# Anaphylaxis and Epinephrine
# AQST-109: Topline Results from Phase 1 PK Study (Study 210010)

**October 25, 2021**

Advancing medicines.
Solving problems.
Improving lives.

# Forward Looking Statement

Certain statements in this presentation 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 potential for AQST-109 as the first orally administered epinephrine prodrug for the treatment of anaphylaxis, the advancement and related timing of AQST-109 through the regulatory and development pipeline and clinical 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 FDA approval of AQST-109, our drug candidate Libervant™ (diazepam) Buccal Film and our other drug candidates or failure to receive FDA 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 legal costs associated with and the outcome of our patent litigation challenging third party at risk generic sale of our proprietary products; 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 liquidity and cash requirements and other cash needs, at the times and in the amounts needed; 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, including patent infringement, 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. 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 presentation whether as a result of new information, future events or otherwise, except as may be required by applicable law.



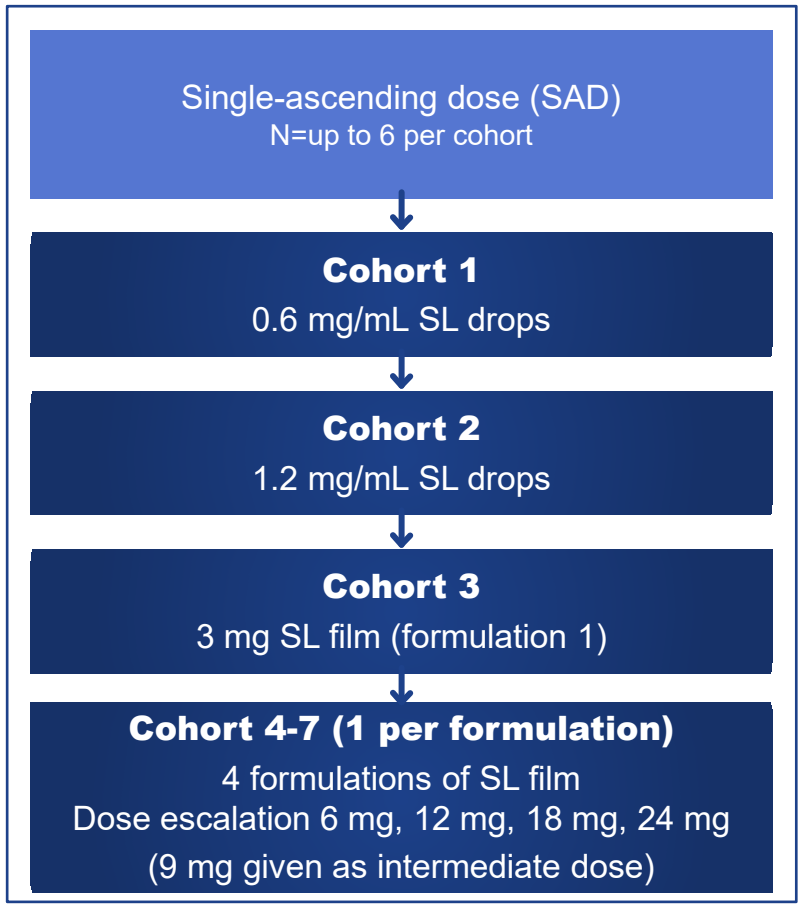
This presentation shall not constitute an offer to sell or the solicitation of an offer to buy these securities, nor shall there be any sale of these securities in any state or jurisdiction in which such offer, solicitation or sale would be unlawful prior to registration or qualification under the securities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

# Executive Summary

- Successful development of a sublingual epinephrine product relies on pharmacokinetic (PK) and pharmacodynamic (PD) comparability to existing epinephrine injection products
- AQST-109 has delivered promising results from a First in Human PK/PD study in healthy volunteers
  - Median time to maximal concentration ($T_{max}$) is 15 minutes (target formulation)
  - Mean maximal concentration ($C_{max}$) values meet or exceed the target range
  - The treatment was well-tolerated, with no serious adverse events reported, and most treatment-emergent adverse events were mild in severity
- The next clinical study in the development program will begin dosing in December, and aims to establish a final dose and formulation for the pivotal trial

# AQST-109: Study 210010* (First in Human) Overview

*Aquestive Therapeutics recently completed Study 210010, a first in human study that evaluated four film formulations at multiple dosage strengths.*




