UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported):
December 6, 2022

Poseida Therapeutics, Inc.
(Exact name of registrant as specified in its charter)

Delaware	001-39376	47-2846548
(State or other jurisdiction of incorporation)	(Commission File Number)	(I.R.S. Employer Identification No.)

9390 Towne Centre Drive, Suite 200, San Diego, California	92121
(Address of principal executive offices)	(Zip Code)

Registrant's telephone number, including area code: (858) 779-3100

N/A
(Former name or former address, if changed since last report.)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.0001 per share	**PSTX**	**Nasdaq Global Select Market**

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

On December 6, 2022, Poseida Therapeutics, Inc. (the "Company") issued a press release announcing the publication of two posters, which present early data from the Company's Phase 1 clinical trials of P-MUC1C-ALLO1 and P-BCMA-ALLO1. The posters will be presented at the European Society for Medical Oncology Immuno-Oncology Annual Congress taking place in Geneva, Switzerland and online from December 7-9, 2022. A copy of the press release and the posters to be presented are attached as Exhibits 99.1, 99.2 and 99.3, respectively, to this report.

The information in this Item 7.01 of this report (including Exhibit 99.1, Exhibit 99.2 and Exhibit 99.3) is furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or subject to the liabilities of that section or Sections 11 and 12(a)(2) of the Securities Act of 1933, as amended. The information shall not be deemed incorporated by reference into any other filing with the Securities and Exchange Commission made by the Company, whether made before or after today's date, regardless of any general incorporation language in such filing, except as shall be expressly set forth by specific references in such filing.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	Description
99.1	Press Release of Poseida Therapeutics, Inc., dated December 6, 2022.
99.2	Poster: Development of an Allogeneic CAR-T Targeting MUC1-C (MUC1, Cell Surface Associated, C-Terminal) for Epithelial Derived Tumors.
99.3	Poster: Phase 1 Study to Assess the Safety and Efficacy of P-BCMA-ALLO1, a Fully Allogeneic CAR-T Therapy, in Patients with Relapsed / Refractory Multiple Myeloma (RRMM).
104	Cover Page Interactive Data File

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Poseida Therapeutics, Inc.

Date: December 6, 2022

By: /s/ Harry J. Leonhardt, Esq.
Name: Harry J. Leonhardt, Esq.
Title: General Counsel, Chief Compliance Officer & Corporate Secretary

Poseida Therapeutics to Present Early Data from Phase 1 Trials of P-MUC1C-ALLO1 and P-BCMA-ALLO1 at ESMO Immuno-Oncology 2022 Annual Congress

P-MUC1C-ALLO1 and P-BCMA-ALLO1 were well tolerated, with no dose-limiting toxicities (DLTs), cytokine release syndrome (CRS), graft vs host disease (GVHD) or immune effector cell-associated neurotoxicity syndrome (ICANS)

P-MUC1C-ALLO1 demonstrated encouraging clinical activity including an objective partial response in a breast cancer patient at the lowest dose

P-BCMA-ALLO1 demonstrated responses in heavily pre-treated patients with relapsed/refractory multiple myeloma at the lowest CAR-T dose tested including in patients who had failed prior BCMA-targeted therapy and patients with high-risk disease

SAN DIEGO, December 6, 2022 — Poseida Therapeutics, Inc. (Nasdaq: PSTX), a clinical-stage cell and gene therapy company advancing a new class of treatments for patients with cancer and rare diseases, today announced it will present early clinical results from its Phase 1 clinical trials of P-MUC1C-ALLO1 and P-BCMA-ALLO1 at the European Society for Medical Oncology Immuno-Oncology (ESMO I-O) 2022 Annual Congress, taking place in Geneva, Switzerland and online from December 7-9, 2022.

"These early data being presented at ESMO I-O for our first two fully allogeneic programs reinforce our belief that our technology and approach have the potential to deliver differentiated off-the-shelf CAR-T cell therapies to patients fighting cancer," said Mark Gergen, Chief Executive Officer of Poseida Therapeutics. "While it is still quite early in both trials, we have seen encouraging responses in both P-MUC1C-ALLO1 and P-BCMA-ALLO1 at the lowest doses as well as favorable tolerability. As we look ahead, we are excited to continue enrolling patients at higher dose levels and explore additional strategies to optimize the therapeutic index, including redosing, cyclic dosing, novel preconditioning regimens and combination therapies. We look forward to providing updates at a medical meeting in 2023."

