

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE PATENT TRIAL AND APPEAL BOARD

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BIONTECH SE AND PFIZER INC.,  
Petitioner,

v.

MODERNA TX, INC.,  
Patent Owner.

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Case IPR2023-01359  
Patent No. 10,933,127

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**PATENT OWNER'S PRELIMINARY STATEMENT REGARDING  
ALLEGED INCONSISTENT POSITIONS**

Patent Owner (“PO”) submits this statement pursuant to the Board’s January 10, 2023 email. PO’s Preliminary Response (“POPR”) explained that Petitioner’s hindsight-driven Grounds do not demonstrate a reasonable likelihood of unpatentability, let alone compelling merits, with respect to the claimed novel and inventive mRNA-LNP betacoronavirus vaccines. The POPR distinguished art about *other* types of vaccines—including self-replicating RNA that is *explicitly excluded* from the invention—and addressed skepticism in the art.

Apparently recognizing the weaknesses of the Petition, Petitioner has engineered not one, but two additional bites at the apple before the Board’s institution decision. In addition to seeking briefing on discretionary denial issues, Petitioner provided PO a chart (Ex. 2060) excerpting documents they allege are “inconsistent” with arguments in the POPR and demanded their disclosure under 37 C.F.R. §§ 42.51(b)(1)(iii), 42.11, 1.56 and 87 FR 45764 (July 29, 2022). These documents are clearly not inconsistent and Petitioner’s attempts to remedy the Petition’s deficiencies through such accusations are misplaced. Each cited document *post-dates the priority date*. *None* contradicts the POPR. The claimed mRNA is *not* self-amplifying RNA. mRNA is different from DNA. *Direct prior art quotations* reflect skepticism. Institution should be denied.

***Stanton (Ex. 2049):*** Stanton is a post-priority publication co-authored by Moderna chemists. Petitioner cites Stanton’s statement in 2018, years after the

claimed invention, that Geall (Ex. 2021), “established amino lipid based LNPs...form stable particles with mRNA...” Ex. 2049, 2. But the POPR correctly explained, and Stanton confirms, that Geall involved “delivery of a *self-amplifying* RNA vaccine” for RSV. *Id.* Geall’s saRNA teaching is distinct from the claimed invention because, as the ’127 patent makes explicit: “the mRNA of the invention are *not self-replicating RNA*.” Ex. 1001, 40:42-44; *see* POPR, 11, 27, 30-31, 38-39, 48-49. The POPR correctly explained that the claimed combination was new, followed an unprecedented route, and that there was *documented* skepticism *in the prior art* that combining mRNA of the invention with LNPs would enable betacoronavirus vaccination to prevent disease. POPR, 13, 48, 55-56, 69-70 (citing Ex. 1031 (Du)). Stanton’s reference to Geall’s example of saRNA *excluded from the invention* does not show otherwise.

***Investigator Brochures (Exs. 2050-2052):*** These exhibits are post-priority Moderna Investigator Brochures from 2016-2019 for other vaccine (not betacoronavirus) candidates. Each has a background section titled “Proof-of-Concept With mRNA-Based Vaccines” and cites (1) Geall (Ex. 2021) for “replicon-based mRNA vaccines” for flu and RSV; and (2) Petsch (Ex. 2025) for a 2-component mRNA complexed with protamine for flu. Ex. 2050; 12-13; Ex. 2051, 198-199; Ex. 2052, 11-12. Inclusion of Geall is not inconsistent with Moderna’s statement that “Geall 2012 discusses saRNA—not mRNA—vaccines.” POPR, 27;

Ex. 2060, 1-2. “Replicon-based mRNA” in the Brochures refers to *self-replicating* (self-amplifying) RNA; Geall refers to saRNA, POPR, 27 (citing Ex. 2021), but the Challenged Claims do not cover “*self-replicating RNA*.” Ex. 1001, 40:38-44. With respect to Petsch, Moderna *submitted* and *accurately quoted* it (Ex. 2025), including to show uncertainty in the prior art. POPR, 48, 53-54. The fact that Petsch addressed studies of mRNA formulated with protamine (not the claimed LNPs), which the POPR cited, *id.*, n.8, is not inconsistent with prior-art uncertainty regarding the claimed betacoronavirus mRNA-LNP formulations. Neither Geall nor Petsch supports reasonable expectation of success with the claimed invention.

**DMID Protocols (Exs. 2053-2055):** Exhibits 2053-2055 are government-authored<sup>1</sup> post-priority (2020) Division of Microbiology and Infectious Diseases (“DMID”) protocols for SARS-CoV-2 mRNA clinical studies. They address mRNA and DNA vaccines five years post-priority (e.g., 2016-2019 studies). Ex. 2053, 16; Ex. 2054, 15; Ex. 2055, 18. Petitioner’s reliance on post-priority information as purportedly inconsistent with PO’s arguments on prior art is inappropriate hindsight.

