# UNITY

BIOTECHNOLOGY

UBX1325
Phase 2 BEHOLD DME Study
12- and 18-Week Data

Robert Bhisitkul, M.D., Ph.D.
Professor of Ophthalmology, UCSF

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

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### 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 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 Quarterly Report on Form 10-Q for the guarter ended March 31, 2022, filed with the Securities and Exchange Commission on May 10, 2022, 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 Achieved Proof-of-Concept in Patients with Diabetic Macular Edema (DME)

### **Phase 2 Data Highlights**

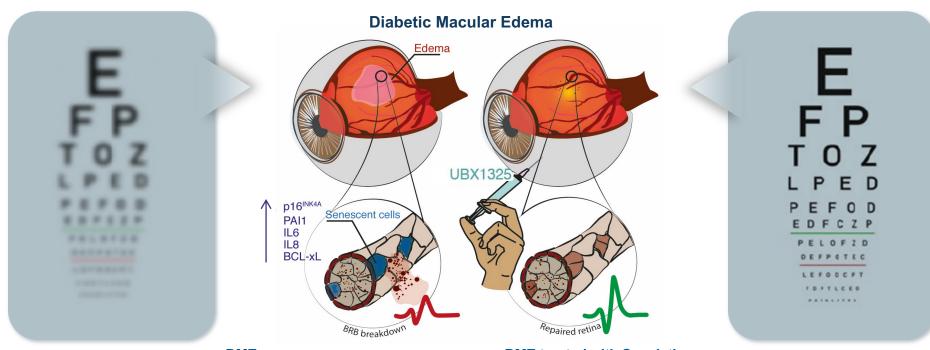
- UBX1325, the first senolytic drug being explored in eye disease, had a favorable safety and tolerability profile, with no
  evidence of intra-ocular inflammation
- A single dose of UBX1325 led to a progressive, statistically significant improvement in vision as measured by BCVA out to 18 weeks in DME patients
- Retinal structure, as measured by CST, was maintained through 18 weeks in UBX1325-treated patients, compared to worsening of CST in sham-treated patients
- This novel mechanism of action could benefit patients as monotherapy or in combination with anti-VEGF agents

### **Built on UNITY's Senescent Cell Biology Platform**

- Preclinical mechanism of action and efficacy data support senolytic therapeutic hypothesis
- Mechanism has broad implication for diseases of aging



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



#### DME:

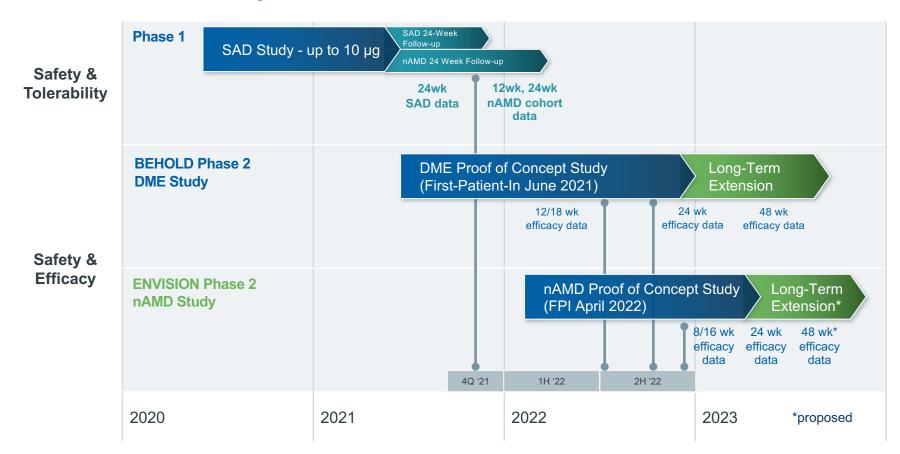
- Increased senescence burden
- Retinal vasculature affected
- Blood retinal barrier (BRB) Breakdown
- Loss of vision

## DME treated with Senolytic intended results:

- · Senescent cells removed
- Retinal vasculature restored
- Improvement in vision



