



Innovation In  
Ophthalmology

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**Corporate Overview**

*May 2021*

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# Disclaimers and Notices

This presentation contains forward looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, that involve substantial risks and uncertainties, including statements regarding Company's products, EYSUVIS®, for the short term (up to two weeks) relief of the signs and symptoms of dry eye disease, INVELTYS®, the first and only topical twice-daily ocular corticosteroid for treatment of post-operative inflammation and pain following ocular surgery; the Company's plans to expand its sales force to approximately 105 ophthalmic sales professionals by the start of the third quarter of 2021, with a subsequent expansion to 125 expected by year-end, pending continued growth in payer coverage and the status of the COVID-19 pandemic; the status of insurance coverage and the availability of reimbursements for EYSUVIS and INVELTYS for commercial and Medicare Part D patients; the commercial potential for EYSUVIS and INVELTYS; Kala's plans to advance its preclinical pipeline of programs and the potential benefits of such programs; and the Company's expectations regarding its use of cash, cash runway and projected revenues. All statements, other than statements of historical facts, contained in this presentation, including statements regarding the Company's strategy, future operations, future financial position, future revenue, projected costs, prospects, plans and objectives of management, are forward looking statements. The words "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "should," "target," "will," "would," and similar expressions are intended to identify forward looking statements, although not all forward-looking statements contain these identifying words. The Company may not actually achieve the plans, intentions or expectations disclosed in its forward-looking statements, and you should not place undue reliance on such forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements as a result of various risks and uncertainties including, but not limited to: the impact of extraordinary external events, such as the current pandemic health event resulting from the novel coronavirus (COVID-19), and their collateral consequences, including disruption of the activities of the Company's sales force and the market for EYSUVIS and INVELTYS; whether the Company will be able to successfully implement its commercialization plans for EYSUVIS and INVELTYS; whether the market opportunity for EYSUVIS and INVELTYS is consistent with the Company's expectations and market research; the Company's ability execute on the commercial launch of EYSUVIS on the timeline expected, or at all, including obtaining Commercial and Medicare Part D payor coverage; whether the Company will be able to generate its projected net product revenue on the timeline expected, or at all; whether the Company's cash resources will be sufficient to fund the Company's foreseeable and unforeseeable operating expenses and capital expenditure requirements for the Company's expected timeline; other matters that could affect the availability or commercial potential of EYSUVIS and INVELTYS; and other important factors, any of which could cause the Company's actual results to differ from those contained in the forward-looking statements, any of which could cause the Company's actual results to differ from those contained in the forward looking statements, discussed in the "Risk Factors" section of the Company's Annual Report on Form 10-K, most recent Quarterly Report on Form 10-Q and other filings the Company makes with the Securities and Exchange Commission.

All information in this presentation is as of May 5, 2021 and should not be considered current after such date. We do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

# Kala is a biopharmaceutical company focused on the discovery, development and commercialization of innovative therapies for diseases of the eye

## Portfolio of Innovative Therapies



- Two marketed products that utilize Kala's proprietary AMPPLIFY® mucus-penetrating particle (MPP) Drug Delivery Technology to address unmet medical needs in Dry Eye Disease and post ocular surgery
- Pipeline with multiple proprietary NCE development programs targeted to address front and back of eye diseases
- Kala holds worldwide rights and IP on all marketed products and pipeline assets

## R&D to Commercial



- Approximately 190 employees
- Recently expanded ophthalmic sales, marketing and market access teams brings proven experience in eye care space
- Deep expertise in discovery, clinical operations and regulatory affairs for both front and back of the eye diseases

## Strong Cash Position



- Cash, cash equivalents and short-term investments of \$156.0 million as of March 31, 2021
- Existing cash resources, along with anticipated revenue from EYSUVIS and INVELTYS, expected to enable funding of operations for at least two years

# Kala Team



**MARK IWICKI**

Chairman, President and Chief  
Executive Officer



**TODD BAZEMORE**

Chief Operating  
Officer



**KIM BRAZZELL, PHD**

Chief Medical Officer



**HONGMING CHEN, SCD**

Chief Scientific Officer



**MARY REUMUTH, CPA**

Chief Financial Officer



**ERIC L.  
TRACHTENBERG**  
General Counsel and  
Chief Compliance Officer



**SUSAN COULTAS, PHD**

SVP, Clinical Development



**NIRANJAN  
KAMESWARAN, PHD**

SVP, Strategy



**KATE KLINE**

SVP, Marketing



**VINCENT KOSEWSKI**

SVP of Manufacturing and  
Supply Chain Management



**STEVEN ZHANG,  
MD, PHD**

SVP of  
Medical Affairs



# Kala Holds Worldwide Rights to a Portfolio of Promising Therapies



## Marketed Products

Two innovative therapies utilizing Kala's proprietary AMPPLIFY® Drug Delivery Technology to address medical needs for front of the eye

**EYSUVIS®**  
(loteprednol etabonate  
ophthalmic suspension) 0.25%

First and only prescription therapy specifically for the short-term management of the signs and symptoms of dry eye disease

**INVELTYS®**  
(loteprednol etabonate  
ophthalmic suspension) 1%

First and only BID corticosteroid indicated for the treatment of post-operative ocular inflammation and pain



## Internal Pipeline

Proprietary NCE development programs targeted to address front and back of the eye diseases

	Discovery	Lead Optimization	Candidate Selection	Formulation Development	IND-Enabling Studies	Clinical Studies
<b>Tyrosine Kinase Inhibitor</b> <i>Retinal diseases, including wet AMD, DME, and RVO</i>	→					
<b>Surface Targeting Steroid (STS)</b> <i>Corneal surface diseases</i>	→					
<b>Selective Glucocorticoid Receptor Modulator (SEGRM)</b> <i>Retinal diseases, including wet AMD, DME, and RVO; corneal surface diseases</i>	→					



# AMPPLIFY® Technology Overview

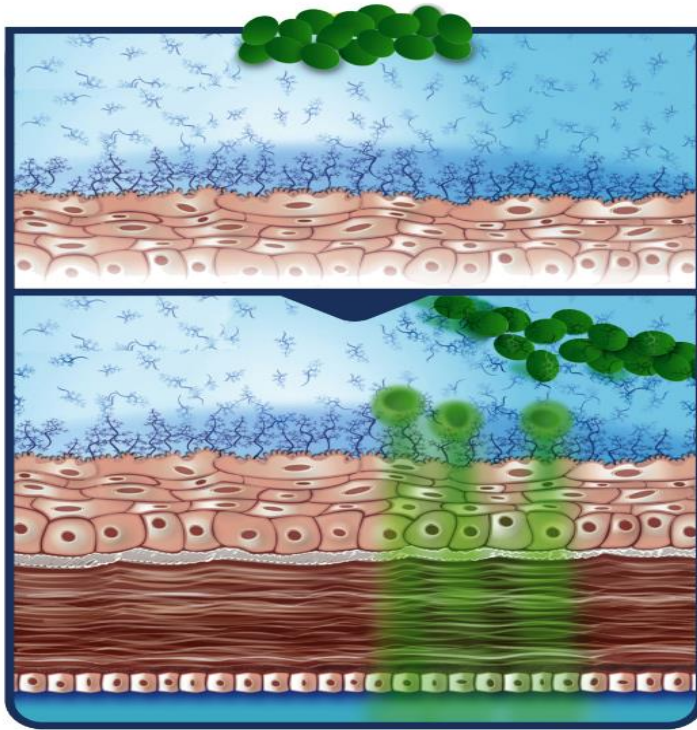
# Mucus is an Innate Defense Mechanism That Can Impair Drug Delivery

- Heterogeneous mesh of mucin fibers present in tear film and other protective coatings in the body
- Mucus binds drugs and other particulate matter to facilitate elimination via tear turnover:
  1. Small particles (<500 nm) penetrate into mucus pores and are bound by charged macromolecules inside the pores
  2. Large particles (larger than mucus pores) are bound to the surface of mucus

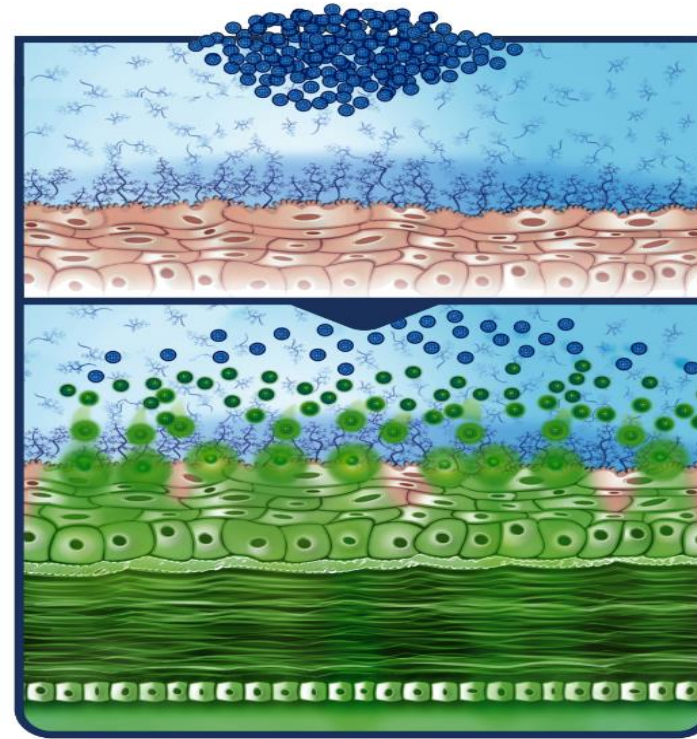
Sources: Olmstead et al. *Biophys J* 2001; Sigurdsson, Kirch & Lehr *Int J Pharm* 2013