## Study 210010 ("010 Study")

- Single-ascending dose study in healthy young male volunteers
  - **Film dose levels of 3 mg, 6 mg, 9 mg, 12 mg, 18 mg, and 24 mg**
- Four different film formulations
- Up to 6 subjects per formulation received up to 4 escalating doses, 24 subjects total
- PK and PD measurements
  - Frequent sampling from pre-dose to 240 minutes post-dose

** From ongoing clinical trial 210010*



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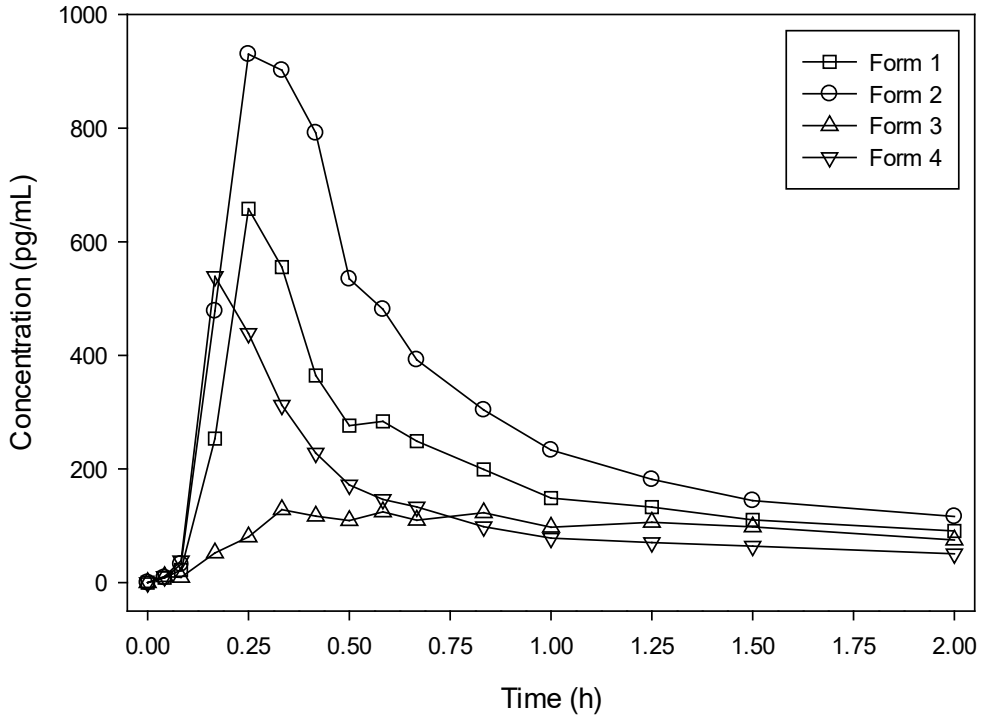
# AQST-109: Absorption and Conversion

*The results from Study 210010 demonstrate that AQST-109 is rapidly absorbed and converted into epinephrine.*

Baseline-Corrected Mean Epinephrine Concentration over Time Following Administration of AQST-109 12 mg




Represents data from top-line results. Figure derived from arithmetic means.

| Description | Form 1 12 mg | Form 2 12 mg | Form 3 12 mg | Form 4 12 mg | EpiPen®* | EpiPen®^ | Auvi-Q®* |
|---|---|---|---|---|---|---|---|
| **Cmax (pg/ml)** | 552 | 762 | 164 | 307 | 518 | 341 | 484 |
| **AUC 0-t (hr*pg/ml)** | 634 | 603 | 329 | 303 | 560 | 328 | 526 |
| **Tmax (min)** | 15 | 15 | 20 | 10 | 10 | 22 | 20 |
| **Tmax Range (min)** | 15-25 | 10-35 | 20-50 | 5-50 | 4-60 | 5-90 | 5-60 |

Represents data from top-line results. Geometric means presented for Cmax and AUC0-t, Median Tmax.

