This presentation and the accompanying oral commentary contain forward-looking statements, including: the expected timing of date from the 24 week endpoints from Unity’s Phase 2 clinical study and Phase 1b high-dose, repeat-dose clinical study of UBX0101, statements regarding Unity’s understanding of cellular senescence and the role it plays in osteoarthritis and retinal diseases, the potential for Unity to develop therapeutics to extend healthspan, including UBX1325 for retinal disease, expectations regarding the results of Unity’s clinical studies 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. 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 the Company in general, see Unity’s most recently filed Quarterly Report on Form 10-Q for the quarter ended June 30, 2020, filed with the Securities and Exchange Commission on July 31, 2020, 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 and 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.
UNITY OVERVIEW, THERAPEUTIC HYPOTHESIS, AND PIPELINE
MANAGEMENT

An experienced team with a track record of success

ANIRVAN GHOSH, PHD
Chief Executive Officer

NATHANIEL DAVID, PHD
President

DAN MARQUESS, D. PHIL
Chief Scientific Officer

JAMIE DANANBERG, MD
Chief Medical Officer

LYNNE SULLIVAN, MS
Chief Financial Officer

TAMMY TOMPKINS, JD
General Counsel

SUSIE LUNDEEN
SVP of People

DOUG RICH, MBA
SVP, Operations

CAMILLE LANDIS, MBA
SVP, Corporate Development
UNITY IS DEVELOPING SENOLYTIC MEDICINES TO SLOW, HALT, OR REVERSE DISEASES OF AGING

NEUROLOGY:
Alzheimer’s, Tauopathies (FTD, PSP), Cognitive Disorders

OPHTHALMOLOGY:
DME, Diabetic Retinopathy, AMD

Broad Therapeutic Potential of Senolytic Medicines
## UNITY OPPORTUNITY

### LEADER IN CELLULAR SENESCENCE
- Emerging research shows that senescent cells are implicated in multiple diseases of aging
- Selectively eliminating senescent cells targets a root cause of age-related disease
- Building on our deep understanding of senescence biology and intellectual property, our approach generates potent senolytic drug candidates
- Pursuing diseases with established endpoints and regulatory pathways

### CLINICAL EVIDENCE
- UBX1325 first-in-human study start expected in 2H 2020 in diabetic macular edema (DME)
- UBX1325 Initial Phase 1 safety data expected in 1H 2021
- UBX1325 Phase 1b proof-of-concept study expected to be initiated in 2021

### EXPERIENCED TEAM
- Seasoned executive team with broad biotech experience
- Strong track record of delivering for patients and investors

### FINANCIAL POSITION
- Cash and cash equivalents of $112 million as of June 30, 2020
- $25M initial tranche of Hercules debt taken down upon closing in August 2020
- Cash runway into mid-2022
SENESCENT CELLS ARE IMPLICATED IN DISEASES OF AGING

SENESCENT CELLS ARE IMPLICATED IN DISEASES OF AGING

Cellular Stress

Cell Cycle Arrest

Initiation of Senescence

Senescence-Associated Secretory Phenotype

Inflammatory Factors
(e.g., MMP1, TNF-α, IL-1β)

Pro-Fibrotic Factors
(e.g., TGFβ1, TIMP-1, MCP-1)

Growth Factors
(e.g., VEGF-A, IL-6, PAI-1)

STRONG EVIDENCE LINKING SENESCENT CELLS TO DISEASES OF AGING

Clearance of senescent glial cells prevents tau-dependent pathology and cognitive decline

Tyler J Ruskin, Aoel Atazi, Charlotte F. Meyer, Barbara L. Swenson, Jan M. van Deursen & Darren J. Baker

Received: 9 December 2019 | Revised: 4 June 2020 | Accepted: 12 June 2020

DOI: 10.1002/head.23170

MINIREVIEWS

Emerging use of senolytics and senomorphics against aging and chronic diseases


BIOMEDICINE

Neutrophil extracellular traps target senescent vasculature for tissue remodeling in retinopathy