**AMPPLIFY utilizes nanoparticles (~300 nm on average) engineered via surface modification to penetrate through mucus pores to the ocular surface without being bound up and eliminated by the tear film**

# AMPPLIFY Technology Increases LE Penetration to Corneal and Aqueous Humor by More Than 3x



Traditional suspension eye drops adhere to mucins and can be rapidly cleared through blinking

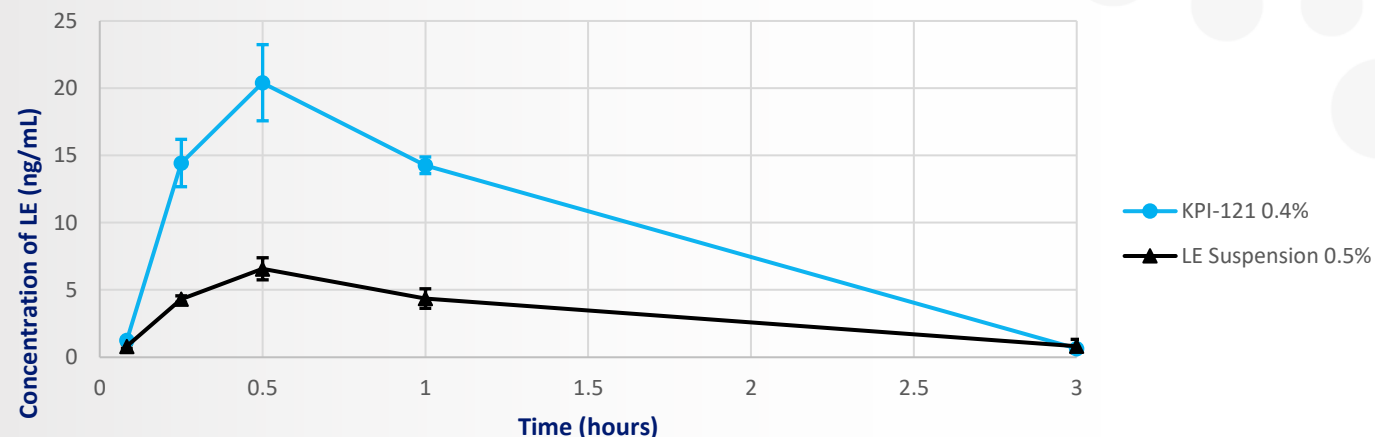


Drug particles formulated with **AMPPLIFY™ Drug Delivery Technology** are designed to enhance penetration through the mucus barrier and deliver increased concentrations of drug to the target ocular tissues

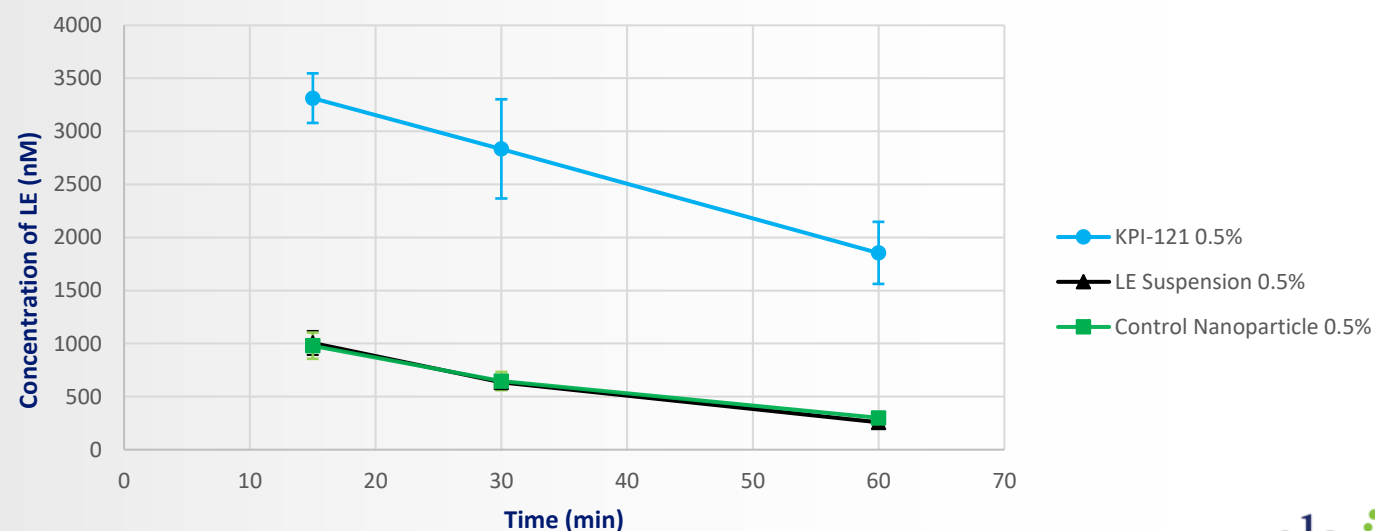
# Leveraging LE MPP to Enhance Delivery to Target Ocular Tissues

- KPI-121: MPP Ioteprednol etabonate (LE)
  - INVELTYS® (KPI-121 1%): Approved Product for Post-Surgical Pain & Inflammation with BID Dosing
  - EYSUVIS™ (KPI-121 0.25%): Approved Product for the Short-term Treatment of the Signs and Symptoms of Dry Eye Disease
- AMPPLIFY technology increases LE penetration to corneal and aqueous humor by more than 3x
- Aqueous Humor concentrations mediate resolution of inflammation following ocular surgery
- Corneal deposition is a key driver for Dry Eye efficacy and resolution of pain following ocular surgery

## LE in Aqueous Humor



## LE in Cornea



Preclinical data from rabbit studies



  
**EYSUVIS<sup>®</sup>**  
(loteprednol etabonate  
ophthalmic suspension) 0.25%

**Short-Term Treatment of Dry Eye Disease**

# EYSUVIS: Potential to Be the Preferred Prescription Therapy for Dry Eye Disease Flares

**EYSUVIS**<sup>®</sup>  
(loteprednol etabonate  
ophthalmic suspension) 0.25%

- 1 First and only prescription therapy specifically for the short-term (up to two weeks) treatment of the signs and symptoms of dry eye disease
- 2 75-90% of dry eye patients routinely experience dry eye flares
- 3 Opportunity to capture a large significant unmet need in dry eye with deep experience in eye care across the organization
- 4 Added to Express Scripts' National Preferred, Basic and High Performance Formularies; Preferred Position on Cigna, effective May 15
- 5 Strong IP position (2033) and proprietary manufacturing process

**Approved October 2020 with U.S. promotional launch in January 2021**

# Strong Demand and Positive Feedback for EYSUVIS to Treat DED Flares

## Strong Demand

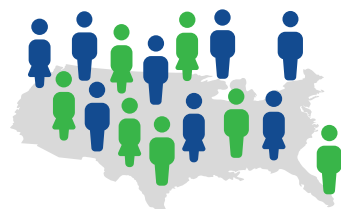
- Between January 2021 launch and April 23:
  - More than 11,600 prescriptions filled
  - More than 2,000 unique prescribers
- To date, more than half of prescriptions written by optometrists
  - Highlights physicians' unmet need for treatment
  - Creating new market segment for Kala



## Positive Feedback

- Qualitative feedback from Eye Care Professionals and patients highlight:
  - Rapid onset of action
  - Comfort of administration
- Quantitative feedback from Eye Care Professionals:
  - Nearly 80% are familiar with EYSUVIS
  - Almost 70% have prescribed or will prescribe EYSUVIS

# Market Overview



## 38M

U.S. prevalence of dry eye, of which **17.2M** have been diagnosed and are under the care of an Eye Care Professional<sup>1</sup>



## 75%

of dry eye patients have **never tried prescription therapy**<sup>2</sup>



## Only ~10%

of dry eye patients are currently on an Rx Chronic therapy<sup>3</sup>



## Only 2.9%

of dry eye patients receive Rx for off-label steroids<sup>3</sup>



## 6.1M

Chronic TRx per year<sup>4</sup>



## ~\$1.5B

Combined Net Revenue for Restasis, Cequa and Xiidra annually<sup>5</sup>



## 80%

of patients discontinue their chronic Rx medication by 4 months<sup>6</sup>



## 75–90%

of dry eye patients **routinely experience dry eye flares**<sup>7,8,9</sup>

1. 2019 Dry Eye Products Market Report, Market Scope, 2. Dry Eye Sufferers 2020 Multi-sponsor Survey, 3. Symphony Rx Data divided by DED Prevalence Study and validated with Market Scope data, 4. Symphony Health National Level Total Pack Unit Data – 52 weeks ending 8/14/2020, 5. Symphony Health Gross Dollar Data - 52 weeks ending 8/14/2020, 6. *NPA Market Dynamics IQVIA data, June 2018-June 2019, as reported in October 2019, Restasis (N=24,340) and Xiidra (N=13,037)* 7. Based on a survey of 297 patients commissioned by Kala and performed by a third party. 8. Based on a survey of 500 patients diagnosed with dry eye disease commissioned by Kala and performed by a third party. 9. Based on a survey of 774 patients performed by a third party.

