Kiniksa Announces Positive Final Data from Phase 1 Trial of KPL-404

May 4, 2021

- Highest dose cohorts confirm and extend previously-reported 3 mg/kg IV cohort data -
- 10 mg/kg IV dose provides full receptor occupancy through Day 71 and complete suppression of TDAR after KLH challenge and re-challenge through at least Day 57 -
- 5 mg/kg SC dose provides full receptor occupancy through Day 43 and complete suppression of TDAR after KLH challenge through at least Day 29 -
- Plan to initiate Phase 2 proof-of-concept trial in patients in 2H 2021 -

HAMILTON, Bermuda, May 04, 2021 (GLOBE NEWSWIRE) -- Kiniksa Pharmaceuticals, Ltd. (Nasdaq: KNSA) ("Kiniksa"), a biopharmaceutical company with a portfolio of assets designed to modulate immunological pathways across a spectrum of diseases, today announced positive final data from the Phase 1 clinical trial of KPL-404 in healthy volunteers. KPL-404 is a monoclonal antibody designed to inhibit interaction of CD40 with CD154 (CD40 ligand), a well-known pathway that plays a critical role in regulating B cell proliferation, T cell activation, and antibody production.

"The final KPL-404 Phase 1 data are very encouraging, as they confirm and extend the findings from the previously-reported lower-dose cohorts," said Sanj K. Patel, Chief Executive Officer and Chairman of the Board of Kiniksa. "The data reinforce our confidence in KPL-404 as a potential best-in-class treatment option and support the optionality for studying chronic KPL-404 dosing in patients with subcutaneous and/or intravenous administration. To this end, we plan to evaluate KPL-404 in a Phase 2 proof of concept study in rheumatoid arthritis patients. We believe that a study in this patient population will be translatable to a spectrum of other devastating autoimmune diseases with high unmet need."

The Phase 1 trial of KPL-404 was a randomized, double-blind, placebo-controlled, single-ascending-dose, first-in-human study in healthy volunteers that was divided into two parts: a single dose of KPL-404 0.03 mg/kg, 0.3 mg/kg, 1 mg/kg, 3 mg/kg or 10 mg/kg administered intravenously (IV) and a single dose of KPL-404 1 mg/kg or 5 mg/kg administered subcutaneously (SC). The primary objective was to assess the safety and tolerability of KPL-404. Secondary endpoints included pharmacokinetics, the immune response, T-cell Dependent Antibody Response (TDAR) to the novel test antigen keyhole limpet hemocyanin (KLH) in clinically-relevant dose level cohorts, and the anti-drug antibody response. CD40 receptor occupancy (RO) was an exploratory endpoint.

KPL-404 showed dose-dependent increases in concentration across cohorts. All dose escalations occurred as per protocol with no dose-limiting safety findings. KPL-404 was well-tolerated, and there were no serious adverse events. Subjects dosed with KPL-404 10 mg/kg IV showed full RO through at least Day 71 and complete suppression of TDAR after KLH challenge and re-challenge through at least Day 57. Subjects dosed with KPL-404 5 mg/kg SC showed full RO through Day 43 and suppression of TDAR after KLH challenge through at least Day 29. These data confirm and extend previously-reported 3 mg/kg IV cohort data, in which RO and suppression of TDAR after KLH challenge were demonstrated through Day 29. The 3 mg/kg IV dose level had previously demonstrated complete suppression of memory TDAR response to a re-challenge on Day 29. Anti-drug antibodies to KPL-404 were suppressed for at least 57 days at 10 mg/kg IV; the suppression of antibody responses to the drug itself is an independent indicator of target engagement and pharmacodynamic effect.

"Dysregulation of the CD40-CD154 pathway has been implicated in the pathophysiology of multiple autoimmune diseases, and the totality of the Phase 1 data underscore the magnitude and duration of memory immune response suppression by KPL-404," said John F. Paolini, MD, PhD, Chief Medical Officer of Kiniksa. "The 10 mg/kg intravenous cohort data demonstrate the full power of KPL-404, and 5 mg/kg subcutaneous cohort data demonstrate practical utility for potential convenient chronic dosing in patients."

Kiniksa plans to initiate a Phase 2 proof-of-concept trial in rheumatoid arthritis in the second half of 2021. The trial will evaluate safety and pharmacokinetics of KPL-404 with subcutaneous administration over 12 weeks. Rheumatoid arthritis was selected as a well-characterized autoimmune disease with decades of published clinical data across diverse mechanistic classes, allowing for objective evaluation in established endpoints. The pharmacokinetic lead-in of the planned trial supports characterization of chronic administration of KPL-404 in a patient population and provides optionality to evaluate the therapeutic potential of KPL-404 across a range of other autoimmune diseases with pathologies believed to be mediated by the CD40-CD154 pathway.

