Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Baden LR, El Sahly HM, Essink B, et al. Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. N Engl J Med. DOI: 10.1056/NEJMoa2035389

Table of Contents **Pg.**

COVE Study Group……... 2

List of COVE Study Trial Investigators and Team…… 4

Supplemental Statistical Methods…….. 8

Fig. S1. Study Disposition in Overall Randomized Set……. 11

Table S1. Primary and Secondary Objectives of the Trial……. 12

Table S2. Baseline Demographics and Characteristics by Randomization Strata……. 14

Table S3. Solicited Adverse Reactions Within 7 Days After First Injection by Grade……. 17

Table S4. Solicited Adverse Reactions Within 7 days After First Injection by Grade…….. 19

Table S5. Number of Days Reporting Solicited Adverse Reactions After First Injection…… 21

Table S6. Solicited ARs by SARS-CoV-2 Baseline Status By Grade After Vaccination 1….. 22

Table S7. Solicited ARs by SARS-COv-2 Baseline Status By Grade After Vaccination 2….. 24

Table S8. Unsolicited AEs 28 Days After Any Injection, Overall Safety Set……... 26

Tables S9-11. Unsolicited AEs, Overall Safety Set……... 27

Table S12. Unsolicited Adverse Events of Hypersensitivity, Overall Safety Set…….. 31

Table S13. Covid-19 Symptoms and Severity……... 32

Table S14. Characteristics of Participants with Severe Covid-19……. 33

Table S15. Serious and Severe Treatment-Related AEs Up to 28 Days After Any Injection... 34

Table S16. Efficacy of Key Secondary Endpoints……. 35

Table S17. Vaccine Efficacy by SARS-COV-2 Status…….. 36

Table S18. Preliminary Analysis of Infection from Randomization…….. 37

COVE Study Group (pubmed listed, and ordered alphabetically by institution affiliation)

Affiliation/Funding*	Study Group	Location
AB Clinical Trials	Atoya Adams, MD, MBA	Las Vegas, NV
Accel Research Sites	Bruce G. Rankin, DO	DeLand, FL
Advanced Clinical Research	Sinikka L. Green, MD	Cedar Park, TX
Alliance for Multispecialty Research	Richard M. Glover, II, MD	Newton, KS
Alliance for Multispecialty Research	Terry L. Poling, MD	Wichita, KS
Alliance for Multispecialty Research	William B. Smith, MD	Knoxville,TN
Baptist Health Center for Clinical Research	Priyantha N. Wijewardane, MD	Little Rock, AR
Baylor College of Medicine NIAID 1UM1AI148575-01S2	Hana El Sahly, MD, Jennifer Whitaker, MD, Catherine Mary Healy, MD, Christine Akamine, MD	Houston, TX
Benchmark Research	Laurence Chu, MD	Austin, TX
Benchmark Research	Michael J. Cotugno, MD	Metairie, LA
Benchmark Research	Greg Hachigian, MD	Sacramento, CA
Benchmark Research	William Seger, MD	Fort Worth, TX
Brigham and Women's Hospital NCATS UL1 RR025758 and NIAID UM1 AI069412	Lindsey R. Baden, MD, Michael Desjardins, MD, Jennifer A Johnson, MD, Amy Sherman, MD, Stephen R Walsh, MD	Boston, MA
Carolina Institute for Clinical Research	Judith Borger, DO	Fayetteville, NC
Centex Studies, Inc.	Joel Solis, MD	McAllen, TX
Clinical Research Atlanta	Nathan Segall, MD	Stockbridge, GA
Clinical Trials of Texas	Douglas Scott Denham, DO	San Antonio, TX
Coastal Carolina Research Center	Cynthia Becher Strout, MD	Mount Pleasant, SC
Cornell Clinical Trials Unit - Weill Cornell Chelsea NIAID UM1AI068619	Kristin Marks, MS, MD, Grant Ellsworth, MD, MS	New York, NY
Covid19 Prevention Network, (CoVPN; NIAID-NIH)	Michele P Andrasnik, Jessica G Andriesen, Gail Broder, Larry Corey, Niles Eaton, Kathy Neuzil, Huub Gelderblom, James Kublin, Nelson Michael, Merlin Robb	Seattle, WA
DM Clinical Research	Vicki E. Miller, MD	Tomball, TX
Emory University - Hope Clinic NIAID 3UM1AI068614-14S1	Colleen Kelley MD, MPH, Valeria Cantos MD, Carlos del Rio MD, Paulina Rebolledo MD	Decatur, GA
Emory University - Hope Clinic NIAID 1UM1AI148576-01	Nadine Rouphael, Srilatha Edupuganti, Daniel Sans Graciaa, Paulina Rebolledo	Decatur, GA
Emory University School of Medicine NIAID 1UM1AI148576-01	Evan J. Anderson, MD, Andres Camacho-Gonzalez, MD, Satoshi Kamidani, MD, Christina A. Rostad, MD, Mehgan Teherani, MD	Atlanta, GA
eStudySite	Jeffrey Scott Overcash, MD	La Mesa, CA
George Washington University NIAID UM1AI068619	David Joseph Diemert, MD	Washington, DC
Hackensack University Medical Center	Bindu Balani, MD	Hackensack, NJ
Henry Ford Health System	Marcus J. Zervos, MD	Detroit, MI
Hope Research Institute	Abram Burgher, MD	Phoenix, AZ
Hope Research Institute	Joseph D. Davis, MD	Chandler, AZ
Hope Research Institute	Matthew W. Doust, MD	Phoenix, AZ
J. Lewis Research	Shane Glade Christensen, MD	Salt Lake City, UT
J. Lewis Research	James Todd Peterson, MD	Salt Lake City, UT
Jacksonville Center For Clinical Research	Michael J. Koren, MD	Jacksonville, FL
Javara	Christina Kennelly, MD	Charlotte, NC
Johnson County Clin-Trials	Carlos A. Fierro, MD	Lenexa, KS
Kaiser Permanente Washington Health Research Institute NIAID 1UM1AI148373-01	Lisa A. Jackson, MD, MPH	Seattle, WA
Laguna Clinical Research Associates	Milton Haber, MD	Laredo, TX
Lynn Health Science Institute	Carl P. Griffin, MD	Oklahoma City, OK
Lynn Institute of the Rockies	Ripley R. Hollister, MD	Colorado Springs, CO
M3 Wake Research	Wayne Lee Harper, MD	Raleigh, NC
MediSync Clinical Research Hattiesburg Clinic	Rambod Rouhbakhsh, MD, MBA	Petal, MS
Meridian Clinical Research	Shishir Kumar Khetan, MD	Rockville, MD
Meridian Clinical Research	Paul Simon Bradley, MD	Savannah, GA
Meridian Clinical Research	Adam Benson Brosz, MD	Grand Island, NE
Meridian Clinical Research	Frank Steven Eder, MD	Binghamton, NY
Meridian Clinical Research	David Jon Ensz, MD	Dakota Dunes, SD
Meridian Clinical Research	Brandon James Essink, MD	Omaha, NE
Meridian Clinical Research	Keith William Vrbicky, MD	Norfolk, NE
Meridian Clinical Research	Jordan L. Whatley, MD	Baton Rouge, LA
NIH	Mamodikoe Makhene, MD, MPH	Bethesda, MD
New Horizons Clinical Research	Gregory Mark Gottschlich, MD	Cincinnati, OH
Optimal Research	Murray A. Kimmel, DO	Melbourne, FL
Optimal Research	Mimi Van Der Leden, MD, PhD	Rockville, MD

Optimal Research	Timothy P. Vachris, MD	Austin, TX
Palm Beach Research Center	Mira Baron, MD	West Palm Beach, FL
Paradigm Clinical Research Center	Jamshid Saleh, MD	Redding, CA
Quality of Life Medical & Research Centers	John W. McGettigan, Jr., MD	Tucson, AZ
Rancho Paseo Medical Group	Judith L. Kirstein, MD	Banning, CA
Rapid Medical Research	Mary Beth Manning, MD	Cleveland, OH
Research Centers of America	Howard I. Schwartz, MD	Hollywood, FL
Rutgers New Jersey Medical School NIAID UM1AI068619	Shobha Swaminathan, MD, Amesika Nyaku, MD, MS	Newark, NJ
Saint Louis University NIAID 1UM1AI148685-01	Sharon E. Frey, MD	St. Louis, MO
St. Vincent's Health System	Leland N. Allen III, MD	Birmingham, AL
Suncoast Research Group	Mark E. Kutner, MD	Miami, FL
Suncoast Research Group	Larkin T. Wadsworth III, MD	St. Louis, MO
Synexus Clinical Research	Michael Ryan Adams, MD	Murray, UT
Synexus Clinical Research	Joseph Lee Newberg, MD	Chicago, IL
Synexus Clinical Research	Paul Joseph Nugent, DO	Cincinnati, OH
Synexus Clinical Research	Michele Diane Reynolds, MD	Dallas, TX
Synexus Clinical Research	Neil Parmanand Sheth, MD	Glendale, AZ
Synexus Clinical Research	Ramy Joseph Toma, MD	Birmingham, AL
Synexus Clinical Research	Judith White, MD	Orlando, FL
Tekton Research, Inc.	Paul Pickrell, MD	Austin, TX
Texas Center for Drug Development, Inc.	Veronica G. Fragoso, MD	Houston, TX
Trial Management Associates	Barton G. Williams, MD	Wilmington, NC
University of California, Los Angeles NIAID UM1AI068619	Jesse L. Clark, MD	Los Angeles, CA
University of California, San Diego NIAID UM1AI068636	Stephen A. Spector, Jill Blumenthal, Amaran Moodley	La Jolla, CA
University of Chicago	Kathleen M. Mullane, DO, PharmD	Chicago, IL
University of Cincinnati NIAID UM1AI068619	Carl Fichtenbaum, MD, Moises A. Huaman, MD, MSc, Margaret Powers-Fletcher, PhD, Michelle Saemann, RN	Cincinnati, OH
University of Colorado Denver, Anschutz Medical Campus NIAID UM1AI068636	Thomas Campbell, M.D.; Jose Castillo-Mancilla, M.D., Hillary Dunlevy, M.D., Steven Johnson, M.D.	Aurora, CO
University of Illinois at Chicago - Project WISH NIAID UM1AI068619	Rick Novak, Scott Borgetti, Tracy Cable, Ben Ladner, Andrew Wendrow,	Chicago, IL
University of Maryland, Baltimore NIAID 1UM1AI148689-01	Karen Kotloff, MD; Matthew Laurens, MD, MPH, Milagritos Tapia, MDs	Baltimore, MD
University of Miami NIAID 3UM1AI068614-14S1	Susanne Doblecki-Lewis, MD, MSP, Maria Alcaide, MD, Jose Gonzales-Zamora, MD, Stephen Morris, MD	Miami, FL
University of North Carolina at Chapel Hill NIAID UM1AI068619	Cynthia Gay, MD, Joseph Eron, MD, David Wohl, MD	Chapel Hill, NC
University of Pennsylvania NIAID 3UM1AI068614-14S1	Ian Frank, MD	Philadelphia, PA
University of Pittsburgh, NIAID 1UM1AI148452-01	Judith M. Martin, MD, Alejandro Hoberman, MD, Gysella Pujalt Muniz, MD, Timothy Shope, MD, MPH	
University of Texas Medical Branch NIAID 1UM1AI148575-01	Richard Rupp; Megan Berman, Laura Porterfield, Amber,Stanford,	Galveston, TX
VA Greater Los Angeles Healthcare System	Michael Lewis, MD	Los Angeles, CA
Vanderbilt University Medical Center NIAID 1UM1AI148452-01	C Buddy Creech, Stephanie L. Rolsma, Robert Samuels, Shannon C. Walker	Nashville, TN
Vanderbilt University Medical Center NIAID 3UM1AI068614-14S1	Spyros Kalams, MD, Greg Wilson, MD	Nashville, TN
Velocity Clinical Research	Gregg H. Lucksinger, MD	Medford, OR
VitaLink Research	Luis I. De La Cruz, MD	Greenville, SC
VitaLink Research	Gowdhami Mohan, MD	Anderson, SC
VitaLink Research- Spartanburg	Gregory J. Feldman, MD	Spartanburg, SC
Wake Forest University Health Sciences	John W. Sanders, MD, MPH	Winston Salem, NC
WR-Clinical Research Center of Nevada	Michael L. Levin, MD	Las Vegas, NV
WR-ClinSearch	Mark Montgomery McKenzie, MD	Chattanooga, TN
WR-Global Medical Research	Valentine Mbepson Ebuh, MD	Dallas, TX
WR-Medical Center for Clinical Research	Laurie J. Han-Conrad, MD	San Diego, CA
*Institutions funded as indicated by National Institute of Allergy and Infectious Diseases (NIAID) and the National center for Advancing Translational Science (NCATS). All other institutions funded by Office of the Assistant Secretary for Preparedness and Response, Biomedical Advanced Research and Development Authority.		

List of COVE Trial Investigators and Study Teams

Principal Investigator	Study Team	Institution	Location
Atoya Adams, MD, MBA	Eric Miller	AB Clinical Trials	Las Vegas, NV
Michael Ryan Adams, MD	Chase Carnahan, Leslie Iverson, Natalie Smith, Rachel Law, Shannon Wright, Stefanie Vasconez	Synexus Clinical Research	Murray, UT
Leland N. Allen III, MD	Vincent Banglini, David House, Cristina Velez, Christy Greenhalgh, Jessica Mena, Zachary McCoy, Candace Robinson, Caitlin Roll, Kimberly Cornelison	St. Vincent's Health System	Birmingham, AL
Evan J. Anderson, MD	Christina Rostad, Andres Camacho-Gonzalez, Satoshi Kamidani, Mehgan Farah Teherani, Teresa Ball, Etza Peters, Peggy Kettle, Lisa Macoy, Cindy Lubbers, Leisa Bower	Emory University School of Medicine	Atlanta, GA
Lindsey R. Baden, MD	Jane Kleinjan, NP, Jon Gothing, NP, Humberto Licona, MD, Paulette Chandler, MD, Elizabeth Karlson, MD, Christin Price, MD, Lewis Novak, Monica Feeley, Xhoi Mitre, Bruce Bausk, Jessica Cauley, Natalie Izaguirre, Hannah Jin, Julia Klopfer, Phoebe Cunningham, Megan Powell, Jun Bai Park Chang, Noah Abasciano, Alexis Liakos, PA, Karina Oganezova, Kirsten Goodman, NP, Karen Magsipoc, NP, Haley Schram, NP, Maureen Macgowan, PA, Elizabeth Sampson, RN, Lauren Donahue, RN, Opeyemi Talabi, Mike Seaman, PHD, Katherine Yanosick, Alka Patel, PharmD, Allison P. Moriarty	Brigham and Women's Hospital	Boston, MA
Bindu Balani, MD	Cristina Cicogna, Steven Spenber	Hackensack University Medical Center	Hackensack, NJ
Mira Baron, MD	Pamela Kane, Maria Bermudez, Mara Kryvicky, Shannen Seversen	Palm Beach Research Center	West Palm Beach, FL
Judith Borger, DO	Scott Syndergaard, Ryan Starr, Lynn Eckert, Ifeanyi Momodu, Cheryl Norris, Nafisa Saleem, Nicole Austin	Carolina Institute for Clinical Research	Fayetteville, NC
Paul Simon Bradley, MD	Amanda Lilienthal, Kay Lynn Olmsted, Anne Crouch, Brooke Halpern	Meridian Clinical Research	Savannah, GA
Adam Benson Brosz, MD	Susan Mae Newman, Lindsey Christel Mattenbrink, Kayla Flege, Douglas Herbek, Luke Friesen	Meridian Clinical Research	Grand Island, NE
Abram Burgher, MD	Marybeth Barcome, Matthew Doust	Hope Research Institute	Phoenix, AZ
Thomas B. Campbell, MD	Hillary Dunlevy, Steven Johnson, Martin Krsak, Andrew Monte, Jose Castillo-Mancilla, Kristine Erlandson, Michelle Barron, Cathi Basler, Andrew Lauria	University of Colorado Denver, Anschutz Medical Campus	Aurora, CO
Shane Glade Christensen, MD	Holly Marie Anderson, Emily Kathleen Bloomquist, Ross Anthony Brunetti, Thomas Conner, Gina Cox, Diana Grazulis, Wesley Lewis, James Longe, Christopher Matich, Bryan Nelson, Emily Raming, Sarah Scott, John Edward Witbeck, Stephen Wood	J. Lewis Research	Salt Lake City, UT
Laurence Chu, MD	R. Michelle Chouteau, Tambra Dora, Pamela Conley, Ruth Fitch, Katherine Davis, Dean Skiles, Brooke Harris, Kelly Weber, Francesca Vigil, Isaiah Knight, Maria Barrientes, Lauren Christal, Clara Loza, Christian Casas, Selena Bermudez	Benchmark Research	Austin, TX
Jesse L. Clark, MD	William Hernandez	University of California, Los Angeles	Los Angeles, CA
Michael J. Cotugno, MD	George Bauer, Edwin Adamson, Julie Bilich, Brenda Lawson, Kim Harper, Lois Eaglin, Kyra Lawson, Shannon Williams	Benchmark Research	Metairie, LA
Clarence Buddy Creech II, MD	Isaac Thomsen, Shannon Walker, Leigh Howard	Vanderbilt University Medical Center	Nashville, TN
Joseph D. Davis, MD	Brendan Levy	Hope Research Institute	Chandler, AZ
Luis I. De La Cruz, MD	David Godwin, Elizabeth Everette, Steven Clemons, Supinder Channa	VitaLink Research	Greenville, SC
Douglas Scott Denham, DO	Ayoade Avworo, Thomas Weiss, Parbe Hedges, Stephen Brick	Clinical Trials of Texas	San Antonio, TX
David Joseph Diemert, MD	Marc Siegel, Gary Simon, David Parenti, Roberts Afsoon, Hana Akselrod, Aimee Desrosiers, Elissa Malkin	George Washington University	Washington, DC
Susanne Doblecki-Lewis, MD	Maria Alcaide, Stephen Morris, Jovanna Bertrean-Lopez, Elisa Corso-Sanchez, Alex Lazo-Vasquez, Leopoldo Cordova-Garcia, Loreta Padron	University of Miami	Miami, FL
Matthew W. Doust, MD	Sandra Erickson, Steven Siwek, Denise Sample	Hope Research Institute	Phoenix, AZ
Valentine Mbepson Ebuh, MD	Elwaleed Elnagar	WR-Global Medical Research	Dallas, TX
Frank Steven Eder, MD	Heather Shaw, Ryan Little, Victoria Engler, John Tarbox	Meridian Clinical Research	Binghamton, NY

