Kezar Life Sciences Presents Positive Complete Results from the MISSION Phase 2 Trial Evaluating Zetomipzomib in Lupus Nephritis at the American College of Rheumatology Convergence 2022

November 14, 2022

- *Overall renal responses (ORR), measured as 50% or greater reduction in proteinuria from baseline, increased from 11 of 17 patients (64.7%) at end of treatment (Week 25) to 15 of 17 patients (88.2%) at end of study (Week 37). The median UPCR at end of study was 0.32.*
- *Reduction in proteinuria was highly correlated with reduction in uCD163, a marker of renal inflammation. The anti-inflammatory activity was maintained up to 12 weeks following discontinuation of zetomipzomib as evidenced by additional reduction in proteinuria and slow recrudescence of SLE disease activity.*
- *Systemic lupus erythematosus disease activity scores including SLEDAI-2K and CLASI were reduced.*
- *Zetomipzomib once-weekly continues to demonstrate a favorable safety and tolerability profile, with no evidence of immunosuppression, and no new safety signals during the follow-up period.*

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--Nov. 14, 2022-- Kezar Life Sciences, Inc. (Nasdaq: KZR), a clinical-stage biotechnology company discovering and developing breakthrough treatments for immune-mediated and oncologic disorders, today announced that it presented the complete data set from the MISSION Phase 2 clinical trial evaluating zetomipzomib in active lupus nephritis (LN) at the American College of Rheumatology (ACR) Convergence 2022 in Philadelphia, PA.

“The MISSION Phase 2 results demonstrate the potential of zetomipzomib, a first-in-class, selective inhibitor of the immunoproteasome, to meaningfully reduce proteinuria, as well as reduce extra-renal manifestations of systemic lupus in patients with LN. By the end of study, the median UPCR was less than 0.5, a clinically important treatment goal. Additionally, the data showed improvements in the skin manifestations of lupus and patient reported outcomes of disease. Importantly, these benefits were accompanied by an overall reduction in the use of corticosteroids,” said Noreen R. Henig, M.D., Kezar’s Chief Medical Officer. “With a well-tolerated safety profile, anti-inflammatory activity, and without indications of suppressing the immune system, zetomipzomib is positioned to be a potentially important therapy for patients with LN and SLE, as well as other autoimmune diseases such as autoimmune hepatitis.”

The MISSION Phase 2 clinical trial was an open-label study designed to demonstrate the responder rate of zetomipzomib in patients with active LN. During the 24-week treatment period, patients received 60 mg of zetomipzomib subcutaneously once weekly (first dose of 30 mg) in addition to stable background therapy. End-of-treatment (EOT) assessments occurred at Week 25, with completion of the study at Week 37 (EOS). Patients in the MISSION Phase 2 clinical trial received zetomipzomib without induction therapy, which represents a significant difference from other recently published clinical trials in LN. The primary efficacy endpoint for this trial was the proportion of patients achieving an overall renal response (ORR), measured as a 50% or greater reduction in urine protein to creatinine ratio (UPCR) at EOT. A key secondary efficacy endpoint was the number of patients with a complete renal response (CRR), measured as an absolute reduction in proteinuria values to a UPCR of 0.5 or less, with preserved renal function (eGFR), and corticosteroid use of 10 mg or less prednisone/prednisone equivalent and no use of prohibited medication. Exploratory endpoints included measures of systemic lupus erythematosus (SLE) disease activity, including Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K), Cutaneous Lupus Erythematosus Severity Index-Activity (CLASI-A), Physician Global Assessment and Patient Global Assessment scores.

Summary of Results from the Completed MISSION Trial

In the MISSION Phase 2 clinical trial, 17 of 21 enrolled patients reached end-of-treatment at Week 25 and end-of-study at Week 37. Zetomipzomib treatment demonstrated steady and clinically meaningful renal responses with additional ORRs and CRRs observed during the safety follow-up period.

- Overall Renal Responses:
  - 10 out 17 patients (58.8%) achieved an ORR as early as Week 13.
  - At EOT, 11 of 17 patients (64.7%) achieved an ORR, measured as a 50% or greater reduction in UPCR compared to baseline, the primary endpoint of the clinical trial.
  - During the safety follow-up period, clinical responses deepened, and ORRs increased to 16 of 17 patients (94.1%) at Week 29 and 15 of 17 patients (88.2%) at EOS. In addition, UPCR was reduced to clinically meaningful levels:
    - 11 of 17 patients (64.7%) achieved a UPCR of 0.5 or less at EOS.
    - 15 of 17 patients (88.2%) achieved a UPCR of 0.7 or less at EOS.
    - Median UPCR was 0.32 at EOS.
- Complete Renal Responses:
  - 5 out 17 patients (29.4%) achieved a CRR as early as Week 13.
  - At EOT, 6 of 17 patients (35.3%) achieved a CRR, a key secondary efficacy endpoint, measured as a UPCR of 0.5 or less, stable eGFR, daily prednisone/prednisone equivalent dose of 10 mg or less, and no use of prohibited medication.

    - During the safety follow-up period, an additional patient achieved a CRR, with the total CRRs increasing to 7 of 17 patients (41.2%) at Week 29 and EOS, demonstrating a deepening renal response throughout the 37-week trial.