* https://www.accessdata.fda.gov/drugsatfda_docs/nda/2012/201739Orig1s000ClinPharmR.pdf

^ Data on file, AQST Study 160445



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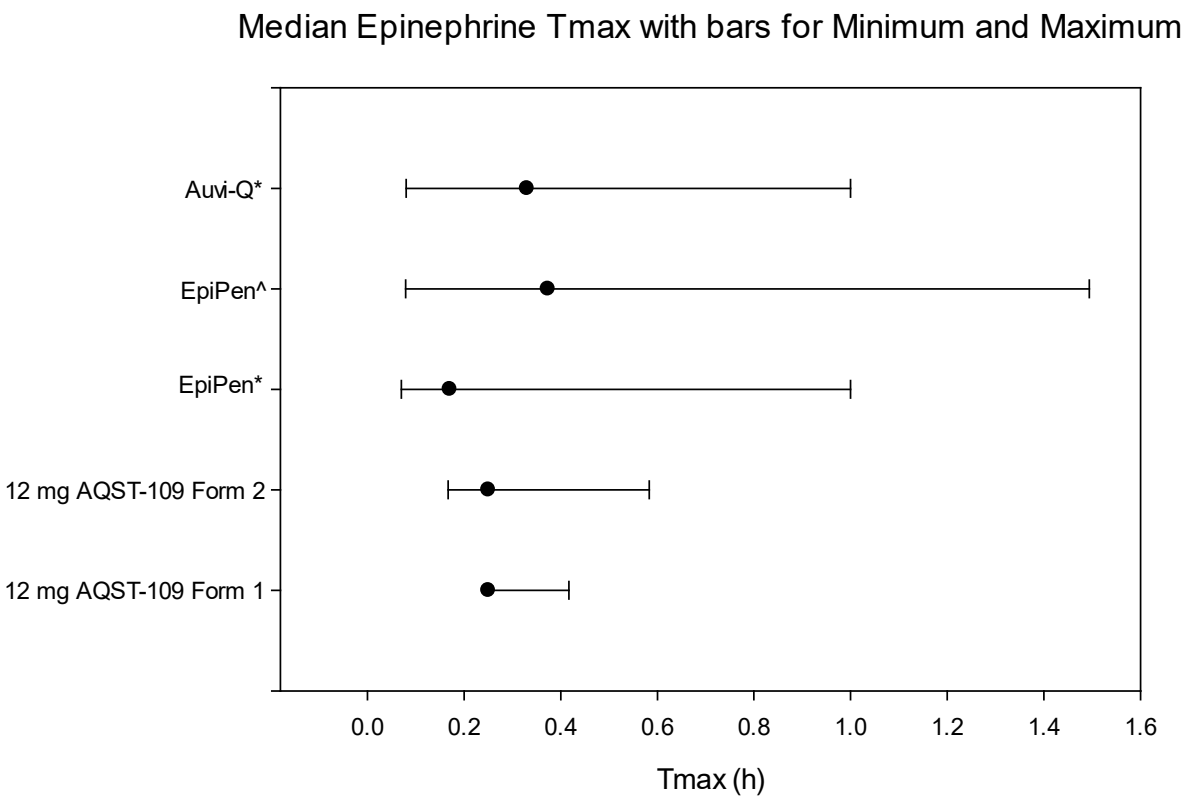
# AQST-109: Tmax Range Comparison

## AQST-109 and Autoinjector Tmax Values




Represents data from top-line results.
* https://www.accessdata.fda.gov/drugsatfda_docs/nda/2012/201739Orig1s000ClinPharmR.pdf
^ Data on file, AQST Study 160445

- Tmax (or time to maximum concentration) is a critical parameter for rescue medications
- The highest observed Tmax values for AQST-109 at 12 mg were below the highest Tmax values for autoinjectors
- The median Tmax values for AQST-109 were comparable to the known values from the autoinjectors