## **UBX1325 Clinical Program Overview**





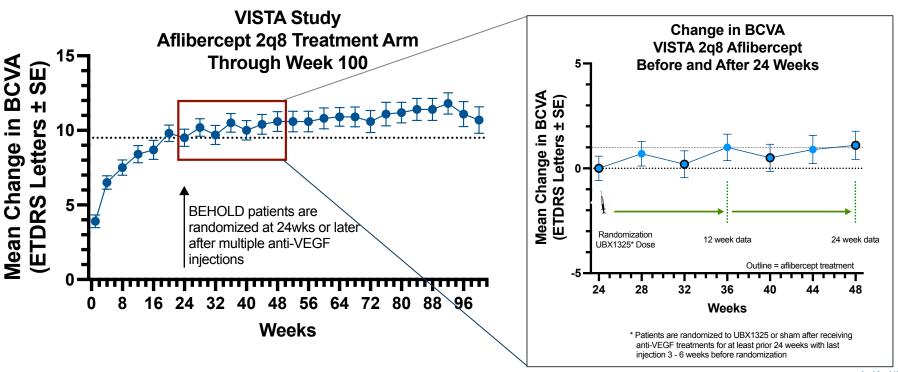
UBX1325 Phase 2 BEHOLD Study

Historic Data on DME Patients treated with Standard of Care

Differences in Patient
Population in Ph1 and Ph2
Studies



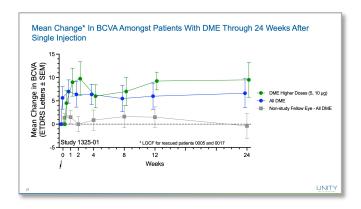
# Context for 12w DME Data: After Anti-VEGF Effect Has Plateaued, Patients Gain Approximately 1 Letter in Subsequent 6 Months on Aflibercept Treatment



## Comparing Patient Populations Between UBX1325 Phase 1 Study and Phase 2 BEHOLD Study

#### Phase 1 Design

- Patients with advanced DME and nAMD
- No previous anti-VEGF treatment for ≥3 months and for whom anti-VEGF agents were no longer considered beneficial



#### Phase 2 (BEHOLD) Design

- Patients with DME with residual visual acuity deficits and macular fluid
- On active anti-VEGF treatment regimen for ≥6 months until randomization





UBX1325 Phase 2 BEHOLD Study

12- and 18-Week Data in Patients With DME





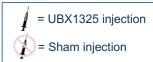
### BEHOLD Study Design, Patient Population, and Endpoints

## Patient Population

Individuals with **Diabetic Macular Edema** (with moderate diabetic proliferative retinopathy or better), **residual retinal fluid** (≥300 µm) and **visual acuity deficit** (73 ETDRS letters or worse) despite having received **repeated anti-VEGF** treatments (≥2 injections over last 6 months, last 3-6 weeks prior to randomization). The majority of subjects had 3 or more injections in preceding 6-month period.



<sup>\* 65</sup> patients were enrolled and used in the 12-Week analysis data set; 54 patients completed 18-Week visit for the respective analysis data set as of cutoff date





### **BEHOLD Study Endpoints and Methodology**

#### BEHOLD Endpoints:

- Safety and Tolerability
- Visual Acuity by Best Corrected Visual Acuity (BCVA, ETDRS Letters)
- Macular Edema Central Subfield Thickness (CST, μm)
- Proportion of patients receiving rescue

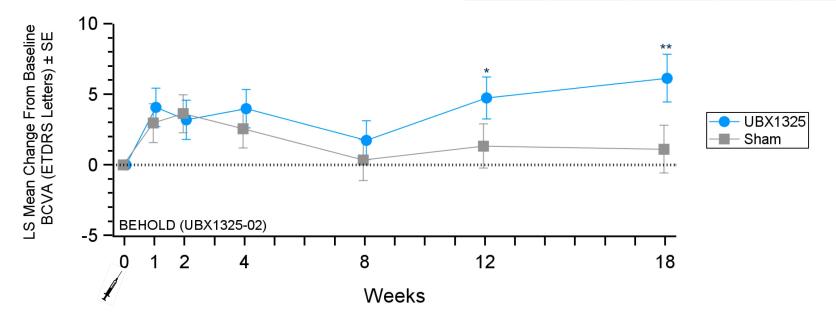
### Methodology

- For all analyses, the primary data sets included 65 patients for data through 12-weeks and 54 patients through 18-weeks
- BCVA and CST analyses were by Mixed Model Repeated Measures (MMRM), a widely used and accepted methodology for analyzing longitudinal data sets
- This methodology effectively addresses post-rescue data so that the analyses presented reflect the treatment effect not confounded by anti-VEGF effect



## 12- and 18-Week BCVA Mean Changes From Baseline Based on MMRM Analysis

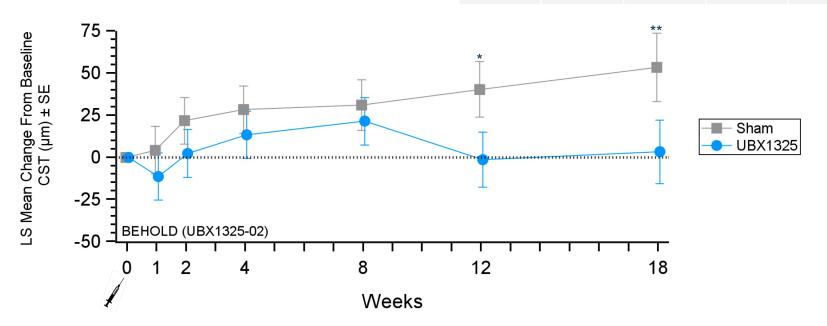
BCVA	Sham	UBX1325	Diff	P-Value
Week 12	1.3	4.7	3.4	0.1148*
Week 18	1.1	6.1	5.0	0.0368**





