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# kala...

#### Innovation In Ophthalmology

**Corporate Overview** *June 2019* 

#### **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 INVELTYS<sup>TM</sup> (loteprednol etabonate ophthalmic suspension) 1% for the treatment of inflammation and pain following ocular surgery and the development and regulatory status of KPI-121 0.25% for the temporary relief of the signs and symptoms of dry eye disease. All statements, other than statements of historical facts, contained in this presentation, including statements regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans and objectives of management, are forward-looking statements. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "target," "potential," "will," "would," "could," "should," "continue" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. 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 as a result of various risks and uncertainties including, but not limited to: whether the Company will be able to successfully implement its commercialization plans for INVELTYS; whether the market opportunity for INVELTYS is consistent with the Company's expectations and market research; uncertainties inherent in the availability and timing of data from ongoing clinical trials, and the results of such trials, including STRIDE 3; whether any additional clinical trials will be required prior to approval of the NDA filed for KPI-121 0.25%, or at all, and whether any such NDA will be approved; 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 INVELTYS and the Company's product candidates, including KPI-121 0.25%; and other important factors, 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 recently filed 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 June 18, 2019, 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.



#### Key Highlights

AMPPLIFY <sup>™</sup> Technology	<ul> <li>Proprietary AMPPLIFY<sup>™</sup> drug delivery technology to enhance delivery to target tissues of the eye</li> <li>IP protection for AMPPLIFY technology and products through 2033</li> </ul>
INVELTYS™	<ul> <li>Approved by FDA on August 22, 2018</li> <li>U.S. launch in January 2019</li> <li>FIRST &amp; ONLY post-surgical steroid with class-leading combination of powerful efficacy, safety profile comparable to vehicle, and BID dosing</li> </ul>
KPI-121 0.25% for Dry Eye Disease	<ul> <li>NDA filed with FDA in October 2018; PDUFA date of August 15, 2019</li> <li>STRIDE 3 Phase 3 trial initiated in July 2018; topline results anticipated Q4 2019</li> </ul>
Commercialization Strategy	<ul> <li>Retained worldwide commercial rights for INVELTYS and pipeline product candidates</li> <li>U.S. specialty sales organization fully hired and calling on eye care professionals</li> </ul>
Corporate Highlights	<ul> <li>Well capitalized, with existing cash as of March 31, 2019 projected to last through at least mid-2020, with additional runway when including revenue from INVELTYS</li> </ul>





## AMPPLIFY<sup>TM</sup> Technology Overview



#### Mucus Is An Innate Defense Mechanism That Can Impair Drug Delivery

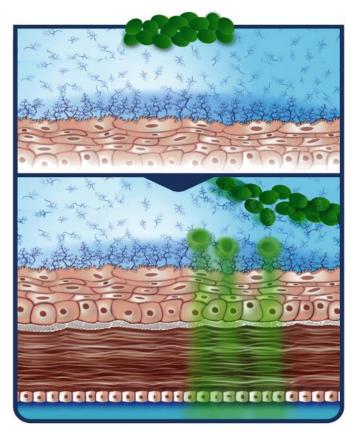
- Heterogeneous mesh of mucin fibers present in tear film and other protective coatings in the body
- Mucus binds drugs and other particulate matter to facilitate elimination via tear turnover:
  - 1. Small particles (<500 nm) penetrate into mucus pores and are bound by charged macromolecules inside 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 & LehrInt J Pharm 2013

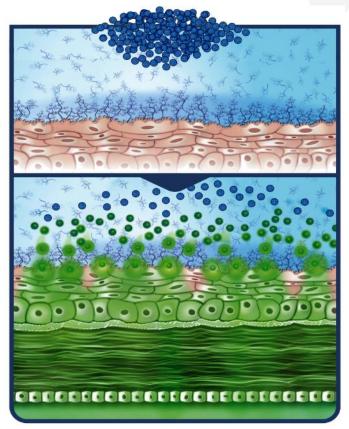
AMPPLIFY utilizes nanoparticles (~300 nm on average) engineered via surface modification to penetrate through mucus pores to the ocular surface without being bound up and eliminated by the tear film



#### In the Eye, AMPPLIFY<sup>TM</sup> Particles Penetrate Through Tear Film Mucins to Enhance Drug Delivery to Target Ocular Tissues



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



#### Drug particles formulated with AMPPLIFY™ Drug Delivery Technology

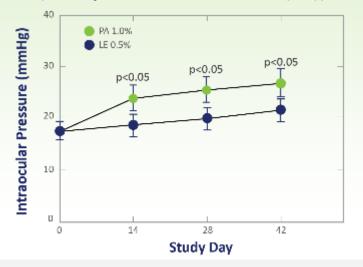
are designed to enhance penetration through the mucus barrier and deliver increased concentrations of drug to the target ocular tissues

