



The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

653.Multiple Myeloma: Prospective Therapeutic Trials

Trial in Progress: A Phase 1 Study of KTX-1001, an Oral, First-in-Class, Selective MMSET Inhibitor in Patients with Relapsed and Refractory Multiple Myeloma

Jesus G. Berdeja, MD¹, David Dingli, MD², Sagar Lonial, MD³, Andrew J. Yee, MD⁴, Alfred Chung, MD⁵, Cristina Gasparetto, MD⁶, P. Leif Bergsagel, MD⁷, Vivek Roy, MD⁸, Al-Ola Abdallah, MD^{9,10}, Sharmilan Thanendrarajan, MD¹¹, Aimaz Afrough, MD¹², Laura Rosiñol, MD PhD¹³, Suzanne Trudel, MD FRCPC¹⁴, Paula Rodriguez Otero, MD PhD¹⁵, Cyrille Touzeau, MD PhD¹⁶, Pierre Bories, MD PhD¹⁷, Soo Bang, MHSA¹⁸, Terry Connolly, PhD¹⁸, Michelle Kim¹⁸, Chad A. Lewis, PhD¹⁸, Bao-Van Tran Linberg¹⁸, M. Travis Quigley¹⁸, Ola Landgren, MD¹⁹, Saad Z Usmani, MD²⁰, Maria-Victoria Mateos²¹, David S. Siegel, MDPhD²²

¹ Sarah Cannon Research Institute, Nashville, TN

² Mayo Clinic, Rochester, MN

³ Department of Hematology and Medical Oncology, Winship Cancer Institute, School of Medicine, Emory University, Atlanta, GA

⁴ Massachusetts General Hospital Cancer Center, Boston, MA

⁵ Helen Diller Family Comprehensive Cancer Center, University of California, San Francisco, San Francisco, CA

⁶ Duke Cancer Institute, Duke University Medical Center, Durham, NC

⁷ Mayo Clinic, Phoenix, AZ

⁸ Division of Hematology-Oncology, Mayo Clinic, Jacksonville, FL

⁹ University of Kansas Medical Center, Kansas City, KS

¹⁰ US Myeloma Innovations Research Collaborative (USMIRC), Kansas City, KS

¹¹ Myeloma Center, Winthrop P. Rockefeller Cancer Institute, University of Arkansas for Medical Sciences, Little Rock, AR

¹² Hematologic Malignancies and Cellular Therapy, University of Texas Southwestern Medical Center, Dallas, TX

¹³ Hematopoietic Cell Transplantation Unit, Hospital Clínic de Barcelona, IDIBAPS, Barcelona, Spain

¹⁴ Division of Medical Oncology and Hematology, Princess Margaret Cancer Centre, Toronto, Canada

¹⁵ Centro de Investigación Biomedica en Red de Cáncer (CIBERONC), Madrid, Spain

¹⁶ University Hospital Nantes, Nantes, France

¹⁷ Toulouse University Institute of Cancer, Toulouse, FRA

¹⁸ K36 Therapeutics, Cambridge, MA

¹⁹ Sylvester Comprehensive Cancer Center, Myeloma Division, University of Miami, Miami, FL

²⁰ Myeloma Service, Division of Hematologic Oncology, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY

²¹ University Hospital of Salamanca/IBSAL, Salamanca, Spain

²² Multiple Myeloma Division, Hackensack Univ. Med. Ctr., Hackensack, NJ

Background: Despite the development and approval of effective therapies for multiple myeloma (MM), MM remains an incurable disease. Moreover, patients with high-risk cytogenetics, like translocation t(4;14), continue to have a poor prognosis compared to standard-risk patients. No novel agents have been approved specifically for this population. There remains an unmet need for precision therapies for MM that can target specific drivers of high-risk MM like t(4;14). Multiple myeloma SET domain-containing protein (MMSET) overexpression observed in 100% of patients with t(4;14) acts through the MMSET-H3K36me2 axis, which promotes malignant transformation through regulation of multiple oncogenic programs. KTX-1001, a methyl transferase inhibitor, is a novel, first-in-class, potent, oral, small molecule that inhibits MMSET and the methylation of lysine K36. KTX-1001 had favorable drug-like properties, demonstrated *in vivo* activity, and was well tolerated in non-clinical studies. Based on these data, KTX-1001 is now being studied in a Phase 1 dose escalation and expansion study in relapsed and refractory multiple myeloma (RRMM).