Petitioner’s assertion that citation to DNA studies in these documents is inconsistent with POPR statements that “DNA and mRNA are materially different in ways that affect their use for vaccines” and prior art “data comparing DNA and

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<sup>1</sup> Petitioner knew this authorship from Moderna testimony, but its chart omits it.

mRNA vaccines suggested vaccine types were not interchangeable” is wrong. Moderna accurately cited references distinguishing DNA and mRNA vaccines and explained their material differences. POPR, 8-9, 54-55, 57-60. To the extent Petitioner suggests the DMID protocols equate mRNA and DNA, Petitioner mischaracterizes them. Exhibits 2053-2055 do **not** state DNA and mRNA vaccines were interchangeable or DNA and mRNA are not materially different. Instead, they cite results years after the invention indicating that despite differences and skepticism, *see* POPR, 8-9, 48, 54-60, 69-70, certain DNA and mRNA vaccines are safe and immunogenic. Exhibits 2053-2055 also cite DNA studies from 2004-2005, but the Petition cites neither and neither addressed ***mRNA***.

Exhibits 2053-2055 and Ex. 2056 (pre-IND document) discuss that coronavirus spike proteins had been studied and found immunogenic. Petitioner wrongly argues this is inconsistent with Moderna's statement that a POSA would have considered Du with “widespread skepticism regarding pursuit of a coronavirus spike protein as a vaccine antigen.” Page 3 of Petitioner's chart (Ex. 2060, 3) truncates the POPR quote and leaves out the part that skepticism arose “particularly” from concerns “that targeting coronavirus spike proteins ***could undesirably lead to enhancement of disease***,” POPR, 55-56, for which the POPR cites supporting evidence. *See id.*, 12, 56, 60, 65, 70. The excerpts of Exhibits 2053-2056 do not concern disease enhancement and there is no inconsistency.

**Watson (Ex. 2057):** Ex. 2057 is a post-priority (2020) document from a Moderna scientist discussing the possibility of disease enhancement from targeting betacoronavirus proteins. *See*, Ex. 2057, 1-2. The excerpt Petitioner cites references published studies not in the Petition that evaluated disease enhancement and Petitioner's chart bolds a hamster study in which SARS-CoV S protein vaccination was not associated with disease enhancement. Ex. 2057, 2. These studies do not make the POPR inconsistent or inaccurate. In fact, Watson evaluates concerns with disease enhancement despite these studies. *Id.*, 1. And Du, which **Petitioner cited**, "**itself** identifies 'concerns about the safety and ultimate protective efficacy of vaccines that contain the full-length SARS-CoV S protein'—despite inducing some neutralizing antibody response—because such vaccines may induce 'harmful immune responses' causing liver damage or enhanced infection." POPR, 56. The POPR accurately quotes Du, which a POSA would consider for all it stated, and notes Petitioner's failure to address its full teaching. *Id.*, 55, 65, 70. Watson's post-priority analysis is consistent with documented pre-priority concerns in the art.

Moderna has fully complied with its duties and Petitioner's incomplete and misleading accusations do not show otherwise. Institution should be denied.

Respectfully submitted,

Date: January 16, 2024

By: /Emily R. Whelan/  
Emily R. Whelan (Reg. No. 50,391)

**CERTIFICATE OF SERVICE**

I hereby certify that on January 16, 2024, I caused a true and correct copy of the following documents:

- Patent Owner's Preliminary Statement Regarding Alleged Inconsistent Positions
- Patent Owner's Exhibit List
- Exhibits 2049-2061

to be served via e-mail, as consented to by Petitioner, upon the following:

COVIDPatentPfizer@wc.com  
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**Patent Owner's Exhibit List**

<b>Exhibit</b>	<b>Description</b>	<b>Bates</b>
2001	Stanley A. Plotkin, <i>Vaccines: Past, Present and Future</i> , 11 Nature Medicine Supplement 55 (2005)	
2002	Lynne Cassimeris et al., <i>Lewin's Cells</i> (2nd ed.) Jones and Bartlett Publishers (2011)	
2003	National Human Genome Research Institute, <i>Central Dogma</i> , <a href="https://www.genome.gov/genetics-glossary/Central-Dogma">https://www.genome.gov/genetics-glossary/Central-Dogma</a>	
2004	National Human Genome Research Institute, <i>Double Helix</i> , <a href="https://www.genome.gov/genetics-glossary/Double-Helix">https://www.genome.gov/genetics-glossary/Double-Helix</a>	
2005	Luis A. Brito et al., <i>A Cationic Nanoemulsion for the Delivery of Next-generation RNA Vaccines</i> , 22 Molecular Therapy 2118 (2014)	
2006	<i>Reserved</i>	
2007	S Withoff et al., <i>Replication-defective Recombinant Semliki Forest Virus Encoding GM-CSF as a Vector System for Rapid and Facile Generation of Autologous Human Tumor Cell Vaccines</i> , 20 Gene Therapy 1515 (2001)	
2008	Alexander E. Gorbalenya, <i>The Species Severe Acute Respiratory Syndrome-related Coronavirus: Classifying 2019-nCoV and Naming it SARS-CoV-2</i> , 5 Nature Microbiology 536 (2020)	



