

**UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION  
WASHINGTON, D.C. 20549**

**FORM 8-K**

**CURRENT REPORT**

**Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934**

**Date of Report (Date of earliest event reported): March 27, 2023**

**UNITY BIOTECHNOLOGY, INC.**

(Exact name of Registrant as Specified in Its Charter)

**Delaware**  
(State or Other Jurisdiction  
of Incorporation)

**001-38470**  
(Commission File Number)

**27-4726035**  
(IRS Employer  
Identification No.)

**285 East Grand Ave.**  
**South San Francisco, California**  
(Address of Principal Executive Offices)

**94080**  
(Zip Code)

**Registrant's Telephone Number, Including Area Code: (650) 416-1192**

(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

**Securities registered pursuant to Section 12(b) of the Act:**

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value \$0.0001 per share	UBX	The Nasdaq Global Select Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

**Item 8.01 Other Events.**

On March 27, 2023, Unity Biotechnology, Inc. (“UNITY” or the “Company”) announced data from its Phase 2 ENVISION study of UBX1325 in patients with wet age-related macular degeneration (AMD). The Company will host a conference call today, Monday, March 27, 2023, at 8:00 a.m., Eastern Time, to discuss the data results.

A copy of the press release and the presentation that will be referenced during the conference call are filed as Exhibit 99.1 and Exhibit 99.2, respectively, to this Current Report on Form 8-K and are incorporated by reference herein.

**Item 9.01 Financial Statements and Exhibits.**

(d) Exhibits

<b>Exhibit No.</b>	<b>Description</b>
99.1	<a href="#">Press release titled “UNITY Biotechnology Announces Results from Phase 2 ENVISION Study of UBX1325 in Patients with Wet Age-Related Macular Degeneration,” dated March 27, 2023</a>
99.2	<a href="#">Presentation of Unity Biotechnology, Inc. dated March 27, 2023</a>
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

**SIGNATURES**

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

UNITY BIOTECHNOLOGY, INC.

Date: March 27, 2023

By: /s/ Anirvan Ghosh  
Anirvan Ghosh, Ph.D.  
Chief Executive Officer

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**UNITY Biotechnology Announces Results from Phase 2 ENVISION Study of UBX1325 in Patients with Wet Age-Related Macular Degeneration**

*UBX1325 monotherapy did not achieve non-inferiority through 24 weeks due, in part, to an unexpected 3.5 letter gain in the anti-VEGF control arm*

*UBX1325 maintained visual acuity in patients with ongoing active disease through 24 weeks with less than one letter mean decrease from baseline*

*52% of UBX1325-treated patients did not require anti-VEGF treatment through 24 weeks*

*Company to share 48-week BEHOLD DME data in April and intends to initiate Phase 2b study in DME in second half of 2023*

*UNITY to host investor call today, March 27, at 8:00 a.m. ET*

**SOUTH SAN FRANCISCO, Calif., March 27, 2023** – UNITY Biotechnology, Inc. (“UNITY”) [Nasdaq: UBX], a biotechnology company developing therapeutics to slow, halt, or reverse diseases of aging, today announced results from Part A of the Phase 2 ENVISION study of UBX1325 in patients with wet age-related macular degeneration (AMD) who were not achieving optimum benefit with their ongoing anti-VEGF therapy. UBX1325 treatment generally maintained visual acuity for 6 months (change of -0.8 ETDRS letters from baseline), with a majority of patients not requiring any anti-VEGF rescue. Patients in the every 8-week aflibercept arm had an early and unexpected gain of 3.5 letters at week 2 which was mostly maintained for the duration of the study. As a result of the strength on the control arm, the study did not meet the non-inferiority threshold compared to aflibercept through 24 weeks.

“Maintenance of visual acuity in hard-to-treat patients with active disease after withdrawal of their anti-VEGF therapy suggests that UBX1325 had an active treatment effect in wet AMD. We continue to be impressed with the durability of effect of UBX1325 in this patient population,” said Anirvan Ghosh, Ph.D., chief executive officer of UNITY. “Following a full analysis of ENVISION results, we will assess and optimize our resource allocation for future development of UBX1325. In the weeks ahead we will provide an update on Part B of the ENVISION study, and importantly, share 48-week data from the Phase 2 BEHOLD DME study. In DME, UBX1325 showed strong evidence of biologic activity and improvement in visual acuity – and, as a result, we plan to initiate a Phase 2b study in the second half of this year.”

The ENVISION study enrolled 51 patients with an average baseline visual acuity of 60.2 ETDRS letters who had ongoing active disease with a baseline CST of approximately 370  $\mu$ m and had been on anti-VEGF treatment for at least 6 months. On average, patients received approximately 4 anti-VEGF injections in the 6 months prior to enrollment. At enrollment, all patients received a single run-in injection of aflibercept. Within 4-8 weeks following the run-in injection, patients were randomized to receive either (a) an injection of UBX1325 at week 0 and at week 4, or (b) an injection of aflibercept at week 0 and every 8 weeks thereafter, and followed for 24 weeks.

**Phase 2 ENVISION data through 24 weeks:**

- UBX1325 demonstrated a favorable safety and tolerability profile with no cases of intraocular inflammation, retinal artery occlusion, endophthalmitis, or vasculitis
- Patients treated with UBX1325 had a mean change from baseline in BCVA of -0.8 ETDRS letters at 24 weeks compared to +3.1 ETDRS letters in the aflibercept control arm
- Patients treated with UBX1325 had a mean change from baseline in CST of +87.3  $\mu\text{m}$  at 24 weeks compared to +30.5  $\mu\text{m}$  in the aflibercept control arm
- 52% of UBX1325-treated patients went at least 24 weeks without receiving anti-VEGF treatment; 92% of UBX1325-treated patients achieved a maximal anti-VEGF treatment-free interval of 12 weeks or longer

The ENVISION study did not meet the non-inferiority margin of -4.5 letters compared to aflibercept with an 85% confidence interval.

“Despite anti-VEGF therapies remaining the standard of care for neovascular AMD for the past two decades, there is an unmet need for treatments with new mechanisms of action to optimize vision outcomes and reduce the treatment burden associated with frequent injections,” said Arshad M. Khanani, MD, MA, FASRS, Director of Clinical Research, Sierra Eye Associates. “The ENVISION study results show that treatment with UBX1325 in nAMD patients with active disease maintained visual acuity with reduced injection burden over six months. The data from the ENVISION AMD and BEHOLD DME studies suggest that UBX1325, with its novel mechanism of action, could lead to a potential treatment option for patients.”

Jamie Dananberg, M.D., chief medical officer of UNITY, added: “Whereas today’s results from the ENVISION study and our Phase 2 BEHOLD study both show encouraging signs of biological activity of UBX1325, the relatively stronger efficacy we observed in DME may be related to the distinct underlying pathophysiologies of the two diseases. We look forward to sharing 48-week data in our BEHOLD DME study in the coming weeks.”

**Conference Call at 8:00 a.m. ET Today**

UNITY will host a video conference call and webcast for investors and analysts today at 8:00 a.m. ET to discuss the most recent UBX1325 clinical data. Members of the UNITY senior management team will lead the discussion on the 24-week ENVISION study results. The live webcast can be accessed in the “Investors and Media” section of our website, [www.unitybiotechnology.com](http://www.unitybiotechnology.com), under “Events & Presentations” or by clicking [here](#). A replay will be available two hours after the completion of the call and can be accessed in the “Investors & Media” section of our website, under “Events and Presentations.”

