

Metaphorical mRNA:

The Current & Future Shape(s) of
the mRNA Therapeutics Industry



ADVANCING
RNA

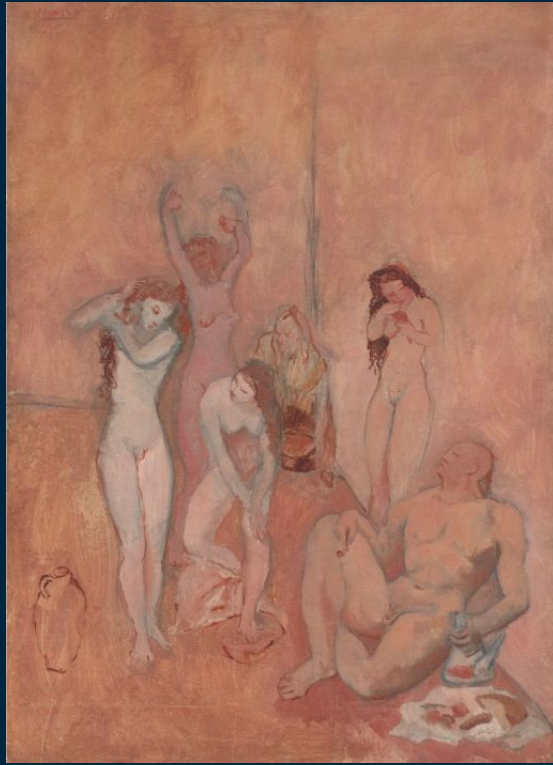
What is Advancing RNA?

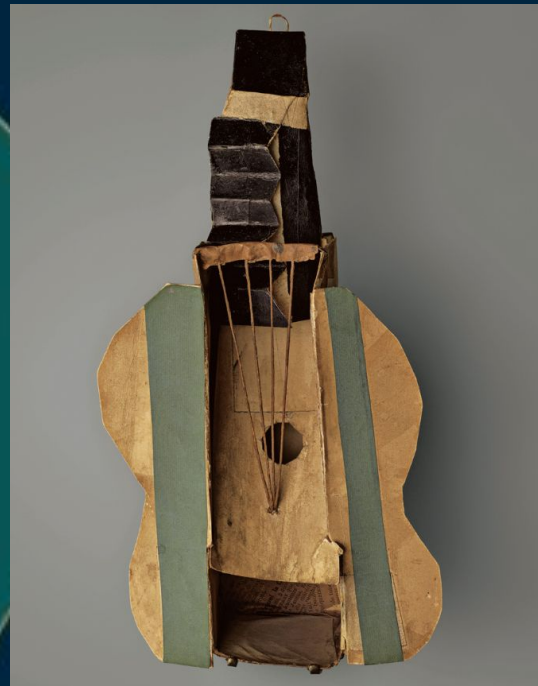
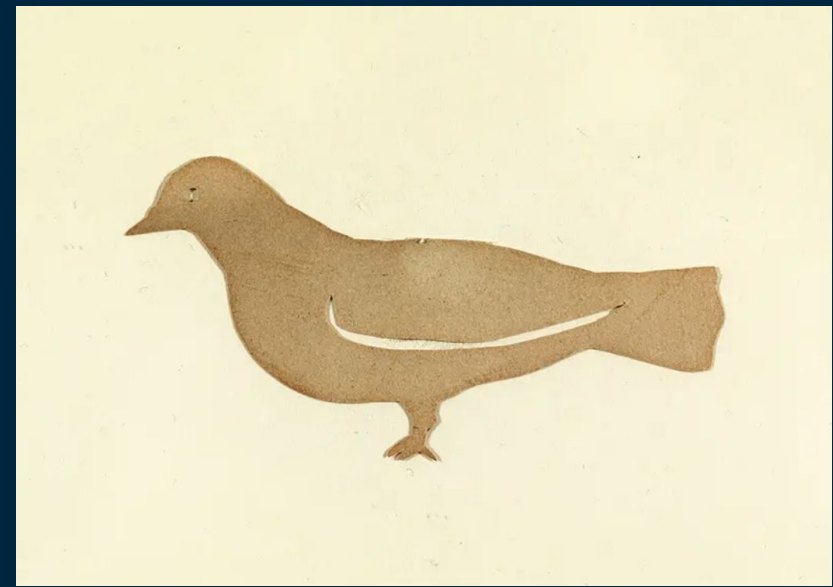
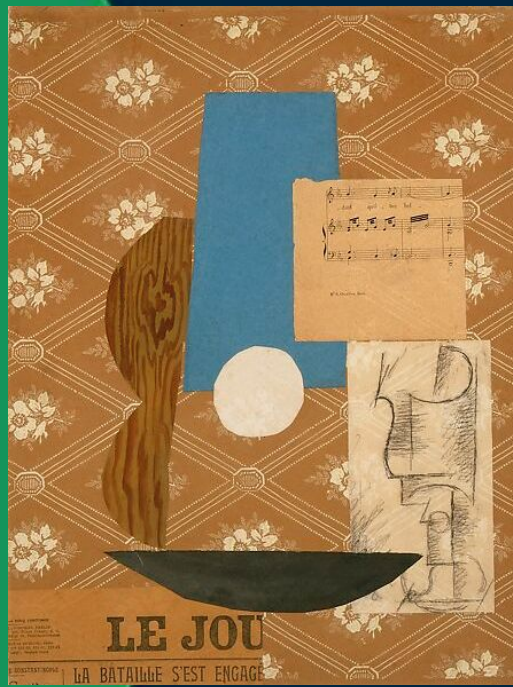
Life Science Connect editorial community launched in January 2024 featuring:

