

# KODIAK

THE OPHTHALMOLOGY MEDICINES COMPANY

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# FORWARD-LOOKING STATEMENTS

These slides contain forward-looking statements and information. The use of words such as "may," "will," "should," "expect," "plan," "anticipate," "believe," "estimate," "project," "intend," "future," "potential," or "continue," and other similar expressions are intended to identify forward-looking statements. Forward-looking statements include statements regarding: the intended benefits and potential differentiating aspects of our ABC Platform, including the possibility that it can enable durability of tarcocimab tedromer (KSI-301, tarcocimab) and KSI-501ABC; the ability of patients requiring anti-VEGF treatment to benefit from tarcocimab and KSI-501ABC: our ability to submit a BLA for tarcocimab in wet AMD. DME and RVO and NDPR; our ability to conduct an additional single pivotal trial for tarcocimab; our ability to accelerate development of KSI-501P and KSI-501ABC; our ability to reduce risk with our trial design for KSI-501P; development plans; clinical and regulatory strategy, including the expected timing of availability of data regarding efficacy, safety and durability of tarcocimab, KSI-501P and KSI-501ABC, and the expected market opportunity for commercialization; the potential for our products to obtain a product label in multiple indications and with the flexibility of a range of dosing intervals: the potential benefits of KSI-501, including its potential to be a first-in-class bispecific ABC inhibiting VEGF and IL-6, and ability to target new market segments with KSI-501P. All forward-looking statements are based on management's current expectations, and future events are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth or implied by such forward-looking statements. These risks and uncertainties include, but are not limited to, the risk that tarcocimab may not demonstrate safety, efficacy or durability in ongoing or future clinical trials; cessation or delay of any clinical studies and/or development of tarcocimab may occur; future regulatory milestones of tarcocimab, including those related to current and planned clinical studies, may be insufficient to support regulatory submissions or approval; our research and development efforts and our ability to advance our product candidates into later stages of development may fail; any one or more of our product candidates may not be successfully developed, approved or commercialized; adverse economic conditions may significantly impact our business and operations, including our clinical trial sites, and those of our manufacturers, contract research organizations or other parties with whom we conduct business; as well as the other risks identified in our filings with the Securities and Exchange Commission. For a discussion of [other] risks and uncertainties, and other important factors, any of which could cause our actual results to differ from those contained in the forward-looking statements, see the sections entitled "Risk Factors" and "Special Note Regarding Forward Looking Statements" in our most recent Annual Report on Form 10-K for the year ended December 31, 2022, subsequent reports on Form 10-Q, as well as discussions of potential risks, uncertainties, and other important factors in our subsequent filings with the Securities and Exchange Commission. Any forward-looking statement speaks only as of the date on which it was made. We undertake no obligation to publicly update or revise any forward-looking statement, whether as a result of new information, future events or otherwise, except as required by law.

#### THE OPHTHALMOLOGY MEDICINES COMPANY

### OUR MISSION



#### TRAILBLAZING SCIENCE

Our creative and thoughtful foundation



#### 2 GENERATION 2.0 MEDICINES

Our challenge to the status quo



### **3** SINGULAR FOCUS IN OPHTHALMOLOGY

Our 24 / 7 / 365

KODIAK SCIENCES

WHERE WE ARE TODAY

• \$346 million in cash and cash equivalents as of end of 3Q23

- Pipeline of 3 clinical prospects advancing to achieve meaningful (pivotal) inflections in 2 – 3 years
- Maturing investments in retina product platforms and technology to enable business development and/or pipeline

#### **TARCOCIMAB TEDROMER**

- 3 positive Phase 3 studies in large indications: Diabetic Retinopathy (NPDR), Retinal Vein Occlusion (RVO) and wet AMD
- Core differentiation based on science and evidence of durability
- Planning towards one confirmatory pivotal study in 1H2024 using a go-to-market formulation to support a single BLA submission across NPDR, RVO and wet AMD
- We believe tarcocimab can fill the leading remaining unmet need of true durability for majority of patients

#### **KSI-501**

- A first-in-class anti-IL-6 and anti-VEGF bispecific therapy designed to treat intraocular inflammation and retinal vascular disease
- Being developed in two therapeutic forms: KSI-501P and KSI-501ABC