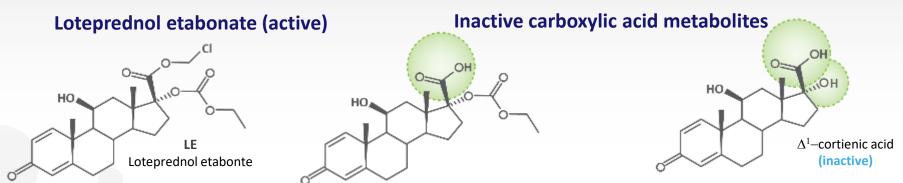


#### Loteprednol Etabonate (LE) Is A Potent Steroid With Improved Safety Characteristics

- Ester steroid differs from traditional ketone-based steroids by its metabolism to inactive metabolites
- 4.3X greater glucocorticoid receptor (GR) binding affinity versus dexamethasone
- Therapeutic effect followed by predictable singlestep de-esterification to inactive carboxylic acid metabolites
- Enhanced clinical safety relative to current ketone steroids
- Clinical efficacy/potency limited by poor penetration into ocular tissues

#### Effect on IOP in steroid responsive patients (LE vs prednisolone acetate (PA))



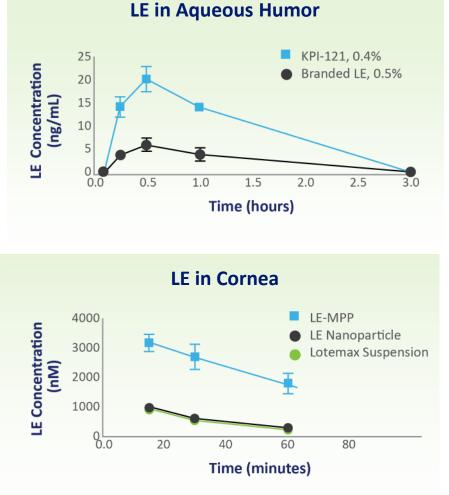




#### Sources: Comstock and DeCory, Int J Inflamm 2012; Bartlett et al, J Ocul Pharm 1993

#### Leveraging LE-MPP to Enhance Delivery to Target Ocular Tissues

- KPI-121: MPP loteprednol etabonate (LE)
  - INVELTYS<sup>™</sup> (KPI-121 1%): Approved
     Product for Post-Surgical Pain &
     Inflammation with BID Dosing
  - KPI-121 0.25%: Product Candidate for 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



Preclinical data from rabbit studies





## INVELTYS<sup>TM</sup>: FIRST AND ONLY Approved BID Post-Surgical Steroid



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

- INVELTYS Launch Meeting week of Jan 28<sup>th</sup>
- Launch WAC price of \$225/Rx
- Ophthalmology Sales organization and Corporate Account team calling on customers
- Commercial and Medicare co-pay assistance programs for eligible patients



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



#### Key Aspects of INVELTYS

- Indication Statement Covers All Ocular Surgery: "INVELTYS is a corticosteroid indicated for the treatment of post-operative inflammation and pain following ocular surgery."
- First FDA Approved Ocular Steroid With BID Dosing: "Instill one to two drops of INVELTYS into the affected eye twice daily beginning the day after surgery and continuing throughout the first 2 weeks of the post-operative period."
- Low Rates of Adverse Events: "The most common adverse drug reactions in the clinical trials with INVELTYS were eye pain and posterior capsular opacification, both reported in 1% of patients. These reactions may have been the consequence of the surgical procedure."
- Intraocular Pressure Results Similar to Vehicle
- Packaged Product Will Have 24 Months of Expiry Dating at Controlled Room Temperature
- No Additional Post-Approval Commitments



#### **INVELTYS Important Safety Information**

INVELTYS, as with other ophthalmic corticosteroids, is contraindicated in most viral diseases of the cornea and conjunctiva including epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, and varicella, and also in mycobacterial infection of the eye and fungal diseases of ocular structures.

A prolonged use of corticosteroids may result in glaucoma with damage to the optic nerve, defects in visual acuity and fields of vision. If this product is used for 10 days or longer, IOP should be monitored.

Use of corticosteroids may result in posterior subcapsular cataract formation.

Use of steroids after cataract surgery may delay healing and increase the incidence of bleb formation. In those diseases causing thinning of the cornea or sclera, perforations have been known to occur with the use of topical steroids. The initial prescription and renewal of the medication order should be made by a physician only after examination of the patient with the aid of magnification such as slit lamp biomicroscopy and, where appropriate, fluorescein staining.

Prolonged use of corticosteroids may suppress the host response and thus increase the hazard of secondary ocular infections. In acute purulent conditions, steroids may mask infection or enhance existing infection.

Use of a corticosteroid medication in the treatment of patients with a history of herpes simplex requires great caution. Use of ocular steroids may prolong the course and may exacerbate the severity of many viral infections of the eye (including herpes simplex).

Fungal infections of the cornea are particularly prone to develop coincidentally with long-term local steroid application. Fungus invasion must be considered in any persistent corneal ulceration where a steroid has been used or is in use.

In clinical trials, the most common adverse drug reactions were eye pain (1%) and posterior capsular opacification (1%). These reactions may have been the consequence of the surgical procedure.