- “ARW on RNA” expert interviews and long-form “From the Editor” features
- Advancing RNA Live bi-monthly virtual panel discussions on industry challenges
- Contributed thought leadership from an expert network of industry contributors
- Free weekly newsletter featuring editorial content and solutions-oriented content from LSC advertising partners

Anna Rose Welch
Editorial & Community Director,
Advancing RNA;
Life Science Connect media group



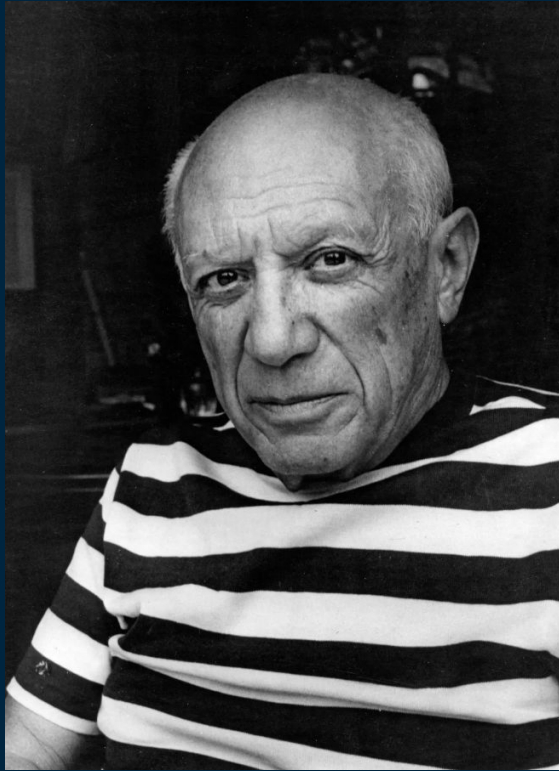






Meet PICASSO!

An mRNA therapeutics industry idol
from 2025-infinity (and beyond)



What Does Picasso Have To Do With mRNA?



3 Lessons the mRNA Industry Can Learn from Picasso's Life & Work

- Being Innovative Comes *After* We Master The Basics
- Innovation Doesn't Occur In a Bubble
- We Won't Win Everyone Over (But We Can/Should Still Try)

LESSON #1: True Innovation Comes After We Master "The Basics"



1. Letting the science catch up
2. Defining DS/DP quality
3. Expanding/advancing our raw material portfolios
4. Exploring methods to reduce/control COGS
5. Drafting RNA-specific regulatory guidance
6. Identifying & Communicating mRNA's value proposition(s)



Letting the Science "Catch Up"

The rise of academic innovation centers

- New UVA Center for RNA Science and Medicine Poised to Become an Epicenter for RNA Innovation
- Hopkins to Establish RNA Innovation Center in Collaboration with TriLink Biotechnologies
- UAlbany, UR Launch New Center of Excellence in RNA Research

From "Alphafold" to "NuFold:" Predictive RNA structure

- *Nature Communications*: "NuFold: end-to-end approach for RNA tertiary structure prediction"

RNA modifications (start to) get the spotlight

- AMM Science & Technology committee hosts RNA modifications webinar

Ongoing exploration of alternative nonviral delivery opportunities

- *Nature Communications*: "Liposomal lipid nanoparticles for extrahepatic delivery of mRNA"
- *Molecular Therapy Nucleic Acids*: "Targeted mRNA delivery with bispecific antibodies that tether LNPs to cell surface markers"

