in January 2027, or for other reasons; risk of loss of U.S. market approval of Libervant for patients aged between two and five resulting from a legal challenge relating to U.S. orphan drug market exclusivity by the owner of the approved nasal spray product with respect to the FDA’s approval for U.S. market access of Libervant for this pediatric patient population, or for other reasons; risks and uncertainties inherent in commercializing a new product (including technology risks, financial risks, market risks and implementation risks and regulatory limitations); risk of development of a sales and marketing capability for commercialization of our product Libervant and other product candidates, including Anaphylm and AQST-108; risk of sufficient capital and cash resources, including sufficient access to available debt and equity financing, including under our ATM facility and the Lincoln Park Purchase Agreement, and revenues from operations, to satisfy all of our short-term and longer-term liquidity and cash requirements and other cash needs, at the times and in the amounts needed, including to fund commercialization activities relating to Libervant for patients between two and five years of age and to fund future clinical development and commercial activities for our product candidates, including Anaphylm, AQST-108 and Libervant for patients aged between six and eleven, should these product candidates be approved by the FDA, and for Libervant patients of six years and older upon expiration of the orphan drug marketing exclusivity period of the nasal spray product; risk that our manufacturing capabilities will be sufficient to support demand for Libervant for patients between two and five years of age and for older patients, should Libervant receive U.S. market access for these older patients, and for demand for our licensed products in the U.S. and abroad; risk of eroding market share for Suboxone® and risk as a sunset product, which accounts for the substantial part of our current operating revenue; risk of default of our debt instruments; risks related to the outsourcing of certain sales, marketing and other operational and staff functions to third parties; risk of the rate and degree of market acceptance in the U.S. and abroad of Libervant for epilepsy patients between two and five years of age, and for older epilepsy patients if approved for U.S. market access and after the expiration of the orphan drug market exclusivity period in January 2027; risk of the rate and degree of market acceptance in the U.S. and abroad of Libervant and Anaphylm, AQST-108 and our other product candidates, should these product candidates be approved by the FDA, and for our licensed products in the U.S. and abroad; risk of the success of any competing products including generics; risk of the size and growth of our product markets; risk 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 our products; risk that our patent applications for our product candidates, including for Anaphylm and AQST-108, will not be timely issued, or issued at all, by the PTO; risk of unexpected patent developments; risk of legislation and regulatory actions and changes in laws or regulations affecting our business including relating to our products and products candidates and product pricing, reimbursement or access thereof; risk of loss of significant customers; risks related to claims and legal proceedings against Aquestive including patent infringement, securities, business torts, investigative, product safety or efficacy and antitrust litigation matters; risk of product recalls and withdrawals; risks related to any disruptions in our information technology networks and systems, including the impact of cybersecurity attacks; risk of increased cybersecurity attacks and data accessibility disruptions due to remote working arrangements; risk of adverse developments affecting the financial services industry; risks related to inflation and rising interest rates; risks related to the impact of the COVID-19 global pandemic and other pandemic diseases on our business, including with respect to our clinical trials and the site initiation, patient enrollment and timing and adequacy of those clinical trials, regulatory submissions and regulatory reviews and approvals of our product candidates, availability of pharmaceutical ingredients and other raw materials used in our products and product candidates, supply chain, manufacture and distribution of our products and product candidates; risks and 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 uncertainties affecting us including those described in the “Risk Factors” section and in other sections included in the Company’s 2023 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 presentation whether as a result of new information, future events or otherwise, except as may be required by applicable law.

This presentation shall not constitute an offer to sell or the solicitation of an offer to buy any of the Company’s securities, nor shall there be any sale of these securities in any state or other jurisdiction in which such offer, solicitation or sale would be unlawful prior to registration or qualification under the securities laws of any such state or other jurisdiction.

PharmFilm® and the Aquestive logo are registered trademarks of Aquestive Therapeutics, Inc. The trade name “Anaphylm” for AQST-109 has been conditionally approved by the FDA. Final approval of the Anaphylm™ proprietary name is conditioned on FDA approval of the product candidate, AQST-109. All other registered trademarks referenced herein are the property of their respective owners.

# Today's agenda

Topic	Presenters
Introductions and company overview	<b>Dan Barber</b> <i>Chief Executive Officer</i> Aquestive Therapeutics
Scientific overview of adrenergic receptors	<b>J. David Farrar, PhD</b> <i>Associate Professor</i> Immunology/Molecular Biology UT Southwestern Medical Center
Adrenaverse™ prodrug platform capabilities	<b>Steve Wargacki, PhD</b> <i>Chief Science Officer</i> Aquestive Therapeutics
AQST 108 (epinephrine) Topical Gel indication and clinical program overview	<b>Carl Kraus, MD</b> <i>Chief Medical Officer</i> Aquestive Therapeutics
Market opportunity	<b>Dan Barber</b> <i>Chief Executive Officer</i> Aquestive Therapeutics
Q&A and Closing Remarks	

# Drug delivery technologies

## PharmFilm®

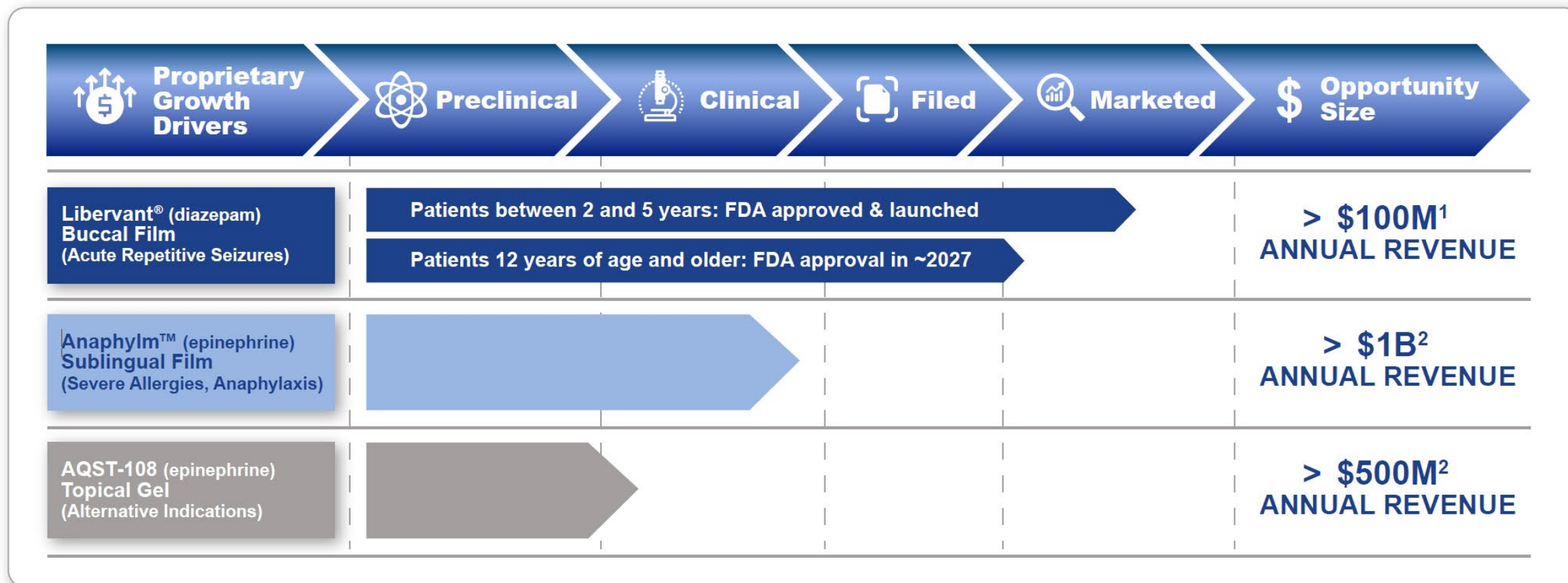


## Adrenaverse™ Prodrug Platform



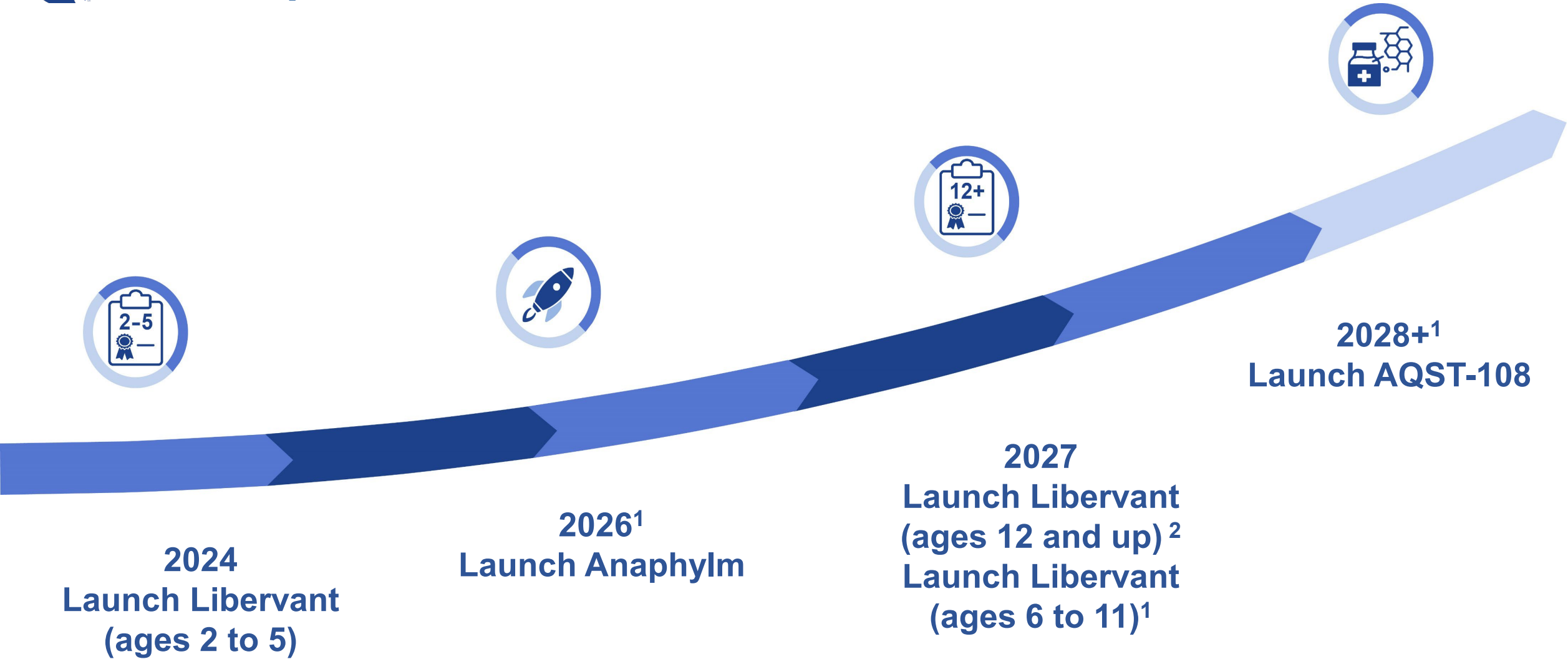
*Adrenaverse platform contains a library of over 20 epinephrine prodrugs that demonstrate control of absorption and conversion rates across a variety of dosage forms and delivery sites, including allergy, topical (dermatological), and more.*

# Diversified pipeline



1. Annual revenue includes revenue for patients 12 and up after launch in 2027. 2. Aquestive Therapeutics data on file.

# Growth plan



1. Assumes satisfaction of all predetermined clinical endpoints and approved by U.S. Food and Drug Administration (FDA). 2. Estimate is based on an orphan drug market exclusivity block until January of 2027 by an FDA approved nasal spray product.

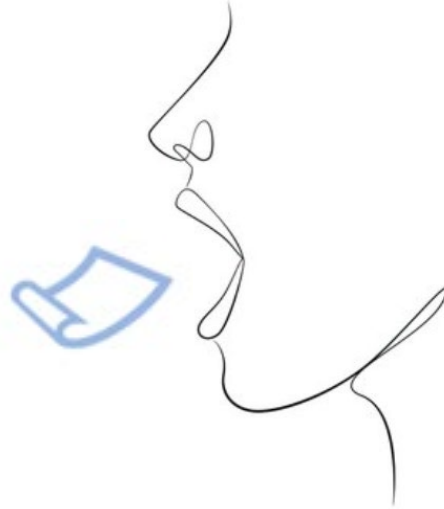
# Anaphylm™ (epinephrine) Sublingual Film

Anaphylm is the first and only non-device based, orally delivered epinephrine product candidate