Principal Investigator	Study Team	Institution	Location
Hana M. El Sahly, MD	Robert L. Atmar, MD, Wendy A Keitel, MD, Barbara Annette Nagel, RN, Sandra Francisco, Coni Cheesman PA-C, Thea Cordero, NP, Carrie Kiebler RN, Janet Brown RPh, Connie Rangel RN, Jennifer Christensen RPh, Chanei Henry, Caroline Doughty Skierski, RN, Chianti Wade Bowers, RN, Kayla Burrell, Kathy Bosworth, Jesus Banay, Trent Davis, Shetel Anassi, Jennifer Whitaker, Catherine Healy, Christine Akamine, Lisreina Toro, Tykel Eddy, Kayla Burrell, Jess Banay, Pedro Piedra, Olga Rybina-Willis	Baylor College of Medicine	Houston, TX
David Jon Ensz, MD	Tavane Harrison, Allie Oplinger, Brandon Essink	Meridian Clinical Research	Dakota Dunes, SD
Brandon James Essink, MD	Jay Meyer, Frederick Raiser III, Kimberly Mueller, Roni Gray, Laura Falcone	Meridian Clinical Research	Omaha, NE
Gregory J. Feldman, MD	Joseph Boscia, Farhan Siddiqui, Catherine Voelker, May-Yin Suen	VitaLink Research-Spartanburg	Spartanburg, SC
Carl J. Fichtenbaum, MD	Lisa Altenau, Kathleen Ballman, Makayla Bishop, Dana Burns, Carrie Christofield, Sherry Donaworth, Pam Fletcher, Jeanine Goddin, Shaina Horner, Judy Houston, Moises Huaman, Tamara Maus, Margaret Powers, Lisa Proffit, Kelly Windholtz	University of Cincinnati	Cincinnati, OH
Carlos A. Fierro, MD	Casey Johnson, Celia Gonzales, Natalia Leinstner	Johnson County Clin-Trials	Lenexa, KS
Veronica G. Fragoso, MD	Vicky Miller, Teresa M. Becker, Cecilia Mckeown, Tracy Kowalski, Lisa Holloway, Robert Weaver, Blanca Gomez	Texas Center For Drug Development, Inc.	Houston, TX
Ian Frank, MD	William Short, Kathleen Degnan, Helen Koening, Dovie Watson, Florence Momplasir, Sarah Wood, Katherine Bar, Jillian Baron, David Mtzger, Jie Ho, Gillain Constantino	University of Pennsylvania	Philadelphia, PA
Sharon E. Frey, MD	Getahun Abate, Shirley Dettlebach, Sabrina DiPiazza, Heather Douds, Carol Duane, Linda Eggemeyer-Sharpe, Sarah George, Geoffrey Gorse, Irene Graham, Daniel Hoft, Rong Hou, Kate Liefer, Tracy Montauk, Karla Mosby, Claudia Paredes, Joan Siegner, Susan Stewart, Janice Tennant, Jin Wang, Qian Wang	Saint Louis University	St. Louis, MO
Cynthia Gay, MD	Joseph Eron, Susan Perdersen, Lina Rosegren-Hovee, David Wohl, Faith Claman, Michael Herce, Suzanne Blevins, Christopher Hurt, Brian Gurney, Tevnan Keller, Michelle Floris-Moore	University of North Carolina at Chapel Hill	Chapel Hill, NC
Richard M. Glover, II, MD	Robyn Hartvickson, Troy Holdeman, Stacy Slechta, Amber Grant, Jeri King, Justin Philips, Eileen Wilbert, Sheri Duncan, Janelle Brown, Katherine Saengerhausen, Jordan Danby, Aaron Nguyen	Alliance for Multispecialty Research	Newton, KS
Gregory Mark Gottschlich, MD	Michael Pordy, Audrius Ruksenas, Lacy Baird, Melissa Gottschlich, Gregory Mark Gottschlich II, Mary Smith	New Horizons Clinical Research	Cincinnati, OH
Sinikka L. Green, MD	Jayasree Krishnankutty, Gregg Lucksinger	Advanced Clinical Research	Cedar Park, TX
Carl P. Griffin, MD	William Schnitz, Raymond Cornelison, Shanda Gower, Angela Genovese	Lynn Health Science Institute	Oklahoma City, OK
Milton Haber, MD	Ronald Meza, Esteban Zurita, Marco Vela	Laguna Clinical Research Associates	Laredo, TX
Greg Hachigian, MD	Peter Wroblicky, Masaru Oshita, Julie Raygoza, Maria Alyssa Lee, Shaila Faulkner, Yaman Darmarathne, Ashley Jungsten, Zuriel Joven	Benchmark Research	Sacramento, CA
Laurie J. Han-Conrad, MD	Dana Maxwell Shipp, Denis Tarakjian, Todd Tyler Simmons	WR-Medical Center for Clinical Research	San Diego, CA
Wayne Lee Harper, MD	Lisa Mauri Cohen, Dougkas Allen Wadeson, Lynn Gordon Eckert	M3 Wake Research	Raleigh, NC
Ripley R. Hollister, MD	Melody Ronk, Jeremy Brown	Lynn Institute of the Rockies	Colorado Springs, CO
Lisa A. Jackson, MD, MPH	Maya Dunstan, Joyce Zorr-Benoit, Roger Calvert, Bruce Douglas, Colin Fields, Paula Lins, Melissa Scheer-Boothe, Karen Sherwin	Kaiser Permanente Washington Health Research Institute	Seattle, WA
Spyros Andrews Kalams, MD	Gregory Wilson	Vanderbilt University Medical Center	Nashville, TN
Colleen Kelley, MD, MPH	Jeffrey Lennox, Valeria Cantos, Paulina Rebolledo, Carlos del Rio, Sheetal Kandiah, Caitlin Moran, Anandi Sheth	Emory University - Hope Clinic	Decatur, GA
Christina Kennelly, MD	David Framm, Gary Rolband, Hala Webster, Gibson Gwyn, Melissa James, Robert Brownlee, Chiedza Hooker, James Alexander	Javara	Charlotte, NC
Shishir Kumar Khetan, MD	Rahul Patel, Asefa Mekonnen, Oyebisi Olanrewaju, Ira Lawrence Berger, Alan Pollack, Allison O'Brien	Meridian Clinical Researc	Rockville, MD
Murray A. Kimmel, DO	Alexa Diec, Ann Riley, Bette Denmat, Bram Swarr, Christina Raidl, Dania Billman, Denise Dixon, Donald Dawson, Elaine Crudo, James Crowley, Katrina Carlson, Kaylie Worzick, Laura Worth, Lisbeth Gordon, Marion Oliver, Robert Holt, Simmy Pinto, Taylor Atkinson, Traci Mitchell	Optimal Research	Melbourne, FL

Principal Investigator	Study Team	Institution	Location
Judith L. Kirstein, MD	Alan Valenzuela, Theodore Wyman, Ana Caroline Remigio, Marcia Bernard	Rancho Paseo Medical Group	Banning, CA
Michael J. Koren, MD	Carolyn Tran, Jeffry Jacqmein, Darlene Bartilucci, Ipa Patel, Janet Garvey, Kenneth Aung-Din, Mitchell Rothstein, Nafisa Ishaku, Margaret Gannaway	Jacksonville Center For Clinical Research	Jacksonville, FL
Karen L. Kotloff, MD	Andrea Berry, Barbara Albert, DeAnna Friedman-Klabanoff, Elizabeth Hammershaimb, James Campbell, Justin Ortiz, Kathleen Neuzil, Kirsten Lyke, Mark Travassos, Matthew Laurens, Meagan Deming, Monica McArthur, Rekha Rapaka, Wilbur Chen	University of Maryland, Baltimore	Baltimore, MD
Mark E. Kutner, MD	Janet Mendez, Marianela Carvajal, Jorge Caso, Maria Hernandez Moran	Suncoast Research Group	Miami, FL
Mimi Van Der Leden, MD, PhD	Peta-Gay Jackson-Booth, Jennifer Yoon, Gloria Kim, Temitope Umah, Atanas Filev	Optimal Research	Rockville, MD
Michael L. Levin, MD	Dana Trippi, Erik Evensen, Marcy Kulic	WR-Clinical Research Center of Nevada	Las Vegas, NV
Michael Lewis, MD	Elham Ghadishah, Joseph Pisegna, Joseph Yusin	VA Greater Los Angeles Healthcare System	Los Angeles, CA
Gregg H. Lucksinger, MD	Kevin Parks, Ryan Israelsen, Jaleh Ostovar, Kary Kelly, Tiffany Smith	Velocity Clinical Research	Medford, OR
Mary Beth Manning, MD	Toby Briskin, Kathryn Bucur, Joan Rothenberg, Devan Patel, Jennifer Gaston, Sarah Dzigiel	Rapid Medical Research	Cleveland, OH
Kristen Marks, MD	Timothy Wilkin, Roy Gulick, Valery Hughes, Tina Wang, Noah Goss, Ole Vielemeyer, Shaun Barcavage	Cornell Clinical Trials Unit - Weill Cornell Chelsea	New York, NY
Judith Martin, MD	Alejandro Hoberman, Nader Shaikh, Timothy Shope, Sonika Bhatnagar, Gysella Muniz, Kumaravel Rajakumar, Anne-Marie Rick, Lalicia Roman, Marcia Pope, Peri Unligil, Diana Kearney	UPMC University Center	Pittsburgh, PA
John W. McGettigan, Jr., MD	Walter Patton, Cynthia Benoy, Karin Choquette, Mikell Karsten, Sheldon Gingrich, Patricia Jalomo, Riemke Brakema	Quality of Life Medical & Research Centers	Tucson, AZ
Mark Montgomery McKenzie, MD	Teresa Deese	WR-ClinSearch	Chattanooga, TN
Vicki E. Miller, MD	Monica Murray, Amy Starr, Muhammad Irfan, Fredic Santiago, Insiya Valika, Blanca Gomez	DM Clinical Research	Tomball, TX
Gowdhami Mohan, MD	Charles Thompson, Steven Clemons	VitaLink Research	Anderson, SC
Kathleen M. Mullane, DO, PharmD	David Pitrak, Stephen Schrantz, Cheryl Nuss	University of Chicago	Chicago, IL
Joseph Lee Newberg, MD	Laura Pearlman	Synexus Clinical Research	Chicago, IL
Richard M. Novak, MD	Scott Borgetti, Brito Maximo, Mahesh Patel	University of Illinois at Chicago - Project WISH	Chicago, IL
Paul Joseph Nugent, DO	Leonard Singer, Georgettea Geuss	Synexus Clinical Research	Cincinnati, OH
Jeffrey Scott Overcash, MD	Hanh Chu, Karla Zepeda, Kia Lee, Michael Waters	eStudySite	La Mesa, CA
James Todd Peterson, MD	Natalie Bee, Alexander Clark, Shana Eborn, Susan Edwards, Dan Henry, Heather Jackson, Gerald Kelty, Issac Pena-Renteria, Jacqueline Rohrer, Jack Taylor	J. Lewis Research	Salt Lake City, UT
Paul Pickrell, MD	David Pampe, Carol Ann Linebarger, Hussain Malbari	Tekton Research, Inc.	Austin, TX
Terry L. Poling, MD	Terry Klein, Tracy Klein, Thomas Klein, Gregory Greer, Taylor Simmons, Christa Shue, Lynn Le, Meenakshi Natesan, Gina Young, Lisa Hemmelgarn, Jill Hiebert, Denise Hole, Melissa Burton, Olivia Eagleson, Laura Holz, Terri Ford, Cindy Thome, Brenna Sprout	Alliance for Multispecialty Research	Wichita, KS
Bruce G. Rankin, DO	John Hill, Daniel Campbell, Steven Shinn, Jennifer Dittman, Crystal Paccione, Dhaneshwar Oomrow, Antonio Rivera, Amber Vasquez, Thais Truffa	Accel Research Sites	DeLand, FL
Michele Diane Reynolds, MD	Jennifer Bashour, Tabitha Stutevoss	Synexus Clinical Research	Dallas, TX
Rambod Rouhbakhsh, MD, MBA	Omelia Danford	MediSync Clinical Research Hattiesburg Clinic	Petal, MS
Nadine Rouphael, MD	Alexis Ahonen, Cassie Ackerley, Colleen Kelley, Daniel Garciaa, Easton Beshears, Jessica Traenkner, Kristen Unterberger, Lauren Nolan, Mary Atha, Matthew Collins, Nicholas Scanlon, Paulina Rebolledo, Srilatha Edupuganti, Varun Phadke	Emory University - Hope Clinic	Decatur, GA
Richard Rupp, MD	Steven Spenber, Richard Rupp, Laura Porterfield, Megan Berman, Cori Burkett, Amber Stanford, Elizabeth Ginn	University of Texas Medical Branch	Galveston, TX

Principal Investigator	Study Team	Institution	Location
Jamshid Saleh, MD	Alisha Garcia, Candice Cabading, Carmen Flores, Emily Crews, Marisol Corrales, Mathew Miles, Mohamed Yassin, Rafael Lupercio, Stephanie Clayton, Vicky Martin	Paradigm Clinical Research Center	Redding, CA
John W. Sanders, MD, MPH	Ann Schweppe, Anna Bowman, James Peacock, John Williamson, Katharine Pearsall, Stacy Harpe-Hall, Stephanie Boothe, Wendy Moore	Wake Forest University Health Sciences	Winston Salem, NC
Howard I. Schwartz, MD	Nelia Sanchez-Crespo, Barbara Corral, Jennifer Schwartz, Surusday Mederos, Peter Ventre, Maria Companioni, José Muniz	Research Centers of America	Hollywood, FL
Nathan Segall, MD	Jon Finley, Pamela Talbott, Mildred Stull, Donna Toepfer, Kwannda Whatley, Michelle Sowell, Jeffrey Jones, Jennifer LeBrun, Nancy Levine, Cynthia Steele	Clinical Research Atlanta	Stockbridge, GA
William Seger, MD	Mohammed Antwi, Jean Seignon, Anthony Kim, Kimberly Pullen	Benchmark Research	Fort Worth, TX
Neil Parmanand Sheth, MD	Kenneth Steil	Synexus Clinical Research	Glendale, AZ
William B. Smith, MD	Richard Gibson, Katherine Buckner	Alliance for Multispecialty Research	Knoxville,TN
Joel Solis, MD	Mratha Carmen Medina, Westly Keating, Edgar Garcia, Samuel Ramirez, Daniel Contreras, Anne McNulty-Paine, Cynthia Bueno, Pedro Penalo	Centex Studies, Inc.	McAllen, TX
Stephen A. Spector, MD	Jill Blumenthal, Amaran Moodley, Lisa Stangl, Karen Deutsch, Carlos Rojas	University of California, San Diego	La Jolla, CA
Cynthia Becher Strout, MD	Rica Santiago, Patty Howenstine, Yvonne Davis, Alison Bondell	Coastal Carolina Research Center	Mount Pleasant, SC
Shobha Swaminathan, MD	Michelle DallaPiazza	Rutgers New Jersey Medical School	Newark, NJ
Ramy Joseph Toma, MD	William Kirby, Rian Montgomery	Synexus Clinical Research	Birmingham, AL
Timothy P. Vachris, MD	Dana Hutchens	Optimal Research	Austin, TX
Keith William Vrbicky, MD	Charles Harper, Wendell Lewis III, Cathy Laflan, Kari Uhlir, Chelsie Nutsch	Meridian Clinical Research	Norfolk, NE
Larkin T. Wadsworth III, MD	Horacio Marafioti, Lyly Dang, Jennifer Berry	Sundance Clinical Research	St. Louis, MO
Jordan L. Whatley, MD	Nicole Harrel, Lindsey Hall, Amie Shannon, Mary Dobson, Kristen Losavio, Crystal Rowell	Meridian Clinical Research	Baton Rouge, LA
Judith White, MD	Christine Murphy, Robert Meyer, Prity Patel, Nicholas Weber, Sejal Patel	Synexus Clinical Research	Orlando, FL
Priyantha N. Wijewardane, MD	A. Michele Maxwell, Amy Cooper, Eric Bravo, Jeffrey Thessing, Richard Pellegrino, Tina Cox	Baptist Health Center for Clinical Research	Little Rock, AR
Barton G. Williams, MD	William Jones	Trial Management Associates	Wilmington, NC
Marcus J. Zervos, MD	John McKinnon, Dee Dee Wang, Mayur Ramesh, Gina Maki, Katherine Reyes, Paul Kilgore, Erica Herc, Brar Indira, Allison Weinmann, Jeffrey Van Laere, Howard Klausner, Joseph Miller, Linda Kaljee	Henry Ford Health System	Detroit, MI

Supplemental Statistical Methods

Statistical aspects of the vaccine efficacy analysis
Vaccine efficacy (VE) is defined as the percent reduction in the hazard, i.e. one minus the hazard ratio (HR, mRNA 1273 vs. placebo).

For the primary efficacy and secondary efficacy endpoints, a stratified Cox proportional hazard (PH) model with Efron's method of tie handling and with vaccine groups (mRNA-1273 or Placebo) as covariate is used to assess the vaccine efficacy (i.e. 1- HR) between mRNA-1273 vs. placebo. The model is adjusted for the same stratification factors used for randomization. The estimator of VE and its 95% CI is provided from the stratified Cox proportional model.

For the primary efficacy endpoint, Covid-19 cases based on adjudication committee assessments starting 14 days after the second injection in the Per-Protocol (PP) set, the one-sided p-value for testing the null hypothesis (VE ≤30%) derived from the stratified Cox model is provided. At IA1, based on a total of 95 cases, the one-sided p-value was <0.0001, and was compared to a one-sided alpha of 0.0047 based on 62.9% information of the target total number (95/151) using the Lan-DeMets O'Brien-Fleming approximation. Therefore, the pre-specified statistical criterion for study success was demonstrated at IA1.

For the primary and secondary efficacy endpoints, incidence rate, defined as the number of participants with an event divided by the number of participants at risk and adjusted by person-years (total time at risk) is calculated. The 95% CI is calculated using the exact method (Poisson distribution) and adjusted by person-years. *VE is defined as 1 — ratio of incidence rate (mRNA-1273 vs. placebo). The 95% CI of the ratio is calculated using the exact method conditional upon the total number of cases, adjusting for person-years.

Stratified Cox regression model to derive estimates of vaccine efficacy as 1-HR.
The assumption of the cox proportional hazard model is that the hazard rate ratio is a constant, i.e. the vaccine efficacy is independent of the rate at which cases occur in the Placebo group in any short time interval. At the first interim analysis with a median follow-up time of 49 days after the second dose, based on 95 cases, the vaccine efficacy estimate from the stratified Cox model was 94.5%. At the primary analysis with a median follow-up time of approximately 9 weeks after the second dose, based on 196 cases, the vaccine efficacy estimate from the stratified Cox model was 94.1%. These results indicate the vaccine efficacy is independent of the rate on Placebo. Analyses based on the exact method conditional on the total number of cases have also been performed and the results are consistent with that from the stratified Cox model.

In addition, the pattern of cumulative incidence curves (based on 1 – Kaplan-Mere estimate) for two treatment groups on Covid-19 counted starting 14 days after second dose in the PP set (primary analysis, Figure 3A) and Covid-19 counted starting from randomization in modified intent-to-treat (mITT) set (sensitivity analysis, Figure 3B) show that the proportional hazard assumption holds: two curves of the treatment groups start together with 0 events, separate around day 42 (14 days after second dose) in Figure 3A and Day 14 in Figure 3B, and then diverge over time without crossing.