**About the ENVISION Study**

The proof-of-concept Phase 2 ENVISION study is a multi-center, randomized, double-masked, active-controlled study designed to evaluate the safety, tolerability, efficacy and durability of a repeat intravitreal injection of UBX1325 in patients with neovascular AMD evaluated through 24 weeks. The study enrolled 51 patients being actively treated with anti-VEGF who had a visual acuity deficit (73 ETDRS letters,

approximately 20/40, or worse) and residual retinal fluid (CST  $\geq$ 300 microns). Patients were randomized into two groups to receive either two 10 mcg doses of UBX1325 at a week 0 and at week 4 or aflibercept 2 mg every 8 weeks. Patients have the option of continuing in the long-term extension (Part B) portion of the study through 48-weeks. To date, a majority of patients have opted to remain in the study. More information about the study is available here (NCT05275205).

#### **About the BEHOLD Study**

The proof-of-concept Phase 2 BEHOLD study is a multi-center, randomized, double-masked, sham-controlled study designed to evaluate the safety, tolerability, efficacy and durability of a single 10 mcg dose of UBX1325 in patients with DME evaluated through 24 weeks. The study enrolled 65 patients being actively treated with anti-VEGF who had a visual acuity deficit (73 ETDRS letters, approximately 20/40, or worse) and residual retinal fluid (CST  $\geq$ 300 microns). Patients have the option of continuing in the long-term extension portion of the study through 48-weeks. To date, a majority of patients have opted to remain in the study. More information about the study is available here (NCT04857996).

#### **About UBX1325**

UBX1325 is an investigational compound being studied for age-related diseases of the eye, including diabetic macular edema (DME), age-related macular degeneration (AMD), and diabetic retinopathy (DR) that is not approved for any use in any country. UBX1325 is a potent small molecule inhibitor of Bcl-xL, a member of the Bcl-2 family of apoptosis regulating proteins. UBX1325 is designed to inhibit the function of proteins that senescent cells rely on for survival. In the 24-week data of the Phase 2 BEHOLD study in patients with DME, a single injection of UBX1325 led to a statistically significant and clinically meaningful improvement in mean Best Corrected Visual Acuity (BCVA) at 24 weeks compared to sham treatment. In a Phase 1 clinical study in advanced wet AMD and DME, UBX1325 showed a favorable safety profile and improvements in visual acuity sustained through 24 weeks following a single intravitreal injection. In preclinical studies, UNITY has demonstrated that targeting Bcl-xL with UBX1325 preferentially eliminated senescent cells from diseased tissue while sparing cells in healthy tissue. UNITY's goal with UBX1325 is to transformationally improve real-world outcomes for patients with DME, AMD, and DR.

#### **About UNITY**

UNITY is developing a new class of therapeutics to slow, halt, or reverse diseases of aging. UNITY's current focus is on creating medicines to selectively eliminate or modulate senescent cells and thereby provide transformative benefit in age-related ophthalmologic and neurologic diseases. More information is available at [www.unitybiotechnology.com](http://www.unitybiotechnology.com) or follow us on Twitter and LinkedIn.

#### **Forward-Looking Statements**

This press release contains forward-looking statements including statements related to UNITY's understanding of cellular senescence and the role it plays in diseases of aging, the potential for UNITY to develop therapeutics to slow, halt, or reverse diseases of aging, including for ophthalmologic and neurologic diseases, UNITY's expectations regarding potential benefits, activity, effectiveness, and safety of UBX1325, the potential for UNITY to successfully commence and complete clinical studies of UBX1325 for DME, AMD, and other ophthalmologic diseases, the expected timing of the results of the clinical trials in UBX1325, and UNITY's expectations regarding the sufficiency of its cash runway. These statements involve substantial known and unknown risks, uncertainties, and other factors that may cause our actual results, levels of activity, performance, or achievements to be materially different from the information expressed or implied by these forward-looking statements, including the risk that the COVID-19 worldwide pandemic may continue to negatively impact the development of preclinical and clinical drug

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candidates, including delaying or disrupting the enrollment of patients in clinical trials, risks relating to the uncertainties inherent in the drug development process, and risks relating to UNITY's understanding of senescence biology. We may not actually achieve the plans, intentions, or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. The forward-looking statements in this press release represent our views as of the date of this release. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we have no current intention of doing so except to the extent required by applicable law. You should, therefore, not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this release. For a further description of the risks and uncertainties that could cause actual results to differ from those expressed in these forward-looking statements, as well as risks relating to the business of UNITY in general, see UNITY's most recent Annual Report on Form 10-K for the year ended December 31, 2022, filed with the Securities and Exchange Commission on March 15, 2023, as well as other documents that may be filed by UNITY from time to time with the Securities and Exchange Commission.

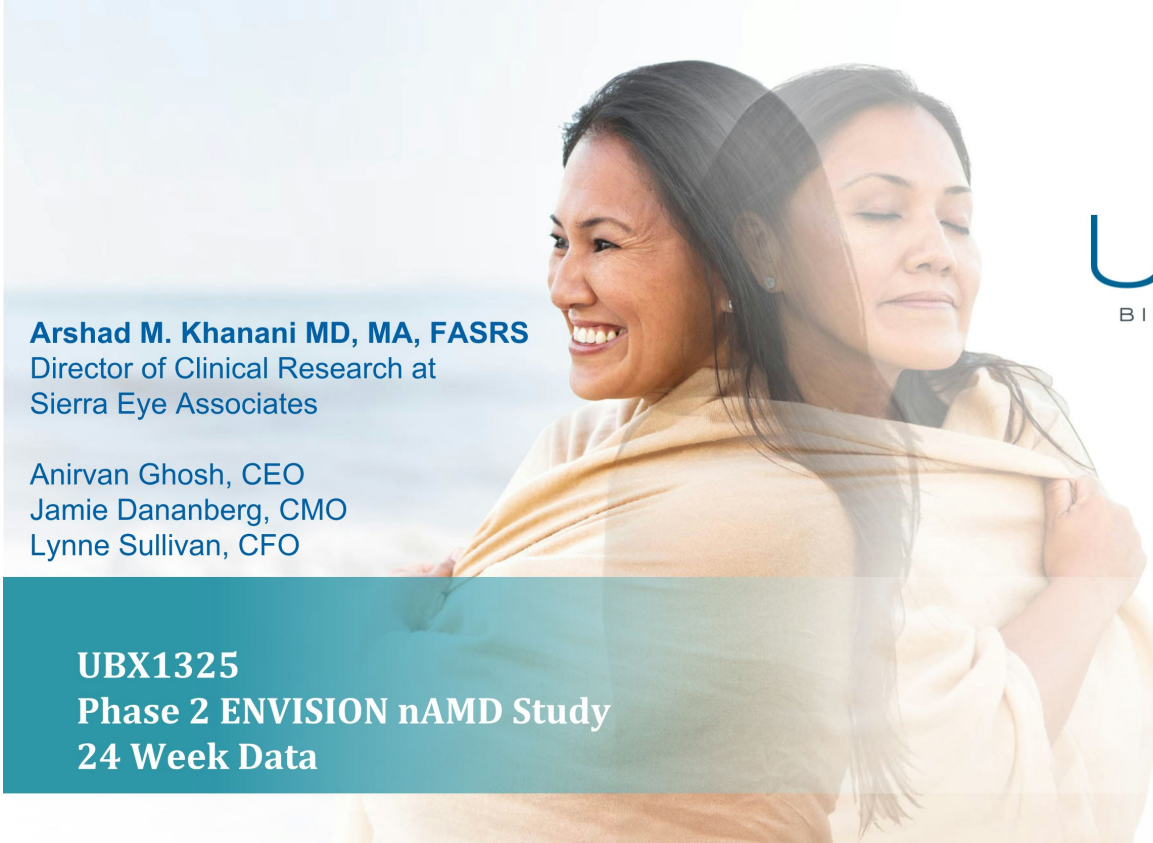
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**UNITY**  
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**Arshad M. Khanani MD, MA, FASRS**  
Director of Clinical Research at  
Sierra Eye Associates