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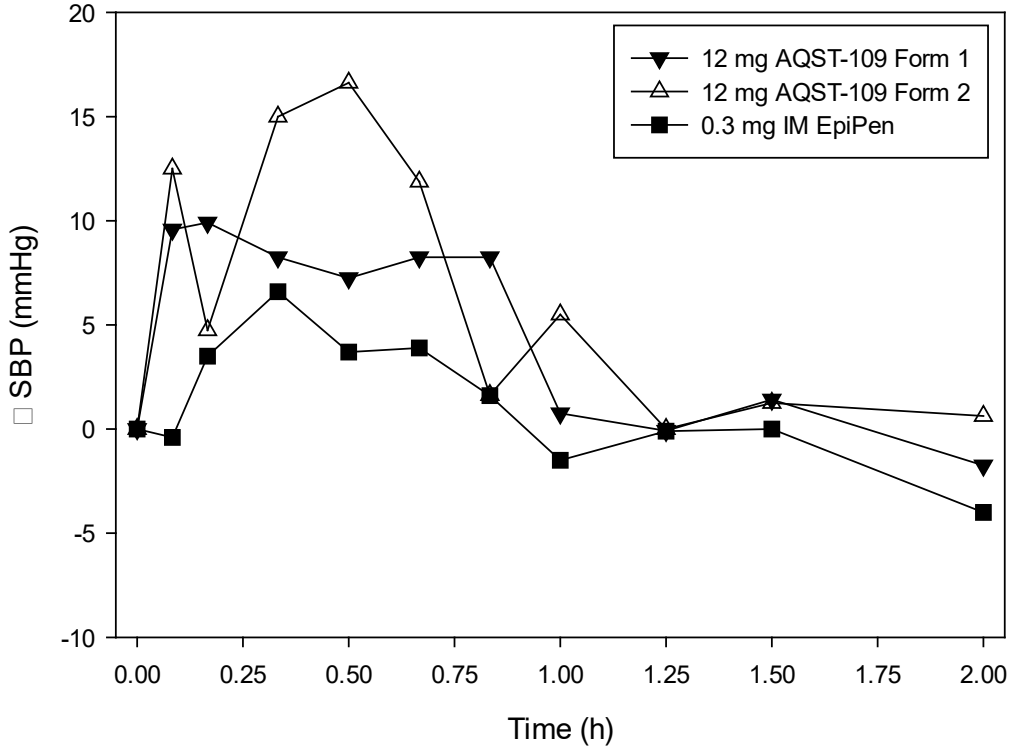
# AQST-109: Pharmacodynamic (PD) Results Consistent with Observed EpiPen Responses

Mean Change from Baseline Systolic Blood Pressure over Time




Represents data from top-line results. EpiPen data overlay is from Study 160445.
SBP=Systolic Blood Pressure

- Literature indicates that subjects should see a change in systolic blood pressure over time after the administration of epinephrine*
- AQST-109 shows a similar change from baseline systolic blood pressure when compared to EpiPen data
- This pharmacodynamic ‘marker’ provides a secondary indication that AQST-109 is working as intended after administration


* **1.** Dworaczyk D, Hunt A. Presented at the American Academy of Allergy, Asthma and Immunology (AAAAI) National Conference, March 16, 2020. https://brynpharma.com/media/content/docs/comparative-delivery-poster.pdf; **2.** Worm M et al. *Clin Transl Allergy*. 2020;10:21; **3.** Duvauchelle T et al. *J Allergy Clin Immunol Pract*. 2018;6(4):1257-1263; **4.** Breuer C et al. *Eur J Clin Pharmacol*. 2013;69:1303-1310.

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# Epinephrine Autoinjector Safety History

*Epinephrine delivered by autoinjectors (EpiPen, Auvi-Q) have affirmed a well-established AE profile*

| | Auvi-Q Doses = 67 | | EpiPen Doses = 135 | |
|---|---|---|---|---|
| | N | (%) | N | (%) |
| General and Admin. Site Conditions | 34 | (50.7) | 79 | (58.5) |
| Nervous System Disorders | 12 | (17.9) | 23 | (17) |
| CV | 2 | (3) | 3 | (2.2) |
| Psychiatric Disorders | 8 | (11.9) | 14 | (10.4) |

Source: https://www.accessdata.fda.gov/drugsatfda_docs/nda/2012/201739Orig1s000MedR.pdf

# AQST-109: Adverse Events Following 12 mg Dose

*The treatments have been generally well-tolerated. Most AEs were of mild severity and there have been no serious* adverse events.*

| | Formulation 1 n=6 | | Formulation 2 n=8 | | Formulation 3 n=6 | | Formulation 4 n=7 | |
|---|---|---|---|---|---|---|---|---|
| | Mild | Moderate | Mild | Moderate | Mild | Moderate | Mild | Moderate |
| Gen. Administration and Site Conditions | 13 | 0 | 31 | 0 | 13 | 0 | 14 | 0 |
| GI | 2 | 0 | 2 | 1 | 0 | 0 | 1 | 0 |
| CV | 1 | 0 | 2 | 0 | 0 | 0 | 0 | 0 |
| Other | 1 | 0 | 3 | 0 | 1 | 0 | 0 | 0 |

n=number of dosings

- General Administration and Site Conditions include stinging, burning, pain, and pseudomembranes/ulcers
- GI AEs include nausea, vomiting, and abdominal pain/discomfort
- Cardiovascular (CV) AEs include heart racing, ECG changes