The plot of log-log transformation of estimated survival probability was examined, based on November 25, 2020 data, of primary endpoint in the PP set. The curves for the two groups were approximately parallel, which supports that the proportional hazard assumption holds

Rationale for Assessment of Vaccine Efficacy in the Per-Protocol Population.

It is not uncommon to use the PP Set as the primary analysis population for efficacy for vaccine studies, as it usually includes participants who have received the intended vaccine regimen. In the PP set, participants are included in the vaccine group to which they were randomized. In our study, the PP Set excluded randomized participants who had positive or missing baseline SARS-CoV-2 status at baseline, who received the incorrect study vaccine, discontinued study before receiving dose 2, or received dose 2 outside of [day 22, 42] window, and other major protocol deviations that impacted critical data. The reasons for exclusions are summarized in Figures 1 and S1. Additionally, sensitivity analyses in the mITT set were performed to assess the consistency of vaccine efficacy.

Additional details supporting Figures 3A and 3B.
In Figures 3 and 4, the time axis started from randomization in days. Figure 3A presents the primary analysis of Covid-19 based on adjudication committee assessments starting 14 days after the second vaccination in the Per-Protocol Set. In this analysis, participants with an onset date of Covid-19 starting 14 days after second dose are events with date of onset; participants with an onset date for Covid-19 <14 days after the second dose (early case) were censored at the date of Covid-19. Participants who did not have Covid-19 were censored at the data cutoff date for efficacy. Participants who discontinued the study early or died due to cause unrelated to Covid-19 without documented Covid-19 are censored at the date of early discontinuation or death. Therefore, the cumulative incidence curves started to separate around 42 days after randomization as the date of Covid-19 in this analysis starts 14 days after second vaccination (with a target day of Day 29). The censoring started around day 29 as the earliest discontinuation in the Per-Protocol Set. Participants who discontinued before dose 2, received dose 2 outside of day [23, 42] window have been excluded from the Per-Protocol Set.

Figure 3B presents a sensitivity analysis of Covid-19 from randomization in the mITT Set. In this analysis, participants who had Covid-19 were events with date of onset. The other censoring rules are the same as above. The mITT Set only excludes randomized participants who did not receive any dose, or had positive or missing baseline SARS-CoV-2 status. Therefore, censoring starts early after randomization (early discontinuations), and the two curves started to separate early.

Baseline demographics and characteristics using the per-protocol set are provided as supportive data for Table 1 based on the randomized participants.

Baseline Demographics and Characteristics Based in the Per-Protocol Set

Characteristics n (%)	Placebo (N=14073)	mRNA-1273 (N=14134)	Total (N=28207)
Sex			
Male	7462 (53.0)	7366 (52.1)	14828 (52.6)
Female	6611 (47.0)	6768 (47.9)	13379 (47.4)
Age at Screening (yr)			
Mean (range)	51.6 (18- 95)	51.6 (18- 95)	51.6 (18- 95)
Age (yr) and health risk for severe Covid-19*			
≥18 and <65 and Not at Risk	8200 (58.3)	8189 (57.9)	16389 (58.1)
≥18 and <65 and at Risk	2324 (16.5)	2367 (16.7)	4691 (16.6)
≥65	3549 (25.2)	3578 (25.3)	7127 (25.3)
Ethnicity			
Hispanic or Latino	2780 (19.8)	2789 (19.7)	5569 (19.7)
Not Hispanic or Latino	11165 79.3)	11212 (79.3)	22377 (79.3)
Not reported and unknown	128 (0.9)	133 (1.0)	261 (0.9)
Race‡			
White	11174 (79.4)	11253 (79.6)	22427 (79.5)
Black or African American	1349 (9.6)	1385 (9.8)	2734 (9.7)
Asian	689 (4.9)	620 (4.4)	1309 (4.6)
American Indian or Alaska Native	111 (0.8)	108 (0.8)	219 (0.8)
Native Hawaiian or Other Pacific Islander	31 (0.2)	35 (0.2)	66 (0.2)
Multiracial	307 (2.2)	295 (2.1)	602 (2.1)
Other	295 (2.1)	299 (2.1)	594 (2.1)
Not reported and unknown	117 (0.9)	139 (1.0)	256 (0.9)
Baseline SARS-CoV-2 Status†			
Negative	14073 (100)	14134 (100)	28207 (100)
Positive	0	0	0
Missing	0	0	0
Baseline RT-PCR			
Negative	14073 (100)	14134 (100)	28207 (100)
Positive	0	0	0
Missing	0	0	0
Baseline bAb Anti-SARS-CoV-2			
Negative	14073 (100)	14134 (100)	28207 (100)
Positive	0	0	0
Missing	0	0	0
Risk Factor for Severe Covid-19 at Screening‡			
Chronic lung disease	688(4.9)	673 (4.8)	1361 (4.8)
Significant cardiac disease	694 (4.9)	711 (5.0)	1405 (5.0)
Severe obesity	936 (6.7)	956 (6.8)	1892 (6.7)
Diabetes	1345 (9.6)	1364 (9.7)	2709 (9.6)
Liver disease	90 (0.6)	95(0.7)	185(0.7)
HIV	77 (0.5)	82 (0.6)	159 (0.6)
Body Mass Index, (kg/m^2)			
Mean (SD)	29.27 (6.650)	29.28 (6.827)	29.28 (6.739)

bAb = binding antibody concentration; IRT = interactive response technology; RT-PCR = reverse transcription polymerase chain reaction. Internet-based randomization was used to randomize participants to treatment groups based on the information the Investigator entered regarding the age and potential comorbid conditions. *Based on stratification factor from IRT, participants who were <65 years old were categorized as at risk for severe Covid-19 illness if they had at least 1 of the risk factors specified in the study protocol at screening. †Baseline SARS-CoV-2 status was positive if there was immunologic or virologic evidence of prior Covid-19, defined as positive RT-PCR test, or bAb against SARS-CoV-2 nucleocapsid above limit of detection; or lower limit of quantification at Day 1. Negative was defined as negative RT-PCR test and negative bAb against SARS-CoV-2 assay result at Day 1. ‡Participants could be under one or more categories and were counted once at each category.

Fig. S1. Study Disposition in Overall Randomized Set

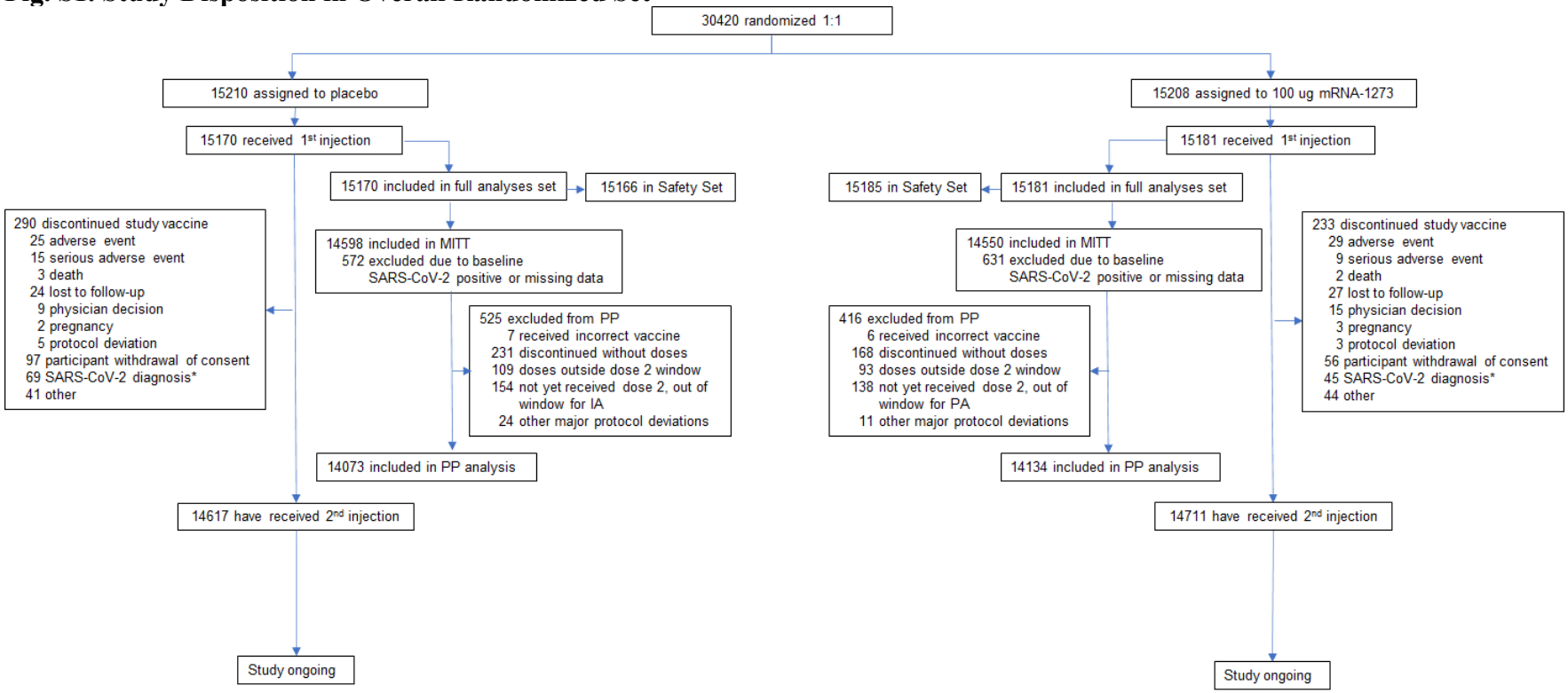

Table S1. Primary and Secondary Objectives of the Trial

Objectives and Endpoints	
Primary Objective	**Primary Endpoints**
Efficacy Objective (Primary): To demonstrate the efficacy of mRNA-1273 to prevent Covid-19.	**Efficacy Endpoints (Primary):** Vaccine efficacy of mRNA-1273 to prevent the first occurrence of Covid-19 starting 14 days after the second dose of investigational product (IP), where Covid-19 is defined as symptomatic disease based on the following criteria: • The participant must have experienced at least TWO of the following systemic symptoms: Fever (≥ 38ºC), chills, myalgia, headache, sore throat, new olfactory and taste disorder(s), OR • The participant must have experienced at least ONE of the following respiratory signs/symptoms: cough, shortness of breath or difficulty breathing, OR clinical or radiographical evidence of pneumonia; AND • The participant must have at least one NP swab, nasal swab, or saliva sample (or respiratory sample, if hospitalized) positive for SARS-CoV-2 by RT-PCR.
Safety Objective (Primary): To evaluate the safety and reactogenicity of 2 injections of the mRNA-1273 vaccine given 28 days apart.	**Safety Endpoint (Primary):** • Solicited local and systemic ARs through 7 days after each dose of IP. • Unsolicited AEs through 28 days after each dose of IP. • Medically attended adverse events (MAAEs) or AEs leading to withdrawal through the entire study period. • SAEs throughout the entire study period.
Efficacy Objectives (Secondary)	**Efficacy Endpoints (Secondary)**
To evaluate the efficacy of mRNA-1273 to prevent severe Covid-19.	• Vaccine efficacy of mRNA-1273 to prevent severe Covid-19, defined as first occurrence of Covid-19 starting 14 days after the second dose of IP, (as per the primary endpoint) AND any of the following: o Clinical signs indicative of severe systemic illness, Respiratory Rate ≥ 30 per minute, Heart Rate ≥ 125 beats per minute, SpO_2 ≤ 93% on room air at sea level or PaO_2/FIO_2 < 300 mm Hg, OR o Respiratory failure or Acute Respiratory Distress Syndrome (ARDS), (defined as needing high-flow oxygen, non-invasive or mechanical ventilation, or ECMO), evidence of shock (systolic blood pressure < 90 mmHg, diastolic BP < 60 mmHg or requiring vasopressors), OR o Significant acute renal, hepatic or neurologic dysfunction, OR o Admission to an intensive care unit or death.
To evaluate the efficacy of mRNA-1273 to prevent serologically confirmed SARS-CoV-2 infection or Covid-19 regardless of symptomatology or severity.	Vaccine efficacy of mRNA-1273 to prevent the first occurrence of either Covid-19 or SARS-CoV-2 infection starting 14 days after the second IP dose. This endpoint is a combination of Covid-19, defined as for the primary endpoint, and asymptomatic SARS-CoV-2 infection, determined by seroconversion assessed by bAb levels against SARS-CoV-2 as measured by a ligand-binding assay specific to the SARS-CoV-2 nucleocapsid protein and with a negative nasopharyngeal (NP) swab sample for SARS-CoV-2 at Day 1.
To evaluate VE against a secondary definition of Covid-19.	Vaccine efficacy of mRNA-1273 to prevent the secondary case definition of Covid-19 starting 14 days after the second IP dose. The secondary case definition of Covid-19 is defined as the following systemic symptoms: fever (temperature ≥ 38ºC), or chills, cough, shortness of breath or difficulty breathing, fatigue, muscle aches or body aches, headache, new loss of taste or smell, sore throat, nasal congestion or rhinorrhea, nausea or vomiting, or diarrhea AND a positive NP swab, nasal swab, or saliva sample (or respiratory sample, if hospitalized) for SARS-CoV-2 by RT-PCR.
To evaluate VE to prevent death caused by Covid-19.	Vaccine efficacy of mRNA-1273 to prevent death due to a cause directly attributed to a complication of Covid-19, starting 14 days after the second IP dose.
To evaluate the efficacy of mRNA-1273 to prevent Covid-19 after the first dose of IP.	Vaccine efficacy of mRNA-1273 to prevent the first occurrence of Covid-19 starting 14 days after the first dose of IP.

To evaluate the efficacy of mRNA-1273 to prevent Covid-19 in all study participants, regardless of evidence of prior SARS-CoV-2 infection.	Vaccine efficacy of mRNA-1273 to prevent the first occurrence of Covid-19 starting 14 days after the second dose of IP regardless of evidence of prior SARS-CoV-2 infection determined by serologic titer against SARS-CoV-2 nucleocapsid (FAS analysis population.
To evaluate the efficacy of mRNA-1273 to prevent asymptomatic SARS-CoV-2 infection.	Vaccine efficacy to prevent the first occurrence of SARS-CoV-2 infection in the absence of symptoms defining Covid-19 starting 14 days after the second IP dose. SARS-CoV-2 infection determined by seroconversion assessed by bAb levels against SARS-CoV-2 as measured by a ligand-binding assay specific to the SARS-CoV-2 nucleocapsid protein and with a negative NP swab sample for SARS-CoV-2 at Day 1.

Table S2. Baseline Demographics and Characteristics by Randomized Strata Groups, Full Analysis Set

	≥18-<65 yr and not at risk			≥18-<65 yr and at risk			≥65 yr			Overall		
	Placebo	mRNA-1273	Total	Placebo	mRNA-1273	Total	Placebo	mRNA-1273	Total	Placebo	mRNA-1273	Total
n (%)	N=8886	N=8888	N=17774	N=2535	N=2530	N=5065	N=3749	N=3763	N=7512	N=15170	N=15181	N=30351
Age at screening, yr mean (range)	43.8 (18-72)	44.0 (18-64)	43.9 (18-72)	49.2 (18-79)	48.9 (18-76)	49.0 (18-79)	70.7 (40-95)	70.4 (64-95)	70.6 (40-95)	51.3 (18-95)	51.4 (18-95)	51.4 (18-95)
Sex												
Male	4632 (52.1)	4544 (51.1)	9176 (51.6)	1329 (52.4)	1305 (51.6)	2634 (52.0)	2101 (56.0)	2074 (55.1)	4175 (55.6)	8062 (53.1)	7923 (52.2)	15985 (52.7)
Female	4254 (47.9)	4344 (48.9)	8598 (48.4)	1206 (47.6)	1225 (48.4)	2431 (48.0)	1648 (44.0)	1689 (44.9)	3337 (44.4)	7108 (46.9)	7258 (47.8)	14366 (47.3)
Race												
White	6789 (76.4)	6756 (76.0)	13545 (76.2)	1870 (73.8)	1900 (75.1)	3770 (74.4)	3336 (89.0)	3373 (89.6)	6709 (89.3)	11995 (79.1)	12029 (79.2)	24024 (79.2)
Black or African American	899 (10.1)	968 (10.9)	1867 (10.5)	413 (16.3)	374 (14.8)	787 (15.5)	215 (5.7)	221 (5.9)	436 (5.8)	1527 (10.1)	1563 (10.3)	3090 (10.2)
Asian	570 (6.4)	501 (5.6)	1071 (6.0)	84 (3.3)	85 (3.4)	169 (3.3)	77 (2.1)	65 (1.7)	142 (1.9)	731 (4.8)	651 (4.3)	1382 (4.6)
American Indian or Alaska Native	72 (0.8)	65 (0.7)	137 (0.8)	23 (0.9)	26 (1.0)	49 (1.0)	26 (0.7)	21 (0.6)	47 (0.6)	121 (0.8)	112 (0.7)	233 (0.8)
Native Hawaiian or Pacific Islander	20 (0.2)	25 (0.3)	45 (0.3)	9 (0.4)	7 (0.3)	16 (0.3)	3 (<0.1)	3 (<0.1)	6 (<0.1)	32 (0.2)	35 (0.2)	67 (0.2)
Multiracial	232 (2.6)	231 (2.6)	463 (2.6)	51 (2.0)	50 (2.0)	101 (2.0)	38 (1.0)	34 (0.9)	72 (1.0)	321 (2.1)	315 (2.1)	636 (2.1)
Other	229 (2.6)	233 (2.6)	462 (2.6)	54 (2.1)	61 (2.4)	115 (2.3)	33 (0.9)	27 (0.7)	60 (0.8)	316 (2.1)	321 (2.1)	637 (2.1)
Not reported	42 (0.5)	67 (0.8)	109 (0.6)	1 (0.7)	16 (0.6)	34 (0.7)	13 (0.3)	13 (0.3)	26 (0.3)	73 (0.5)	96 (0.6)	169 (0.6)
Unknown	33 (0.4)	42 (0.5)	75 (0.4)	13 (0.5)	11 (0.4)	24 (0.5)	8 (0.2)	6 (0.2)	14 (0.2)	54 (0.4)	59 (0.4)	113 (0.4)
Race and Ethnicity Group*												
White	4975 (56.0)	5005 (56.3)	9980 (56.1)	1426 (56.3)	1456 (57.5)	2882 (56.9)	3060 (81.6)	3068 (81.5)	6128 (81.6)	9461 (62.4)	9529 (62.8)	18990 (62.6)
Communities of color	3903 (43.9)	3869 (43.5)	7772 (43.7)	1104 (43.6)	1068 (42.2)	2172 (42.9)	676 (18.0)	689 (18.3)	1365 (18.2)	5683 (37.5)	5626 (37.1)	11309 (37.3)
Missing	8 (<0.1)	14 (0.2)	22 (0.1)	5 (0.2)	6 (0.2)	11 (0.2)	13 (0.3)	6 (0.2)	19 (0.3)	26 (0.2)	26 (0.2)	52 (0.2)
Ethnicity												
Hispanic or Latino	2228 (25.1)	2209 (24.9)	4437 (25.0)	552 (21.8)	558 (22.1)	1110 (21.9)	334 (8.9)	354 (9.4)	688 (9.2)	3114 (20.5)	3121 (20.6)	6235 (20.5)
Not Hispanic or Latino	6585 (74.1)	6599 (74.2)	13184 (74.2)	1960 (77.3)	1953 (77.2)	3913 (77.3)	3372 (89.9)	3366 (89.4)	6738 (89.7)	11917 (78.6)	11918 (78.5)	23835 (78.5)
Not Reported	43 (0.5)	58 (0.7)	101 (0.6)	15 (0.6)	14 (0.6)	29 (0.6)	27 (0.7)	32 (0.9)	59 (0.8)	85 (0.6)	104 (0.7)	189 (0.6)
Unknown	30 (0.3)	22 (0.2)	52 (0.3)	8 (0.3)	5 (0.2)	13 (0.3)	16 (0.4)	11 (0.3)	27 (0.4)	54 (0.4)	38 (0.3)	92 0.3)
BMI kg/m2, mean (SD)	28.0 (5.2)	28.0 (5.3)	28.0 (5.2)	35.0 (9.2)	35.2 (9.6)	35.1 (9.4)	28.7 (5.9)	28.7 (5.9)	28.7 (5.9)	29.3 (6.7)	29.3 (6.9)	29.3 (6.8)
At risk for severe Covid-19 at screening												
Yes	141 (1.6)	127 (1.4)	268 (1.5)	2163 (85.3)	2171 (85.8)	4334 (85.6)	1114 (29.7)	1101 (29.3)	2215 (29.5)	3418 (22.5)	3399 (22.4)	6817 (22.5)
No	8745 (98.4)	8761 (98.6)	17506 (98.5)	372 (14.7)	359 (14.2)	731 (14.4)	2635 (70.3)	2662 (70.7)	5297 (70.5)	11752 (77.5)	11782 (77.6)	23534 (77.5)