Anirvan Ghosh, CEO  
Jamie Dananberg, CMO  
Lynne Sullivan, CFO

**UBX1325**  
**Phase 2 ENVISION nAMD Study**  
**24 Week Data**

NASDAQ: UBX



## Special Note Regarding Forward-Looking Statements

This presentation and the accompanying oral commentary contain forward-looking statements including statements related to Unity Biotechnology Inc.'s ("UNITY's") understanding of cellular senescence and the role it plays in diseases of aging, the potential for UNITY to develop therapeutics to slow, halt, or reverse diseases of aging, including for ophthalmologic and neurologic diseases, the potential for UNITY to successfully commence and complete clinical studies of UBX1325 for DME, AMD, and other ophthalmologic diseases, the expected timing of enrollment and results of the clinical trials in UBX1325, and UNITY's expectations regarding the sufficiency of its cash runway. These statements involve substantial known and unknown risks, uncertainties, and other factors that may cause our actual results, levels of activity, performance, or achievements to be materially different from the information expressed or implied by these forward-looking statements, including the risk that the COVID-19 worldwide pandemic may continue to negatively impact the development of preclinical and clinical drug candidates, including delaying or disrupting the enrollment of patients in clinical trials, risks relating to the uncertainties inherent in the drug development process, including the risk that interim results of our clinical studies may not be indicative of future results, and risks relating to UNITY's understanding of senescence biology. We may not actually achieve the plans, intentions, or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. The forward-looking statements in this presentation represent our views as of the date of this release. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we have no current intention of doing so except to the extent required by applicable law. You should, therefore, not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this release. For a further description of the risks and uncertainties that could cause actual results to differ from those expressed in these forward-looking statements, as well as risks relating to the business of UNITY in general, see UNITY's most recent Annual Report on Form 10-K for the year ended December 31, 2022, filed with the Securities and Exchange Commission on March 15, 2023, as well as other documents that may be filed by UNITY from time to time with the Securities and Exchange Commission. This presentation concerns drug candidates that are under clinical investigation which have not yet been approved for marketing by the U.S. Food and Drug Administration. They are currently limited by Federal law to investigational use, and no representation is made as to their safety or effectiveness for the purposes for which they are being investigated. This presentation does not constitute an offer or invitation for the sale or purchase of securities and has been prepared solely for informational purposes.

# UBX1325 Phase 2 ENVISION Study in Patients with Neovascular AMD

## Phase 2 ENVISION Part A Study Data Highlights

*UBX1325 monotherapy did not achieve non-inferiority through 24 weeks due, in part, to an unexpected 3.5 letter gain in the anti-VEGF control arm*

*UBX1325 maintained visual acuity in patients with ongoing active disease through 24 weeks with less than one letter mean decrease from baseline*

*52% of UBX1325-treated patients did not require anti-VEGF treatment through 24 weeks*

*UBX1325 was well tolerated with no instances of intraocular inflammation*

## Additional Insights from Secondary Analysis

- A single dose of run-in aflibercept may not have been sufficient to get patients entering study to anti-VEGF BCVA plateau
- UBX1325 may be more effective in patients with longer disease duration who may have greater senescence burden

**Disease Pathophysiology**

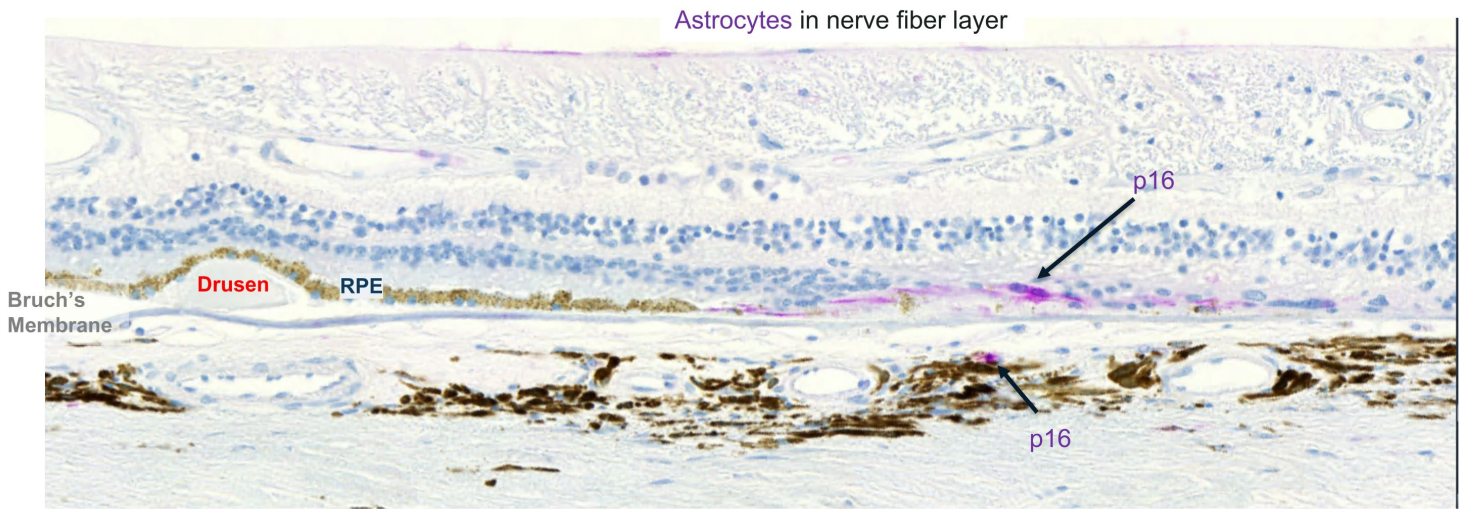
**UBX1325 Rationale and  
Mechanism of Action**

**Clinical Development  
Plan**



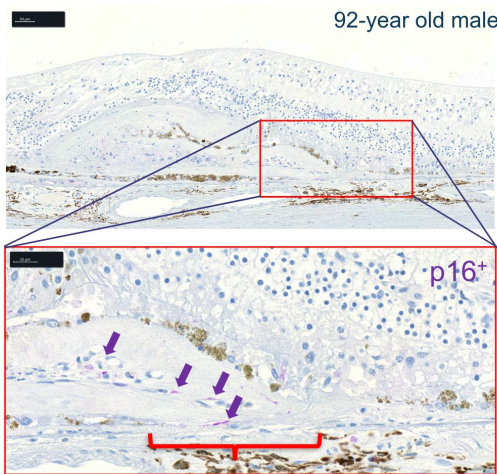
# Senescent cells are Associated with Disease Pathology in AMD