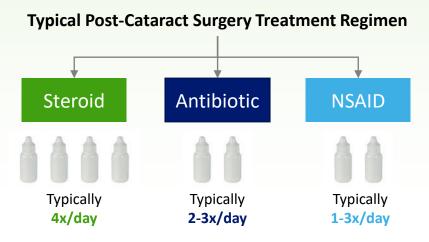
Please see the full prescribing information available at: www.inveltys.com



#### Steroids are Standard of Care for Treating Inflammation & Pain Following Ocular Surgery

- Eye care professionals (ECPs) report prescribing steroids in greater than 90% of cataract, glaucoma and refractive surgeries<sup>\*</sup>
- Current ocular steroids are approved for 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



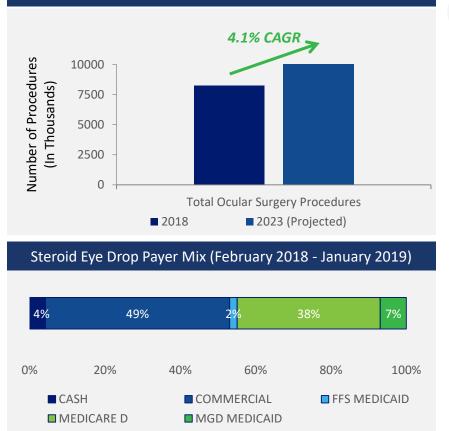




#### The Ocular Surgery Market is Large and Growing

- ~8.2M ocular surgery procedures in 2018 in the U.S.; projected to grow at a CAGR of 4.1%
- Branded products account for ~25% of prescriptions and ~60% of gross sales
- At current branded prices, the market is estimated to be valued at ~\$1.7B
- Approximately 6,500 Eye Care Professionals (ECPs) account for 80% of the target surgical business
- Steroid market payer mix is ~50%
   Commercial/Cash and ~38% Medicare

US Ocular Surgery Procedures, 2018-2023





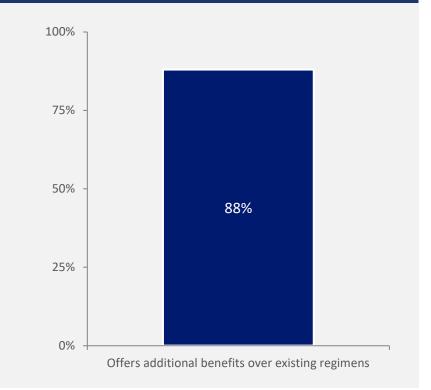
Sources: Ocular Surgery Procedures: Market Scope US Procedures data, 2017; Pricing: AnalySource data 2019;

Rx and Sales: IQVIA NPA and NSP data February 2018-January 2019; Payer mix: IQVIA FIA claims data February 2018-January 2019; Prescriber-level data: IQVIA Xponent Nov 2016-Oct 2017; Ocular Steroid Market includes INVELTYS, Prednisolone Acetate, Pred Forte, Lotemax, Durezol, FML, Flarex, Flourometholone and Dexamethasone

#### Our Market Research Indicates INVELTYS Could Address Key Treatment Gaps with Current Products\*

- Currently ECPs make tradeoffs when selecting ocular steroids for patients
  - Some steroids are viewed to be efficacious but carry a higher risk of IOP increases
  - Others are perceived to be less effective but with a more favorable IOP profile
  - All currently marketed steroids, generic and branded, are only approved for 4x/day dosing
- INVELTYS is viewed to address key unmet needs for ocular surgery patients by delivering strong efficacy with a favorable safety profile and less frequent dosing
- 88% of ophthalmologists report they believe INVELTYS will offer an advantage over existing treatment options

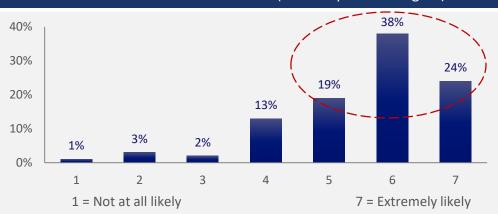
#### Perception of INVELTYS Benefit Over Existing Treatment Options\* (n=100 Ophthalmologists)



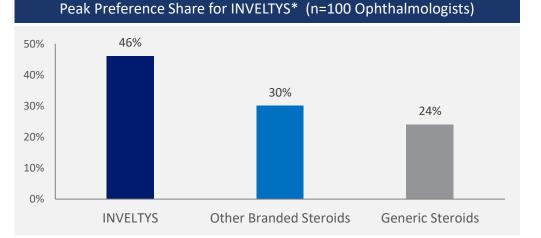


## Surveyed Ophthalmologists Rate the INVELTYS Profile as Highly Compelling and Express Strong Intent to Prescribe\*

- Ophthalmologists indicated that INVELTYS will be an important addition to their treatment options
- 81% of Ophthalmologists report that they are "Likely" to "Extremely Likely" to prescribe INVELTYS
- Ophthalmologists had a 46% stated peak preference share for INVELTYS based on the market today
- Future generic availability of Lotemax<sup>®</sup> and Durezol<sup>®</sup> still results in a stated peak preference share of 40% for INVELTYS



