UNITY BIOTECHNOLOGY Corporate Overview

January 2025

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 retinal diseases and 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 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 risks relating to the uncertainties inherent in the drug development process, 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 presentation. 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 presentation. 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 September 30, 2024, filed with the Securities and Exchange Commission on November 4, 2024, 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.

Executive Leadership Team



ANIRVAN GHOSH, PhD Chief Executive Officer





LYNNE SULLIVAN, MS Chief Financial Officer Biogen Merck Serono



FEDERICO GROSSI, MD, PhD Chief Medical Officer Apellis



ALEX NGUYEN, JD Chief Legal Officer/ Head of Ops ROIVANT Alyvant



ALICIA TOZIER, MBA Chief Strategy Officer

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MIKE SAPIEHA, PhD Chief Scientist



Steering Team Arshad Khanani, MD, MA I Raj Maturi, MD I Dante Pieramici, MD I Victor Gonzales, MD I Quan Nguyen, MD

Advisory Team Jeff Heier, MD I David Boyer, MD I Bob Bhisitkul, MD, PhD I Quan Nguyen, MD, MSc I Diana Do, MD

Senior Clinical Advisor Robert Bhisitkul, MD, PhD



Developing Transformative Medicines for Retinal Disease based on a Senolytic Mechanism of Action





Focus Area: Ophthalmology

DME (Diabetic Macular Edema),

Diabetic Retinopathy,

Geographic Atrophy



Investment Highlights: Recent Achievements and UBX1325 Clinical Studies

Senolytic platform to develop transformative therapeutics

Developing a novel therapeutic approach to remodel the retina based on Senolytic Mechanism of Action

Potential to be valuable as monotherapy or in combination with anti-VEGF agents to shift the treatment paradigm for progressive vision loss

Lead asset UBX1325 (foselutoclax) has best in class potential for DME

Novel MOA to overcome limitations of current standard of care, including heavy treatment burden and sub-optimal response

A single dose of foselutoclax led to strong visual acuity gains through 48 weeks in Phase 2 BEHOLD study in patients with DME

Recent achievements and ongoing studies

Phase 2b ASPIRE study, evaluating UBX1325 head-to-head against aflibercept in DME,

- Enrollment completed in Q3 2024
- Type C Engagement with FDA provides opportunity for pivotal study largely in line with Ph2 ASPIRE trial
- 24-week data expected in 1Q25 and 36-week data expected in 2Q25

UBX1325 (Foselutoclax) Clinical Program in Diabetic Macular Edema BEHOLD and ASPIRE Studies





UNITY Pipeline

Targeting Cellular Senescence and Aging-Related Biology in Indications with Established Endpoints and Well-Defined Regulatory Pathways to Approval

	Mechanism	Indication	Research	Lead Optimization	IND-enabling	Phase 1	Phase 2	Phase 3
	BCL-xL Inhibition	Diabetic Macular Edema (ASPIRE)	Foselutoclax (UBX1325, Phase 2b)					
		Diabetic Macular Edema (BEHOLD)						
Ophthalmology			Foselutoclax (UBX1	oselutoclax (UBX1325, Phase 2)				
	Tie2/aVEGF bi-specific	Retinal Vascular Diseases	UBB2048					
	Tie2 Agonistic Antibody	Retinal Vascular Diseases	UBX 2050					
Neurology	α-Klotho	Cognitive Disorders						
			UBX 2089		Partnered	Partnered with Jocasta Neuroscience		



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Unmet Need in DME and the Opportunity for UBX1325

Diabetic Macular Edema (DME) Represents a Large Underserved Market

35.5 million people with DME worldwide

1.7 million in the US¹ with ~750,000 diagnosed and treated² and ~30% affected in both eyes²

Inadequate Response to Anti-VEGF Standard of Care

- > One half of patients achieve a weak or suboptimal response^{3,8}
- 30% may not respond to anti-VEGF⁴ at all
- > Approximately one-third of patients require monthly dosing⁷

Continued Vision Loss Over Time Despite Treatment

- > Most visual acuity (VA) improvements occur within the first year²
- > Vision gains plateau at 24 months then decline through year 5^5
- > 28% lose the ability to drive by Year 4⁶