# Majority of DED Patients Suffer from Episodic Flares, Not Continual Symptoms

## Dry Eye Disease (DED) Flare Definition<sup>1</sup>:

**Rapid-onset, inflammation-driven response** to a variety of triggers that **typically cannot be adequately managed with patient's current therapy** (e.g., artificial tears, chronic Rx therapies)

**~75-90%**

of all DED patients report they **suffer from flares**<sup>2,3,4</sup>

**~81%**

of patients on artificial tears report they **suffer from flares**<sup>4</sup>

**~91%**

of patients on prescription medications report they **suffer from flares**<sup>4</sup>

1. ASCRS EyeWorld. <https://www.eyeworld.org/download/file/fid/453>. Published May 2019. Accessed May 24, 2019.

2. Based on a survey of 297 patients commissioned by Kala and performed by a third party.

3. Based on a survey of 500 patients diagnosed with dry eye disease commissioned by Kala and performed by a third party.

4. Based on a survey of 774 patients performed by a third party.



Patients Suffer  
a Median of  
**5.5 Flares a year**<sup>4</sup>

# Eye Care Professional (ECP) Key Insights



ECPs believe there is an **opportunity to better manage many mild-to-moderate DED** patients that currently go untreated with Rx therapy because current therapies take too long to work, and often have significant tolerability issues



ECPs have a **large proportion of patients that suffer from flares**, and intend to discuss the topic of flares more proactively with patients now that there is an FDA-approved, short-term treatment option



ECPs cited **rapid relief and safety/tolerability profile of EYSUVIS as top advantages** vs. other DED therapies



ECPs indicate that **EYSUVIS is suitable for a wide variety of dry eye patients**, including chronic dry eye patients who may benefit from treatment for induction or breakthrough therapy, patients on an artificial tear only, and patients currently using an off-label steroid<sup>1</sup>



**ECPs are using EYSUVIS as a first-line treatment for dry eye flares:** Approximately 50% of EYSUVIS prescriptions are from new-to-market patients<sup>3</sup>

1. Symphony Vantage April 5, 2021 \*History defined as 12-month lookback on product classes.DE Market Defined as Restasis, Restasis MD, Xiidra, Cequa and EYSUVIS. Ocular steroid market includes Alrex, Dexamethasone, Durezol, Flarex, Fluorometholone, FML Fort, Inveltys, Lotemax, Lotemax SM, Loteprednol, ECP
2. Multi Wave Survey (200 ECPs) , Wave 1 Jan 25-27, Wave 2: Feb. 10-12, Wave 3: Feb. 26-Mar 2, Wave 4: March 18-13
3. Symphony Patient Source February 2021

# Key Patient Insights



Once diagnosed, patients are typically first recommended to try an OTC artificial tear, but **continue to suffer with symptoms from episodic DED flares**



**Continuous source of frustration** – Artificial tears provide minimal palliative relief, but do not address inflammation – Patients on current Rx therapy often report limited satisfaction due to unwanted side effects and the time it takes to work (slow onset of weeks to months)



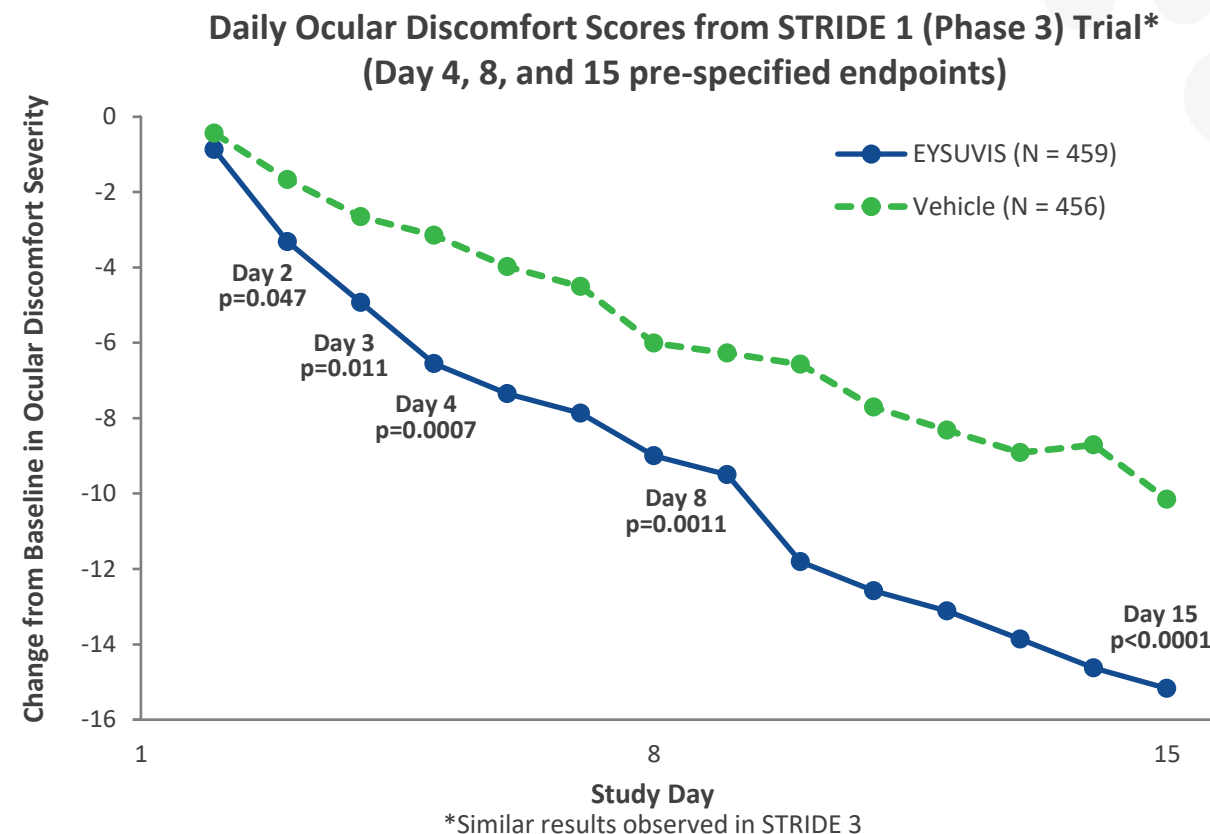
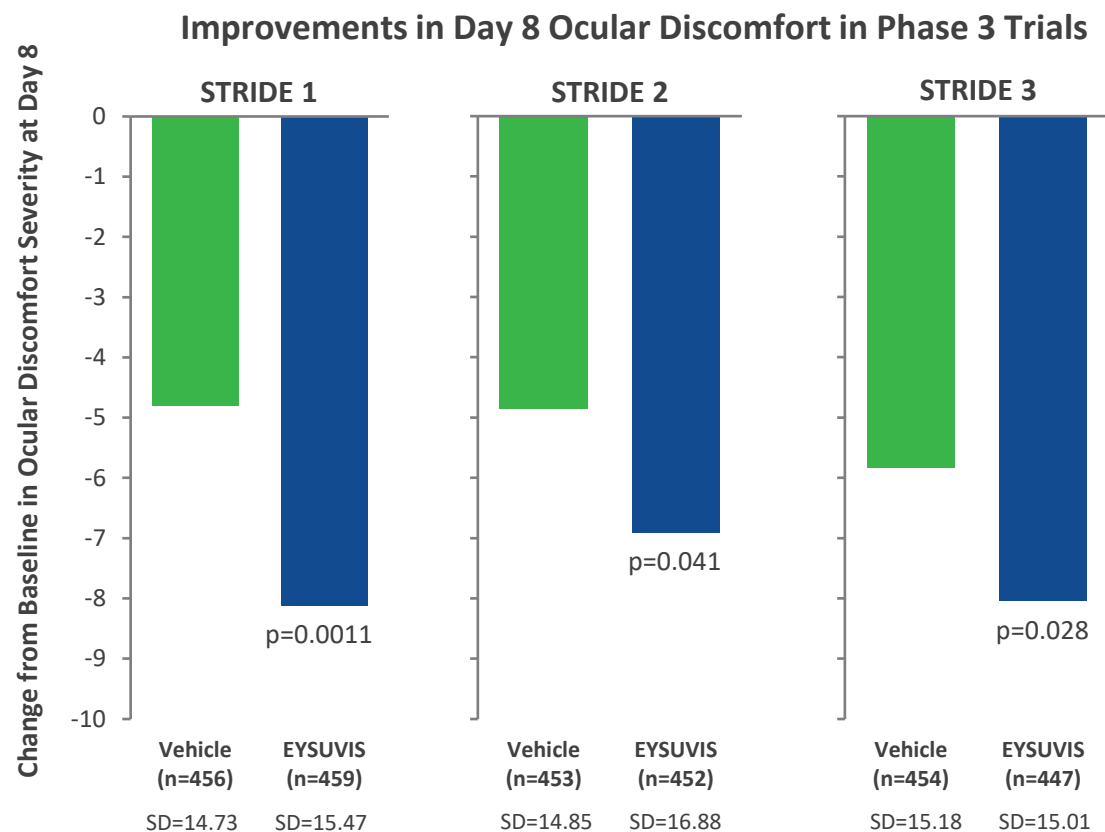
Regardless of DED severity, majority of patients say they suffer from flares and **desire a fast-acting treatment they can use short term**, during times when they are experiencing symptoms