#### Likelihood to Prescribe INVELTYS\* (n=100 Ophthalmologists)



#### We expect INVELTYS peak net revenues in the U.S. to be in excess of \$300M



#### **INVELTYS Launch In Full Swing**

**Reprint and Carrier:** Phase III INVELTYS data published in Clinical Ophthalmology



**Rep Promotion:** Sales Aid, Coupon card, Journal Ads



INVELTYS Early Experience Program: Trade size samples sent to top cataract surgeons to gain early trial of INVELTYS



**INVELTYS Supplement:** 4 KOLs discuss how INVELTYS helps control pain and inflammation published in Cataract Refractive Surgery Today



# Medical Educational Programs



#### Increasing INVELTYS Awareness at National and Local Conferences

#### **2019 National Conferences**

- January: Hawaiian Eye
- February: Controversies in Cataract Surgery, South Eastern Optometry Conference (SECO)
- March: Vision Expo East
- April: Cornea 360, American Research in Vision and Ophthalmology (ARVO)
- May: American Society of Cataract and Refractive Surgeons (ASCRS)
- June: American Optometric Association (AOA)
- September: Vision Expo West
- October: American Academy of Ophthalmology (AAO)
- November: American Academy of Optometry (AAOpt)

#### 2019 Regional and Local Conferences

 March-December: 50-75 local/regional programs across the country





#### **INVELTYS Commercial Opportunity: Summary**

- The ocular surgery market is large, with ~8.2M procedures in 2018 in the U.S. and projected to grow at a CAGR of 4.1% over the next 5 years
  - Branded steroids account for ~25% of TRxs and ~60% of sales
- There is an unmet need for a product that delivers strong efficacy with a favorable safety profile and less frequent dosing
- INVELTYS is the *FIRST AND ONLY* post-surgical steroid proven effective and approved with BID dosing (all other steroids only approved for QID dosing)
- Ophthalmologists see a need for INVELTYS in their treatment regimens\*:
  - 88% view INVELTYS as offering a benefit over current treatment options
  - 81% are "Likely" to "Extremely Likely" to prescribe INVELTYS
  - 46% stated peak preference share for post-operative use
- U.S. launch in January 2019; specialty sales organization of 57 sales representatives and 7 sales managers fully on-boarded and calling on eye care professionals
- Corporate account director team in place and calling on payor customers
- We expect INVELTYS peak net revenues in the U.S. to be in excess of \$300M





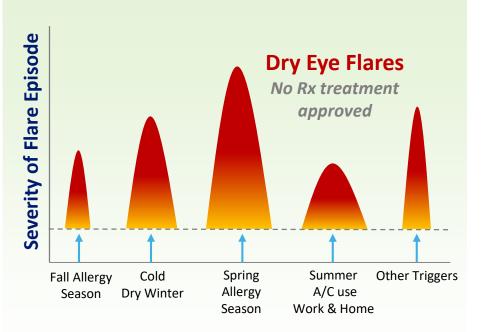
## KPI-121 0.25% for Dry Eye Disease



#### Dry Eye Is An Inflammation Driven Ocular Surface Disease

## ~90% of surveyed dry eye patients experience flares and the majority have multi-day episodes<sup>1</sup>

- Dry eye disease is a chronic, episodic disease of ocular inflammation
  - Ocular surface inflammation and tear film instability lead to discomfort, visual disturbances, hyperemia, and tissue damage
- ~33 million people in the U.S. with dry eye, ~16 million of whom are diagnosed<sup>2</sup>
- For most patients, dry eye is an episodic disease, not one of continual symptoms
  - Patients have symptom "flares" that wax and wane in response to environmental triggers
  - For these patients, chronic therapy may not be necessary or appropriate
- Currently there is no approved product for the short-term rapid relief of episodic symptoms (i.e., flares)



#### **Episodic Flare Drivers**

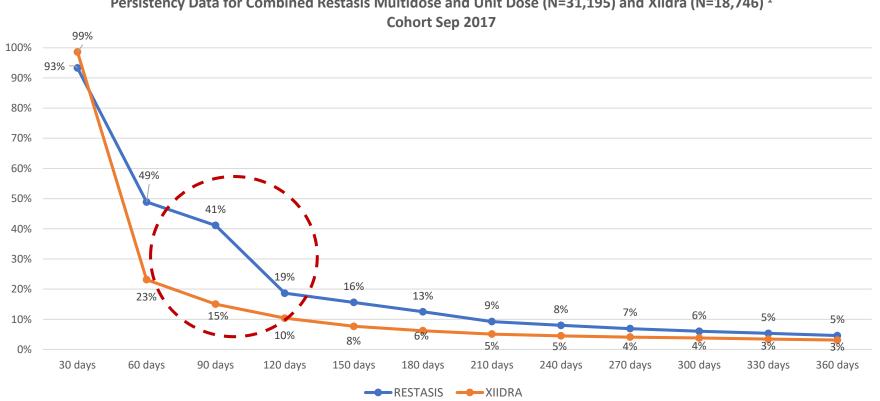
This graphic is included for illustrative purposes only