Study Design and Methods: This multi-country, Phase 1, open-label study (NCT05651932) is designed to assess the safety, tolerability, and initial clinical activity of KTX-1001. The study will also examine the recommended phase 2 dose (RP2D), phar-

macokinetics (PK) and pharmacodynamics (PD). Part A of this trial includes an accelerated titration, followed by 3+3 dose escalation with backfill of cohorts for dose optimization prior to moving to Part B, which is an expansion phase at the RP2D (please see Figure 1 for study design schematic). The expansion phase will only include patients with t(4;14). KTX-1001 will be administered orally daily and given until disease progression, unacceptable toxicity, or withdrawal from the study.

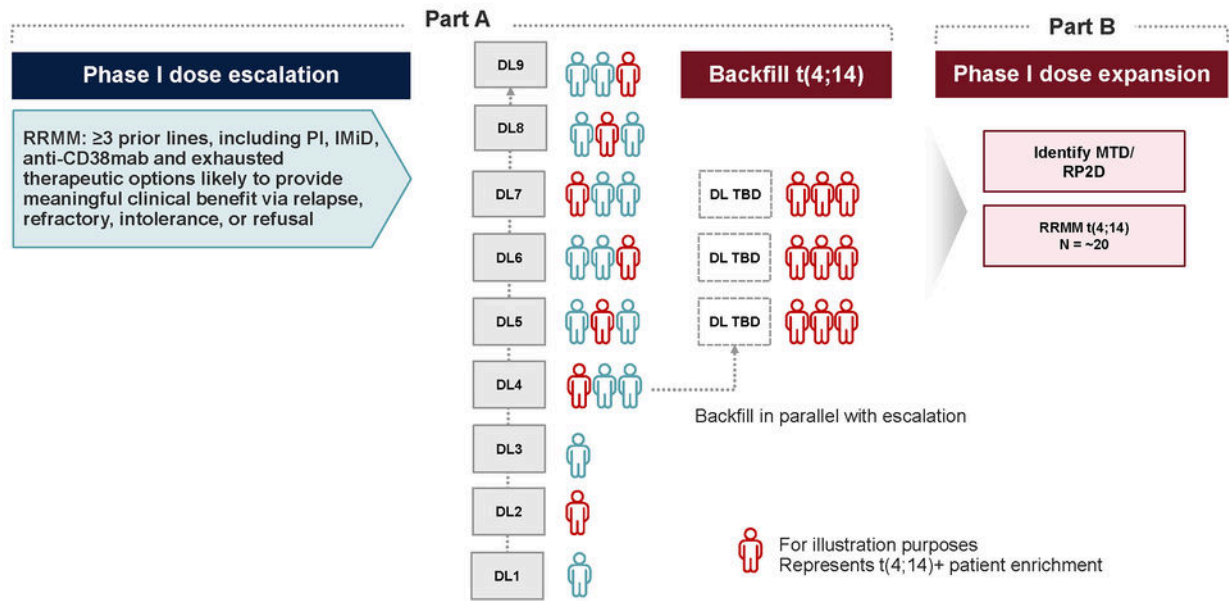
Estimated enrollment for Parts A and B will be approximately 60 patients. The study will enroll patients with RRMM who have received ≥ 3 prior lines of therapy, including a proteasome inhibitor (PI), immunomodulatory drug (IMiD), and anti-CD38 antibody. Patients must have measurable disease, be ≥ 18 years of age, have an Eastern Cooperative Oncology Group score of ≤ 2 , and adequate bone marrow, liver, and kidney function. Key exclusion criteria include history of or current plasma cell leukemia, active central nervous system (CNS) disease, or active unstable cardiovascular function.

The primary endpoints of safety and tolerability include incidence of dose-limiting toxicity (DLTs), treatment-emergent adverse events (AEs), and treatment-related AEs. Secondary endpoints include plasma concentrations of KTX-1001 and efficacy outcomes such as objective response rate (ORR), duration of response (DOR), progression-free survival (PFS), and overall survival (OS). Exploratory biomarker and pharmacodynamic assessments will also be performed. The sample size was not determined by formal statistical methods but will be sufficient to provide preliminary information on safety, PK, PD, and efficacy. Statistical analyses will be primarily descriptive.

Conclusion: This Phase 1 study will evaluate a potential treatment for RRMM utilizing KTX-1001, which is a novel, first-in-class, potent, oral small-molecule MMSET inhibitor. The study is open and actively enrolling patients at centers in the United States, Spain, France, and Canada.