p16-positive senescent cells in 86y/o AMD posterior retina and choroid

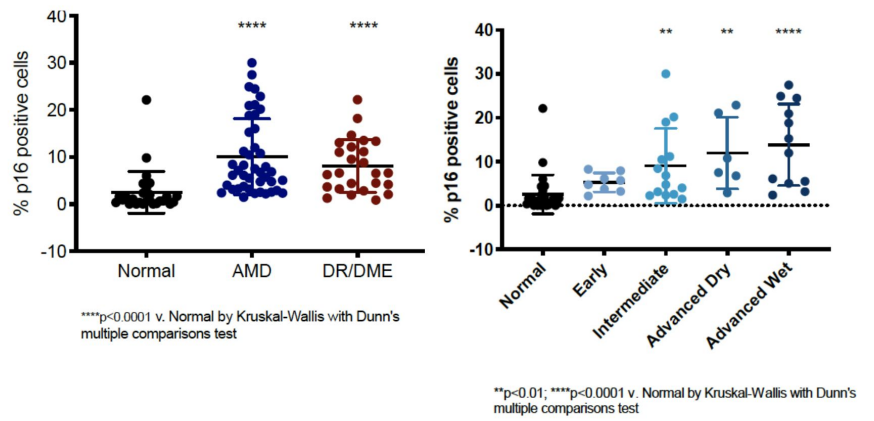


# There is a Higher Burden of Senescent Cells in Advanced Disease

## Macular region of patient with wAMD

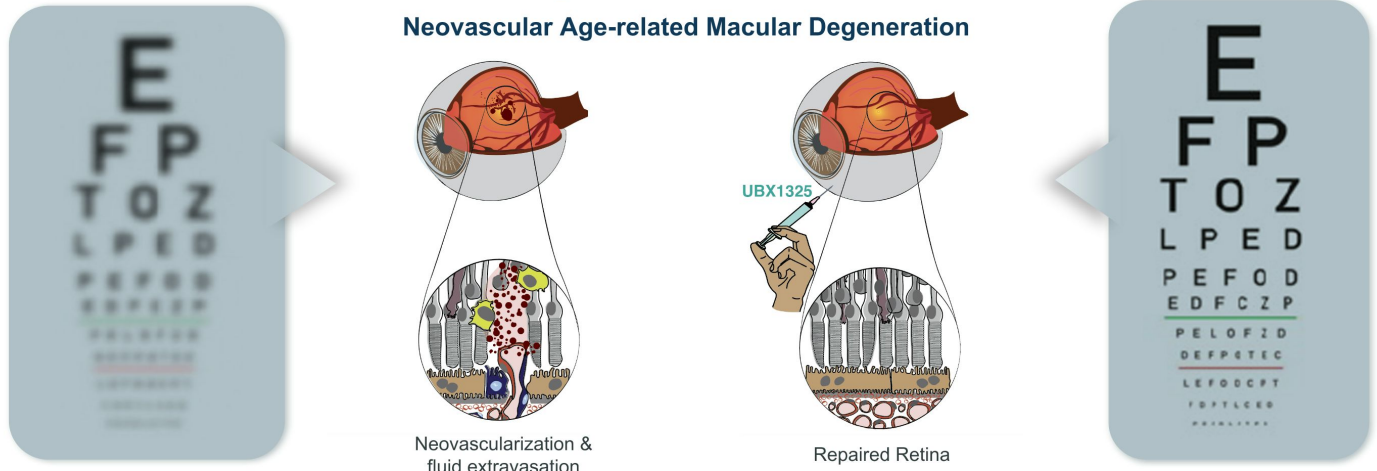


## % of p16<sup>+</sup> cells



Percentage p16<sup>+</sup> cells in human ocular normal (n=28), AMD (n=43) and DR/DME (n=25) samples. Each point represents a single whole globe.

# UNITY Is Developing Senolytic Medicines to Eliminate Senescent Cells to Restore Vascular Health and Improve Vision



## Neovascular Age-related Macular Degeneration

Neovascularization & fluid extravasation

### nAMD:

- Increased senescence burden
- Choroidal vasculature affected
- Neovascularization and vascular leakage
- Loss of vision

UBX1325

Repaired Retina

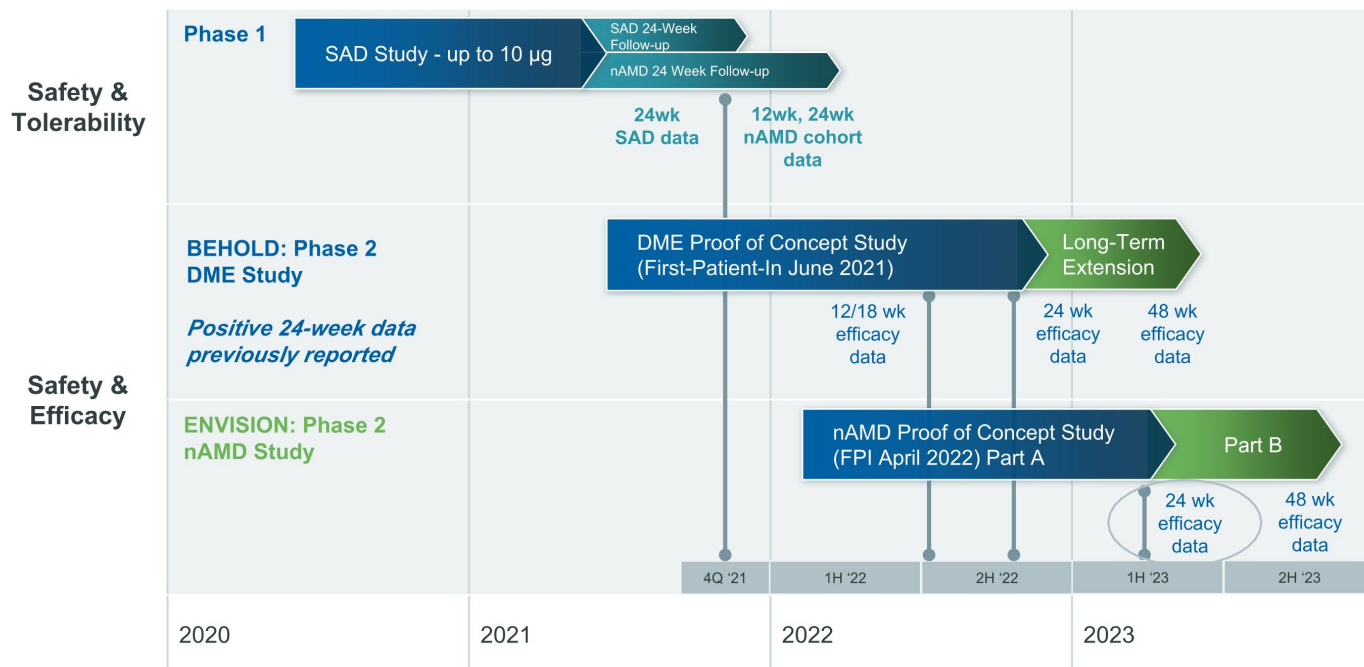
### nAMD treated with Senolytic intended results:

- Senescent cells removed
- Choroidal vasculature and outer retina restored
- Improvement in vision

UNITY illustration.

