Poseida Therapeutics Provides Update on Phase 1 Study of P-BCMA-101 CAR-T Product Candidate at the 2018 American Society of Hematology Annual Meeting

P-BCMA-101 showed a 100% ORR with patients achieving rapid and deep responses with no CRS or neurotoxicity observed at the planned Phase 2 dose

SAN DIEGO – Dec. 3, 2018 – Poseida Therapeutics Inc., a clinical-stage biopharmaceutical company leveraging proprietary non-viral gene engineering technologies to create life-saving therapeutics, today provided an update on the ongoing Phase 1 clinical trial of its autologous P-BCMA-101, a chimeric antigen receptor T-cell (CAR-T) product candidate in relapsed/refractory multiple myeloma, during an oral presentation at the 2018 American Society of Hematology (ASH) Annual Meeting. As of the data cutoff date, 23 patients had been treated across five dosing cohorts with no dose limiting toxicities observed, including two patients in cohort five who had been dosed with more than one billion (1000 x 10e6) CAR-T cells each. All patients in each of the five cohorts had responded to P-BCMA-101 and showed improved markers of disease.

P-BCMA-101 showed a 100% objective response rate (ORR) in patients receiving the planned Phase 2 dose, and rapid and deep responses were observed in all patients. Patients receiving this dose include one patient in partial response who continues to improve and was negative for minimal residual disease (MRD-) with no detectable disease in the bone marrow. A second patient was in very good partial response (VGPR) and awaiting a bone marrow biopsy, while a third patient reached VGPR with no detectable disease in the bone marrow. Notably, no patient at the highest dosing levels in cohort 4 or cohort 5 has had any cytokine release syndrome (CRS) or neurotoxicity.

Overall, of the 19 patients evaluable by International Myeloma Working Group (IMWG) criteria, 15 showed meaningful responses, including 13 who reached stringent complete response (sCR), complete response (CR), VGPR or partial response (PR), and two patients in minor response (MR) who were dosed within the last 60 days and continue to show improvement. Of these, five patients had reached sCR, including MRD-, CR or VGPR as of the cutoff date. P-BCMA-101 continued to be well tolerated in the trial, with two mild and transient instances of suspected cytokine release syndrome (CRS) observed, and one patient with possible neurotoxicity, each of which occurred at doses below the planned Phase 2 dose.

“These data suggest that our CAR-T product candidate, which is comprised of a high percentage of stem cell memory T cells (Tscm), has the potential to be truly differentiated and result in more gradual peak expansion leading to deep responses and lower toxicity as observed so far in this trial,” said Eric Ostertag, M.D., Ph.D., chief executive officer of Poseida Therapeutics. “Although CRS and neurotoxicity have been significant risk factors in other CAR-T therapies with reported rates as high as 90% for some products, we have observed very little CRS or neurotoxicity and, when it has been suspected, it has been mild and transient.”

P-BCMA-101 is composed primarily of Tscm, a very young subset of T cells that are long-lived, self-renewing and multipotent, with the capacity to reconstitute the entire spectrum of T cell subsets, including T effector cells. They also survive for decades, and potentially for entire lifespans, with non-CAR-Tscm cells normally providing lifelong T cell immunity against some infectious agents.

As of November 29, 2018, 23 patients had been treated across five dose groups in the clinical trial. Patients are treated with a single weight-based dose of P-BCMA-101. The doses received by the patients are listed by dose group in the table below:

Dose Group	CAR-T cells administered (mean)	Patients (#)
1	$51x10^6$	3
2	$152x10^6$	7
3	$456x10^6$	7
4	$845x10^6$	4
5	$1143x10^6$	2

The median patient age was 61, with 13 patients considered high-risk, including those with high-risk cytogenetics. The majority of patients received six or more prior lines of therapy and all patients had received at least one proteasome inhibitor and at least one IMiD. Ninety-one percent of the patients had received daratumumab and eighty-six percent of the patients had received an autologous stem cell transplant. Peak T-cell expansion was observed between days 14 and 21, which is more gradual than the five to 14-day peak expansion typically seen with other CAR-T therapies and was associated with less acute cytokine release and other adverse effects. Poseida has not conducted a head-to-head study comparing P-BCMA-101 to other CAR-T therapies.

Interim Safety Update

All 23 patients treated to as of the data cutoff date received a single dose of P-BCMA-101 following a standard conditioning regimen of lymphodepleting chemotherapy consisting of 300 mg/m2 cyclophosphamide and 30 mg/m2 fludarabine. Two cases of suspected CRS (9.5%) were observed, one Grade 1 and one Grade 2. In both cases, the suspected CRS was minimal and transient and neither patient was treated with an IL-6 inhibitor or steroids, which are standard therapies for CRS. In addition, no patient has required admittance to the intensive care unit for CRS or neurotoxicity. In both patients, peak measured IL-6 levels, a suspected correlate marker for CRS, were under 50 pg/ml, well below the levels typically associated with meaningful or serious CRS. One case of suspected neurotoxicity (4.8%) was observed in a patient with mental status changes prior to treatment and was treated with an IL-6 inhibitor and steroids. No dose limiting toxicities have been reported. To date, use of the safety switch has not been indicated in any patient.

“We recently received RMAT designation from the FDA and believe the data support our plan to pursue a registrational clinical trial for P-BCMA-101 to begin in the first half of 2019, with the goal of moving toward a potential biologics license application filing by the end of 2020 subject to positive data from such study,” continued Ostertag.

This open-label, multicenter, single-ascending dose, Phase 1 study is designed to assess the safety of P-BCMA-101 in up to 40 subjects with relapsed and/or refractory multiple myeloma. The primary objective of this study is to determine the safety and maximum-tolerated dose of P-BCMA-101. Secondary objectives include anti-myeloma effect of P-BCMA-101. This study is funded in part by the California Institute for Regenerative Medicine. Additional information about the Phase 1 clinical study of P-BCMA-101 is available at www.clinicaltrials.gov using identifier: NCT03288493

About P-BCMA-101

P-BCMA-101 is an autologous CAR-T therapeutic candidate being developed to treat patients with relapsed/refractory multiple myeloma. P-BCMA-101 targets cells that express B cell maturation antigen, or BCMA, which is expressed on essentially all multiple myeloma cells. P-BCMA-101 is engineered with Poseida's non-viral piggyBac™ DNA Modification System, resulting in a high percentage of T stem cell memory cells. Preliminary results from the company's ongoing Phase 1 clinical trial suggest that P-BCMA-101 may have improved response rates with a favorable safety profile compared to published results from clinical trials of other CAR-T therapies at similar doses. The Phase 1 study is funded in part by the California Institute for Regenerative Medicine.

About Poseida Therapeutics, Inc.

Poseida Therapeutics is a clinical-stage biotechnology company leveraging proprietary next-generation non-viral, gene engineering technologies to create life-saving therapeutics for patients with high unmet medical need. The company is developing a wholly-owned pipeline of autologous and allogeneic CAR-T product candidates, initially focused on the treatment of hematological malignancies and solid tumors. Poseida's product candidates are designed to address the limitations of other CAR-T therapies, including duration of response, the ability to treat solid tumors and safety concerns. P-BCMA-101 is Poseida's lead CAR-T product candidate, currently in Phase 1 clinical development for the treatment of relapsed/refractory multiple myeloma.

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