Disclosures Berdeja: Amgen: Research Funding; Poseida: Research Funding; Celgene: Consultancy, Research Funding; Acetylon: Research Funding; Incyte: Research Funding; Celularity: Research Funding; CRISPR Therapeutics: Consultancy, Research Funding; EMD Serono: Research Funding; Ichnos Sciences: Research Funding; AbbVie: Research Funding; Bristol Myers Squibb: Consultancy, Research Funding; Genentech: Research Funding; Fate Therapeutics: Research Funding; GSK: Research Funding; 2seventy bio: Consultancy, Research Funding; Novartis: Research Funding; Lilly: Research Funding; Cartesian: Research Funding; CARsgen: Research Funding; Janssen: Consultancy, Research Funding, Speakers Bureau; C4 Therapeutics: Research Funding; Sanofi: Research Funding; Legend Biotech: Consultancy; Kite Pharma: Consultancy; Karyopharm: Research Funding; Takeda: Consultancy, Research Funding; Roche: Consultancy; Teva: Research Funding. **Dingli:** Novartis: Consultancy; Sanofi: Consultancy; Sorrento: Membership on an entity's Board of Directors or advisory committees; K-36 Therapeutics: Research Funding; Genentech: Consultancy; BMS: Consultancy; Apellis: Consultancy; Janssen: Consultancy; Alexion (AstraZeneca); Apellis Pharmaceuticals; BMS; GSK; Janssen; Novartis; Sanofi; Takeda: Consultancy; BioCryst: Consultancy. **Lonial:** TG Therapeutics Inc: Other: Board of Directors with Stock; AbbVie Inc, Amgen Inc, Bristol-Myers Squibb Company, Celgene Corporation, Genentech, a member of the Roche Group, GlaxoSmithKline, Janssen Biotech Inc, Novartis, Pfizer Inc, Takeda Pharmaceuticals USA Inc: Consultancy, Other: Advisory Committee; Bristol-Myers Squibb Company, Janssen Biotech Inc, Novartis, Takeda Pharmaceuticals USA Inc.: Other: Contracted Research, Research Funding; Janssen: Research Funding; Novartis: Research Funding. **Yee:** Karyopharm: Consultancy; BMS: Consultancy, Research Funding; GSK: Consultancy; Amgen: Research Funding; Adaptive: Consultancy; AbbVie: Consultancy; Takeda: Research Funding; Sanofi: Consultancy; Regeneron: Consultancy; Janssen: Consultancy, Research Funding. **Chung:** Janssen: Membership on an entity's Board of Directors or advisory committees; Sanofi: Honoraria; AbbVie Inc., Bristol Myers Squibb, Caelum Biosciences, CarsGen Therapeutics, Cellectis, Janssen, K36, Merck: Research Funding. **Gasparetto:** Karyopharm, Sanofi, BMS: Speakers Bureau; BMS, GSK, Amgen, Janssen: Consultancy. **Bergsagel:** Salarius: Consultancy; Janssen: Consultancy; Pfizer: Research Funding; Mayo Clinic: Patents & Royalties: Royalty for hCRBN and Vk*MYC mice; Aptitude Health: Honoraria; Novartis: Patents & Royalties: Royalty for hCRBN mice; CellCentric: Consultancy; Omeros: Consultancy; Radmetrix: Consultancy. **Rosñol:** Sanofi: Other: Honoraria for lectures; GlaxoSmithKline: Other: Honoraria for lectures; Takeda: Other: Honoraria for lectures; Amgen: Other: Honoraria for lectures; Bristol Myers Squibb/Celgene: Other: Honoraria for lectures; Janssen: Other: Honoraria for lectures. **Trudel:** FORUS: Consultancy; Pfizer: Honoraria, Research Funding; Amgen: Honoraria, Research Funding; Janssen: Honoraria, Research Funding; K36: Consultancy; Genentech: Research Funding; BMS: Consultancy, Honoraria, Research Funding; Sanofi: Honoraria; Roche: Consultancy, Research Funding; GSK: Consultancy, Honoraria, Research Funding. **Rodriguez Otero:** AbbVie: Consultancy, Membership on an entity's Board of Directors or advisory committees; Regeneron: Other: Honoraria for lectures; Amgen: Other: Honoraria for lectures; GlaxoSmithKline: Membership on an entity's Board of Directors or advisory committees, Other: Honoraria for lectures; Sanofi: Membership on an entity's Board of Directors or advisory committees, Other: Honoraria for lectures; Janssen: Consultancy, Membership on an entity's Board of Directors or advisory committees, Other: Honoraria for lectures; Bristol Myers Squibb: Consultancy, Membership on an entity's Board of Directors or advisory committees, Other: Honoraria for lectures; Oncopeptides: Membership on an entity's Board of Directors or advisory committees; Pfizer: Consultancy, Membership on an entity's Board of Directors or advisory committees, Other: Travel grants; Roche: Consultancy. **Touzeau:** Bristol Myers Squibb: Honoraria, Membership on an entity's Board of Directors or advisory committees. **Bories:** Abbvie, BMS, Celgene, Gilead, Kite: Honoraria. **Bang:** K36 Therapeutics: Current Employment. **Connolly:** K36 Therapeutics: Current Employment, Current equity holder in private company, Membership on an entity's Board of Directors or advisory committees. **Kim:** K36 Therapeutics: Current Employment, Current holder of stock options in a privately-held company. **Lewis:** K36 Therapeutics: Current Employment. **Linberg:** K36 Therapeutics: Current Employment. **Quigley:** K36 Therapeutics: Current Employment, Current holder of stock options in a privately-held company, Divested equity in a private or publicly-traded company in the past 24 months. **Landgren:** Merck: Consultancy, Honoraria, Membership on an entity's Board

