Kala Pharmaceuticals Submits New Drug Application to U.S. Food and Drug Administration for KPI-121 0.25% for Dry Eye Disease

October 16, 2018

WALTHAM, Mass.--(BUSINESS WIRE)--Oct. 16, 2018-- Kala Pharmaceuticals, Inc. (Kala) (NASDAQ:KALA), today announced that it has submitted a New Drug Application (NDA) to the United States Food and Drug Administration (FDA) for KPI-121 0.25%, a topical product candidate which, if approved, could be the first FDA-approved product for the temporary relief of signs and symptoms of dry eye disease.

There are an estimated 33 million patients with dry eye disease in the U.S. and Kala's market research indicates that approximately 90% of these patients have flares associated with their dry eye disease. If approved, KPI-121 0.25% could offer a favorable management option for these dry eye flares and other dry eye-associated conditions.

KPI-121 0.25% utilizes Kala's AMPPLIFY ^{TM} mucus-penetrating particle (MPP) Drug Delivery Technology, which are selectively-sized nanoparticles with proprietary coatings that significantly enhance drug penetration and distribution in ocular tissues. In preclinical studies, MPPs increased drug delivery into ocular tissues more than three-fold by facilitating penetration through the tear film mucus.

The NDA filing is supported by three clinical trials studying approximately 2,000 patients with dry eye disease, including one Phase 2 trial 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). KPI-121 0.25% achieved statistical significance for the primary sign endpoint of conjunctival hyperemia in the intent to treat (ITT) population in the Phase 2 trial and both Phase 3 trials. KPI-121 0.25% also achieved statistical significance for the primary symptom endpoint of ocular discomfort severity at Day 15 in the ITT population in STRIDE 1 with a trend towards a treatment effect in STRIDE 2, as well as a positive treatment effect observed in Phase 2. Statistical significance was achieved in STRIDE 1 for the second primary symptom endpoint of ocular discomfort severity at Day 15 in patients with a more severe baseline discomfort, with a strong trend towards a treatment effect observed for the same endpoint in STRIDE 2. Positive treatment effects were also observed in both trials for the symptom endpoint of ocular discomfort severity in the ITT population at Day 8, which was a key pre-specified secondary endpoint. KPI-121 0.25% was well-tolerated in all three trials with elevation in intra-ocular pressure, a known side effect with topical corticosteroids, similar to vehicle (placebo).

"We are pleased to submit the NDA for KPI-121 0.25% to the FDA," said Kim Brazzell, Ph.D., Chief Medical Officer of Kala Pharmaceuticals. "We believe the data from STRIDE 1, STRIDE 2 and the Phase 2 trials demonstrate a robust data package supporting the clinically meaningful efficacy, safety and tolerability of KPI-121 0.25%. Today, there are limited treatment options for dry eye disease and KPI-121 0.25% has the opportunity to address significant unmet needs for patients and health care professionals."

Kala has also initiated a third Phase 3 clinical trial, STRIDE 3, evaluating KPI-121 0.25% for the temporary relief of the signs and symptoms of dry eye disease. The primary endpoints for the study will be symptom-focused. Kala has conducted a comprehensive analysis of the data generated in the previous three clinical trials and believes it has identified key factors that contributed to the differences observed in the results from STRIDE 2 compared to those of STRIDE 1 and Phase 2. Kala has integrated these factors into the trial design of STRIDE 3, which it believes will improve the probability of success for the trial. The Company expects to report top-line results for STRIDE 3 in the fourth quarter of 2019.

About STRIDE 3 Phase 3 Trial Design
The STRIDE 3 trial is a multicenter, randomized, double-blind, placebo controlled, parallel-arm study comparing KPI-121 0.25% to placebo, each dosed four times a day (QID) for 14 days, in approximately 900 patients with dry eye disease. Subjects who meet initial screening and inclusion/exclusion criteria undergo a 2-week run-in period with placebo. Subjects who continue to meet inclusion/exclusion criteria after the run-in are randomized to either KPI-121 0.25% or placebo. The primary endpoints, Day 15 ocular discomfort severity in the ITT population and Day 15 ocular discomfort severity in patients with a more severe baseline discomfort, are based upon a patient diary in which ocular discomfort is recorded daily over the entire course of the trial using a visual analog grading scale. Topline data from this study is expected in the fourth quarter of 2019.

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 administered four times a day. 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 loteprednol etabonate (LE) into ocular tissues more than three-fold compared to current LE products by facilitating penetration through the tear film mucus. Kala has completed one Phase 2 and two Phase 3 clinical trials 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.

About Kala Pharmaceuticals, Inc.
Kala is a biopharmaceutical company focused on the development and commercialization of therapeutics using its proprietary AMPPLIFY Drug Delivery Technology, with an initial focus on the treatment of eye diseases. Kala has applied the AMPPLIFY Drug Delivery Technology to a corticosteroid, LE, designed for ocular applications, resulting in recently approved INVELTYS^{TM} 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 the Company's lead product candidate, KPI-121 0.25% for the temporary relief of

the signs and symptoms of dry eye disease, KPI-121 0.25% potentially being the first FDA-approved product for the treatment of dry eye flares, KPI-121 0.25% having the opportunity to address significant unmet needs for patients and health care professionals, and the Company's expectation to report top-line results for STRIDE 3 in the fourth quarter of 2019. 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; data from the Company's Phase 3 clinical trials of KPI-121 0.25% will warrant filing of the NDA; whether any additional clinical trials will be initiated or required for KPI-121 0.25% prior to submission or filing of an NDA, or at all, and whether any such NDA will be accepted for filing and/or 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 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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