About KPL-404
KPL-404 is an investigational humanized monoclonal antibody that is designed to inhibit CD40-CD154 (CD40 ligand) interaction, a key T-cell co-stimulatory signal critical for B-cell maturation and immunoglobulin class switching and Type 1 immune responses. Kiniksa believes disrupting the CD40-CD154 interaction is an attractive approach for multiple autoimmune disease pathologies such as rheumatoid arthritis, Sjogren's syndrome, Graves' disease, systemic lupus erythematosus and solid organ transplant. Kiniksa owns or controls the intellectual property related to KPL-404.

About KPL-404 Phase 1 Trial
The Phase 1 trial of KPL-404 is a randomized, double-blind, placebo-controlled, single-ascending-dose, first-in-human study that is divided into two parts: a single dose of KPL-404 0.03 mg/kg, 0.3 mg/kg, 1 mg/kg, 3 mg/kg or 10 mg/kg intravenously (IV) and a single dose of KPL-404 1 mg/kg or 5 mg/kg subcutaneously (SC). The primary objective is to assess the safety and tolerability of KPL-404. Secondary endpoints include pharmacokinetics, the immune response to the novel test antigen keyhole limpet hemocyanin (KLH) in clinically relevant dose cohorts, and the anti-drug antibody response. CD40 receptor occupancy (RO) was an exploratory endpoint.

About Kiniksa

Kiniksa is a biopharmaceutical company focused on discovering, acquiring, developing and commercializing therapeutic medicines for patients suffering from debilitating diseases with significant unmet medical need. Kiniksa's portfolio of assets, ARCALYST ®, mavrilimumab, vixarelimab and KPL-404, are based on strong biologic rationale or validated mechanisms, target underserved conditions and offer the potential for differentiation. These assets are designed to modulate immunological pathways across a spectrum of diseases. For more information, please visit www.kiniksa.com.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. In some cases, you can identify forward looking statements by terms such as "may," "will," "should," "expect," "plan," "anticipate," "could," "intend," "target," "project," "contemplate," "believe," "estimate," "predict," "potential" or "continue" or the negative of these terms or other similar expressions, although not all forward-looking statements contain these identifying words. All statements contained in this press release that do not relate to matters of historical fact should be considered forward-looking statements, including without limitation, statements regarding: our beliefs about the final data from the Phase 1 clinical trial of KPL-404 in healthy volunteers and its potential, including its potential to be a best-in-class treatment option; our beliefs about what the totality of the Phase 1 data show and support, including the optionality of dosing administrations in patients; expected timing for initiating a Phase 2 proof-of-concept trial of KPL-404 in in rheumatoid arthritis patients; our rationale for selecting rheumatoid arthritis for the trial patient population, including our belief that a study in that patient population being translatable to a spectrum of other devastating autoimmune diseases with high unmet need; our planned trial design; our beliefs about the mechanisms of action of our product candidates and potential impact of their approach, including our belief that KPL-404's disruption of the CD40-CD154 interaction is an attractive approach for multiple autoimmune disease pathologies; and our belief that all of our product candidates offer the potential for differentiation.

These forward-looking statements are based on management's current expectations. These statements are neither promises nor guarantees, but involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements, including without limitation, the following: delays or difficulty in initiating, enrolling and completing our Phase 2 proof-of-concept clinical trial of KPL-404 in patients with rheumatoid arthritis; our potential inability to replicate in later clinical trials the positive final data from our earlier clinical trials or studies; impact of additional data from us or other companies, including the potential for our data to produce negative, inconclusive or commercially uncompetitive results; potential undesirable side effects caused by KPL-404; our reliance on third parties to manufacture our product candidates; drug substance and/or drug product shortages; our reliance on third parties to conduct research, clinical trials, and/or certain regulatory activities for our product candidates, including for KPL-404; potential complications in coordinating requirements, regulations and guidelines of regulatory authorities across jurisdictions for our clinical trials, including for the Phase 2 clinical trial; the potential impact of the COVID-19 pandemic and measures taken in response to the pandemic on our business and operations as well as the business and operations of our manufacturers, CROs upon whom we rely to conduct our clinical trials, and other third parties with whom we conduct business or otherwise engage, including the FDA and other regulatory authorities; changes in our operating plan and funding requirements; and existing or new competition.

These and other important factors discussed under the caption "Risk Factors" in our Annual Report on Form 10-K filed with the Securities and Exchange Commission ("SEC") on February 25, 2021 and our other reports subsequently filed with the SEC could cause actual results to differ materially from those indicated by the forward-looking statements made in this press release. Any such forward-looking statements represent management's estimates as of the date of this press release. While we may elect to update such forward-looking statements at some point in the future, we disclaim any obligation to do so, even if subsequent events cause our views to change. These forward-looking statements should not be relied upon as representing our views as of any date subsequent to the date of this press release.

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