#### KSI-501P (Unconjugated Bispecific Protein)

- Being developed for retinal inflammatory diseases, i.e. patients who have retinal fluid and signs of inflammation (irrespective of prior treatment)
- A new market segment separate from the established anti-VEGF market
- Planning towards pivotal study initiation in 2024
- Risks and opportunities not tied to ABC platform

#### KSI-501ABC (Bispecific Antibody Biopolymer Conjugate)

- Being developed for the high prevalence retinal vascular diseases, with future potential to address broader patient populations and unmet needs of efficacy and durability
- Planning towards pivotal study initiation in 2024

## Kodiak aims to address multiple unmet needs within retinal disease therapy area with a diversified pipeline

#### Antibody Biopolymer Conjugate ("ABC") Platform-derived biologics

Precision engineered for increased durability in high prevalence retinal diseases



- A mono or bispecific protein therapeutic, engineered for high affinity and specificity, is combined with a bioinspired polymer designed to make medicines last longer and extend their therapeutic benefit
- Commercial scale formulations decrease the gel-like nature of earlier formulations with benefits to usability and safety
- Product candidates: Tarcocimab tedromer, KSI-501ABC

#### Unconjugated biologic

Novel "free" protein engineered for retinal inflammatory diseases where extended durability is not an unmet need where there are no approved therapies



Product candidate: KSI-501P

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A pipeline of 3 clinical programs with significant synergy but also a diversification

### TARCOCIMAB TEDROMER



### Three successful Phase 3 studies in NPDR, RVO and wet AMD with compelling durability demonstrated

	Study design	Primary endpoint	Extended durability	
NPDR Phase 3 GLOW Study	<ul> <li>Superiority study</li> <li>tarcocimab Q24W after 3 initiating doses vs sham</li> </ul>	$\checkmark$	$\checkmark$	Signature durability demonstrated with all patients on 6-month dosing
<b>RVO</b> Phase 3 BEACON Study	<ul> <li>Tarcocimab Q8W after 2 monthly loading doses vs aflibercept Q4W</li> </ul>	$\checkmark$	$\checkmark$	Tarcocimab demonstrated strong durability at primary endpoint at month 6 and at Year 1
Wet AMD Phase 3 DAYLIGHT Study	<ul> <li>Tarcocimab Q4W vs aflibercept Q8W after 3 monthly loading doses</li> </ul>	$\checkmark$	Not Applicable	Monthly dosing of tarcocimab demonstrated favorable safety and non- inferior efficacy

 In addition to these studies, tarcocimab was also studied in wet AMD (Phase 2b/3 study) and DME (Phase 3 GLEAM and GLIMMER studies). These studies did not meet primary endpoint but did demonstrate strong 5 and 6-month durability in the majority of patients. Across the pivotal program, tarcocimab's durability was consistently differentiated. In multiple indications, it delivered on 5- to 6-month durability for the majority of patients



Study did not meet primary endpoint believed to be due to the undertreatment of a minority of patients.
 Studies did not meet primary endpoints due to an unforeseen increase in cataracts in tarcocimab-treated patients: Kodiak's new commercial formulation may mitigate this liability.

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aflibercept-treated patients.

Tarcocimab and the ABC Platform have demonstrated a favorable safety profile with more than 2,400 patient years of exposure across the full clinical program



- Tarcocimab demonstrated low IOI rates pooled across six pivotal studies
- IOI rates observed with tarcocimab were comparable to those demonstrated by other anti-VEGF agents in Phase 3 studies\*
- No events of vascular occlusion or vasculitis associated with IOI have been observed with >1,500 patients dosed with tarcocimab, indicating a favorable overall safety profile for tarcocimab and the ABC Platform

### In NPDR, tarcocimab established superior efficacy with every 6-month dosing and reduced the risk of developing sight-threatening complications by ~90%

#### Results from the GLOW Phase 3 study in NPDR

- Patients treated with tarcocimab received only 4 injections in Year 1<sup>1</sup>
- Tarcocimab demonstrated superiority in ≥2-step and ≥3-step improvement in DRSS
- Tarcocimab reduced the risk of developing pre-specified sight-threatening complications by ~90%





#### Any Sight-Threatening Complication

 DME
 CST of ≥320 and a 5-letter decrease in BCVA from Day 1; or CST of ≥350

 PDR
 NVD or NVE; or VH

 ASNV
 ASNV; or NVG

1. All patients were randomized to receive either tarcocimab every six months after 3 initiating doses or to receive sham injections.

