Ethics Approval The study was approved by participating study sites' Institutional Review Boards and the Sponsor has conducted the trial in full compliance with all GCP and FDA regulations.

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Clinical trials in-progress

798 SAFETY, TOLERABILITY, AND IMMUNOGENICITY OF MRNA-4157 IN COMBINATION WITH PEMBROLIZUMAB IN SUBJECTS WITH UNRESECTABLE SOLID TUMORS (KEYNOTE-603): AN UPDATE

[1]Julie Bauman*, [2]Howard Burris, [3]Jeffrey Clarke, [4]Manish Patel, [5]Daniel Cho, [6]Martin Gutierrez, [1]Ricklie Julian, [1]Aaron Scott, [7]Pamela Cohen, [7]Joshua Frederick, [7]Celine Robert-Tissot, [7]Honghong Zhou, [7]Kinjal Mody, [7]Karen Keating, [7]Robert Meehan, [8]Justin Gainor. *[1]University of Arizona, Tuscon, AZ, USA; [2]SCRI, Nashville, TN, USA; [3]Duke, Durham, NC, USA; [4]Florida Cancer Specialists, Sarasota, FL, USA; [5]NYU, New York, NY, USA; [6]Hackensack, Hackensack, NJ, USA; [7]Moderna, Tenafly, NJ, USA; [8]Mass General Hospital, Boston, MA, USA*

Background T-cell targeting of mutation-derived epitopes (neoantigens) has shown to drive anti-tumor responses. Immunizing patients against such neoantigens in combination with a checkpoint inhibitor (CPI) may elicit greater anti-tumor responses than CPI alone. Mutations are rarely shared between patients, thus requiring a personalized approach to vaccine design. mRNA-4157 is a lipid encapsulated mRNA based personalized cancer vaccine encoding neoantigens selected using a proprietary algorithm to induce neoantigen specific T cells and associated anti-tumor responses. This report includes updates from the mRNA-4157 Phase1(P1) study. The initial data was presented at ASCO2019.[1]

Methods This study evaluates the safety and efficacy of mRNA-4157 as monotherapy in patients with resected solid tumors (Part A) and in combination with pembrolizumab in patients with advanced/metastatic solid tumors (Parts B). The selected solid tumors in Part A-B includes melanoma, bladder carcinoma, HPV-negative (HPV-neg) HNSCC, NSCLC, SCLC, MSI-High (MSI-h), or TMB-High cancers. Expansion cohorts includes patients with CPI-naïve MSS-CRC and HPV-neg HNSCC (Part C) and with resected melanoma (Part D). Patients receive up to 9 cycles (Q3W) of mRNA-4157 by intramuscular injection at up to 1 mg alone (Part A) or in combination with pembrolizumab (200 mg IV Q3W, Parts B-D). Pembrolizumab is administered for two cycles before the first dose of mRNA-4157 and may continue after 9 cycles of combination. Endpoints include safety, tolerability, efficacy and biomarker assessments.

Results 79 patients received mRNA-4157; 16 as monotherapy and 63 in combination with pembrolizumab. Only low grade and reversible treatment related AEs were reported. 14/16 Part A patients (3 melanoma, 11 NSCLC, 2 MSI-h CRC) remained disease free on study. 28 patients in Parts B (6 bladder, 2 HNSCC, 3 melanoma, 10 NSCLC, 2 SCLC, 4 MSI-h tumor, 1 TMB-h tumor), 27 patients in Part C (10 HNSCC and 17 MSS-CRC), and 8 patients with resected melanoma (Part D) received combination. 3 CR (1 HNSCC, 1 MSI-h CRC and 1 MSI-h prostate), and 8 PR (1 bladder, 4 HNSCC, 2 SCLC and 1 MSI-h endometrial) were observed with combination. Of 10 CPI-naïve HPV-neg HNSCC patients, the response rate was 50% (1CR, 4PR, 4SD) mPFS 9.8months, which compared favorably to published rates of ~14.6% mPFS 2.0months for pembrolizumab monotherapy.[2 3] Biomarker assessments including immune gene expression profiling will be presented.