François Bénet, Gail Capone, Sergio Crespo-García, Masayuki Hata, Mathieu Neauzy, Agnieszka Dejde, Ariel M. Wolm, Manuel Bascuñán, Gaëlle Thérèse Mavoungou, José P. Romão, Roberto Díaz-Mazuelas, Celia Parinello, Vera Guber, Frédérique Blondel, Rachel Jawad, Rémi Lafiore, Cristina Sañé, Karine Soulier, Severine Lecker, Alain Abu-Thoraya, Jean-François Gédé, Gregor Anstett, Flavio A. Rosende, Florian Sempé, Jean-Sébastien Joly, Frédéric A. Mallette & Przemysław Sapieha

RESEARCH

Senolytic CART cells reverse senescence-associated phenotype

Cara K. Murray, Judith Freudenreich, Justin K. Davis, Dong Hoon Lee, Chengjun Yu, Nora Green, M. Reza Emami, Nינה Abu-Elheiga, Ronald A. DePinho, Alexander Perrimon & Michael Yaffe

PULMONARY ARTERIAL HYPERTENSION

Cellular senescence impairs the reversibility of pulmonary arterial hypertension

Diederik L. van der Flier, Celso P. L. Bosron, Giacomo S. Giordano, Jan-Remier Monner, Kondoboku Kuratsuka, Robert Souslov, James Chapell, Francesco Vannucci, Michele Demery, Klaus Kolb, Jackson S. Kroll, Arjan M. Petersen, Tom van Lingen, Marco Demarco, Marine Jose, Sébastien M. Giroux, Robert A. Deysse, Pervez Khatri, Marlene Rabkowska, Rolf M. F. Berger, Beatriz Bartels

Pulmonary arterial hypertension (PAH) is a congenital cardiac disease that can be reversed by hemodynamic unloading (HED) through short-term closure. However, this reversibility potential is lost beyond a certain point in time. The process is mediated by cellular senescence, which can be reversed by senolytics, a class of pharmacological agents that induce apoptosis of senescent cells.

RESEARCH ARTICLE

Senescence-associated secretory phenotype promotes chronic ocular graft-vs-host disease in mice and humans

Mie Yamane, Shinobu Sato, Einako Shinizumi, Shin-Insuke Shibata, Motohisa Hayano, Tomomori Yaguchi, Hajime Kamiyama, Mamoru Ogawa, Takanari Suzuki, Shin Mukai, Shigeto Shimura, Hideyuki Okano, Tetsuo Takouchi, Yutaka Kawakami, Yoko Ogawa & Kazuo Tsubota

Opinion

Reducing Senescent Cell Burden in Aging and Disease

Robert B. Pignolo, John P. Passos, Sundarp Khosla, Tamara Tokonina, and James L. Kirkland

Senescent intimal foam cells are deleterious at all stages of atherosclerosis

Steven L. Gillis, James J. Tuder, Alicia Neal-Patrick, David A. Cosentino, Judith Campisi & Joe W. van Staa

Frontiers in Aging Neuroscience

Astrocyte Senescence and Alzheimer’s Disease: A Review

Nianjun Han, Tieying Zhang, Wenhuan Xu, Yang-Ming Gu & Xingjun Gou

AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE
THERAPEUTIC RATIONALE FOR SENOLYTIC MEDICINES

**CELLULAR STRESS** → **ACCUMULATION OF SnCs** → **SnCs, INFLAMMATION, TISSUE DYSFUNCTION** → **CLEARANCE OF SnCs WITH SENOLYTIC Tx** → **REGENERATION AND RESTORATION OF FUNCTION**

**DISEASED TISSUE** → **FUNCTIONAL TISSUE**
UNITY PIPELINE
Pursuing indications with established endpoints and regulatory pathways