of Directors or advisory committees, Other: Membership on independent data monitoring committees; *Amgen*: Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Membership on independent data monitoring committees; *Takeda*: Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Membership on independent data monitoring committees; *Janssen*: Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Membership on independent data monitoring committees; *Celgene*: Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Membership on independent data monitoring committees; *Adaptive*: Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Membership on independent data monitoring committees; *Theradex*: Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Membership on independent data monitoring committees; **Usmani**: *SecuraBio*: Membership on an entity's Board of Directors or advisory committees; *Gilead Sciences*: Membership on an entity's Board of Directors or advisory committees, Research Funding; *Merck*: Research Funding; *Oncopeptides*: Membership on an entity's Board of Directors or advisory committees; *Pharmacyclics*: Research Funding; *EdoPharma*: Membership on an entity's Board of Directors or advisory committees; *GSK*: Membership on an entity's Board of Directors or advisory committees, Research Funding; *Genentech*: Membership on an entity's Board of Directors or advisory committees; *Seattle Genetics*: Membership on an entity's Board of Directors or advisory committees, Research Funding; *Novartis*: Membership on an entity's Board of Directors or advisory committees; *Moderna*: Membership on an entity's Board of Directors or advisory committees; *SkylineDX*: Membership on an entity's Board of Directors or advisory committees, Research Funding; *K36 Therapeutics*: Membership on an entity's Board of Directors or advisory committees; *Array Biopharma*: Research Funding; *Sanofi*: Membership on an entity's Board of Directors or advisory committees, Research Funding; *Janssen*: Membership on an entity's Board of Directors or advisory committees, Research Funding; *TeneoBio*: Membership on an entity's Board of Directors or advisory committees; *Takeda*: Membership on an entity's Board of Directors or advisory committees, Research Funding; *Celgene*: Membership on an entity's Board of Directors or advisory committees, Research Funding; *Bristol Meyer Squibb*: Membership on an entity's Board of Directors or advisory committees, Research Funding; *Amgen*: Membership on an entity's Board of Directors or advisory committees, Research Funding; *Abbvie*: Membership on an entity's Board of Directors or advisory committees, Research Funding. **Mateos**: *Janssen*: Honoraria, Membership on an entity's Board of Directors or advisory committees; *BMS/Celgene*: Honoraria, Membership on an entity's Board of Directors or advisory committees; *GSK*: Honoraria, Membership on an entity's Board of Directors or advisory committees; *Sanofi*: Honoraria, Membership on an entity's Board of Directors or advisory committees; *Pfizer*: Honoraria, Membership on an entity's Board of Directors or advisory committees; *Abbvie*: Honoraria, Membership on an entity's Board of Directors or advisory committees; *Stemline*: Honoraria, Membership on an entity's Board of Directors or advisory committees; *Oncopeptides*: Honoraria, Membership on an entity's Board of Directors or advisory committees; *Amgen*: Honoraria; *Takeda*: Honoraria; *Regeneron*: Honoraria. **Siegel**: *BMS*: Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding, Speakers Bureau; *Novartis*: Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding, Speakers Bureau; *Karyopharm*: Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding, Speakers Bureau; *Janssen*: Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding, Speakers Bureau; *Celgene*: Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding, Speakers Bureau; *Celularity Scientific*: Consultancy, Membership on an entity's Board of Directors or advisory committees; *Amgen*: Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding, Speakers Bureau; *Takeda*: Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding, Speakers Bureau.



CD, cluster of differentiation; DL, dose level; IMiD, immunomodulatory drug; mab, monoclonal antibody; MTD, maximum tolerated dose; PI, proteasome inhibitor; RP2D, recommended phase 2 dose; RRMM, relapsed and refractory multiple myeloma; TBD, to be determined

Figure 1

<https://doi.org/10.1182/blood-2023-174550>

Downloaded from http://ashpublications.net/blood/article-pdf/142/Supplement_1/3391/2205197/blood-9993-main.pdf by guest on 28 May 2024