DRSS: diabetic retinopathy severity scale; DME; diabetic macular edema; PDR; proliferative diabetic retinopathy; ASNV: anterior segment neovascularization; CST; central subfield thickness; BCVA; best corrected visual acuity; NVD: neovascularization of the disc; NVE; neovascularization elsewhere; VH: vitreous hemorrhage; NVG; neovascular glaucoma.

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Weighted percentages are based on weighted average of observed estimates across strata using CMH weights. p-values are based on the difference in response rates

#### In RVO, tarcocimab demonstrated strong durability, matched efficacy and comparable safety profile with fewer doses than aflibercept

#### Results from the BEACON Phase 3 study in RVO

- Tarcocimab Q8W was non-inferior to aflibercept Q4W in all RVO patients at 6 months, thereby doubling the treatment interval
- Approximately half of tarcocimab-treated patients required no additional injections in the second 6 months of the study
- Despite fewer injections in tarcocimab-treated patients, vision outcomes at Year 1 favored tarcocimab-treated patients achieving an observed mean of 74.6 letters versus 74.3 letters for aflibercept-treated patients



#### Number of injections from Week 24 to 48

In wet AMD, monthly dosing of tarcocimab demonstrated a favorable safety profile and noninferior efficacy profile, supporting monthly dosing and wet AMD indication in label

#### Results from the DAYLIGHT Phase 3 study in wet AMD

Tarcocimab dosed monthly demonstrated non-inferior visual acuity gains at Year 1 compared to aflibercept dosed per label Continued dosing through Year 1 resulted in comparable drying effect of tarcocimab compared to aflibercept (OCT CST change from baseline of -117 µm versus -109 µm, respectively) Tarcocimab on intensive monthly dosing is safe and well tolerated – low rate of intraocular inflammation and no cases of intraocular inflammation with vasculitis or vascular occlusion

#### DAYLIGHT met its objectives

- Provide monthly dosing support for other indications in regulatory submission
- Support a wet AMD Biologics License Application and other regulatory applications
- Safety outcomes from DAYLIGHT provide support for the favorable safety profile of Kodiak's ABC Platform

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### Tarcocimab's breadth of indications, differentiation (science of durability), and a thoughtful commercial strategy may translate into meaningful commercial opportunity

#### The branded anti-VEGF market continues to grow, making room for more differentiated branded therapies

- The branded anti-VEGF market is >\$13B with a decade of >10% annual growth
- Within the anti-VEGF market, diabetic retinopathy is expected to be a growth driver given limited penetration of agents today
- Branded anti-VEGF competition is expected to remain similar when tarcocimab enters the market
  - Existing anti-VEGFs (Eylea HD and Vabysmo) are expected to remain as the major branded competition
- A meaningful commercial product in this landscape does not require dominant market share

#### Tarcocimab's signature durability profile has gathered early positive feedback

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• Tarcocimab is on a path to fulfilling the attributes that retina practices have indicated are important for adoption:

Important Attributes for Adoption		Tarcocimab
6-month dosing where appropriate	$\checkmark$	• Phase 3 data supporting 6-month dosing in the majority of patients
• Flexibility of monthly dosing	$\checkmark$	Phase 3 data supporting monthly dosing with a favorable safety profile
• Breadth of indications	$\checkmark$	Potential for a single BLA across 3 indications at launch
Underlying science of durability	$\checkmark$	• The ABC Platform is purposefully designed for durability. We will find creative and impactful ways to communicate our science of durability
Commercial strategy	$\checkmark$	<ul> <li>Understanding the buy-and-bill market is critical in retina, and our commercial strategy will be thoughtfully designed to support physician adoption</li> </ul>