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# UBX1325 Clinical Program Overview



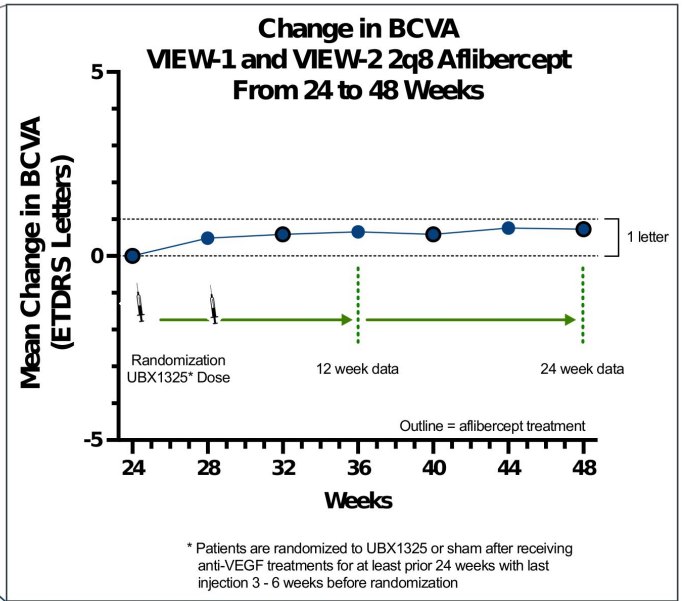
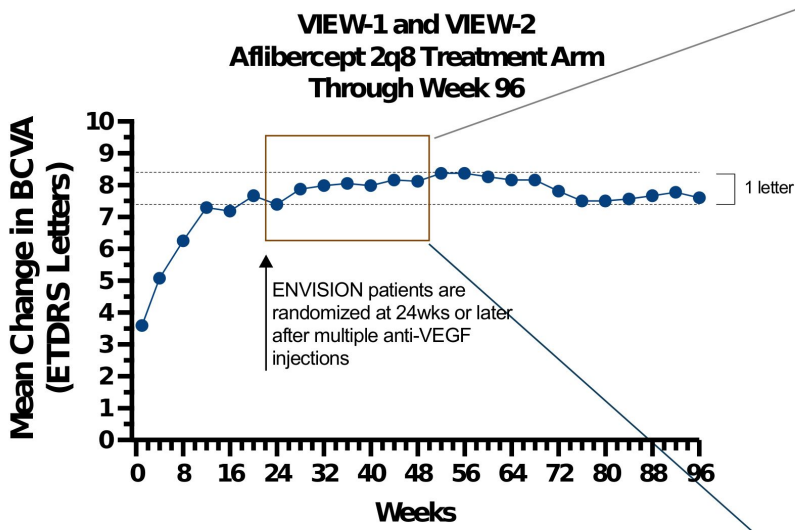


**Clinical Context:  
Response of nAMD Patients  
to anti-VEGF Treatment**





# Context for AMD Data: Majority of Anti-VEGF BCVA Benefit is in First Six Months After Which Gains Are Limited To ~One or Fewer Letters



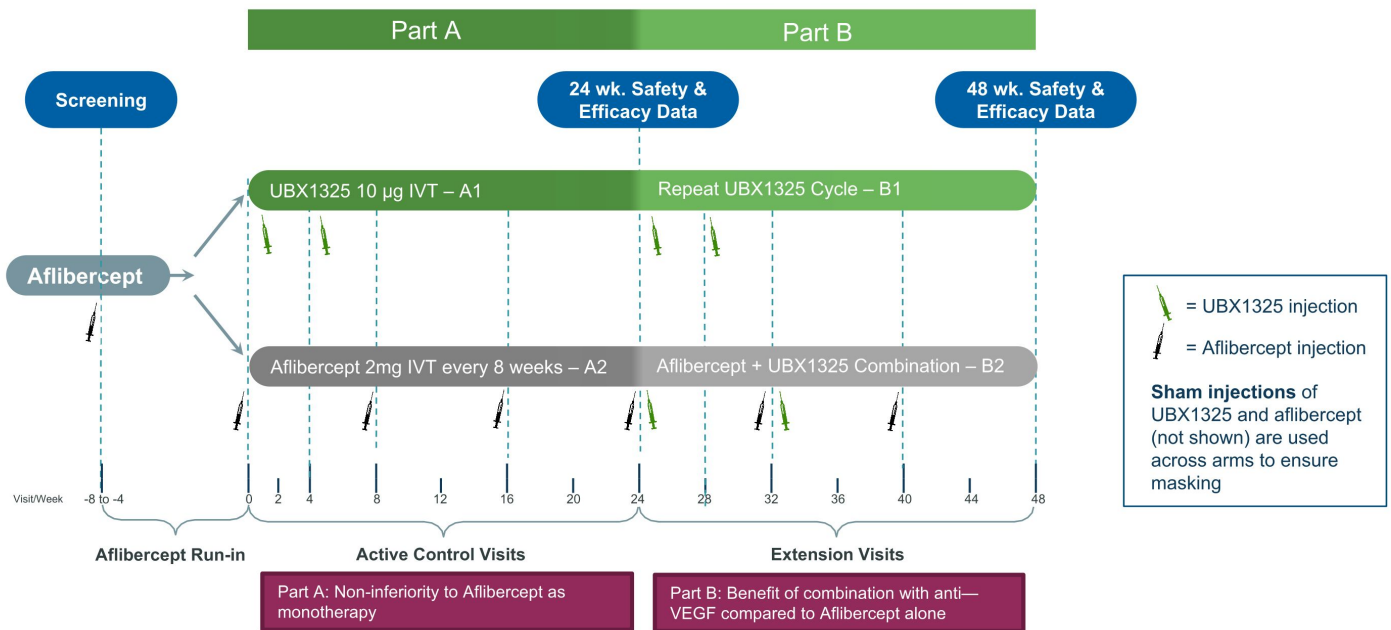
Aflibercept AMD BLA 125387 Orig-1, 11 Nov 2011  
Heier, J. S., et al and the VIEW 1 and VIEW 2 Study Groups (2012).  
Ophthalmology, 119(12), 2537-2548.

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**UBX1325 Phase 2  
ENVISION Study  
24-Week Data in Patients  
With nAMD**



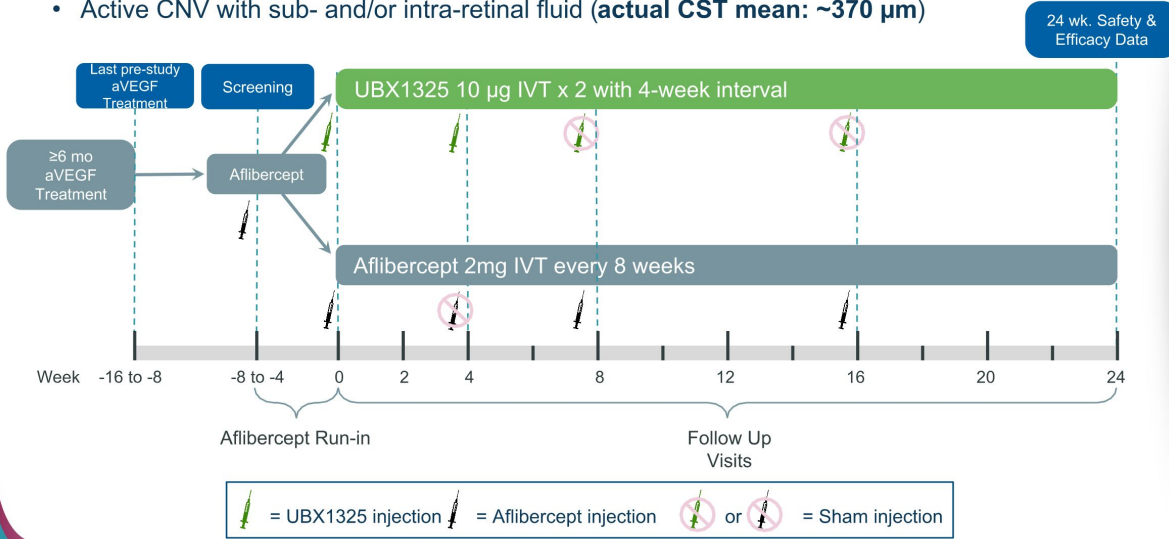
# ENVISION: nAMD Phase 2 Study Design



# ENVISION: nAMD Phase 2 Proof-of-Concept Study Design – Part A

Population (actual enrolled 51) patients with AMD who had:

- At least 2 anti-VEGF IVTs in the preceding 6-month period (**actual ~4**)
- BCVA 70 – 20 ETDRS letters (**actual mean: ~60**)
- Active CNV with sub- and/or intra-retinal fluid (**actual CST mean: ~370  $\mu$ m**)



## Endpoints

- Safety and tolerability
- BCVA change from baseline
- CST change from baseline
- Non-inferiority vs aflibercept (BCVA and CST)
- Durability of response
- Sub- and intra-retinal fluid
- Changes in perfusion (FA and OCTA)
- Changes in photoreceptor function (mfERG)

## ENVISION: Demographics at baseline

	Aflibercept	UBX1325
<b>Baseline BCVA (ETDRS Letters)</b>		
n	25	25
Mean	<b>62.4</b>	<b>58.0</b>
SD	9.46	13.47
Median	64.0	60.0
Min, Max	36.0, 77.0	25.0, 79.0
<b>Baseline CST (<math>\mu\text{m}</math>)</b>		
n	25	25
Mean	<b>367.5</b>	<b>370.8</b>
SD	151.75	108.85
Median	284.0	374.0
Min, Max	198.0, 683.0	206.0, 665.0
<b>Duration of neovascular AMD (Years)</b>		
n	25	25
Mean	<b>3.9</b>	<b>3.8</b>
SD	2.04	3.40
Median	3.3	2.4
Min, Max	1.1, 9.1	0.4, 14.6

## Summary of Treatment Emergent Adverse Events

	Aflibercept 2mg Total 25 n (%)	UBX1325 10µg Total 25 n (%)
Subjects with at least one TEAE	19 (76.0)	20 (80.0)
Grade ≥3 TEAE	1 (4.0)	2 (8.0)
Serious TEAE	0	2 (8.0)
Ocular TEAE for Study Eye	14 (56.0)	15 (60.0)
Treatment-related Ocular TEAE for Study Eye	3 (12.0)	1 (4.0)
TEAE leading to death	0	1 (4.0) *
<b>Intraocular inflammation, endophthalmitis, retinal artery occlusion, or vasculitis</b>	<b>0</b>	<b>0</b>

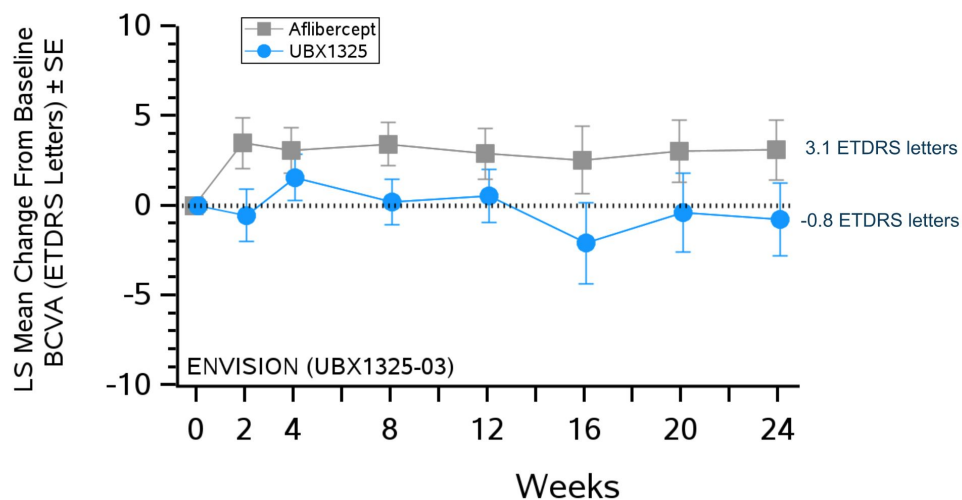
\* Unrelated to treatment

Source: L\_14\_3\_1\_4

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# Change from baseline in BCVA excluding post-rescue data

## UBX1325 Patients Maintained BCVA Through 24 Weeks; non-inferiority not met



Average CFBL Weeks 16 – 24 ETDRS letters (85% CI)	
Aflibercept	2.9 (0.7 – 5.1)
UBX1325	-1.1 (-3.6 – 1.4)

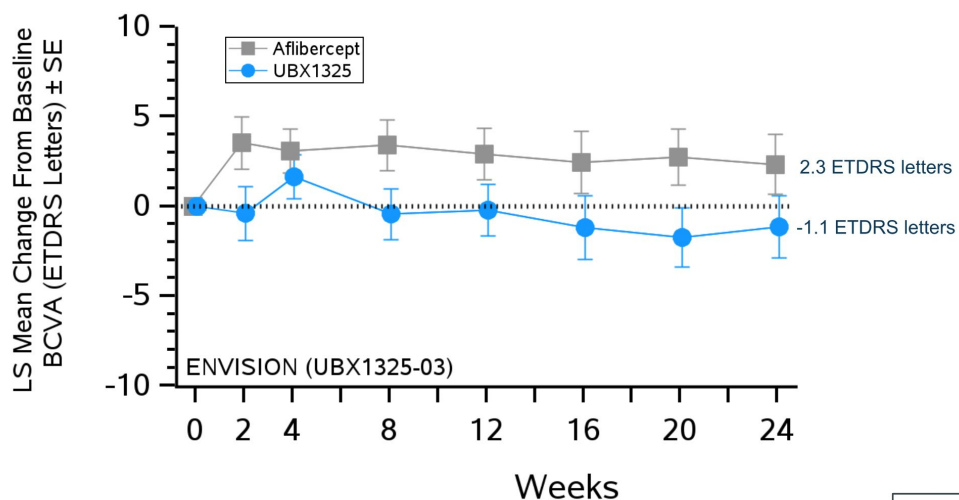
	Number of Subjects							
	0	2	4	8	12	16	20	24
Aflibercept	24	25	25	25	25	25	25	23
UBX1325	22	24	22	21	21	13	11	12

UBX1325 dosed at 0 and 4 weeks  
Aflibercept dosed at 0, 8, and 16 weeks



# Change from baseline in BCVA including post-rescue data

## UBX1325 patients maintained BCVA through 24 Weeks



	Average CFBL Weeks 16 – 24 ETDRS letters (85% CI)
Aflibercept	2.5 (0.5 – 4.5)
UBX1325	-1.4 (-3.4 – 0.7)

	Number of Subjects							
	0	2	4	8	12	16	20	24
Aflibercept	24	25	25	25	25	25	25	24
UBX1325	22	25	25	24	24	23	21	21