<table>
<thead>
<tr>
<th>MECHANISM</th>
<th>INDICATION</th>
<th>RESEARCH</th>
<th>LEAD OPTIMIZATION</th>
<th>IND-ENABLING</th>
<th>PHASE 1</th>
<th>PHASE 2</th>
<th>PHASE 3</th>
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</thead>
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<tr>
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• UBX0101 Phase 2 12-week data in painful arthritis of the knee showed no separation from placebo in any treatment group
• Phase 2 24-week data & Phase 1b 12- and 24-week data expected from UBX0101 shortly
• Data will be shared at a scientific meeting
• Unity does not intend to advance UBX0101 to a pivotal study
AGE-RELATED EYE DISEASES ARE SIGNIFICANT PUBLIC HEALTH BURDENS AND MAY BE TREATABLE WITH A SENOLYTIC

**Diabetic Retinopathy (DR)**

- **90M** Global Prevalence
- **8M** US Prevalence
- **1.4M** US Patients with Vision Threatening DR

- **PDR**
- **SEvere NPDR**
- **MOD NPDR**
- **MILD NPDR**

**Diabetic Macular Edema (DME)**

- **20M** Global Prevalence
- **2M** US Prevalence (Across all stages of DR)
- **1M** US Patients with Symptomatic DME

**Age-Related Macular Degeneration (AMD)**

- **170M** Global Prevalence
- **11M** US Prevalence (90% have dAMD, 10% have wAMD)
- **.8M** US Patients with Advanced DAMD / Geographic Atrophy
- **1.1M** US Patients with Symptomatic WAMD

---

Estimated numbers for DR/DME based on sources 1-7: 

AMD, age-related macular degeneration; dAMD, dry AMD; wAMD, wet AMD; DM, diabetes mellitus; DME, diabetic macular edema; DR, diabetic retinopathy.
# Role of Senescence in Age-Related Eye Disease

SnCs accumulate in the retina, potentially contributing to disease phenotypes.

## DR & DME

**SnCs** accumulate in the retina with age and diabetic disease.

**SASP** → ocular inflammation

- Abnormal blood vessel growth

**Disease** → vision loss

## AMD

**SnCs** accumulate with age in the retina retinal pigment epithelium (RPE) layer.

**SASP** → choroidal remodeling & RPE dysfunction → atrophy

**Disease** → Central vision loss

---

**SASP FACTORS**
- PAI-1, IL-6, IL-8, VEGF, IL-1β
- VEGF-α, IP-10

---

*Oubaha et al., Senescence-associated secretory phenotype contributes to pathological angiogenesis in retinopathy, Sci. Transl. Med. 8, 362ra144 (2016)*
AGE-RELATED EYE DISEASES ARE MULTIFACTORIAL

Factors beyond VEGF are detected in the vitreous of DR patients

**P<0.01; ***P<0.0001

SENESCENCE BURDEN IN AMD AND DR/DME

- SnC burden is associated with disease activity
- DR/DME patients show SnC in the retina and choroid
- SnC is associated with drusen accumulation

GCL
INL
ONL
RPE
Choroid
Sclera

GCL
INL
ONL
RPE
Choroid
Sclera

GCL
INL
ONL
RPE
Choroid
Sclera

GCL
INL
ONL
RPE
Choroid
Sclera

Drusen

NORMAL (71F)

AMD (93M)

DR (64M)

INTERMEDIATE AMD (86F)
SENESCENCE IS OBSERVED IN PRE-CLINICAL MODELS

Senescence burden in pre-clinical models supports identification of novel senolytics
UBX1325 selectively inhibits Bcl-xL without driving apoptosis in a normal retina

TE: Target engagement
ME: Mechanism Engagement
UBX1325 IMPROVES RETINAL VASCULATURE IN MOUSE OIR

Bcl-xL TE drives apoptosis in OIR

Retinal Bcl-xL TE

Neovascularization

Avascular area

Retinal caspase activation

% retinal area

% retinal area
UBX1325 DEMONSTRATES EFFICACY IN MOUSE STZ
Streptozotocin-induced diabetic retinopathy model

VASCULAR LEAK

PHOTORECEPTOR FUNCTION

CYTOKINES

Intravitreal dosing reduces vascular leakage and protects retinal function in diabetic mice
VALUE PROPOSITION FOR SENOLYTICS IN MULTIPLE AGE-RELATED EYE DISEASES