Both posters will be presented at ESMO I-O on Thursday, December 8, 2022 at 12:30-1:15 PM CET in Foyer ABC at the Palexpo Exhibition Centre in Geneva and are now available on the Poseida website at www.poseida.com.

In the poster titled *"Development of an allogeneic CAR-T targeting MUC1-C (MUC1, cell surface associated, C-terminal) for epithelial derived tumors"* (abstract #407, presentation 46P), David Oh, M.D., Ph.D., Assistant Professor, University of California, San Francisco, will highlight:

- As of the cutoff date of November 14, 2022, the study had dosed seven patients with epithelial-derived cancers, including esophageal, colorectal, breast, pancreatic and prostate carcinomas, of which four were evaluable for response.

- Only one patient with breast cancer has been dosed to date; this patient with HR+, HER2- breast cancer, with four prior lines of treatment, achieved a partial response at a dose of $0.75x10^6$ cells/kg.
- Two other patients with heavily pretreated gastrointestinal tumors (colorectal and pancreatic cancer) achieved stable disease at a dose of $0.75x10^6$ cells/kg and $2x10^6$ cells/kg each.
- P-MUC1C-ALLO1 was safe and well tolerated, with no DLTs, CRS, GVHD or ICANS.

“We are very encouraged by these early data highlighting initial safety and tolerability as well as signs of clinical activity of P-MUC1C-ALLO1 even at very low doses,” said Dr. Oh, an investigator on the trial. “Importantly, for a novel target such as MUC1-C it has been a key focus to monitor for any evidence of on-target off-tumor toxicity, and we are pleased that we have not observed any such significant toxicity to date. Overall, we believe that these data support MUC1-C as a target with the potential to address the significant unmet need in patients with advanced carcinomas. We look forward to continuing to evaluate the safety, efficacy and durability of responses as we continue to enroll additional patients into the study.”

In the poster titled *“Phase 1 Study to Assess the Safety and Efficacy of P-BCMA-ALLO1, a Fully Allogeneic CAR-T Therapy, In Patients with Relapsed/Refractory Multiple Myeloma (RRMM)”* (abstract #705, presentation 47P), Mehmet Hakan Kocoglu, M.D., Assistant Professor, University of Maryland Medical Center, will highlight:

- As of the cutoff date of November 11, 2022, the study had dosed 10 patients with relapsed/refractory (R/R) multiple myeloma, Of these ten patients, six are evaluable for response (all at the lowest dose level of 0.75×10^6 cells/kg).
- The response evaluable patients were heavily pre-treated, having received an average of 6.5 prior lines of therapy with a median time since diagnosis of 5 years. Three patients had previously received BCMA-targeted therapy and four patients had high-risk cytogenetics, of which two had p53 deletions.
- As of the cutoff date, P-BCMA-ALLO1 achieved a 50% (3/6) overall response rate, with a 66% (2/3) ORR in patients who had previously received BCMA-targeted therapy and a 50% (2/4) ORR in patients with high-risk cytogenetics.
- Of the three responders in the first cohort ($0.75x10^6$ cells/kg), two patients were partial responses and one patient achieved a very good partial response.
- P-BCMA-ALLO1 was extremely well tolerated. There were no cases of CRS, GVHD or ICANS. No DLTs were observed. There was one case of febrile neutropenia.

“To date, P-BCMA-ALLO1 has demonstrated a favorable safety and tolerability profile in patients with R/R multiple myeloma. We have also observed encouraging efficacy signals even at the lowest doses highlighting the potential of Poseida’s proprietary genetic editing platforms in allogeneic cell therapies,” said Dr. Kocoglu, an investigator on the trial. “In particular, we have seen responses in patients with p53 mutations, a known marker for aggressive multiple myeloma as well as in patients who had received prior BCMA-targeted therapy. These early results support the potential of P-BCMA-ALLO1 to treat a broad patient population with an off-the-shelf CAR-T therapy and we look forward to continuing enrollment in the study.”