Baseline RT-PCR												
Negative	8755 (98.5)	8728 (98.2)	17483 (98.4)	2474 (97.6)	2478 (97.9)	4952 (97.8)	3694 (98.5)	3711 (98.6)	7405 (98.6)	14923 (98.4)	14917 (98.3)	29840 (98.3)
Positive	65 (0.7)	64 (0.7)	129 (0.7)	20 (0.8)	16 (0.6)	36 (0.7)	10 (0.3)	7 (0.2)	17 (0.2)	95 (0.6)	87 (0.6)	182 (0.6)
Missing	66 (0.7)	96 (1.1)	162 (0.9)	41 (1.6)	36 (1.4)	77 (1.5)	45 (1.2)	45 (1.2)	90 (1.2)	152 (1.0)	177 (1.2)	329 (1.1)
Baseline bAb Anti-SARS-CoV-2												
Negative	8595 (96.7)	8555 (96.3)	17150 (96.5)	2449 (96.6)	2451 (96.9)	4900 (96.7)	3682 (98.2)	3684 (97.9)	7366 (98.1)	14726 (97.1)	14690 (96.8)	29416 (96.9)
Positive	216 (2.4)	230 (2.6)	44 (2.5)	59 (2.3)	42 (1.7)	101 (2.0)	28 (0.7)	33 (0.9)	61 (0.8)	303 (2.0)	305 (2.0)	608 (2.0)
Missing	75 (0.8)	103 (1.2)	178 (1.0)	27 (1.1)	37 (1.5)	64 (1.3)	39 (1.0)	46 (1.2)	85 (1.1)	141 (0.9)	186 (1.2)	327 (1.1)
Baseline SARS-CoV-2 Status†												
Negative	8532 (96.0)	8468 (95.3)	17000 (95.6)	2415 (95.3)	2427 (95.9)	4842 (95.6)	3651 (97.4)	3655 (97.1)	7306 (97.3)	14598 (96.2)	14550 (95.8)	29148 (96.0)
Positive	239 (2.7)	260 (2.9)	499 (2.8)	65 (2.6)	47 (1.9)	112 (2.2)	33 (0.9)	36 (1.0)	69 (0.9)	337 (2.2)	343 (2.3)	680 (2.2)
Missing	115 (1.3)	160 (1.8)	275 (1.5)	55 (2.2)	56 (2.2)	111 (2.2)	65 (1.7)	72 (1.9)	137 (1.8)	235 (1.5)	288 (1.9)	523 (1.7)
Age Subgroup at Screening (yr)												
≥18 and <65	8885 (>99.9)	8888 (100)	17773 (>99.9)	2532 (99.9)	2524 (99.8)	5056 (99.8)	1 (<0.1)	1 (<0.1)	2 (<0.1)	11418 (75.3)	11413 (75.2)	22831 (75.2)
≥65 and <75	1 (<0.1)	0	1 (<0.1)	2 (<0.1)	5 (0.2)	7 (0.1)	3008 (80.2)	3105 (82.5)	6113 (81.4)	3011 (19.8)	3110 (20.5)	6121 (20.2)
≥75 and <85	0	0	0	1 (<0.1)	1 (<0.1)	2 (<0.1)	691 (18.4)	616 (16.4)	1307 (17.4)	692 (4.6)	617 (4.1)	1309 (4.3)
≥85 Years	0	0	0	0	0	0	49 (1.3)	41 (1.1)	90 (1.2)	49 (0.3)	41 (0.3)	90 (0.3)
Risk Factor for Severe Covid-19 at Screening												
Chronic lung disease	17 (0.2)	19 (0.2)	36 (0.2)	485 (19.1)	455 (18.0)	940 (18.6)	242 (6.5)	236 (6.3)	478 (6.4)	744 (4.9)	710 (4.7)	1454 (4.8)
Significant cardiac disease	11 (0.1)	12 (0.1)	23 (0.1)	285 (11.2)	306 (12.1)	591 (11.7)	448 (11.9)	434 (11.5)	882 (11.7)	744 (4.9)	752 (5.0)	1496 (4.9)
Severe obesity	69 (0.8)	59 (0.7)	128 (0.7)	809 (31.9)	807 (31.9)	1616 (31.9)	143 (3.8)	159 (4.2)	302 (4.0)	1021 (6.7)	1025 (6.8)	2046 (6.7)
Diabetes	33 (0.4)	32 (0.4)	65 (0.4)	871 (34.4)	876 (34.6)	1747 (34.5)	536 (14.3)	527 (14.0)	1063 (14.2)	1440 (9.5)	1435 (9.5)	2875 (9.5)
Liver disease	8 (<0.1)	6 (<0.1)	14 (<0.1)	62 (2.4)	76 (3.0)	138 (2.7)	26 (0.7)	18 (0.5)	44 (0.6)	96 (0.6)	100 (0.7)	196 (0.6)
HIV	13 (0.1)	14 (0.2)	27 (0.2)	59 (2.3)	62 (2.5)	121 (2.4)	15 (0.4)	16 (0.4)	31 (0.4)	87 (0.6)	92 (0.6)	179 (0.6)
Occupational Risk	7962 (89.6)	7929 (89.2)	15891 (89.4)	2165 (85.4)	2144 (84.7)	4309 (85.1)	2378 (63.4)	2356 (62.6)	4734 (63.0)	12505 (82.4)	12429 (81.9)	24934 (82.2)
Healthcare Workers	2734 (30.8)	2735 (30.8)	5469 (30.8)	593 (23.4)	595 (23.5)	1188 (23.5)	504 (13.4)	460 (12.2)	964 (12.8)	3831 (25.3)	3790 (25.0)	7621 (25.1)
Emergency Response	220 (2.5)	233 (2.6)	453 (2.5)	58 (2.3)	49 (1.9)	107 (2.1)	19 (0.5)	20 (0.5)	39 (0.5)	297 (2.0)	302 (2.0)	599 (2.0)
Retail/Restaurant	689 (7.8)	683 (7.7)	1372 (7.7)	186 (7.3)	171 (6.8)	357 (7.0)	99 (2.6)	100 (2.7)	199 (2.6)	974 (6.4)	954 (6.3)	1928 (6.4)
Manufacturing and Production	306 (3.4)	289 (3.3)	595 (3.3)	85 (3.4)	102 (4.0)	187 (3.7)	30 (0.8)	34 (0.9)	64 (0.9)	421 (2.8)	425 (2.8)	846 (2.8)
Warehouse Shipping and Fulfillment	121 (1.4)	138 (1.6)	259 (1.5)	42 (1.7)	44 (1.7)	86 (1.7)	12 (0.3)	9 (0.2)	21 (0.3)	175 (1.2)	19 (1.3)	366 (1.2)

Transportation and Delivery	313 (3.5)	335 (3.8)	648 (3.6)	9 (3.9)	97 (3.8)	195 (3.8)	62 (1.7)	50 (1.3)	112 (1.5)	473 (3.1)	482 (3.2)	955 (3.1)
Border Protection and Military Personnel	51 (0.6)	53 (0.6)	104 (0.6)	11 (0.4)	13 (0.5)	24 (0.5)	6 (0.2)	3 (<0.1)	9 (0.1)	6 (0.4)	69 (0.5)	137 (0.5)
Personal Care and In-Home Services	330 (3.7)	299 (3.4)	629 (3.5)	78 (3.1)	103 (4.1)	181 (3.6)	61 (1.6)	67 (1.8)	128 (1.7)	469 (3.1)	469 (3.1)	938 (3.1)
Hospitality and Tourism Workers	149 (1.7)	163 (1.8)	312 (1.8)	40 (1.6)	38 (1.5)	78 (1.5)	43 (1.1)	36 (1.0)	79 (1.1)	232 (1.5)	237 (1.6)	469 (1.5)
Pastoral, Social or Public Health Workers	264 (3.0)	296 (3.3)	560 (3.2)	101 (4.0)	90 (3.6)	19 (3.8)	138 (3.7)	147 (3.9)	285 (3.8)	503 (3.3)	533 (3.5)	1036 (3.4)
Educators and Students	1113 (12.5)	1083 (12.2)	2196 (12.4)	270 (10.7)	276 (10.9)	546 (10.8)	169 (4.5)	184 (4.9)	353 (4.7)	1552 (10.2)	1543 (10.2)	3095 (10.2)
Other	2591 (29.2)	2582 (29.1)	5173 (29.1)	789 (31.1)	810 (32.0)	1599 (31.6)	1423 (38.0)	1426 (37.9)	2849 (37.9)	4803 (31.7)	4818 (31.7)	9621 (31.7)
Location and Living Circumstances Risk	7444 (83.8)	7481 (84.2)	14925 (84.0)	2080 (82.1)	2046 (80.9)	4126 (81.5)	3089 (82.4)	3119 (82.9)	6208 (82.6)	12613 (83.1)	12646 (83.3)	25259 (83.2)
Nursing Home or Assisted Living Facility	6 (<0.1)	11 (0.1)	17 (<0.1)	3 (0.1)	11 (0.4)	14 (0.3)	20 (0.5)	11 (0.3)	31 (0.4)	29 (0.2)	33 (0.2)	62 (0.2)
Multi-Family Dwelling	266 (3.0)	304 (3.4)	570 (3.2)	80 (3.2)	92 (3.6)	172 (3.4)	63 (1.7)	66 (1.8)	129 (1.7)	409 (2.7)	462 (3.0)	871 (2.9)
High Density Housing	873 (9.8)	839 (9.4)	1712 (9.6)	195 (7.7)	195 (7.7)	390 (7.7)	239 (6.4)	251 (6.7)	490 (6.5)	1307 (8.6)	1285 (8.5)	2592 (8.5)
Low Density, Multi-Family Setting	952 (10.7)	934 (10.5)	1886 (10.6)	275 (10.8)	301 (11.9)	576 (11.4)	255 (6.8)	244 (6.5)	499 (6.6)	1482 (9.8)	1479 (9.7)	2961 (9.8)
Single Family Home	4739 (53.3)	4771 (53.7)	9510 (53.5)	1366 (53.9)	1288 (50.9)	2654 (52.4)	2245 (59.9)	2270 (60.3)	4515 (60.1)	8350 (55.0)	8329 (54.9)	16679 (55.0)
Other	1306 (14.7)	1329 (15.0)	2635 (14.8)	331 (13.1)	315 (12.5)	646 (12.8)	528 (14.1)	545 (14.5)	1073 (14.3)	2165 (14.3)	2189 (14.4)	4354 (14.3)

Percentages are based on the number of participants in full analysis set (FAS), presented for overall and 3 age stratification groups. Baseline SARS-CoV-2 status was positive if there was immunologic or virologic evidence of prior Covid-19, defined as positive RT-PCR test or positive bAb result at day 1; negative was defined as negative RT-PCR test and negative bAb result at day 1. *White was defined as white and non-Hispanic, and communities of color includes all the others whose race or ethnicity is not unknown, unreported or missing. †Baseline SARS-CoV-2 Status was considered positive if there was immunologic or virologic evidence of prior Covid-19, defined as positive RT-PCR test or bAb result at day 1; negative was defined as negative RT-PCR test and bAb results at day 1. Age and health risk for severe Covid-19 are derived from age and risk factors collected on case report form. Note that some participants were incorrectly stratified on the basis of Covid-19 risk.

Table S3. Solicited Adverse Reactions Within 7 Days After First Vaccination by Grade, Solicited Safety Set

Adverse reaction Vaccination 1 n (%)	Overall Safety Set			≥18-<65 years			≥65 years		
	Placebo (N=15155)	mRNA-1273 (N=15168)	Total (N=30323)	Placebo (N=11407	mRNA-1273 (N=11406)	Total (N=22813)	Placebo N=3748	mRNA-1273 N=3762	Total N=7510
Any solicited AR	7284 (48)	13319 (87.8)	20603 (67.9)	5738 (50.3)	10261 (90.0)	15999 (70.1)	1546 (41.2)	3058 (81.3)	4604 (61.3)
Grade 1	5147 (34.0)	9342 (61.6)	14489 (47.8)	4003 (35.1)	6959 (61.0)	10962 (48.1)	1144 (30.5)	2383 (63.3)	3527 (47.0)
Grade 2	1770 (11.7)	3124 (20.6)	4894 (16.1)	1459 (12.8)	2593 (22.7)	4052 (17.8)	311 (8.3)	531 (14.1)	842 (11.2)
Grade 3	361(2.4)	848 (5.6)	1209 (4.0)	272 (2.4)	704 (6.2)	976 (4.3)	89 (2.4)	144 (3.8)	233 (3.1)
Grade 4	6 (<0.1)	5 (<0.1)	11 (<0.1)	4 (<0.1)	5 (<0.1)	9 (<0.1)	2 (<0.1)	0	2 (<0.1)
Any Local AR	2997 (19.8)	12765 (84.2)	15762 (52.0)	2430 (21.3)	9960 (87.4)	12390 (54.3)	567 (15.1)	2805 (74.6)	3372 (44.9)
Grade 1	2837 (18.7)	10731 (70.8)	13568 (44.8)	2333 (20.5)	8154 (71.5)	10487 (46.0)	504 (13.5)	2577 (68.5)	3081 (41.0)
Grade 2	82 (0.5)	1505 (9.9)	1587 (5.2)	58 (0.5)	1354 (11.9)	1412 (6.2)	24 (0.6)	151 (4.0)	175 (2.3)
Grade 3	78 (0.5)	529 (3.5)	607 (2.0)	39 (0.3)	452 (4.0)	491 (2.2)	39 (1.0)	77 (2.0)	116 (1.5)
Grade 4	0	0	0	0	0	0	0	0	0
Local AR									
Pain	2658 (17.5)	12690 (83.7)	15348 (50.6)	2177 (19.1)	9908 (86.9)	12085 (53.0)	481 (12.8)	2782 (74.0)	3263 (43.5)
Grade 1	2549 (16.8)	10990 (72.5)	13539 (44.7)	2114 (18.5)	8362 (73.3)	10476 (45.9)	435 (11.6)	2628 (69.9)	3063 (40.8)
Grade 2	54 (0.4)	1284 (8.5)	1338 (4.4)	40 (0.4)	1180 (10.3)	1220 (5.3)	14 (0.4)	104 (2.8)	118 (1.6)
Grade 3	55 (0.4)	416 (2.7)	471 (1.6)	23 (0.2)	366 (3.2)	389 (1.7)	32 (0.9)	50 (1.3)	82 (1.1)
Erythema	67 (0.4)	430 (2.8)	497 (1.6)	47 (0.4)	344 (3.0)	391 (1.7)	20 (0.5)	86 (2.3)	106 (1.4)
Grade 1	47 (0.3)	267 (1.8)	314 (1.0)	32 (0.3)	212 (1.9)	244 (1.1)	15 (0.4)	55 (1.5)	70 (0.9)
Grade 2	7 (<0.1)	121 (0.8)	128 (0.4)	4 (<0.1)	98 (0.9)	102 (0.4)	3 (<0.1)	23 (0.6)	26 (0.3)
Grade 3	13 (<0.1)	42 (0.3)	55 (0.2)	11 (<0.1)	34 (0.3)	45 (0.2)	2 (<0.1)	8 (0.2)	10 (0.1)
Swelling	52 (0.3)	932 (6.1)	984 (3.2)	34 (0.3)	767 (6.7)	801 (3.5)	18 (0.5)	165 (4.4)	183 (2.4)
Grade 1	39 (0.3)	605 (4.0)	644 (2.1)	28 (0.2)	500 (4.4)	528 (2.3)	11 (0.3)	105 (2.8)	116 (1.5)
Grade 2	7 (<0.1)	245 (1.6)	252 (0.8)	3 (<0.1)	205 (1.8)	208 (0.9)	4 (0.1)	40 (1.1)	44 (0.6)
Grade 3	6 (<0.1)	82 (0.5)	88 (0.3)	3 (<0.1)	62 (0.5)	65 (0.3)	3 (<0.1)	20 (0.5)	23 (0.3)
Axillary swelling/tenderness*	722 (4.8)	1553 (10.2)	2275 (7.5)	567 (5.0)	1322 (11.6)	1889 (8.3)	155 (4.1)	231 (6.1)	386 (5.1)
Grade 1	668 (4.4)	1395 (9.2)	2063 (6.8)	534 (4.7)	1181 (10.4)	1715 (7.5)	134 (3.6)	214 (5.7)	348 (4.6)
Grade 2	27 (0.2)	109 (0.7)	136 (0.4)	20 (0.2)	104 (0.9)	124 (0.5)	7 (0.2)	5 (0.1)	12 (0.2)
Grade 3	27 (0.2)	49 (0.3)	76 (0.3)	13 (0.1)	37 (0.3)	50 (0.2)	14 (0.4)	12 (0.3)	26 (0.3)
Any Systemic AR	6399 (42.2)	8320 (54.9)	14719 (48.5)	5065 (44.4)	6503 (57.0)	11568 (50.7)	1334 (35.6)	1817 (48.3)	3151 (42.0)
Grade 1	4346 (28.7)	5372 (35.4)	9718 (32.0)	3375 (29.6)	4092 (35.9)	7467 (32.7)	971 (25.9)	1280 (34.0)	2251 (30.0)
Grade 2	1739 (11.5)	2496 (16.5)	4235 (14.0)	1438 (12.6)	2043 (17.9)	3481 (15.3)	301 (8.0)	453 (12.0)	754 (10.0)
Grade 3	308 (2.0)	447 (2.9)	755 (2.5)	248 (2.2)	363 (3.2)	611 (2.7)	60 (1.6)	84 (2.2)	144 (1.9)
Grade 4	6 (<0.1)	5 (<0.1)	11 (<0.1)	4 (<0.1)	5 (<0.1)	9 (<0.1)	2 (<0.1)	0	2 (<0.1)
Systemic AR									
Fever	44 (0.3)	115 (0.8)	159 (0.5)	37 (0.3)	105 (0.9)	142 (0.6)	7 (0.2)	10 (0.3)	17 (0.2)
Grade 1	29 (0.2)	74 (0.5)	103 (0.3)	26 (0.2)	67 (0.6)	93 (0.4)	3 (<0.1)	7 (0.2)	10 (0.1)
Grade 2	7 (<0.1)	26 (0.2)	33 (0.1)	6 (<0.1)	24 (0.2)	30 (0.1)	1 (<0.1)	2 (<0.1)	3 (<0.1)
Grade 3	2 (<0.1)	11 (<0.1)	13 (<0.1)	1 (<0.1)	10 (<0.1)	11 (<0.1)	1 (<0.1)	1 (<0.1)	2 (<0.1)

