Kala Pharmaceuticals Announces New Drug Application for KPI-121 0.25% for Dry Eye Disease Has Been Accepted for Review by the U.S. Food and Drug Administration

December 26, 2018

- KPI-121 0.25% expected to be the first product indicated for the temporary relief of signs and symptoms of dry eye disease, if approved -

- PDUFA target action date of August 15, 2019 -

WALTHAM, Mass.--(BUSINESS WIRE)--Dec. 26, 2018-- Kala Pharmaceuticals, Inc. (NASDAQ:KALA), a biopharmaceutical company focused on the development and commercialization of therapeutics using its proprietary AMPPLIFY™ mucus-penetrating particle (MPP) Drug Delivery Technology, today announced that the New Drug Application (NDA) for KPI-121 0.25%, a product candidate for the temporary relief of signs and symptoms of dry eye disease utilizing a two-week course of therapy, has been accepted for review by the United States Food and Drug Administration (FDA). The FDA has set a target action date under the Prescription Drug User Fee Act (PDUFA) of August 15, 2019. If approved, KPI-121 0.25% is expected to be the first product indicated for the temporary relief of the signs and symptoms of dry eye disease, which would include treatment of dry eye flares.

“All currently marketed FDA-approved pharmaceutical treatments for dry eye disease are chronic therapies and are typically used in patients with chronic or persistent dry eye symptoms,” said Dr. Edward Holland, Director of Cornea Services, Cincinnati Eye Institute and Professor of Clinical Ophthalmology, University of Cincinnati. “The vast majority of patients experience episodic dry eye flares that are characterized by acute exacerbations of signs and/or symptoms. An FDA-approved, safe and effective short-term treatment for dry eye disease, including dry eye flares, will represent an important new treatment option for patients and prescribers.”

KPI-121 0.25% utilizes Kala’s proprietary AMPPLIFY Drug Delivery Technology to enhance penetration into target tissues of the eye. In preclinical studies, the AMPPLIFY technology increased delivery of loteprednol etabonate (LE) into ocular tissues more than three-fold compared to current LE products by facilitating penetration through the tear film mucins. The AMPPLIFY technology also underpins INVELTYS™ (loteprednol etabonate ophthalmic suspension) 1%, the first twice-a-day corticosteroid for the treatment of post-operative inflammation and pain following ocular surgery, which was approved by the FDA in August 2018.

The NDA submission for KPI-121 0.25% was supported by data from one Phase 2 and two Phase 3 efficacy and safety trials, STRIDE 1 and STRIDE 2 (STRIDE - **S**hort **T**erm **R**elief **I**n **D**ry **E**ye), studying over 2,000 patients with dry eye disease. Based upon the FDA’s recommendation, Kala also initiated an additional Phase 3 clinical trial, STRIDE 3, in July 2018, evaluating KPI-121 0.25% for the temporary relief of the signs and symptoms of dry eye disease. The Company expects to report top-line results for STRIDE 3 in the fourth quarter of 2019.

About Dry Eye Disease
Dry eye disease is a chronic, episodic, multifactorial disease affecting the tears and ocular surface that can result in tear film instability, inflammation, discomfort, visual disturbance and ocular surface damage. Dry eye disease is estimated to affect approximately 33 million people in the United States, based on an estimated prevalence of 14.5% as described in The Beaver Dam Offspring Study, a major epidemiological study published in 2014 in the American Journal of Ophthalmology. Dry eye disease can have a significant impact on quality of life and can potentially cause long-term damage to the ocular surface. In addition, the vast majority of dry eye patients experience acute exacerbations of their symptoms, which are commonly referred to as flares, at various times throughout the year. These flares can be triggered by numerous factors which cause ocular surface inflammation and impact tear production and/or tear film stability.

About KPI-121 0.25%
Kala is developing KPI-121 0.25% for the temporary relief of the signs and symptoms of dry eye disease utilizing a two-week course of therapy. Dry eye disease is a chronic, episodic, multifactorial disease affecting the tears and ocular surface and can involve tear film instability, inflammation, discomfort, visual disturbance and ocular surface damage. KPI-121 0.25% utilizes Kala's AMPPLIFY™ mucus-penetrating particle (MPP) Drug Delivery Technology to enhance penetration of loteprednol etabonate (LE) into target tissue of the eye. In preclinical studies, the AMPPLIFY Drug Delivery Technology increased delivery of LE into ocular tissues more than three-fold compared to current LE products by facilitating penetration through the tear film mucins. Kala has completed one Phase 2 and two Phase 3 clinical trials, STRIDE 1 and STRIDE 2 (STRIDE - **S**hort **T**erm **R**elief **I**n **D**ry **E**ye), of KPI-121 0.25%. Kala believes that KPI-121 0.25%'s broad mechanism of action, rapid onset of relief of both signs and symptoms, favorable tolerability and safety profile and the potential to be complementary to existing therapies, could result in a favorable profile for the management of dry eye flares and other dry eye associated conditions. Kala has filed an NDA with the FDA and has been granted a PDUFA target action date of August 15, 2019. Based upon the FDA’s recommendation, Kala has also initiated an additional Phase 3 clinical trial in July 2018, STRIDE 3, evaluating KPI-121 0.25% for the temporary relief of the signs and symptoms of dry eye disease. Kala believes that it has identified key factors that contributed to the differences observed in the results from STRIDE 2 compared to those of STRIDE 1 and the Phase 2 study, and that changes made to the inclusion/exclusion criteria of STRIDE 3 based on these analyses will improve the probability of success. The Company expects to report top-line results for STRIDE 3 in the fourth quarter of 2019.

About INVELTYS™
INVELTYS™ (loteprednol etabonate ophthalmic suspension) 1% is a twice-a-day corticosteroid for the treatment of post-operative inflammation and pain following ocular surgery. INVELTYS utilizes Kala’s proprietary AMPPLIFY™ mucus-penetrating particle (MPP) Drug Delivery Technology to enhance penetration into target tissues of the eye. In preclinical studies, the AMPPLIFY Drug Delivery Technology increased delivery of loteprednol etabonate (LE) into ocular tissues more than three-fold compared to current LE products by facilitating penetration through the tear film mucins. INVELTYS was approved by the FDA on August 22, 2018. Kala believes INVELTYS has a favorable profile for the treatment of inflammation and pain following ocular surgery, due to its twice-a-day dosing regimen. A link to the full product label can be found at: www.inveltys.com.

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

About Kala Pharmaceuticals, Inc.
Kala is a biopharmaceutical company focused on the development and commercialization of therapeutics using its proprietary AMPPLIFY™ mucus-penetrating particle (MPP) Drug Delivery Technology, with an initial focus on the treatment of eye diseases. Kala has applied the AMPPLIFY Drug Delivery Technology to a corticosteroid, loteprednol etabonate (LE), designed for ocular applications, resulting in recently approved INVELTYS™ for the treatment of inflammation and pain following ocular surgery and its lead product candidate, KPI-121 0.25%, for the temporary relief of the signs and symptoms of dry eye disease.

Forward Looking Statements
This press release 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 for the treatment of inflammation and pain following ocular surgery and the Company's lead product candidate, 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 Press Release, 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," "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. 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: 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 initiated or required for KPI-121 0.25% prior to approval of the NDA, or at all, and whether any such NDA will be approved; the Company's ability to build a specialty sales force and prepare for commercial launch of INVELTYS 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 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. These forward-looking statements represent the Company's views as of the date of this release and should not be relied upon as representing the Company's views as of any date subsequent to the date hereof. The Company does 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.

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