Anaphylm™ (dibutepinephrine) Sublingual Film
Complete Response Letter
Supplemental Material

February 3, 2026

Disclaimer

This presentation has 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™ (dibutepinephrine) Sublingual Film through clinical development and approval by the FDA, including: whether our clinical and other data will be adequate enough to address the concerns raised by the FDA in the Complete Response Letter dated January 30, 2026 (CRL) provided to the Company and for the FDA to finally approve Anaphylm or whether the FDA may request further information from us, disagree with our findings or otherwise undertake a lengthy review of our resubmission, and challenges regarding the following commercial launch of Anaphylm, if approved by the FDA; the advancement and related timing of potential international regulatory filings and marketing authorization of Anaphylm outside of the U.S.; 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 potential benefits Anaphylm could bring to patients, if approved by the FDA; the advancement and related timing of our product candidate AQST-108 (epinephrine) Topical Gel through clinical development and FDA regulatory approval process, including design and timing of clinical studies including those necessary to support the targeted indication of alopecia areata for AQST-108; our future financial and operating results and financial position, including with respect to our 2025 financial outlook, estimated cash runway and sufficiency to support the Company's long-term growth strategy for the potential regulatory approval and subsequent launch of Anaphylm in the U.S. and around the world, if approved by the respective regulatory authorities in such jurisdictions; 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 for Anaphylm; risk of delays in advancement of the regulatory approval process through the FDA of our product candidate Anaphylm, or failure to receive FDA approval at all; risk of FDA inspections of manufacturing and clinical study sites for any of our product candidates, including Anaphylm; risk of government shutdowns or actions to reduce government workforces on the ability of the FDA to act on the approval of our product candidates, including Anaphylm; risk of the Company's ability to generate sufficient clinical and other human factor data, including with respect to our submission of pharmacokinetic and pharmacodynamic (PK/PD) comparability data for FDA approval of Anaphylm; risks associated with our ability to address the FDA's comments on and identified deficiencies in our NDA, including the concerns raised by the FDA in the Complete Response Letter dated January 30 2026 issued to the Company for approval of Anaphylm; risk that the FDA may consider issues raised in the citizen petition submitted to the FDA regarding Anaphylm on October 1, 2025; risks associated with the success of any competing products, including generics; 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 candidates, including Anaphylm, if approved by the FDA; risks associated with the potential impact on the value of the Company of the sale or outlicensing of our product and product candidates, including Anaphylm; risk of sufficient capital and cash resources, including sufficient access to available debt and equity financing, including under our ATM facility, and revenues from operations, to satisfy all of our short-term and longer-term liquidity and cash requirements to support our growth strategy, and other cash needs, at the times and in the amounts needed, including to commence principal payments on our 13.5% Senior Secured Notes in 2026, and to fund future clinical development and commercial activities for our product candidates, including Anaphylm, should these product candidates be approved by the FDA; risk of the impact of our obligations under the Company's Purchase Agreement and the Royalty Rights Agreement with third parties, each of which agreements requires the Company to make payments to each counterparty thereof, respectively, of a portion of our revenues, on our ability to contribute to the funding of our operations and the payment of principal and interest on our debt; the risk of our obligations under such Purchase Agreement and Royalty Rights Agreement impacting our ability to refinance our 13.5% Senior Secured Notes; risk that our manufacturing capabilities will be sufficient to support demand of our product candidates in the U.S. and abroad, including Anaphylm, if such product candidates should be approved by the FDA and other regulatory authorities, and our licensed products in the U.S. and abroad; risk of eroding market share for Suboxone® as a sunsetting product, which accounts for a 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 Anaphylm and our other product candidates, should these product candidates be approved by the FDA and other regulatory authorities, and for our licensed products in the U.S. and abroad; risk associated with the size and growth of our product markets; risk associated with our 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, will not be timely issued, or issued at all, by the U.S. Patent and Trademark Office or, if issued, will be sufficient to provide long-term commercial success of these product candidates; 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 product candidates and product pricing, reimbursement or access therefor; risk of loss of significant customers; risks related to claims and legal proceedings against us 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 changing interest rates; risks related to the impact of pandemic diseases on our business; 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; risks related to uncertainty about presidential administration initiatives and their impact on our business, including imposition of government tariffs and other trade restrictions; and other uncertainties affecting the Company including those described in the "Risk Factors" section and in other sections included in the Company's Annual Report on 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.

The Aquestive logo is a registered trademark of Aquestive Therapeutics, Inc. and 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.