Grade 4	6 (<0.1)	4 (<0.1)	10 (<0.1)	4 (<0.1)	4 (<0.1)	8 (<0.1)	2 (<0.1)	0	2 (<0.1)
Headache	4027 (26.6)	4951 (32.7)	8978 (29.6)	3304 (29.0)	4030 (35.3)	7334 (32.2)	723 (19.3)	921 (24.5)	1644 (21.9)
Grade 1	3306 (21.8)	3953 (26.1)	7259 (23.9)	2676 (23.5)	3174 (27.8)	5850 (25.7)	630 (16.8)	779 (20.7)	1409 (18.8)
Grade 2	525 (3.5)	727 (4.8)	1252 (4.1)	466 (4.1)	637 (5.6)	1103 (4.8)	59 (1.6)	90 (2.4)	149 (2.0)
Grade 3	196 (1.3)	271 (1.8)	467 (1.5)	162 (1.4)	219 (1.9)	381 (1.7)	34 (0.9)	52 (1.4)	86 (1.1)
Fatigue	4133 (27.3)	5635 (37.2)	9768 (32.2)	3282 (28.8)	4384 (38.4)	7666 (33.6)	851 (22.7)	1251 (33.3)	2102 (28.0)
Grade 1	2709 (17.9)	3599 (23.7)	6308 (20.8)	2104 (18.4)	2744 (24.1)	4848 (21.3)	605 (16.2)	855 (22.7)	1460 (19.5)
Grade 2	1319 (8.7)	1885 (12.4)	3204 (10.6)	1095 (9.6)	1519 (13.3)	2614 (11.5)	224 (6.0)	366 (9.7)	590 (7.9)
Grade 3	105 (0.7)	150 (1.0)	255 (0.8)	83 (0.7)	120 (1.1)	203 (0.9)	22 (0.6)	30 (0.8)	52 (0.7)
Grade 4	0	1 (<0.1)	1 (<0.1)	0	1 (<0.1)	1 (<0.1)	0	0	0
Myalgia	2071 (13.7)	3441 (22.7)	5512 (18.2)	1628 (14.3)	2699 (23.7)	4327 (19.0)	443 (11.8)	742 (19.7)	1185 (15.8)
Grade 1	1567 (10.3)	2445 (16.1)	4012 (13.2)	1205 (10.6)	1876 (16.5)	3081 (13.5)	362 (9.7)	569 (15.1)	931 (12.4)
Grade 2	457 (3.0)	906 (6.0)	1363 (4.5)	385 (3.4)	750 (6.6)	1135 (5.0)	72 (1.9)	156 (4.1)	228 (3.0)
Grade 3	47 (0.3)	90 (0.6)	137 (0.5)	38 (0.3)	73 (0.6)	111 (0.5)	9 (0.2)	17 (0.5)	26 (0.3)
Arthralgia	1783 (11.8)	2511 (16.6)	4294 (14.2)	1327 (11.6)	1893 (16.6)	3220 (14.1)	456 (12.2)	618 (16.4)	1074 (14.3)
Grade 1	1341 (8.9)	1846 (12.2)	3187 (10.5)	970 (8.5)	1371 (12.0)	2341 (10.3)	371 (9.9)	475 (12.6)	846 (11.3)
Grade 2	405 (2.7)	604 (4.0)	1009 (3.3)	328 (2.9)	474 (4.2)	802 (3.5)	77 (2.1)	130 (3.5)	207 (2.8)
Grade 3	37 (0.2)	60 (0.4)	97 (0.3)	29 (0.3)	47 (0.4)	76 (0.3)	8 (0.2)	13 (0.3)	21 (0.3)
Grade 4	0	1 (<0.1)	1 (<0.1)	0	1 (<0.1)	1 (<0.1)	0	0	0
Nausea/vomiting	1074 (7.1)	1262 (8.3)	2336 (7.7)	908 (8.0)	1068 (9.4)	1976 (8.7)	166 (4.4)	194 (5.2)	360 (4.8)
Grade 1	890 (5.9)	1048 (6.9)	1938 (6.4)	752 (6.6)	889 (7.8)	1641 (7.2)	138 (3.7)	159 (4.2)	297 (4.0)
Grade 2	172 (1.1)	204 (1.3)	376 (1.2)	148 (1.3)	173 (1.5)	321 (1.4)	24 (0.6)	31 (0.8)	55 (0.7)
Grade 3	12 (<0.1)	10 (<0.1)	22 (<0.1)	8 (<0.1)	6 (<0.1)	14 (<0.1)	4 (0.1)	4 (0.1)	8 (0.1)
Chills	878 (5.8)	1253 (8.3)	2131 (7.0)	730 (6.4)	1051 (9.2)	1781 (7.8)	148 (4.0)	202 (5.4)	350 (4.7)
Grade 1	706 (4.7)	940 (6.2)	1646 (5.4)	584 (5.1)	781 (6.8)	1365 (6.0)	122 (3.3)	159 (4.2)	281 (3.7)
Grade 2	158 (1.0)	289 (1.9)	447 (1.5)	138 (1.2)	253 (2.2)	391 (1.7)	20 (0.5)	36 (1.0)	56 (0.7)
Grade 3	14 (<0.1)	24 (0.2)	38 (0.1)	8 (<0.1)	17 (0.1)	25 (0.1)	6 (0.2)	7 (0.2)	13 (0.2)

n=Number of exposed participants who submitted any for the event; percentages are based on the number of exposed participants who submitted any data for the event in the solicited safety set. Any = Grade 1 or higher. Toxicity grade for Erythema (Redness) is defined as: G1 = 25 - 50 mm; G2 = 51 -100 mm; G3 = >100 mm. Toxicity grade for fever is defined as: G1 = 38 - 38.4 C; G2 = 38.5 - 38.9 C; G3 = 39 -40 C; G4 = >40 C. *Localized axillary swelling or tenderness ipsilateral to the vaccination arm.

Table S4. Solicited Adverse Reactions Within 7 Days After Second Vaccination by Grade, Solicited Safety Set

Adverse reaction Vaccination 2 n (%)	Overall Safety Set			≥18-<65 years			≥65 years		
	Placebo (N=14566)	mRNA (N=14677)	Total (N=29243)	Placebo (N=10918)	mRNA-1273 (N=10985)	Total (N=21903)	Placebo N=3648	mRNA-1273 N=3692	Total 7340
Any solicited AR	6232 (42.8)	13534 (92.2)	19766 (67.6)	4902 (44.9)	10231 (93.1)	15133 (69.1)	1330 (36.5)	3303 (89.5)	4633 (63.1)
Grade 1	4354 (29.9)	4855 (33.1)	9209 (31.5)	3397 (31.1)	3294 (30.0)	6691 (30.5)	957 (26.2)	1561 (42.3)	2518 (34.3)
Grade 2	1534 (10.5)	5781 (39.4)	7315 (25.0)	1248 (11.4)	4576 (41.7)	5824 (26.6)	286 (7.8)	1205 (32.6)	1491 (20.3)
Grade 3	341 (2.3)	2884 (19.6)	3225 (11.0)	255 (2.3)	2349 (21.4)	2604 (11.9)	86 (2.4)	535 (14.5)	621 (8.5)
Grade 4	3 (<0.1)	14 (<0.1)	17 (<0.1)	2 (<0.1)	12 (0.1)	14 (<0.1)	1 (<0.1)	2 (<0.1)	3 (<0.1)
Any Local AR	2735 (18.8)	13006 (88.6)	15741 (53.8)	2244 (20.6)	9915 (90.3)	12159 (55.5)	491 (13.5)	3091 (83.8)	3582 (48.8)
Grade 1	2581 (17.7)	8778 (59.8)	11359 (38.9)	2135 (19.6)	6410 (58.4)	8545 (39.0)	446 (12.2)	2368 (64.2)	2814 (38.4)
Grade 2	82 (0.6)	3208 (21.9)	3290 (11.3)	67 (0.6))	2703 (24.6)	2770 (12.6)	15 (0.4)	505 (13.7)	520 (7.1)
Grade 3	72 (0.5)	1020 (7.0)	1092 (3.7)	42 (0.4)	802 (7.3)	844 (3.9)	30 (0.8)	218 (5.9)	248 (3.4)
Grade 4	0	0	0	0	0	0	0	0	0
Local AR									
Pain	2477 (17.0)	12943 (88.2)	15420 (52.7)	2040 (18.7)	9873 (89.9)	11913 (54.4)	437 (12.0)	3070 (83.2)	3507 (47.8)
Grade 1	2378 (16.3)	9498 (64.7)	11876 (40.6)	1972 (18.1)	6923 (63.0)	8895 (40.6)	406 (11.1)	2575 (69.8)	2981 (40.6)
Grade 2	59 (0.4)	2841 (19.4)	2900 (9.9)	46 (0.4)	2444 (22.3)	2490 (11.4)	13 (0.4)	397 (10.8)	410 (5.6)
Grade 3	40 (0.3)	604 (4.1)	644 (2.2)	22 (0.2)	506 (4.6)	528 (2.4)	18 (0.5)	98 (2.7)	116 (1.6)
Erythema	56 (0.4)	1257 (8.6)	1313 (4.5)	43 (0.4)	982 (8.9)	1025 (4.7)	13 (0.4)	275 (7.5)	288 (3.9)
Grade 1	38 (0.3)	442 (3.0)	480 (1.6)	28 (0.3)	352 (3.2)	380 (1.7)	10 (0.3)	90 (2.4)	100 (1.4)
Grade 2	3 (<0.1)	528 (3.6)	531 (1.8)	3 (<0.1)	420 (3.8)	423 (1.9)	0	108 (2.9)	108 (1.5)
Grade 3	15 (0.1)	287 (2.0)	302 (1.0)	12 (0.1)	210 (1.9)	222 (1.0)	3 (<0.1)	77 (2.1)	80 (1.1)
Swelling	49 (0.3)	1789 (12.2)	1838 (6.3)	36 (0.3)	1389 (12.6)	1425 (6.5)	13 (0.4)	400 (10.8)	413 (5.6)
Grade 1	29 (0.2)	890 (6.1)	919 (3.1)	24 (0.2)	700 (6.4)	724 (3.3)	5 (0.1)	190 (5.2)	195 (2.7)
Grade 2	9 (<0.1)	645 (4.4)	654 (2.2)	8 (<0.1)	507 (4.6)	515 (2.4)	1 (<0.1)	138 (3.7)	139 (1.9)
Grade 3	11 (<0.1)	254 (1.7)	265 (0.9)	4 (<0.1)	182 (1.7)	186 (0.8)	7 (0.2)	72 (2.0)	79 (1.1)
Axillary swelling/tenderness*	567 (3.9)	2090 (14.2)	2657 (9.1)	470 (4.3)	1775 (16.2)	2245 (10.3)	97 (2.7)	315 (8.5)	412 (5.6)
Grade 1	521 (3.6)	1737 (11.8)	2258 (7.7)	433 (4.0)	1469 (13.4)	1902 (8.7)	88 (2.4)	268 (7.3)	356 (4.9)
Grade 2	27 (0.2)	286 (1.9)	313 (1.1)	26 (0.2)	260 (2.4)	286 (1.3)	1 (<0.1)	26 (0.7)	27 (0.4)
Grade 3	19 (0.1)	67 (0.5)	86 (0.3)	11 (0.1)	46 (0.4)	57 (0.3)	8 (0.2)	21 (0.6)	29 (0.4)
Any Systemic AR	5323 (36.5)	11652 (79.4)	16975 (58.1)	4192 (38.4)	8999 (81.9)	13191 (60.2)	1131 (31.0)	2653 (71.9)	3784 (51.6)
Grade 1	3526 (24.2)	3723 (25.4)	7249 (24.8)	2734 (25.0)	2618 (23.8)	5352 (24.4)	792 (21.7)	1105 (29.9)	1897 (25.8)
Grade 2	1512 (10.4)	5590 (38.1)	7102 (24.3)	1233 (11.3)	4441 (40.4)	5674 (25.9)	279 (7.6)	1149 (31.1)	1428 (19.5)
Grade 3	282 (1.9)	2325 (15.8)	2607 (8.9)	223 (2.0)	1928 (17.6)	2151 (9.8)	59 (1.6)	397 (10.8)	456 (6.2)
Grade 4	3 (<0.1)	14 (<0.1)	17 (<0.1)	2 (<0.1)	12 (0.1)	14 (<0.1)	1 (<0.1)	2 (<0.1)	3 (<0.1)
Systemic AR									
Fever	43 (0.3)	2278 (15.5)	2321 (7.9)	39 (0.4)	1908 (17.4)	1947 (8.9)	4 (0.1)	370 (10.0)	374 (5.1)
Grade 1	33 (0.2)	1364 (9.3)	1397 (4.8)	31 (0.3)	1111 (10.1)	1142 (5.2)	2 (<0.1)	253 (6.9)	255 (3.5)
Grade 2	5 (<0.1)	699 (4.8)	704 (2.4)	4 (<0.1)	601 (5.5)	605 (2.8)	1 (<0.1)	98 (2.7)	99 (1.3)
Grade 3	2 (<0.1)	202 (1.4)	204 (0.7)	2 (<0.1)	184 (1.7)	186 (0.8)	0	18 (0.5)	18 (0.2)
Grade 4	3 (<0.1)	13 (<0.1)	16 (<0.1)	2 (<0.1)	12 (0.1)	14 (<0.1)	1 (<0.1)	1 (<0.1)	2 (<0.1)
Headache	3410 (23.4)	8602 (58.6)	12012 (41.1)	2760 (25.3)	6898 (62.8)	9658 (44.1)	650 (17.8)	1704 (46.2)	2354 (32.1)

Grade 1	2739 (18.8)	4804 (32.7)	7543 (25.8)	2180 (20.0)	3658 (33.3)	5838 (26.7)	559 (15.3)	1146 (31.1)	1705 (23.2)
Grade 2	509 (3.5)	3139 (21.4)	3648 (12.5)	451 (4.1)	2687 (24.5)	3138 (14.3)	58 (1.6)	452 (12.3)	510 (7.0)
Grade 3	162 (1.1)	659 (4.5)	821 (2.8)	129 (1.2)	553 (5.0)	682 (3.1)	33 (0.9)	106 (2.9)	139 (1.9)
Fatigue	3403 (23.4)	9582 (65.3)	12985 (44.4)	2687 (24.6)	7430 (67.6)	10117 (46.2)	716 (19.6)	2152 (58.3)	2868 (39.1)
Grade 1	2182 (15.0)	3432 (23.4)	5614 (19.2)	1700 (15.6)	2525 (23.0)	4225 (19.3)	482 (13.2)	907 (24.6)	1389 (18.9)
Grade 2	1115 (7.7)	4722 (32.2)	5837 (20.0)	901 (8.3)	3731 (34.0)	4632 (21.2)	214 (5.9)	991 (26.9)	1205 (16.4)
Grade 3	106 (0.7)	1428 (9.7)	1534 (5.2)	86 (0.8)	1174 (10.7)	1260 (5.8)	20 (0.5)	254 (6.9)	274 (3.7)
Myalgia	1809 (12.4)	8508 (58.0)	10317 (35.3)	1411 (12.9)	6769 (61.6)	8180 (37.4)	398 (10.9)	1739 (47.1)	2137 (29.1)
Grade 1	1300 (8.9)	3239 (22.1)	4539 (15.5)	994 (9.1)	2411 (22.0)	3405 (15.6)	306 (8.4)	828 (22.4)	1134 (15.5)
Grade 2	457 (3.1)	3951 (26.9)	4408 (15.1)	375 (3.4)	3245 (29.5)	3620 (16.5)	82 (2.2)	706 (19.1)	788 (10.7)
Grade 3	52 (0.4)	1318 (9.0)	1370 (4.7)	42 (0.4)	1113 (10.1)	1155 (5.3)	10 (0.3)	205 (5.6)	215 (2.9)
Arthralgia	1569 (10.8)	6284 (42.8)	7853 (26.9)	1172 (10.7)	4993 (45.5)	6165 (28.2)	397 (10.9)	1291 (35.0)	1688 (23.0)
Grade 1	1142 (7.8)	2802 (19.1)	3944 (13.5)	837 (7.7)	2105 (19.2)	2942 (13.4)	305 (8.4)	697 (18.9)	1002 (13.7)
Grade 2	383 (2.6)	2712 (18.5)	3095 (10.6)	298 (2.7)	2241 (20.4)	2539 (11.6)	85 (2.3)	471 (12.8)	556 (7.6)
Grade 3	44 (0.3)	770 (5.2)	814 (2.8)	37 (0.3)	647 (5.9)	684 (3.1)	7 (0.2)	123 (3.3)	130 (1.8)
Nausea/vomiting	934 (6.4)	2785 (19.0)	3719 (12.7)	801 (7.3)	2348 (21.4)	3149 (14.4)	133 (3.6)	437 (11.8)	570 (7.8)
Grade 1	756 (5.2)	2090 (14.2)	2846 (9.7)	646 (5.9)	1752 (16.0)	2398 (11.0)	110 (3.0)	338 (9.2)	448 (6.1)
Grade 2	167 (1.1)	674 (4.6)	841 (2.9)	147 (1.3)	586 (5.3)	733 (3.3)	20 (0.5)	88 (2.4)	108 (1.5)
Grade 3	11 (<0.1)	20 (0.1)	31 (0.1)	8 (<0.1)	10 (<0.1)	18 (<0.1)	3 (<0.1)	10 (0.3)	13 (0.2)
Grade 4	0	1 (<0.1)	1 (<0.1)	0	0	0	0	1 (<0.1)	1 (<0.1)
Chills	809 (5.6)	6482 (44.2)	7291 (24.9)	658 (6.0)	5341 (48.6)	5999 (27.4)	151 (4.1)	1141 (30.9)	1292 (17.6)
Grade 1	626 (4.3)	2899 (19.8)	3525 (12.1)	502 (4.6)	2307 (21.0)	2809 (12.8)	124 (3.4)	592 (16.0)	716 (9.8)
Grade 2	166 (1.1)	3392 (23.1)	3558 (12.2)	141 (1.3)	2870 (26.1)	3011 (13.8)	25 (0.7)	522 (14.2)	547 (7.5)
Grade 3	17 (0.1)	191 (1.3)	208 (0.7)	15 (0.1)	164 (1.5)	179 (0.8)	2 (<0.1)	27 (0.7)	29 (0.4)

n=Number of exposed participants who submitted any for the event; percentages are based on the number of exposed participants who submitted any data for the event. Any = Grade 1 or higher. Toxicity grade for Erythema (Redness) is defined as: G1 = 25 — 50 mm; G2 = 51 — 100 mm; G3 = > 100 mm. Toxicity grade for Fever is defined as: G1 = 38 — 38.4 C; G2 = 38.5 — 38.9 C; G3 = 39 — 40 C; G4 = > 40 C. *Localized axillary swelling or tenderness ipsilateral to the vaccination arm.