<sup>1</sup>Kala survey of 503 diagnosed dry eye patients, December 2017

<sup>2</sup>Source for dry eye disease market data: Epidemiology research commissioned by Kala and performed by a third party

#### Most Patients Discontinue Chronic Dry Eye Therapies Within 3-4 Months of Initiation of Treatment



Persistency Data for Combined Restasis Multidose and Unit Dose (N=31,195) and Xiidra (N=18,746)<sup>1</sup>

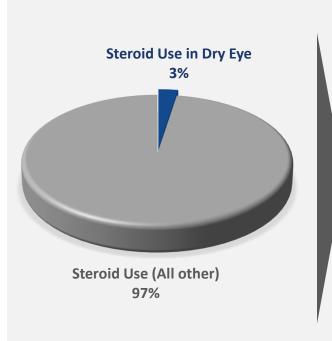
The main reasons cited by patients for discontinuing Restasis and Xiidra were insufficient efficacy and side effects<sup>2</sup>

<sup>1</sup> NPA Market dynamics IMS data, October 2018 <sup>2</sup> Kala survey of 503 diagnosed dry eye patients, December 2017

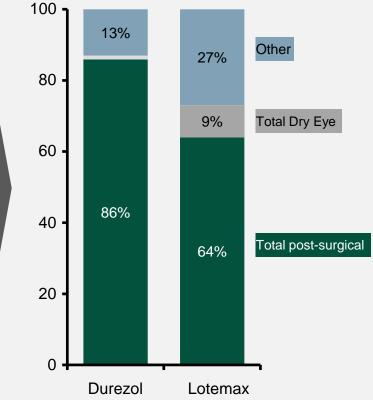


#### Dry Eye Represents a Very Small Percentage of Ophthalmic Steroid Use

#### Use in Dry Eye for all ophthalmic steroids (2011-2017)



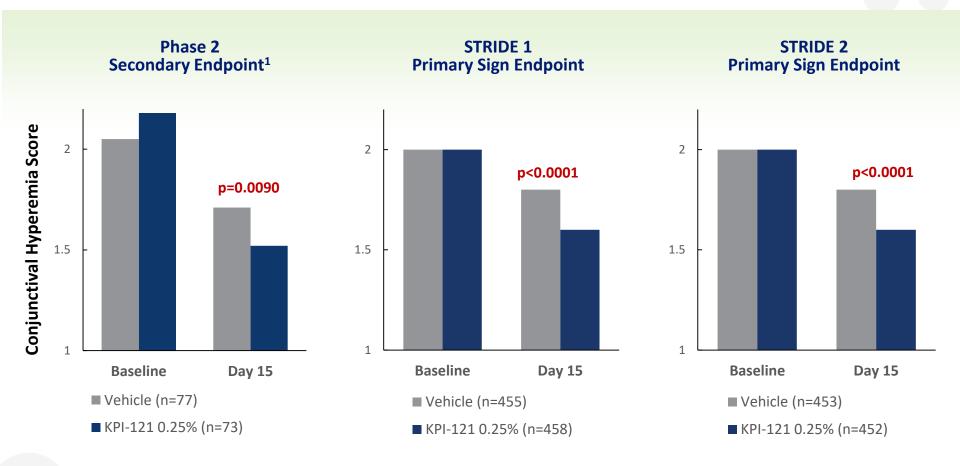
#### Drug use by indication for select drugs (2011-2017)



- ~8.5M ocular steroid prescriptions from September 2017 to August 2018
- 3% of Steroid prescriptions (~255k RXs) are for Dry Eye
- ~16M diagnosed dry eye patients in the U.S.
- Less than 2% of diagnosed dry eye patients get a prescription of an ocular steroid



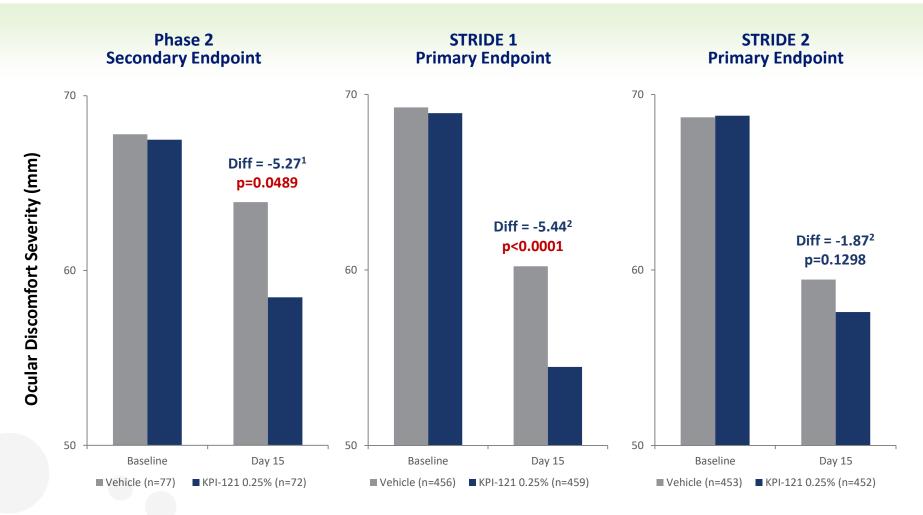
#### Statistically Significant Improvements in Conjunctival Hyperemia (Primary Sign Endpoint) in Phase 2 and Both Phase 3 Trials