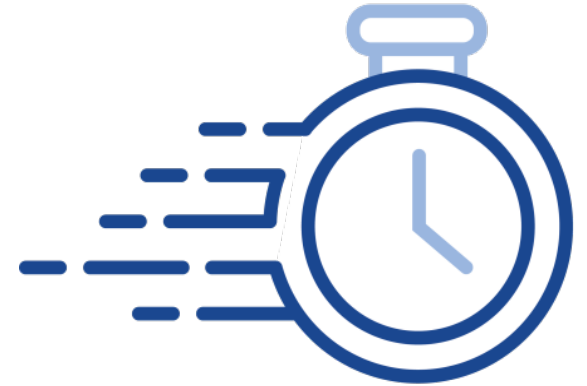
Easy To Carry

+



Easy To Administer

+



Works Quickly<sup>1</sup>

# Anaphylm is fast-acting and well-tolerated, with a safety profile comparable to standard of care (SOC)<sup>1</sup>

1

**Rapid absorption as demonstrated by:**

**Consistent time to peak drug concentration (T<sub>max</sub>) of 12-15 minutes**

**Onset of pharmacodynamics (PD) effects within 2-5 minutes**

2

**Consistent pharmacokinetics (PK) demonstrated across 5 administration procedures:**

**Performed consistently in the presence of food (clinically), drink, temperature, and local swelling (non-clinically)**

**Same peak concentration levels as autoinjectors of epinephrine**

3

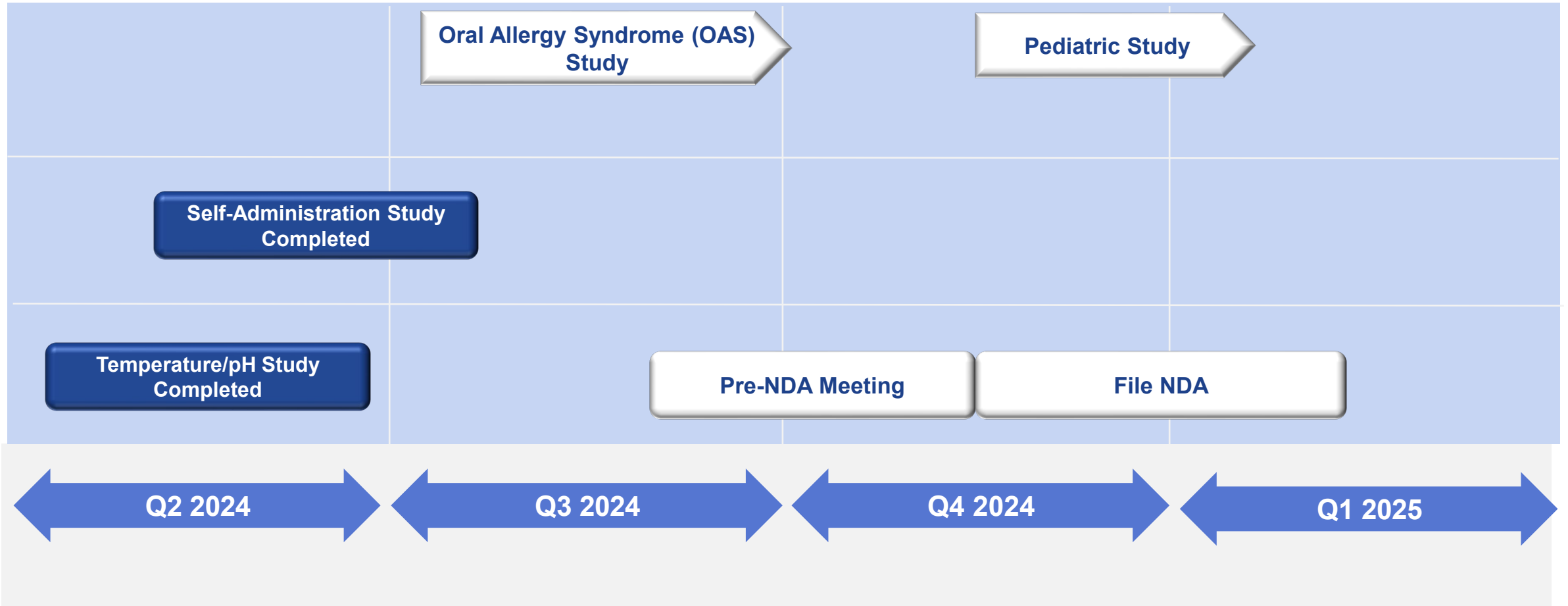
**Safety and tolerability:**

**Adverse events (AE's) were generally mild, all were transient and resolved without intervention**

1. Aquestive Therapeutics data on file.

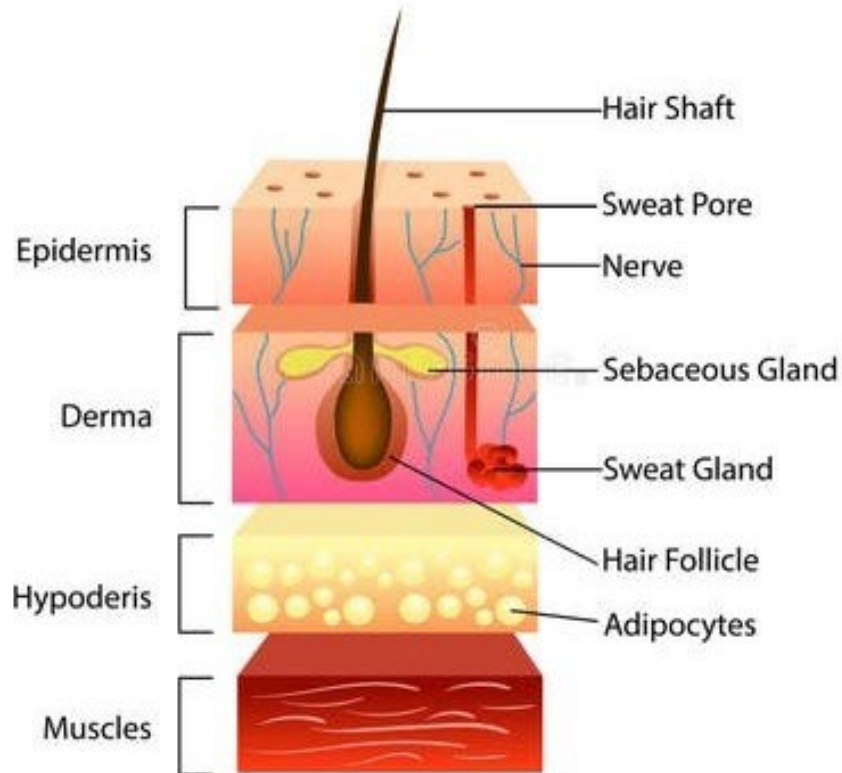


# Expected clinical timeline for Anaphlym™



# Our thesis (the big idea)

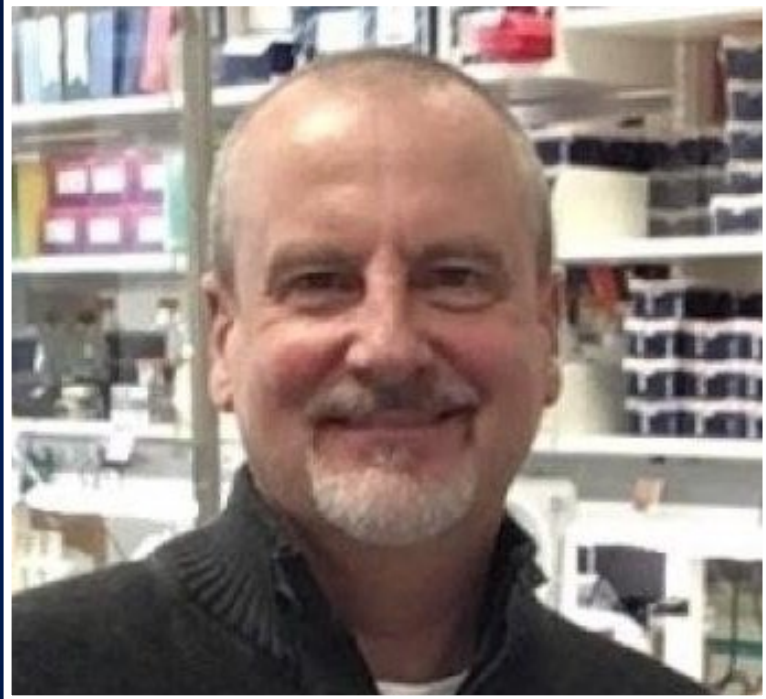
## Human Skin Structure



- The utility of exogenous epinephrine for the treatment of medical conditions has been limited due to the molecule's five-minute half-life as well as poor absorption capabilities<sup>1</sup>
- Aquestive's Adrenaverse technology unlocks the potential of epinephrine by addressing both problems<sup>2</sup>

# Scientific Overview of **Adrenergic Receptors**

Dr. J. David Farrar

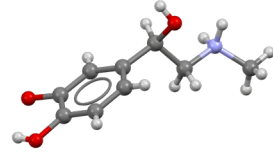


# **J. David Farrar, PhD**

- **Associate Professor**
- **UT Southwestern Medical Center, Dallas, TX**
- **PhD in Immunology**
- **53 Publications with >4000 citations**
- **Specializes in neural regulation of immune function**

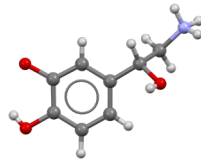
# Epinephrine and Norepinephrine regulate key biological functions

**Adrenaline (Epinephrine)**



Secreted predominantly by the adrenal gland

**Noradrenaline (Norepinephrine)**



Secreted by sympathetic nerve fibers that innervate peripheral tissues

## Physiological Regulation

- Digestion
- Body temperature
- Blood pressure
- Heart rate
- Breathing
- “Fight or Flight” response

## Effects on Immune Cells

- Pathogen recognition
- Antibody production
- Immune cell trafficking
- General immune suppression

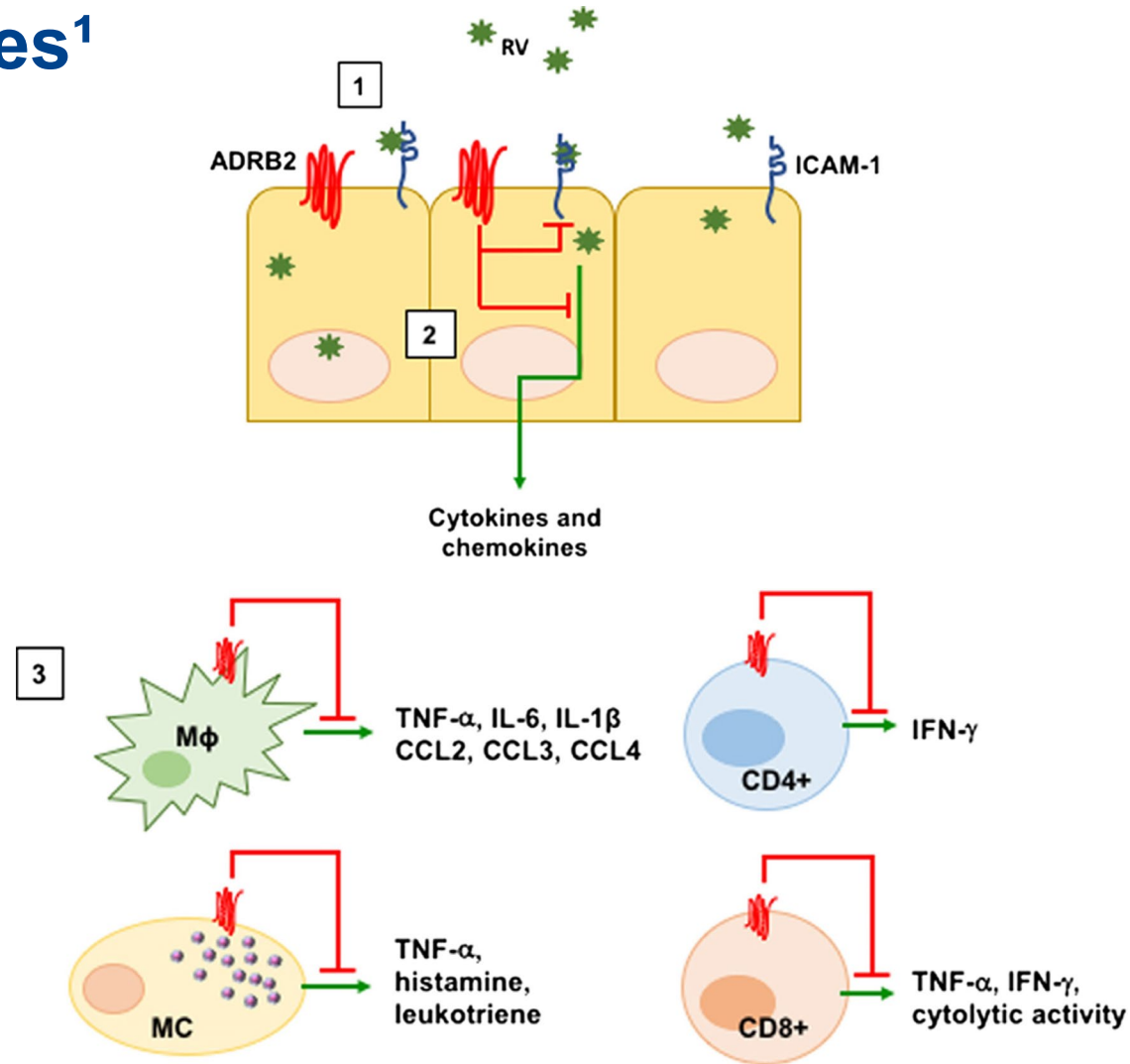
# Signaling through the adrenergic receptor suppresses a variety of inflammatory processes<sup>1</sup>

## Innate immune cells

- Macrophages
- Neutrophils
- Mast cells
- Dendritic cells
- Natural Killer (NK) cells

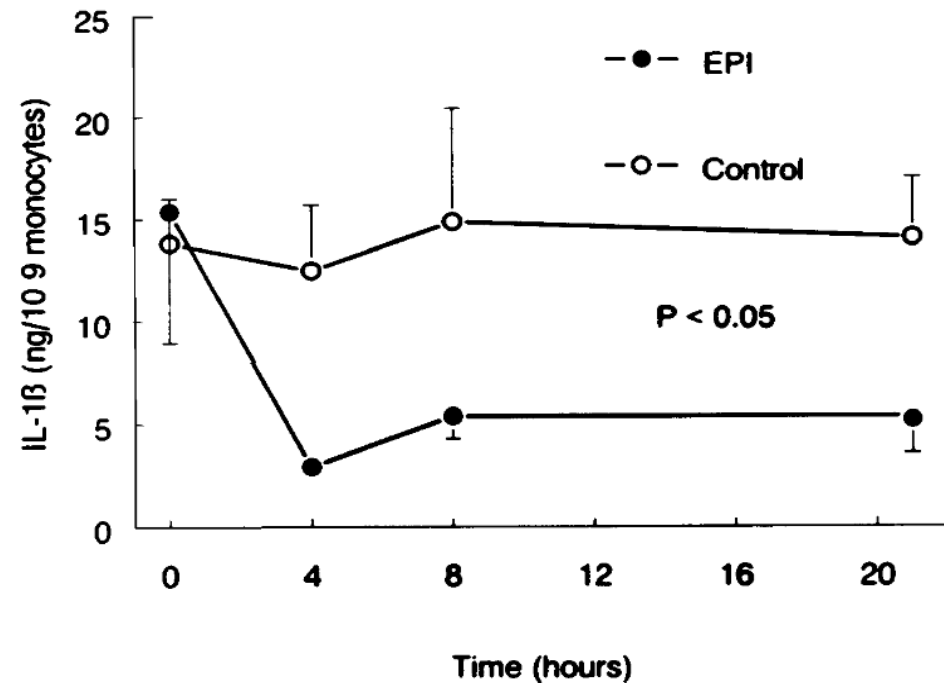
## Adaptive immune cells

- T cells
- NK T cells
- B cells



# Epinephrine is a potent inhibitor of inflammatory cytokines in humans

Epinephrine inhibits endotoxin-induced IL-1beta production; roles of tumor necrosis factor – alpha and IL-10<sup>1</sup>

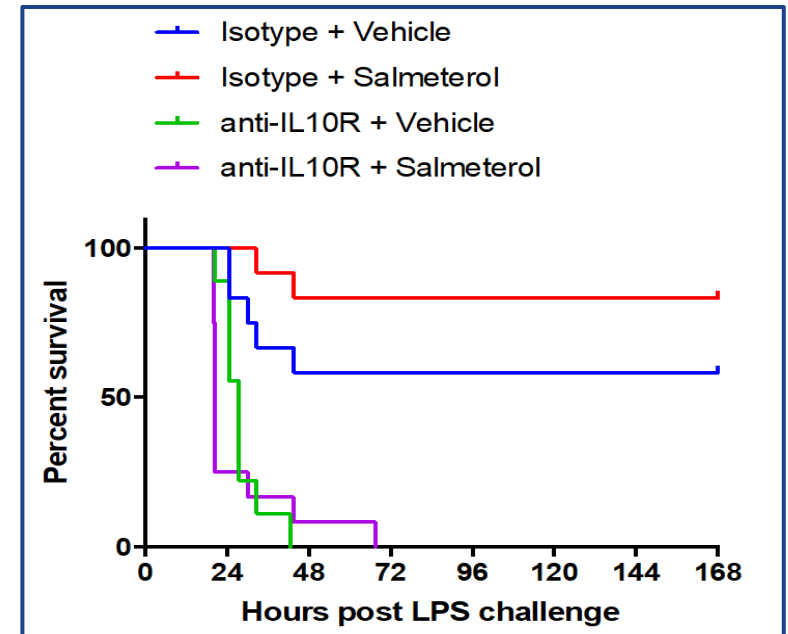
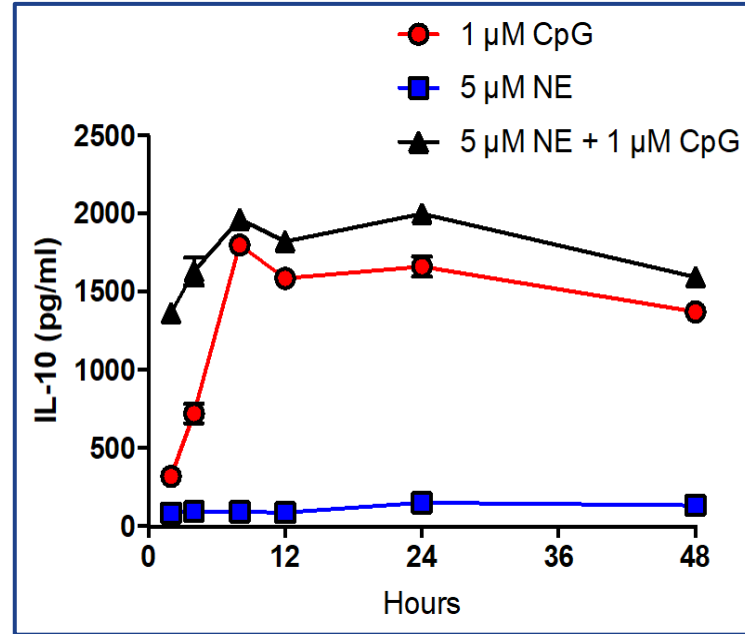
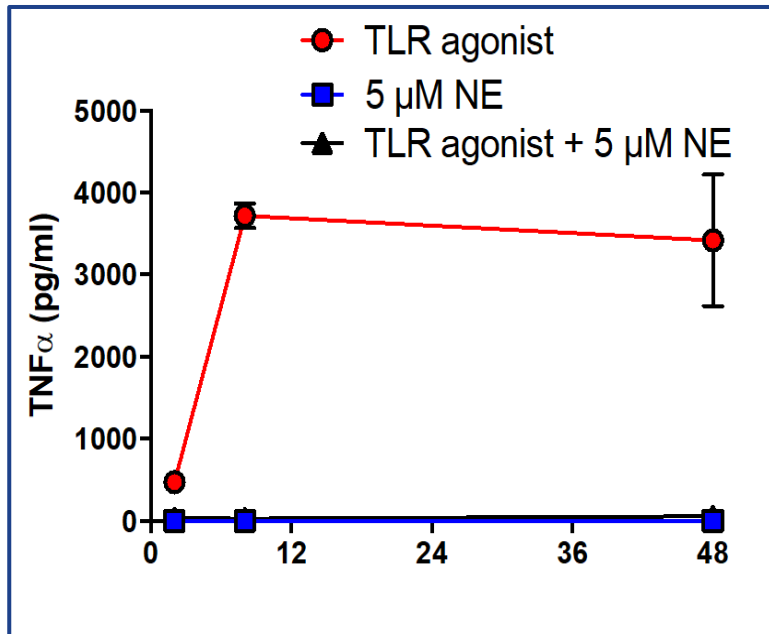