### **Tarcocimab tedromer in summary**

- Across the entire tarcocimab clinical program, tarcocimab and the ABC Platform demonstrated consistent and differentiated durability as well as favorable safety
- Successful pivotal data demonstrated in NPDR, RVO and wet AMD. Plan to initiate an additional pivotal study in 1H 2024 to support a single BLA in these three indications
  - NPDR GLOW study was the first time 6-month dosing in all patients successfully treated moderate-to-severe NPDR
  - In RVO BEACON study, tarcocimab demonstrated strong durability, matched efficacy and favorable safety with fewer doses than aflibercept; both in a fixed dose regimen in the 1<sup>st</sup> 6 months & in a flexible dose regimen in the 2<sup>nd</sup> 6 months
  - In wet AMD DAYLIGHT study, monthly dosing of tarcocimab demonstrated favorable safety and non-inferior efficacy, supporting wet AMD indication in label and monthly dosing across indications in label
- We believe tarcocimab's breadth of indications, signature durability, combined with an appropriate commercial strategy, could support physician adoption and translate into a meaningful commercial product in the growing anti-VEGF market
- Kodiak believes a 4<sup>th</sup> confirmatory pivotal study can be completed within 24 months

### **KSI-501**

#### Negative-stain electron microscopy images of KSI-501ABC

# anti-IL6 Fab Fc Biopolymer

**KSI-501ABC** 

In the absence of VEGF, VEGF trap arms are not seen

KSI-501ABC + VEGF



Upon VEGF binding, VEGF trap arms are oriented in an optimal configuration and become visible

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### ANTI-IL-6 & ANTI-VEGF DUAL INHIBITION

A new category of retinal medicine: to address inflammation and the underlying inflammatory cascade present in many patients

#### SUPERIOR MOLECULAR DESIGN

Anti-IL-6 therapeutic to address inflammation directly as well as inflammation-mediated retinal fluid

plus

#### A potent anti-VEGF therapeutic similar to aflibercept for strong fluid control and anti-VEGF action

Preclinical and clinical evidence suggest synergy of the two mechanisms



#### DUAL THERAPEUTIC DEVELOPMENT STRATEGY

#### KSI-501P – unconjugated bispecific protein

- Being developed for retinal inflammatory diseases, i.e. patients who have retinal fluid and signs of inflammation (irrespective of prior treatment)
- A new market segment separate from the established anti-VEGF market
- Planning to initiate pivotal studies in 2024
- Risks uncoupled from the ABC platform

### KSI-501ABC – ABC platform commercial formulation with a defined ratio of unconjugated protein and bioconjugate

- Being developed in high prevalence retinal diseases to address broader patient populations and unmet needs of efficacy and durability
- Commercial formulation contains a defined ratio of unconjugated protein and bioconjugate
- Planning to initiate pivotal studies in 2024



A substantial portion of patients underperform in vision and anatomical improvement compared to the mean BCVA and OCT responses, suggesting the need for additional mechanisms of action

BCVA change from baseline during year 1 for individual patients treated with Q8W aflibercept

### OCT CST change from baseline during year 1 for individual patients treated with Q8W aflibercept

KODIAK Aflibercept-treated subjects completing Year 1 of Phase 2b/3 study of tarcocimab tedromer in wet AMD, NCT04049266. BCVA, best corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; OCT, optical coherence tomography; CST, central subfield thickness

#### "Two hands on the ball"



"One hand on the ball"



KSI-501 bispecific protein features unique design that enables highly efficient binding to both IL-6 and VEGF

#### ENHANCED BINDING CAPACITY

Each molecule has the ability to inhibit up to two VEGF molecules, depending on the concentration of VEGF, in addition to two IL-6 molecules, simultaneously Both arms inhibit multiple targets, unlike the canonical bispecific where each arm of the antibody binds to one target, limiting binding capacity

#### **ADAPTABILITY**

The VEGF trap of KSI-501 has flexible arms that can bind and inhibit two VEGF molecules in a "one-hand-on-the-ball" fashion or bind to one VEGF firmly in a "twohands-on-the-ball" fashion

#### BEST-IN-CLASS VEGF INHIBITION

The VEGF trap mimics the native receptor and binds multiple targets including VEGF-A, VEGF-B and PIGF

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\*Fc region contains engineered mutations to silence effector function (•) and to allow site-specific conjugation of biopolymer (•).