- Urinary CD163, a biomarker that is associated with active inflammation in the kidney, decreased and showed a strong correlation to UPCR across all timepoints in the study. These data suggest that patients had active inflammation at baseline despite standard-of-care therapy and that the addition of zetomipzomib reduced inflammation.
- By Week 13, 14 of 17 patients (82.4%) achieved a daily corticosteroid dose of 10 mg or less, despite no protocol-mandated steroid taper. Doses of background immunosuppressive agents remained stable throughout the study, including during the 12-week safety follow-up.
- Key measurements of SLE disease activity were reduced. There was no evidence of early rebound of inflammation following discontinuation of zetomipzomib.
    - SLEDAI-2K, a global assessment of SLE disease activity, reduced from a mean of 11.3 at baseline to 6.5 at EOT and 5.8 at EOS.
    - CLASI-A, a measure of active SLE skin disease, was elevated in 11 patients at baseline, and was reduced from a mean of 5.7 at baseline to 2.6 at EOT and 3.0 at EOS.
    - Physician Global Assessment scores reduced from a mean of 57.2 at baseline to 23.9 at EOT and 16.2 at EOS.
    - Patient Global Assessment scores reduced from a mean of 23.6 at baseline to 10.7 at EOT and 6.6 at EOS.
- Biomarkers of SLE activity improved or normalized in patients with abnormal baseline levels.
    - Of the 12 patients with abnormal levels of double-stranded DNA antibody levels (anti-dsDNA) at baseline, 10 patients showed improved or normalized levels of anti-dsDNA at EOT, and improvement was maintained in 9 patients at EOS.
    - 4 of 5 patients with abnormally low C3 complement at baseline demonstrated improvement at EOT. 3 of 4 patients with abnormally low C4 complement at baseline demonstrated improvement at EOT.

Safety

Zetomipzomib continued to be well-tolerated over the course of the 37-week trial, demonstrating a favorable safety and tolerability profile with no new safety signals during the follow-up period. Overall, adverse events were generally mild-to-moderate (Grade 1 or 2) and were consistent with what was previously reported with topline data from the MISSION Phase 2 clinical trial. Early terminations occurred in 4 out of 21 patients. No opportunistic or Grade 3 infections were reported in the trial.

Poster Presentation Details:

Abstract Title: Interim Results from the Phase 2 MISSION Study Evaluating Zetomipzomib (KZR-616), a First-in-Class Selective Immunoproteasome Inhibitor for the Treatment of Lupus Nephritis
Session: SLE – Treatment Poster II
Date/Time: November 13, 2022 from 9:00 AM - 10:30 AM ET
Presenter: Amit Saxena, MD, Assistant Professor, NYU Grossman School of Medicine

The MISSION poster presentation is currently available in the “Scientific Publications” section of Kezar Life Science’s website at www.kezarlifesciences.com.

About Zetomipzomib

Zetomipzomib (KZR-616) is a novel, first-in-class, selective immunoproteasome inhibitor with broad therapeutic potential across multiple autoimmune diseases. Preclinical research demonstrates that selective immunoproteasome inhibition results in a broad anti-inflammatory response in animal models of several autoimmune diseases, while avoiding immunosuppression. Data generated from Phase 1 and Phase 2 clinical trials provide evidence that zetomipzomib exhibits a favorable safety and tolerability profile for development in severe, chronic autoimmune diseases.

About Lupus Nephritis

Lupus nephritis (LN) is one of the most serious complications of systemic lupus erythematosus (SLE). LN is a disease comprising a spectrum of vascular, glomerular and tubulointerstitial lesions and develops in approximately 50% of SLE patients within 10 years of their initial diagnosis. LN is associated with considerable morbidity, including an increased risk of end-stage renal disease requiring dialysis or renal transplantation and an increased risk of death. There are limited approved therapies for the treatment of LN. Management typically consists of induction therapy to achieve remission and long-term maintenance therapy to prevent relapse.

About Kezar Life Sciences

Kezar Life Sciences is a clinical-stage biopharmaceutical company discovering and developing novel treatments for immune-mediated and oncologic disorders. The company is pioneering first-in-class, small-molecule therapies that harness master regulators of cellular function to inhibit multiple drivers of disease via single, powerful targets. Zetomipzomib, its lead development asset, is a selective immunoproteasome inhibitor has completed a Phase 2 clinical trial in lupus nephritis. This product candidate also has the potential to address multiple chronic immune-mediated diseases. KZR-261 is the first anti-cancer clinical candidate from the company’s platform targeting the Sec61 translocon and the protein secretion pathway. An open-label dose-escalation Phase 1 clinical trial of KZR-261 to assess safety, tolerability and preliminary tumor activity in solid tumors is underway. For more information, visit www.kezarlifesciences.com.

Cautionary Note on Forward-looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Words such as

“may,” “will,” “can,” “should,” “expect,” “believe”, “potential,” “plan” and similar expressions (as well as other words or expressions referencing future events, conditions or circumstances) are intended to identify forward-looking statements. These forward-looking statements are based on Kezar’s expectations and assumptions as of the date of this press release. Each of these forward-looking statements involves risks and uncertainties that could cause Kezar’s clinical development programs, future results or performance to differ materially from those expressed or implied by the forward-looking statements. Forward-looking statements contained in this press release include, but are not limited to, statements about the design, progress, timing, scope and results of clinical trials, the anticipated therapeutic benefit, regulatory development and future clinical trials involving zetomipzomib, the likelihood that data will support future development and therapeutic potential, the association of data with treatment outcomes and the likelihood of obtaining regulatory approval of zetomipzomib. Many factors may cause differences between current expectations and actual results, including unexpected safety or efficacy data observed during clinical studies, changes in expected or existing competition, the uncertainties and timing of the regulatory approval process, and unexpected litigation or other disputes. Other factors that may cause actual results to differ from those expressed or implied in the forward-looking statements in this press release are discussed in Kezar’s filings with the U.S. Securities and Exchange Commission, including the “Risk Factors” contained therein. Except as required by law, Kezar assumes no obligation to update any forward-looking statements contained herein to reflect any change in expectations, even as new information becomes available.

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