About P-MUC1C-ALLO1

P-MUC1C-ALLO1 is an allogeneic CAR-T product candidate in Phase 1 development for multiple solid tumor indications. Poseida believes P-MUC1C-ALLO1 has the potential to treat a wide range of solid tumors derived from epithelial cells, such as breast, ovarian, colorectal, lung, pancreatic and renal carcinomas, as well as other cancers expressing a cancer-specific form of the Mucin 1 protein, or MUC1-C. P-MUC1C-ALLO1 is designed to be fully allogeneic, with genetic edits to eliminate or reduce both host-vs-graft and graft-vs-host alloreactivity. Poseida has demonstrated the elimination of tumor cells to undetectable levels in preclinical models of both breast and ovarian cancer. Additional information about the Phase 1 study is available at www.clinicaltrials.gov using identifier: NCT05239143.

About P-BCMA-ALLO1

P-BCMA-ALLO1 is an allogeneic CAR-T product candidate, partnered with Roche, targeting B-cell maturation antigen (BCMA) for the treatment of relapsed/refractory multiple myeloma in Phase 1 development. In vitro and in vivo P-BCMA-ALLO1 preclinical studies showed effective, targeted cancer cell killing and cytokine secretion, with similar or superior anti-tumor efficacy compared to an autologous CAR-T therapy. Additional information about the Phase 1 study is available at www.clinicaltrials.gov using identifier: NCT04960579.

About Poseida Therapeutics, Inc.

Poseida Therapeutics is a clinical-stage biopharmaceutical company advancing differentiated cell and gene therapies with the capacity to cure certain cancers and rare diseases. The Company's pipeline includes allogeneic CAR-T cell therapy product candidates for both solid and liquid tumors as well as in vivo gene therapy product candidates that address patient populations with high unmet medical need. Poseida's approach to cell and gene therapies is based on its proprietary genetic editing platforms, including its non-viral Super piggyBac® DNA Delivery System, Cas-CLOVER™ Site-Specific Gene Editing System and nanoparticle and hybrid gene delivery technologies. The Company has formed global strategic collaborations with Roche and Takeda to unlock the promise of cell and gene therapies for patients. Learn more at www.poseida.com and connect with Poseida on Twitter and LinkedIn.

Forward-Looking Statements

Statements contained in this press release regarding matters that are not historical facts are "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. Such forward-looking statements include statements regarding, among other things, expected plans with respect to clinical trials, including timing of clinical data updates; the potential benefits of Poseida's technology platforms and product candidates; and Poseida's plans and strategy with respect to developing its technologies and product candidates. Because such statements are subject to risks and uncertainties, actual results may differ materially from those expressed or implied by such forward-looking statements. These forward-looking statements are based upon Poseida's current expectations and involve assumptions that may never materialize or may prove to be incorrect. Actual results could differ materially from those anticipated in such forward-looking statements as a result of various risks and uncertainties, which include, without limitation, Poseida's reliance on third parties for various aspects of its business; risks and uncertainties associated with development and regulatory approval of novel product candidates in the biopharmaceutical industry; Poseida's ability to retain key scientific or management personnel; and the other risks described in Poseida's filings with the Securities and Exchange Commission. All forward-looking statements contained in this press release speak only as of the date on which they were made. Poseida undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made, except as required by law.

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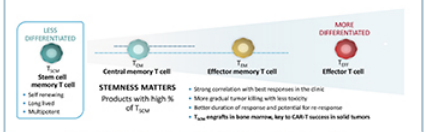
46P - Development of an allogeneic CAR-T targeting MUC1-C (MUC1, cell surface associated, C-terminal) for epithe

David Y. Oh,[1] Jason T. Henry,[2] Joaquina Baranda,[3] Ecaterina E. Dumbrava,[4] Ezra Cohen,[5] Rajesh Belani,[6] Jeff D. Eskew,[6] Joanne McCaigue,[6] Hamid Namini,[6] Christopher E. Martin,[6] Ann Murphy,[6] Eric Ostertag,[6] Julia Coronella,[6] Devon J. Shedlock,[6] Ilde
[1]University of California San Francisco, Helen Diller Family Comprehensive Cancer Center, San Francisco, CA; [2]Sarah Cannon Research Institute at HealthOne, Denver, CO; [3]University of Kansas Cancer Center, Kansas City, KS; [4]MD Anderson Cancer Center, Houston, TX; [5]
CA; [6]Poseida Therapeutics, Inc., San Diego, CA; [7]NEXT Oncology, San Antonio, TX