## KSI-501P and KSI-501ABC demonstrate comparable VEGF binding affinity and potency to REGN aflibercept and comparable IL-6 potency as Roche vamikibart

Key disease drivers in retinal diseases	Aflibercept	Vamikibart (anti-IL-6 mAb)	KSI-501P & KSI-501ABC^
Inflammation	×	$\checkmark$	$\checkmark$
Angiogenesis	$\checkmark$	×	$\checkmark$
Barrier function	×	$\checkmark$	$\checkmark$
Vascular leakage	$\checkmark$	×	$\checkmark$
Preclinical potency			
Binding affinity to VEGF-A*	0.49 pM	N / A	1.02 pM
Inhibition of VEGF-A binding to VEGF-R^^^	IC <sub>50</sub> =129.6 pM	N/A	IC <sub>50</sub> =163.7 рМ
Inhibition of IL-6 <i>cis</i> signaling	N/A	IC <sub>50</sub> = 41 pM	IC <sub>50</sub> = 66 pM
Inhibition of IL-6 trans signaling	N/A	IC <sub>50</sub> = 1.0 nM	IC <sub>50</sub> = 2.1 nM

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mAb; monoclonal antibody; TVEGF-A binding affinity determined by Kodiak from Kinetic Exclusion Assay for tarcocimab and KSI-501 and determined by Regeneron from Biacore assay for aflibercept; ^1CS0 determined by Kodiak from VEGF bioluminescent cell-based assay; ^Values for KSI-501P are shown, except for VEGF-A binding affinity, for which values for KSI-501ABC was shown. KSI-501ABC and KSI-501P have similar binding affinity and potency in preclinical assays

## Powerful effect on barrier biology: KSI-501ABC inhibits angiogenesis and normalizes inner and outer blood retinal barriers in preclinical studies

- Inner blood-retinal barrier: leakage from vascular endothelium disruption leads to macular edema and hemorrhage<sup>1</sup>
- Outer blood-retinal barrier: RPE integrity prevents choroidal vascularization from invading the retina<sup>2</sup>



## Strong scientific rationale: dual inhibition of VEGF and IL-6 by KSI-501ABC confers superior normalization vs either anti-VEGF or anti-IL-6 monotherapy



RPE Cells

Vascular Cells



## **KSI-501P**

## Unconjugated Bispecific Protein

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High unmet need for safer, disease modifying therapies. The opportunity is primed for safe and effective biologics to move up the treatment pathway towards first line therapy

#### **Current treatment algorithm for retinal inflammatory diseases**

### 1L: Local or systemic corticosteroids

- Mainstay of therapies and used first line
- Associated with elevated intraocular pressure / glaucoma that often require therapy and even surgery as well as cataract progression
- 30 40% of UME patients do not respond

#### **2L: Immunomodulators**

- Off-label use
- Used as steroid-sparing agents
- Up to 50% of patients do not have UME resolved
- ~35% of patients do not experience improvement in UME

#### 2L or 3L: Biologics

- Adalimumab (anti-TNFα) is currently the only FDA-approved non-steroid therapy for noninfectious uveitis (NIU)
- Used as a steroid-sparing therapy
- ~55% of patients experienced treatment failure over 85 weeks
- Associated with serious side effects (e.g., infections, malignancies)

#### 3L or 4L or adjunct: anti-VEGF agents

Used for patients with persistent UME that fail conventional therapies

However, the underlying inflammatory component of the pathophysiological process is not addressed by inhibiting VEGF alone

## IL-6 plays a key role in retinal inflammatory diseases and is a newly validated target for Uveitic Macular Edema (UME) treatment

- IL-6 has been consistently demonstrated to be elevated in ocular compartments and in serum in patients with non-infectious uveitis
- IL-6 has been shown to be further elevated in uveitis patients who have macular edema
- Targeting IL-6 has demonstrated clinically meaningful improvement in vision and resolution of macular edema in UME patients