High Treatment Burden Leading to Discontinuation

 $\rightarrow 50\%^+$ discontinue anti-VEGF treatment by 6 months²

DME=Diabetic Macular Edema; AE=Adverse Events; VEGF=Vascular Endothelial Growth Factor; Newest agents=VABYZMO and EYLEA HD

1. Downs P. Global Retinal Pharmaceuticals Market Report. Market Scope; 2023 Aug; 2. Kuo B, et al. Long-term Treatment Patterns for Diabetic Macular Edema – Up to 6 Year Follow-up in the IRIS Registry. Ophthalmology Retina. Articles in Press. 2024 Jun 01; 3. Gonzales V et al. Early and Long-Term Responses to Anti-Vascular Endothelial Growth Factor Therapy in Diabetic Macular Edema. American Journal of Ophthalmology. 2016 Dec. 172:72:79; 4. Sharma D et al. Mechanisms of Acquired Resistance to Anti-VEGF. iovs.arvojournals.org; ISSN: 1552-5783; May 2023; 5. Glassman AR et al, Diabetic Retinopathy Clinical Research Network. Ophthalmol. 2020 Aug; 127 (9): 1201-10, 6. Emami-Naeini, P et al. Ophthalmology Retina. 2024 Apr. Volume 8, Issue 4, 388 – 398. 7. Giust J et al. Treat and Extend Versus Bi-monthly Dosing with Aflibercept for the Treatment of Diabetic Macular Edema, One Year Outcomes (EVADE STUDY). ARVO Abstract. 2018; 8. Sun J et al. Defining "Strong" versus "Weak" Response to Anti-VEGF Treatment for Center-Involved Diabetic Macular EdemaRetina. 2023 April 01; 43(4): 616–623.



UBX1325 Has a Differentiated Profile With Best-In-Disease Potential in DME

Safety and Efficacy Profile	Current standard of care (Aflibercept)	aVEGF/Ang2 bispecific (Faricimab)	UBX1325
Favorable safety and PK profile	\bigcirc		Ø
Strong efficacy signal in broad patient population including sub-optimal anti-VEGF responders	\mathbf{c}	\mathbf{e}	Ø
>50% patients achieve 6-month treatment free interval after single injection	$\mathbf{\mathfrak{S}}$	\mathbf{S}	Ø
Reduction of ischemic regions of the retina and potential for disease modification	\mathbf{S}	$\mathbf{ eta}$	

Not based on head-to-head trials

supported by clinical data

supported by preclinical data



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Senolytic Therapeutic Hypothesis

Mechanism of Action

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





UNITY illustration of proposed mechanism of action

Proposed Mechanism of Action for UBX1325 in Retinal Disease



Diabetic blood vessel

Senescent (Sn) ECs accumulate in diabetic retinas in areas of disease activity

Vessel remodeling

UBX1325 selectively triggers cell death of Sn ECs. UBX1325 reduces retinal inflammation and leakage

Repaired blood vessel

Preclinical data predicts progressive disease modification through vascular remodeling



Senescent Cells & Inflammatory Factors Increase in Patients with DME











BCL-xL Inhibition Reduces Inflammation in a Mouse Model of Diabetes



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BCL-xL Inhibition Reduces Vascular Leakage in a Mouse Model of Diabetes



UBX1325 Improves Retinal Vasculature in Mouse Model of Neovascularization





OIR Vasculature following UBX1325





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UBX1325 Phase 2 BEHOLD Study in Patients with DME

Context for Novel Therapeutic Options for Patients with DME: Patients on anti-VEGF Plateau After 6 months of Treatment and Stop Gaining Vision



BEHOLD Study Design, Patient Population, and Endpoints

Patient Population

- Individuals with Diabetic Macular Edema
- Repeated anti-VEGF treatments (≥2 injections/6 months) Actual: 4.1 injections in prior 6 months
- Residual retinal fluid (≥300 µm) Actual: 439.6 µm
- Visual acuity deficit (73 ETDRS letters or worse) Actual: 61.4 ETDRS letters



	Sham	UBX	Total
Full Analysis Set	33	32	65
Completed to 24 Weeks only	4	5	9
Lost to follow-up	1	3	4
Site Closure	1	0	1
Patient withdrawal	1	0	1
Available through 48 Weeks	26	24	50