- Decreased serum concentrations of IL-1beta in septic patients following treatment with epinephrine
- Similar effects seen with other inflammatory cytokines
- Epinephrine increases serum concentrations of the anti-inflammatory cytokine, IL-10

1. Van Der Poll and Lowry, Am J Physiol., 1997, 273:R1829-R2137.

# Epinephrine is a potent inhibitor of inflammatory cytokines in mouse models<sup>1</sup>

The  $\beta$ 2-adrenergic receptor controls inflammation by driving rapid IL-10 secretion



Norepinephrine (NE) potently suppresses TNF $\alpha$  while inducing rapid IL-10 secretion

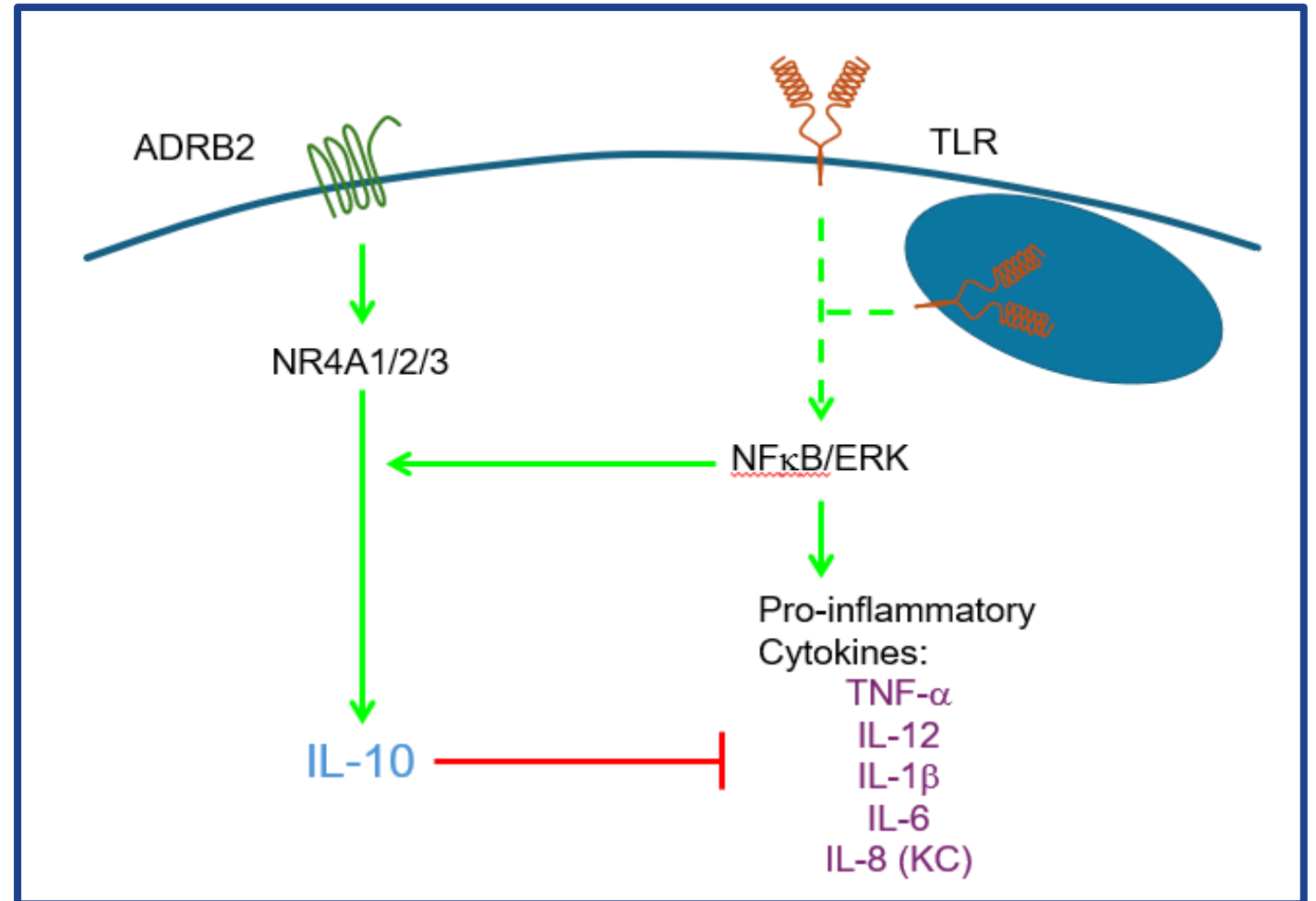
1. Brain, Behav. Immun., 2018, Didem Agac, Leonardo D. Estrada, Robert Maples, Lora V. Hooper, J. David Farrar.



# Adrenergic receptor beta 2 (ADRB2)-mediated suppression of inflammation

Adrenergic regulation of immune cell function and inflammation<sup>1</sup>

Unlike JAK inhibitors, which temporarily block inflammatory cytokine signaling, adrenergic signaling converts an inflammatory environment to an anti-inflammatory pathway.



1. Drashya Sharma, J. David Farrar, Seminars in Immunopathology (2020) 42:709-717; <https://doi.org/10.1007/s00281-020-00829-6>.

## Key takeaways

- **Epinephrine and Norepinephrine are natural immune modulators that act both systemically and locally to inhibit the magnitude of normal inflammation**
- **Pharmacological application of epinephrine inhibits inflammatory activities of both innate and adaptive arms of the immune system**



# Adrenaverse™ Prodrug Platform

# **R&D Overview**

**Stephen Wargacki, Ph.D.**  
Chief Science Officer

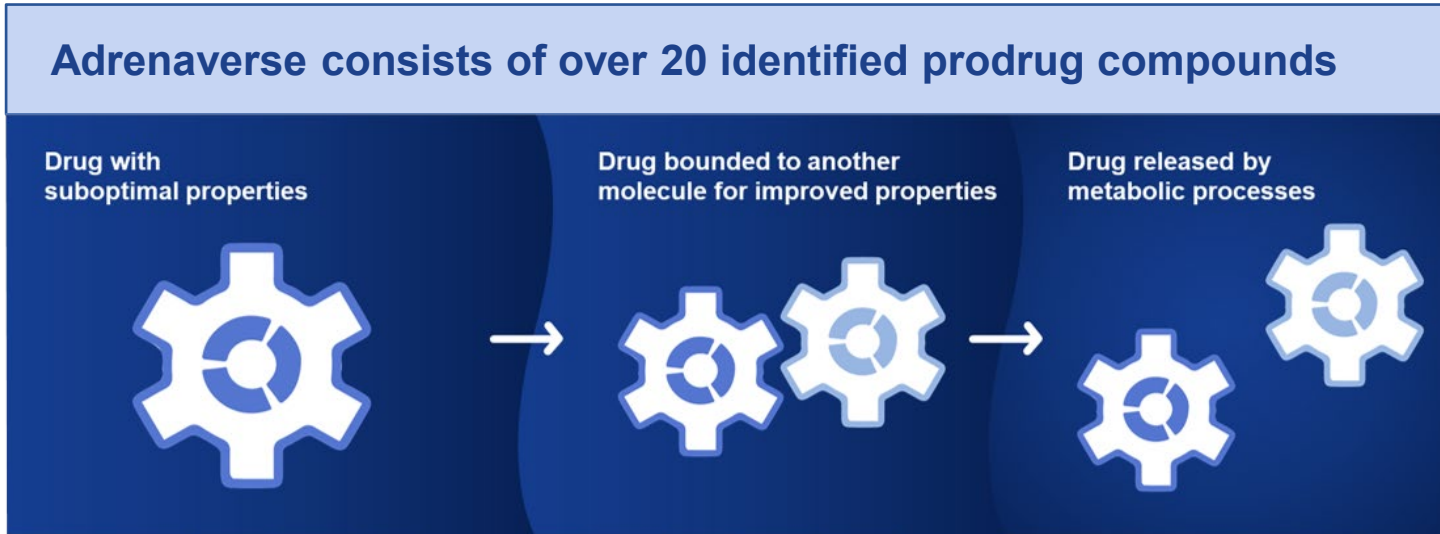


# **Stephen Wargacki, PhD**

## **Chief Science Officer**

- **PhD, Polymer Chemistry  
University of Tennessee**
- **Postdoctoral Fellow  
Air Force Research Laboratory**
- **15+ years experience in alternative drug delivery**
- **29 publications (414 citations)**
- **122 patents/applications (26 patent families)**

# Adrenaverse™: A robust and versatile prodrug platform

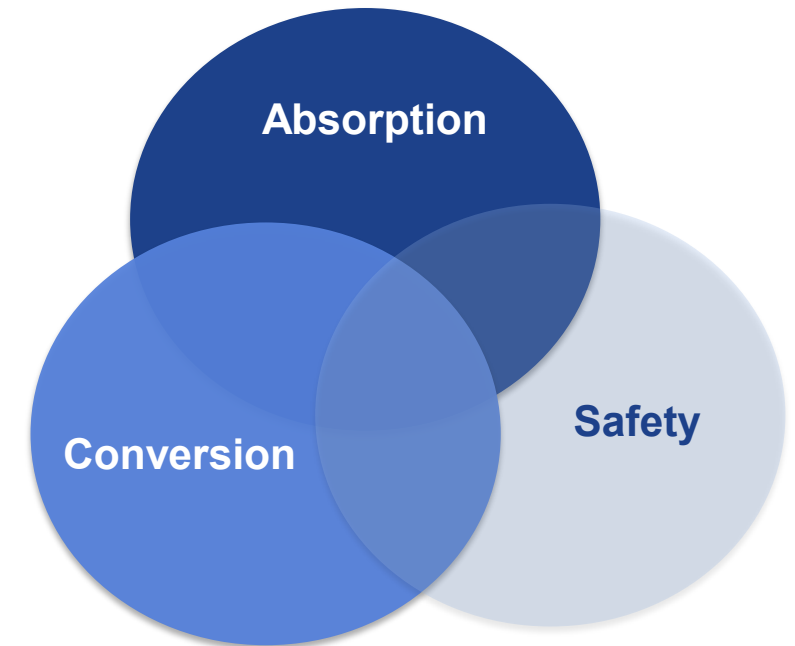


Aquestive's topical platform allows for:

- Simple fast drying formulations
- Ability to accommodate single or multiple prodrugs
- Ability to include additional components without impacting performance
- Robust stability through six months accelerated conditions

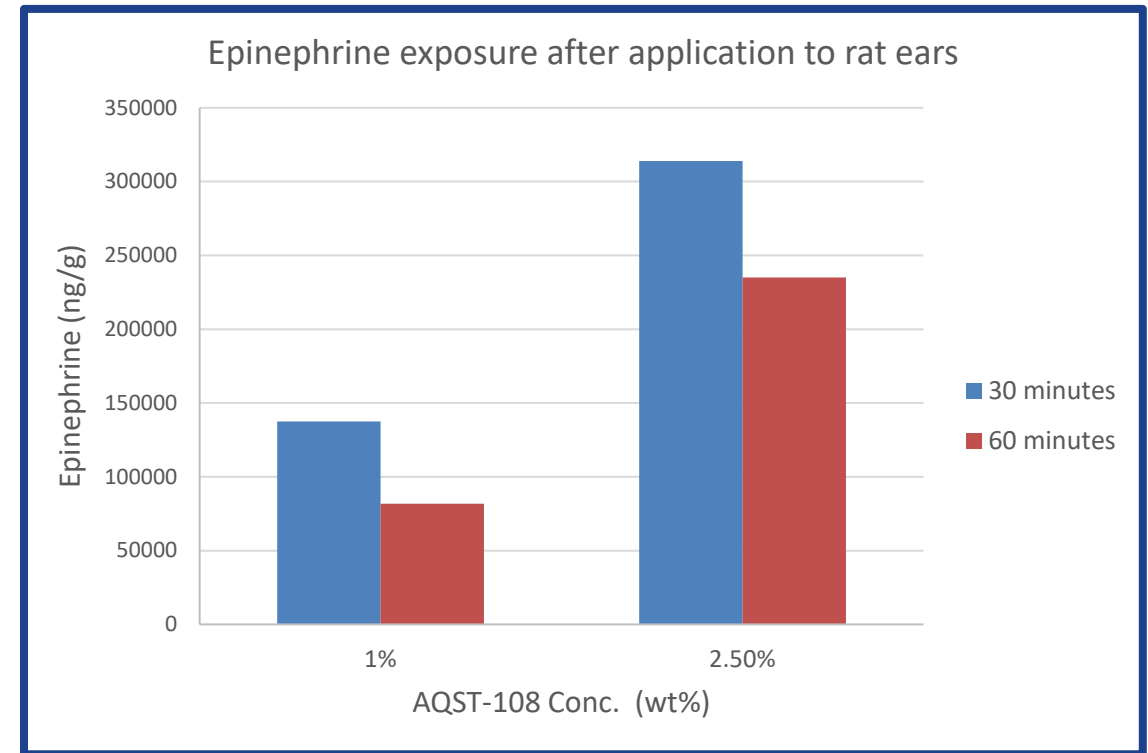
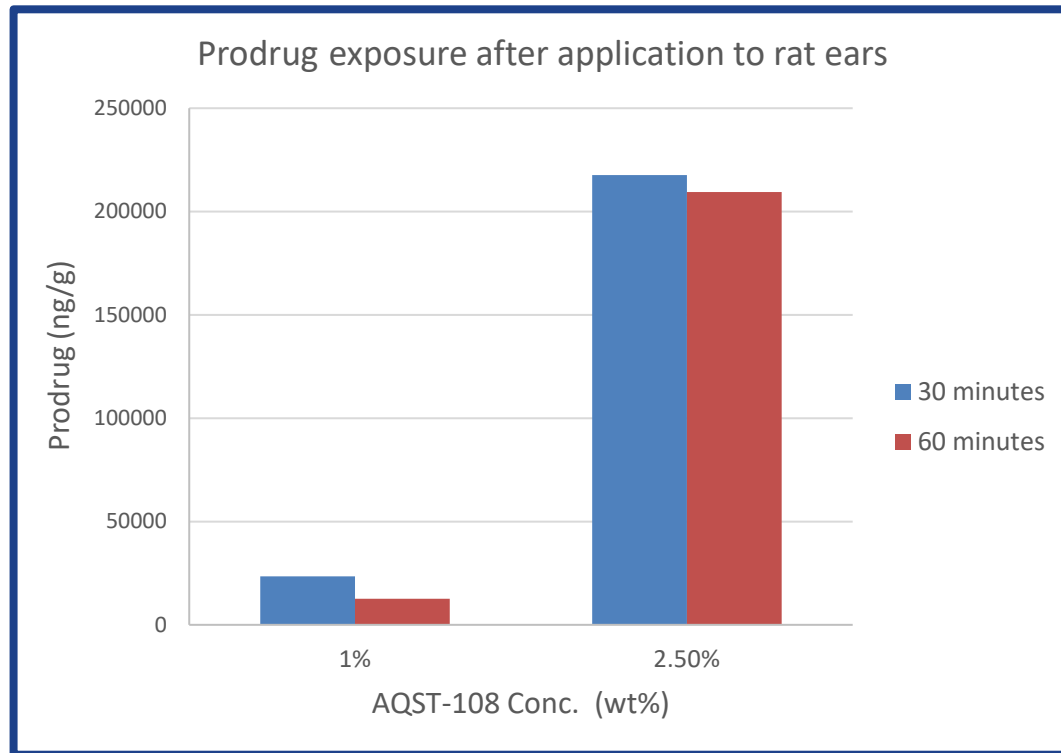
Allows for different critical profiles of key properties