BACKGROUND

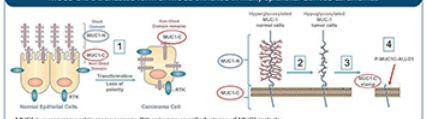
- Most solid tumors are of epithelial origin and express mucin 1 (MUC1) and its C-terminal domain MUC1-C (MUC1, cell surface associated, C-terminal), such as breast, ovarian, prostate, colorectal, pancreatic, gastric, esophageal, nasopharyngeal, as well as non-small cell lung cancer, renal cell carcinoma, head-and-neck squamous cell carcinoma, and others
- There have been multiple clinical-stage therapeutics targeting MUC1, including chimeric antigen receptor (CAR)-T therapies, antibody-drug conjugates, and bispecific T-cell engagers which have thus far demonstrated little evidence for "on-target, off-tumor" toxicity[1-3]
- MUC1-C is expressed broadly and accessibly throughout tumor tissue due to the loss of cell polarity, one of the hallmarks of tumorigenesis
- We have developed a fully allogeneic CAR-T cell therapy, called P-MUC1C-ALLO1, that targets a MUC1-C epitope. P-MUC1C-ALLO1 is manufactured using non-viral transposon-based integration (piggyBac® DNA Delivery System), resulting in a highly enriched T stem cell memory (T_{SCM}) product, and is gene edited with Cas-CLOVER to knock out B2M and TRBC. P-MUC1C-ALLO1 administration resulted in complete elimination of solid tumors in murine models
- This first-in-human Phase 1 clinical trial is evaluating a CAR-T in epithelial-based solid tumors

P-MUC1C-ALLO1 is highly enriched for T stem cell memory CAR-Ts



Allogeneic platform incorporates learnings from our autologous experience

MUC1-C is a truncated form of MUC1 enriched in many epithelial-derived carcinomas

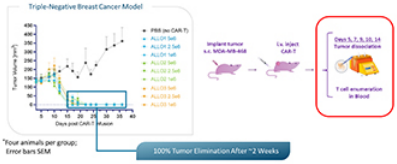


MUC1 is overexpressed in many cancers. Other tumor-specific features of MUC1 include:
1. MUC1 is normally expressed on apical surface of epithelium, but globally on all surfaces of cancer cells due to loss of cell polarity
2. MUC1 is hypoglycosylated on tumor cells
3. Increased shedding of MUC1-N due to proteases in the tumor microenvironment, producing high levels of monomeric MUC1-C
4. The presence of cryptic epitopes on MUC1-C in the tumor microenvironment, hypothesized to be the result of proteolysis

Disclosures: The presenter has the following relevant financial and non-financial relationships to disclose: Financial interests relating to Research Support: Merck Sharp and Dohme, PACT Pharma, Poseida Therapeutics, TCR2 Therapeutics, Roche/Genentech, Nutcracker Therapeutics. Regents of the University of California; Financial interests relating to Travel/Accommodations: Roche/Genentech
Presenting author: David.Oh@ucsf.edu
Clinical trial identifier: NCT05123443
Study sponsored by Poseida Therapeutics

PRECLINICAL RATIONALE

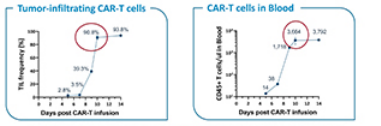
Can P-MUC1C-ALLO1 Infiltrate into Solid Tumor?



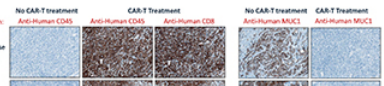
*Four animals per group; Error bars SEM

100% Tumor Elimination After ~2 Weeks

Massive P-MUC1C-ALLO1 Tumor Infiltration and loss of MUC1-C+ tumor cells post CAR-T Infusion



Xenograft immunohistochemistry after CAR-T cell infusion



- Maximum tumor infiltration at 10 days post CAR-T infusion resulting in **>90% of cells in tumor mass at day 10 are CAR-T (TIL)**
- TIL at day 10 are more differentiated T_{SCM} while reservoir of T_{SCM} / T_{CM} resides in bone marrow
- Data previously presented on Poseida's P-PSMA-101 show CAR-T bone trophic activity in mCRPC in which a biopsy of prior bone metastasis showed CAR-T cells, bone remodeling, and bone marrow but no tumor cells[4]

P-MUC1C-ALLO1 epitope highly prevalent in solid tumor indications

- A high percentage of tumor samples tested positive for staining with scFv binder used by P-MUC1C-ALLO1 CAR
  - ~90% of breast and colon tumors were positive, as were 88% of ovary, 81% of lung, and 81% of renal tumors
- Expression profile was consistent with what has been widely reported for full-length MUC1