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Key takeaways from the FDA's Complete Response Letter (CRL)

In the following slides, we provide exact language in the comments contained in the CRL and Aquestive's viewpoint.

Of note:

- Deficiencies limited to packaging and administration
- Company believes it can rapidly resolve deficiencies and expects to resubmit as early as Q3 2026, assuming completion of planned responsive Human Factor (HF) study and pharmacokinetic (PK) study and typical response times from the FDA
- Remains well-capitalized and anticipates ending 2026 with significant cash
- Reiterates plans to submit for regulatory approval in Canada and EU in the second half of 2026

CRL Comments and Aquestive Viewpoint

HUMAN FACTORS AND CLINICAL

The results of the human factors (HF) validation study demonstrated several use errors/close calls/use difficulties with critical tasks that may result in harm to the patient. Specifically:

- Participants demonstrated difficulty opening the pouch, were unable to open the pouch, or tore the film while opening the pouch. Resulting delays in dose administration, inability to administer a dose, or underdosing raises significant safety concerns in the setting of anaphylaxis.
- Participants placed the film in incorrect locations or chewed the film. The impact on PK and clinical efficacy related to the chewing or incorrect placement of the film (i.e. placing it on the roof of the mouth or on the tongue) is uncertain.
- Some participants, mainly pediatric participants, identified "tingling" or "burning" and/or taste that led them, or would lead them, to remove the film prematurely. We note the HF study used a placebo with a different formulation compared to dibutepinephrine sublingual film that limits interpretation of these results. However, based on this finding in the HF study and the high rate of local adverse events reported in the pivotal PK trials, tolerability of dibutepinephrine sublingual film is a concern.
- We also note that there were several use issues with other critical tasks (besides the ones noted above) where several participants provided subjective feedback that they did not see instructions/were not aware of the instructions or pointed to label organization as the root cause.

- 1 participant (pediatric) was unable to open the (current child resistant) pouch (n=166 participants)
- The median time to open the 1st dose pouch was 17 seconds, 2nd dose was 8 seconds; this compares favorably to epinephrine medical device data
- There were 6 instances of torn film; all resulted in full dose administration (n=404 doses)
- Aquestive's approved film product complaint database includes only 1 product complaint related to potential tearing of a strip when opening a pouch (out of approximately 2.5 billion doses)

- 4 participants noted chewing the film; 3 of 4 participants were not provided the Instructions for Use (IFU) per protocol
- 19 participants misplaced film on top of tongue; 11 out of 19 participants were not provided the Instructions for Use (IFU) per protocol
- 1 participant placed film on roof of mouth

- 4 participants removed film; 2 due to burning and 2 due to taste (*e.g.*, "I do not like mint taste, but if I had to save my life, I would stick it there for like 10 minutes"
- No participants removed the film due to tingling
- The placebo used was similar but not identical to the Anaphylm formulation; Aquestive will use an exact Anaphylm placebo formulation in the repeat HF validation study
- Tolerability is discussed further in Aquestive viewpoint on slide 7

- Aquestive will continue to analyze and provide information to FDA

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CRL Comments and Aquestive Viewpoint (continued)

We acknowledge the additional risk controls implemented post-validation; however, our review indicates that additional risk controls are necessary.

To resolve the deficiencies, you need to:

1. Review the HF study results and subjective feedback *for all tasks* to identify additional, potential areas of optimization. Additionally, we acknowledge you implemented post-validation risk controls to address some identified use issues (i.e., incorrect placement of the film); however, based on the criticality of the impacted tasks, the revised user interface and additional risk controls should be evaluated for effectiveness.

Aquestive will conduct the analysis as requested by the FDA

2. Implement additional design modifications and user interface revisions identified in item #1 above, along with the following recommendations:

    a. Container Closure Design

        i. Revise the opening mechanism of the proposed container closure or consider an alternative container closure design to address the observed use issues with opening the proposed container closure. When redesigning the opening mechanism, consider the risk of the film being torn during opening and a user not being aware of the tear, which may lead to underdosing.