Enables the development of patient centric formulations tailored to the needs of the indication



# Non-clinical results (pharmacokinetics in rat ears)<sup>1</sup>

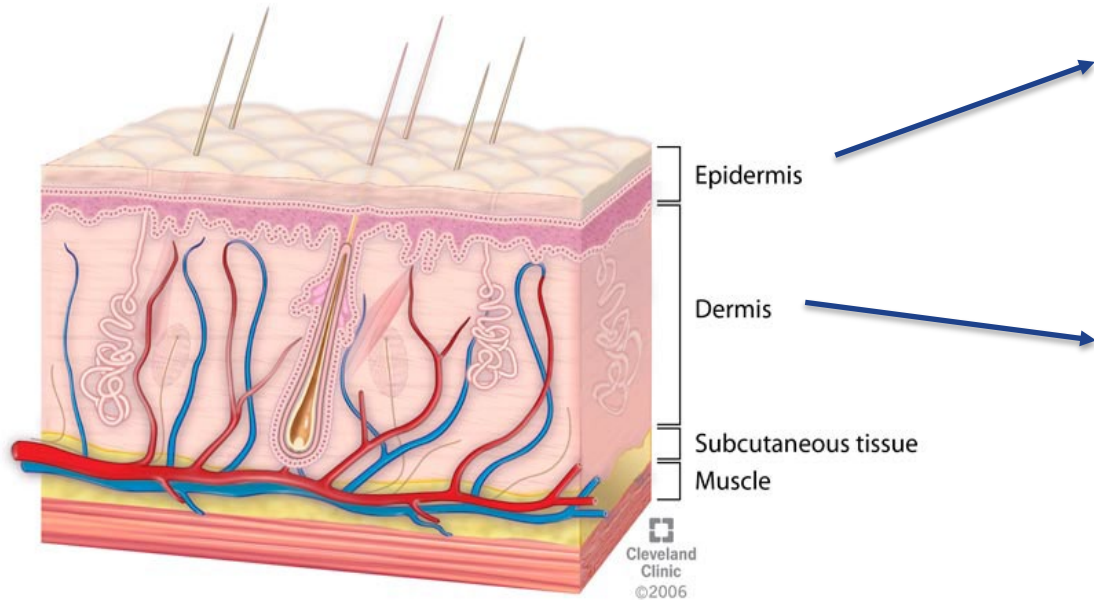
**AQST-108 (epinephrine) Topical Gel demonstrates significant local absorption for over one hour without systemic exposure**



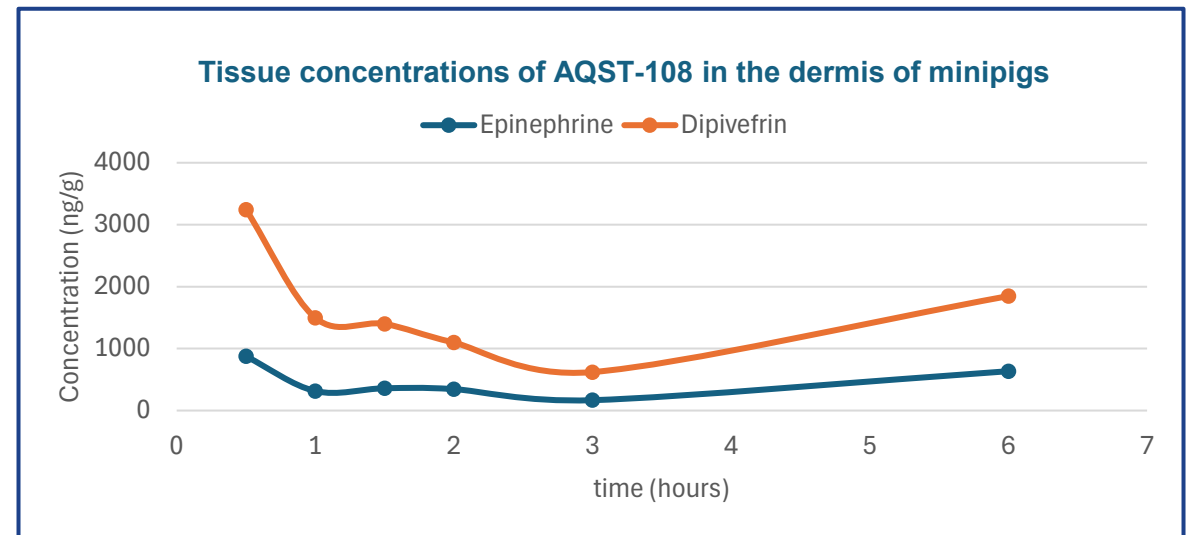
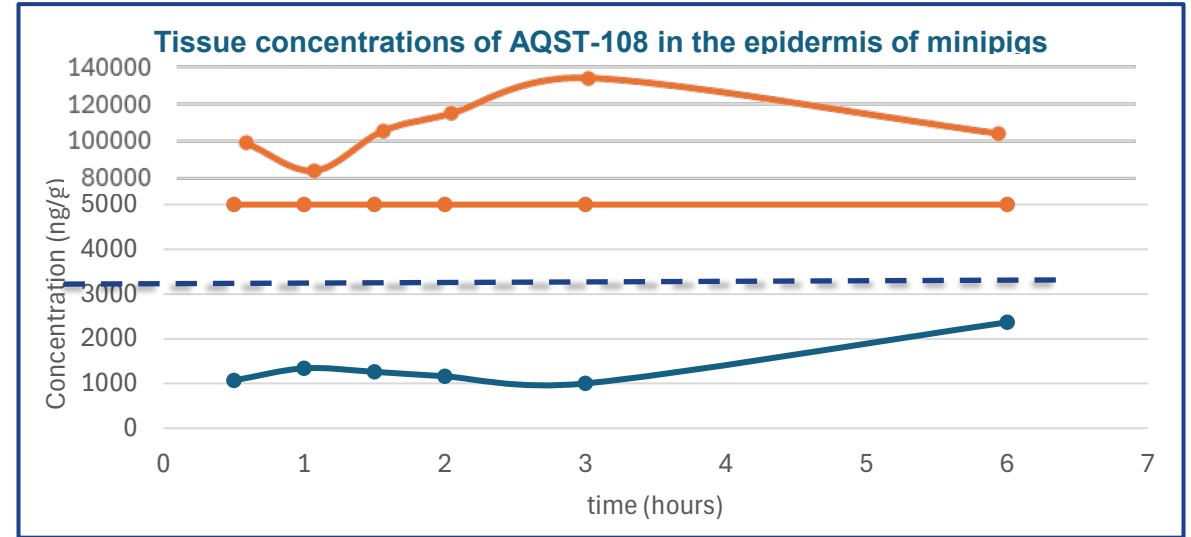
1. Aquestive Therapeutics data on file.

# Non-clinical pharmacokinetic (PK) results in minipigs<sup>1</sup>

Results show high exposure in both dermis and epidermis lasting > 6 hours and no systemic exposure even at high body surface area coverage



2.5% topical gel applied at 30mg/cm<sup>2</sup>  
7, 10, and 12% Body Surface Area (BSA) coverage<sup>2</sup>



# Non-clinical results - passive cutaneous anaphylaxis in rat ears<sup>1</sup>

## AQST-108 resolves cutaneous anaphylaxis in rat ears, preventing dye profusion

Group 1:  
Naive



Group 2:  
Placebo



Group 3: Test  
item 1%



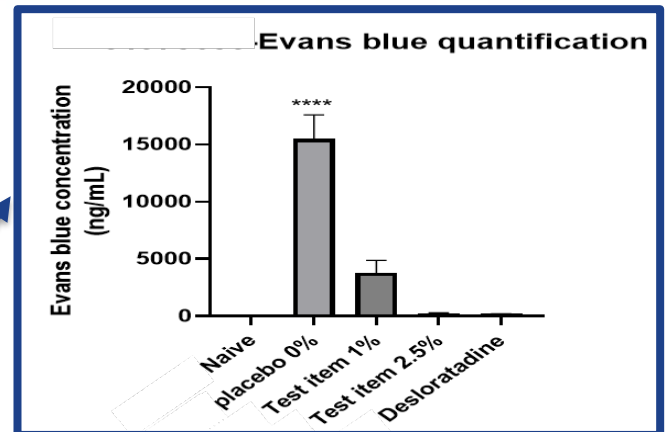
Group 4: Test  
item 2.5%



Group 5:  
Desloratadine



- N=10 rats per group (except N=5, naïve control) were given either topical application of: Placebo, 1% or 2.5% AQST-108 was applied, high dose oral histamine (desloratadine) as positive control
- Injection of 2,4-dinitrophenol (DNP), an immunoglobulin E (IgE) specific antibody, which induces mast cell degranulation releasing histamine and proinflammatory cytokines
- Evans Blue dye was also injected to observe increased capillary profusion (see chart)

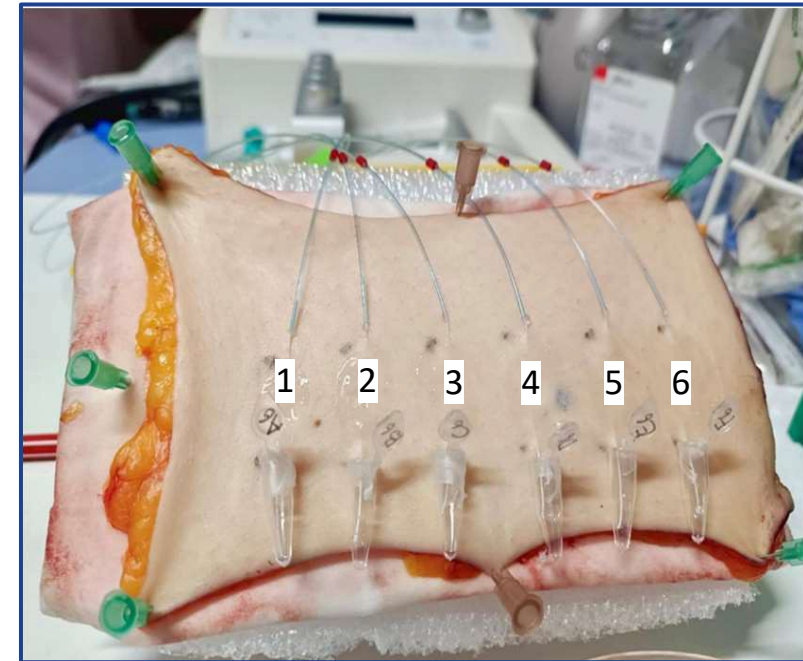
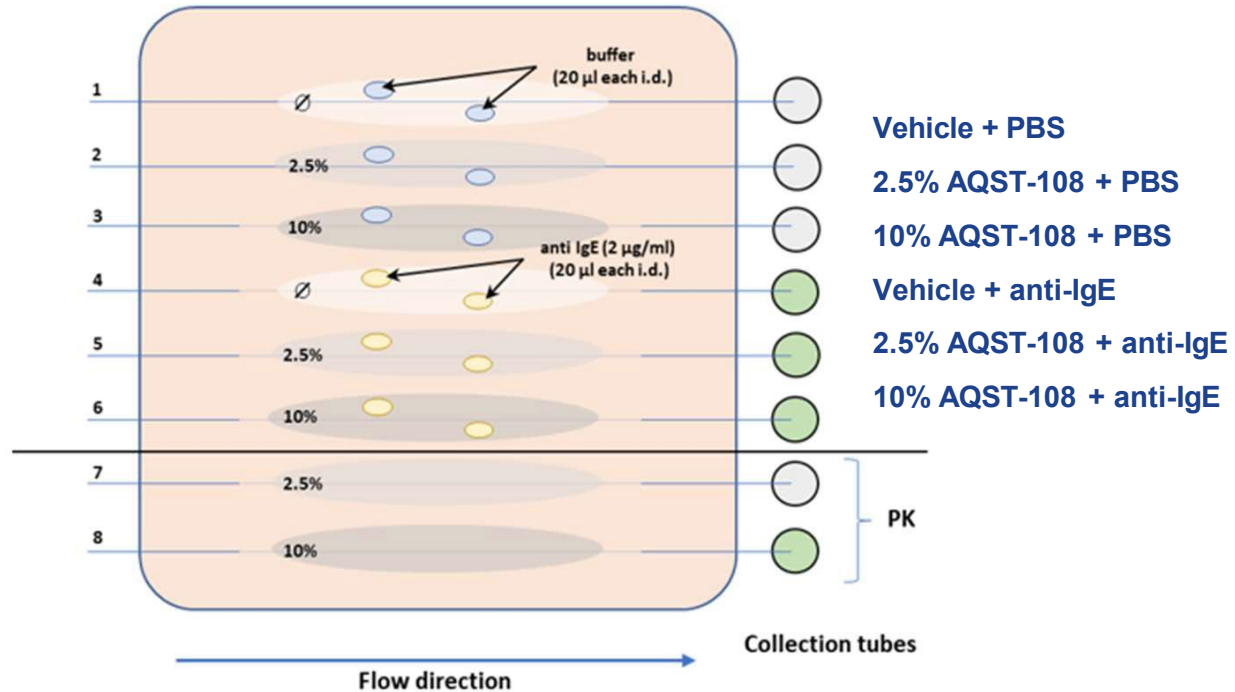


1. Aquestive Therapeutics data on file.



# Ex-Vivo human skin microdialysis

Design: Freshly excised human skin used for microdialysis of interstitial fluid across multiple treatment groups<sup>1</sup>