*Numbers above bar indicate number of samples analyzed

ABBREVIATIONS: AE = adverse event; ALT = alanine aminotransferase; ANC = absolute neutrophil count; AST = aspartate aminotransferase; BLI = bioluminescent imaging; CNS = central nervous system; CRS = cytokine release syndrome; CTC = circulating tumor cells; DOR = duration of response; Hb = hemoglobin; HLH = hemophagocytic lymphohistiocytosis; ICANS = immune effector cell-associated neurotoxicity; LTFU = long-term follow-up; LVEF = left ventricular ejection fraction; MAS = macrophage activation syndrome; MTD = maximum tolerated dose; ORR = overall response rate; OS = overall survival; PBS = phosphate-buffered saline; PFS = progression-free survival; PTFU = post-treatment follow-up; Q2W, every 2 weeks; RECIST = Response Evaluation Criteria in Solid Tumors; RP2D = recommended Phase 2 dose; SAD = single ascending dose; TTR = time to response; ULN = upper limit of normal.

CLINICAL STUDY METHODS AND DESIGN

Topic	Detail
Study information	Phase 1, dose escalation, and expanded cohort study of P-MUC1C-ALLO1 in adults with advanced or metastatic solid tumors (NCT05239143). The study will include 15 years of follow-up and evaluate the safety, MTD, and antitumor effect of P-MUC1C-ALLO1
Study design	Part 1: Standard 3+3 design of dose-escalating cohorts **Arm A (SA):** single dose after cy/flu lymphodepletion **Arm B (CYC):** multiple doses in cycles q2W after cy/flu lymphodepletion with ≤2 additional lymphodepletion in cycles ≥6-week intervals **Arm C (SA-RIT):** singe dose after cy/flu plus rituximab lymphodepletion **Arm D (CYC-RIT):** multiple doses in cycles q2W after cy/flu/rit lymphodepletion with ≤2 additional lymphodepletion in cycles ≥6-week intervals Part 2: RP2D at cMTD in groups of up to 15 patients with defined characteristics
Study patient population	Adults with confirmed unresectable, locally advanced or metastatic epithelial-derived solid tumors refractory to standard of care therapy or ineligible or refused another existing treatment option
Proposed sample size	Up to 100 patients (including up to 40 in the expansion)
Evaluation criteria: efficacy, safety, and other variables	Safety/feasibility: AEs, labs, CRS, neurotoxicity, and MAS/HLH* Efficacy: RECIST v1.1 and secondarily iRECIST; ORR, TTR, DOR, PFS, OS, CTCs, P-MUC1C-ALLO1 cells (vectors/clonality)
Exploratory	MUC1-C expression in tumor biopsies and by related markers CA15-3 and CA27-29; P-MUC1C-ALLO1 cell kinetics and phenotype including β2M expression; immunogenicity in context of patient-donor match metrics. Cytokine correlates of lymphodepletion, safety, and efficacy

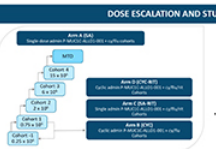
Major inclusion criteria

- Advanced or metastatic epithelial-derived solid tumor with measurable disease per RECIST v1.1
- Refractory to standard of care treatment or ineligible/refused other existing treatment options
- ANC ≥1000 /µL, platelets 50,000 /µL, Hb ≥8 g/dL
- Ferritin ≤5000 ng/mL. Creatinine ≤1.5 mg/dL, LFTs ≤1.5 x ULN

Major exclusion criteria

- No active second primary malignancies
- No active autoimmune disease
- No active systemic infections
- No significant CNS, liver or heart disease

DOSE ESCALATION AND STUDY SCHEMATIC



Planned dose escalation*

If the Maximum Tolerated Dose (MTD) has not been reached in Arm A following completion of Cohort 4, the dose of P-MUC1C-ALLO1 may be increased by 5-10 x10^6 cells/kg for the subsequent dose levels as agreed upon with the safety committee and the FDA

* Doses are weight-based (cells/kg)

P-MUC1C-ALLO1 MANUFACTURING CHARACTERISTICS

Mean (Range)	Clinical Lots (n = 6)
CD4/CD8 Ratio	0.9 (0.3, 2.0)
Stem cell memory CD8 T cells, %	54.8 (32.9, 73.9)
Central memory CD8 T cells, %	44.4 (19.2, 66.7)
Effector memory CD8 T cells, %	0.6 (0.2, 1.8)
Effector CD8 T cells, %	0.2 (0, 0.6)
% CCR7 +	95.0 (94.0, 95.8)
% CAR +	38.3 (36.7, 38.9)