Endpoints

Safety and tolerability BCVA change from baseline Durability of response Sub- and intra-retinal fluid, CST changes Proportion of UBX1325 patients requiring 2 or more rescue treatments

Patient Characteristics at Baseline Were Well Balanced Between Groups

	Sham (n=33)	UBX1325 (n=32)
Age (Mean / Median)	61.4 (9.09)	63.6 (9.33)
HBA1c, %	7.4 (1.36)	8.0 (1.68)
Diabetes Dx, Years	17.5 (10.53)	17.2 (11.41)
DME Dx, Years	3.0 (2.32)	3.5 (3.60)
BCVA, ETDRS letters	61.8 (9.61)	60.9 (9.97)
CST, μm	456.2 (98.07)	422.5 (84.16)
Anti VEGF prior 190 days		
Aflibercept	13	13
Aflibercept, bevacizumab	4	1
Bevacizumab	15	16
Ranibizumab	1	2

Balanced on other parameters at baseline: ethnicity & race, BMI, DRSS score

UBX1325-treated Patients had Marked Reduction in Need for Anti-VEGF Rescue Compared to Sham-treated Patients Through 48 weeks

- Median Time-To-First-Rescue in UBX arm was >48 weeks (at least 30 weeks greater than Sham arm)
- ~50% of UBX-treated patients went without rescue through 48 weeks
- ~80% of sham-treated patients required rescue before 48 weeks

Rescue Criteria (Either)

Decrease of 10 ETDRS or more letters from any peak value

Increase in CST of 75 μ m or more from baseline

Physician discretion

Efficacy analyses excluding and including data post anti-VEGF rescue show a treatment benefit of UBX1325



Median Time to First Rescue Sham: 17.5 Weeks

BEHOLD Ph2 Study in Patients with DME



UBX1325-treated Patients had a Significant Improvement in BCVA from Baseline at Weeks 24 and 48



MMRM analysis, excluding post-rescue data



Between Group

p-value

0.0031

0.1198

Delta

8.1

5.6

UBX1325-treated Patients had Significant Visual Acuity Gains Compared to Sham Based on Analysis of Last Observation Prior to Rescue or End of Study[†]





CST Remained Stable or Improved in UBX1325-treated Patients Compared to Worsening in Sham Patients



MMRM analysis, excluding post-rescue data



UBX1325-treated Patients had Significantly Lower CST Compared to Sham Based on Analysis of Last Observation Prior to Rescue or End of Study[†]





53% of UBX1325-Treated Patients Did Not Require Anti-VEGF Rescue Through 48 weeks



Rescue Criteria (EITHER)

Decrease of 10 ETDRS or more letters from any peak value

Increase in CST of 75 μ m or more baseline

Physician discretion



Diabetic Retinopathy is Assessed Based on the Diabetic Retinopathy Severity Score (DRSS)







30% of UBX1325-treated Patients Had a 2-step Improvement in Diabetic Retinopathy Severity Score (DRSS) at Week 48 Compared to No Improvement in the Sham Arm



MMRM analysis, excluding post-rescue data



Over 40% of UBX1325-treated Patients Had a DRSS Score Improvement at Week 48 Compared to No Improvement or Worsening in the Sham Arm





UBX1325 Demonstrated a Favorable Overall Safety and Tolerability Profile with no Instances of Intraocular Inflammation

Parameter	Sham (n=33)	UBX1325 10 μg (n=32)
Subjects with at least one TEAE	31 (93.9)	26 (81.3)
Related TEAE	3 (9.1)	6 (18.8)
Grade >=3 TEAE	4 (12.1)	5 (15.6)
Serious TEAE	3 (9.1)	5 (15.6)
Ocular TEAE for Study Eye	28 (84.8)	23 (71.9)
Treatment-related Ocular TEAE for Study Eye	3 (9.1)*	6 (18.8)*
TEAE leading to death	0	0
Intraocular inflammation, endophthalmitis, retinal artery occlusion, or vasculitis	0	0