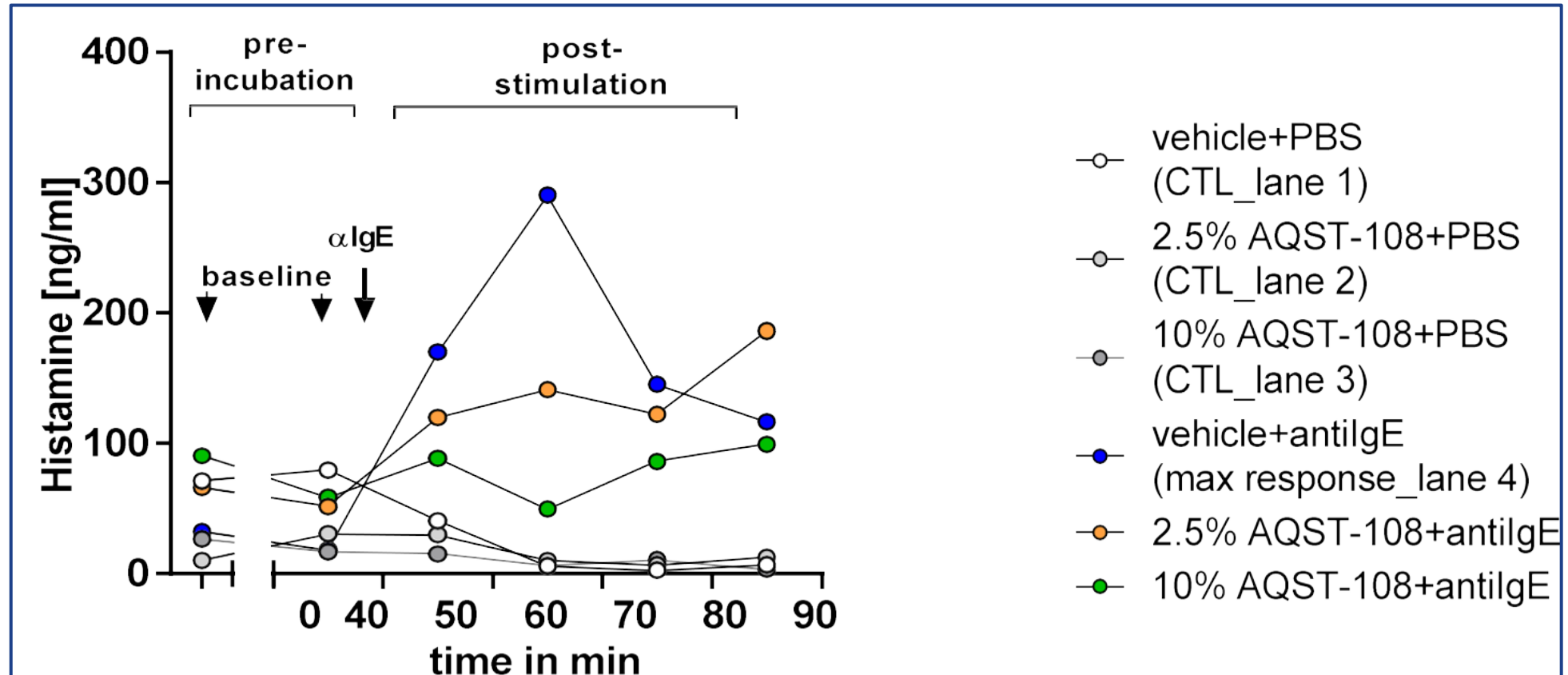


Ex vivo skin explant with sampling lanes 1– 6

1. Aquestive Therapeutics data on file.

# Topical AQST-108 human skin microdialysis results<sup>1</sup>

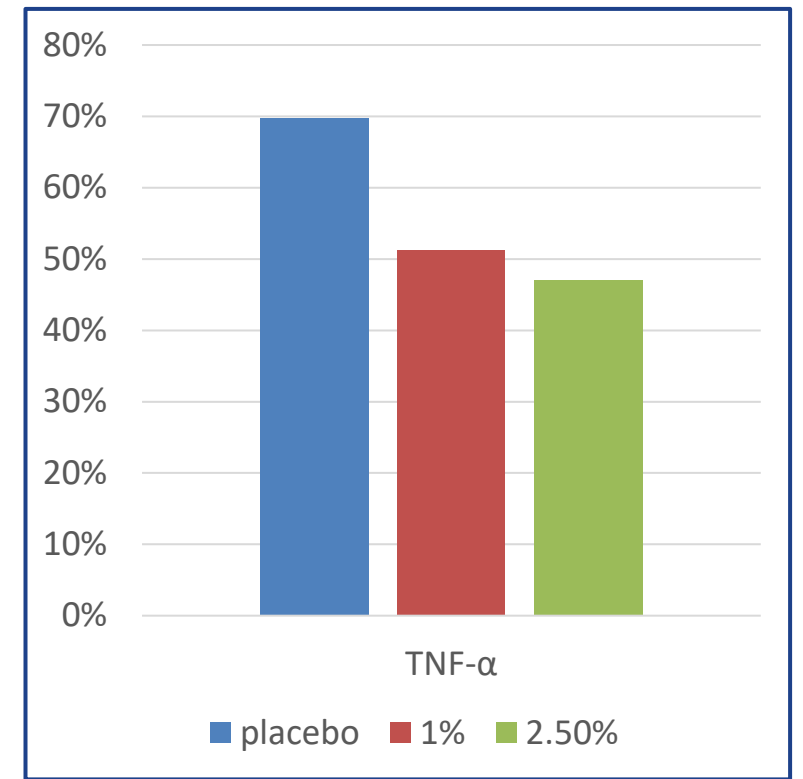
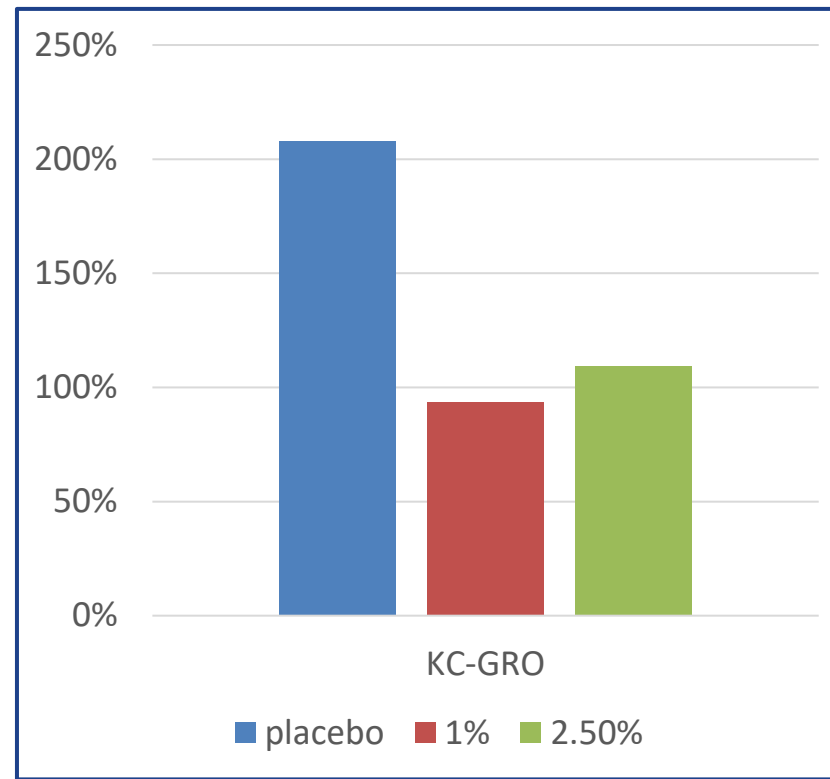
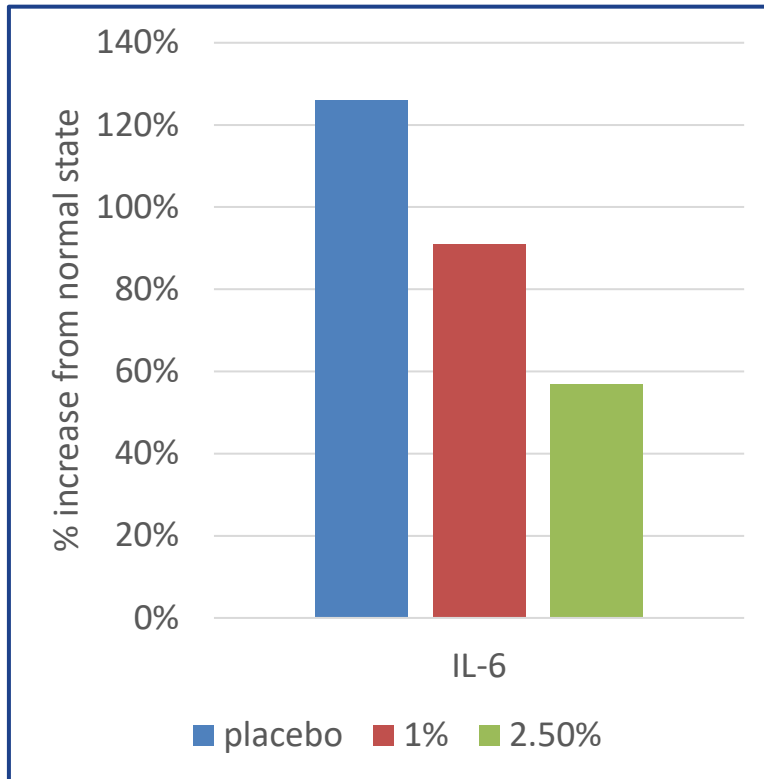
AQST-108 demonstrates that histamine release is inhibited through mast cell stabilization in ex-vivo human skin provoked with IgE antibodies



1. Aquestive Therapeutics data on file.

# Cytokine analysis from passive cutaneous anaphylaxis (PCA) model<sup>1</sup>

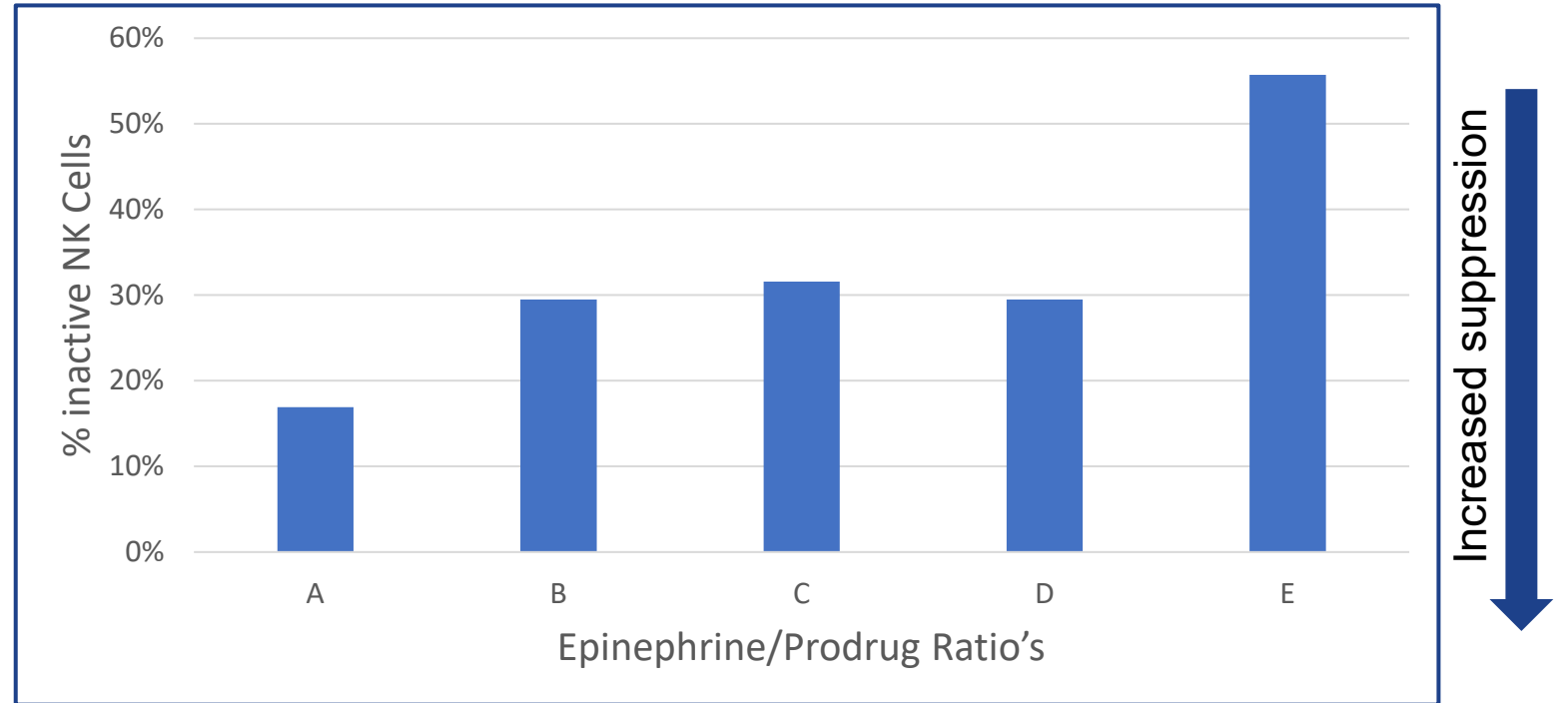
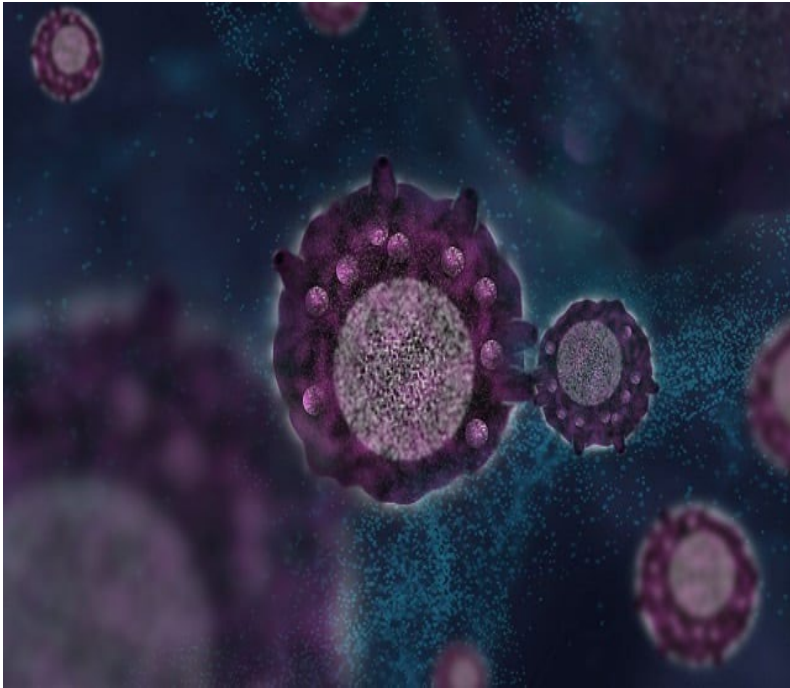
AQST-108 demonstrates immunomodulation across multiple cytokines monitored in the PCA model. Graphs represent % cytokine presence during PCA relative to the naive state<sup>2</sup>



1. Aquestive Therapeutics data on file. 2.  $p < 0.01$  compared to Placebo; Utilized One way ANOVA; Dunnett's test for multiple comparisons.

# Modulation of NK cell activity<sup>1</sup>

AQST-108 suppressed NK cell activation across of range of concentrations exceeding the half-maximal inhibitory concentration (IC<sub>50</sub>) above a 750nM <sup>2</sup>



	ritlecitinib <sup>3</sup>	cortisol	108
Inhibition (IC <sub>50</sub> ) - NK cells	509nM	200nM	750nM

1. Aquestive Therapeutics data on file. 2. IC<sub>50</sub> is a measurement of how much of a drug is needed to inhibit a biological process by half. 3. ritlecitinib IC<sub>50</sub> extracted from FDA summary basis of approval for Litfulo™, results shown are a cross-study comparison.