* Definition: https://www.fda.gov/safety/reporting-serious-problems-fda/what-serious-adverse-event



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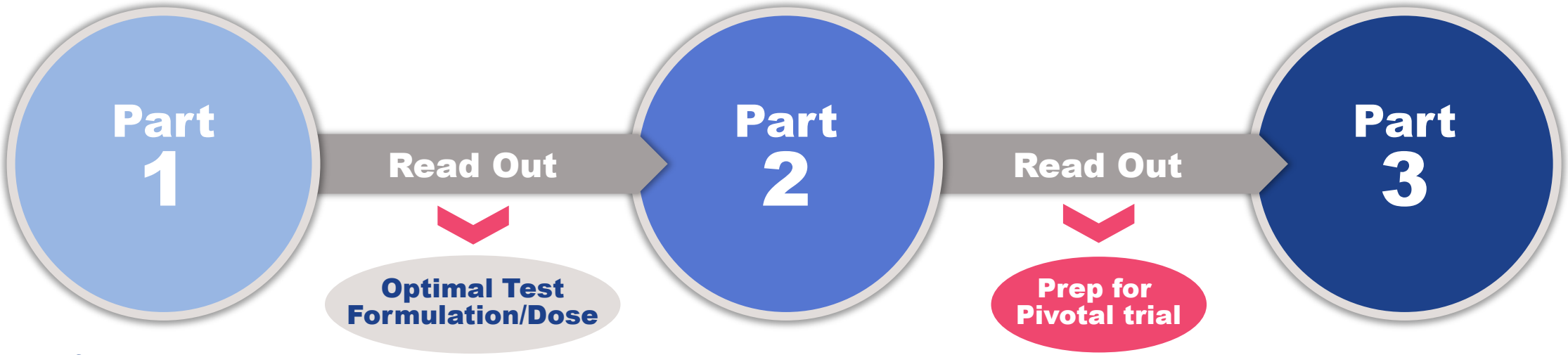
# What Comes Next: Adaptive Design Study for AQST-109




- Preferred Formulation/ Dose from 010 Study
- 6 Formulation/Dose Optimizations
- 0.5 mg IM injection

- Crossover, Balanced, Incomplete Block
- 1 week washout

- Test
- Test (Replicate)
- 0.3 mg IM inj
- 0.3 mg IM inj (replicate)

- Crossover
- 1 week washout

- Repeat Dose
- Dosing Conditions
- Administration Change*

*Administration change options include swallowing time, speaking during disintegration and buccal administration.

*Successful completion assumes positive outcomes from each Part*



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# PharmFilm® Platform Projecting Robust Stability

## Chemical Stability

- ≥ 2 years room temperature
- ≥ 6 months accelerated conditions

## Environmental Stability

- Light resistant
- Water resistant
- Withstands extreme cold conditions
- Exploring high temperature excursions



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# Patent Applications Extending into 2042

| Title | Patent Status |
|---|---|
| **ENHANCED DELIVERY EPINEPHRINE COMPOSITIONS** | • 1 US patent application allowed<br>• 8 Foreign applications<br>• **Priority date:** May 5, 2016<br>• Possible patent term to 2037 |
| **ENHANCED DELIVERY EPINEPHRINE AND PRODRUG COMPOSITIONS** | • 2 US applications<br>• 8 Foreign applications<br>• **Priority date:** May 4, 2017<br>• Possible patent term to 2037 |
| **PRODRUG COMPOSITIONS AND METHODS OF TREATMENT** | • 2 US applications<br>• 1 Foreign application<br>• **Priority date:** late 2019<br>• Possible patent term to 2041 |
| **PHARMACEUTICAL COMPOSITIONS WITH ENHANCED STABILITY PROFILES** | • 1 US application<br>• **Priority date:** October 2021<br>• Possible patent term to 2042 |