## 12- and 18-Week CST Mean Changes From Baseline Based on MMRM Analysis

CST	Sham	UBX132 5	Diff	P-Value
Week 12	40.3	-1.4	-41.7	0.0747*
Week 18	53.5	3.2	-50.2	0.0719**





## Study Met Statistical Significance Based on Pre-specified Proof of Concept\* Criteria for Both BCVA and CST

PoC criteria were met for BCVA and CST at Week 12 based on p-values

Week 12	Difference	p-value
BCVA (ETDRS letters)	3.4	0.1148
CST (µm)	-41.7	0.0747

Treatment effect improved through Week 18

Week 18	Difference	p-value
BCVA (ETDRS letters)	5.0	0.0368
CST (µm)	-50.2	0.0719

- Numerically **greater use of rescue on Sham vs UBX1325** (12 vs 10 subjects with ≥1 rescue, 4 vs 3 patients with ≥2 rescues)
- Use of rescue attenuated the treatment effect for BCVA, as expected, but had a much smaller impact on CST

\*This PoC study was powered for false positive rate (alpha) for BCVA of 15% or p<0.15

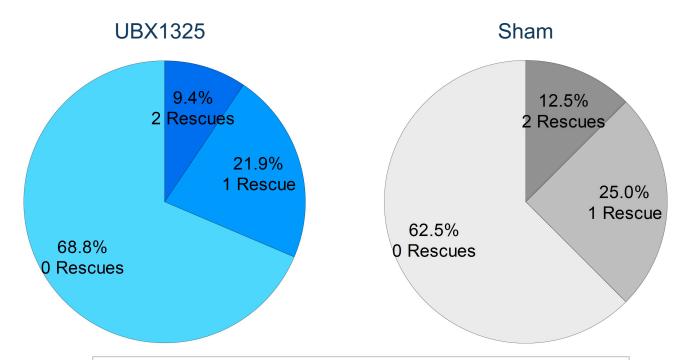


### Summary of Subgroup Analyses

- In BEHOLD, 4 subgroup factors with 8 total subgroups (2 each) were evaluated based on baseline values for:
  - BCVA (≤60 vs. >60 ETDRS letters)
  - CST (≤400 vs. >400μm)
  - DRSS Score (<47 vs. ≥47)</li>
  - A1c (≤7 vs. >7%)
- For the response of BCVA, there was a numeric advantage in all 8 subgroups for UBX1325-treated subjects
- For the response of CST, there was a numeric advantage in 7/8 subgroups for UBX1325treated patients



## Proportion of Subjects Requiring Anti-VEGF Rescue Through 12 Weeks



#### **Rescue Criteria (Either Triggers Rescue):**

- Increase in CST of +75µm from the lowest value (trough)
- Decrease in BCVA of -10 ETDRS letters from the highest value (peak)



## **Summary of Treatment Emergent Adverse Events**

	Sham (%) (N = 33)	UBX1325 10 μg (%) (N = 32)	Overall (%) (N = 65)
Subjects with at least one TEAE	21 (63.6)	20 (62.5)	41 (63.1)
Related TEAE	3 (9.1)	6 (18.8)	9 (13.8)
Grade ≥3 TEAE	3 (9.1)	2 (6.3)	5 (7.7)
Serious TEAE	1 (3.0)	2 (6.3)	3 (4.6)*
Ocular TEAE for Study Eye	17 (51.5)	16 (50.0)	33 (50.8)
Treatment-related Ocular TEAE for Study Eye	3 (9.1)	6 (18.8)	9 (13.8)**
TEAE leading to death	0	0	0
Intraocular inflammation, endophthalmitis, retinal vein occlusion, or vasculitis	0	0	0

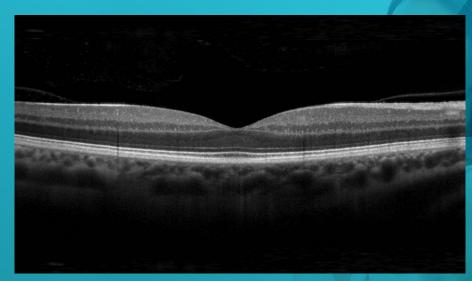
Data as of 22 July 2022 or Week 12 visit