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Exhibit	Description	Bates
2009	Andrew M.Q. King et al., <i>Virus Taxonomy: Classification and Nomenclature of Viruses</i> , Elsevier Academic Press (2012)	
2010	Package Insert for Spikevax (COVID-19 Vaccine, mRNA) – 2023-2024 Formula	
2011	Civil Docket Report for <i>ModernaTX, Inc. et al. v. Pfizer Inc. et al.</i> , C.A. No. 22- 11378-RGS (D. Mass.)	
2012	Complaint, <i>ModernaTX, Inc. et al. v. Pfizer Inc et al.</i> , C.A. No. 22-11378, Dkt. No. 1 (D. Mass, Aug. 26, 2022)	
2013	United States District Courts – National Judicial Caseload Profile, Federal Court Management Statistics (June 2023), available at: <a href="https://www.uscourts.gov/sites/default/files/data_tables/fcms_na_distprofile0630.2023.pdf">https://www.uscourts.gov/sites/default/files/data_tables/fcms_na_distprofile0630.2023.pdf</a>	
2014	<i>Reserved</i>	
2015	Excerpts from Defendants' Supplemental Patent-Related Disclosures, Exhibit D – Invalidity Contentions of U.S. Patent No. 10,933,127 (June 27, 2023)	
2016	<i>Reserved</i>	
2017	Excerpts from U.S. Patent No. 10,702,599 File History	
2018	Excerpts from U.S. Patent No. 10,064,934 File History	
2019	U.S. Patent Application Publication No. 2014/0193482 (“the ’482 Publication”)	

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Exhibit	Description	Bates
2020	International Patent Publication No. WO 2005/027963 (“Nabel”)	
2021	Andrew J. Geall, <i>Nonviral Delivery of Self-Amplifying RNA Vaccines</i> , 109 Proceedings of the Nat’l Acad. of Sci. 14604 (2012) (“Geall 2012”)	
2022	International Patent Publication No. WO 2003/072720 (“Haller”)	
2023	<i>Reserved</i>	
2024	Karl-Josef Kallen et al., <i>A Novel, Disruptive Vaccination Technology: Self-adjuvanted RNActive Vaccines</i> , 9 (10) Human Vaccines & Immunotherapeutics 2263 (2013)	
2025	Benjamin Petsch, <i>Protective Efficacy of In Vitro Synthesized, Specific mRNA Vaccines Against Influenza A Virus Infection</i> , 30 Nature Biotechnology 1210 (2012)	
2026	U.S. Patent No. 10,487,332 File History	
2027	Norbert Pardi et al., <i>mRNA Vaccine – A New Era in Vaccinology</i> , 17 Nature Reviews 261 (2018)	
2028	Laura DeFrancesco, <i>The ‘Anti-hype’ Vaccine</i> , 35 Nature Biotechnology 193(2017)	
2029	Harry Vennema et al., <i>Early Death After Feline Infectious Peritonitis Virus Challenge due to Recombinant Vaccinia Virus Immunization</i> , 64 Journal of Virology 1407 (1990) (“Vennema”)	
2030	Martial Jaume et al., <i>Anti-Severe Acute Respiratory Syndrome Coronavirus Spike</i>	

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Exhibit	Description	Bates
	<i>Antibodies Trigger Infection of Human Immune Cells via a pH- and Cysteine Protease-Independent FcγR Pathway</i> , 85 Journal of Virology 10582 (2011) (“Jaume”)	
2031	Amarendra Pegu et al., <i>Durability of mRNA-1273 vaccine-induced antibodies against SARS-CoV-2 variants</i> , 373 Science 1372 (2021)	
2032	European Medicines Agency Assessment Report for COVID-19 Vaccine Moderna (Mar. 11, 2021)	
2033	Japanese Package Insert for Spikevax Intramuscular Injection (Monovalent: Omicron XBB.1.5)	
2034	Moderna, Inc., <i>Patents</i> , <a href="https://www.modernatx.com/patents">https://www.modernatx.com/patents</a>	
2035	E.J. Anderson et al., <i>Safety and Immunogenicity of SARS-CoV-2 mRNA-1273 Vaccine in Older Adults</i> , 383 The New England Journal of Medicine 2427 (2020)	
2036	Spyros Chalkias et al., <i>Safety, immunogenicity and antibody persistence of a bivalent Beta-containing booster vaccine against COVID-19: a phase 2/3 trial</i> , 28 Nature Medicine (2022)	
2037	Denise Grady, <i>Vaccine's Early Test Result Elevates Hopes and Stocks</i> , 169 N.Y. Times, May 19, 2020, at A1.	
2038	Peter Loftus, <i>Moderna Says Initial Covid-19 Vaccine Results Are Positive</i> , Wall Street Journal (2020)	