# AQST-108 patent applications potentially extending into 2046<sup>1</sup>

## TITLE

## PATENT STATUS

### ENHANCED DELIVERY EPINEPHRINE COMPOSITIONS

- ▶ **Priority date:** May 5, 2016
- ▶ Possible patent term to 2037

### ENHANCED DELIVERY EPINEPHRINE AND PRODRUG COMPOSITIONS

- ▶ **Priority date:** May 4, 2017
- ▶ Possible patent term to 2037

### PRODRUG COMPOSITIONS AND METHODS OF TREATMENT

- ▶ **Priority date:** Late 2019
- ▶ Possible patent term to 2040

### TOPICAL DELIVERY OF EPINEPHRINE AND PRODRUG COMPOSITIONS

- ▶ **Priority date:** March 2025
- ▶ Possible patent term to 2046

- **AQST-108 non-clinical development demonstrates valuable proof points about absorption and conversion potentially resulting in durable local exposure in the skin without undesirable systemic exposure**
- **Models successfully demonstrated desired pharmacology and immunomodulation that can be harnessed clinically and is patent-protected**



AQST-108 (epinephrine) Topical Gel

# **Initial Indication and Clinical Overview**

Dr. Carl Kraus

Chief Medical Officer



## **Carl Kraus, MD**

### **Chief Medical Officer**

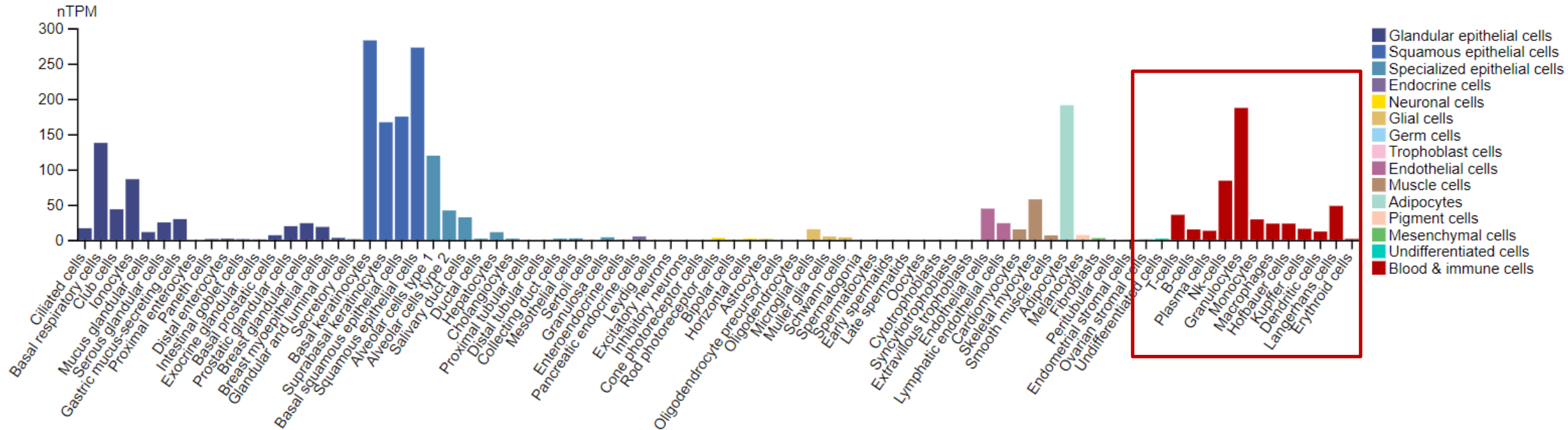
- **M.D., Washington University in St. Louis**
- **Residency, University of Chicago**
- **Fellowship, National Institutes of Health**
- **Clinical Reviewer, CDER, FDA**
- **18+ years experience in multiple therapeutic development programs from preclinical – Phase IV**





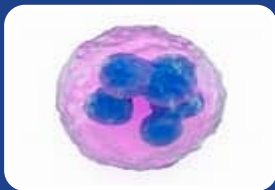
# The Human Protein Atlas: clues from receptor expression

In addition to high expression on skin tissue, ADRB2 has high expression on immune cells<sup>1</sup>



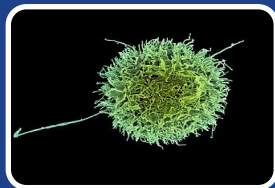


# Skin disorders potentially addressable by adrenergic receptor-mediated immune cell targeting



## Granulocytes

- Mast cells – Cutaneous mastocytosis, MCAS<sup>1</sup>, Alopecia areata
- Neutrophils – Chronic granulomatous disease, Leukocyte adhesion deficiencies



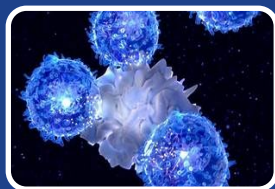
## Natural Killer Cells

- Increased activity – Alopecia areata, Lupus, Rheumatoid Arthritis
- Decreased activity – Viral infections, proliferative diseases including cancers



## Langerhans Cells<sup>2</sup>

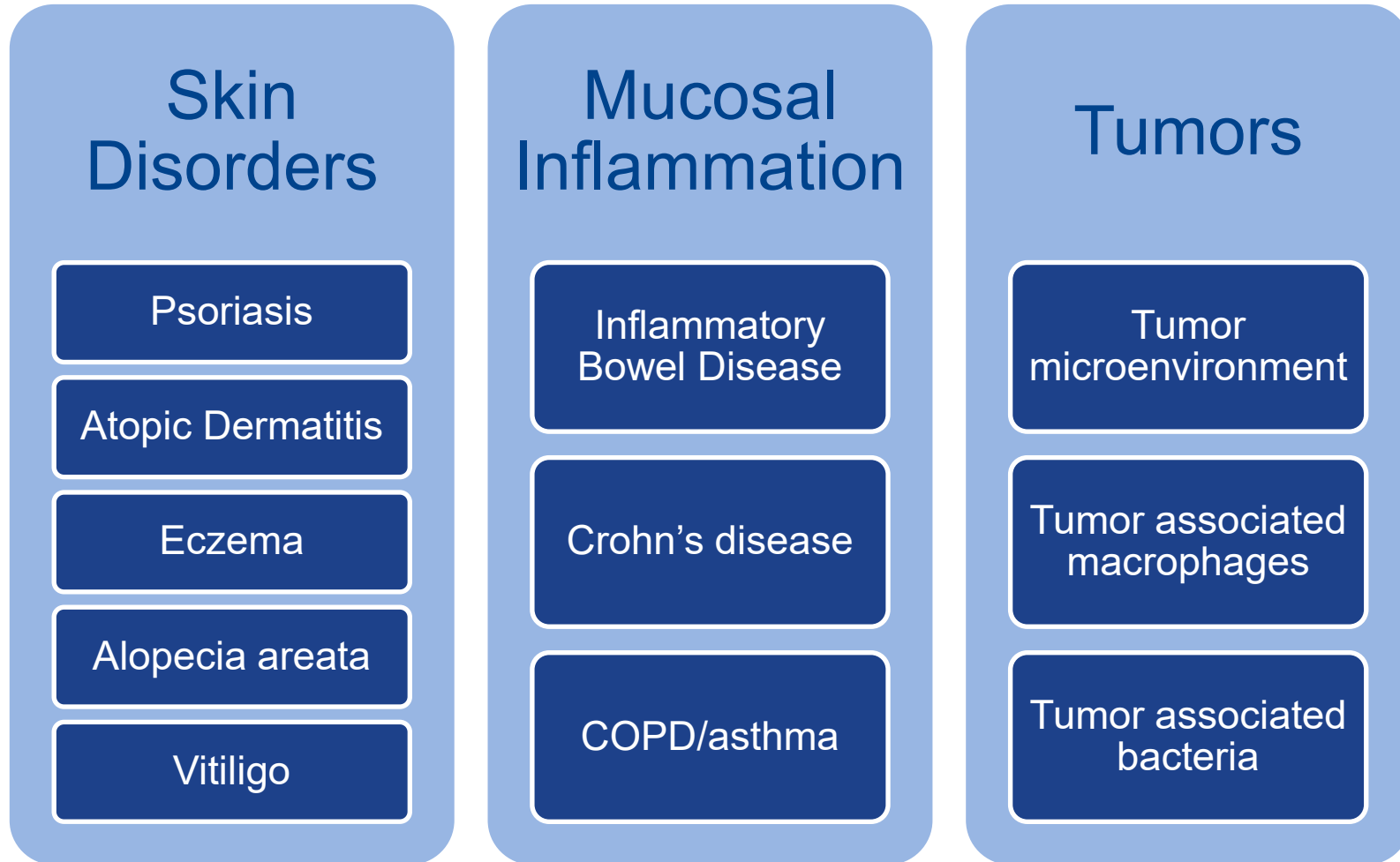
- Alopecia areata
- Langerhans cell histiocytosis – Skin manifestations are common and mimic other conditions



## T-cells

- Cytotoxic – Autoimmune diseases (Alopecia areata), viral infections
- Helper – Atopic Dermatitis, mycobacterial infections, Asthma

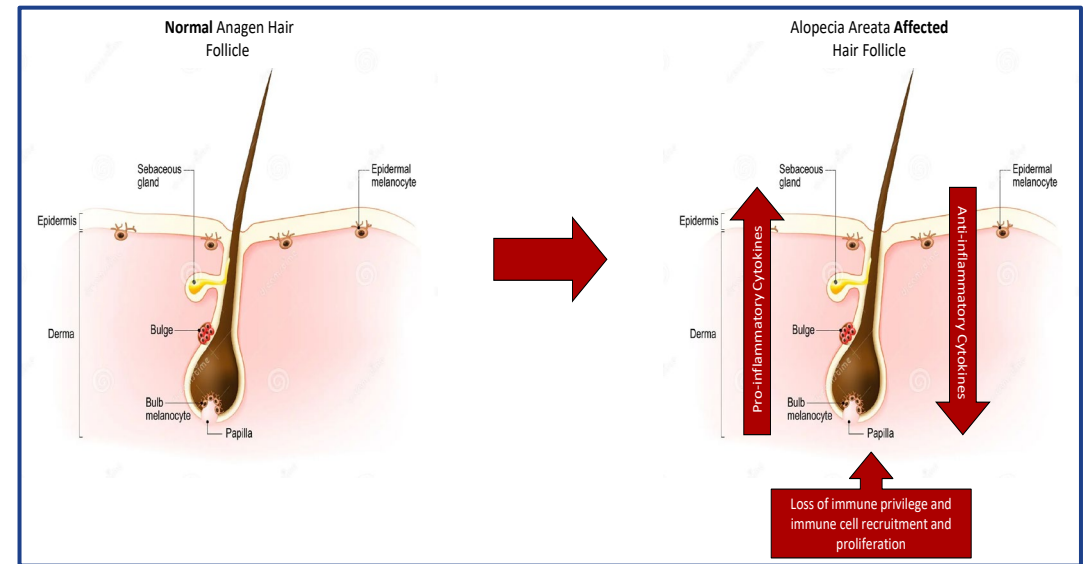
# Potential indications for Adrenaverse™ technology<sup>1</sup>



1. Not yet in development; assumes successful clinical development and approval by FDA.

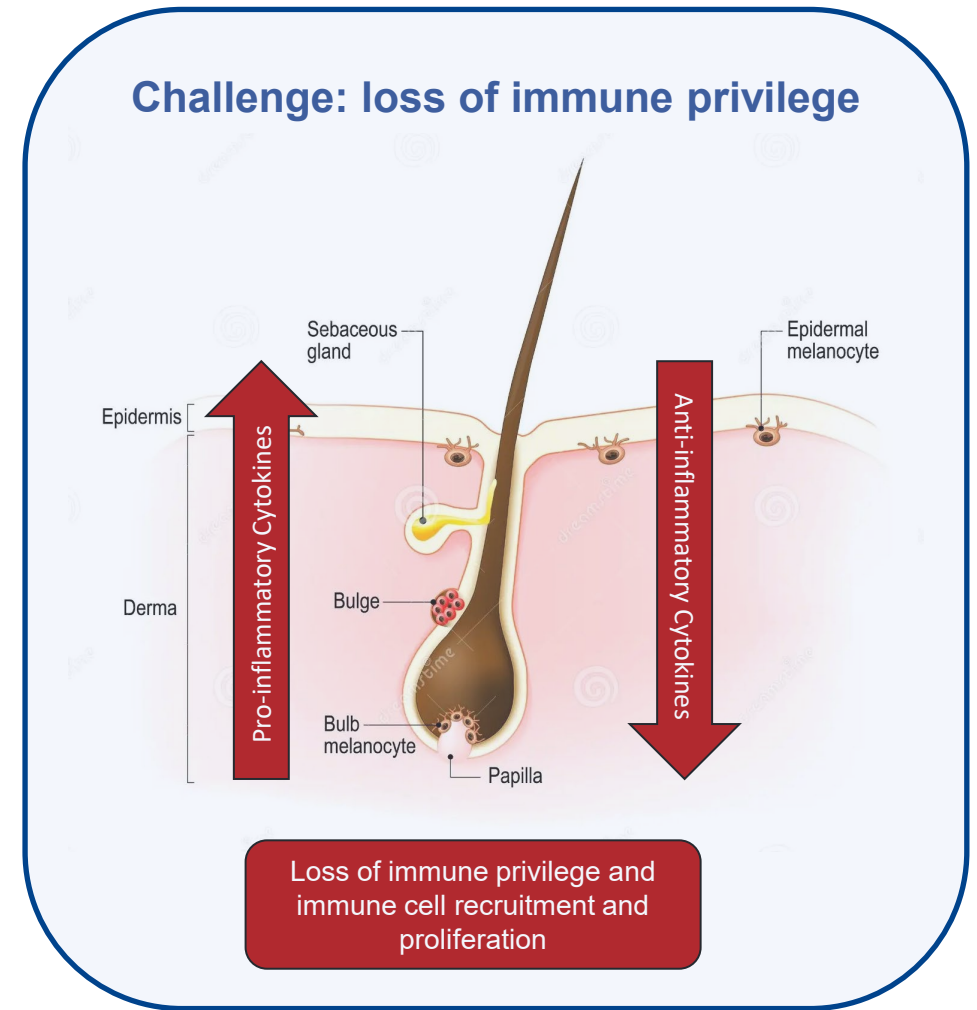
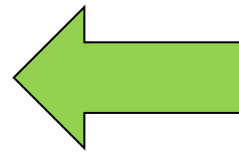
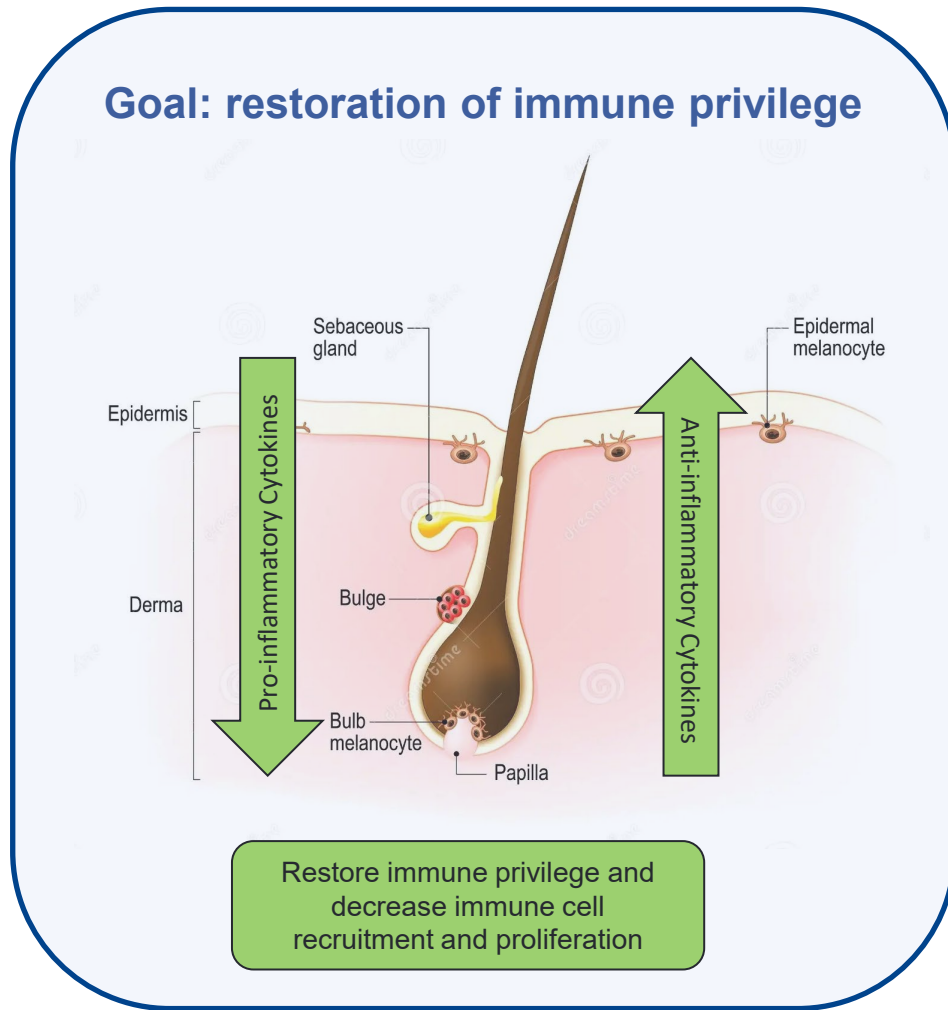
# Alopecia areata (AA) background<sup>1</sup>

- AA is an autoimmune disease leading to hair loss on the scalp, face, and in more severe cases, other body areas
- The mechanisms leading to AA are multifactorial, including an autoimmune response that results in the loss of hair follicle immune privilege
- The patient will begin treatment based on disease severity (> 50% involvement – JAK inhibitors; < 50% involvement – corticosteroids)



1. UpToDate; NAAF.org; BioMedTracker; Benigno et al. A large cross-sectional survey study of the prevalence of AA in the US. 2020; Litfulo Pfizer HCP Page. SALT Evaluation; King et al. Defining severity in Alopecia areata: current perspectives and a multidimensional framework. 2022, accessed January 2024.