Patients see EYSUVIS as a breakthrough therapy because it provides rapid relief and is used short term vs chronically – **90% of respondents report they intend to ask their ECP about EYSUVIS**



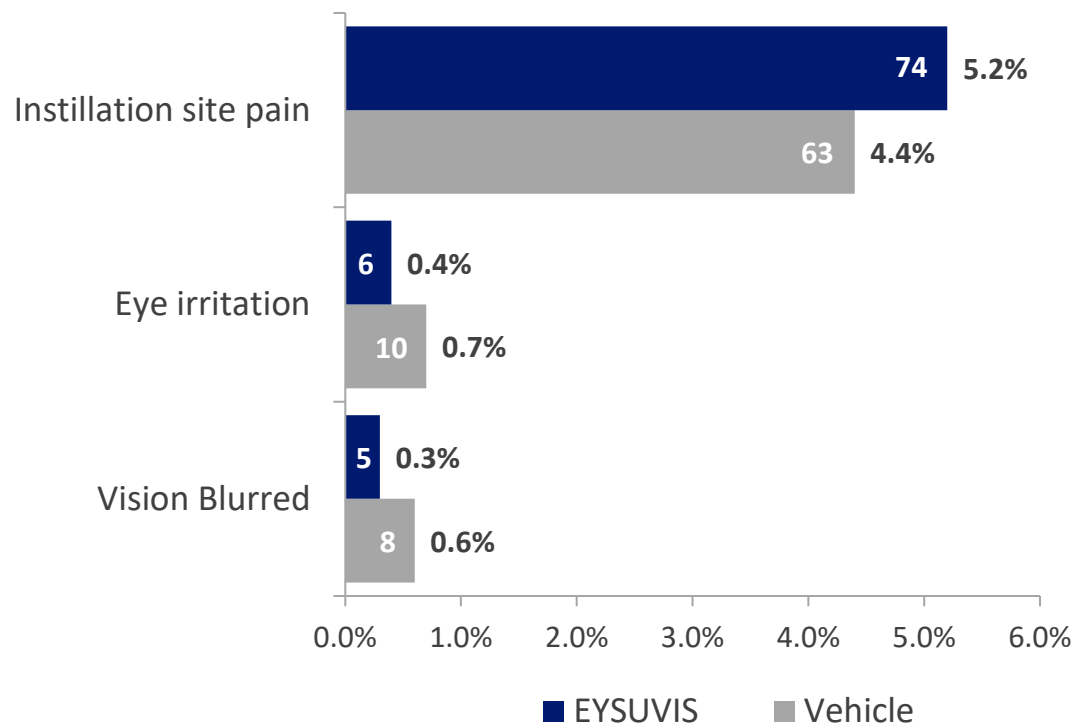
# Rapid Onset of Relief for Ocular Discomfort



- Day 8 and 15 were pre-specified efficacy endpoints in STRIDE 1, STRIDE 2 and STRIDE 3
- Day 4, Day 8 and Day 15 were pre-specified efficacy endpoints in STRIDE 1
- Day 2 and day 3 are exploratory efficacy endpoints in STRIDE 1
- p values for the Day 8 and day 15 results in each study were analyzed on the days following Day 7 and 14 using the 3 day mean prior to Day 8 (Days 5, 6 and 7) and the 3 day mean prior to Day 15 (days 12, 13 and 14) compared to the 3 day mean prior to Day 1 (Baseline)
- The daily ocular discomfort change from baseline data presented in the graph on the right are derived comparing the single day data from each time point to the 3 day mean prior to Day 1 (baseline)

# Pooled Safety Findings from Over 2,800 Patients Across Four Clinical Trials

## Percentage of Subjects Reporting Treatment-related Adverse Event by >0.3% of Subjects

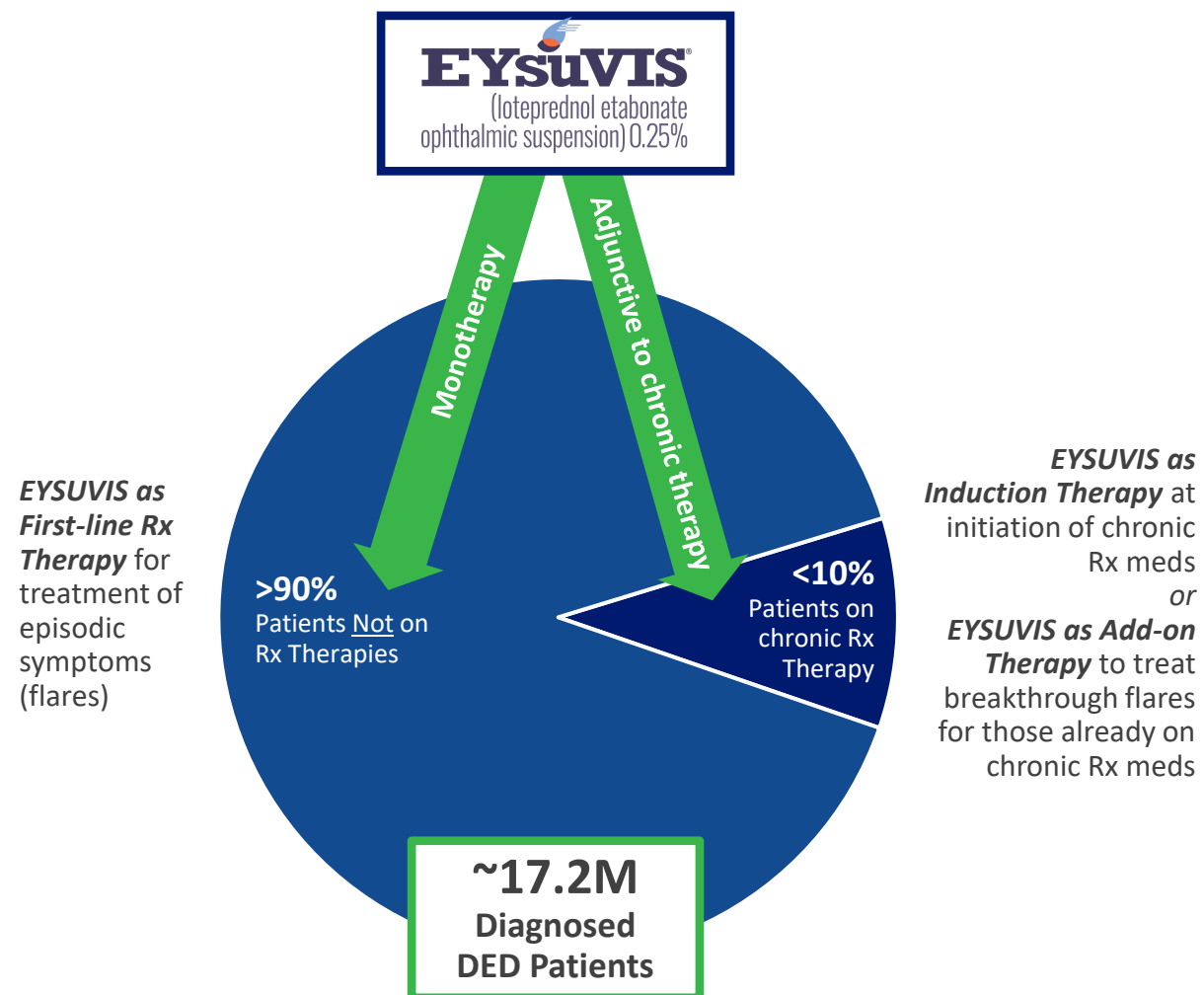


## Number (%) of Subjects with Increased Intraocular Pressure Compared with Baseline at any Postbaseline Visit

	Study Eye		Fellow Eye	
	EYSUVIS (n = 1430)	Vehicle (n = 1438)	EYSUVIS (n = 1430)	Vehicle (n = 1438)
≥ 10 mmHg increase from BL and ≥ 21 mmHg	3 (0.2%)	0	2 (0.1%)	1 (0.1%)

The most frequently reported treatment-related AE was instillation site pain, reported by 5.2% of subjects in the EYSUVIS group and 4.4% of subjects in the vehicle group

# EYSUVIS May Be Suitable for the Vast Majority of Patients with Dry Eye Disease



## Patients with DED are in the Office Seeking Treatment

**2-3x**

Patients with DED are in the Eye Care Professional (ECP) office an average of 2-3 times per year

**42%**

of annual ECP office visits are for DED flares

# EYSUVIS is Poised to Answer Unmet Needs in DED

- **Broad anti-inflammatory activity** addresses key driver of DED
- In clinical trials, **EYSUVIS** provided **rapid onset of relief** of signs and symptoms of DED
- In clinical trials, **EYSUVIS** was **well tolerated** with low incidence of IOP elevations (similar to vehicle)
- **EYSUVIS** is the **first and only** ocular corticosteroid indicated for dry eye disease

## Eye Care Professionals (ECPs) Prefer an On-label Steroid for DED:<sup>1</sup>

- Off-label steroids have varied safety profiles
- Risk of IOP elevation when prescribing steroids off-label
- The DED indication provides patient comfort and confidence
- Efficacy and safety reviewed by the FDA

**99%** of ECPs are interested in the availability of a steroid with a DED indication<sup>2</sup>

1. Third Party Qualitative Physician Market Research with 70 ECPs (34 OPH and 36 OPT).  
2. Quantitative Market Research with 201 ECPs (101 OPH and 100 OPT).