Table S5. Number of Days Reporting Solicited Adverse Reactions After First and Second Vaccinations, Solicited Safety Set

Adverse reaction duration days	Vaccination 1			Vaccination 2		
	Placebo (N=15155)	mRNA-1273 (N=15168)	Total (N=30323)	Placebo (N=14566)	mRNA-1273 (N=14677)	Total (N=29243)
Any solicited (n)	7284	13319	20603	6232	13534	19766
Mean days (SD)	3.2 (4.2)	3.4 (3.3)	3.3 (3.6)	3.4 (5.7)	4.0 (4.8)	3.8 (5.1)
Any local (n)	2997	12765	15762	2735	13006	15741
Mean days (SD)	1.9 (2.6)	2.6 (2.0)	2.5 (2.0)	2.1 (4.1)	3.2 (2.9)	3.0 (3.2)
Pain (n)	2658	12690	15348	2477	12943	15420
Mean, days (SD)	1.7 (2.1)	2.4 (1.4)	2.3 (1.5)	1.8 (3.3)	3.0 (2.2)	2.8 (2.4)
Erythema (n)	67	430	497	56	1257	1313
Mean, days (SD)	3.2 (5.6)	2.5 (4.1)	2.6 (4.4)	3.8 (10.6)	2.7 (3.9)	2.7 (4.4)
Swelling (n)	52	932	984	49	1789	1838
Mean, days (SD)	5.1 (7.8)	2.1 (2.2)	2.2 (2.8)	2.7 (4.9)	2.6 (4.1)	2.6 (4.2)
Axillary swelling/tenderness* (n)	722	1553	2275	567	2090	2657
Mean, days (SD)	2.1 (2.8)	2.3 (2.9)	2.2 (2.9)	2.6 (5.3)	2.4 (3.2)	2.4 (3.7)
Any Systemic AR	6399	8320	14719	5323	11652	16975
Mean, days (SD)	3.1 (4.2)	2.9 (3.7)	3.0 (3.9)	3.4 (5.6)	3.1 (4.6)	3.2 (4.9)
Fever (n)	44	115	159	43	2278	2321
Mean, days (SD)	1.4 (0.6)	1.3 (0.7)	1.3 (0.7)	1.2 (0.5)	1.2 (1.7)	1.2 (1.7)
Headache (n)	4027	4951	8978	3410	8602	12012
Mean, days (SD)	2.1 (2.4)	2.1 (2.2)	2.1 (2.3)	2.3 (3.3)	2.3 (2.9)	2.3 (3.0)
Fatigue (n)	4133	5635	9768	3403	9582	12985
Mean, days (SD)	2.8 (3.7)	2.7 (3.6)	2.7 (3.6)	3.0 (5.1)	2.6 (3.7)	2.7 (4.1)
Myalgia (n)	2071	3441	5512	1809	8508	10317
Mean, days (SD)	2.7 (3.7)	2.3 (3.2)	2.4 (3.4)	3.2 (6.1)	2.1 (3.1)	2.3 (3.8)
Arthralgia (n)	1783	2511	4294	1569	6284	7853
Mean, days (SD)	3.2 (5.0)	2.6 (4.1)	2.9 (4.5)	3.7 (7.0)	2.3 (3.5)	2.5 (4.5)
Nausea/vomiting (n)	1074	1262	2336	934	2785	3719
Mean, days (SD)	1.8 (2.2)	1.7 (1.5)	1.7 (1.9)	1.9 (3.8)	1.7 (2.4)	1.8 (2.8)
Chills (n)	878	1253	2131	809	6482	7291
Mean, days (SD)	1.7 (1.7)	1.5 (1.7)	1.6 (1.7)	1.9 (3.2)	1.5 (1. 6)	1.5 (1.8)

n = Number of exposed participants who reported the event on any day within 7 days of the first injection. Number of days is calculated as the days of the solicited adverse reaction reported within the 7 days of injection including the day of injection. If the solicited AR continued beyond 7 days, the consecutive days a solicited adverse reaction was reported after 7 days are included. *Localized axillary swelling or tenderness ipsilateral to the vaccination arm.

Table S6. Solicited Adverse reactions by SARS-CoV-2 Baseline Status by Grade After Vaccination 1, Solicited Safety Set

Vaccination-1 ARs n (%)	Baseline SARS-CoV-2 negative			Baseline SARS-CoV-2 positive			Missing data		
	Placebo (N=14583)	mRNA-1273 (N=14538)	Total (N=29121)	Placebo (N=337)	mRNA-1273 (N=342)	Total (N=679)	Placebo (N=235)	mRNA-1273 (N=288)	Total N=523
Any solicited AR	7023 (48.2)	12800 (88.0)	19823 (68.1)	137 (40.7)	261 (76.3)	398 (58.6)	124 (52.8)	258 (89.6)	382 (73.0)
Grade 1	4978 (34.1)	9029 (62.1)	14007 (48.1)	82 (24.3)	136 (39.8)	218 (32.1)	87 (37.0)	177 (61.5)	264 (50.5)
Grade 2	1696 (11.6)	2972 (20.4)	4668 (16.0)	41 (12.2)	96 (28.1)	137 (20.2)	33 (14.0)	56 (19.4)	89 (17.0)
Grade 3	344 (2.4)	795 (5.5)	1139 (3.9)	13 (3.9)	28 (8.2)	41 (6.0)	4 (1.7)	25 (8.7)	29 (5.5)
Grade 4	5 (<0.1)	4 (<0.1)	9 (<0.1)	1 (0.3)	1 (0.3)	2 (0.3)	0	0	0
Any Local AR	2891 (19.8)	12276 (84.5)	15167 (52.1)	60 (17.8)	246 (71.9)	306 (45.1)	46 (19.6)	243 (84.4)	289 (55.3)
Grade 1	2738 (18.8)	10352 (71.2)	13090 (45.0)	56 (16.6)	178 (52.0)	234 (34.5)	43 (18.3)	201 (69.8)	244 (46.7)
Grade 2	80 (0.5)	1423 (9.8)	1503 (5.2)	1 (0.3)	55 (16.1)	56 (8.2)	1 (0.4)	27 (9.4)	28 (5.4)
Grade 3	73 (0.5)	501 (3.4)	574 (2.0)	3 (0.9)	13 (3.8)	16 (2.4)	2 (0.9)	15 (5.2)	17 (3.3)
Grade 4	0	0	0	0	0	0	0	0	0
Local AR									
Pain	2563 (17.6)	12207 (84.0)	14770 (50.7)	56 (16.6)	244 (71.3)	300 (44.2)	39 (16.6)	239 (83.0)	278 (53.2)
Grade 1	2459 (16.9)	10601 (72.9)	13060 (44.9)	54 (16.0)	183 (53.5)	237 (34.9)	36 (15.3)	206 (71.5)	242 (46.3)
Grade 2	52 (0.4)	1211 (8.3)	1263 (4.3)	1 (0.3)	51 (14.9)	52 (7.7)	1 (0.4)	22 (7.6)	23 (4.4)
Grade 3	52 (0.4)	395 (2.7)	447 (1.5)	1 (0.3)	10 (2.9)	11 (1.6)	2 (0.9)	11 (3.8)	13 (2.5)
Erythema	63 (0.4)	409 (2.8)	472 (1.6)	3 (0.9)	9 (2.6)	12 (1.8)	1 (0.4)	12 (4.2)	13 (2.5)
Grade 1	45 (0.3)	254 (1.7)	299 (1.0)	1 (0.3)	5 (1.5)	6 (0.9)	1 (0.4)	8 (2.8)	9 (1.7)
Grade 2	7 (<0.1)	115 (0.8)	122 (0.4)	0	2 (0.6)	2 (0.3)	0	4 (1.4)	4 (0.8)
Grade 3	11 (<0.1)	40(0.3)	51(0.2)	2 (0.6)	2 (0.6)	4 (0.6)	0	0	0
Swelling	49 (0.3)	895 (6.2)	944 (3.2)	2 (0.6)	19 (5.6)	21 (3.1)	1 (0.4)	18 (6.3)	19 (3.6)
Grade 1	36 (0.2)	582 (4.0)	618 (2.1)	2 (0.6)	10 (2.9)	12 (1.8)	1 (0.4)	13 (4.5)	14 (2.7)
Grade 2	7 (<0.1)	235 (1.6)	242 (0.8)	0	8 (2.3)	8 (1.2)	0	2 (0.7)	2 (0.4)
Grade 3	6 (<0.1)	78 (0.5)	84 (0.3)	0	1 (0.3)	1 (0.1)	0	3 (1.0)	3 (0.6)
Axillary swelling/tenderness*	689 (4.7)	1465 (10.1)	2154 (7.4)	18 (5.3)	53 (15.5)	71 (10.5)	15 (6.4)	35 (12.2)	50 (9.6)
Grade 1	637 (4.4)	1327 (9.1)	1964 (6.7)	17 (5.0)	38 (11.1)	55 (8.1)	14 (6.0)	30 (10.4)	44 (8.4)
Grade 2	27 (0.2)	94 (0.6)	121 (0.4)	0	11 (3.2)	11 (1.6)	0	4 (1.4)	4 (0.8)
Grade 3	25 (0.2)	44 (0.3)	69 (0.2)	1 (0.3)	4 (1.2)	5 (0.7)	1 (0.4)	1 (0.3)	2 (0.4)
Any Systemic AR	6167 (42.3)	7954 (54.7)	14121 (48.5)	121 (35.9)	210 (61.4)	331 (48.7)	111 (47.2)	156 (54.2)	267 (51.1)
Grade 1	4203 (28.8)	5171 (35.6)	9374 (32.2)	69 (20.5)	107 (31.3)	176 (25.9)	74 (31.5)	94 (32.6)	168 (32.1)
Grade 2	1665 (11.4)	2367 (16.3)	4032 (13.8)	40 (11.9)	80 (23.4)	120 (17.7)	34 (14.5)	49 (17.0)	83 (15.9)
Grade 3	294 (2.0)	412 (2.8)	706 (2.4)	11 (3.3)	22 (6.4)	33 (4.9)	3 (1.3)	13 (4.5)	16 (3.1)
Grade 4	5 (<0.1)	4 (<0.1)	9 (<0.1)	1 (0.3)	1 (0.3)	2 (0.3)	0	0	0
Systemic AR									
Fever	38 (0.3)	79 (0.5)	117 (0.4)	6 (1.8)	32 (9.4)	38 (5.6)	0	4 (1.4)	4 (0.8)
Grade 1	26 (0.2)	51 (0.4)	77 (0.3)	3 (0.9)	20 (5.8)	23 (3.4)	0	3 (1.0)	3 (0.6)
Grade 2	5 (<0.1)	16 (0.1)	21 (<0.1)	2 (0.6)	9 (2.6)	11 (1.6)	0	1 (0.3)	1 (0.2)
Grade 3	2 (<0.1)	9 (<0.1)	11 (<0.1)	0	2 (0.6)	2 (0.3)	0	0	0
Grade 4	5 (<0.1)	3 (<0.1)	8 (<0.1)	1 (0.3)	1 (0.3)	2 (0.3)	0	0	0
Headache	3865 (26.5)	4723 (32.5)	8588 (29.5)	82 (24.3)	131 (38.3)	213 (31.4)	80 (34.0)	97 (33.7)	177 (33.8)
Grade 1	3182 (21.8)	3795 (26.1)	6977 (24.0)	59 (17.5)	88 (25.7)	147 (21.6)	65 (27.7)	70 (24.3)	135 (25.8)
Grade 2	496 (3.4)	679 (4.7)	1175 (4.0)	16 (4.7)	31 (9.1)	47 (6.9)	13 (5.5)	17 (5.9)	30 (5.7)
Grade 3	187 (1.3)	249 (1.7)	436 (1.5)	7 (2.1)	12 (3.5)	19 (2.8)	2 (0.9)	10 (3.5)	12 (2.3)

Fatigue	3988 (27.4)	5400 (37.2)	9388 (32.2)	72 (21.4)	134 (39.2)	206 (30.3)	73 (31.1)	101 (35.1)	174 (33.3)
Grade 1	2618 (18.0)	3468 (23.9)	6086 (20.9)	40 (11.9)	69 (20.2)	109 (16.1)	51 (21.7)	62 (21.5)	113 (21.6)
Grade 2	1271 (8.7)	1793 (12.3)	3064 (10.5)	28 (8.3)	56 (16.4)	84 (12.4)	20 (8.5)	36 (12.5)	56 (10.7)
Grade 3	99 (0.7)	138 (0.9)	237 (0.8)	4 (1.2)	9 (2.6)	13 (1.9)	2 (0.9)	3 (1.0)	5 (1.0)
Grade 4	0	1 (<0.1)	1 (<0.1)	0	0	0	0	0	0
Myalgia	1987 (13.6)	3244 (22.3)	5231 (18.0)	47 (13.9)	124 (36.3)	171 (25.2)	37 (15.7)	73 (25.3)	110 (21.0)
Grade 1	1510 (10.4)	2318 (15.9)	3828 (13.1)	27 (8.0)	70 (20.5)	97 (14.3)	30 (12.8)	57 (19.8)	87 (16.6)
Grade 2	433 (3.0)	845 (5.8)	1278 (4.4)	18 (5.3)	48 (14.0)	66 (9.7)	6 (2.6)	13 (4.5)	19 (3.6)
Grade 3	44 (0.3)	81 (0.6)	125 (0.4)	2 (0.6)	6 (1.8)	8 (1.2)	1 (0.4)	3 (1.0)	4 (0.8)
Arthralgia	1707 (11.7)	2381 (16.4)	4088 (14.0)	40 (11.9)	85 (24.9)	125 (18.4)	36 (15.3)	45 (15.6)	81 (15.5)
Grade 1	1294 (8.9)	1761 (12.1)	3055 (10.5)	21 (6.2)	53 (15.5)	74 (10.9)	26 (11.1)	32 (11.1)	58 (11.1)
Grade 2	379 (2.6)	565 (3.9)	944 (3.2)	17 (5.0)	27 (7.9)	44 (6.5)	9 (3.8)	12 (4.2)	21 (4.0)
Grade 3	34 (0.2)	54 (0.4)	88 (0.3)	2 (0.6)	5 (1.5)	7 (1.0)	1 (0.4)	1 (0.3)	2 (0.4)
Grade 4	0	1 (<0.1)	1 (<0.1)	0	0	0	0	0	0
Nausea/vomiting	1033 (7.1)	1193 (8.2)	2226 (7.6)	26 (7.7)	42 (12.3)	68 (10.0)	15 (6.4)	27 (9.4)	42 (8.0)
Grade 1	860 (5.9)	998 (6.9)	1858 (6.4)	18 (5.3)	30 (8.8)	48 (7.1)	12 (5.1)	20 (6.9)	32 (6.1)
Grade 2	161 (1.1)	186 (1.3)	347 (1.2)	8 (2.4)	12 (3.5)	20 (2.9)	3 (1.3)	6 (2.1)	9 (1.7)
Grade 3	12 (<0.1)	9 (<0.1)	21 (<0.1)	0	0	0	0	1 (0.3)	1 (0.2)
Chills	836 (5.7)	1144 (7.9)	1980 (6.8)	27 (8.0)	80 (23.4)	107 (15.8)	15 (6.4)	29 (10.1)	44 (8.4)
Grade 1	675 (4.6)	878 (6.0)	1553 (5.3)	17 (5.0)	43 (12.6)	60 (8.8)	14 (6.0)	19 (6.6)	33 (6.3)
Grade 2	148 (1.0)	246 (1.7)	394 (1.4)	9 (2.7)	34 (9.9)	43 (6.3)	1 (0.4)	9 (3.1)	10 (1.9)
Grade 3	13 (<0.1)	20 (0.1)	33 (0.1)	1 (0.3)	3 (0.9)	4 (0.6)	0	1 (0.3)	1 (0.2)

CI = Confidence intervals. N1 = Number of exposed participants who submitted any data for the event. Any = Grade 1 or higher. Percentages are based on the number of exposed participants who submitted any data for the event. 95% CI is calculated using the Clopper-Pearson method. Toxicity grade for Erythema (Redness) is defined as: G1 = 25 — 50 mm; G2 = 51 — 100 mm; G3 = > 100 mm. Toxicity grade for Fever is defined as: G1 = 38 — 38.4 C; G2 = 38.5 — 38.9 C; G3 = 39 — 40 C; G4 = > 40 C.
*Localized axillary swelling or tenderness ipsilateral to the vaccination arm.

