Kezar Announces Topline Results from PRESIDIO Trial of Zetomipzomib for the Treatment of Dermatomyositis and Polymyositis

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- *Most patients saw clinically meaningful improvements in the primary endpoint measure of Total Improvement Score (TIS), but no differentiation from placebo was observed*
- *Zetomipzomib demonstrates a favorable safety and tolerability profile, including in the PRESIDIO Open-label Extension Study where weekly zetomipzomib has been administered for up to an additional 77 weeks*
- *Topline data from MISSION Phase 2 trial of zetomipzomib in lupus nephritis (LN) is on track and expected in June 2022, consistent with previous guidance*

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)-- Kezar Life Sciences, Inc., (Nasdaq: KZR), a clinical-stage biotechnology company discovering and developing breakthrough treatments for immune-mediated and oncologic disorders, today announced topline results from the PRESIDIO Phase 2 clinical trial of zetomipzomib (KZR-616) in patients with dermatomyositis (DM) and polymyositis (PM).

In PRESIDIO, 25 patients enrolled with either DM (n=13) or PM (n=12) with active disease despite best available treatments, and 20 patients completed through end-of-treatment. During the 32-week study period, all patients received 16 weeks of zetomipzomib treatment: patients received either 45 mg of zetomipzomib or placebo subcutaneously (SC) once weekly for 16 weeks on top of standard of care, followed by a crossover to the other arm of placebo or zetomipzomib, respectively, for an additional 16 weeks. Patients continued their background therapy but could taper medications as clinically indicated. The primary endpoint of PRESIDIO was the mean change in the Total Improvement Score (TIS).

Topline results of the PRESIDIO trial showed that most DM and PM patients saw clinically meaningful improvements in TIS, but zetomipzomib demonstrated no significant differentiation from placebo. At Week 16, the zetomipzomib 45 mg SC weekly group achieved a mean TIS of 25.5 versus the control group mean TIS of 25. Following cross-over, at Week 32, the arm receiving zetomipzomib beginning at Week 16 achieved a mean TIS of 32.5 versus the control group mean TIS of 31.3.

Safety

Zetomipzomib was well tolerated over the course of the PRESIDIO trial. Adverse events were generally mild-to-moderate (Grade 1 or 2), and the most common treatment-emergent adverse events (TEAEs) were injection site reactions, which were transient and manageable. One subject withdrew from the study following an injection site reaction at Week 9. There were three Grade 3 serious adverse events in the zetomipzomib arms, all deemed unrelated to zetomipzomib, which occurred in two patients and did not result in discontinuation from the study or change in dose. One patient experienced a mechanical fall and syncope, and another patient had a retinal detachment. There was one Grade 3 adverse event in a placebo arm identified as a worsening rash. No opportunistic infections or cytopenias were observed. Safety data is summarized in the table below.

Safety and Tolerability of Zetomipzomib for the 32-week PRESIDIO Trial

Patients Experiencing Adverse Events: N (%)	Zetomipzomib N=25	Placebo N=22*
Any adverse event	22 (88.0)	16 (72.7)
At least 1 TEAE	22 (88.0)	16 (72.7)
Nausea	3 (12.0)	3 (13.6)
Vomiting	1 (4.0)	1 (4.5)
Most Common TEAEs		
Injection-site Reaction	18 (72.0)	8 (36.4)
TEAEs = Grade 3 (all unrelated)	2 (8.0)	1 (4.5)
Infectious TEAEs ≥ Grade 3	0	0
Infectious TEAEs, all Grades	7 (28.0)	6 (27.3)
Opportunistic Infections	0	0
Serious TEAE (all unrelated)	2 (8.0)	0

*Three patients withdrew in Period 1 prior to receiving placebo in Period 2

Open-label Extension Study

KZR-616-003E is an open-label extension (OLE) study available to patients who completed 32 weeks in the PRESIDIO trial. Following completion of PRESIDIO, 18 out of 20 patients enrolled in the OLE. For the first time, patients have the option to self-administer zetomipzomib in the OLE. Current active participation in the OLE ranges from 2 to 77 weeks. 6 patients have discontinued participation in OLE for reasons unrelated to zetomipzomib.

No additional safety or tolerability issues have been observed, and mean TIS scores have improved over scores observed at the 32-week conclusion of PRESIDIO.

“I want to thank all the investigators, site staff, Kezar employees and most importantly the patients for their commitment to this study in the face of profound pandemic-related headwinds. While we are disappointed with the results of this trial, we are encouraged by the favorable safety data and we maintain our strong conviction in the promise of zetomipzomib in lupus nephritis and our commitment to development of this novel agent in autoimmune disease,” said John Fowler, CEO. “The strong response rates we’ve seen to date in MISSION – utilizing objective endpoints in LN patients – informs this conviction, and we look forward to sharing topline results from that trial in June. Furthermore, our strong financial position provides ample runway for both our zetomipzomib and protein secretion programs, including our Phase 1 trial of KZR-261 in solid tumors.”

Kezar’s unaudited cash position is approximately $253 million, including cash, cash equivalents and marketable securities as of April 30, 2022. The company plans to report the MISSION Phase 2 topline data in lupus nephritis (LN) at a Kezar corporate event in June 2022.

About Zetomipzomib (KZR-616)

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 clinical trials provide evidence that zetomipzomib exhibits a favorable safety and tolerability profile for development in severe, chronic autoimmune diseases.

In addition to PRESIDIO, Kezar is conducting the MISSION Phase 2 trial in patients with lupus nephritis. Interim data from this trial reported in November 2021 showed that of the five patients who completed the full course of 24 weeks of weekly treatment with zetomipzomib 60 mg doses, two achieved partial renal responses (PRRs) and two achieved complete renal responses (CRRs).

About Dermatomyositis and Polymyositis

Dermatomyositis and Polymyositis are two of the five types of autoimmune myositis diseases. Both are chronic, debilitating, inflammatory autoimmune myopathies that are distinguished by inflammation of the muscles as well as the skin (in DM). Approximately 30,000 to 120,000 people in the United States are living with these severe and progressive inflammatory myopathies that are characterized by marked morbidity and associated mortality. While debilitating muscle weakness is the hallmark of these myopathies, including compromised muscles of respiration, other internal organ system dysfunctions can be equally disabling. The aim of treatment for these diseases is to suppress inflammation, increase muscle strength and prevent long-term damage to muscles and extramuscular organs; however, treatment options are limited for DM, and there are currently no approved treatments for PM.

About Kezar Life Sciences

Kezar Life Sciences is a clinical-stage biopharmaceutical company discovering and developing breakthrough 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 being evaluated in Phase 2 clinical trials in lupus nephritis, dermatomyositis and polymyositis. 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,” “should,” “expect,” “believe,” “promise,” “potential,” “look forward,” “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 sufficiency of Kezar’s capital and other resources, the anticipated clinical and regulatory development of Kezar’s product candidates, the anticipated approval of the nonproprietary name of KZR-616, the preliminary nature of interim and topline data, 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 Kezar’s product candidates. Many factors may cause differences between current expectations and actual results, including the availability of additional data, the confirmation of interim and topline data resulting from trial audit and verification procedures, unexpected safety or efficacy data observed during clinical studies, the impacts of the COVID-19 pandemic and other global events on the company’s business and clinical trials, changes in expected or existing competition, changes in the regulatory environment, 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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