EYSUVIS Has  
Potential to Be the  
**Preferred Rx Therapy  
for DED Flares**

# Annual Total Addressable US Market for Dry Eye Disease Flares

**75-90%**<sup>1-3</sup>



of the 17.2M<sup>4</sup>

diagnosed  
DED patients  
experience

**Flares**<sup>1-3</sup>



Of these,

**~13-15M**

patients  
have about

**5.5 Flares**

per year<sup>4,5</sup>



**330M**

treatable

**Flare Days**

per year



- Only ~15% of diagnosed DED patients are currently on an Rx medication
- 75% of diagnosed DED patients have never tried prescription therapy
- Less than 3% of diagnosed DED patients receive a prescription for an off-label steroid
- U.S. Dry Eye Market expected to exceed \$2.6B in annual revenues by 2026<sup>6</sup>

1. Based on a survey of 297 patients commissioned by Kala and performed by a third party. 2. Based on a survey of 500 patients diagnosed with dry eye disease commissioned by Kala and performed by a third party. 3. Based on a survey of 774 patients performed by a third party. 4. Schaumberg et al, 2013, Prevalence of diagnosed dry eye in the US, MarketScope 2018 report – Diagnosed Dry Eye patients in the US; 5. Based on a survey of 297 patients commissioned by Kala and performed by a third party 6. Evaluatepharma Report: Available USA Sales by Indication (Indications) (Marketed & PII+) 8Jan2021



INVELTYS®: *FIRST AND ONLY* Approved  
BID Post-Surgical Steroid

# INVELTYS: The First & Only Post-Surgical Steroid Approved with BID Dosing



INVELTYS launched January 2019

INVELTYS is indicated to treat inflammation and pain following **ALL** ocular surgeries

INVELTYS is the **FIRST AND ONLY** post-surgical steroid shown to be effective and approved with BID dosing

INVELTYS has an excellent safety and tolerability profile, with IOP results similar to placebo

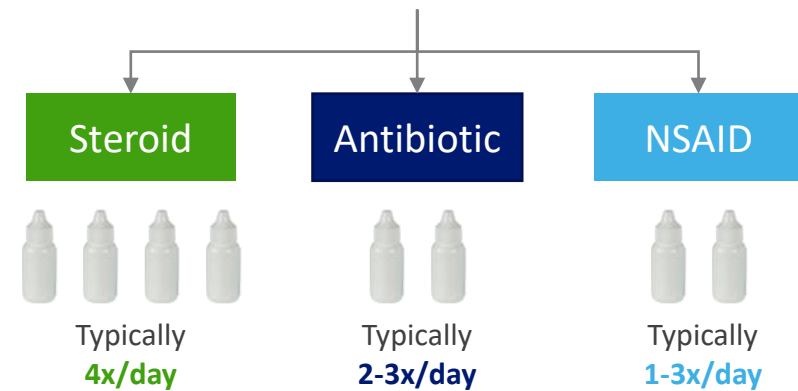
INVELTYS utilizes AMPPLIFY nanoparticle technology that delivers more loteprednol directly to the target ocular tissue while maintaining an excellent safety profile

# Steroids Are Standard of Care for Treating Inflammation and Pain Following Ocular Surgery

- Eye care professionals (ECPs) report prescribing steroids in greater than 90% of cataract, glaucoma and refractive surgeries<sup>1</sup>
- Current ocular steroids are approved for TID or QID dosing, which can lead to issues with adherence to the steroid regimen
- An effective and safe topical steroid with BID dosing would be a significant benefit in the management of patients following ocular surgery



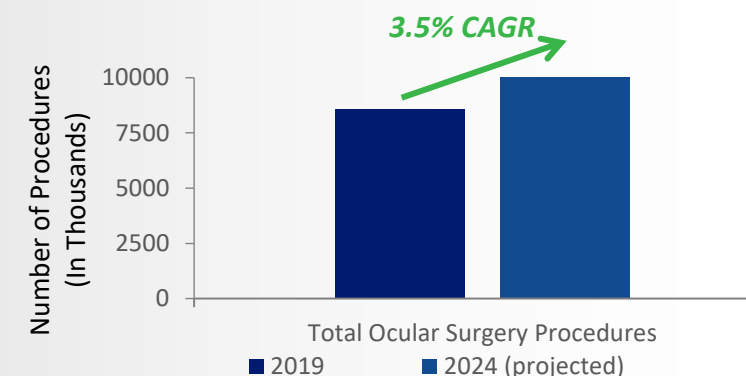
Typical Post-Cataract Surgery Treatment Regimen



# The Ocular Surgery Market is Large and Expected to Continue to Grow

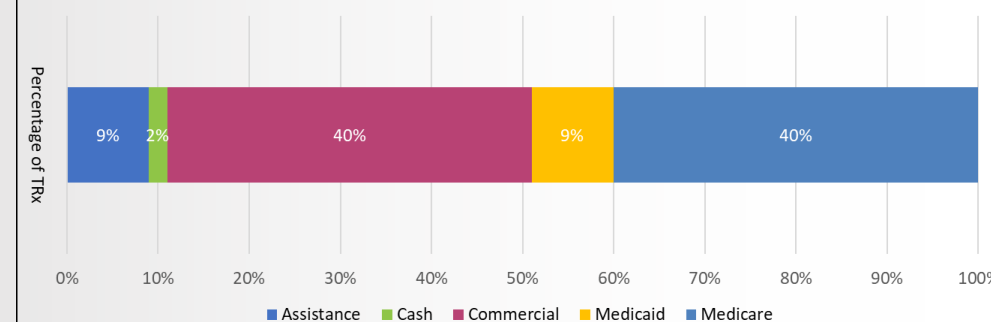
- ~8.6M ocular surgery procedures in 2019 in the U.S.; projected to grow at a CAGR of 3.5% through 2024<sup>1</sup>
- Branded products currently account for ~17% of prescriptions and ~41% of gross sales<sup>2</sup>
- At current branded prices, the market is estimated to be valued at ~\$1.9B<sup>2</sup>
- ~6,600 Eye Care Professionals (ECPs) account for 75% of the target surgical business and over 99.5% of INVELTYS business<sup>3</sup>
- Steroid market payer mix for Q1 2021 is 40% Commercial and 40% Medicare<sup>4</sup>

US Ocular Surgery Procedures, 2019-2024



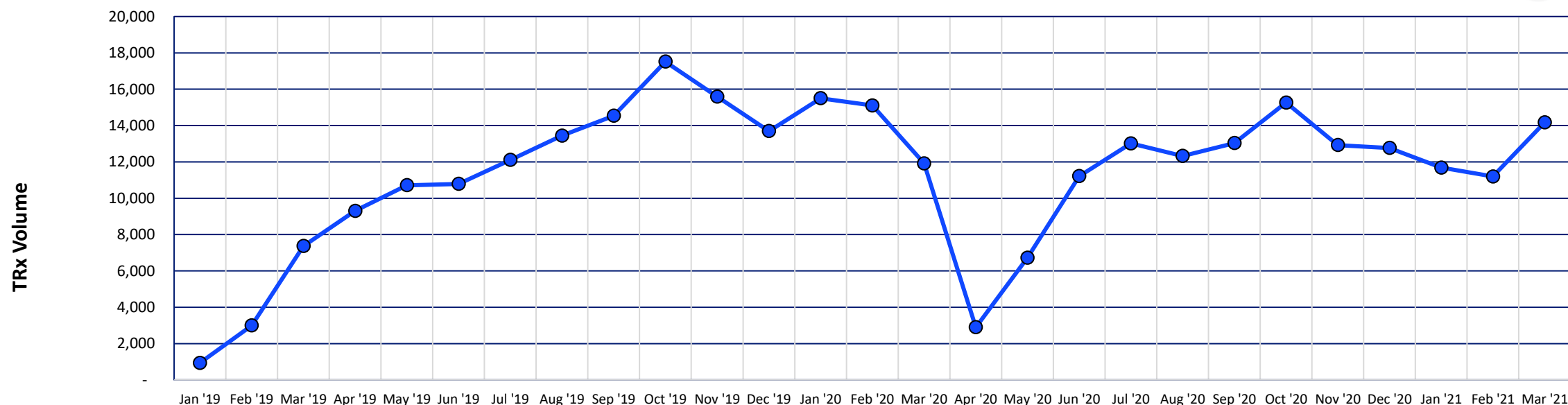
Steroid Market Payer Mix

January 2021 – March 2021, n = 2,104,287



1. Ocular Surgery Procedures: Market Scope US Procedures 2019, impact on growth rate expected in 2020 due to COVID-19; 2. Symphony PHAST December 2019-November 2020; 3. Symphony METYS and Symphony Prescriber December 2019-November 2020 4. Payer Mix based on MMIT channels mapped to Symphony TRx data for Q1 2021; Ocular Steroid Market includes INVELTYS, Prednisolone Acetate, Pred Forte, Lotemax, Durezol, FML, Alrex, Flarex, Flourometholone, Loteprednol Etabonate and Dexamethasone. Channel Notes: "Assistance" represents Copay TRx, "Commercial" includes TriCare, VA, PBM, and "Medicaid" includes Managed and Fee for Service.