Table S7. Solicited Adverse reactions by SARS-COv-2 Baseline Status by Grade After Vaccination 2, Solicited Safety Set

	Baseline SARS-CoV-2 negative			Baseline SARS-CoV-2 positive			Missing data		
Vaccination-2 ARs n (%)	**Placebo (N=14119)**	**mRNA-1273 (N=14183)**	**Total (N=28302)**	**Placebo (N=232)**	**mRNA-1273 (N=230)**	**Total (N=462)**	**Placebo (N=215)**	**mRNA-1273 (N=264)**	**Total N=479**
Any solicited AR	6056 (42.9)	13101 (92.4)	19157 (67.7)	81 (34.9)	186 (80.9)	267 (57.8)	95 (44.2)	247 (93.6)	342 (71.4)
Grade 1	4235 (30.0)	4676 (33.0)	8911 (31.5)	51 (22.0)	91 (39.6)	142 (30.7)	68 (31.6)	88 (33.3)	156 (32.6)
Grade 2	1485 (10.5)	5609 (39.5)	7094 (25.1)	27 (11.6)	66 (28.7)	93 (20.1)	22 (10.2)	106 (40.2)	128 (26.7)
Grade 3	333 (2.4)	2802 (19.8)	3135 (11.1)	3 (1.3)	29 (12.6)	32 (6.9)	5 (2.3)	53 (20.1)	58 (12.1)
Grade 4	3 (<0.1)	14 (<0.1)	17 (<0.1)	0	0	0	0	0	0
Any Local AR	2650 (18.8)	12594 (88.8)	15244 (53.9)	42 (18.2)	172 (74.8)	214 (46.4)	43 (20.0)	240 (90.9)	283 (59.1)
Grade 1	2505 (17.7)	8489 (59.9)	10994 (38.9)	35 (15.2)	125 (54.3)	160 (34.7)	41 (19.1)	164 (62.1)	205 (42.8)
Grade 2	77 (0.5)	3122 (22.0)	3199 (11.3)	5 (2.2)	35 (15.2)	40 (8.7)	0	51 (19.3)	51 (10.6)
Grade 3	68 (0.5)	983 (6.9)	1051 (3.7)	2 (0.9)	12 (5.2)	14 (3.0)	2 (0.9)	25 (9.5)	27 (5.6)
Grade 4	0	0	0	0	0	0	0	0	0
Local AR									
Pain	2403 (17.0)	12536 (88.4)	14939 (52.8)	36 (15.6)	169 (73.5)	205 (44.5)	38 (17.7)	238 (90.2)	276 (57.6)
Grade 1	2310 (16.4)	9194 (64.8)	11504 (40.7)	32 (13.9)	125 (54.3)	157 (34.1)	36 (16.7)	179 (67.8)	215 (44.9)
Grade 2	56 (0.4)	2758 (19.5)	2814 (9.9)	3 (1.3)	36 (15.7)	39 (8.5)	0	47 (17.8)	47 (9.8)
Grade 3	37 (0.3)	584 (4.1)	621 (2.2)	1 (0.4)	8 (3.5)	9 (2.0)	2 (0.9)	12 (4.5)	14 (2.9)
Erythema	52 (0.4)	1227 (8.7)	1279 (4.5)	1 (0.4)	8 (3.5)	9 (2.0)	3 (1.4)	22 (8.3)	25 (5.2)
Grade 1	35 (0.2)	434 (3.1)	469 (1.7)	0	2 (0.9)	2 (0.4)	3 (1.4)	6 (2.3)	9 (1.9)
Grade 2	3 (<0.1)	521 (3.7)	524 (1.9)	0	3 (1.3)	3 (0.7)	0	4 (1.5)	4 (0.8)
Grade 3	14 (<0.1)	272 (1.9)	286 (1.0)	1 (0.4)	3 (1.3)	4 (0.9)	0	12 (4.5)	12 (2.5)
Swelling	47 (0.3)	1746 (12.3)	1793 (6.3)	1 (0.4)	11 (4.8)	12 (2.6)	1 (0.5)	32 (12.1)	33 (6.9)
Grade 1	28 (0.2)	874 (6.2)	902 (3.2)	0	4 (1.7)	4 (0.9)	1 (0.5)	12 (4.5)	13 (2.7)
Grade 2	8 (<0.1)	629 (4.4)	637 (2.3)	1 (0.4)	5 (2.2)	6 (1.3)	0	11 (4.2)	11 (2.3)
Grade 3	11 (<0.1)	243 (1.7)	254 (0.9)	0	2 (0.9)	2 (0.4)	0	9 (3.4)	9 (1.9)
Axillary swelling/tenderness*	546 (3.9)	2018 (14.2)	2564 (9.1)	11 (4.8)	30 (13.0)	41 (8.9)	10 (4.7)	42 (15.9)	52 (10.9)
Grade 1	503 (3.6)	1682 (11.9)	2185 (7.7)	8 (3.5)	20 (8.7)	28 (6.1)	10 (4.7)	35 (13.3)	45 (9.4)
Grade 2	24 (0.2)	271 (1.9)	295 (1.0)	3 (1.3)	8 (3.5)	11 (2.4)	0	7 (2.7)	7 (1.5)
Grade 3	19 (0.1)	65 (0.5)	84 (0.3)	0	2 (0.9)	2 (0.4)	0	0	0
Any Systemic AR	5168 (36.6)	11290 (79.6)	16458 (58.2)	71 (30.6)	150 (65.2)	221 (47.8)	84 (39.1)	212 (80.3)	296 (61.8)
Grade 1	3427 (24.3)	3593 (25.3)	7020 (24.8)	42 (18.1)	61 (26.5)	103 (22.3)	57 (26.5)	69 (26.1)	126 (26.3)
Grade 2	1462 (10.4)	5414 (38.2)	6876 (24.3)	28 (12.1)	68 (29.6)	96 (20.8)	22 (10.2)	108 (40.9)	130 (27.1)
Grade 3	276 (2.0)	2269 (16.0)	2545 (9.0)	1 (0.4)	21 (9.1)	22 (4.8)	5 (2.3)	35 (13.3)	40 (8.4)
Grade 4	3 (<0.1)	14 (<0.1)	17 (<0.1)	0	0	0	0	0	0
Systemic AR									
Fever	42 (0.3)	2223 (15.7)	2265 (8.0)	1 (0.4)	31 (13.5)	32 (6.9)	0	24 (9.1)	24 (5.0)
Grade 1	32 (0.2)	1326 (9.4)	1358 (4.8)	1 (0.4)	20 (8.7)	21 (4.6)	0	18 (6.8)	18 (3.8)
Grade 2	5 (<0.1)	685 (4.8)	690 (2.4)	0	9 (3.9)	9 (2.0)	0	5 (1.9)	5 (1.0)
Grade 3	2 (<0.1)	199 (1.4)	201 (0.7)	0	2 (0.9)	2 (0.4)	0	1 (0.4)	1 (0.2)
Grade 4	3 (<0.1)	13 (<0.1)	16 (<0.1)	0	0	0	0	0	0
Headache	3311 (23.5)	8348 (58.9)	11659 (41.2)	43 (18.6)	97 (42.2)	140 (30.4)	56 (26.0)	157 (59.5)	213 (44.5)
Grade 1	2655 (18.8)	4648 (32.8)	7303 (25.8)	36 (15.6)	60 (26.1)	96 (20.8)	48 (22.3)	96 (36.4)	144 (30.1)
Grade 2	497 (3.5)	3058 (21.6)	3555 (12.6)	7 (3.0)	31 (13.5)	38 (8.2)	5 (2.3)	50 (18.9)	55 (11.5)
Grade 3	159 (1.1)	642 (4.5)	801 (2.8)	0	6 (2.6)	6 (1.3)	3 (1.4)	11 (4.2)	14 (2.9)

Fatigue	3294 (23.3)	9310 (65.7)	12604 (44.5)	53 (22.9)	104 (45.2)	157 (34.1)	56 (26.0)	168 (63.6)	224 (46.8)
Grade 1	2115 (15.0)	3332 (23.5)	5447 (19.3)	30 (13.0)	42 (18.3)	72 (15.6)	37 (17.2)	58 (22.0)	95 (19.8)
Grade 2	1077 (7.6)	4583 (32.3)	5660 (20.0)	22 (9.5)	50 (21.7)	72 (15.6)	16 (7.4)	89 (33.7)	105 (21.9)
Grade 3	102 (0.7)	1395 (9.8)	1497 (5.3)	1 (0.4)	12 (5.2)	13 (2.8)	3 (1.4)	21 (8.0)	24 (5.0)
Grade 4	0	0	0	0	0	0	0	0	0
Myalgia	1738 (12.3)	8229 (58.0)	9967 (35.2)	32 (13.9)	115 (50.0)	147 (31.9)	39 (18.1)	164 (62.1)	203 (42.4)
Grade 1	1252 (8.9)	3117 (22.0)	4369 (15.4)	20 (8.7)	59 (25.7)	79 (17.1)	28 (13.0)	63 (23.9)	91 (19.0)
Grade 2	436 (3.1)	3828 (27.0)	4264 (15.1)	12 (5.2)	45 (19.6)	57 (12.4)	9 (4.2)	78 (29.5)	87 (18.2)
Grade 3	50 (0.4)	1284 (9.1)	1334 (4.7)	0	11 (4.8)	11 (2.4)	2 (0.9)	23 (8.7)	25 (5.2)
Arthralgia	1516 (10.7)	6083 (42.9)	7599 (26.9)	24 (10.4)	76 (33.0)	100 (21.7)	29 (13.5)	125 (47.3)	154 (32.2)
Grade 1	1102 (7.8)	2717 (19.2)	3819 (13.5)	17 (7.4)	37 (16.1)	54 (11.7)	23 (10.7)	48 (18.2)	71 (14.8)
Grade 2	371 (2.6)	2613 (18.4)	2984 (10.5)	7 (3.0)	35 (15.2)	42 (9.1)	5 (2.3)	64 (24.2)	69 (14.4)
Grade 3	43 (0.3)	753 (5.3)	796 (2.8)	0	4 (1.7)	4 (0.9)	1 (0.5)	13 (4.9)	14 (2.9)
Grade 4	0	0	0	0	0	0	0	0	0
Nausea/vomiting	912 (6.5)	2700 (19.0)	3612 (12.8)	13 (5.6)	34 (14.8)	47 (10.2)	9 (4.2)	51 (19.3)	60 (12.5)
Grade 1	740 (5.2)	2022 (14.3)	2762 (9.8)	10 (4.3)	26 (11.3)	36 (7.8)	6 (2.8)	42 (15.9)	48 (10.0)
Grade 2	161 (1.1)	658 (4.6)	819 (2.9)	3 (1.3)	7 (3.0)	10 (2.2)	3 (1.4)	9 (3.4)	12 (2.5)
Grade 3	11 (<0.1)	19 (0.1)	(0.1)	0	1 (0.4)	1 (0.2)	0	0	0
Grade 4	0	1 (<0.1)	1 (<0.1)	0	0	0	0	0	0
Chills	778 (5.5)	6292 (44.4)	7070 (25.0)	17 (7.4)	78 (33.9)	95 (20.6)	14 (6.5)	112 (42.4)	126 (26.3)
Grade 1	604 (4.3)	2807 (19.8)	3411 (12.1)	14 (6.1)	39 (17.0)	53 (11.5)	8 (3.7)	53 (20.1)	61 (12.7)
Grade 2	157 (1.1)	3296 (23.2)	3453 (12.2)	3 (1.3)	39 (17.0)	42 (9.1)	6 (2.8)	57 (21.6)	63 (13.2)
Grade 3	17 (0.1)	189 (1.3)	206 (0.7)	0	0	0	0	2 (0.8)	2 (0.4)

CI = Confidence intervals. N1 = Number of exposed participants who submitted any data for the event. Any = Grade 1 or higher. Percentages are based on the number of exposed participants who submitted any data for the event. 95% CI is calculated using the Clopper-Pearson method. Toxicity grade for Erythema (Redness) is defined as: G1 = 25 — 50 mm; G2 = 51 — 100 mm; G3 = > 100 mm. Toxicity grade for Fever is defined as: G1 = 38 — 38.4 C; G2 = 38.5 — 38.9 C; G3 = 39 — 40 C; G4 = >40 C. *Localized axillary swelling or tenderness ipsilateral to the vaccination arm.

Table S8. Unsolicited Adverse Events 28 Days after Any Injection, Overall Safety Set

Unsolicited Adverse Event n (%)	Overall Safety Set			≥18-<65 years			≥65 years		
	Placebo N=15166	mRNA-1273 N=15185	Total N=30351	Placebo (N=11416)	mRNA-1273 (N=11415)	Total (N=22831)	Placebo N=3750	mRNA-1273 N=3770	Total N=7520
Regardless of relationship to study vaccination									
All	3277 (21.6)	3632 (23.9)	6909 (22.8)	2463 (21.6)	2674 (23.4)	5137 (22.5)	814 (21.7)	958 (25.4)	1772 (23.6)
Serious	89 (0.6)	93 (0.6)	182 (0.6)	46 (0.4)	54 (0.5)	100 (0.4)	43 (1.1)	39 (1.0)	82 (1.1)
Fatal	3 (<0.1)	2 (<0.1)	5 (<0.1)	1 (<0.1)	1 (<0.1)	2 (<0.1)	2 (<0.1)	1 (<0.1)	3 (<0.1)
Medically-attended	1465 (9.7)	1372 (9.0)	2837 (9.3)	1051 (9.2)	991 (8.7)	2042 (8.9)	414 (11.0)	381 (10.1)	795 (10.6)
Leading to discontinuation from study vaccine*	80 (0.5)	50 (0.3)	130 (0.4)	62 (0.5)	37 (0.3)	99 (0.4)	18 (0.5)	13 (0.3)	31 (0.4)
Leading to discontinuation from study†	2 (<0.1)	2 (<0.1)	4 (<0.1)	0	1 (<0.1)	1 (<0.1)	2 (<0.1)	1 (<0.1)	3 (<0.1)
Severe	202 (1.3)	234 (1.5)	436 (1.4)	132 (1.2)	156 (1.4)	288 (1.3)	70 (1.9)	78 (2.1)	148 (2.0)
Related to study vaccination									
All	686 (4.5)	1242 (8.2)	1928 (6.4)	526 (4.6)	938 (8.2)	1464 (6.4)	160 (4.3)	304 (8.1)	464 (6.2)
Serious	4 (<0.1)	6 (<0.1)	10 (<0.1)	3 (<0.1)	4 (<0.1)	7 (<0.1)	1 (<0.1)	2 (<0.1)	3 (<0.1)
Fatal	0	0	0	0	0	0	0	0	0
Medically-attended	83 (0.5)	140 (0.9)	223 (0.7)	68 (0.6)	110 (1.0)	178 (0.8)	15 (0.4)	30 (0.8)	45 (0.6)
Leading to discontinuation from study vaccine*	15 (<0.1)	18 (0.1)	33 (0.1)	10 (<0.1)	14 (0.1)	24 (0.1)	5 (0.1)	4 (0.1)	9 (0.1)
Leading to discontinuation from study†	0	0	0	0	0	0	0	0	0
Severe	28 (0.2)	71 (0.5)	99 (0.3)	19 (0.2)	49 (0.4)	68 (0.3)	9 (0.2)	22 (0.6)	31 (0.4)

An adverse event is defined as any event not present before exposure to study vaccination or any event already present that worsens in intensity or frequency after exposure. Percentages are based on overall safety set. *AEs leading to study discontinuation 28 days after first dose. †AEs leading to discontinuation from study after either dose.

Tables S9-11. Unsolicited Adverse Events, Overall Safety Set

Table S9. Summary of Unsolicited AE Reported by ≥1% of Participants in Any Treatment Group up to 28 Days After Any Injection

System Organ Class Preferred Term n (%)	Placebo (N=15166)	mRNA-1273 (N=15185)
Number of participants reporting unsolicited AEs	3277 (21.6)	3632 (23.9)
Number of unsolicited AEs	6085	6798
Nervous system disorders	622 (4.1)	684 (4.5)
Headache	458 (3.0)	466 (3.1)
Respiratory, thoracic and mediastinal disorders	583 (3.8)	536 (3.5)
Cough	156 (1.0)	164 (1.1)
Oropharyngeal pain	203 (1.3)	147 (1.0)
Gastrointestinal disorders	440 (2.9)	478 (3.1)
Diarrhea	162 (1.1)	189 (1.2)
Musculoskeletal and connective tissue disorders	617 (4.1)	671 (4.4)
Arthralgia	167 (1.1)	207 (1.4)
Myalgia	181 (1.2)	200 (1.3)
General disorders and administration site conditions	622 (4.1)	1006 (6.6)
Fatigue	336 (2.2)	372 (2.4)
Injection site pain	54 (0.4)	151 (1.0)

AE = adverse event. An AE is defined as any event not present before exposure to study vaccination or any event already present that worsens in intensity or frequency after exposure. Percentages are based on the number of participants in the safety set. All AEs were coded using MedDRA Version 23.0.

Table S10. Unsolicited Severe AEs Reported by ≥5 Participants in Any Treatment Group up to 28 Days After Any Injection, Overall Safety Set

System Organ Class Preferred Term n (%)	Placebo (N=15166)	mRNA-1273 (N=15185)
Number of participants reporting unsolicited severe AEs	202 (1.3)	234 (1.5)
Nervous system disorders	21 (0.1)	30 (0.2)
Headache	12 (<0.1)	20 (0.1)
Cardiac disorders	13 (<0.1)	13 (<0.1)
Bradycardia	5 (<0.1)	4 (<0.1)
Atrial Fibrillation	3 (<0.1)	4 (<0.1)
Vascular disorders	43 (0.3)	30 (0.2)
Hypertension	32 (0.2)	23 (0.2)
Musculoskeletal and connective tissue disorders	24 (0.2)	23 (0.2)
Myalgia	2 (<0.1)	10 (<0.1)
Arthralgia	2 (<0.1)	8 (<0.1)
Back pain	7 (<0.1)	1 (<0.1)
General disorders and administration site conditions	13 (<0.1)	49 (0.3)
Fatigue	6 (<0.1)	12 (<0.1)
Injection site erythema	0	11 (<0.1)
Injection site pain	1 (<0.1)	3 (<0.1)
Investigations	13 (<0.1)	23 (0.2)
Blood pressure increased	6 (<0.1)	11 (<0.1)
Blood pressure systolic increased	7 (<0.1)	7 (<0.1)

An AE is defined as any event not present before exposure to study vaccination or any event already present that worsens in intensity or frequency after exposure. Percentages were based on the number of safety set participants. All AEs were coded using MedDRA Version 23.0.