Letting the Science "Catch Up"

- *Ongoing publication of preclinical and clinical data*
 - Metagenomi Presents Updated Preclinical Data in Hemophilia A at American Society of Hematology (ASH) 66th Annual Meeting
 - Strand Therapeutics To Present Potential First-In-Class Preclinical Data for STX-003, a Programmable mRNA Therapy to Treat Solid Tumor Cancers
 - Intellia Announces Positive Two-Year Follow-Up Data from Ongoing Phase 1 Study of Nexiguran Ziclumeran (nex-z), in Patients with Hereditary Transthyretin (ATTR) Amyloidosis with Polyneuropathy
 - BioNTech to Present Clinical and Preclinical Data Across mRNA and Next-Generation Immuno-Oncology Priority Programs at AACR 2025
 - Patient-Specific In Vivo Gene Editing to Treat a Rare Genetic Disease (NEJM)
 - Replicate Bioscience Announces Publication of First-in-Human Data for Its Optimized srRNA Rabies Vaccine in Nature Communications
 - Sail Biomedicines Presents Preclinical Data on In Vivo eRNA™ CAR-T Candidate for Autoimmune Diseases at ASGCT 2025
 - Orna Therapeutics Presents New Preclinical Data Supporting its in vivo CAR Therapy Approach in Autoimmune Diseases at ASGCT 2025

Defining Drug Substance/Drug Product Quality

European Pharmacopoeia Commission general texts:

- mRNA vaccines for human use
- mRNA substances for the production of mRNA vaccines for human use
- DNA templates for preparation of mRNA substances

USP Analytical Procedures for Quality of mRNA Vaccines & Therapeutics Draft Guidelines (*THIRD* edition) + USP mRNA Virtual Summit: Joining Forces to Advance the Quality of mRNA Therapeutics

Ongoing research around plasmid, mRNA, and LNP quality

- *Advancing RNA*: "What Do We Really Know About DNA for IVT?"
- *Molecular Therapy Nucleic Acids*: "Removal of dsRNA Byproducts Using Affinity Chromatography
- *Biology Methods & Protocols*: Mass Photometry as a fast, facile tool for direct measurement of mRNA length
- *Advancing RNA*: "Points to Consider for Assessing Lipid Quality for LNP Manufacturing"

Communicating mRNA's Value

“One of biggest challenges facing the industry in the years ahead will not only be figuring out what an mRNA therapeutic can do clinically, but it will be asking — and answering — why and when it should/must be an mRNA therapeutic.”



The Many "Forms" of Collaboration in the mRNA Space

Where can we find our inspiration?

- (Non-RNA-specific) ATMP Regulatory/Sector Milestones
- Partnerships & Acquisitions (Vendor-Vendor)
 - Evonik partners with ST Pharm to increase its offerings for RNA and nucleic acid delivery
 - TriLink BioTechnologies® and Aldevron enter into non-exclusive license and supply agreement for CleanCap® mRNA capping technology
 - Aldevron Announces Strategic Partnership with Acuitas Therapeutics
 - Wacker Biotech announces strategic collaboration with RNAV8 Bio to enhance mRNA therapeutics development
- Partnerships & Acquisitions (Biotech-Biotech)
 - Chroma Medicine & Nvelop Tx Merge to Create nChroma
 - Orna Therapeutics Announces Acquisition of ReNAgade Tx
 - Eptopia & Genevant Sciences Announce Collaboration Agreement
 - Orna Enters Alliance with Vertex for Next-Gen Gene Tx



The Many "Forms" Of Collaboration in the mRNA Space, Cont.

Global RNA Ecosystem Development

- Academic RNA Innovation Hubs
- UK, Quebec, & Australian RNA hubs

Innovative (Multi-Stakeholder) Access Models

- NHS Cancer Vaccine Launch Pad (mRNA immunotherapies)
- Brazilian Productive Development Partnerships (PDPs)
- CTMC (JV between MD Anderson, Resilience, cell therapy biotechs)

Combination Therapies On The Rise

- MRNA = a great “side kick” to other modalities

“Where do we need to recreate our own wheels?”



