Kala Pharmaceuticals Announces Update to KPI-121 0.25% Development Plan

June 19, 2018

– Expects to submit NDA for KPI-121 0.25% in the second half of 2018 –

– Expects to initiate Phase 3 STRIDE 3 trial in the third quarter of 2018 –

WALTHAM, Mass.--(BUSINESS WIRE)--Jun. 19, 2018-- Kala Pharmaceuticals, Inc. (NASDAQ:KALA), today provided an update on the development plan for KPI-121 0.25%, which if approved could be the first FDA-approved product for the short-term treatment of dry eye disease.

The Company announced that it plans to submit a New Drug Application (NDA) to the U.S. Food and Drug Administration (FDA) during the second half of 2018. The NDA will include data from three clinical trials studying approximately 2000 patients, including one Phase 2 trial and two Phase 3 efficacy and safety trials.

In addition, based upon the recommendation of the FDA, Kala plans to initiate an additional Phase 3 clinical trial evaluating KPI-121 0.25% for the temporary relief of the signs and symptoms of dry eye disease. The Company plans to initiate the new trial, STRIDE 3 (STRIDE - **S**hort **T**erm **R**elief **I**n **D**ry **E**ye), in the third quarter of 2018. Top-line results for STRIDE 3 are anticipated in the fourth quarter of 2019.

The Company has conducted a comprehensive analysis of data generated in its 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. The Company has integrated these factors into the trial design of STRIDE 3, which the Company believes will improve the probability of success for the trial.

Kala remains committed to developing KPI-121 0.25% for the millions of patients suffering from dry eye disease for whom there is currently no product approved for the temporary relief of signs and symptoms of the disease.

Kala also continues to prepare for the potential approval and launch of INVELTYS™, which, if approved, is expected to be the first twice-daily ocular corticosteroid indicated for the treatment of post-operative ocular inflammation and pain. The FDA accepted the INVELTYS NDA for review in January 2018 and provided a target action date under the Prescription Drug User Fee Act (PDUFA) of August 24, 2018. The brand name for KPI-121 1%, INVELTYS, has been conditionally approved by the FDA.

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 mucus-penetrating particle (MPP) technology to enhance penetration of loteprednol etabonate (LE) into target tissue of the eye. In preclinical studies, MPP technology increased delivery of 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 which could benefit from temporary relief of dry eye signs and symptoms.

In January 2018, Kala announced topline results for two Phase 3 trials (STRIDE 1 and STRIDE 2), evaluating the safety and efficacy of KPI-121 0.25% versus placebo in patients with dry eye disease. The two Phase 3 clinical trials were each multicenter, randomized, double-masked, placebo-controlled, parallel-arm studies comparing KPI-121 0.25% to placebo each dosed four times a day (QID) for 14 days. Subjects who met initial screening and inclusion/exclusion criteria underwent a 2-week run-in period with placebo dosed in each eye QID for 14 days. Subjects who continued to meet inclusion and exclusion criteria after the run-in were randomized to either KPI-121 or placebo. A total of 918 patients were randomized in STRIDE 1 and 909 patients were randomized in STRIDE 2. Ocular discomfort severity was graded daily by the patient over the entire course of the trial using a visual analog grading scale recorded in a patient diary.

KPI-121 0.25% achieved statistical significance for the primary sign endpoint of conjunctival hyperemia at Day 15 in the ITT population in 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. Statistical significance was achieved for the second primary symptom endpoint of ocular discomfort severity at Day 15 in patients with a more severe baseline discomfort in STRIDE 1 with a strong trend towards a treatment effect observed for the same endpoint in STRIDE 2. Positive treatment effects were also observed for the symptom endpoint of ocular discomfort severity in the ITT population at Day 8 in both trials, which was a key pre-specified secondary endpoint.

KPI-121 0.25% was well-tolerated in both Phase 3 trials with elevation in intra-ocular pressure, a known side effect with topical corticosteroids, similar to placebo.

In March 2018, Kala announced additional analyses of the STRIDE 1, STRIDE 2 and Phase 2 data. The Phase 2 ocular discomfort data was analyzed using the analysis method defined in the Phase 3 statistical analysis plan, and Kala observed a positive treatment effect for ocular discomfort at day 15 ($p=0.0489$) using this analysis method. A similar magnitude of effect was observed in the Phase 2 trial as observed in STRIDE 1 (5.27 mm and 5.44 mm differences vs. vehicle, respectively).

Additionally, a positive treatment effect was observed for the primary symptom endpoint of ocular discomfort at day 15 ($p<0.0001$) when pooling the data from STRIDE 1 and STRIDE 2.

Furthermore, the effect on ocular discomfort on each of the days between days 8 and 14 in STRIDE 1 and STRIDE 2 using the analysis that was pre-specified for day 15. P-values of less than 0.002 were observed for all days during that time period in STRIDE 1, and p-values less than 0.05 were observed on 6 of the 7 days during that time period in STRIDE 2.

About INVELTYS™

INVELTYS™ (KPI-121 1%) is a twice-a-day corticosteroid for the treatment of inflammation and pain following ocular surgery. INVELTYS utilizes Kala's proprietary mucus-penetrating particle (MPP) technology to enhance penetration into target tissues of the eye. In preclinical studies, MPP increased delivery of a corticosteroid into ocular tissues more than three-fold by facilitating penetration through the tear film mucus. Two Phase 3 clinical trials have been successfully completed for INVELTYS and statistical significance was achieved for both primary efficacy endpoints in both trials. In each of these trials, INVELTYS was well tolerated with no treatment-related serious adverse events observed. Kala believes INVELTYS has a favorable treatment profile compared to the standard of care for the treatment of inflammation and pain following ocular surgery, due to its twice-a-day dosing regimen and rapid onset of relief. The NDA for INVELTYS was accepted for review by the FDA in January 2018 and given a target action date under the Prescription Drug User Fee Act (PDUFA) of August 24, 2018. The brand name for KPI-121 1%, INVELTYS, has been conditionally approved by the FDA.

About Kala

Kala is a biopharmaceutical company focused on the development and commercialization of therapeutics using its proprietary mucus-penetrating particle (MPP) technology, with an initial focus on the treatment of eye diseases. Kala has applied the MPP technology to a corticosteroid designed for ocular applications, resulting in two lead product candidates. Kala's product candidates are INVELTYS™ (KPI-121 1%) for the treatment of inflammation and pain following ocular surgery, for which an NDA has been accepted for review by the FDA, and 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 product candidates, including INVELTYS (KPI-121 1%) for the treatment of inflammation and pain following ocular surgery and 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 data from the Company's Phase 3 clinical trials of KPI-121 0.25% will warrant submission and filing of an NDA on the timeline expected, or at all; 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 approved; the Company's ability to initiate and complete clinical trials on the timeline expected, or at all; whether the results of clinical trials will be positive and/or replicate the results from earlier clinical development and/or preclinical studies; that post-hoc analyses are normally given less weight by regulatory authorities than pre-specified analyses; whether the Company's NDA for INVELTYS will be approved by its PDUFA date, or at all; uncertainties inherent in the availability and timing of data from ongoing clinical trials; uncertainties related to the Company's ability to obtain regulatory approvals to conduct trials or to market products; the Company's ability to build a sales force and prepare for commercial launch 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 the Company's product candidates; 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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