<sup>24</sup> <sup>1</sup>Statistical significance achieved (p=0.0405) for Phase 2 primary sign endpoint (conjunctival hyperemia at Day 29)

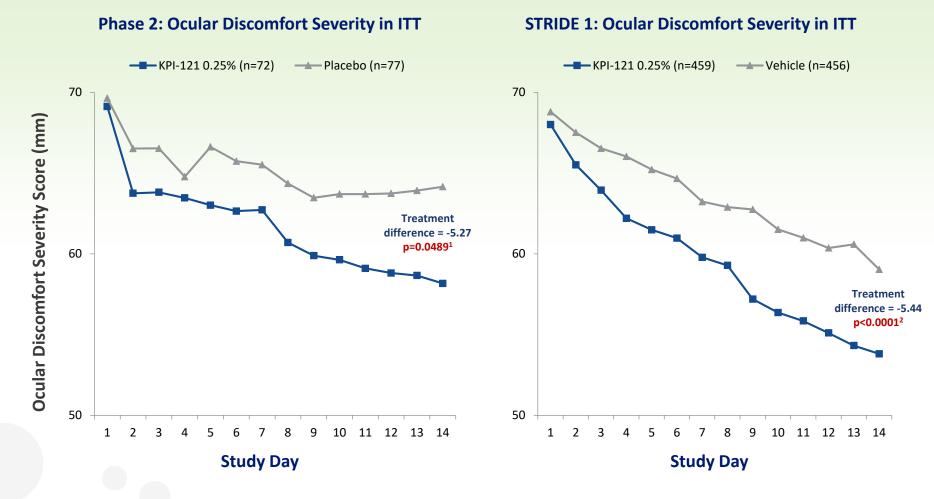
#### Statistically Significant Improvement in Ocular Discomfort in ITT Population at Day 15 in STRIDE 1; Positive Treatment Effect Observed in Phase 2



<sup>1</sup>Using statistical analysis defined in STRIDE 1/2 Statistical Analysis Plan (comparison of 3 day means) <sup>2</sup>Using pre-specified statistical analysis as per Statistical Analysis Plan (comparison of 3 day means)



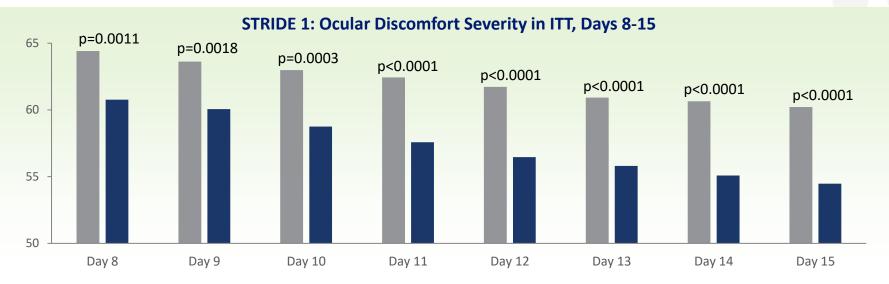
#### Similar Treatment Benefit Seen in Phase 2 and STRIDE 1



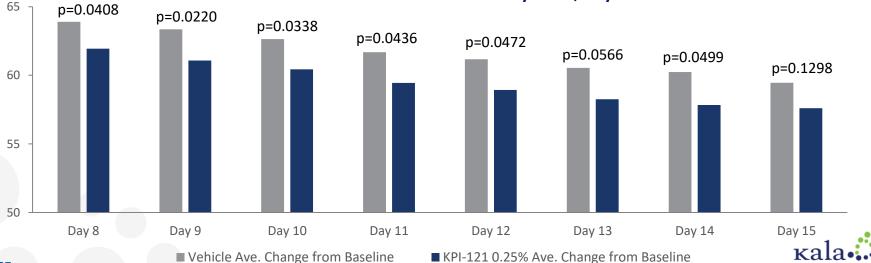
<sup>1</sup>Using statistical analysis defined in STRIDE 1/2 Statistical Analysis Plan (comparison of 3 day means) <sup>2</sup>Using pre-specified statistical analysis as per Statistical Analysis Plan (comparison of 3 day means)