An alternate opening mechanism is available, has been successfully tested in a human factors formative study, and will be included in the requested human factors validation study

CRL Comments and Aquestive Viewpoint (continued)

b. Instructions for Use

i. Revise the instructions to improve clarity and prominence of the important information related to the correct placement of the film.

ii. Revise the IFU to include the following statement under Step 3 "Use Anaphylm even if torn" to improve emphasis of this important information. Additionally, we recommend including this or a similarly phrased statement on the carton labeling and pouch label if space allows.

iii. Revise the statement "If symptoms continue or get worse take a 2nd Anaphylm (repeat steps 1-5 with a new pouch)" to read as follows, "If symptoms continue or come back, get a new pouch to take a 2nd Anaphylm."

iv. Step 3 in the IFU to read as follows to improve clarity and emphasis:
"**Dry hands** and remove Anaphylm from the pouch
- Avoid touching Anaphylm until you are ready to use."

c. Pouch Label

i. Improve the prominence of the statement "Follow all instructions on the back" and relocate it to a more central location.

ii. Revise the instructions to increase the font size, as several participants commented on the small font size being difficult to read.

iii. Add the statement "Place 1 film under the tongue for 1 dose" directly under the image on the principal display panel. Alternatively, you could consider shifting the image to the right and adding the statement "Place 1 film under the tongue for 1 dose" to the left of the image with an arrow pointing to the film/tongue in the image.

iv. Revise the statement "1 sublingual film (under tongue)" to read as "each pouch contains 1 sublingual film dose".

v. Revise the statement under Step 3 "Wipe hands dry, remove film" to read as "**Dry hands** and remove film."

vi. Revise the statement "If symptoms continue or get worse take a 2nd Anaphylm (repeat steps 1-5 with a new pouch)" to read as follows "If symptoms continue or come back, get a new pouch to take a 2nd Anaphylm".

d. Carton Labeling

i. Revise the statement under Step 3 "Wipe hands dry, remove film from pouch" to read as "**Dry hands** and remove film from pouch."

ii. Revise the instructions to add more white space/spacing between the instructions under step 4 to improve readability. Further, increase the font size of the instructions.

Aquestive will incorporate the FDA's proposed labeling changes

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CRL Comments and Aquestive Viewpoint (continued)

3. Conduct another HF validation study to demonstrate that the revised user interface supports the safe and effective use of the product. In your HF validation study, include a placebo with the same formulation as dibutepinephrine sublingual film (without the active ingredient).

4. Address potential tolerability use issues in your resubmission.

Aquestive will conduct another human factors validation study, as requested

Aquestive will continue to provide information on potential tolerability issues
However, we note:

- In our pivotal clinical data set in the NDA (*n*=142), tolerability was cited in ***only one*** participant withdrawal (withdrawal due to tremors and tolerability relating to administration site reactions)
- ***All*** subject-reported local adverse events were mild in severity and self-resolved

CRL Comments and Aquestive Viewpoint (continued)

CLINICAL PHARMACOLOGY

Given findings from the HF validation study, there are uncertainties regarding how some use errors may impact the epinephrine pharmacokinetic (PK) concentration-time profile following the incorrect administration of dibutepinephrine sublingual film. To address these uncertainties, evaluate epinephrine PK under the following three conditions (you may choose to evaluate these three conditions in a parallel-group design):

1. Dibutepinephrine sublingual film administered with chewing the film both with and without swallowing.

2. Dibutepinephrine sublingual film administered at alternative sites consistent with observations in the HF validation study (e.g., top of tongue, roof of the mouth).

3. Dibutepinephrine sublingual film given via self-administration with final instructions that reflect the recommended design modifications and user interface revisions based on the new HF validation study.

To better interpret the PK/PD results under these conditions and to compare the results to the existing results obtained from the completed clinical pharmacology studies, it is pertinent that every subject in this study also receive two additional control treatments:

1. Dibutepinephrine sublingual film administered by trained staff with instructions consistent with those used in Trial AQ109301.

2. A listed epinephrine injection product.

Of note, future revisions of the design, user interface, and administration instructions, and results of the new HF validation study will not obviate the need to evaluate epinephrine PK following the administration of dibutepinephrine sublingual film under the aforementioned conditions.

Aquestive will discuss with the clinical pharmacology team at the Type A meeting and will conduct the study as requested

CRL Comments and Aquestive Viewpoint (continued)

ADDITIONAL COMMENTS

We have the following comment/recommendation that is not an approvability issue:

Refer to the Filing Communication dated June 13, 2025. The uncertainty of the impact of drinking liquid/water immediately before the administration of dibutepinephrine sublingual film on epinephrine PK remains, as Trial AQ109203 did not include a within-study comparison to epinephrine PK following administration of injection products and dibutepinephrine sublingual film given with the same instructions used in Trial AQ109301 (i.e., no fluid/water administration prior to dibutepinephrine sublingual film dosing). Therefore, we recommend you evaluate epinephrine PK following dibutepinephrine sublingual film administration with or without immediate prior water intake and compare to epinephrine PK following administration of a listed injection product.