- P-MUC1C-ALLO1 is largely comprised of early memory T cells, i.e., T_{SCM} and T_{CM} (CD45RO$^-$CD45RA$^+$CD62L$^+$ or CD45RO$^+$CD45RA$^-$CD62L+, respectively)
- Low composition of late memory T cells (<5%)
- Products are consistently >90% CCR7+
- Reliably high frequency of CAR+ cells (>95%) across clinical lots

PHASE 1 DOSE-ESC

Patient demogra

CAR-T cells administered, cells/kg	
Cohort 1: 0.75 x 10^6 single infusion	
Cohort 2: 2.0 x 10^6 single infusion	
Parameter (n=6)	
Age, median (min, max), years	
Time since diagnosis, median (min, max), years	
Baseline ECOG performance status, 0/1, n (%)	
Prior therapy	
No. of prior regimens, all patients (n=6): median (mi	

Cohort	Patient #	Sex	
1	1	M	Esophag
1	2	M	
1	3	F	Bre
2	4	M	
2	5	F	
2	6	M	

*Cutoff: 14 Nov 2022

PATIENT SAFE

Cohort/ cell dose	Patient #	Dose-limiting toxicities
Cohort 1 0.75 x 10^6 cells/kg	1	None
	2	None
	3	None
Cohort 2 2 x 10^6 cells/kg	4	None
	5	None
	6	None

*NE = Not evaluable as subject has not completed D28 DLT ev

Safety

- No dose-limiting toxicities or SAEs considered relat
- No CRS, ICANS, or graft vs host disease were obser
- Grade 3-4 treatment-emergent AEs were anemia ((n=2) and subclavian vein thrombosis (n=1)

Efficacy

- Six heavily pretreated patients have been dosed w of PR and 1 had SD at the low starting dose of 0.7

CO

- P-MUC1C-ALLO1 is largely comprised of e
- The Phase 1 trial for P-MUC1C-ALLO1 was across 15 sites
- Three patients have been treated with P-M
- Both cohort 1 and cohort 2 were complete observed
- Early signs of clinical activity were observe dose and two other patients with gastroin
- P-MUC1C-ALLO1 Phase 1 trial enrollment cohort 3 dose-level (Arm A) and cyclic dos per protocol for re-treatment at the origin

REFERENCES: 1. Taylor-Papadimitriou J et al. Biochem Soc Trans. 2
3. Specht J et al. J Clin Oncol. 2021;39(suppl 15). Abstract 4. Lee D

ACKNOWLEDGEMENTS: The authors and Poseida Therapeutics, Inc.,
study. This study was funded by Poseida (San Diego, CA).

47P - Phase I Study to Assess the Safety and Efficacy of P-BCMA-ALLO1, a Fully Allogeneic CAR T T Patients with Relapsed / Refractory Multiple Myeloma (RRMM)

Mehmet Kocoglu,[1] Adam Asch,[2] Aravind Ramakrishnan,[3] Carlos Bachier,[4] Thomas Martin III,[5] Tulio Rodriguez,[6] Katherine McArthur,[7] Joanne McCaigue,[7] Christopher E. Martin,[7] Maggie Zhang,[7] Hamid Namini ,[7] Eric Ostertag,[7] Matthew A. Spear,[8] Ellen Christie,[7] Rajesh Belani,[7] Stacey Cranert,[7] Julia Corone

[1]University of Maryland Greenebaum Cancer Center, Baltimore, MD; [2]Stephenson Cancer Center, Oklahoma University, Oklahoma City, OK; [3]Sarah Cannon Transplant and Cellular Therapy Program at St. David's South Austin Medical Center, Austin, TX; [4]Sarah Cannon Transplant and Cellular Therapy Progr Medical Center at Parnassus, San Francisco, CA; [6]Bone Marrow Transplantation, Advocate Lutheran General Hospital, Park Ridge, IL; [7]Poseida Therapeutics, Inc., San Diego, CA; [8]Denovo Biopharma, San Diego, CA; [9]UCSD Moores Cancer Center, La Jolla, CA