# Strong INVELTYS Growth Despite COVID-19 Impact



- 1<sup>st</sup> Quarter 2021 – 37,057 TRx
- Achieved 11% TRx growth in 2020
  - 2020 – approximately 143,000 TRx
  - 2019 – approximately 129,000 TRx
- Steady growth back to pre-COVID prescription levels
  - Beginning in late April ocular surgeries were allowed to recommence in many parts of the country
  - Q4 TRx exceeded Q3 by approximately 8%



## Development-Stage Programs

# Significant Unmet Need Remains for Effective Therapies to Treat Retinal Disorders



## Wet Age-related Macular Degeneration

A leading cause of irreversible blindness and visual impairment worldwide



# 288M

Number of people living with macular degeneration is expected to reach **288 million worldwide by 2040**<sup>1</sup>



# 5.4M

By 2050, an estimated **5.4 million Americans** are expected to have wet AMD<sup>2</sup>



## Diabetic Retinopathy and Diabetic Macular Edema (DME)

The leading cause of vision loss in working adults



# 93M

Approximately **93 million people worldwide** have diabetic retinopathy<sup>3</sup>



# 16M

Number of **Americans** with diabetic retinopathy is expected to grow to **16 million by 2050**<sup>4</sup>



## Retinal Vein Occlusion (RVO)

Second most common cause of vision loss due to retinal vascular disease



# 16.4M

Globally, an estimated **16.4 million** adults are affected by RVO<sup>5</sup>



# 1.26M

Estimated number of patients with retinal vein occlusion in the US<sup>6, 7</sup>

1. National Institutes of Health. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5178091/>. Published December 2016. Accessed January 4, 2021.

2. National Eye Institute. <https://www.nei.nih.gov/learn-about-eye-health/resources-for-health-educators/eye-health-data-and-statistics/age-related-macular-degeneration-amd-data-and-statistics>. Published July 2019. Accessed February 19, 2021.

3. American Diabetes Association. <https://care.diabetesjournals.org/content/35/3/556>. Published March 2012. Accessed January 4, 2021.

4. American Journal of Managed Care. <https://www.ajmc.com/view/addressing-unmet-needs-in-diabetic-retinopathy>. Published October 2019. Accessed January 4, 2021.

5. National Library of Medicine. <https://pubmed.ncbi.nlm.nih.gov/20022117/>. Published February 2010. Accessed January 6, 2021.

6. Rogers S et al Ophthalmology 2010, 117(2): 313–9.

7. US Census Data 2020 [www.census.gov](http://www.census.gov) Accessed Jan 9, 2021


# Advancing Multiple NCE Development Programs Targeted to Address Front and Back of the Eye Diseases



## Internal Pipeline

Proprietary NCE development programs targeted to address front and back of the eye diseases

	Discovery	Lead Optimization	Candidate Selection	Formulation Development	IND-Enabling Studies	Clinical Studies
<b>Tyrosine Kinase Inhibitor</b> <i>Retinal diseases, including wet AMD, DME, and RVO</i>						
<b>Surface Targeting Steroid (STS)</b> <i>Corneal surface diseases</i>						
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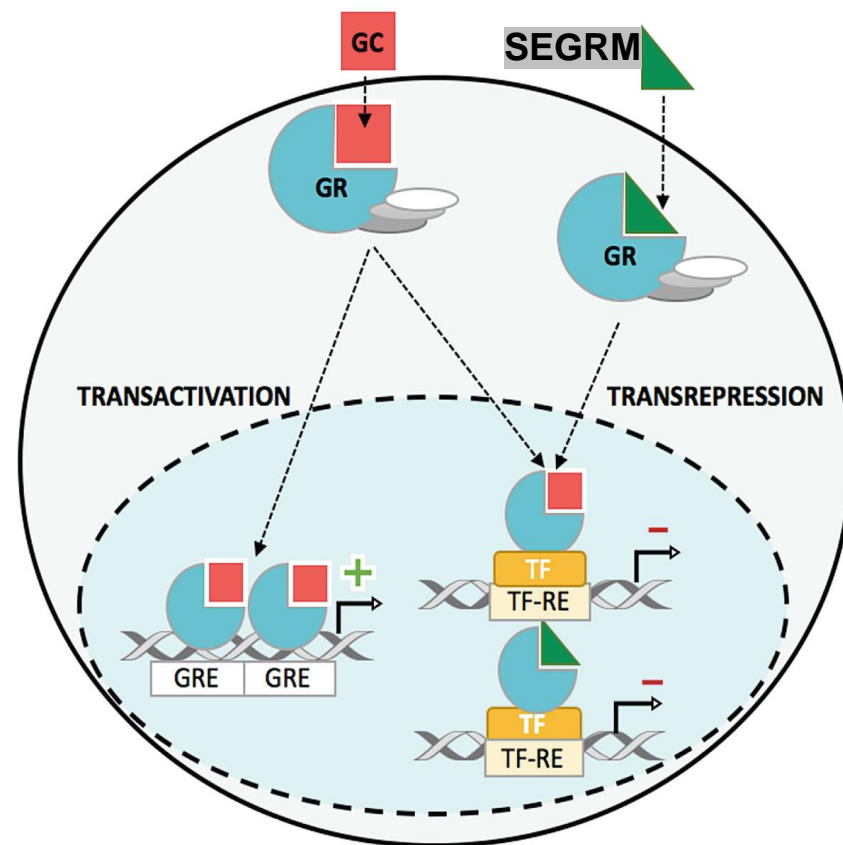
A close-up photograph of a human eye, looking slightly to the right. The image has a soft, ethereal quality with a color palette dominated by light blues and greens. The iris is a pale, hazy blue, and the pupil is dark. The eyelashes are visible, and the skin around the eye is smooth. Overlaid on the right side of the image are several semi-transparent circles in various shades of blue and white, creating a modern, scientific aesthetic. A semi-transparent white horizontal band runs across the middle of the image, serving as a background for the text.

# KPI-415: Selective Glucocorticoid Receptor Modulators (SEGRM)

# SEGRMs (Selective Glucocorticoid Receptor Modulators)

Novel Anti-inflammatory Compounds to Address Significant Unmet Needs in Ophthalmology and Systemic Diseases

- Activation of glucocorticoid receptor (GR) can result in regulation of gene expression along both the transactivation (TA) and transrepression (TR) pathways
- Considerable evidence that the TR pathway alone is sufficient for anti-inflammatory and immunomodulatory activity
- The TA pathway is thought to be responsible for the untoward effects associated with ocular and systemic administration of corticosteroids
  - Elevated IOP, hypertension, osteoporosis, skin atrophy, etc.
- SEGRMs:
  - Novel class of compounds designed to selectively regulate gene expression through the TR pathway, avoiding the TA pathway
  - Potential for comparable anti-inflammatory activity to the corticosteroid class of therapies without their associated side effects