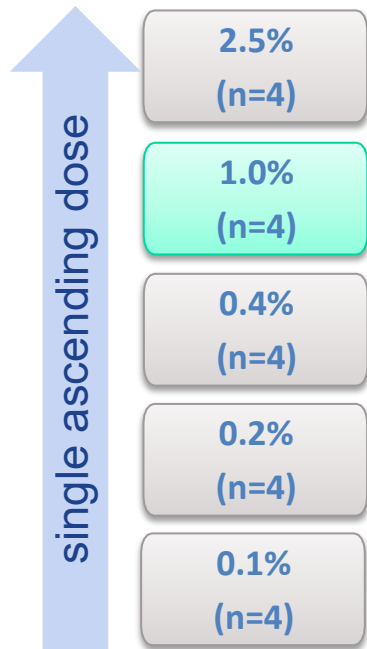
# Adrenergic receptor agonism may address early AA pathology<sup>1</sup>



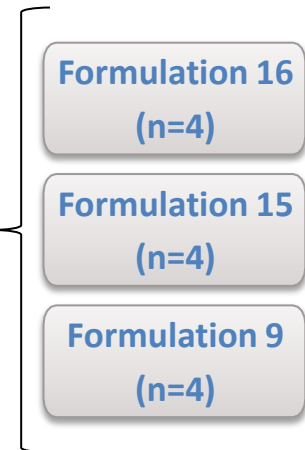
1. Hair follicle immune privilege and its collapse in Alopecia areata - Bertolini - 2020 - Experimental Dermatology - Wiley Online Library.

# Completed first in human (FIH) two-part study<sup>1</sup>

**Part 1** – single ascending doses of a single formulation of AQST-108



**Part 2** – a single dose of 1 of 3 formulations of 1.0% AQST-108



## Part 1 outcomes:

- No serious adverse events (SAE) or topical adverse events (AE)
- Calculated % AQST-108 in skin remained relatively consistent, between 9-14%
- No AQST-108 concentration in plasma observed
- Systemic epinephrine concentrations remained within normal physiologic range for all doses

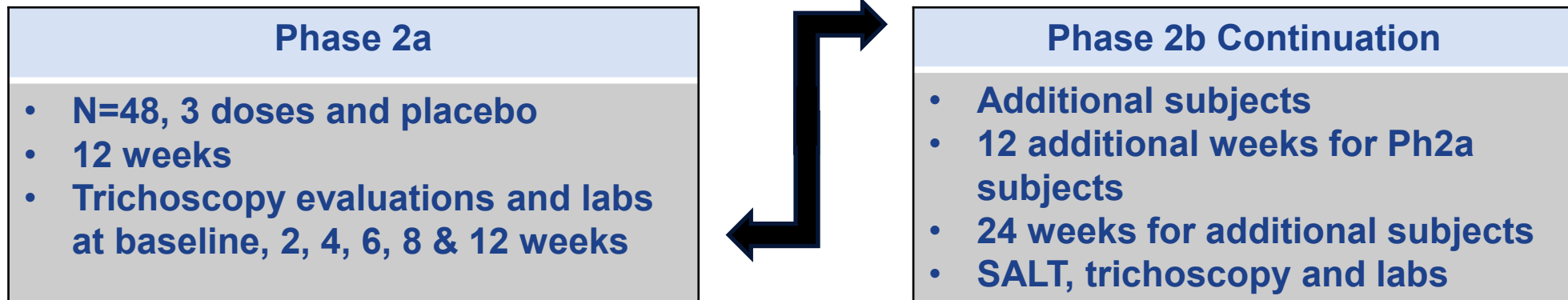
**1.0% AQST-108 strength down-selected to Part 2**

## Part 2 outcomes:

- No SAEs or topical AEs
- Calculated % AQST-108 in skin remained relatively consistent across formulations (11-12%)
- No AQST-108 concentration in plasma observed

# AQST-108 planned Phase 2 Alopecia areata clinical study<sup>1</sup>

A Phase 2, multi-center, double-blind, placebo-controlled, dose-ranging, adaptive study to evaluate the safety and efficacy of AQST-108 in mild to moderate Alopecia areata patients



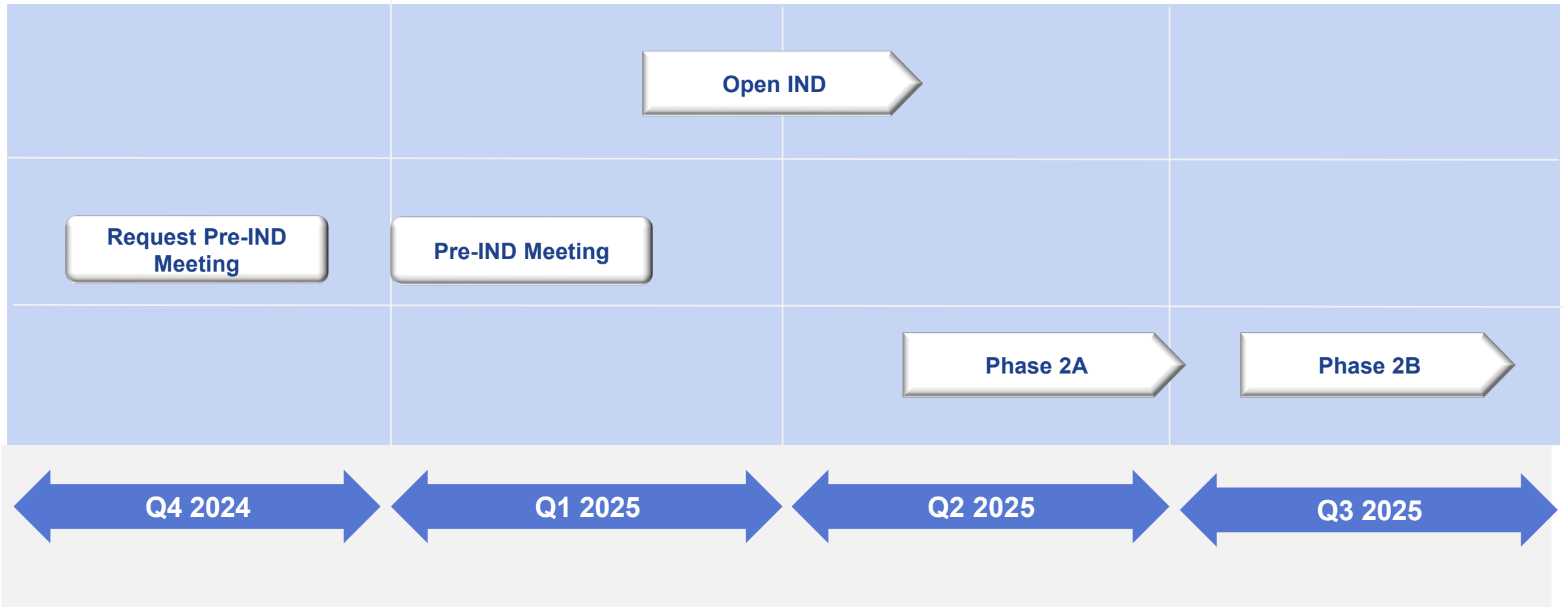
## Objectives of Phase 2a Study

Assess the safety and efficacy of AQST-108 in Alopecia areata patients following 12 weeks of treatment as determined by digital imagery (Canfield)

## Objectives of Phase 2b Study

To evaluate the safety and efficacy of AQST-108 compared to placebo in AA patients with less than 50% scalp hair loss, on regrowth of lost hair (as measured by change from baseline in Severity of Alopecia Tool (SALT) Score) at week 24

# Planned AQST-108 clinical and regulatory pathway<sup>1</sup>



1. End of phase 2 meeting with the FDA is planned for the fourth quarter of 2025 or the first quarter of 2026.



## Key takeaways

- **AQST-108 demonstrated no serious adverse events or topical adverse events**
- **Lack of plasma concentration after application of AQST-108 may indicate conversion in the dermis at the targeted site of action**
- **Plan to hold pre-IND meeting and advance AQST-108 into a Phase 2 clinical study for mild to moderate Alopecia areata**

Alopecia areata

# Market Potential

Dan Barber

# Patient unmet needs in moderate to severe Alopecia areata<sup>1</sup>

## Existing JAK inhibitor therapies

- are systemic and have known side effects
- have a black box warning
- only show significant improvement in approximately one out of three cases
- have an unacceptable relapse rate
- are expensive

# Alopecia areata represents a potential opportunity<sup>1</sup>



## Reasons to Believe

- Patient unmet need is well-documented and understood
- Planned development endpoints that are potentially achievable
- Competitive landscape indicates pricing will continue to be reasonable (severe is high)
- Commercial opportunity can fit within a growing Aquestive commercial infrastructure

Initial Target Product Profile <sup>2</sup>	
Description	<ul style="list-style-type: none"><li>• Topical gel form of AQST-108</li></ul>
Indication	<ul style="list-style-type: none"><li>• Moderate and severe Alopecia areata patients</li></ul>
Dosage and Administration	<ul style="list-style-type: none"><li>• Apply once in the morning and once at night</li></ul>
Safety	<ul style="list-style-type: none"><li>• Potential for no black box warning</li><li>• No systemic effect may limit side effects</li></ul>
Value Proposition	<ul style="list-style-type: none"><li>• May be an alternative to using JAK inhibitors</li><li>• May improve treatment for the two-thirds of severe patients who see no improvement with JAK inhibitors</li><li>• May improve treatment in conjunction with JAK inhibitors</li></ul>

1. Aquestive Therapeutics data on file. 2. Dependent on final clinical and regulatory outcomes.

# Alopecia areata occurs in ~2% of the population

## Alopecia areata by the Numbers



Estimated 6.7M people in the U.S. have been affected by Alopecia areata<sup>1</sup>



Equally prevalent between male and females<sup>2</sup> (average age of diagnosis is 31 years for males and 36 years for females)<sup>3</sup>



Evidence suggests there may be a genetic link for some patients<sup>4</sup>



~39% of patients with Alopecia areata also have atopic dermatitis<sup>5</sup>









~43% of Alopecia areata patients are considered severe<sup>6</sup>



1. National Alopecia Areata Foundation, What you need to know about Alopecia areata, <https://www.naaf.org/alopecia-areata>, Accessed August 2024; 2. National Organization for Rare Disorders, Alopecia areata, <https://rarediseases.org/rare-diseases/alopecia-areata/>, Last Updated July 12, 2022; 3. Mirzoyev S., et al., Lifetime incidence risk of Alopecia areata estimated at 2. 1% by Rochester epidemiology project, 1990–2009, Journal of Investigative Dermatology, April 2014; 4. Lepe K., et al., Alopecia Areata, StatPearls, National Library of Medicine, Updated March 7, 2023; 5. Kolb L., et al., Atopic Dermatitis, StatPearls, National Library of Medicine, Updated August 8, 2022; 6. Benigno et al. A large cross-sectional survey study of the prevalence of AA in the US. 2020.


# Currently marketed products for severe AA are JAK inhibitors


## Alopecia areata Treatment Landscape<sup>1</sup>


	Product/ Generic	Company	Mechanism of Action <sup>2</sup>	Route of Administration <sup>2</sup>	Dosing Frequency <sup>5</sup>	Approval Year (Indication) <sup>3</sup>	Monthly Treatment Cost (WAC) <sup>4</sup>
On-Label Branded Therapies	 olumiant <sup>®</sup> (baricitinib) tablets 4mg, 2mg, 1mg		JAK1/2 inhibitor	Oral	Once daily	2022	\$2,740 (2mg) – \$5,480 (4mg)
	 Litfulo <sup>®</sup> (ritlecitinib) capsules 50mg		JAK3 inhibitor	Oral	Once daily	2023	\$4,240 (50mg)
	 LEQSELVI <sup>®</sup> (deuruxolitinib) tablets 8mg		JAK1/2 inhibitor	Oral	Twice daily	2024	<i>Not yet announced by Sun Pharma</i>
Corticosteroids	Triamcinolone acetonide	Generic Rx	Steroid	Topical / Intralesional	Twice daily / Every 4-6 weeks until regrowth or failure	N/A	\$50 <sup>†</sup>
	Betamethasone	Generic Rx	Topical	Topical / Intralesional	Twice daily / Every 4-6 weeks until regrowth or failure	N/A	\$50 <sup>††</sup>
	Desoximetasone	Generic Rx	Topical	Topical / Intralesional	Twice daily / Every 4-6 weeks until regrowth or failure	N/A	\$20 <sup>††</sup>
Non-Steroidals	DPCP*	Generic Rx	Calcineurin inhibitor	Topical	Once weekly	N/A	- <sup>§</sup>
	SADBE**	Generic Rx	IL-13 & IL-4 antagonist	Topical	Once weekly	N/A	- <sup>§</sup>
	Methotrexate	Generic Rx	JAK1 inhibitor	Oral	Once weekly	N/A	\$10
	Minoxidil	Generic Rx	Anti-hypertensive	Oral / Topical	Twice daily	N/A	\$30
	Dupixent	Sanofi	IL-13 & IL-4 antagonist	SQ Injection	Every 2-4 weeks	N/A	\$3,800

# JAK inhibitors pricing for severe AA remains high




List Price (WAC, 4mg tablets): <b>\$5,480/ month<sup>1,2</sup></b>
Indication(s): Adults with Severe Alopecia; Moderate-to-Severe RA*
Black Box Warning on Label