BACKGROUND

- Multiple myeloma (MM) is an incurable plasma cell malignancy with high expression of B-cell Maturation Antigen (BCMA)
- Autologous Chimeric Antigen Receptor T-cell (CAR T) therapies targeting BCMA have shown significant activity in MM
- Unfortunately, autologous CAR T poses several challenges including the need for apheresis, long manufacturing times, high manufacturing costs, costs and poor product quality because the T-cells are obtained from myeloma patients
- An allogeneic "off the shelf" CAR T could address these unmet needs by eliminating the need for apheresis, providing on demand therapy and better-quality T-cells from healthy donors for manufacturing
- P-BCMA-ALLO1 is an allogeneic CAR T targeting BCMA being investigated for the treatment of relapsed refractory multiple myeloma (RRMM)
- P-BCMA-ALLO1 utilizes non-viral transposon-based integration (piggyBac® DNA Delivery System) that introduces a humanized anti-BCMA VH-based CAR producing a highly enriched T stem cell memory (T_{SCM}) product
- The Cas-CLOVER™ Site-Specific Gene Editing System eliminates endogenous T cell receptor (TCR) expression via knockout of the *TCR beta chain 1* gene to prevent graft-vs-host disease and reduces MHC class I expression to eliminate host-vs-graft responses via *beta-2 microglobulin* gene knockout
- P-BCMA-ALLO1 demonstrated compelling activity in MM xenografts, providing rationale for this first-in-human phase I study

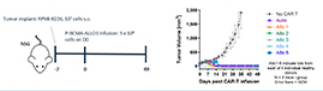
CAS-CLOVER: CLEAN GENE EDITING

Potentially the Cleanest Gene Editing Platform
with important ability to efficiently edit resting cells enables fully **Allogeneic CAR-T** products and **Gene Therapy** applications including ongoing development for non-viral in vivo gene editing

ALLOGENEIC PLATFORM

PRECLINICAL RESULTS

Efficacy in the RPMI-8226 Multiple Myeloma Model



CLINICAL STUDY METHODS AND DESIGN

Topic	Detail
Study information	Open label, multicenter, Phase 1, dose escalation study to assess the safety and efficacy of P-BCMA-ALLO1, which will be administered intravenously as a single dose. Dose levels will be tested in 3+3 escalation design in approximately 40 RRMM patients
Study design	**Dose escalation**: Standard 3+3 design is utilized in the dose-escalating cohorts to evaluate DLTs within 28 days post P-BCMA-ALLO1 administration. Adverse events (AE), Serious Adverse Events (SAE) and Treatment Emergent Adverse Events (TEAEs) will be evaluated throughout the study. If cohort 5 is completed without a Maximum Tolerated Dose (MTD), the Safety Committee may elect to assess further escalation cohorts in higher dose levels. P-BCMA-ALLO1 will be administered on D0 following lymphodepleting chemotherapy: Fludarabine 30 mg/m²/day and cyclophosphamide 300 mg/m²/day on D-5, -4, -3
Study patient population	RRMM patients who have received greater than 3 lines of therapy, which must include a proteasome inhibitor (PI), immunomodulatory drug (IMiDs) and CD38 monoclonal antibody (mAb)
Evaluation criteria: efficacy, safety, and other variables	Safety/Teasibility: AE, Cytokine Release Syndrome (CRS), neurotoxicity, Graft vs Host Disease (GVHD) Efficacy: IMWG criteria will be used for response. Overall Response Rate (ORR), Time to Response (TTR), Duration of Response (DOR), Progression Free Survival (PFS), Overall Survival (OS) will be analyzed.
Exploratory	P-BCMA-ALLO1 cellular kinetics; T cell composition in P-BCMA-ALLO1 drug product; immune response in the context of patient-donor match metrics; soluble BCMA levels; BCMA expression on MM cells; putative blood markers of safety and efficacy.