# Kala Advancing Toward Lead SEGRM Candidate

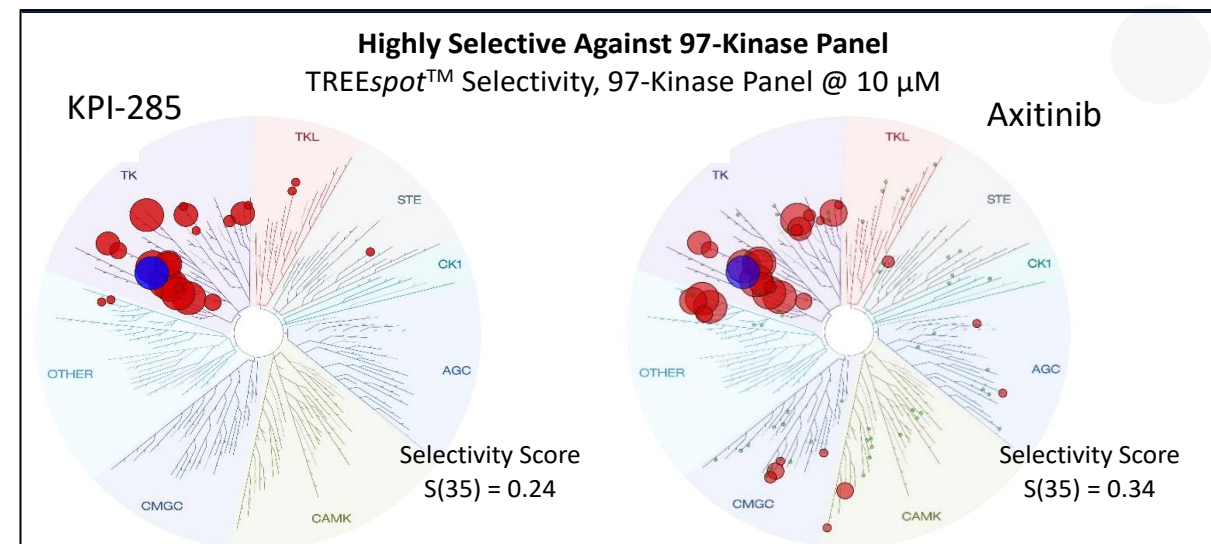
- Kala SEGRM program focused on developing novel NCEs that specifically target the TR pathway of the glucocorticoid receptor
  - Will address key unmet needs in both ophthalmic and systemic disease
- Target profile - Novel glucocorticoid receptor modulator with:
  - Potent anti-inflammatory and immunomodulatory effect with favorable therapeutic index
  - Favorable side effect profile, devoid of typical steroid side effects with both ocular and systemic administration
  - Ability to be safely administered long-term
- Good progress on program to date:
  - Promising *in vitro* selectivity data on several NCEs
  - Good separation of transrepression (TR) and transactivation (TA) effects
  - Program currently in Lead Optimization phase
  - Promising candidates moving into in vivo testing in 1Q 2021; targeting a lead compound by year-end 2021
- SEGRM product candidates also have potential to be developed for non-ophthalmic disease
- Kala owns all IP and WW rights

A close-up photograph of a human eye, looking directly at the camera. The image has a soft, ethereal quality with a color palette dominated by blues and greens. The iris is a light, hazy blue, and the pupil is dark. The surrounding skin and eyelashes are softly blurred. Overlaid on the right side of the image are several semi-transparent circles in various shades of blue and white, creating a modern, scientific aesthetic. A horizontal white band runs across the middle of the image, serving as a background for the text.

Potent and Selective NCE Tyrosine Kinase Inhibitor (TKI)

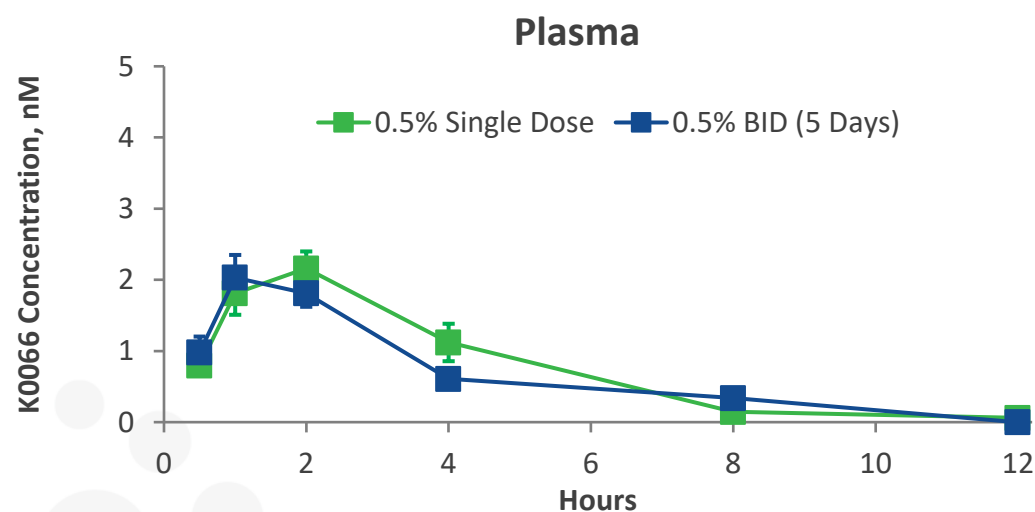
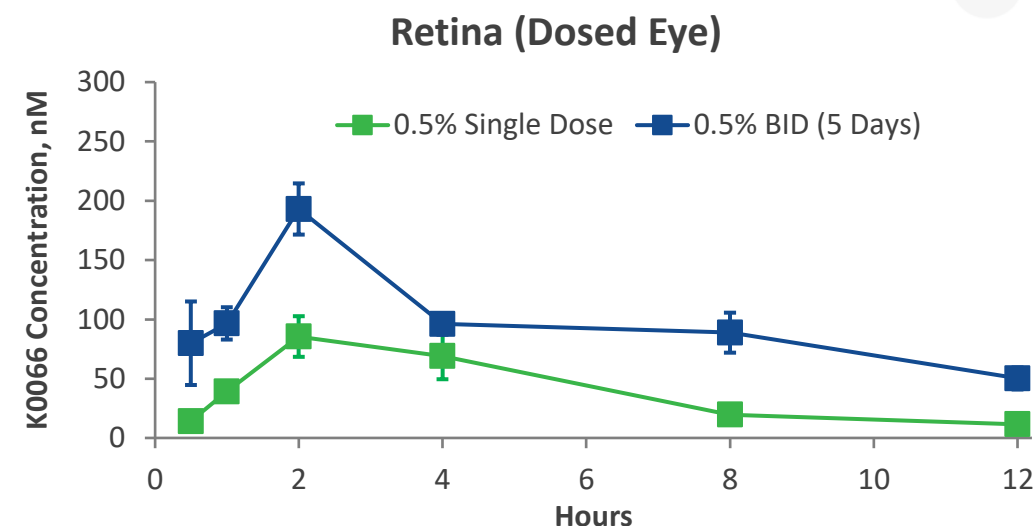
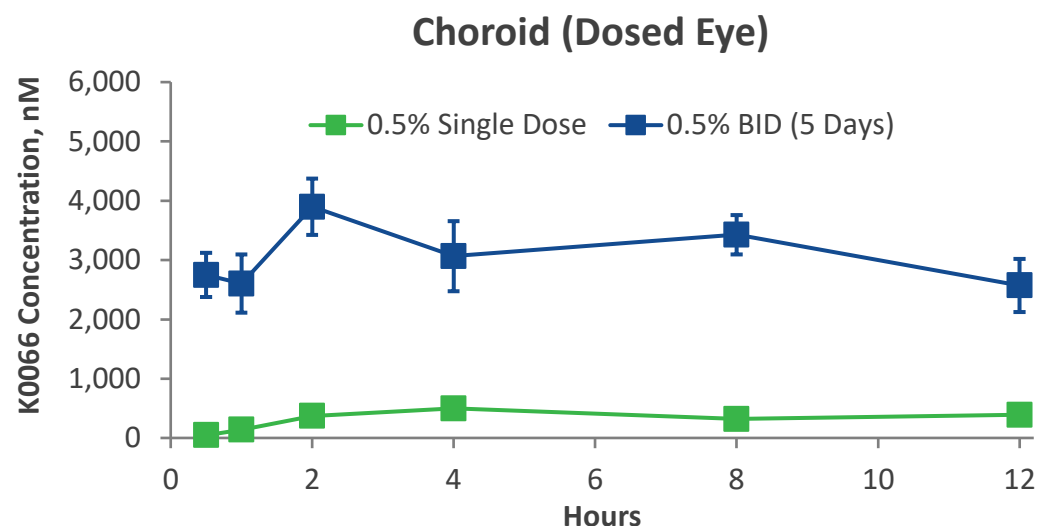
# Proprietary Potent and Selective NCE Tyrosine Kinase Inhibitor (TKI) for Treatment of Age-Related Macular Degeneration (AMD) and Other Retinal Diseases

- >100 NCEs synthesized and characterized
- Highly selective and potent lead compound identified
- Compelling preclinical PK and efficacy data generated with topical delivery (KPI-285)
  - Significant drug concentrations achieved in retina and choroid
  - Comparable efficacy to intravitreal Avastin in relevant animal model
  - Topical program (KPI-285) is ready to enter IND-enabling studies
- Injectable depot delivery for sustained delivery (KPI-286) currently in formulation development



Potent VEGFR-2 Inhibitor HUVEC IC <sub>50</sub> : 0.2 $\pm$ 0.1 nM (n=6)	
Target	K <sub>d</sub> (nM)
KDR (VEGFR-2)	0.5
FLT1 (VEGFR-1)	0.8
FLT4 (VEGFR-3)	6.2
PDGFRB	1.3
PDGFRA	0.2

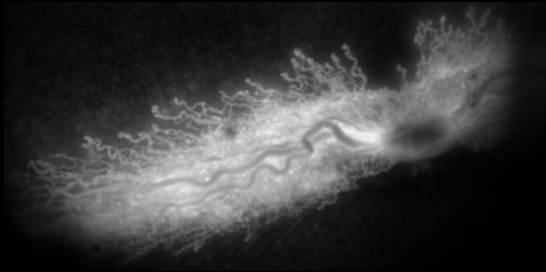
# KPI-285 Delivers Significant Levels to the Retina and Choroid in Rabbits