Conclusions mRNA-4157 has an acceptable safety profile along with observed clinical responses in combination with pembrolizumab. Preliminary efficacy analysis from CPI-naïve relapsed/refractory HPV-neg HNSCC cohort suggests activity of this combination. Study is ongoing.

Trial Registration NCT03313778

Ethics Approval The study was approved by each participating sites' local IRB.

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799 DURABLE RESPONSES AND IMMUNE ACTIVATION WITH INTRATUMORAL ELECTROPORATION OF PIL-12 PLUS PEMBROLIZUMAB IN ACTIVELY PROGRESSING ANTI-PD-1 REFRACTORY ADVANCED MELANOMA: KEYNOTE 695 INTERIM DATA

[1]Pablo Fernandez-Penas, [1]Matteo Carlino, [2]Katy Tsai, [3]Victoria Atkinson, [4]Monaster Shaheen, [5]Sajeve Thomas, [6]Catalin Mihalcioiu, [7]Tom Van Hagen, [8]Rachel Roberts-Thomson, [9]Andrew Haydon, [10]Andrew Mant, [11]Marcus Butler, [12]Gregory Daniels, [13]Elizabeth Buchbinder, [14]John Hyngstrom, [15]Mecker Moller, [16]Igor Puzanov, [17]C Lance Cowey, [18]Eric Whitman, [19]Carmen Ballesteros-Merino, [19]Shawn Jensen, [19]Bernard Fox, [20]Emmett Schmidt, [20]Clemens Krepler, [20]Scott Diede, [21]Erica Browning, [21]Reneta Hermiz, [21]Lauren Svenson, [21]Jon Salazar, [21]Jack Lee, [21]Christopher Baker, [21]Donna Bannavong, [21]Jendy Sell, [21]Kellie Malloy Foerter, [21]David Canton, [21]Sandra Aung, [21]Christopher Twitty, [2]Alain Algazi, [2]Adil Daud*. *[1]Westmead Hospital, University of Sydney, Westmead, Australia; [2]University of California, San Francisco, San Francisco, CA, USA; [3]Princess Alexandra Hospital, University of Queensland, Woolloongabba, Australia; [4]University of Arizona, Tucson, AZ, USA; [5]UF Health Cancer Center at Orlando Health, Orlando, FL, USA; [6]McGill University Health Centre, Montreal, Canada; [7]St. John of God Hospital, Subiaco, Australia; [8]Adelaide Oncology and Haematology, Adelaide, Australia; [9]The Alfred Hospital, Victoria, Australia; [10]Box Hill Hospital, Box Hill, Australia; [11]Princess Margaret Cancer Centre, Toronto, Ontario, Canada; [12]University of California, San Diego, La Jolla, CA, USA; [13]Dana Faber Cancer Institute, Boston, MA, USA; [14]University of Utah Healthcare Huntsman Cancer Institute, Salt Lake City, UT, USA; [15]University of Miami Sylvester Cancer Center, Miami, FL, USA; [16]Roswell Park Cancer Institute, Buffalo, NY, USA; [17]Baylor University Medical Center, Dallas, TX, USA; [18]Atlantic Health System, Morristown, NJ, USA; [19]Earle A. Chiles Research Institute, Portland, OR, USA; [20]Merck and Co., Inc., Kenilworth, NJ, USA; [21]Oncosec Medical Incorporated, San Diego, CA, USA*

Background Electroporated plasmid IL-12 (TAVO or tavokinogene telseplasmid) is a novel pro-inflammatory intratumoral therapy with substantial single agent activity in melanoma, which has been shown to synergize with anti-PD-1 antibodies in patients predicted as non-responders to anti-PD-1.[1 2] Interim data from patients with stage III/IV melanoma actively progressing on anti-PD-1 antibody are presented herein.

Methods Patients with confirmed disease progression by RECIST v1.1 after at least 12 weeks of treatment on pembrolizumab or nivolumab (or combination checkpoint blockade) and within 12 weeks of last dose (with no intervening