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Exhibit	Description	Bates
2039	Carolyn Y. Johnson, <i>Moderna's coronavirus vaccine shows encouraging early results</i> , The Washington Post (2020)	
2040	<i>'Heroes of Chemistry' recognized for contributions to health, medicine and more</i> , American Chemical Society (2022)	
2041	<i>The Galien Foundation Announces Winners of the 2022 Prix Galien UK Awards at the Natural History Museum, London</i> (2022)	
2042	<i>Pharma Awards 2022: The Winners Interviews</i>	
2043	Jeffrey M. Jacobson et al., <i>Dendritic Cell Immunotherapy for HIV-1 Infection Using Autologous HIV-1 RNA: A Randomized, Double-Blind, Placebo-Controlled Clinical Trial</i> , 72 J. Acquired Immune Deficiency Syndromes 31 (2016)	
2044	Wesley de Jong, <i>Therapeutic Vaccine in Chronically HIV-1-Infected Patients: A Randomized, Double-Blind, Placebo-Controlled Phase IIa Trial with HTI-TriMix</i> , 209 Vaccines (2019)	
2045	Nick Paul Taylor, <i>Translate Bio's mRNA Fails to Improve Lung Function in Cystic Fibrosis Patients</i> , Biotech (2021)	
2046	Martin Alberer et al., <i>Safety and Immunogenicity of a mRNA Rabies Vaccine in Healthy Adults: an Open-label, Non-randomised, Prospective, First-in-human Phase 1 Clinical Trial</i> , 390 The Lancet 1511 (2017)	

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Exhibit	Description	Bates
2047	<i>Reserved</i>	
2048	Excerpts from Defendants' Patent-Related Disclosures, Exhibit D – Invalidity Contentions of U.S. Patent No. No. 10,933,127 (Mar. 31, 2023)	
2049	Excerpts from Matthew G. Stanton & Kerry E. Murphy-Benenato, <i>Messenger RNA as a Novel Therapeutic Approach</i> , Topics in Medicinal Chemistry RNA Therapeutics 237 (2017)	MOD_000773684- MOD_000773700 at MOD_000773688
2050	Excerpts from Investigator's Brochure mRNA-1325 (Sept. 23, 2016) (PROTECTIVE ORDER MATERIAL)	MOD_001416753- MOD_001416784 at MOD_001416764- MOD_001416765
2051	Excerpts from Pre-IND Meeting Background Document, mRNA-1325 (PROTECTIVE ORDER MATERIAL)	MOD_001417294- MOD_001417512 at MOD_001417309, MOD_001417492
2052	Excerpts from mRNA-1893 Investigator's Brochure (June 4, 2019) (PROTECTIVE ORDER MATERIAL)	MOD_000337172- MOD_000337198 at MOD_000337182, MOD_000337183
2053	Excerpts from Division of Microbiology and Infectious Diseases (DMID) Protocol (Mar. 30, 2020)	MOD_000477134- MOD_000477212 at MOD_000477149
2054	Excerpts from Division of Microbiology and Infectious Diseases (DMID) Protocol (Feb. 14, 2020)	MOD_000477491- MOD_000477561 at MOD_000477497, MOD_000477505

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<b>Exhibit</b>	<b>Description</b>	<b>Bates</b>
2055	Excerpts from Division of Microbiology and Infectious Diseases (DMID) Protocol (May 20, 2020)	MOD_000471975- MOD_000472059 at MOD_000471981, MOD_000471991
2056	Excerpts from Type B Pre-IND Meeting Request for mRNA-1273 (PROTECTIVE ORDER MATERIAL)	MOD_000205848- MOD_000205881 at MOD_000205868
2057	Excerpts from SARS-CoV-2, Disease Enhancement & Vaccination (Apr. 7, 2020) (PROTECTIVE ORDER MATERIAL)	MOD_000329613- MOD_000329628 at MOD_000329616- MOD_000329617
2058	Redline Stipulated Protective Order	
2059	Stipulated Protective Order	
2060	Petitioner's Chart (PROTECTIVE ORDER MATERIAL)	
2061	Petitioner's Chart – Redacted	