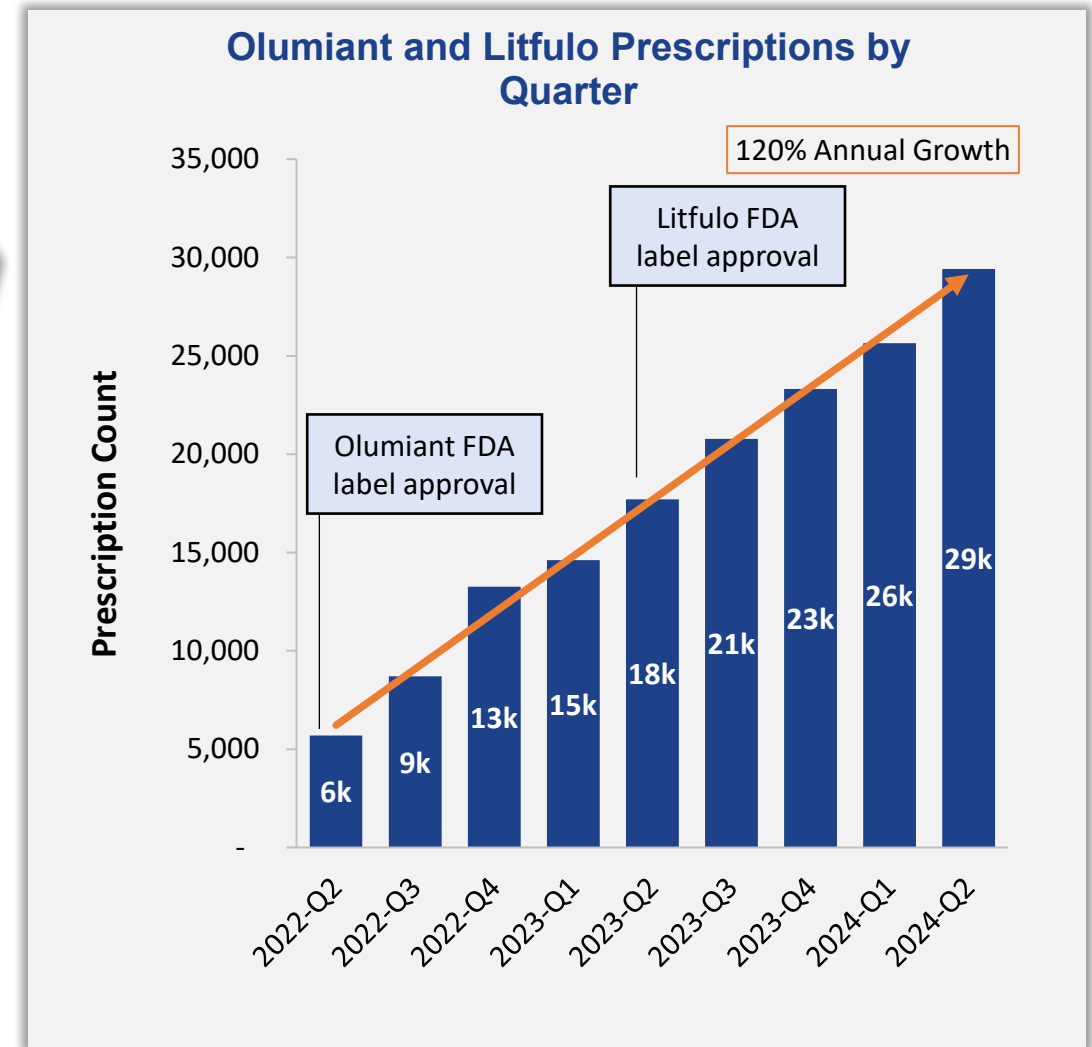

List Price (WAC, 50mg tablets): <b>\$4,240/ month<sup>2</sup></b>
Indication(s): Adults and Pediatric Patients >17 YoA with Severe Alopecia
Black Box Warning on Label


List Price (WAC, 50mg tablets): <b>Not yet announced by Sun Pharma</b>
Indication(s): Adults with Severe Alopecia
Black Box Warning on Label

\*Rheumatoid Arthritis; following inadequate response to anti-TNF therapy

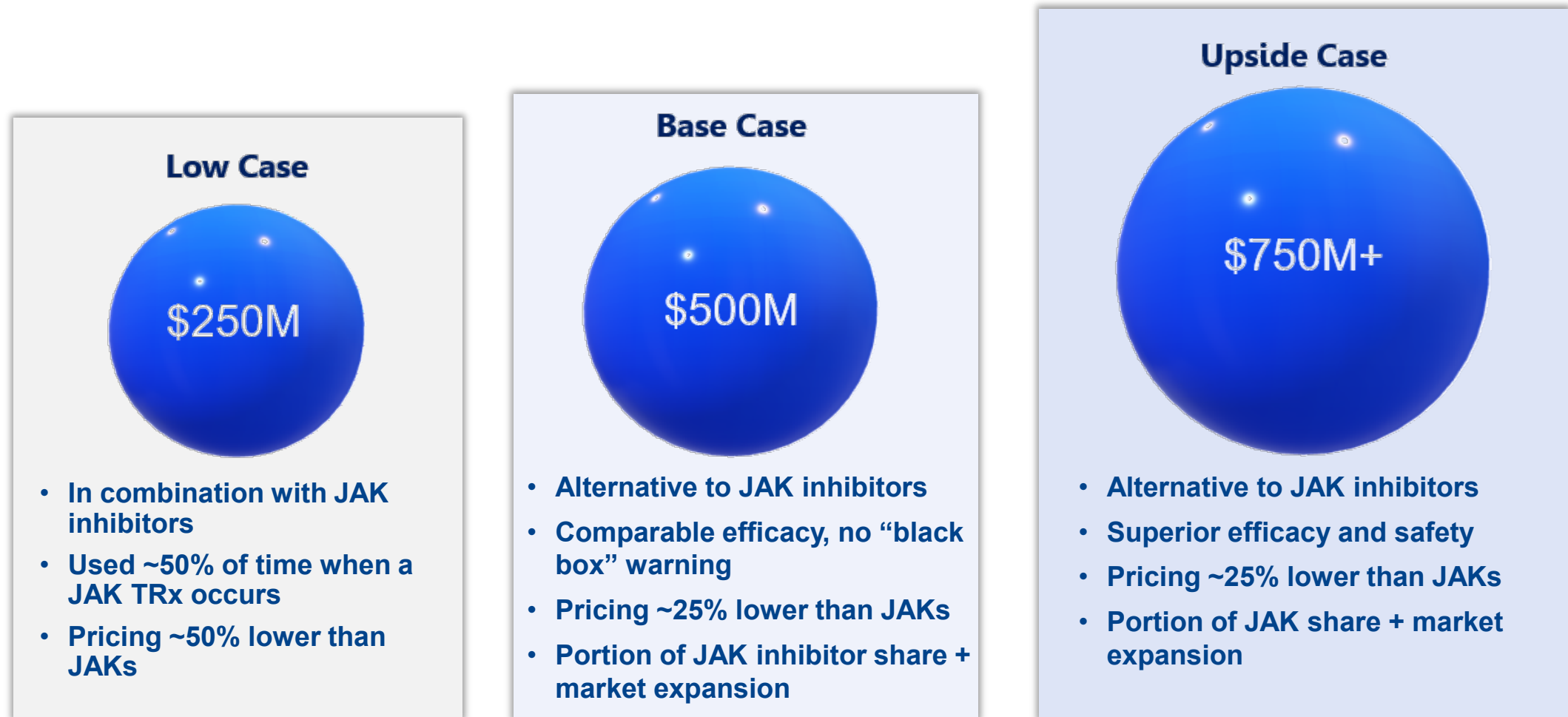
# Estimated \$1 billion+ opportunity for JAK inhibitors<sup>1</sup>

- Olumiant label for AA granted in June 2022
- Litfulo label for AA granted in June 2023
- Combined prescriptions for Olumiant and Litfulo in 2<sup>nd</sup> quarter of 2024 totaled ~30K, representing a small fraction of the severe AA patient population
- This still represents a small fraction of the patient prevalence for severe AA, for which awareness is building





# AQST-108 – potential annual peak net sales<sup>1</sup>

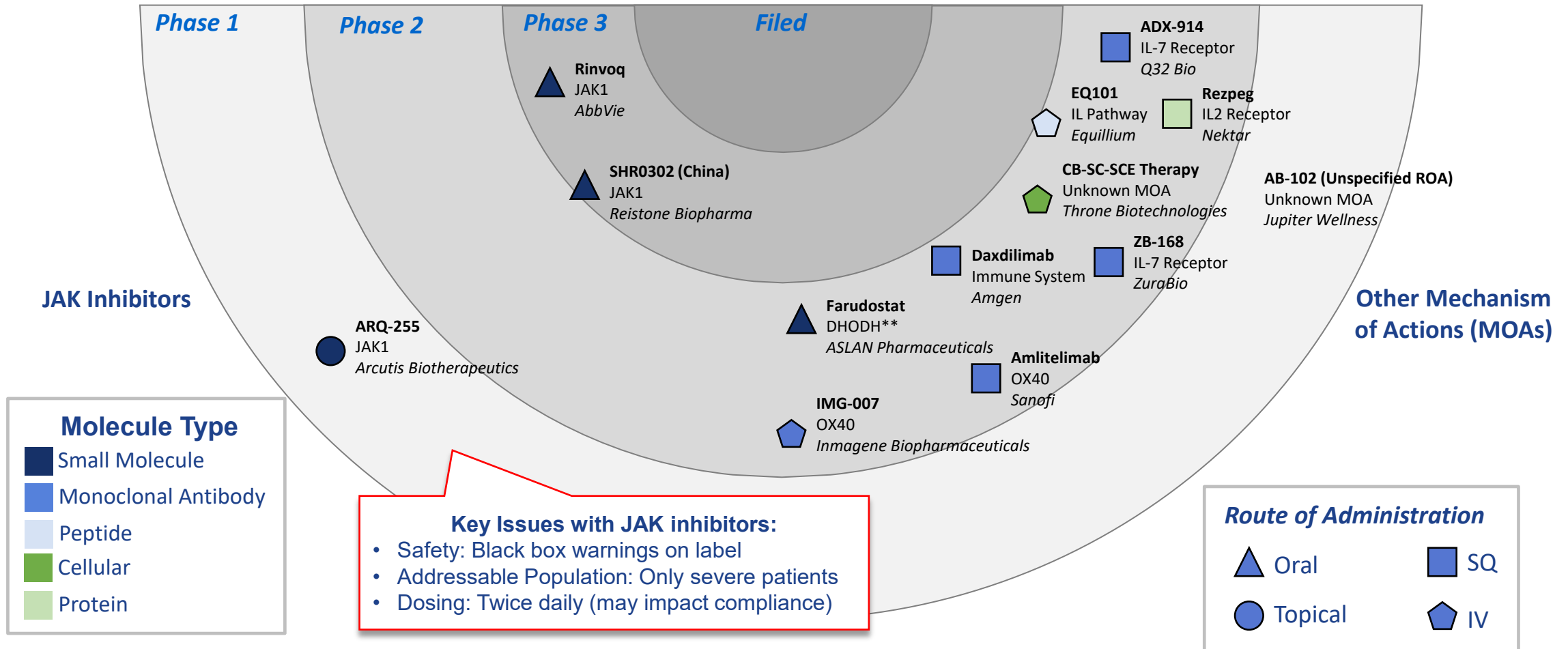


1. Aquestive Therapeutics data on file; potential revenues are Aquestive Therapeutics estimates based on current information; peak year sales are assumed ~5 years post launch.



# Late-stage pipeline assets of competitors include multiple JAK inhibitor products, creating a unique space for AQST-108, if approved by FDA

## Alopecia areata competitive pipeline<sup>1</sup>

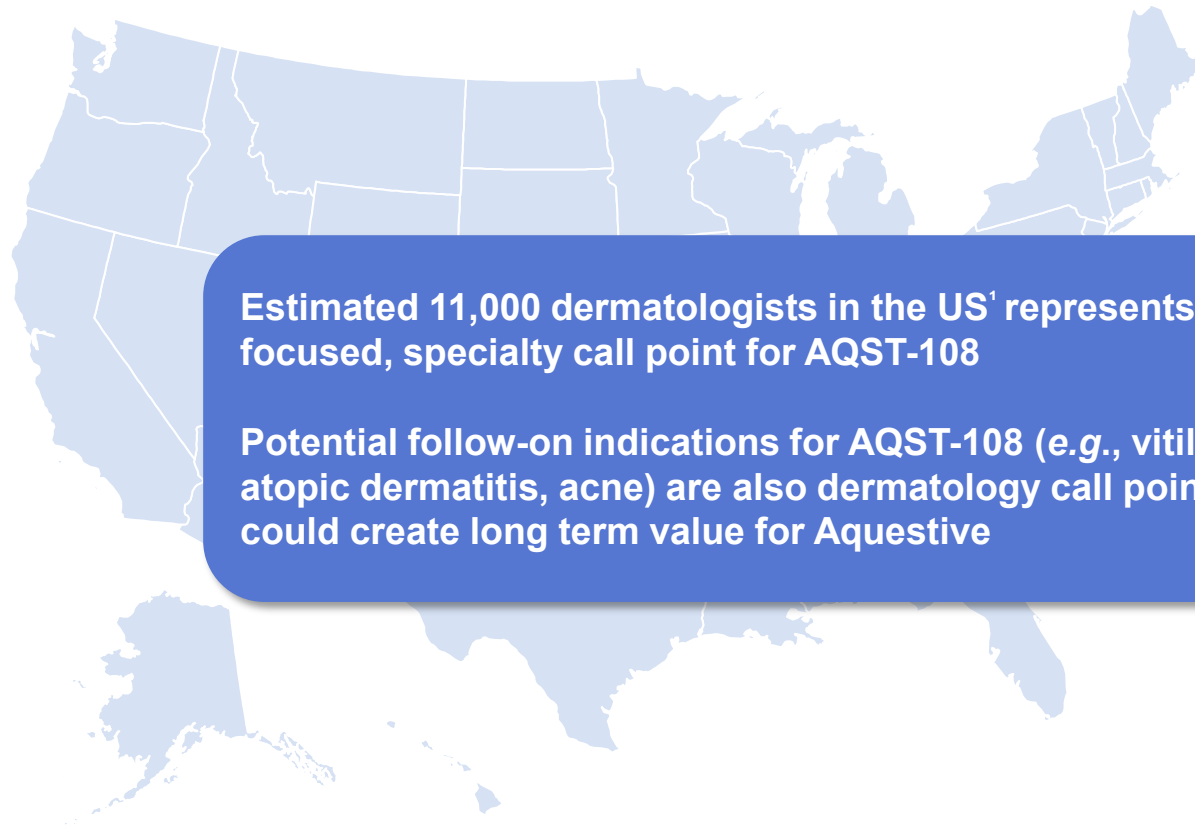


1. Aquestive Therapeutics data on file.



# Planned commercialization efforts would focus on a dermat call point

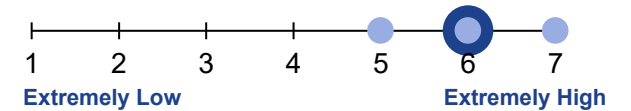
Focused commercialization effort with a dermatology call point



Estimated 11,000 dermatologists in the US<sup>1</sup> represents a focused, specialty call point for AQST-108

Potential follow-on indications for AQST-108 (e.g., vitiligo, atopic dermatitis, acne) are also dermatology call points – could create long term value for Aquestive

Dermatologist-Expressed Level of **Unmet Need** for **severe Alopecia areata patients<sup>1</sup>** and **Receptivity to AQST-108**



*“Product X [AQST-108], due to its superior safety profile, could likely be used for extended durations [compared to topical corticosteroids], given its lack of systemic absorption or local side effects. I think that’s very beneficial.”*

- Dermatologist

*“If Product X’s efficacy is comparable to that of class I topical steroids, then it’s going to be very desirable. And I could see this being first-line therapy.”*

- Dermatologist

## Final key takeaways

- **The Adrenaverse™ platform opens a new development pipeline for the Company**
- **AQST-108 for Alopecia areata has the potential to be an important opportunity**



# Closing Remarks and Q&A



**Thank You**