Finding The "Right" Audience

Reputation/Policy Challenges We're Facing

- *AMM: "U.S. Government policies & funding cuts to mRNA research represent a critical threat..."*
- *The EMA has not "admitted" that mRNA vaccines are 'experimental'*
- *States [Idaho, Iowa, Montana] Push Fight Against mRNA Vaccines*
- *Idaho House Bill seeks to criminalize mRNA vaccine administration*
- *"Texas Attorney General Sues Pfizer for Misrepresenting COVID-19 Vaccine Efficacy & Conspiring to Censor Public Discourse"*



Engaging Our Public — Positive Examples

- *Former Moderna CSO Melissa Moore's TED Talk: "How mRNA medicine will change the world"*
- *Moderna's "Welcome to the mRNAge" commercial*
- *Pfizer's "Meet mRNA" & LNPs (i.e., mRNA's "Custom Trucks") series*
- *"Antigen Hero:" A satirical mRNA-specific rewrite of Taylor Swift's song "Anti-Hero" [National Center for Therapeutics Manufacturing]*
- *Physician education video: "How mRNA therapeutics work (medieval village analogy) [Sketchy Group, LLC]*
- *The Vaccine Museum— Inaugurated in 2023 at the Butantan Institute, São Paulo, Brazil*



WORKS CONSULTED

AMM. (2025, May). Threats to mRNA Put Jobs, Cures, National Security, and U.S. Biomedical Leadership at Risk. <https://mrnamedicines.org/new-amm-survey-the-future-of-mrna-is-at-risk/>

BioPhorum. (2023, July). Defining the required CQAs & phase requirements for mRNA/LNP product development and manufacture. <https://www.biophorum.com/download/defining-the-required-critical-quality-attributes-cqas-and-phase-requirements-for-mrna-lnp-product-development-and-manufacture/>

Bot, A. Geall, A., Kassim, S., Ripley, S. (2023, Oct.). *Science Slam: The role of mRNA in enabling a new generation of immuno-oncology products*. [Panel Discussion.] Alliance for Regenerative Medicine Meeting on the Mesa, Carlsbad, CA, U.S.A. <https://www.youtube.com/watch?v=A9SthXTx5yU>

Fujimori, S. (2022). Inside the Delivery Vehicles Critical to the Success of mRNA. Pfizer. <https://www.pfizer.com/news/behind-the-science/inside-delivery-vehicles-critical-success>

Hoch, P., Peters, E. (2024). Understanding CQAs for mRNA/LNP Product Development & Manufacture. *Advancing RNA*. <https://www.advancingrna.com/doc/understanding-cqas-for-mrna-lipid-nanoparticle-product-development-and-manufacture-0001>

Jones, C., Androsavich, J., So, N. (2024). Breaking The Mold With RNA— a “RNAissance” of Life Science. NPJ Genomic Medicine (9). <https://www.nature.com/articles/s41525-023-00387-4>

Kagaya, Y. (2025, Jan.) NuFold: end-to-end approach for RNA tertiary structure prediction with flexible nucleobase center representation. *Nature Communications*. <https://www.nature.com/articles/s41467-025-56261-7>

WORKS CONSULTED

Moderna. (2023). Welcome to the mRNAge. [Video.] YouTube. <https://www.youtube.com/watch?v=v7M-MbSZokQ>
National Center for Therapeutics Manufacturing. (Oct. 2023). Antigen Hero: A Taylor Swift “Anti-Hero Parody Music Video. [Video.] YouTube. <https://www.youtube.com/watch?v=dry11OYkrWw>

National Center for Therapeutics Manufacturing. (Oct. 2023). Antigen Hero: A Taylor Swift “Anti-Hero Parody Music Video. [Video.] YouTube. <https://www.youtube.com/watch?v=dry11OYkrWw>

Peters, E. (2022, Sept. 21). *Redefining Scale-Up Challenges From Bench To Clinic & Beyond*. [Presentation]. mRNA Process Development & Manufacturing Summit, Boston, MA, U.S.A. <https://mrna-processandmanufacturing.com/>

Probert, P. (2025, Feb.) What Do We (Really) Know About DNA Quality for In Vitro Transcription. *Advancing RNA*. <https://www.advancingrna.com/doc/what-do-we-really-know-about-dna-quality-for-in-vitro-transcription-0001>

Sketchy Group, LLC. (April 2023). *How mRNA Therapeutics Work*. [Video.] YouTube. <https://www.youtube.com/watch?v=vlXu58mjUaM&t=1s>

TED. Melissa Moore, Moderna. (2022, May 18). *How mRNA Medicine Will Change The World*. [Video]. YouTube. <https://www.youtube.com/watch?v=h5D3mv8ewCY>

U.S. Pharmacopeia. (Feb 2025). *USP mRNA Virtual Summit: Joining Forces to Advance the Quality of mRNA Therapeutics* . [Online Conference]. <https://www.usp.org/sites/default/files/usp/document/events-and-training/mrna-agenda-final.pdf>