DIFFERENTIATING PRECLINICAL FEATURES

1. **Bcl senolytic**: Potent inhibitor of Bcl-xL in the retina

2. **Novel MOA**: eliminates SnCs → reduces multicomponent SASP

3. **in vivo efficacy** → activity in two preclinical models of retinopathy

PROPOSED CLINICAL BENEFITS

- Potential for improvements in visual function over anti-VEGF therapy
- Potential for efficacy in patients that don’t respond to anti-VEGF therapy
- Potential for efficacy in combination with anti-VEGF therapy

Potential for disease modification in the aging retina
SENESCENCE DISEASE HYPOTHESIS IN THE BRAIN

SnCs accumulate in the brain, promote inflammation and Tau accumulation, and induce neurodegeneration.

**REFERENCE:** Chinta et al., Cellular senescence and the aging brain, Exp Gerontol. 68:3-7 (2015)
Characteristic FTD/PSP tauopathy including (A) a tufted astrocytes in mid-frontal cortex and (B) a globose neuronal tau tangle in midbrain. CBD characteristic tau pathology showing (C) glial astrocytic plaques in the mid-frontal cortex, (D) a ballooned neuron in the anterior cingulate gyrus and (E) oligodendrocyte coiled bodies in the mid-frontal cortex. Note ballooned neurons and coiled bodies may be present in other tauopathies to a lesser extent. GGT (F) globular oligodendrocytes in white matter and (G) astrocytic tau inclusions in grey matter of the mid-frontal cortex show distinct globular morphology from PSP and CBD tau pathology. AGD associated (H) small comma-shaped 4R tau reactive grains (arrows) in the amygdala.
TAU PATHOLOGY PRECEDES COGNITIVE SYMPTOMS IN AD

Jack et al., Lancet Neurology, 2010
ELEVATED SENESCENCE BURDEN IN AD/PSP/FTD IS CORRELATED WITH TAU PATHOLOGY

Luth et al., Brain Research, 2000; Musi et al., Aging Cell, 2018
ELIMINATION OF SnCs REDUCES TAU BURDEN IN P301S TAU MOUSE MODEL

ELIMINATION OF SnCs RESTORES COGNITION IN P301S TAU MOUSE MODEL

FINANCIAL METRICS AND MILESTONES
FINANCIAL METRICS AND MILESTONES

FINANCIALS

• $112 million cash and cash equivalents as of June 30, 2020, excluding Hercules debt facility
• $25M initial tranche of Hercules debt taken down upon closing in August 2020
• Refocusing capital allocation to extend cash runway into mid-2022, thus enabling UBX1325 Phase 1b proof-of-concept

MILESTONES

• 2H 2020 – UBX1325 Phase 1 study first-patient dosing in DME
  – To enable multiple indications (e.g. DME, DR, AMD)
• 1H 2021 – UBX1325 Phase 1 safety and tolerability data
• 2021 – UBX1325 Phase 1b proof-of-concept study initiation
UBX0101 and UBX1325 Clinical Development Plan

**2020**
- **UBX1325** (Bcl-xL)
  - Ph1 FPI 2H2020
- **UBX0101** (MDM2 / p53) Osteoarthritis
  - Ph1b & Ph 2 24-wk 2H2020*

**2021 and Beyond**
- **UBX1325** (Bcl-xL) Ph1 Tolerability 1H2021
- **UBX1325** (Bcl-xL) Ph1 POC
- **UBX1325** (Bcl-xL) Ph2/3 Study start

UBX0101 (MDM2 / p53) Osteoarthritis
- Ph2 12 wk Readout 3Q2020*

* Detailed data presentation at future medical meeting
UNITY IS DEVELOPING SENOLYTIC MEDICINES TO SLOW, HALT, OR REVERSE DISEASES OF AGING

**NEUROLOGY:**
Alzheimer’s, Tauopathies (FTD, PSP), Cognitive Disorders

**OPHTHALMOLOGY:**
AMD, Diabetic Retinopathy, DME

**Broad Therapeutic Potential of Senolytic Medicines**