Major Inclusion Criteria

- Relapsed / Refractory Multiple Myeloma as defined by the IMWG
- Must have received at least three lines of therapy that must include a PI, IMiDs and CD38 mAb
- Have a measurable disease as defined by one of the following: 1) serum M-protein > 1.0g/dL; 2) Urine M-protein > 200mg/24hr; 3) FLC > 10 mg/dL; 4) Bone marrow plasma cells > 30%
- ANC ≥1000 /mL, platelets 50,000 /mL, Hb >8 g/dL
- Creatinine ≤1.5 mg/dL, SGOT < 3x ULN
- LVEF ≥45%

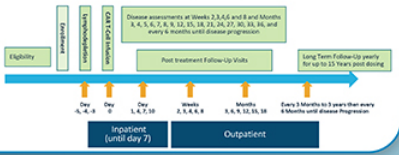
Major Exclusion Criteria

- Active hemolytic anemia; plasma cell leukemia, etc.
- Active second malignancies other than multiple myeloma
- Active autoimmune disease
- History of significant central nervous system disease
- Active systemic infections
- History of hepatitis; HTLV or HIV infection
- Has NYHA Class III or IV heart failure
- Received prior gene therapy

DOSE ESCALATION PLAN AND STUDY SCHEMATIC

Single infusion Dose Levels (cells/kg/dose) include:	
Cohort minus 2:	0.0625 x 10^6
Cohort minus 1:	0.25 x 10^6
Cohort 1:	0.75 x 10^6
Cohort 2:	2 x 10^6
Cohort 3:	6 x 10^6
Cohort 4:	10 x 10^6
Cohort 5:	15 x 10^6

If cohort 5 is completed without concluding an MTD, the safety Committee may elect to assess further escalation cohorts in 5-10 X 10^6 P-BCMA-ALLO1 cells/kg increments.



PHASE 1 DOSE-ESCALATION CLINICAL RESULTS

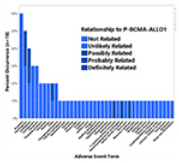
PATIENT DEMOGRAPHICS AND CHARACTERISTICS

CAR-T cells Administered: Cells/kg	Mean (Min/Max) x 10^6	Patients, n
Cohort 1: 0.75 x 10^6 single infusion	48 (37/ 64)	7
Cohort 2: 2.0 x 10^6 single infusion	142 (126/210)	3
Age / Gender/ Time since Diagnosis / Performance Status (n=10)		
Median (min, max) age, y		75 (33, 85)
Male, n (%)		9 (90)
Median (min, max) time since diagnosis, y		5.17 (3.48, 18.85)
Diagnosis Subtype, n (%)*		IgG, 7 (70)
		IgA, 2 (20)
		Kappa FLC, 5 (50)
		Lambda FLC, 5 (50)
Cytogenetic High-risk, n (%)		5 (50)
ECOG (Baseline) PS, 0 (%) /1 (%)		3 (30) / 7 (70)
Prior Therapy Exposure (n=10)		
Median (min, max) # prior regimens		6.5 (4, 10)
Prior anti-BCMA therapy, n (%)		3 (30)

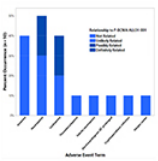
*No patients with IgM, IgE, IgD or Non-Secretory Diagnosis Subtypes

SAFETY RESULTS

Safety Population: All TEAEs



TEAEs Grade ≥ 3

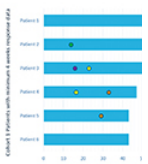


SUMMARY

- A total of 10 patients were treated with P-BCMA-ALLO1, 7 in cohort 1, and 3 in cohort 2
- Three SAE occurred in cohort 1 (G3 Febrile Neutropenia, G3 Disseminated Herpes Zoster, G3 Cryptosporidiosis infection)
- No SAE were related to P-BCMA-ALLO1
- **No CRS, GVHD, neurotoxicity, DLT or Adverse Events of Special Interest (AESI) have been observed as of the data cutoff**
- Six cohort 1 patients are available for response evaluation

EFFI

Patient	Cohort	Age	Prior Lines therapy
1	1	79	8
2	1	69	5
3	1	75	5
4	1	33	10
5	1	75	4
6	1	66	4



- All enrolled patients are heavily
- 3 out of 6 evaluable cohort 1 pat
- 4 out of 6 evaluable cohort 1 pat
- ORR for Cohort 1 is 50%
- ORR in patients who have receiv
- ORR in patients with high-risk cy

C

- P-BCMA-ALLO1 is an allogeneic "off t demonstrates compelling anti-myelo the lowest dose tested, while demon
- It is active in patients who have failed risk myeloma
- The clinical activity is seen without C
- P-BCMA-ALLO1 represents an import attractive treatment option for multip
- Dose escalation is ongoing
- Additional treatment regimens includ and fixed (non-weight based) dosing

Disclosures: The presenter has the following relevant financial and non-financial relationships to disclose: Financial Interests relating to research Support: Poseida Therapeutics
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