Welch, A.R. (2017, July). A Deep Dive Into Brazil’s Biosimilar PDPs. Biosimilar Development. <https://www.biosimilardevelopment.com/doc/a-deep-dive-into-brazil-s-biosimilar-pdps-0001>

Welch, A.R. (2024, Aug.) Is This The Hardest Question Facing mRNA Therapeutics Makers? *Advancing RNA*. <https://www.advancingrna.com/doc/is-this-the-hardest-question-facing-mrna-therapeutics-makers-0001>

Welch, A.R. (2023). A Meditation on mRNA Reputation & Regulatory Complexities. *Advancing RNA*. <https://www.advancingrna.com/doc/muddy-waters-run-deep-a-meditation-on-mrna-s-regulatory-reputation-complexities-0001-0001>

Welch, A.R. (2024, May). Multidisciplinary mRNA: What Can We Learn From Other CGTs? *Advancing RNA*. <https://www.advancingrna.com/doc/multidisciplinary-mrna-what-can-we-learn-from-other-cgts-0001>

Welch, A.R. (2024, Dec.) Top 5 mRNA/RNA Developments of 2024 (Pt 1 & 2). Advancing RNA.
<https://www.advancingrna.com/doc/top-mrna-rna-developments-of-part-0001> &
<https://www.advancingrna.com/doc/top-mrna-rna-advancements-of-part-0001>

Welch, A.R. (Sept. 2023). “I’ve argued it before & will no doubt continue to reiterate... [LinkedIn Post + Image].
https://www.linkedin.com/posts/annarosewelch_ive-argued-it-before-httpsshorturlat-activity-7113165372802957312-rvSo/?utm_source=share&utm_medium=member_desktop

Industry News — Clinical Development Press Releases:

- Metagenomi:
<https://ir.metagenomi.co/news-releases/news-release-details/metagenomi-presents-updated-preclinical-data-hemophilia-american>
- Strand Therapeutics:
<https://www.strandtx.com/potential-first-in-class-data-from-preclinical-program-for-stx-003-a-programmable-mrna-therapy-to-treat-solid-tumor-cancers/>
- Intellia:
<https://ir.intelliatx.com/news-releases/news-release-details/intellia-announces-positive-two-year-follow-data-ongoing-phase-1>
- BioNTech:<https://investors.biontech.de/news-releases/news-release-details/biontech-present-clinical-and-preclinical-data-across-mrna-and>
- CHOP/Danaher: <https://www.nejm.org/doi/full/10.1056/NEJMoa2504747>
- Replicate Biosciences:
<https://replicatebioscience.com/replicate-bioscience-announces-publication-of-first-in-human-data-for-its-optimized-srrna-rabies-vaccine-in-nature-communications/>
- Sail Biomedicines:
<https://www.sail.bio/news/sail-biomedicines-presents-preclinical-data-on-in-vivo-erna-car-t-candidate-for-autoimmune-diseases-at-asgct-2025/>
- Orna Therapeutics:
<https://www.prnewswire.com/news-releases/orna-therapeutics-presents-new-preclinical-data-supporting-its-in-vivo-car-therapy-a-approach-in-autoimmune-diseases-at-the-american-society-of-gene-and-cell-therapy-annual-meeting-302456153.html>

Industry News — Partnership Press Releases

- Aldevon/Acuitas: <https://www.aldevron.com/about-us/news/acuitas-aldevron-partnership>
- Wacker/RNAV8:
https://www.wacker.com/cms/media/en/documents/pressrelease-pdf/pm2025/cooperation_wacker_biotech_rnav8_bio.pdf
- TriLink/Aldevron:
<https://www.trilinkbiotech.com/press-releases/trilink-biotechnologies-and-aldevron-enter-into-non-exclusive-license-and-supply-agreement-for-cleancap-mrna-capping-technology>
- Evonik/ST Pharm:
<https://healthcare.evonik.com/en/news-and-events/press-releases/evonik-partners-with-st-pharm-to-increase-its-offerings-for-rna-and-nucleic-acid-delivery-268818.html>
- Chroma & Nvelop:
<https://www.businesswire.com/news/home/20241211660902/en/Chroma-Medicine-and-Nvelop-Therapeutics-Unite-to-Form-nChroma-Bio-Securing-%2475-Million-to-Accelerate-Genetic-Medicines>
- Orna & ReNAgade:
<https://www.ornatx.com/orna-therapeutics-announces-strategic-acquisition-of-renagade-therapeutics-to-solidify-leadership-in-circular-rna-therapies/>
- Epitopia & Genevant: <https://www.genevant.com/epitopea-and-genevant-sciences-announce-collaboration-agreement/>