* Most are likely procedural related, all were mild-mod, and self-limited: Sham: 1 conj. hemorrhage, 1 conj. hyperemia, 1 diabetic macular edema. UBX: 5 conj. hemorrhage, 1 ant. chamber pigmentation, 1 eye irritation



In the BEHOLD Study, UBX1325:

- Improved visual acuity at 48 weeks by 6.2 letters from baseline after a single injection
- Led to ~50% of patients achieving a rescue-free interval of at least 48
 weeks and may represent the potential for disease modification
- **Maintained retinal structure** throughout the duration of the study without the need for anti-VEGF rescue
- Had a generally favorable safety and tolerability profile with no intraocular inflammation or other serious TEAE

UBX1325 may be an important future therapeutic option for patients with diabetic macular edema

UBX1325

Summary of Findings and Concordance of Evidence Supporting a Treatment Effect of UBX1325 in Diabetic Macular Edema

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ASPIRE Ph2b Study

UBX1325 head-to-head against aflibercept in patients with DME



ASPIRE: DME Phase 2b Study Design (Head-to-head against aflibercept)



Patient Population: Participants with NPDR who have active DME despite treatment with \geq 3 anti-VEGF injections in preceding 6 months; BCVA 70 – 30 ETDRS letters; CST >325µm

- Duration: 36 Weeks; Randomization: 1:1
- Size: n=50 (25 /arm); powered for 4.5 letter NI

Endpoints

Primary endpoint: BCVA change from baseline to week 24 (noninferiority)

Secondary endpoints include: BCVA change from BL over time • CST change from BL over time • proportion of patients gaining ≥ 15 , ≥ 10 , ≥ 5 , or ≥ 0 letters from BL • safety and tolerability • proportion of participants who do not require anti-VEGF rescue

Exploratory endpoints: DRSS change from BL at weeks 24 and 36



FDA Type C Interaction and Implications for Ph3 Design

Type C Engagement

Recent FDA Type C engagement with written feedback received on Ph3 Study expectations

Opportunity for a **pivotal study largely in line** with Ph2 ASPIRE trial

Ph3 Design Implications

Primary Endpoint: Non-Inferiority to Aflibercept as assessed by BCVA with 4.0-letter non-inferiority margin

Comparator: Aflibercept 2mg Q8 weeks



ASPIRE Top Line Results expected in Q1 2025 to inform End of Ph2 meeting and final Phase 3 design



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DME Unmet Need and Market Opportunity

Expansive Revenue Potential for UBX1325 in DME if Approved



DME=Diabetic Macular Edema; BCVA=Best Corrected Visual Acuity

1. Global Data. Diabetic Macular Market 2021-2031. 2022 Aug 01; 2. Sharma D et al. Mechanisms of Acquired Resistance to Anti-VEGF. iovs. arvojournals.org; ISSN: 1552-5783; May 2023; 3. Kuo B, et al. Long-term Treatment Patterns for Diabetic Macular Edema – Up to 6 Year Follow-up in the IRIS Registry. Ophthalmology Retina. Articles in Press. 2024 Jun 01; 4. Gonzales V et al. Early and Long-Term Responses to Anti-Vascular Endothelial Growth Factor Therapy in Diabetic Macular Edema. American Journal of Ophthalmology. 2016 Dec. 172:72:79; 5. Glassman AR et al, Diabetic Retinopathy Clinical Research Network. Ophthalmol. 2020 Aug; 127 (9): 1201-10; 6. Emami-Naeini, P et al. Ophthalmology Retina. 2024 Apr. Volume 8, Issue 4, 388 – 398. 7. Giust J et al. Treat and Extend Versus Bi-monthly Dosing with Aflibercept for the Treatment of Diabetic Macular Edema, One Year Outcomes (EVADE STUDY). ARVO Annual Meeting Abstract. 2018; 8. Sun J et al. Defining "Strong" versus "Weak" Response to Anti-VEGF Treatment for Center-Involved Diabetic Macular EdemaRetina. 2023 April 01; 43(4): 616–623.