<sup>\*\*</sup> most are likely procedural related



<sup>\*</sup> unrelated or likely unrelated to study drug

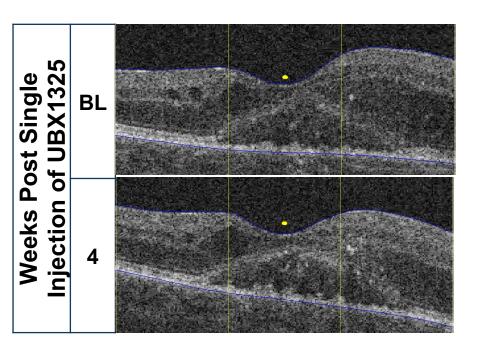
Examples of Imaging Data

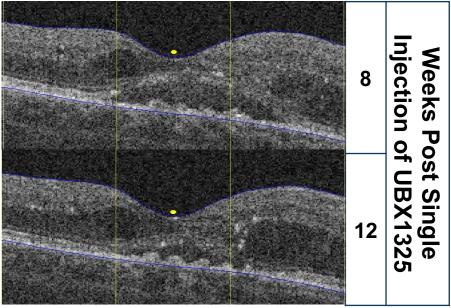


Normal Optical Coherence Tomograph (OCT)



### **PATIENT A**



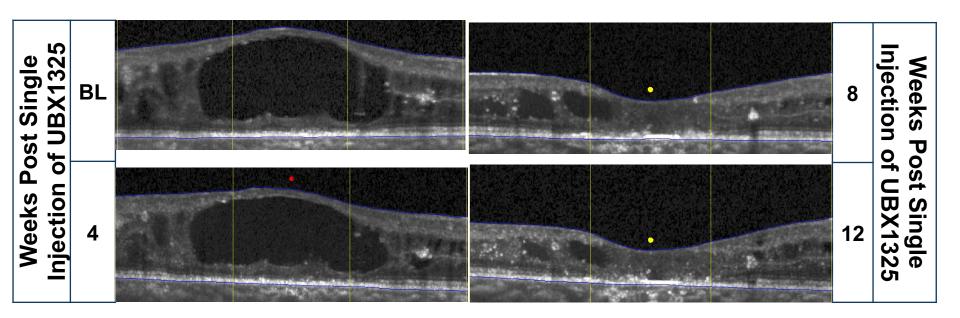


#### From Baseline to Week 12:

- Decrease in IRF
- Decrease in SRF
- Decrease in volume
- Decrease in CST ~85 microns



### **PATIENT B**



#### From Baseline to Week 12:

- Decrease in IRF
- Decrease in volume (mm3) ~10%
- Decrease in CST ~250 microns



# A Single Injection of UBX1325 Demonstrated Evidence of a Senolytic Agent Improving Visual Acuity in Patients with Diabetic Macular Edema



In the BEHOLD Study, UBX1325:

Was well tolerated with a favorable safety profile and no intraocular inflammation

Improved BCVA that was durable through 18-weeks

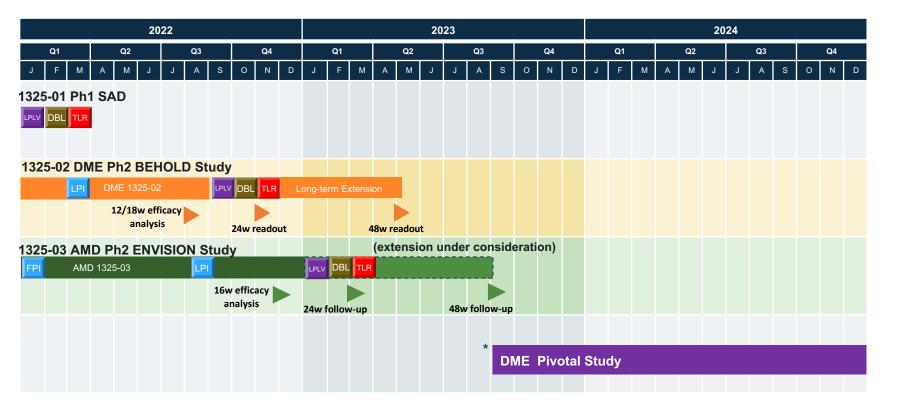
BCVA gains were robust across a range of disease severity

Maintained retinal structure vs. sham-treated subjects

**UBX1325 Provides an Opportunity for a Transformative First-in-Class and Best-in-Disease Therapy** 



## 1325 Program Overview and Data Readouts 2022-24





## Key Highlights from Phase 2 BEHOLD DME Study 12- and 18-week data underscore the therapeutic potential of UBX1325