### IL-6 levels are elevated in vitreous fluid of patients with active uveitis<sup>1,2,3</sup>

• Aqueous Humor IL-6 levels were further elevated in uveitis patients with cystoid macular edema vs patients without (p=0.026)





KODINK I. Perez et al. Ocul Immunol Inflamm. 2004;12(3):193-201.2. de Boer et al. Curr Eye Res. 1992;11 Suppl:181-186.3. Valentincic et al. Molecular Vision 2011; 17: 2003-2010.4. 2023 ASRS presentation, A Novel Intravitreal Anti-IL-6 Monoclonal Antibody for Uveitic Macular Edema (UME): Preliminary Results From the Phase I DOVETAIL Study

## The addition of anti-VEGF to anti-inflammatory agents may provide further clinical benefit in treatment of retinal inflammatory diseases

- Role of VEGF is well established in macular edema
- VEGF levels are found to be elevated in aqueous humor of eyes with uveitis and UME
- Anti-VEGF agents are currently used to treat UME patients that fail conventional therapies based on clinical evidence from off-label use in UME patients

VEGF levels are elevated in aqueous humor of uveitis patients with macular edema vs without macular edema<sup>1</sup>



Combined therapy of anti-VEGF with STA led to faster and greater reduction in CMT and UME resolution vs STA alone<sup>2</sup>





## **KSI-501ABC**

Bispecific Antibody Biopolymer Conjugate

### KSI-501ABC for high prevalence retinal diseases: maintains signature durability of the ABC platform while benefiting from learnings of tarcocimab program

- KSI-501ABC is currently in a Ph1 study in DME patients and aims to evaluate safety, tolerability and early signals of bioactivity; data is expected in 1Q24
- Further studies will be conducted with a commercial formulation that contains a defined ratio of unconjugated bispecific proteins and bioconjugates and is expected to improve injectability / user experience and mitigate cataract events while maintaining the signature durability of the platform
- Exploring initiation of dual Ph 2/3 pivotal studies in 2024 in high prevalence retinal vascular diseases, potentially with early interim analysis to support accelerated development towards pivotal data

Phase 1 study of KSI-501ABC has completed enrollment of DME patients; data to be shared at Angiogenesis, Exudation, and Degeneration 2024 virtual meeting



- Multiple ascending dose design
- 3 subjects enrolled for each dosing group, with option for expansion if indicated
- Each subject receives 3 monthly doses and will be followed for 24 weeks total
- Enrollment across all dose levels are completed; last patient last visit expected Jan 2024

#### **Key Inclusion Criteria**

- Adults ≥21 years of age
- Diabetes mellitus type 1 and 2 (HbA1c ≤12%)
- Vision loss due to DMF
  - BCVA between 25 and 70 ETDRS letters (20/40 20/320 Snellen)
  - DME (CST 320 microns)
- Treatment naïve or previously treated with defined washout period

### KSI-501P and KSI-501ABC in summary

#### KSI-501P – unconjugated bispecific protein

- Novel anti-IL-6 and VEGF trap bispecific protein being developed in retinal inflammatory diseases
- Risk profile uncoupled from ABC platform-derived pipeline & defines a new market segment separate from the established anti-VEGF market
- Development path with sham / placebo comparator, smaller sample sizes and shorter duration to primary endpoint
- Ph1/2 expansion study planned for 1H24 with plans to initiate Phase 2/3 pivotal studies in 2024 with early interim analysis

### KSI-501ABC – ABC platform commercial formulation with a defined ratio of unconjugated protein and bioconjugate

- Novel anti-IL-6 and VEGF trap bispecific antibody biopolymer conjugate being developed in high prevalence retinal vascular diseases
- Revised formulation is expected to improve injectability and mitigate cataract risks while maintaining the signature durability of the ABC platform
- Plans to initiate Phase 2/3 pivotal studies in 2024 with early interim analysis
- Development path to be accelerated with the goal of obtaining interim if not topline pivotal data within 2 years

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# WHERE WE ARE TODAY

- Pipeline of three clinical prospects moving forward expeditiously to achieve pivotal value inflections in 2 3 years
- \$346M in cash and cash equivalents as of the end of 3Q23
- Maturing investments in retina product platforms and technology to enable business development and/or pipeline