## Ocular Discomfort Severity in ITT Population Assessed for Days 8-15 in STRIDE 1 & 2

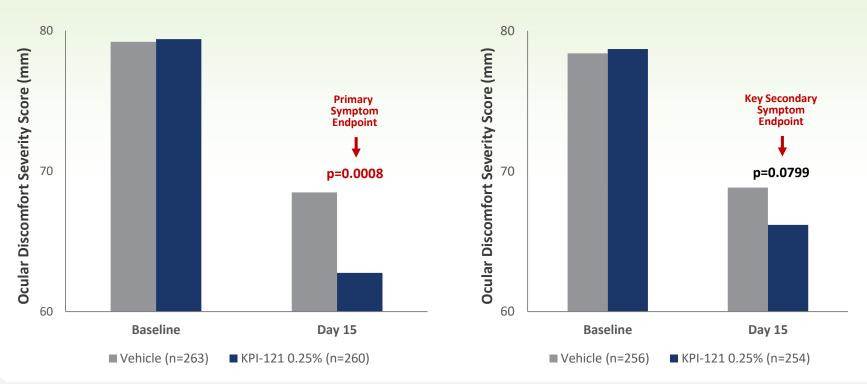


**STRIDE 2: Ocular Discomfort Severity in ITT, Days 8-15** 



## Statistically Significant Improvements in Ocular Discomfort in Patients with More Severe Baseline Discomfort in STRIDE 1

STRIDE 1 Ocular Discomfort Severity in Patients with Baseline Discomfort ≥ 68 mm STRIDE 2 Ocular Discomfort Severity in Patients with Baseline Discomfort ≥ 68 mm



## Statistical significance achieved for second predefined primary symptom endpoint in STRIDE 1 but not for key secondary symptom endpoint in STRIDE 2



#### KPI-121 0.25% Was Well-Tolerated and Demonstrated Similar IOP Profile to Vehicle in Both STRIDE 1 and 2

#### AEs Reported by >1% of Patients

**STRIDE 1** 

	KPI-121 0.25%	Vehicle
Instillation site pain	28/459 (6.1%)	28/456 (6.1%)
Eye irritation	5/459 (1.1%)	7/456 (1.5%)

#### STRIDE 2

	KPI-121 0.25%	Vehicle
Instillation site pain	26/453 (5.7%)	20/452 (4.4%)
Vision blurred	1/453 (0.2%)	6/452 (1.3%)

Number of Patients with IOP Increase > 5 mmHg Leading to IOP ≥ 21 mmHg

#### **STRIDE 1**

KPI-121 0.25%	Vehicle
2/455	2/453
(0.4%)	(0.4%)

#### STRIDE 2

KPI-121 0.25%	Vehicle
5/448	0/448
(1.1%)	(0.0%)

#### Combined

KPI-121 0.25%	Vehicle
7/903	2/901
(0.8%)	(0.2%)



#### Summary of KPI-121 0.25% Data to Date and Next Steps

#### Summary of KPI-121 0.25% Data:

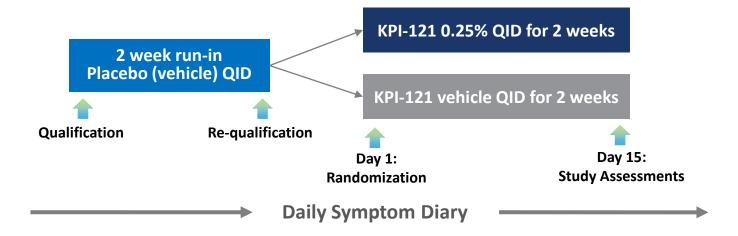
- Sign endpoint achieved in all 3 studies
  - Statistically significant improvements in pre-specified sign endpoint of Conjunctival Hyperemia in STRIDE 1, STRIDE 2 and Phase 2
- Primary symptom endpoints (Ocular Discomfort in overall ITT population and severe subgroup) achieved in STRIDE 1
  - Statistically significant improvement in pre-specified primary symptom endpoint of Ocular Discomfort in ITT Population at Day 15 in STRIDE 1
  - Statistically significant improvement in pre-specified primary symptom endpoint of Ocular Discomfort in Severe Population at Day 15 in STRIDE 1
  - Applying the STRIDE 1/2 statistical analysis plan to the Phase 2 study results in a p-value of 0.0489 for Ocular Discomfort in ITT Population at Day 15
- KPI-121 0.25% well-tolerated with IOP profile similar to vehicle

#### Next Steps for KPI-121 0.25% Program:

- NDA filing accepted by FDA, with PDUFA date of August 15, 2019
- STRIDE 3 trial initiated in July 2018; topline results anticipated in Q4 2019



#### STRIDE 3 Study Initiated in July 2018; Similar Design to STRIDE 1 & 2 With Focus on Symptom Endpoints



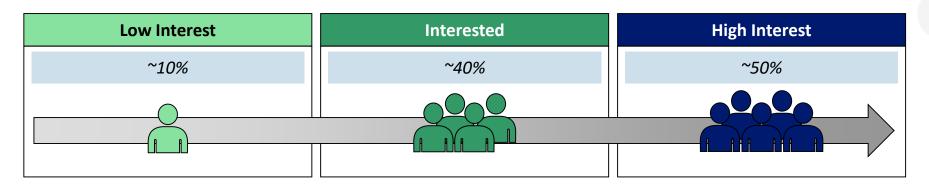
#### Key Aspects of STRIDE 3 Study Design:

- Similar design to STRIDE 1 and 2
- Specific modifications made to inclusion/exclusion criteria to address key factors which are expected to improve the probability of success
- Independent primary endpoints of Day 15 Ocular Discomfort in ITT population and severe subgroup
  - Achieving either endpoint should satisfy symptom requirement
- Topline results anticipated in Q4 2019



## Our Market Research Suggests Strong Patient Interest in KPI-121 0.25%\*

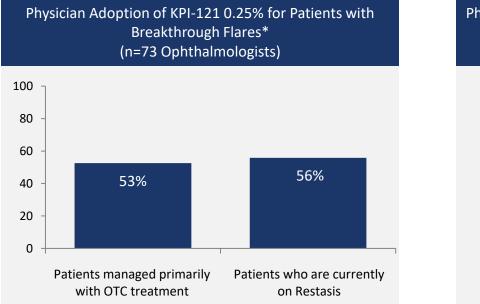
#### The majority of surveyed patients expressed interest in the KPI-121 0.25% profile



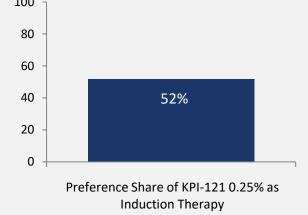
- Patients were very interested in the profile and would ask their physicians for more information about KPI-121 0.25%
- Patients specifically commented they would like an "as-needed" flare treatment vs. a chronic medicine
- The majority of patients indicated they want to try KPI-121 0.25%, expressing high levels of interest
- Patients highlighted they want rapid and strong efficacy with a reduction of "redness", and short-term and "as-needed" flare treatment



#### Significant Market Opportunity for KPI-121 0.25% in Dry Eye



Physician Adoption of KPI-121 0.25% as Induction Therapy for Patients Initiating Restasis\* (n=73 Ophthalmologists)

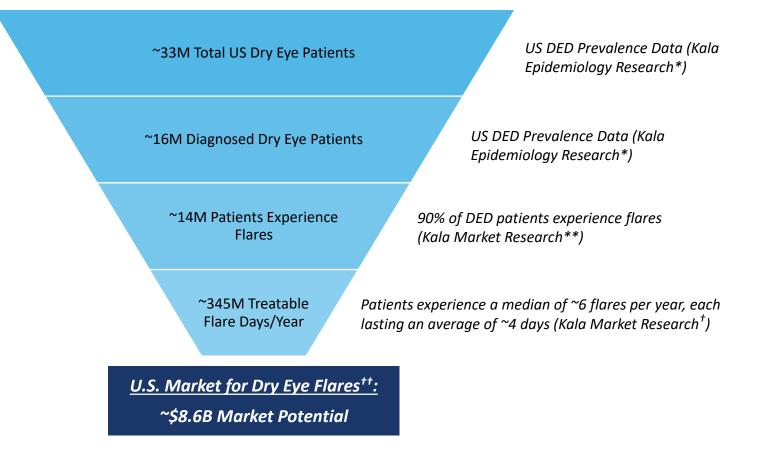


- ~16M diagnosed dry eye sufferers in the U.S., of whom ~90% experience flares<sup>\*\*</sup>
- Patients state that they experience a median of ~6 flares per year, each lasting an average of ~4 days<sup>†</sup>
- Market research indicates physicians would prescribe KPI-121 0.25% for ~55% of patients with flares and for 52% of patients being initiated on Restasis<sup>\*</sup>

\*Based on a survey of 73 ophthalmologists commissioned by Kala and performed by a third party. \*\*Based on a survey of 503 patients commissioned by Kala and performed by a third party. \*Based on a survey of 297 patients commissioned by Kala and performed by a third party.



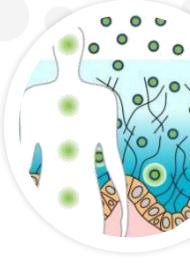
#### Dry Eye Flares – Market Potential



\*Epidemiology research commissioned by Kala and performed by a third party. \*\*Based on a survey of 503 patients commissioned by Kala and performed by a third party. <sup>†</sup>Based on a survey of 297 patients commissioned by Kala and performed by a third party. <sup>††</sup>Assuming \$350 WAC for a 2-week Rx



#### Summary



**INVELTYS<sup>™</sup>:** FIRST and ONLY BID ocular steroid

~8.2M ocular surgery procedures in the U.S. in 2018, projected to grow at a 4.1% CAGR over the next 5 years

**KPI-121 0.25%:** Potential first-line Rx therapy to treat dry eye flares

~33M dry eye sufferers in U.S.

AMPPLIFY<sup>™</sup> Platform Enhances Mobility of Drug Particles Through Mucus Layers INVELTYS U.S. Launch in Jan 2019; Peak Net Revenues Expected To Be In Excess of \$300M KPI-121 0.25% PDUFA Date of Aug 15, 2019; STRIDE 3 Phase 3 Trial Topline Results Anticipated in 4Q2019



Source for ocular surgery market data: Market Scope

Source for dry eye disease market data: Epidemiology research commissioned by Kala and performed by a third party

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### **Thank You**