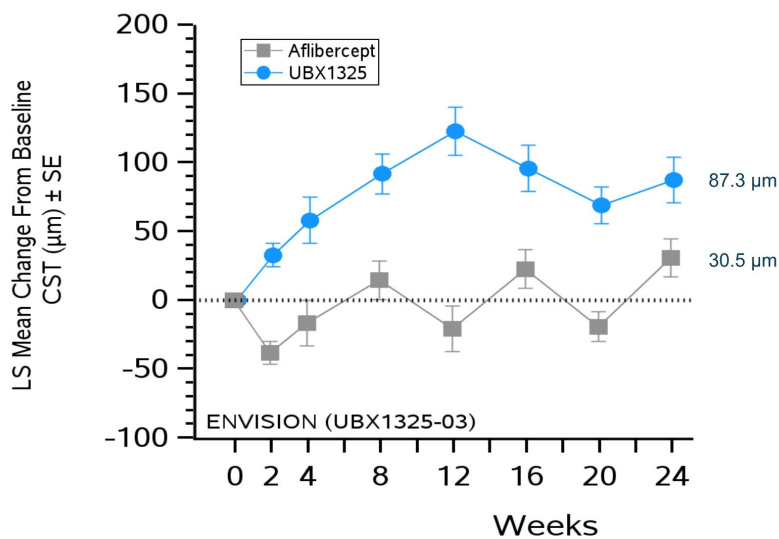
UBX1325 dosed at 0 and 4 weeks  
Aflibercept dosed at 0, 8, and 16 weeks





# Change from baseline in CST excluding post-rescue data

*Delayed impact on CST is consistent with potential time-course for senolytic mechanism to exert effect*



	Average CFBL Weeks 16 – 24 µm (85% CI)
Aflibercept	11.3 (-4.9 – 27.4)
UBX1325	84.0 (65.8 – 102.3)

UBX1325 dosed at 0 and 4 weeks  
Aflibercept dosed at 0, 8, and 16 weeks

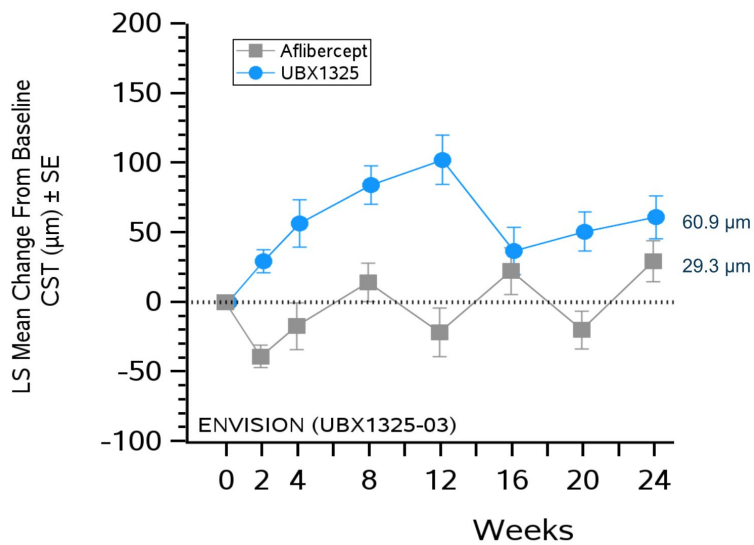
	Number of Subjects							
	0	2	4	8	12	16	20	24
UBX1325	21	24	22	21	13	11	12	
Aflibercept	24	25	25	25	25	24	22	

Source: f\_14\_2\_1\_3



# Change from baseline in CST including post-rescue data

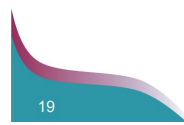
## Anti-VEGF rescue appears to improve CST in UBX1325-treated patients



Average CFBL Weeks 16 – 24 µm (85% CI)	
Aflibercept	10.5 (-7.0 – 28.1)
UBX1325	49.4 (31.4 – 67.3)

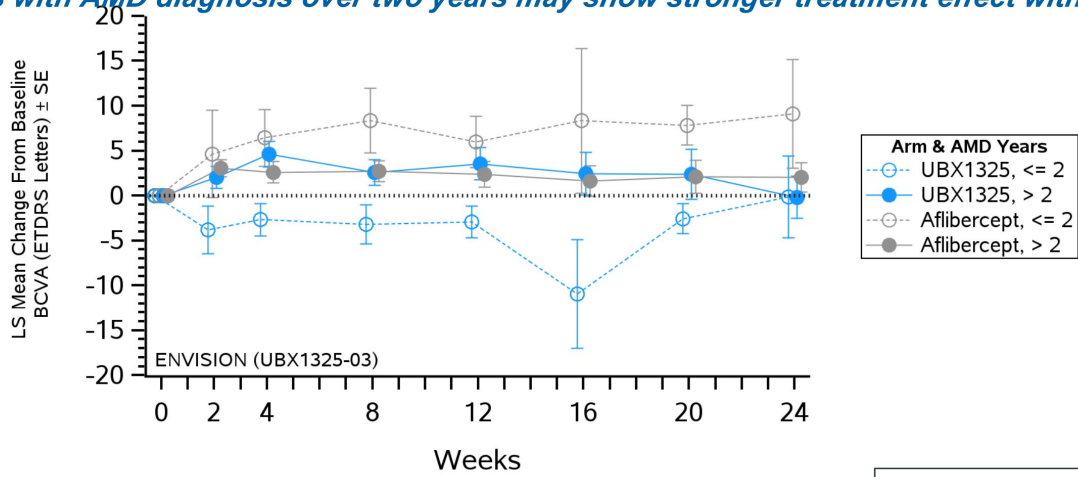
	0	4	8	12	16	20	24
UBX1325	21	25	25	24	23	21	21
Aflibercept	24	25	25	25	25	24	23

UBX1325 dosed at 0 and 4 weeks  
Aflibercept dosed at 0, 8, and 16 weeks



# Impact of AMD diagnosis duration on BCVA response *excluding* post-rescue data

*Patients with AMD diagnosis over two years may show stronger treatment effect with UBX1325\**



	Number of Subjects						
	0	4	8	12	16	20	24
UBX1325, <= 2	10	9	8	7	4	4	4
UBX1325, > 2	12	15	14	14	9	7	8
Aflibercept, <= 2	3	3	3	3	3	3	3
Aflibercept, > 2	21	22	22	22	22	22	20

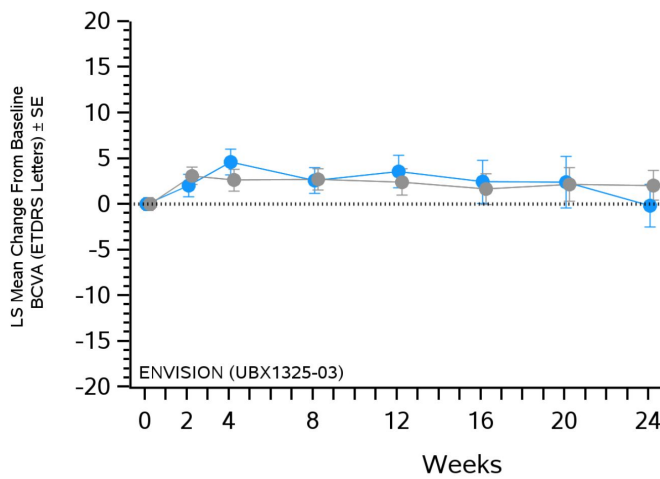
UBX1325 dosed at 0 and 4 weeks  
Aflibercept dosed at 0, 8, and 16 weeks

\* *Post hoc* analysis expanding on a *priori* hypothesis

Source: f\_14\_2\_3\_17



# BCVA change in patients with wAMD diagnosis >2 years excluding post-rescue data is similar between UBX1325 and aflibercept-treated patients\*



	Number of Subjects							
	0	2	4	8	12	16	20	24
UBX1325	12	15	14	14	9	7	8	
Aflibercept	21	22	22	22	22	22	20	

	Average CFBL Weeks 16 – 24 ETDRS letters (85% CI)
Aflibercept	1.9 (-0.2 – 4.0)
UBX1325	1.6 (-1.3 – 4.4)