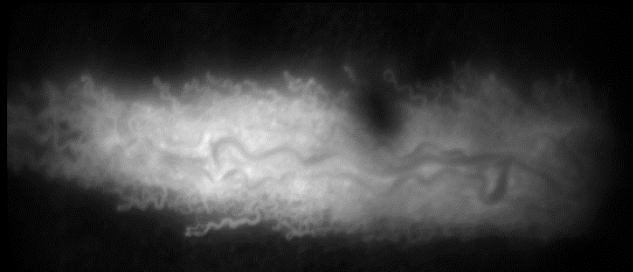
- MPP delivered back-of-eye concentrations well above  $IC_{50}$ 
  - Tissue to plasma ratio ~40–400 fold
- Multi-day dosing (5 days BID) vs. single dose results in:
  - 8-fold higher choroid levels
  - 2-fold higher retina levels
  - Little-or-no change in plasma levels

# KPI-285 Demonstrates Similar Efficacy to IVT Avastin in a Rabbit VEGF-induced Vascular Leakage Model

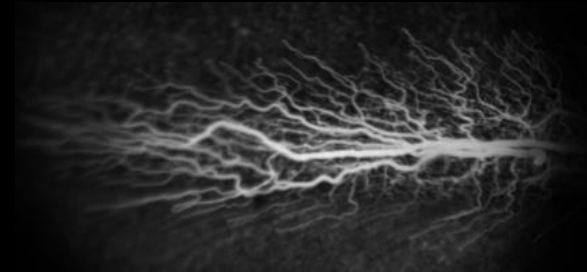
Vehicle  
Topical TID x 6 days  
Score = 3



Vehicle  
Topical every 4hrs x 6 days  
Score = 4



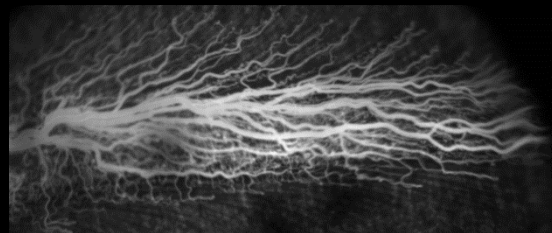
Avastin (IVT injected)  
Score = 0



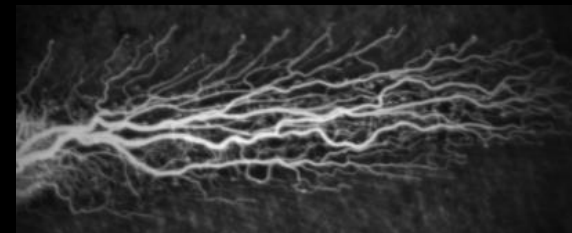
1.0% KPI-285  
Topical TID x 6 days  
Score = 2



1.0% KPI-285  
Topical every 4hrs x 6 days  
Score = 1



5.0% KPI-285  
Topical QID x 6 days  
Score = 0



No observed ocular irritation for KPI-285 (*Draize score*)

A close-up photograph of a human eye, looking slightly to the right. The eye is light-colored, and the eyelashes are visible. A white horizontal band runs across the middle of the image, containing the text 'KPI-333: Surface Targeted Steroid (STS)'. The background is a soft, out-of-focus blue and green. On the right side of the image, there are several semi-transparent blue circles of varying sizes, creating a bokeh effect.

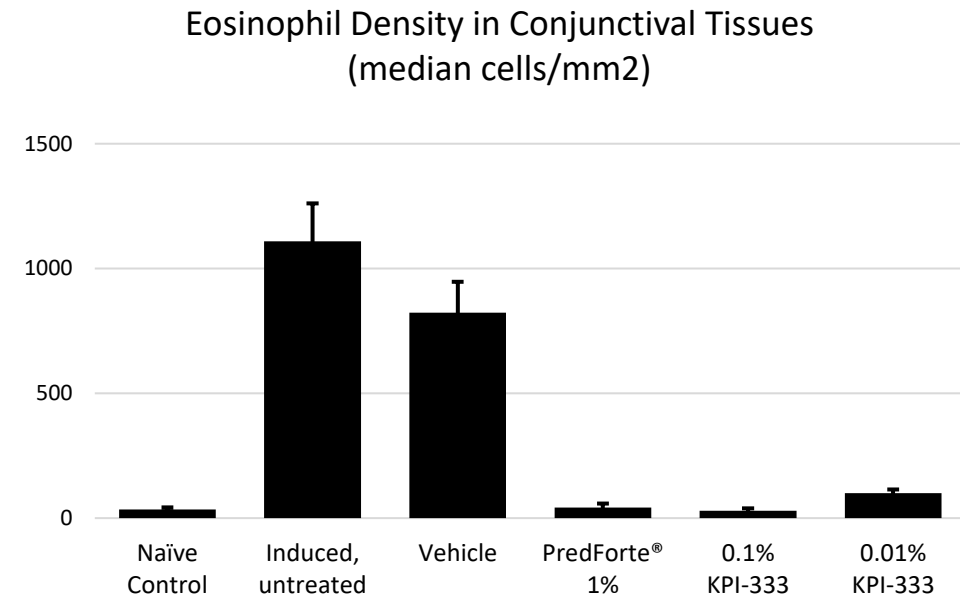
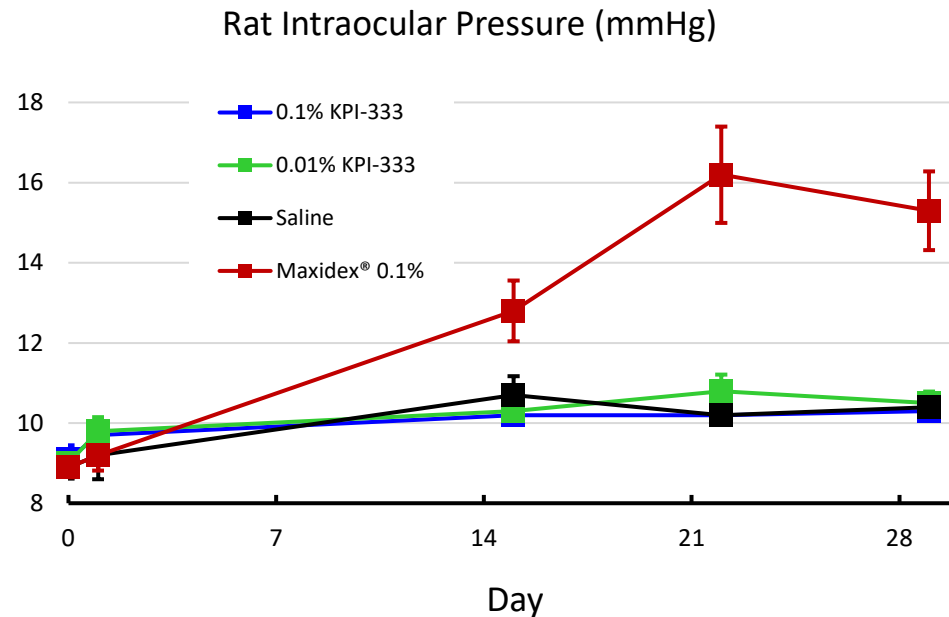
# KPI-333: Surface Targeted Steroid (STS)

# The Need for a Surface Targeted Steroid (STS)

- Corticosteroids are potent inhibitors of ocular surface inflammation
  - However long-term use is limited by significant untoward effects such as elevated IOP and cataract formation
  - These adverse events are mediated by absorption of the steroid into the aqueous humor and subsequent penetration into the trabecular meshwork and lens
- A topical steroid that targets the ocular surface without significant absorption into the aqueous humor could overcome the safety issues associated with long-term use of steroids
- A unique combination of potent anti-inflammatory activity, rapid onset of action and absence of impact on IOP and cataract would address a key unmet need for chronic management of ocular surface inflammation
- Kala is developing KPI-333, an NCE which has demonstrated the potential to be an effective STS in preclinical studies
- KPI-333 has the potential to address the significant unmet need for an effective chronic treatment of ocular surface inflammation associated with diseases such as dry eye

# Topical Administration of KPI-333 Demonstrates Strong Anti-inflammatory Activity Without Inducing IOP Elevation in Validated Animal Models

- No IOP elevation after repeated topical administrations to rats (BID for 28 days)
- Comparable efficacy to PredForte® 1% in an allergic conjunctivitis mouse model despite 10–100×-fold lower doses



# Kala is Positioned to be a Leader in Ophthalmics



- First and only prescription therapy specifically for the short-term (up to two weeks) treatment of the signs and symptoms of dry eye disease
- 75-90% of dry eye patients suffer from short-term, episodic flares
- Approved by FDA on October 26, 2020 with U.S. promotional launch in January 2021
- Added to Express Scripts' National Preferred, Basic and High Performance Formularies; Preferred Position on Cigna, effective May 15

- First and only post-surgical steroid with combination of powerful efficacy, a safety profile comparable to vehicle and approved for BID dosing
- Approved by FDA in August 2018 with U.S. launch in January 2019

- Deep experience in clinical development, commercial and medical affairs across multiple ophthalmic brands
- Expanded ophthalmic sales team deepens experience in dry eye and across overall eye care space

- Advancing multiple NCE development programs targeted to address front and back of eye diseases

- Cash, cash equivalents and short-term investments of \$156.0 million as of March 31, 2021
- Existing cash resources, along with anticipated revenue from EYSUVIS and INVETYS, expected to enable funding of operations for at least two years



**Thank You**