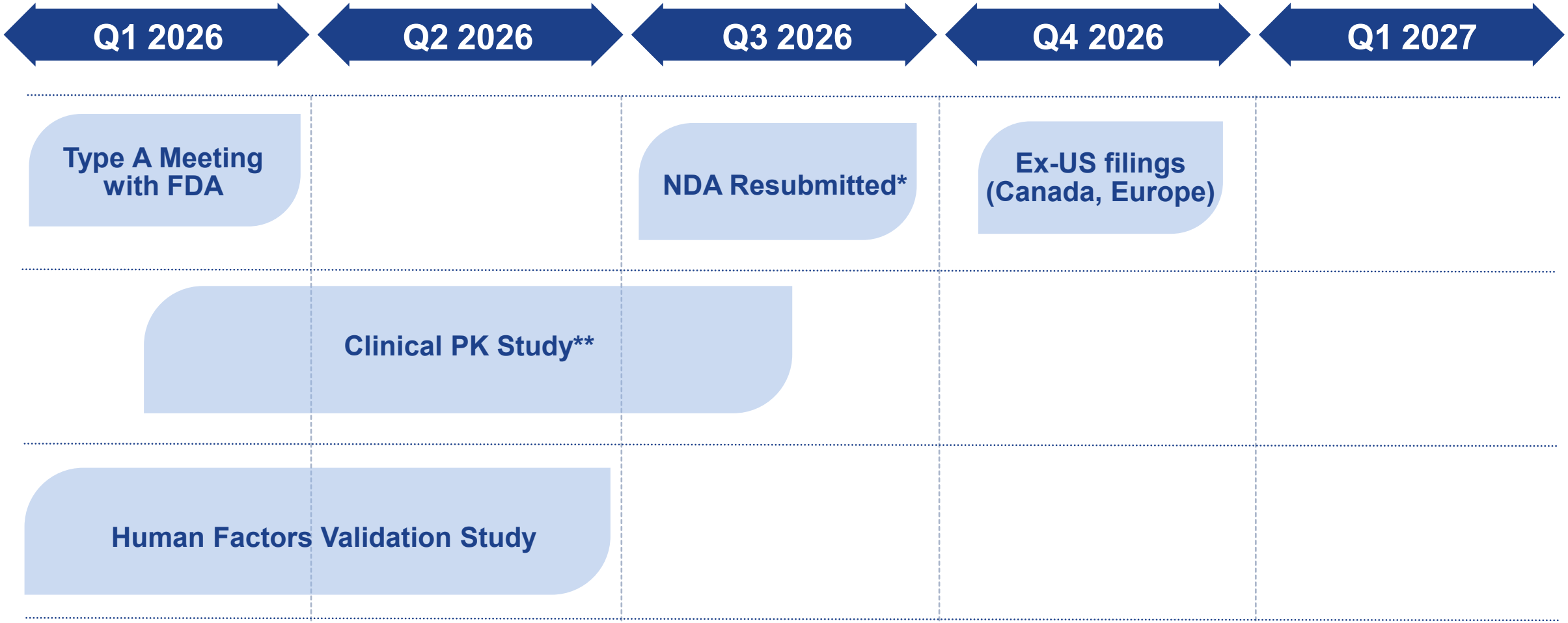
Aquestive is assessing the potential label impact and if additional clinical data generation is warranted

OTHER

We note that on October 1, 2025, ARS Pharmaceuticals Inc., through Arnall Golden Gregory, LLP, submitted a citizen petition to FDA (FDA-2025-P-4612) regarding AQST-109 Epinephrine Sublingual Film ("Anaphylm"). The issues raised by that petition are currently under review by the Agency, and FDA has not made any final decisions with respect to the petition. The comments included in this communication reflect the deficiencies that CDER has determined preclude approval of the NDA in its current form, and do not represent a final decision by the Agency on approval of the NDA or the issues raised in the pending citizen petition.

Language matches boilerplate language provided to nasal spray manufacturer in response to auto-injector manufacturer submitted citizen petition (CP), and other FDA issued CRLs which referenced unresolved pre-submitted CPs

Planned AnaphyIm Key Milestones



*Typical FDA response time is six (6) months; Aquestive intends to request expedited review of the NDA resubmission.
**Study timeline reflects startup to final report.

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Thank You