Table S11. Serious AEs Reported by Preferred Term in Any Treatment Group, Overall Safety Set

System Organ Class Preferred Term n (%)	Placebo (N=15166)	mRNA-1273 N=15185
Number of participants reporting serious AEs	153 (1.0)	147 (1.0)
Number of serious AEs	211	207
Atrial fibrillation	5 (<0.1)	5 (<0.1)
Myocardial infarction	3 (<0.1)	5 (<0.1)
Pneumonia	7 (<0.1)	5 (<0.1)
Pulmonary embolism	5 (<0.1)	4 (<0.1)
Abdominal pain upper	0	3 (<0.1)
Cardiac failure congestive	3 (<0.1)	3 (<0.1)
Cerebrovascular accident	1 (<0.1)	3 (<0.1)
Cholecystitis	0	3 (<0.1)
Dehydration	3 (<0.1)	3 (<0.1)
Dyspnoea	0	3 (<0.1)
Nausea	1 (<0.1)	3 (<0.1)
Nephrolithiasis	0	3 (<0.1)
Prostate cancer	3 (<0.1)	3 (<0.1)
Acute respiratory failure	2 (<0.1)	2 (<0.1)
Acute coronary syndrome	0	2 (<0.1)
Acute myocardial infarction	4 (<0.1)	2 (<0.1)
Appendicitis	3 (<0.1)	2 (<0.1)
Arthritis	1 (<0.1)	2 (<0.1)
Cervical vertebral fracture	0	2 (<0.1)
Chest pain	1 (<0.1)	2 (<0.1)
Colitis	1 (<0.1)	2 (<0.1)
Coronary artery disease	2 (<0.1)	2 (<0.1)
Deep vein thrombosis	0	2 (<0.1)
Diarrhoea	1 (<0.1)	2 (<0.1)
Embolic stroke	0	2 (<0.1)
Fall	3 (<0.1)	2 (<0.1)
Hiatus hernia	1 (<0.1)	2 (<0.1)
Hypertension	1 (<0.1)	2 (<0.1)
Respiratory Failure	1 (<0.1)	2 (<0.1)
Road traffic accident	1 (<0.1)	2 (<0.1)
Seizure	0	2 (<0.1)
Spinal stenosis	1 (<0.1)	2 (<0.1)
Subdural hematoma	0	2 (<0.1)
Swelling face	1 (<0.1)	2 (<0.1)
Syncope	4 (<0.1)	2 (<0.1)
Acute kidney injury	3 (<0.1)	1 (<0.1)
Covid-19	15 (<0.1)	1 (<0.1)
Hip fracture	2 (<0.1)	1 (<0.1)
Thyroidectomy	0	1 (<0.1)
Abdominal pain	2 (<0.1)	0
Anaemia	2 (<0.1)	0
Ankle fracture	3 (<0.1)	0
Chronic obstructive pulmonary disease	4 (<0.1)	0
Confusional state	2 (<0.1)	0
Depression	3 (<0.1)	0
Diverticulitis	2 (<0.1)	0
Hypertensive emergency	2 (<0.1)	0
Intervertebral disc protrusion	1 (<0.1)	0
Intraductal proliferative breast lesion	2 (<0.1)	0
Major depression	2 (<0.1)	0
Urinary tract infection	4 (<0.1)	0

AE is defined as any event not present before exposure to study vaccination or any event already present that worsens in intensity or frequency after exposure. Percentages are based on the number of participants in the safety set. All AEs were coded using MedDRA Version 23.0.

Table S12. Unsolicited Adverse Events of Hypersensitivity, Overall Safety Set

Preferred term n (%)	Placebo (N=15166)	mRNA-1273 (N=15185)
Participants reporting hypersensitivity	166 (1.1)	233 (1.5)
Allergic sinusitis	1 (<0.1)	2 (<0.1)
Anaphylactic reaction	1 (<0.1)	1 (<0.1)
Angioedema	3 (<0.1)	1 (<0.1)
Bronchospasm	0	1 (<0.1)
Conjunctivitis allergic	2 (<0.1)	2 (<0.1)
Dermatitis	8 (<0.1)	8 (<0.1)
Dermatitis allergic	3 (<0.1)	2 (<0.1)
Dermatitis atopic	7 (<0.1)	4 (<0.1)
Dermatitis bullous	2 (<0.1)	0
Dermatitis contact	29 (0.2)	21 (0.1)
Drug hypersensitivity	4 (<0.1)	4 (<0.1)
Eczema	4 (<0.1)	3 (<0.1)
Exfoliative rash	0	1 (<0.1)
Eye swelling	2 (<0.1)	2 (<0.1)
Hand dermatitis	0	2 (<0.1)
Hypersensitivity	4 (<0.1)	5 (<0.1)
Idiopathic urticaria	1 (<0.1)	0
Injection related reaction	1 (<0.1)	1 (<0.1)
Injection site rash	1 (<0.1)	37 (0.2)
Injection site urticaria	0	15 (<0.1)
Laryngeal oedema	1 (<0.1)	0
Lip swelling	2 (<0.1)	2 (<0.1)
Palatal oedema	1 (<0.1)	0
Periorbital oedema	1 (<0.1)	0
Periorbital swelling	2 (<0.1)	0
Rash	34 (0.2)	45 (0.3)
Rash erythematous	2 (<0.1)	6 (<0.1)
Rash follicular	1 (<0.1)	0
Rash macular	4 (<0.1)	6 (<0.1)
Rash maculo-papular	2 (<0.1)	11 (<0.1)
Rash pruritic	4 (<0.1)	6 (<0.1)
Rash vesicular	0	3 (<0.1)
Rhinitis allergic	13 (<0.1)	10 (<0.1)
Serum sickness	1 (<0.1)	0
Swelling face	2 (<0.1)	4 (<0.1)
Swelling of eyelid	1 (<0.1)	2 (<0.1)
Swollen tongue	0	2 (<0.1)
Type IV hypersensitivity reaction	0	1 (<0.1)
Urticaria	23 (0.2)	27 (0.2)
Urticaria papular	5 (<0.1)	3 (<0.1)
Vaccination site rash	0	1 (<0.1)

Percentages are based on the number of participants in the safety set. Preferred term by MedDRA version 23.0. Hypersensitivity was identified through selected SMQ.

Table S13. Covid-19 Symptoms and Severity, Per-protocol Set

Covid-19 Symptom n (%)	All Covid-19 cases		Severe Covid-19 cases	
	Placebo (N=185)	mRNA-1273 (N=11)*	Placebo (N=30)	mRNA-1273 (N=0)
Number of participants with any symptom	185 (100)	11 (100)	30 (100)	0
Respiratory symptom				
Clinical evidence of pneumonia	4 (2.2)	0	4 (13.3)	0
Cough	155 (83.8)	6 (54.5)	28 (93.3)	0
Difficulty breathing	55 (29.7)	1 (9.1)	16 (53.3)	0
Radiographical evidence of pneumonia	3 (1.6)	0	3 (10.0)	0
Shortness of breath	78 (42.2)	2 (18.2)	23 (76.7)	0
Systemic symptom				
Body aches	111 (60.0)	7 (63.6)	26 (86.7)	0
Chills	95 (51.4)	4 (36.4)	19 (63.3)	0
Diarrhea	70 (37.8)	2 (18.2)	14 (46.7)	0
Fatigue	156 (84.3)	9 (81.8)	27 (90.0)	0
Fever†	54 (29.2)	2 (18.2)	13 (43.3)	0
Headache	145 (78.4)	10 (90.9)	25 (83.3)	0
Muscle aches (myalgia)	114 (61.6)	5 (45.5)	24 (80.0)	0
Nasal congestion	138 (74.6)	8 (72.7)	21 (70.0)	0
Nausea	65 (35.1)	3 (27.3)	13 (43.3)	0
New loss of smell	115 (62.2)	3 (27.3)	16 (53.3)	0
New loss of taste	106 (57.3)	3 (27.3)	15 (50.0)	0
Runny nose (rhinorrhea)	121 (65.4)	6 (54.5)	18 (60.0)	0
Sore throat	85 (45.9)	7 (63.6)	15 (50.0)	0
Vomiting	18 (9.7)	1 (9.1)	7 (23.3)	0
Number of participants with any severe symptom	32 (17.3)	0	30 (100)	0
Acute renal dysfunction	2 (1.1)	0	2 (6.7)	0
Acute Respiratory Distress Syndrome	1 (0.5)	0	1 (3.3)	0
ECMO	0	0	0	0
High-flow oxygen	1 (0.5)	0	1 (3.3)	0
Mechanical ventilation	0	0	0	0
Non-Invasive ventilation	1 (0.5)	0	1 (3.3)	0
Admission to an intensive care unit due to SARS-CoV-2	1 (0.5)	0	1 (3.3)	0
Heart Rate ≥125 beats per minute	0	0	0	0
Hepatic dysfunction	0	0	0	0
Neurologic dysfunction	1 (0.5)	0	1 (3.3)	0
Oxygen saturation ≤93‡	28 (15.1)	0	27 (90.0)	0
Oxygen saturation SpO2 ≤93% on room air at sea level	29 (15.7)	0	28 (93.3)	0
PaO2/FIO2 ratio <300 mmHg	0	0	0	0
Respiratory failure	1 (0.5)	0	1 (3.3)	0
Respiratory rate ≥30 per minute	0	0	0	0
Systolic blood pressure <90 mmHg, diastolic blood Pressure <60 mmHg	5 (2.7)	0	4 (13.3)	0
Vasopressors required	0	0	0	0

Note symptoms are shown for participants with all cases of 196 Covid-19 and those 30 that were considered severe cases. All symptoms reported are included, regardless of relationship with the positive RT-PCR test used to define the case of Covid-19 in PP set. Participants can be counted in more than one category. *There were 7 Covid-19 cases reported before 14 days post-dose 2. †Derived based on temperature collected on case report form (CRF) symptoms. ‡Derived based on oxygen saturation collected on CRF symptom log page.

Table S14. Characteristics of Participants with Severe Covid-19 Cases, Per-protocol Set

Characteristics n (%)	**Covid-19 cases Placebo N=30**
Sex	
Female	17 (57)
Male	13 (43)
Age, years	
Mean (range)	54.4 (23-80)
≥65 years	10 (33)
Race/Ethnicity	
White, not hispanic or Latino	24 (80)
White, Hispanic or Latino	2 (7)
Black/African American, Not Hispanic or Latino	1 (3)
Not reported/other, Hispanic or Latino	2 (7)
Multiple, Not Hispanic or Latino	1 (3)
Hospitalized	9 (30)
ICU	2 (7)
Co-morbid conditions (chronic lung, severe obesity, cardiac, diabetes, hypertension and/or asthma)	20 (67)
Clinical signs indicative of severe system illness	
Oxygen saturation ≤93%*	28 (93)
Respiratory failure or Acute Respiratory Distress Syndrome	6 (20)
Significant acute renal or neurologic dysfunction	2 (7)
*Derived based on oxygen saturation collected on CRF symptom log page. Covid-19 cases in the PP set. Data from December 3rd, 2020.	

Table S15. Serious and Severe Treatment-related AEs Up to 28 days after Any Injection, Overall Safety Set

System organ class, preferred term n (%)	Placebo N=15166	mRNA-1273 N=15185	Total (N=30351)
Serious AEs			
Incidence of unsolicited AEs	4 (<0.1)	6 (<0.1)	10 (<0.1)
Autonomic nervous system imbalance	0	1 (<0.1)	1 (<0.1)
Paraesthesia	1 (<0.1)	0	1 (<0.1)
Dyspnoea	0	1 (<0.1)	1 (<0.1)
Pulmonary embolism	1 (<0.1)	0	1 (<0.1)
Nausea	0	1 (<0.1)	1 (<0.1)
Vomiting	0	1 (<0.1)	1 (<0.1)
Rheumatoid arthritis	0	1 (<0.1)	1 (<0.1)
Polymyalgia rheumatica	1 (<0.1)	0	1 (<0.1)
Swelling face	1 (<0.1)	2 (<0.1)	3 (<0.1)
Edema peripheral	0	1 (<0.1)	1 (<0.1)
Feeling hot	1 (<0.1)	0	1 (<0.1)
Immunization anxiety-related reaction	1 (<0.1)	0	1 (<0.1)
Procedural haemorrhage	1 (<0.1)	0	1 (<0.1)
Severe AEs			
Incidence of unsolicited severe AEs	28 (0.2)	71 (0.5)	99 (0.3)
Lymphadenopathy	1 (<0.1)	1 (<0.1)	2 (<0.1)
Type IV hypersensitivity reaction	0	1 (<0.1)	1 (<0.1)
Headache	8 (<0.1)	9 (<0.1)	17 9<0.1)
Dizziness	1 (<0.1)	1 (<0.1)	2 (<0.1)
Movement disorder	0	1 (<0.1)	1 (<0.1)
Syncope	0	1 (<0.1)	1 (<0.1)
Migraine	1 (<0.1)	0	1 (<0.1)
Vertigo	0	0	1 (<0.1)
Hypertension	9 (<0.1)	4 (<0.1)	13 (<0.1)
Nausea	0	1 (<0.1)	1 (<0.1)
Dermatitis	0	1 (<0.1)	1 (<0.1)
Rash	0	1 (<0.1)	1 (<0.1)
Rash macular	0	1 (<0.1)	1 (<0.1)
Myalgia	0	6 (<0.1)	6 (<0.1)
Arthralgia	2 (<0.1)	3 (<0.1)	5 (<0.1)
Muscle spasms	0	2 (<0.1)	2 (<0.1)
Neck pain	0	1 (<0.1)	1 (<0.1)
Pain in extremity	0	1 (<0.1)	1 (<0.1)
Temporomandibular joint syndrome	0	1 (<0.1)	1 (<0.1)
Back pain	1 (<0.1)	0	1 (<0.1)
Polymyalgia rheumatica	1 (<0.1)	0	1 (<0.1)
Injection site erythema	0	11 (<0.1)	11 (<0.1)
Fatigue	2 (<0.1)	9 (<0.1)	11 (<0.1)
Injection site swelling	0	4 (<0.1)	4 (<0.1)
Injection site macule	0	3 (<0.1)	3 (<0.1)
Chills	0	2 (<0.1)	2 (<0.1)
Injection site lymphadenopathy	0	2 (<0.1)	2 (<0.1)
Injection site pain	1 (<0.1)	2 (<0.1)	3 (<0.1)
Adverse drug reaction	0	1 (<0.1)	1 (<0.1)
Chest discomfort	0	1 (<0.1)	1 (<0.1)
Injection site induration	0	1 (<0.1)	1 (<0.1)
Injection site rash	0	1 (<0.1)	1 (<0.1)
Malaise	0	1 (<0.1)	1 (<0.1)
Pyrexia	0	1 (<0.1)	1 (<0.1)
Swelling face	0	1 (<0.1)	1 (<0.1)
Asthenia	1 (<0.1)	0	1 (<0.1)
Blood pressure increased	2 (<0.1)	5 (<0.1)	7 (<0.1)
Blood pressure systolic increased	0	1 (<0.1)	1 (<0.1)

Adverse event (AE) was defined as any event not present before exposure to study vaccination or any event already present that worsens in intensity or frequency after exposure. Percentages are based on the number of participants in the safety set. All AEs were coded using MedDRA Version 23.0.

Table S16. Efficacy of Key Secondary Endpoints, Per-protocol Set

Secondary endpoint	Placebo (N=14073)	mRNA-1273 (N=14073)
Severe Covid-19 starting 14 days after second injection, adjudicated		
n, events, PP	30	0
VE Based on Hazard Ratio (95% CI)*		1.00 (NE-1.00)
Covid-19 after the first dose†		
n, events, PP	225	11
VE Based on Hazard Ratio (95% CI)		0.952 (0.912-0.974)
Secondary definition of Covid-19 starting 14 days after second injection‡		
n, events, PP	221	11
VE Based on Hazard Ratio (95% CI)		0.951 (0.911-0.973)
Covid-19 after the second injection regardless of prior SARS-CoV-2 infection, adjudicated		
n/N events§ FAS	187/15170	12/15181
VE Based on Hazard Ratio (95% CI)		0.936 (0.886-0.965)

PP=per-protocol set; FAS=full analysis set. *Vaccine efficacy (VE), defined as 1 - hazard ratio (mRNA-1273 vs placebo), and 95% CI estimated using a stratified Cox proportional hazard model with Efron's method of tie handling and with the treatment group as a covariate, adjusting for stratification factor. †Inclusive of second doses. ‡Secondary case definition of Covid-19 was defined as including systemic symptoms: fever (temperature ≥ 38ºC) or chills, cough, shortness of breath or difficulty breathing, fatigue, muscle aches or body aches, headache, new loss of taste or smell, sore throat, nasal congestion or rhinorrhea, nausea or vomiting or diarrhea AND a positive NP swab, nasal swab, or saliva sample (or respiratory sample, if hospitalized) for SARS-CoV-2 by RT-PCR. §n and N are based on the number of participants in the FAS.

Table S17. Vaccine Efficacy by SARS-COV-2 Status, Modified Intent-to-Treat

Baseline SARS-CoV-2 Status n (%)	**Placebo**	**mRNA-1273**
Negative	**N=14598**	**N=14550**
Number with Covid-19	185 (1.3)	12 (<0.1)
Number censored	14413 (98.7)	14538 (>99.9)
VE Based on HR (95% CI)		0.936 (0.885-0.964)
Person-Years	3382.9	3390.1
Incidence rate per 1,000 Person-Years (95% CI)	54.7 (47.1- 63.2)	3.6 (1.8-6.2)
VE based on incidence rate (95% CI)		0.935 (0.884-0.967)
Positive	**N=337**	**N=343**
Number with Covid-19	1 (0.3)	0
Number Censored	336 (99.7)	343 (100)
VE Based on HR (95% CI)		1.000 (NE-1.000)
Person-Years	71.9	71.4
Incidence rate per 1,000 Person-Years (95% CI)*	13.9 (0.4-77.5)	0.0 (NE-51.7)
VE based on incidence rate (95% CI)		1.000 (-38.3-NE)

HR=hazard ratio. VE=vaccine efficacy. VE was defined as 1 - hazard ratio (mRNA-1273 vs. placebo); 95% CI were estimated using a stratified Cox proportional hazard model with Efron's method of tie handling with the treatment group as a covariate, adjusting for stratification factor if applicable in mITT set. Person-years was defined as the total years from randomization date to the date of Covid-19, last date of study participation, or efficacy data cutoff date, whichever was earlier. *Incidence rate was defined as the number of participants with an event divided by the number of participants at risk, adjusted by person-years (total time at risk) in each treatment group; the 95% CI was calculated using the exact method (Poisson distribution) adjusted by person-years and VE was defined as 1 — ratio of incidence rate (mRNA-1273 vs. placebo). Baseline SARS-CoV-2 Status was considered positive based on immunologic or virologic evidence of prior Covid-19, defined as positive RT-PCR test or bAb result at day 1; negative was defined as negative RT-PCR test and bAb results at day 1. Covid-19 cases were diagnosed by symptoms and RT-PCR.

Table S18. Preliminary Analysis of Infection from Randomization, Modified Intent-to-Treat

	Placebo N=14598	mRNA-1273 N=14550	Vaccine efficacy (95% CI)
Symptomatic Covid-19	293	20	
Covid -19	269	19	
Secondary definition of Covid -19	24	1	
Positive RT-PCR at scheduled pre-dose 2*	39	15	
Total infection (symptomatic or RT-PCR+ at pre-dose 2)	332	35	89.6% (85.2%-92.6%)†
Person-years‡	3365.6	3386.6	
Incidence rate (95% CI)§	98.6 (88.3-109.8)	10.3 (7.2-14.4)	89.5% (85.1%-92.8%)

Preliminary analysis of infection from randomization performed based on the modified intent-to-treat set (data cut-off November 25, 2020). Infection was defined as symptomatic Covid-19, either Covid-19 (positive RT-PCR with two eligible systemic or one eligible respiratory symptom), or secondary/CDC definition of Covid-19 requiring one symptom, or, asymptomatic infection, as measured by positive RT- PCR at the scheduled pre-Dose 2 visit.). *Positive RT-PCR at the scheduled pre-Dose 2 visit and no Covid-19 symptoms. †From stratified Cox proportional model adjusting for the stratification factor. ‡Person-years defined as the total years from randomization date to the date of Covid-19, last date of study participation, or efficacy data cutoff date, whichever was earlier. §Incidence rate was defined as the number of participants with an event divided by the number at risk adjusted by person-years (total time at risk) in each treatment group and 95% CI calculated using the exact method (Poisson distribution) conditional on total number of events adjusted by person-years.