UBX1325 dosed at 0 and 4 weeks  
Aflibercept dosed at 0, 8, and 16 weeks

\* Post hoc analysis expanding on a priori hypothesis

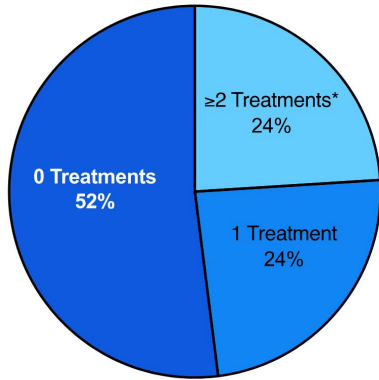
Source: f\_14\_2\_3\_17; t\_14\_2\_3\_17



# ENVISION: Durability of effect of UBX1325

Majority of patients went 24 weeks without requiring anti-VEGF treatments

# of aVEGF Treatments over 24 Weeks



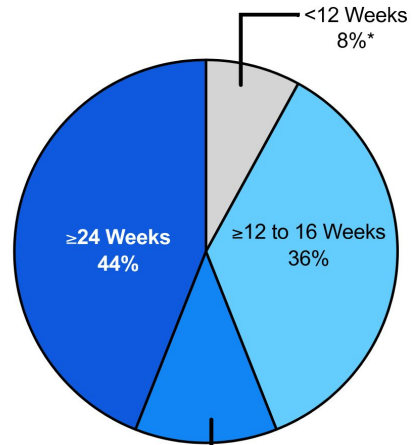
\* Includes single patient misdosed with monthly aflibercept after first treatment

**UBX1325**  
ITT Population

Treatment Criteria (either):

- Loss of 10 letters from any highest value (peak)
- Gain of 75  $\mu$ m CST from any lowest value (trough)

Maximal aVEGF-Free Interval



\* Single patient misdosed with monthly aflibercept after first treatment

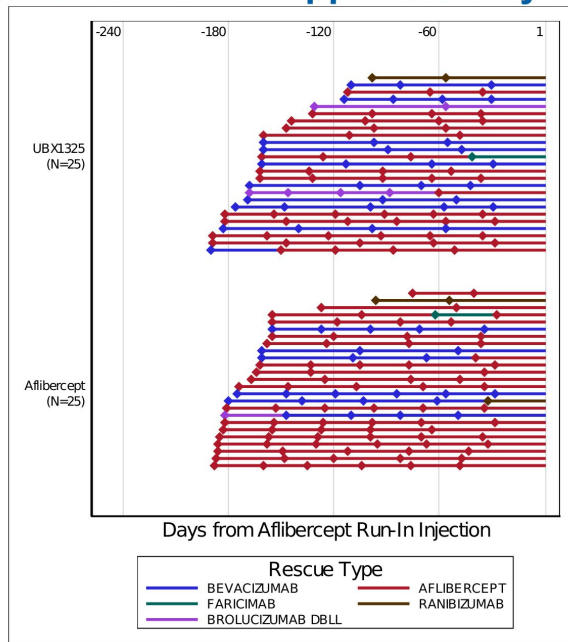
Total ≥16 weeks = 56%

**UBX1325**  
ITT Population

Source: f\_14\_2\_4\_1; f\_14\_2\_4\_4\_all\_aflib\_swimmer



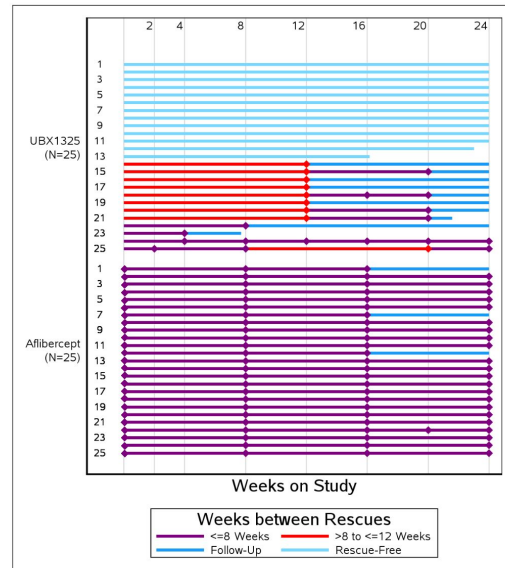
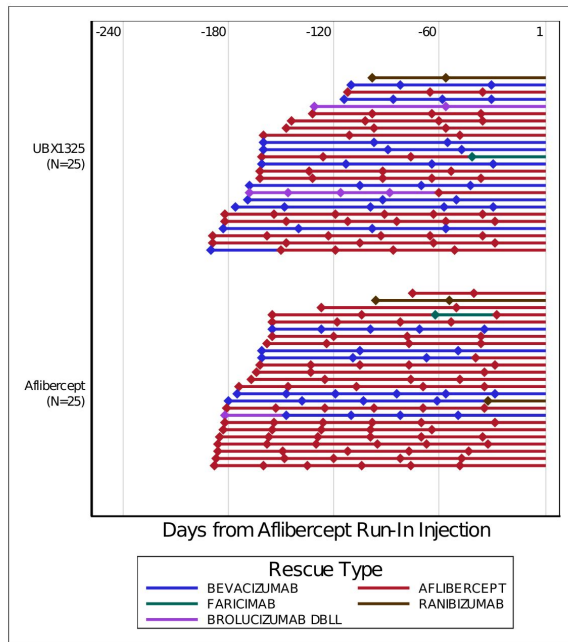
## Patients in ENVISION were high-need patients with active disease requiring anti-VEGF treatment approximately every 6 weeks



Avg prior aVEGF use from -190d: 4.0  
CST 370.8  $\mu\text{m}$

Avg prior aVEGF use from -190d: 4.5  
CST 367.5

# In UBX1325-treated patients 52% went without requiring anti-VEGF



Source: f\_prior\_avegf; f\_correlation\_tranch1\_tables

## Summary of UBX1325 ENVISION Phase 2 Study in nAMD



UBX1325

### In the ENVISION Study, UBX1325:

- ✓ Was generally well tolerated with no intraocular inflammation
- ✓ Maintained visual acuity through 24 weeks in patients with active disease; there was a 3.5 letter gain in aflibercept arm at 2 weeks and non-inferiority to aflibercept was not met
- ✓ Allowed 52% of patients to avoid anti-VEGF treatment for at least 6 months
- ✓ May have greater treatment effect in patients with AMD diagnosis greater than two years based on post-hoc assessments

Part B of ENVISION study is exploring the potential benefit of UBX1325 in combination with anti-VEGF



## Summary and Development Plans for UBX1325

### Phase 2 ENVISION Part A Study Data Highlights

*UBX1325 monotherapy did not achieve non-inferiority through 24 weeks due, in part, to an unexpected 3.5 letter gain in the anti-VEGF control arm*

*UBX1325 maintained visual acuity in patients with ongoing active disease through 24 weeks with less than one letter mean decrease from baseline*

*52% of UBX1325-treated patients did not require anti-VEGF treatment through 24 weeks*

*UBX1325 was well tolerated with no instances of intraocular inflammation*

### Additional Insights from Secondary Analysis

- A single dose of run-in aflibercept may not have been sufficient to get patients entering study to anti-VEGF BCVA plateau
- UBX1325 may be more effective in patients with longer disease duration who may have greater senescence burden

*Company to share 48-week BEHOLD DME data in April and intends to initiate Phase 2b study in DME in second half of 2023*

Q&A