UBX1325 is Designed to Address Current DME Unmet Needs

POOR VISUAL OUTCOMES	One half of patients do not achieve > 5 letters of vision gain ⁸ With anti-VEGF agents, vision gains plateau at 24 months & then continue to decline ⁵
HIGH TREATMENT BURDEN	Approximately one third of DME patients still require monthly dosing ⁷ Dosing frequencies are burdensome leading to >50% dropping out after 6 months ³
NEW MECHANISM OF ACTION	Sub-optimal response to anti-VEGF point to the need for additional mechanisms of action ^{1,2,3,4} Patients with diabetes are 2x more likely to experience systemic AEs ⁶ with anti-VEGF therapy
STRONG UBX1325 OPPORTUNITY	A novel therapeutic approach with the potential to improve long-term visual outcomes for DME patients, via a proven and safe IVT route of administration

1. Global Data. Diabetic Macular Market 2021-2031. 2022 Aug 01; 2. Hahn P, Garg SJ, eds. Membership Preferences and Trends (PAT). American Society of Retina Specialists. 2023; 3. Kuo B, et al. Long-term Treatment Patterns for Diabetic Macular Edema – Up to 6 Year Follow-up in the IRIS Registry. Ophthalmology Retina. Articles in Press. 2024 Jun 01; 4. Sharma S, Joshi SN, Karki P, HbA1c as a predictor for response of beva dzumab in diabetic macular oed ema. BMJ Open Ophthalmol. 2020;5(1):e000449; 5. Glassman A Ret al. Diabetic Retinopathy Clinical Research Network. Diabetic Macular Edema Protocol T Extension Study. Ophthalmol. 2020;9(1):e002409; 127 (9): 1201-10. 6. Zafae S et al. Systemic Adverse Events Among Patients With Diabetes Treated For Vascular Edema, One Year Outcomes Growth Fador Injections. JAMA Ophthalmol. 2023;141(7):658-666. doi:10.1001/jamaophthalmol.2023.2098. 2023 Jun 01; 7. Giust J et al. Treat and Extend Versus Bi-monthly Dosing with Aflib ercept for the Treatment of Diabetic Macular Edema, One Year Outcomes (EVADE STUDY). ARVO Annual Meeting Abstract. 2018. 8. Gonzales V et al. Early and Long-Term Responses to Anti-Vascular Endothelial Growth Fador Injections. JAMA Ophthalmology. 2016 Dec. 172:72:79;



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Preclinical Pipeline Tie2/aVEGF Bispecific Program



Tie-2 mAb Represents an Orthogonal Approach Restoring Vascular Integrity

Tie-2 mAb explores restoring vascular function in DME/DR independent of Bcl-xLi



Senescence biology

DR & DME

SnCs accumulate diabetic in the retina with age and disease



SASP \rightarrow ocular inflammation abnormal blood vessel growth

Disease \rightarrow vision loss





Vascular and endothelial growth factor (VEGF)





Junctional instability and pericyte death. Barrier integrity lost: Ocular edema/critical organ edema



Tie2/VEGF Bispecific Mechanism of Action

Healthy Vasculature
Tie2 is constitutively activated by <u>Ang1</u>



Diseased Vasculature Tie2 is inactivated by <u>Ang2</u>



Inducers of Ang-2:



Vasculature Homeostasis Restored by Tie2/aVEGF Bispecific Molecule



Junctional stability
Barrier integrity maintained

Junctional instability Barrier integrity lost: vascular leak in eye Junctional stability, Restoration of choriocapillaris, Inhibition of

neovascularization

Barrier integrity restored



UNITY's Tie2/VEGF Bispecific Molecules Are Differentiated from Competition

	Current standard of care (Aflibercept)	Anti-VEGF-Ang1 Bispecific (Faricimab)	Tie2/VEGF bispecific (Target Profile)
Neutralization of VEGF-A			
Neutralization of VEGF-B, PIGF and other angiogenic factors		\bigotimes	
Ang1-independent activation of Tie2	8		
Potential to improve ischemic areas of eye (preclinical data)	\mathbf{c}	$\boldsymbol{\bigotimes}$	



Multi-valent VEGFneutralizing domain

Financial Metrics



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Financials: Market Snapshot

\$29.0 million cash, cash equivalents and marketable securities as of September 30, 2024

UNITY believes that focused capital allocation are sufficient to fund operations into the third quarter of 2025